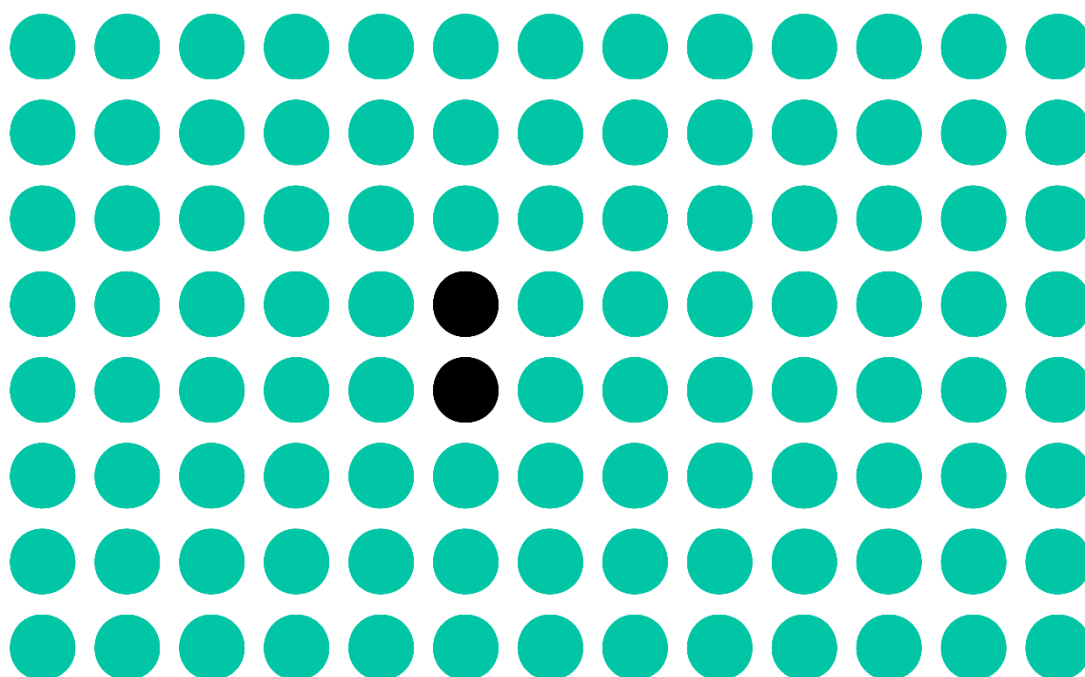




Instituto
de Medicina
Molecular

João
Lobo
Antunes

Scientific Report 2021



Lisbon, March 2022

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Organization and Structure

Research and development in the Biomedical Sciences plays a central role in generating knowledge and in the application of this knowledge to improving the quality of life.

The mission of the Instituto de Medicina Molecular João Lobo Antunes (iMM) is to foster basic, clinical and translational biomedical research with the aim of contributing to a better understanding of disease mechanisms, developing novel predictive tests, improving diagnostics tools and developing new therapeutic approaches.

Located on the campus of the Faculdade de Medicina da Universidade de Lisboa (FMUL), iMM is a Research Unit of the National Ministry of Science and Higher Education. iMM is mainly supported by national public funds and European Union funds. The research expenditure includes additional funds obtained from peer-reviewed competitive grants, private donations and industrial partnerships.

Created in December 2002, iMM results from the association of five former research units from FMUL: The Biology and Molecular Pathology Center, the Lisbon Neurosciences Center, the Microcirculation and Vascular Pathobiology Center, the Gastroenterology Center and the Nutrition and Metabolism Center. The institute is a Private, Non-profit Association.

iMM Associated Members

Universidade de Lisboa

Faculdade de Medicina da Universidade de Lisboa

Centro Hospitalar Universitário Lisboa Norte – Hospital de Santa Maria

Associação para a Investigação e o Desenvolvimento da Faculdade de Medicina

Fundação Oriente

Board of Trustees

The Board of Trustees is composed by representatives of the Associated Members and meets at least once per year to analyse the scientific and finance report and to approve the plan of activities and budget for the next year.

Board of Directors

The Board of Directors is responsible for the management of the Institute according to the plans approved by the Trustees. The Board of Directors is elected by the Trustees.

M. Carmo-Fonseca, MD, PhD
President

Maria M. Mota, PhD
Executive Director

Bruno Silva-Santos, PhD
Vice-Director

Council of Scientists

The Council of Scientists is composed by all Group Leaders. It meets at least once per year to discuss the scientific strategies and plan of actions proposed by the Board of Directors. This council elects two representatives to participate in the meetings of the Board of Trustees.

Scientific Advisory Board

Undertake periodic evaluations to the iMM specific programmes and include international experts of scientific fields.

Carlos Caldas, MD, PhD, *Chairman* – Cancer Research UK Cambridge Institute, Cambridge Cancer Center UK

Caetano Reis e Sousa, PhD, – Francis Crick Institute, London, UK

Elaine Mardis, PhD – Institute for Genomic Medicine at NationWide Children’s Hospital, USA

Paul Peter Tak, MD, PhD – University of Amsterdam, Netherlands

Yasmine Belkaid, PhD – National Institutes of Health, USA

Industry Advisory Board

The Industry Advisory Board will assist to the Technology Transfer Office team in the definition of a strategy and action plan to drive innovation at iMM.

Daniela Couto – Biogeneration Ventures Fund

David Malta – Vesalius Biocapital

Isabel Ferreira – Versameb

Miguel Forte – Zelluna Immunotherapy

Pascale Redig – Janssen

Societal Advisory Board

António Barreto, *Chairman* – Sociologist and Columnist

Graça Franco – Renascença Group

Paula Martinho da Silva – Lawyer

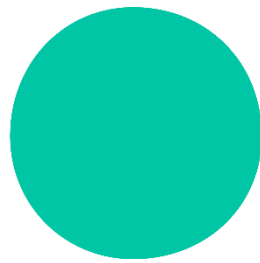
Diogo Lucena – NOVA School of Business and Economics

João Filipe Queiró – Faculdade de Ciências e Tecnologia da Universidade de Coimbra

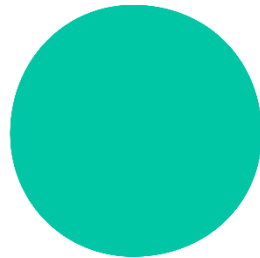
Henrique Leitão – Faculdade de Ciências da Universidade de Lisboa

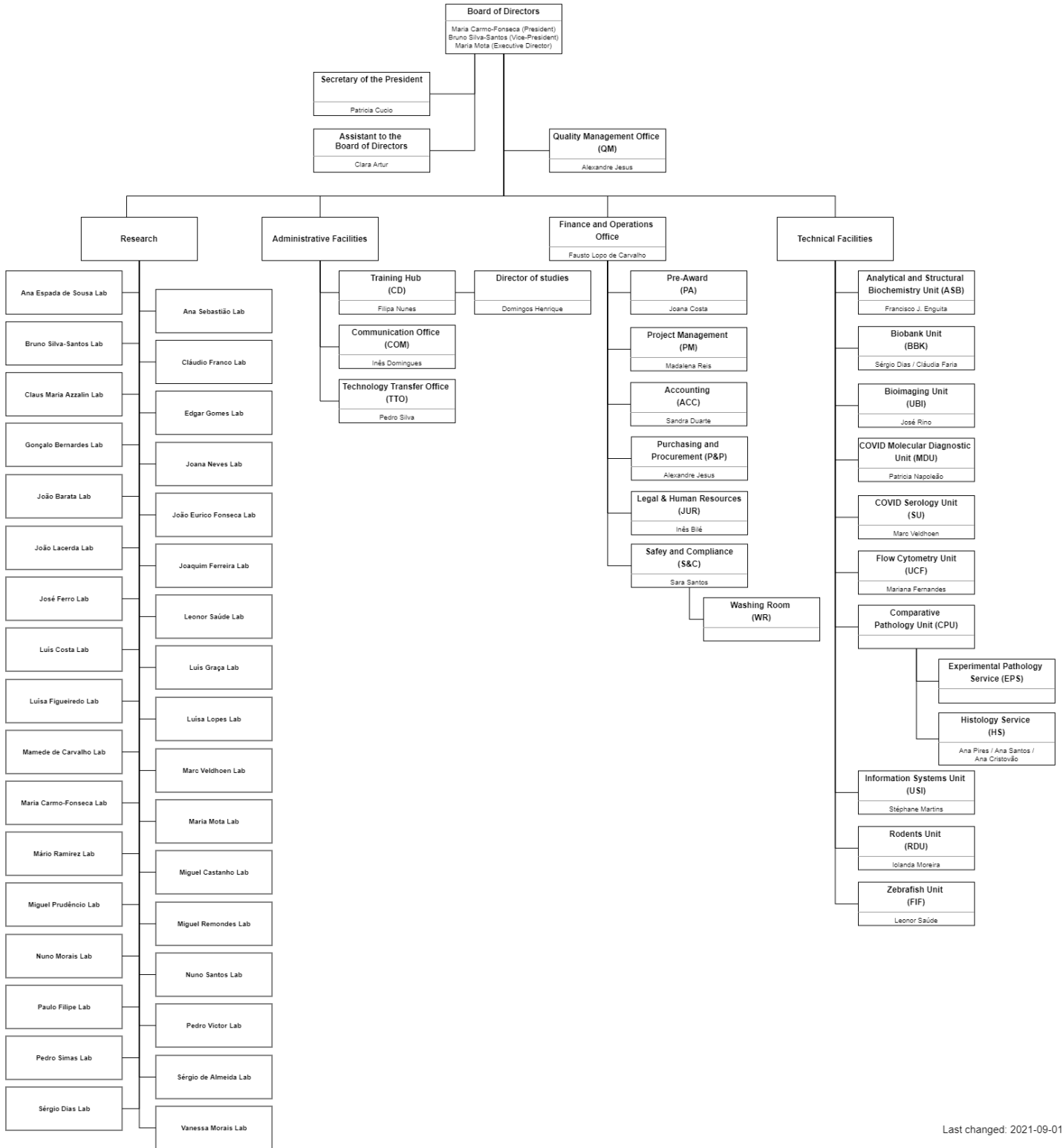
Pedro Norton – Finerge

Domília dos Santos – The dos Santos Group



Organigram





Last changed: 2021-09-01

Evaluation Report

Avaliação Laboratórios Associados

CRITERION A

Technological capacity to sustainably support and promote the response of public policies

Rating: 5

Comments:

A.1 Relevance, scope and impact of the support to public policies in the last 5 years by the constituent entities of the Associate Laboratory The iMM is one of the very top-level institutes in Portugal that gathers some 650 staff with 85% researchers, and does biomedical research at an excellent level, being internationally competitive. The iMM Associate Laboratory (AL) does basic, translational and clinical biomedical research along 4 Thematic Lines (TLs) whose objectives are perfectly aligned with the national, as well as European public policies. Another important aspect is the iMM strategy of patient centered research, which becomes increasingly important to understand and treat disease. The success stories (Clinical Research Centre, COLife, Biobanco, Lymphact, COVID-19) demonstrate very clearly the breath of action of iMM. The iMM is a very active player in the Portuguese Roadmap for infrastructures. They contribute to GenomePT, PPBI Bioimaging, Congento for genetically tractable organisms, Biobanco.pt linked to the EU initiative EATRIS and BBMRI. iMM is also a member in PtCRIN and PtCAC. The iMM has been also instrumental to create in 2015 the Lisbon Academic Medical Center (CAML) and subsequently in regulating patient trials through the Clinical Research Center of the CAML (CiC-CAML). The iMM also joined a very important initiative (COLife) in the greater Lisbon area, which assembles a large critical mass of scientists and infrastructures. How efficient CoLife will be is at present unclear. Synergies leading to success will depend on the will to promote inter-institutional collaboration by overcoming psychological barriers and egocentric tendencies. The iMM AL is very efficient also in creating successful start-up companies and keeping contact with them. Since the setting up of the Technology Transfer Office (TTO) in 2018, 96 contracts with international and national companies were signed. Also, 15 licencing agreements and 43 technology transfer agreements were established. After singular success cases of technology transfer resulting from initiative of individual researchers (e.g. the start-up Lymphatic that was acquired by GammaDelta Therapeutics), iMM has decided to take a more pro-active role to expand and consolidate this area, namely by reinforcing the TTO office, increasing the awareness of researchers and promoting instruments for the financing of early stage projects.

A.2 Relevance and scope of the proposed 2 / 4 thematic lines and their specific objectives in response to public policies The organization in four TLs (Molecular and Cellular Biology; Development, Aging and Cancer; Infection and Immunity and Neurosciences and Behaviour) provides scope for focusing in important scientific and clinical issues, while enabling ample opportunities for interconnected cross-disciplinary approaches. The 4 TLs are very well presented in the proposal and address major health issues.

A.3 Adequacy of the governance model to secure effective support to public policies The iMM governance is strictly horizontal without departmental "boundaries" and the Group Leaders (GL) and Heads of Facilities report directly to the Board of Directors (BoD). There is little information about the BoD, which is responsible for all aspects of iMMs operations. The risk of a top-down government cannot be excluded and the efficiency of the iMM depends on the individuals constituting the BoD. With the right leaders, this can be very efficient, as it is apparently the case for the iMM at present.

Problems may occur if "breeding of novel leaders" is sub-optimal or if those leaders have a different, more ego-centric understanding of leadership. In such a situation there is not a compensatory effect possible that emanates from a secondary executive level. The BoD should have a leading role in defining long-term strategies to support public policies, with the active involvement of GL other researchers and staff.

CRITERION B

Promotion of scientific or technical careers at doctoral level & Attraction of Talent

Rating: 5

Comments:

B.1 Demonstrated track record and capacity to develop and sustain scientific and technical careers for PhDs through permanent or open-ended employment contracts. iMM has a consistent and well-proven record in scouting, attracting, monitoring and mentoring of talent, combined with providing a scientific infrastructure and stimulatory leadership. The iMM has established a model for career development, evaluation and attracting talent. This concerns the regular courses on leadership and management for senior iMM researchers and the adoption of Responsible Research and Innovation (RRI) culture. iMM aims to create a supportive, fair, creative and non-discriminatory environment is very much appreciated. The involvement of external experts in the selection of GL, based on merit and capacity to be internationally competitive, is praised. Also, clear guidelines for the recruitment of other staff have been established. iMM is implementing the European Human Research Strategy for Researchers (HRS4R). The proposal documents a very high dedication to supporting of young scientists and attraction of talent. The proposal mentions on p. 4 that 25% of the contracts are permanent, but in reality only 21 are group leaders, while 26 post-docs have permanent positions that are inherent to their contracts with FMUL and or HSM/CHLN. Since the latter are not considered staff scientists (scientists with over 6 years of research experience), although they may acquire this category based on evaluation, a distinction between both groups is recommended. Also, the consideration of a group of 31 postdocs with other type of contracts (p.4) creates confusion between the two groups of postdocs. B.2 Capacity to attract talent to Portugal, in particular PhD students and PhD researchers. About 35% of iMM members are MSc and PhD students, which places iMM as a very strong training academic centre. Every year, iMM receives 55 students from different national Master's programs, as well national and international PhD students (number not provided). Every year around 20 students 3 / 4 complete their doctoral studies. Doctoral researchers play a critical role in continuously providing mentoring as well as scientific and transferable skills. The guidance of postdoctoral researches is provided by 2 offices, the Training Hub and the Human Resources, engaged in providing guidance to postdoctoral researches, emphasizing equal opportunities, transparent career pathways and framework conditions to maintain high quality standards. The iMM LisbonBioMed International PhD programme, together with the Md-intern-PhD programme, create excellent opportunities for multidisciplinary and translational research. Every annual edition of this programme starts with a 8 week training module entitled "Towards a creative and critical mind", which is aimed at promoting student integration, fostering team attitude, and raising awareness to skills required for a successful career. Other initiatives include an annual meeting where the students have the opportunity to gain further insight and inspiration from international invited keynote speakers and a merit award to recognize iMM students with outstanding performance in their

doctoral studies. The plan to establish a programme for Breakthrough Ideas (high-risk and multidisciplinary) is an important instrument to engage in high-risk/high-gain initiatives and to foster research outside comfort zones. B.3 Adequacy of the governance model to secure careers and employment for PhDs and attract talent The reviewers appreciate that cornerstones of career development at iMM are scientific freedom and progression and retention of researchers, solely based on their merit, evaluation of results and alignment with the scientific strategy of the AL. The plan for the next five years is to establish 35 permanent contracts (10 for technical career, 10 for staff scientists and 15 for Group Leaders).

CRITERION C

International projection & Securing diversified funding

Rating: 5

Comments:

C.1 Demonstrated track record and capacity to secure international funding, in particular from EU R&D Programmes iMM has been very successful in securing international funding (60% of funding), mainly from the EU Commission (ca. 30%). The success of iMM in obtaining international grants is also of benefit for all iMM scientists who gain access to international contacts (PhD, post-doc, PI opportunities), reinforce networking and the capacity to attract further international funding. This is particularly the case for the various networks in which iMM researchers are partner or coordinator. Remarkably, iMM researchers got 2 FET-Open, 5 MSCA-ITNs, 3 MSCA-RISE, 9 MSCA-IF, 1 ERA-Chair and 7 Twinning network projects, resulting in the recruitment of more than 30 million Euros. Moreover, they participate in two IMI2 projects, European Joint Partnerships and will join the Digital Transformation in Health and Care. The iMM has to be commended for their achievements in terms of external financing, which is certainly due on its politics to attract, monitor, support and keep talent. C.2 Scientific and technological capacity to leverage the international prominence of science and technology activities The track record of iMM and its present leadership provide the foundations to leverage the prominence of the AL. C.3 Adequacy of the governance model to leverage international prominence and secure funding Please refer to comments made above regarding the governance model.

Overall

Rating: 100

Recommended annual funding: 1 823 562,73 €

Comments:

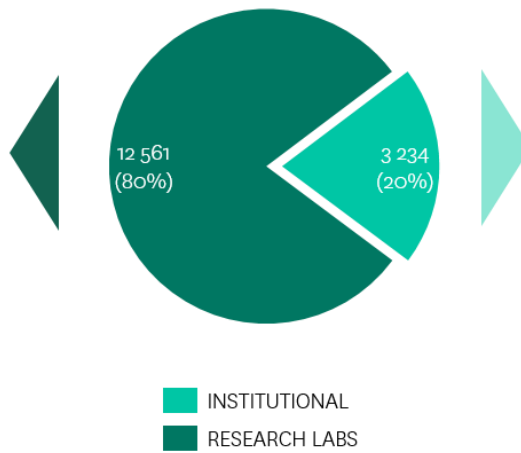
According to the comments above, the Panel recommends the award of the title of Laboratório Associado for the period of ten years. The Panel recommends complementary funding, as annual average for the period 2021-2025, of 1,823,562.73 .

Research Funding

Expenditure in 2021

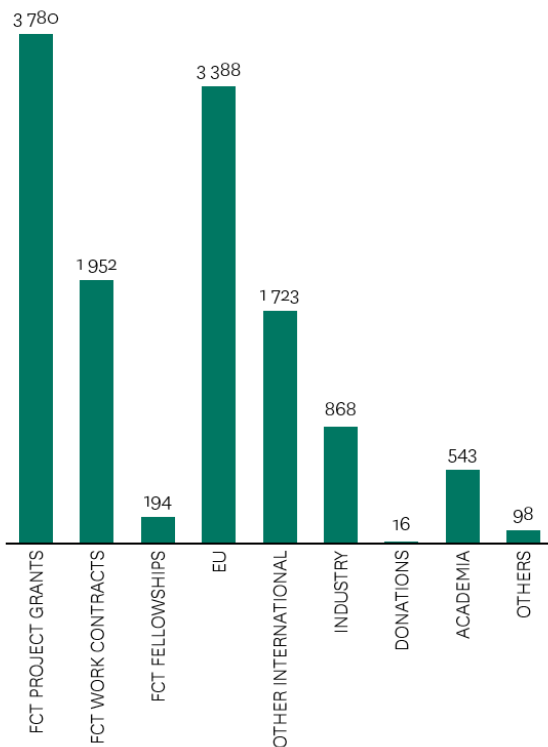
Total Expenditure: € 15.795.680¹

Total Expenditures 15,8 M



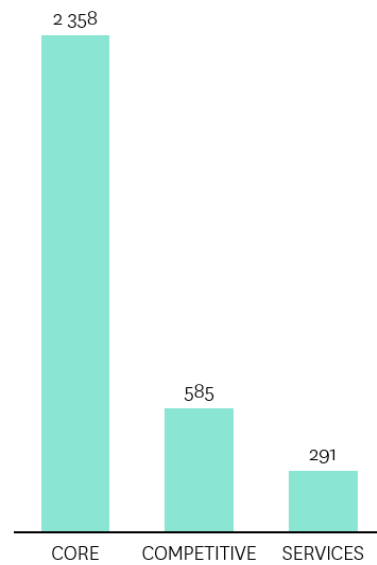
Research Labs

All Values in 000 Euros



Institutional

All Values in 000 Euros



¹ Figures for this exercise only consider costs registered in the exercise of 2021, from Jan 1 to Dec 31. In previous reports the numbers presented also took in consideration payments occurred in the exercise of the report but referring to expenses from the previous year. In order to reflect the yearly operations of IMM, this change in the referential was put in place from 2021 onwards. All expenditures regarding COVID-19 diagnostic testing operation were excluded from the relation above.

Total Expenditures 2021

			(EUROS)
INSTITUTIONAL	CORE	2.357.955	
	COMPETITIVE	585.309	
	SERVICES	291.098	3.234.362
RESEARCH LABS	FCT PROJECT GRANTS	3.779.937	
	FCT WORK CONTRACTS	1.952.243	
	FCT FELLOWSHIPS	194.000	
	EU	3.387.866	
	OTHER INTERNATIONAL	1.723.406	
	INDUSTRY	867.516	
	ACADEMIA	15.548	
	DONATIONS	542.961	
	OTHERS	97.840	12.561.318
TOTAL			15 795 680 ²

² Figures for this exercise only consider costs registered in the exercise of 2021, from Jan 1 to Dec 31. In previous reports the numbers presented also took in consideration payments occurred in the exercise of the report but referring to expenses from the previous year. In order to reflect the yearly operations of iMM, this change in the referential was put in place from 2021 onwards. All expenditures regarding COVID-19 diagnostic testing operation were excluded from the relation above.

Number of Ongoing Research Grants in 2021

176 Research Grants:

Public National FCT: 71

Private National: 20

Public National Other: 3

Of which with the industry – 4

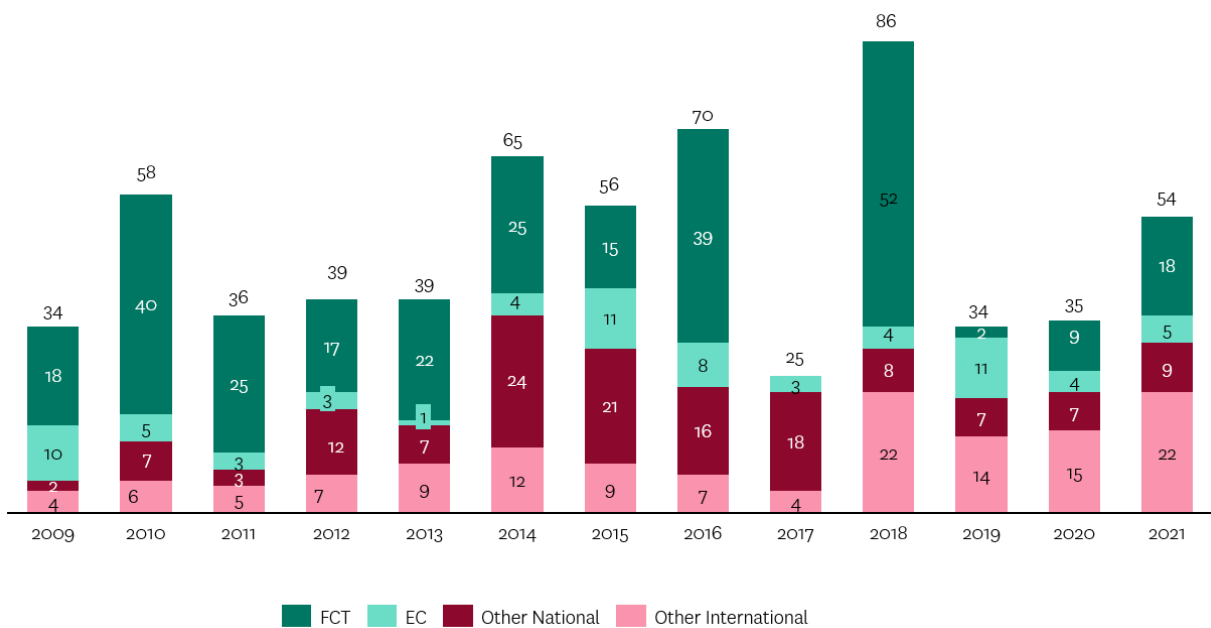
Public European Commission: 29

Private International: 50

Public International Other: 3

Of which with the industry – 27

Number of Research Grants Initiated at iMM from 2009 to 2021



Number of Research Funding Grants Initiated in 2021

Research Grants (54):

National Public: 18

International Public: 5

National Private: 9

International Private: 22

Projects Initiated in 2021 through Competitive Funds

FUNDING AGENCY	RESEARCHER	iMM BUDGET
Fundação para a Ciência e a Tecnologia (FCT)	Vanessa Morais	249 987,50€
	Pedro Sousa-Victor	249 967,50€
	Luisa Lopes	218 050,00€
	Claus Azzalin	249 511,56€
	Bruno de Sousa e Silva	249 761,57€
	Sérgio de Almeida	249 925,00€
	Bruno André e Silva Miranda	61 064,98€
	Mamede de Carvalho	30 832,50€
	Ana Espada de Sousa	249 998,75€
	João Forjaz de Lacerda	249 886,57€
	Julie Ribot	250 000,01€
	Miguel Castanho	77 500,00€
	Nuno Santos	181 950,00€
	Bruno Silva-Santos	250 000,00€
	Cláudio Franco	249 950,00€
	Gonçalo Bernardes	249 995,00€
	iMM	1 823 562,00€
Marc Veldhoen	249 995,00€	
European Commission	Mamede de Carvalho	315 690,00€
	Gonçalo Bernardes	159 815,04€
	Nuno Santos	148 090,04€
"la Caixa" Foundation	Luis Graça	237 772,24€
	Luísa Figueiredo	499 400,00€
	João Barata	489 158,00€
	Miguel Prudêncio	758 082,50€
	Miguel Castanho	184 600,00€
Portugal 2020	Claus Azzalin	495 792,00€
	Miguel Castanho	165 634,72€

Protocols, Donations & Awards³

FUNDING AGENCY	RESEARCHER	iMM BUDGET
AbbVie Inc	João Eurico da Fonseca	27 422,05€
CENTOGENE GmbH	Joaquim Ferreira	8 000,00€
CSL Behring	Ana Espada de Sousa	5 100,00€
Dompé	Pedro Simas	25 759,50€
European Molecular Biology Organisation	Claus Azzalin	104 000,00€
Fundação para a Ciência e a Tecnologia	Gonçalo Bernardes	249 995,00€
Gilead Sciences, Lda	Ana Espada de Sousa	25 100,00€
International Society for Neurochemistry	Ana Sebastião	6 607,20€
Janssen - Cilag Farmacêutica, Lda	Luís Costa	56 771,00€
Leo Farmacêutica	Paulo Filipe	81 000,00€
Liga Portuguesa Contra o Cancro	Ângela Afonso	20 060,00€
Limm Therapeutics	Luis Graça	5 000,00€
National Institutes of Health (NIH)	Pedro Simas	50 000,00€
	Tiago Maia	41 038,61€
Novartis	Inês Domingues	41 400,00€
ONO Pharma	Luis Graça	253 454,25€
Pfizer	Luís Costa	15 000,00€
Portugal 2020	Miguel Castanho	165 634,72€
Proterris	Tiago Maia	38 160,00€
Rett Foundation	Sérgio de Almeida	50 000,00€
Universidade Lisboa	Edgar Gomes	1 000,00€
University College London	Maria Carmo-Fonseca	8 572,00€

³ Considered protocols, donations and awards that fund projects, infrastructures and seminars.

iMM Applications and Secured Competitive Funding

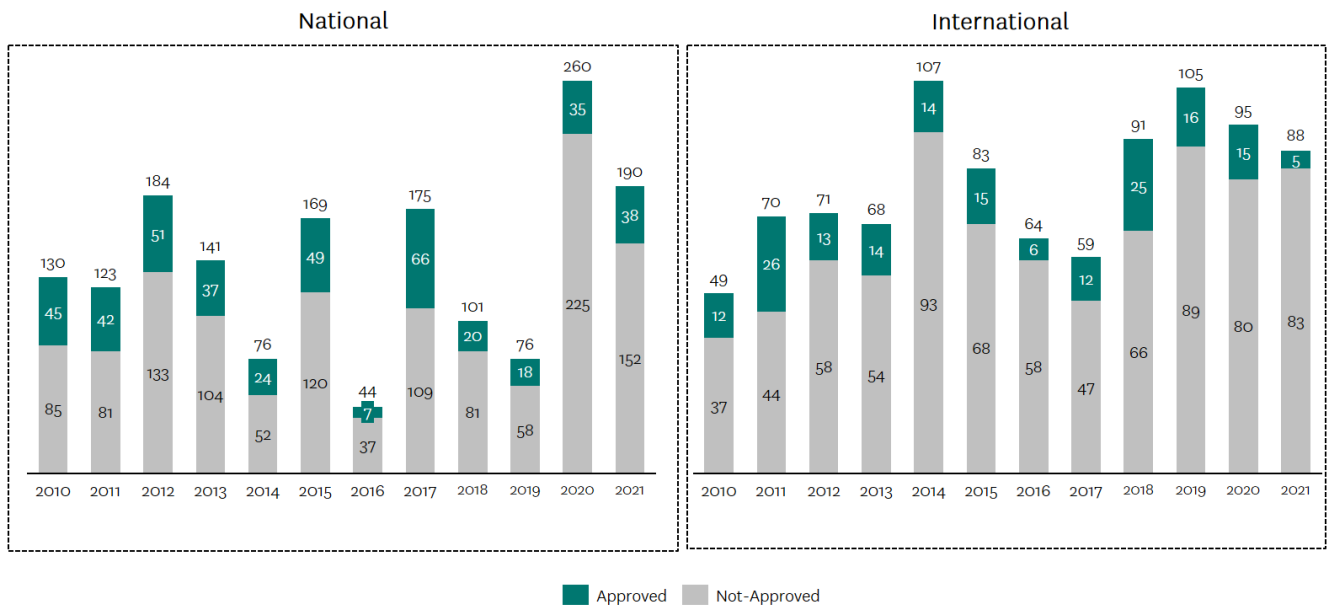


Figure 1: Submitted and approved applications to national and international competitive funding schemes since 2011. The number of submitted applications corresponds to those effectively communicated to the Pre-Award. The number of approved applications for 2021 corresponds to those with known results as of January 2022.

Funds Secured

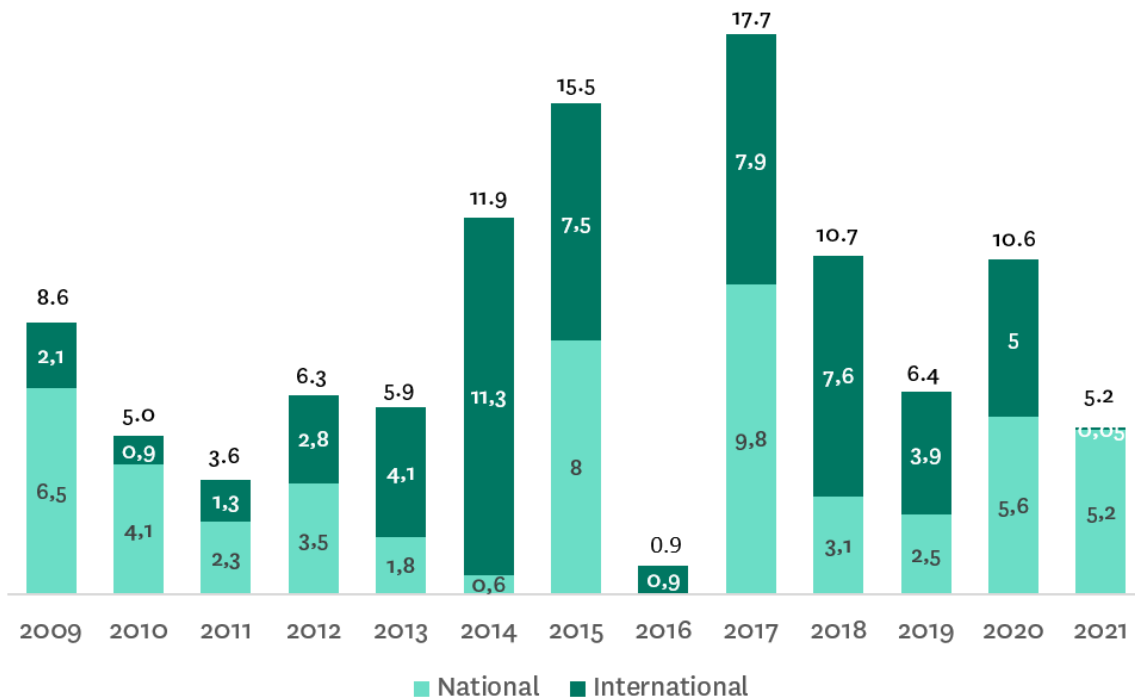


Figure 2: Total funds secured by iMM (in millions of €) in international and national competitive funding schemes since 2009. Secured funds per year correspond to the sum of the iMM budget of the approved applications submitted in the corresponding year (irrespectively to the project starting date). Information for 2021 corresponds to known results as of January 21, 2022.

Funding Sources of iMM Applications

In 2021, iMM researchers and staff have submitted grants to the following funding schemes:

INTERNATIONAL						
PRIVATE		PUBLIC				
Alzheimer's Association	Alzheimer's Drug Discovery Foundation	European Comission - Horizon Europe	Pillar 1 - Excellent Science	European Research Council	Starting Grants	
Brain & Behaviour Research Foundation	British Society for Antimicrobial Chemotherapy				Consolidator Grants	
Chan Zuckerberg Initiative	Crohn's & Colitis Foundation				Advanced Grants	
CURE	European Foundation for the Study of Diabetes				Proof-of-Concept	
European Hematology Association	Gilead Sciences			Marie Skłodowska-Curie Actions	Postdoctoral Fellowships	
Human Frontier Science Program	International Brain Research Organization				Doctoral Networks	
International Rett Syndrome Foundation	International Society for Neurochemistry			Pillar 2 - Global Challenges and European Industrial Competitiveness	Health	
Kenneth Rainin Fondation	Leukemia & Lymphoma Society					
la Caixa	Junior Leader Fellowship					
	Health Research projects			Pillar 3 - Innovative Europe	European Innovation Council	Pathfinder Open Pathfinder Challenges
Merck/EMD Serono	Michael J. Fox Foundation	Widening				
Motor Neurone Disease Association	MS Society	National Institute for Health (NIH), US				
Muscular Dystrophy Association	Myotubular Trust	US Department of Defense				
National Multiple Sclerosis Society	New York Stem Cell Foundation					
One Mind	Simons Foundation					
Start2Cure	Wings for Life					

NATIONAL			
PRIVATE		PUBLIC	
Bial Foundation	Maratona da Saúde	Fundação para a Ciência e Tecnologia	Scientific Employment Stimulus
Fundação Rui Osório de Castro	Gilead Sciences		R&D Project Grants in all Scientific Domains
Pfizer Global Medical Grants	Pfizer Sociedade das Ciências Médicas de Lisboa		ERA-NET on neurodegenerative diseases (JPCOFUND2)
LPCC	LPCC - Terry Fox		ERA-NET on Cancer Research (TRANSCAN-3)
	Bolsa LPCC / Lions		International Partnerships UT Austin-Portugal
Santa Casa da Misericórdia de Lisboa			Plano de Recuperação e Resiliência

Funding Programmes

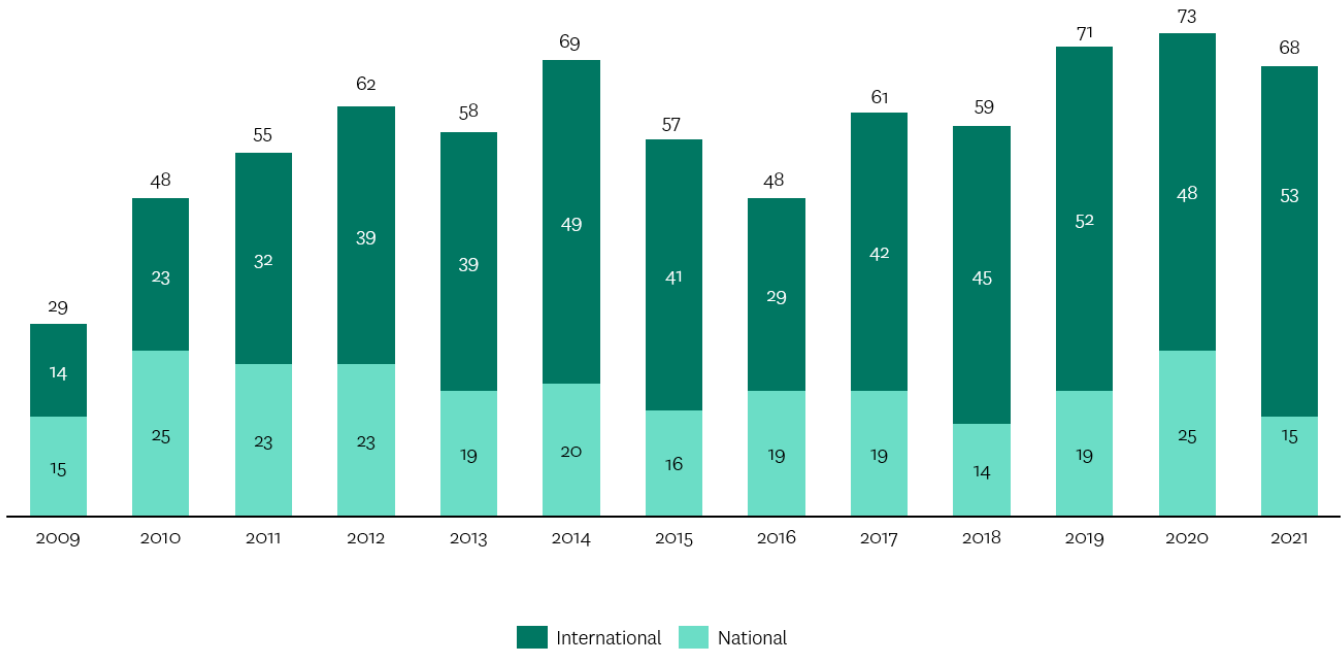


Figure 3: Evolution of the diversity of international and national funding schemes for which iMM researchers submitted applications from 2009 to 2021.

2021 iMM Activities Highlights

Human Resources 2021

		2020	2021
Researchers	PhD	242	229
	PhD Students	127	135
	MSc Students	112	117
	Master	44	45
	Graduate	21	26
	Other	7	11
		553	563
Technical Staff	PhD	8	12
	Master	58	51
	Graduate	21	20
	Other	14	17
		101	100
Administrative Staff	PhD	12	7
	Master	17	13
	Graduate	16	19
	Other	9	9
		54	48
TOTAL		708	711

Selection of Prizes and Awards

2020 Ferreira da Silva Award - Vicente de Seabra Medal

Gonçalo Bernardes (Group Leader)

Liga Portuguesa Contra o Cancro & Lions Clube Portugal Award

Cláudia Faria (João Barata Lab and Biobank)

European Vascular Biology Organization Council (EVBO) - Elected Member

Cláudio Franco (Group Leader)

“la Caixa” Foundation – Health Research 2021

Claus M. Azzalin (Group Leader)

João Barata (Group Leader)

Miguel Castanho (Group Leader)

Miguel Prudêncio (Group Leader)

Gilead GÉNESE Program

Ana Espada de Sousa (Group Leader)

International Brain Research Organization Early Career Grant

Sara Xapelli (Ana Sebastião Lab)

Expertscape “World Expert” in Venous Thrombosis

José Ferro (Group Leader)

Pfizer Award 2021 – Basic Research

João Barata (Group Leader)

Leonor Saúde (Group Leader)

1st Edition: Maria de Sousa Award (BIAL Foundation and Ordem dos Médicos)

Sara Silva Pereira (Luísa Figueiredo Lab)

2020 João Lobo Antunes Merit PhD Thesis Award (Announced in 2022)

Diana Aguiar de Sousa (José Ferro Lab)

Adam Armada-Moreira (Ana Sebastião Lab)

Mantero Belard Award – Santa Casa Neurociências Awards

Maria José Diógenes (Ana Sebastião Lab)

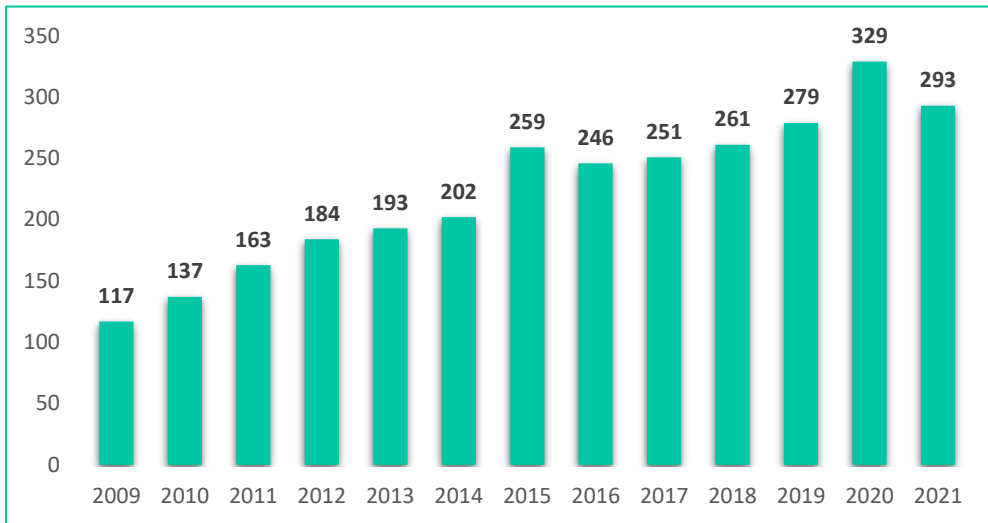
Productivity at a Glance

	2020	2021
Total Publications in Peer-Reviewed Journals	321	293 ⁴
Communications in International Conferences	296	269
Communications in National Conferences	157	303
Invited Lectures & Seminars	250	361
Organization of Conferences	47	50
Prizes & Honours	63	179
PhD Theses Completed	29	23
MSc Theses Completed	45	70

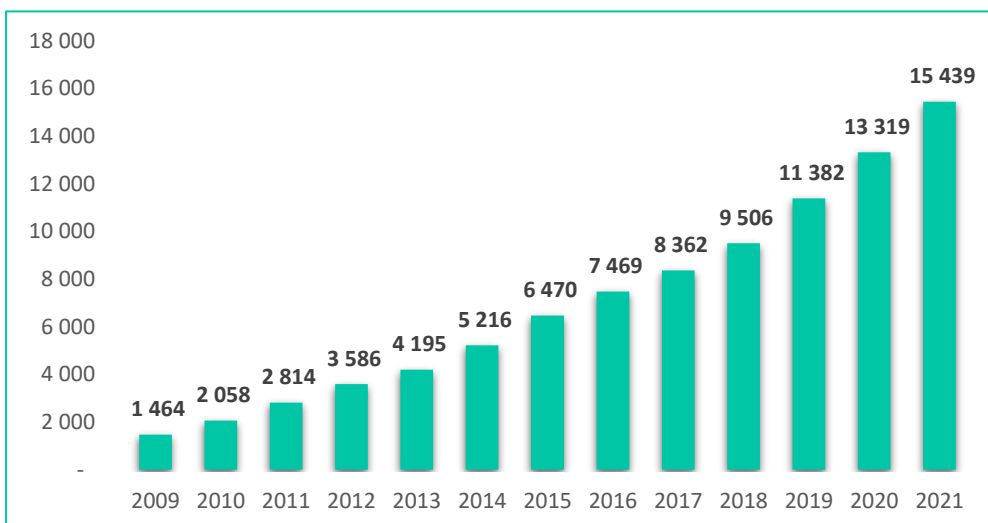
⁴ Errata: The total number of publications in peer-reviewed journals in 2021 is 293, not 638, based on the information available on the Web of Science.

iMM Publications in International Journals

(Source: Web of Science™)



Published Items in Each Year: 2009-2021



Citations in Each Year: 2009-2021

Papers in 2021: **293**

Sum of the times cited: **96.162**

Average citations per item: **29.22**

h-index: **124**

Query: ADDRESS: (Inst Med Molec SAME Portugal) OR ADDRESS: (Mol Med Inst SAME Portugal) OR ADDRESS: (Inst Mol Med SAME Portugal) OR ADDRESS: (Inst Med Mol SAME PORTUGAL)

Refined by: [excluding] DOCUMENT TYPES=(EDITORIAL MATERIAL OR CORRECTION OR MEETING ABSTRACT OR BOOK CHAPTER OR REVIEW)

Timespan: 2009-2021. Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC.

Note: This data is based on the information available on the Web of Science; hence, it is not an exhaustive analysis of the iMM publications.

10 Most Cited Articles 2002-2021

(Source: Web of Science™)

Ostrowski M, Carmo NB, Krumeich S et al (2010). Rab27a and Rab27b control different steps of the exosome secretion pathway. *Nature Cell Biology* 12(1):19-30.

Lefaucheur J, Andre-Obadia N, Antal A et al (2014). Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clinical Neurophysiology* 125(11):2150- 2206.

Colombo M, Moita C, van Niel G et al (2013). Analysis of ESCRT functions in exosome biogenesis, composition and secretion highlights the heterogeneity of extracellular vesicles. *Journal of Cell Science* 126(24):5553-5565.

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[Note](#): This data is based on the information available on the Web of Science; hence, it is not an exhaustive analysis of the iMM publications.

Selected Publications

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Bouca-Machado R, Pona-Ferreira F, Leitão M., Clemente A, Vila-Vicosa D, Kauppila LA, Costa RM, Matias R, Ferreira JJ (2021). Feasibility of a Mobile-Based System for Unsupervised Monitoring in Parkinson's Disease. **Sensors**, 21(15): 4972.

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Calero-Cuenca FJ, Osorio DS, Carvalho-Marques S, Sridhara SC, Oliveira LM, Jiao Y, Diaz J, Janota CS, Cadot B, Gomes ER (2021). Ctdnep1 and Eps8L2 regulate dorsal actin cables for nuclear positioning during cell migration. **Current Biology**, S0960-9822(21)00040-3.

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Dias M, Ferreira R, Remondes M (2021). Medial entorhinal cortex is necessary for estimation of elapsed time. **Journal of Neuroscience**, 41(48):9932-9943.

Kumar S, Fonseca VR, Ribeiro F, Basto AP, Agua-Doce A, Monteiro M, Miragaia RJ, Gomes T, Piaggio E, Segura E, Gama-Carvalho M, Teichmann SA, Graca L (2021). Developmental bifurcation of human T follicular regulatory cells. **Science Immunology**, 6: eabd8411.

Laserna V, Abegg D, Afonso CF, Martin EM, Adibekian A, Ravn P, Corzana F, Bernardes GJL (2021). Dichloro butendiamides as irreversible site-selective protein conjugation reagent. **Angewandte Chemie (International Edition English)**, 60:23750–23755.

Mainoli B, Machado T, Duarte GS, Prada L, Goncalves N, Ferreira JJ, Costa J (2021). Analysis of clinical and methodological characteristics of early COVID-19 treatment clinical trials: so much work, so many lost opportunities. **BMC Medical Research Methodology**, 21(1:42).

Mendonça DA, Bakker M, Cruz-Oliveira C, Neves V, Jiménez MA, Defaus S, Cavaco M, Veiga AS, Cadima-Couto I, Castanho MARB, Andreu D, Todorovski T (2021). Penetrating the blood-brain barrier with new peptide–porphyrin conjugates having anti-HIV activity. **Bioconjugate Chemistry**, (32):1067–1077.

Paramos-de-Carvalho D, Martins I, Cristóvão AM, Dias AF, Pereira T, Chapela D, Farinho A, Neves-Silva D, Jacinto A, Saúde L (2021). Targeting senescent cells improves functional recovery after spinal cord injury. **Cell Reports**, 36(1):109334.

Pinheiro H, Pimentel MR, Sequeira C, Oliveira LM, Pezzarossa A, Roman W, Gomes ER (2021). mRNA distribution in skeletal muscle is associated with mRNA size. **Journal of Cell Science**, 134.

Roman W, Pinheiro H, Pimentel MR, Segalés J, Oliveira LM, García-Domínguez E, Gómez-Cabrera MC, Serrano AL, Gomes ER, Muñoz-Cánoves P (2021). Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction. **Science**, 374:355–359.

Silva A, Almeida ARM, Cachucho A, Neto JL, Demeyer S, de Matos M, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT (2021). Overexpression of wild-type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. **Blood**, 138(12):1040-1052.

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Seminars, Workshops & Events

Computational Biology and Bioinformatics Seminar

January 6

“Acute stress impairs reward learning by blunting prediction-error signaling in men”

Vasco Conceição – Mamede de Carvalho Lab

January 20

“Exploring the role of interactions between circular RNAs and RNA binding proteins in Atrial Fibrillation: From Wet to Dry lab”

André Gabriel – Francisco Enguita Lab

February 3

“Selection Detection From the Masses - a tale of bibliographic research, automation and best scientific practices”

Francisco Pina-Martins – CE3C, FCUL

February 17

“Basal and IL-7-dependent transcriptomics of healthy and malignant T-cells”

Daniel Ribeiro – João Barata Lab

March 3

“A Git a day pushes the Docker away: a guide to container deployment and version control”

Inês Mendes and Nuno Agostinho – Mário Ramirez Lab and Nuno Morais Lab

March 31

“High-throughput studies to decipher Trypanosoma congolense sequestration”

Sara Silva Pereira – Luísa Figueiredo Lab

April 14

“Lobo Cluster - The iMM Supercomputer”

Pedro Luiz de Castro – Information Systems Unit

April 28

“From academic bioinformatics to corporate data science: a n = 1 study”

Filipe Tavares-Cadete – Santander

May 12

“Scientists hate her: discover this simple trick for consistent results with image analysis”

Clara Barreto – Bioimaging Unit

May 26

“Impossible task of today: Create an interactive stand-alone and dependency-free report”

Pedro Cerqueira – Mário Ramirez Lab

June 30

“The role of cingulate cortex in memory guided choices”

Sofia Cruz – Miguel Remondes Lab

July 21

“Bioinformatics Matters: more than a cause, an action!”

Marta Bica, Rita Silva and Rita Belo – Bioinformatics Matters

October 27

How to detect and diagnose a liver stage of Plasmodium infection?”

Bárbara Teixeira – Maria Mota Lab and Miguel Prudêncio Lab

“Exploring the repeatome of the human brain: Dynamics of transposable elements during neurodevelopment and in neurodevelopmental diseases”

Miguel Casanova – Nuno Morais Lab

November 10

“Unveiling the phosphorylation of RNA Polymerase II CTD associated to co-transcriptional splicing”

Ana Líbano Monteiro – Carmo-Fonseca Lab

“Profiling aging-associated gene expression alterations in human astrocytes using single cell transcriptomics”

Rita Silva – Nuno Morais Lab

November 24

“Targeting induced-senescent cells: a novel approach to promote spinal cord regeneration in mammals”

Daniel Ribeiro – Leonor Saúde Lab

“Bayesian modelling of splicing kinetics”

Rosina Savisaar – Carmo-Fonseca Lab

December 15

“Heterogeneity among parasite tissues population”

Lara Escobar – Luísa Figueiredo Lab

“Disease-associated T cell subsets with single-cell resolution”

Rui Vieira – Luís Graça Lab

Immunology Club

January 13

“Stem Cell Memory CD8 T cells in Graft versus Host Disease, the evidence so far and future studies”

Maria Soares – João Lacerda Lab

January 27

“Longitudinal profiling of innate immune response in COVID-19 patients”

Amelia Chiara Trombetta and André Gomes – Ana Espada Sousa Lab

February 10

“Characterization of B and follicular T cell subpopulations in Juvenile Idiopathic Arthritis”

Catarina Tomé – Luís Graça Lab and João Eurico da Fonseca Lab

February 24

“Dissecting the role of microRNAs on effector and regulatory CD4+ T cell differentiation during immune responses in vivo”

Carolina Cunha – Bruno Silva-Santos Lab

March 10

“The role of AIP (Aryl hydrocarbon receptor Interacting Protein) in T cell biology”

Silvia Ariotti – Marc Veldhoen Lab

March 24

“The signature of human cd4 regulatory thymocytes and its modulation by the chromatin landscape”

Pedro Rosmaninho – Ana Espada de Sousa Lab

April 7

“Study of the interaction between diet, microbiome, gut permeability and metabolomics in Systemic Lupus Erythematosus”

Inês Correia and Miguel Castro – João Eurico da Fonseca Lab

April 21

“Unraveling the heterogeneity of T cell help to B cells”

Saumya Kumar – Luís Graça Lab

May 19

“Targeting macrophages for breast cancer immunotherapy”

Mariana Reis Sobreiro – Bruno Silva-Santos Lab

June 2

“Interaction between Intraepithelial lymphocytes, microbiota and GLP-1 in context of small intestine parasite infection”

Patricia Campos – Marc Veldhoen Lab

June 16

“Mapping the glycan structures across thymic T cell development: impact in disease”

Manuel Vicente & Salomé Pinho – i3S

Host: Ana Espada de Sousa Lab

June 30

“Designing of Chimeric Antigen Receptor (CAR) T cells for cancer immunotherapy using sequences from malaria parasites: novel ways to distinguish friend from foe”

Diogo Silva – João Lacerda Lab

October 27

“Immune response to hepatitis B and influenza vaccines in patients under biological therapies”

Pedro Ribeiro – Luís Graça Lab

November 10

“Intestinal tissue resident T cell activation depends on metabolite availability”

Marc Veldhoen – iMM

November 24

“A role for CCR10+ILC2 in COVID-19 recovery”

Susana Fernandes & André Gomes – Ana Espada de Sousa Lab

Internal Seminar

March 3

“Long noncoding RNA-mediated alterations of telomeric chromatin”

Claus Azzalin – iMM

March 31

“Breaking News on gamma-delta T cells: Mums, Neonates and Metabolism”

Bruno Silva-Santos – iMM

April 14

“X-Chromosome Inactivation in Systemic Lupus Erythematosus”

Patrícia Costa Reis and Simão Rocha – João Eurico da Fonseca Lab and Carmo-Fonseca Lab

April 28

“New insights on vascular biology”

Cláudio Franco – iMM

May 12

“IL-7 deadly sins”

João Barata – iMM

May 26

“Tissue resident T lymphocytes”

Marc Veldhoen – iMM

June 9

“Amyotrophic Lateral Sclerosis: more than just a motor neuron disease?”

Ana Sebastião – iMM

July 21

“RNA splicing in the heart”

M. Carmo-Fonseca – iMM

October 6

“Modulation of inflammation in aging and tissue repair”

Joana Neves – iMM

October 20

Maria Mota – iMM

November 3

“Functions for nuclear positioning within cells”

Edgar Gomes – iMM

November 17

“How LDL cholesterol favors breast cancer cells migration and metastasis formation”

Sérgio Dias – iMM

December 15

“The biology of regeneration failure and success after spinal cord injury”

Leonor Saúde – iMM

Monday Lecture

January 4

“Emergent cellular ecosystems in melanoma revealed by single cell analysis”

Arjun Raj – University of Pennsylvania, Dept of Bioengineering and Dept of Genetics

Host: Domingos Henrique

January 11

“Lifestyle and cardiovascular disease”

Filip Swirski – Harvard Medical School, Massachusetts General Hospital

Host: Marc Veldhoen

January 18

“Learning and forgetting in olfactory cortex”

Carl Schnoonover – University of Colombia

Host: PhD Students Committee

January 25

“Multispectral functional genetics to unravel cardiovascular biology”

Rui Benedito – CNIC

Host: Domingos Henrique

February 8

“i-Rheo & Microrheology: Essential tools for biophysical studies”

Manlio Tassieri – Division of Biomedical Engineering, School of Engineering, University of Glasgow

Host: Nuno Santos

February 22

“Insights into Neuronal Kinesin Function from Mutations that Cause Hereditary Spastic Paraplegia”

Thomas M Huckaba – Department of Biology, Xavier University of Louisiana

Host: Edgar Gomes

March 1

“Importance of the origins in monocyte/macrophage functional phenotype”

Alberto Yanez – Instituto de Biotecnología y Biomedicina (BIOTECMED), University of Valencia

Host: Mariana Sobreiro and Karine Serre (Bruno Silva-Santos Lab)

March 8

“Understanding cerebral malaria with novel computational and 3D bioengineered vascular models”

Maria Bernabeu – EMBL Barcelona

Host: Luísa Figueiredo Lab

March 15

“Molecular and cellular origins of blood clot mechanical properties”

John Weisel – University of Pennsylvania School of Medicine, Philadelphia

Host: Nuno Santos

March 22

“Cytoskeletal crosstalk in cell mechanical behavior”

Gijsje Koenderink – TU Delft

Host: Nuno Santos

March 29

“Circadian Clock Genes and the Importance of Timing in Aging and Longevity”

Joseph Takahashi – Department of Neuroscience and Howard Hughes Medical Institute - UT Southwestern

Host: Bruno Cardoso (João Barata Lab)

April 12

“The evolution of mammalian organ development”

Margarida Cardoso Moreira - Francis Crick Institute, London, UK

Host: Nuno Morais

April 19

“Novel strategies to combat hard-to-treat infections”

Peter H. Nibbering – Leiden University Medical Center, The Netherlands

Host: Miguel Castanho

April 26

“High-resolution intravital microscopy reveals the plastic behavior of metastatic cancer cells”

Javier Bravo-Cordero – Icahn School of Medicine, Mount Sinai

Host: Ana Magalhães (Sérgio Dias Lab)

May 3

“Cell-type specialization in the brain is encoded by specific long-range chromatin topologies”

Ana Pombo – Berlin Institute for Medical Systems Biology (BIMSB) at the Max Delbrück Center for Molecular Medicine (MDC), Berlin

Host: Domingos Henrique

May 10

“The structure of cell fate decisions in the neural crest lineage”

Igor Adameyko – Center for Brain Research, Medical University of Vienna & Karolinska Institutet, Stockholm

Host: Nuno Morais

May 17

“Unifying CD8 T cell differentiation in mice and men”

Carmen Gerlach – Karolinska Institute

Host: Marc Veldhoen

May 24

“B cell circuits in homeostasis and disease”

João Pedro Pereira – Yale University

Host: Bruno Silva-Santos

May 31

“Keeping in touch - systematic identification of contact site residents”

Maya Schuldiner – Weizmann Institute of Sciences

Host: PhD Students Committee

June 7

“Understanding TB: a view from the pathogen”

Margarida Saraiva – i3S

Host: Luís Graça

June 14

“Open cutting-edge super-resolution and machine-learning technology for the study of cell biology and viral infection”

Ricardo Henriques – i3S

Host: Edgar Gomes

June 28

“Chromosome Dynamics during Mitosis”

Raquel Oliveira – IGC

Host: Sérgio de Almeida

July 5

“In vivo Imaging of Alzheimer’s pathology and related memory dysfunction in human aging”

Anne Maass – DZNE Magdberg

Host: Luísa Lopes

July 12

“New paradigms in influenza A virus infection”

Maria João Amorim – IGC

Host: Pedro Simas

September 13

“Sensorimotor Organoids as models of Amyotrophic Lateral Sclerosis”

João Pereira – Tufts School of Biomedical Sciences

Host: Leonor Saúde

September 20

“Using scRNA-seq to map cell diversity in human liver regeneration”

Tomás Gomes – ETH Zurich

Host: Nuno Morais

October 11

“Metabolic regulation of developmental rate in mouse and human cells”

Margarete Diaz-Quadros – Genetics Department - Harvard Medical School

Host: Domingos Henrique

October 25

“Characterizing and targeting non-genetic mechanics of tumorigenesis in blood cancer”

Panagiotis Ntziachristos – Ghent University

Host: João Barata

November 22

“Measles virus: Endgame?”

Benhur Lee – Icahn School of Medicine at Mount Sinai

Host: Nuno Santos

November 29

“Telomere shortening: why and how?”

Titia deLange – The Rockefeller University, NYC

Host: Claus Azzalin

December 6

“Metabolic control of disease tolerance to infection”

Miguel Soares – IGC

Host: Domingos Henrique

December 13

“Multimodal Optical Microscopy to study biological systems”

Alberto Diaspro – Università di Genova and Istituto Italiano di Tecnologia

Host: Nuno Santos

Neurosciences Seminar

January 4

“Role of Brain-Derived Neurotrophic Factor on Childhood Absence Epilepsy: from circuits to behavior”

Mariana Sottomayor – Ana Sebastião Lab

“Search for novel compounds to prevent TrkB-FL cleavage”

Sara Oliveira – Ana Sebastião Lab

January 11

“Function of the Hippocampal-Retrospenial Cortex Circuit in the Resolution of a Spatial Conflict Task”

Patrícia Bernardo – Miguel Remondes Lab

“Characterization of neuroinflammatory and synaptic plasticity dysfunction in Wistar-Kyoto model of depression”

Hugo Simões – Miguel Remondes Lab

January 18

“Neuroinflammation and substance abuse: partners in crime”

Teresa Summavielle – i3S

January 25

“Unveiling the effects of caffeine in adult neurogenesis and synaptogenesis”

João Moreira – Ana Sebastião Lab

February 1

“Modulation of synaptic cooperation and competition by the endocannabinoids”

Rosalina Fonseca – CEDOC

February 8

“Zooming in on the effects of Diabetes in Parkinson’s disease neuropathology”

Hugo Vicente Miranda – CEDOC

February 22

“Rett Syndrome, Adenosine and BDNF: a tale of the last four years”

Catarina Lourenço – Ana Sebastião Lab

March 1

“Impact of NLRP3 Inflammasome Inhibition on a Model of A β -Induced Toxicity”

Diogo Dias – Ana Sebastião Lab

March 8

“Role of the mitochondrial kinase PINK1 in mitochondria quality control pathways in Parkinson’s disease models”

Renata Couto – Vanessa Morais Lab

March 15

“Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β induced toxicity”

Mariana Van Zeller – Ana Sebastião Lab

March 22

“Synaptic mitochondria: In search of its functional fingerprint”

Andreia Pereira – Vanessa Morais Lab

March 29

“Medial entorhinal cortex excitatory neurons are necessary for accurate timing”

Marcelo Dias – Miguel Remondes Lab

April 5

“NLRP3 inflammasome-driven neurodegeneration and epileptiform activity in a model of epileptogenesis in organotypic slices”

Francisco Meda – Ana Sebastião Lab

April 12

“The Metabolic Profile of Brain Mitochondria”

Bernardo Cetra Antunes – Vanessa Morais Lab

April 19

“Unveiling the NLRP3 Inflammasome Cascade in Ageing and Social Isolation”

Daniela Magalhães – Ana Sebastião Lab

April 26

“Unravelling the contribution of astrocytes for the neuroinflammatory milieu of epileptic-like organotypic slices”

Jacinta Manta – Ana Sebastião Lab

May 3

“The role of asymmetric post-translational modifications on the behavior of protein homodimers and oligomers”

Federico Herrera – Laboratory Head of the Cell Structure and Dynamics Laboratory, BioISI Research Unit, Faculty of Sciences, University of Lisbon

May 10

“Unravelling mitochondrial turnover at the synapse”

Carlos Cardanho-Ramos – Vanessa Morais Lab

May 17

“KTP vs KTP-NH2: Should KTP arrive to the party alone or with a plus one?”

Rita Belo – Ana Sebastião Lab

May 24

“Neuronal TrkB-ICD fragment in Alzheimer's disease: an unexpected journey”

Tiago Coelho – Ana Sebastião Lab

May 31

“Is seizure severity related to increased TrkB-FL cleavage?”

Leonor Rodrigues – Ana Sebastião Lab

June 7

“Extracellular regulation of protein aggregation in Alzheimer's Disease”

Cláudio Gomes – Protein Misfolding and Amyloids in Biomedicine Laboratory BioISI/FCUL

June 14

“Dissecting the Determinants of Dysfunctional Sensory Processing in Autism”

Jorge Cardoso – Miguel Remondes Lab

June 21

“The involvement of astrocytes in cortico-limbic function and cognition”

João Oliveira – ICVS-Universidade do Minho

June 28

“The role of brain-derived neurotrophic factor (BDNF) in amyotrophic lateral sclerosis (ALS)”

Mariana Vendeirinho – Ana Sebastião Lab

July 5

“Mechanisms of Neuronal Aging relevant for Alzheimer’s disease”

Cláudia Almeida – CEDOC

July 12

“Adenosine receptors impact on astroglial CB1R: relevance for synaptic function”

Joana Gonçalves-Ribeiro – Ana Sebastião Lab

July 19

“Unravelling the role of the non-psychotomimetic cannabinoid Cannabidivarin in the modulation of neurogenesis – Relevance for Rett Syndrome”

Diogo Lourenço – Ana Sebastião Lab

July 26

“Microtubule nucleation during brain development: from mitosis to neuronal morphology augmin takes the lead”

Ricardo Viais – Ana Sebastião Lab

September 6

“An adenosine A1R agonist with anticonvulsant properties but devoid of effect on excitatory hippocampal synaptic transmission”

Anwasha Ghosh – Ana Sebastião Lab

September 13

“What is hAPPening at the synapse: from development to Alzheimer’s Disease”

Joana Saraiva – Luísa Lopes Lab

September 20

“BDNF receptor cleavage: a novel biomarker for Alzheimer's disease”

Carolina Borlido – Ana Sebastião Lab

October 11

"Adenosine signaling detects and stabilizes newly formed GABAergic synapses during development"

Sabine Levi – École des Neurosciences de Paris, Île de France

October 25

"Is memory a matter of time?"

Inês Morgado – Luísa Lopes Lab and Miguel Remondes Lab

November 8

"Memory traces of a drug-led life"

Joana Gomes Ribeiro – Luísa Lopes Lab

November 15

"Optogenetic dissection of cortico-striatal connectivity"

Nicolas Morgenstern – Luísa Lopes Lab

November 22

"From unconventional niches to adult hypothalamic neurogenesis in Alzheimer's Disease"

Sara Paulo – Ana Sebastião Lab

November 29

"Characterization of the metabolic profile of differentiated cells derived from Subventricular Zone Neural Stem Cells"

Isa Mota – Ana Sebastião Lab and Vanessa Morais Lab

"Developing a strategy to improve neuronal regeneration after glial scar formation"

Gonçalo Costa – Ana Sebastião Lab

December 6

"Pyroptotic Deadly Curse of Neurons in Alzheimer's Disease – Unravelling the NLRP3 Inflammasome pathway"

Tiago Ferreira – Ana Sebastião Lab

December 13

"Drogas: Contexto Sócio-Histórico e Cultural"

Adriana Marcassa Tucci – Departamento de Saúde, Educação e Sociedade, Universidade Federal de São Paulo

December 20

"Information processing challenges to cognitive control"

Gonçalo Aires de Oliveira – Miguel Remondes Lab

Oncobiology Club

January 6

“TNF α Inhibits Sodium-Iodide Symporter Expression In Thyroid Cells Through Nf-Kb Activation”

Márcia Faria – Research Group on Endocrine Tumors and Signaling, Hospital de Santa Maria

January 20

“Molecular characterization of early breast cancer”

Célia Carvalho – Carmo-Fonseca Lab

February 3

“Horizontal transfer of therapy resistance in cancer cells”

José Carlos Machado – i3S

February 17

“Targeting microRNAs for modulation of the anti-tumor human $\gamma\delta$ T cell differentiation”

Gisela Silva Gordino – Bruno Silva-Santos Lab

March 3

“Transcriptomic signatures of the INK4A/ARF locus in senescence regulation and cancer”

José Ferrão – Nuno Morais Lab

March 17

“RANKL/RANK pathway blockade: an opportunity to overcome resistance to CDK4/6 inhibitors in breast cancer”

Inês Gomes – Luís Costa Lab

April 14

“The role of UBE2C in Brain Metastases”

Eunice Paisana – João Barata Lab

April 28

“LDL-Cholesterol in HER2+ Breast Cancer”

Ana Magalhães – Sérgio Dias Lab

May 12

“Functional and Metabolic Characterization of Antitumour Macrophages”

Afonso Teixeira Mota – Bruno Silva-Santos Lab

May 26

“Development of multiparameter medical imaging tools for cancer diagnosis”

Mar Cabeza-Cabrerizo – Gonçalo Bernardes Lab

June 9

“What are these dots in my plots? A guide to understanding scRNA-seq data analysis applied to the tumour microenvironment”

Marta Bica – Nuno Morais Lab

June 23

“The controversial roles of PLC γ 1 across different tumor types”

Raquel Cruz-Duarte – Luís Costa Lab

July 7

“Sphingosine Kinases are essential positive modulators of IL-7/IL-7R signaling in Acute Lymphoblastic Leukemia”

Marta Fernandes – João Barata Lab

October 6

"Multi-Dimensional Cartography the Breast Cancer Microenvironment"

Karine Serre – iMM-Laço Hub

October 20

"Cholesterol Metabolism in Breast Cancer"

Ana Magalhães – Sérgio Dias Lab

November 3

“Big data, big picture - how we help looking at cancer transcriptomes”

Mariana Ferreira and Nuno Agostinho – Nuno Morais Lab

November 24

“RANK pathway blockade in combination with CDK4/6 inhibitors as a therapeutic approach for hard-to-treat metastatic breast cancers: what we know and the (nearby) future”

Sandra Casimiro – Luís Costa Lab

December 15

“A Bispecific antibody to block iron-endocytosis-driven metastasis”

Marta Marques – Gonçalo Bernardes Lab

Other Events

January 14

COLife Scientific Webinar

“Modeling human development and disease in cerebral organoids”

Jürgen Knoblich – IMBA - Institute of Molecular Biotechnology of the Austrian Academy of Science part of Vienna Biocenter

January 20

EpiEpiNet Kick-Off Meeting

January 21

Out of Our Box

“Seagrass guardians: fisherwomen leaders of ocean conservation”

Raquel Gaspar – Co-Founder of Ocean Alive

February 5

Webinar “Bullying in Science”

“Filling the space: Integrative responding to academic incivility in higher education”

Morteza Mahmoudi – Michigan State University

February 11

SIMICA Seminar

“Profiling drug action in primary human patient tissues with high content imaging and deep learning”

Nikolaus Krall – Scientific Co-Founder of Allcyte GmbH

March 4

COLife Community Webinar

“Bioimaging @ COLife”

March 9

NeuroSeS Seminar

“Complicações neurológicas da COVID-19”

José Ferro – Group Leader, IMM

March 10

RiboMed Innovation Challenges: Presentation and Q&A Session

March 11

COLIFE | Towards diversity and equality in science: "Picture a Scientist" Doc & Panel Discussion

March 12

Ximbio Seminar

“Unlock the value of your research tools”

Estela Pérez Santamarina & Julia Appelhans

SIMICA Seminar

“Getting published in 2021 and beyond: How to adapt to a rapidly changing publication landscape”

Ruben Ragg – Chem BioChem Wiley-VCH GmbH

April 6

CAML Rheumatology Series

“Early diagnosis of SLE”

Marta Mosca – Department of Clinical and Experimental Medicine, University of Pisa, Italy

April 16
RiboMed Innovation Challenges
“Reaching Out to Industry” Workshop
Joachim Vogt (Abbvie) and Pascale Redig (Janssen)

April 20
CAML Rheumatology Series
“Regulation of tertiary lymphoid structures and their translational relevance in Sjogren’s syndrome”
Michele Bombardieri – Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London

April 22
ACORN Seminar
“Introduction to optical, ultrasound and photoacoustic imaging”
Timo Schomann – Percuros B.V.

April 29
ACORN Seminar
“Defying Conventional Wisdom: Developing Carbon Monoxide as a Therapeutic Agent”
Binghe Wang – Department of Chemistry and Center for Diagnostics and Therapeutics Georgia State University

Out of Our Box – XIV CAML/IV NeurULisboa
“Making graphics and animations in National Geographic”
Fernando Baptista – National Geographic

May 4
CAML Rheumatology Series
“Dissecting phases of psoriatic disease – from psoriasis to arthritis”
Axel Hueber – Section Rheumatology, Sozialstiftung Bamberg, Bamberg, Germany

May 4-7
XIV CAML · IV NeurULisboa PhD Students Virtual Meeting

May 5
FLxFlow Network Seminar
“Fluorochromes - brightness, detection and resolution”
Andrew Filby – Newcastle Flow Cytometry Core Facility

May 6
COLife Webinar | COLife/MyoChip Microfabrication and Microfluidics Symposium
“Microfabrication & Microfluidics meets Life Sciences”

May 11

NeuroSeS Seminar

“Potencial regenerativo das células estaminais neurais em doenças neurológicas”

Sara Xapelli – Ana Sebastião Lab

May 13

Out of Our Box

“Wonder, groundbreaking technology and big-scale human collaboration - essential tools to communicate particle physics”

Ana Godinho – Head of Education, Communications and Outreach CERN (European Laboratory for Particle Physics)

May 20

SIMICA Seminar

“Rational Design of Conformation-Specific Antibodies Targeting Protein Aggregates”

Michele Vendruscolo – Centre for Misfolding Diseases, University of Cambridge, UK

May 21

SIMICA Seminar

“Extracellular vesicles for drug delivery: Enhancing uptake and efficacy of chemotherapy towards cancer-specific cells”

Pablo Lara – Percuros B.V., Netherlands

May 27

iMM Postdoc Day

June 1

CAML Rheumatology Series

“What can synovial tissue research teach us about preventing arthritis?”

Carl Orr – Centre for Arthritis and Rheumatic Diseases, Saint Vicent’s University Hospital, University College Dublin, Dublin, Ireland

Let’s Talk About Biomedical Research – Q&A Session

Luís Graça, Luísa Lopes, Pedro Simas & Filipa Nunes

Moderator: Inês Domingues

June 2

Master Students Day

COLife Community Webinar

“Histology and Pathology Series: RNAscope™ @ COLife”

Ana M. Biscaia Santos (Facility Manager, iMM Comparative Pathology Unit) and Paolo Ferro (Genomics sales specialist, Biotechne)

June 17-18
EXCELLtoINNOV Final Meeting

June 17
Flow Cytometry Seminar
“Pushing the Limits of Fluorescence in a Fluorescent Limited World”
Yacine Kharraz – Cytex® Biosciences Inc.
Host: iMM Flow Cytometry Unit

June 29
CAML Rheumatology Series
“Manipulating signalling pathways for the treatment of rheumatoid arthritis”
Peter Taylor – Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Botnar Research Centre, University of Oxford

NeuroSeS Seminar
“Obsessive-Compulsive Disorder: from brain dysfunction to new therapeutic approaches”
Pedro Morgado – ICVS/3B’s, UMinho

September 14
NeuroSeS Seminar
“Desenvolvimento clínico de tecnologias em saúde: Quando um produto é testado em humanos”
Mário Miguel Rosa – FMUL, iMM, HSM/CHLN

October 29
Comparative Pathology Unit | 1st Users Meeting

November 9
NeuroSeS Seminar
“Flow-migration coupling and cerebral vascular malformations”
Cláudio Franco – iMM

November 25
Out of Our Box
“Research (in)Security for a more secure world”
Pedro Adão – Associate Professor at the Department of Computer Science and Engineering of Instituto Superior Técnico (IST) and a researcher from Instituto de Telecomunicações
Host: Nuno Morais

December 10
SIMICA Seminar
“The Art of Conveying and Convincing - From Grant Writing To Lay-Level Presentations”
Alan Chan – Percuros

December 16

Out of Our Box

“The Serengeti Rules: The Regulation and Restoration of Biodiversity”

Sean B. Carroll - Howard Hughes Medical Institute, HHMI Tangled Bank Studios

Host: Leonor Saúde

Parasitology Club

January 5

“Plasmodium cross-stage interplay modulates parasite virulence”

Sónia Pereira – Maria Mota Lab

January 12

“Persister-like parasites in a Trypanosoma brucei infection”

Sandra Trindade – Luísa Figueiredo Lab

January 19

“Hypothesis: Interference of COVID-19 with lung homeostasis”

Cristina Arias – Maria Mota Lab

January 26

“Is replication a damage? From one to thousands in Plasmodium liver infection”

Inês Bento – Maria Mota Lab

February 2

“Microbiota”- A new player in the Host-Plasmodium affair”

Debanjan Mukherjee – Maria Mota Lab

February 9

“3D hepatic models – an innovative platform for the screening of anti-plasmodial drugs”

Diana Fontinha – Miguel Prudêncio Lab

February 23

Henrique Machado – Luísa Figueiredo

March 2

“Methionine metabolism in Plasmodium blood-stage development”

Maria Inês Marreiros – Maria Mota Lab

March 9

“Development of a multi stage Plasmodium vaccine”

Raquel Azevedo – Miguel Prudêncio Lab

March 16

“gRABing the APPLe : Plasmodium hijacks a host endosomal adaptor during liver stage development”

Aparajita Lahree – Maria Mota Lab

March 23

“Effect of Antiretroviral Therapy on Liver Stage Development of Plasmodium Parasites and Whole-Organism Vaccination against Malaria”

Gonçalo Nogueira – Miguel Prudêncio Lab

April 13

Denise Francisco – Miguel Prudêncio Lab

April 20

“Impact of dietary protein deficiency on the generation of an efficient immune response to malaria vaccination”

Helena Cabaço – Miguel Prudêncio Lab

April 27

“Lysine Residues Matter”

Sara Baptista – Maria Mota Lab

May 4

“Hijacking of the host cell Golgi by Plasmodium berghei liver stage parasites”

Mariana De Niz – Luísa Figueiredo Lab

May 11

“Plasmodium infection: What happens in the liver... doesn't stay in the liver.”

Ângelo Chora – Maria Mota Lab

May 19

“Nutrient sensing in Plasmodium falciparum”

Yvonne Azasi – Maria Mota Lab

June 1

“Grumpy lncRNA and parasite differentiation: a new link via rRNA methylation”

Fabien Guegan – Luísa Figueiredo Lab

June 15

“Liver stage Plasmodium infection: from one to thousands parasites”

Soraia Caetano – Maria Mota Lab

June 22

“Characterization of a novel mRNA methylation mechanism in Trypanosoma brucei”

Lúcia Serra – Luísa Figueiredo Lab

June 29

“Cell-to-cell heterogeneity among parasite tissue population”

Lara Escobar – Luísa Figueiredo Lab

July 13

“Endosomal dynamics at the Host-Plasmodium interface through liver stage parasite development”

Aparajita Lahree – Maria Mota Lab

July 20

“Immunopathology and parasite sequestration cause severe cerebral animal African trypanosomiasis”

Sara Silva Pereira – Luísa Figueiredo Lab

July 27

“Whole-sporozoite vaccines against malaria: how different can they be?”

Diana Moita – Miguel Prudêncio Lab

September 21

“Excreted Trypanosoma brucei proteins inhibit Plasmodium hepatic infection”

Adriana Temporão – Miguel Prudêncio Lab

September 28

“Sirtuins in Plasmodium nutrient sensing and responses”

Yash Pandya – Maria Mota Lab

October 12

Idálio Viegas – Luísa Figueiredo Lab

October 20

“Killing the competition: a theoretical framework of liver-stage malaria”

Cristina Arias – Maria Mota Lab

October 26

“Persistent Parasite Squad: A New Platoon in the Fat”

Sandra Trindade – Luísa Figueiredo Lab

November 9

Inês Bento – Maria Mota Lab

November 16

“Microbiota-Host-Plasmodium” A three-way axis dictating severe malaria pathology”

Debanjan Mukherjee – Maria Mota Lab

November 23

“Trypanosoma brucei triggers a broad immune response in the adipose tissue”

Henrique Machado – Luísa Figueiredo Lab

November 30

“Circumsporozoite protein polyubiquitination impairs the establishment of Plasmodium liver infection”

Sara Baptista – Maria Mota Lab

December 7

“Development of a multi stage malaria vaccine”

Raquel Azevedo – Miguel Prudêncio Lab

Pizza Seminar

January 12

“Mechanisms of astrocytic dysfunction in ALS”

Sara Pinto – Ana Sebastião Lab

“Mechanisms of T follicular regulatory cell differentiation”

Filipa Ribeiro – Luís Graça Lab

January 26

“Modulating adult oligodendrogenesis”

Joana Mateus – Ana Sebastião Lab

“How to prepare a perfect pizza... oh sorry, develop trans-BBB antiviral conjugates”

Diogo Mendonça – Miguel Castanho Lab

February 9

“Regulation of in vitro postnatal neurogenesis by TRPV1”

Diogo Lourenço – Ana Sebastião Lab

“Unveiling the effects of Myh9 in pericytes during sprouting angiogenesis”

Andreia Pena – Cláudio Franco Lab

February 23

“Modelling and interpreting the impact of splicing variants on human health”

Pedro Barbosa – Carmo-Fonseca Lab

“Trypanosoma brucei: New ally in the fight against malaria?”

Adriana Temporão – Miguel Prudêncio Lab

March 9

“Using the regenerative potential of zebrafish extracellular matrix to promote spinal cord repair in mammals”

Dalila Silva – Leonor Saúde Lab

“Exploiting innate immune responses to enhance whole sporozoite antimalarial vaccination”

Diana Moita – Miguel Prudêncio Lab

March 23

“Targeting the CCL2/CCR2 signaling axis in metastatic medulloblastoma”

Carlos Custódia – João Barata Lab

“Monocytes as allies against cancer: how to instruct them to prevent primary tumour growth and metastasis formation?”

Carolina Jardim – Bruno Silva-Santos Lab

April 6

“Exercising on cannabinoids: targeting adult neural stem cells to treat Major Depression”

Rui Rodrigues – Ana Sebastião Lab

“Modification of therapeutic monoclonal antibodies towards reduction of immunogenicity”

Rodrigo Pedroso – Luís Graça Lab

April 20

“Targeting microRNAs for modulation of the anti-tumor human gamma-delta T cell differentiation”

Gisela Gordino – Bruno Silva-Santos Lab

“At last, the secret of targeting BTK for the treatment of B-cell malignancies is revealed”

Bárbara Sousa – Gonçalo Bernardes Lab

May 11

“Unveiling the neuroinflammatory mediators in Ageing and Social Isolation”

Daniela Magalhães – Ana Sebastião Lab

“Characterizing the risk for IL-7R-mediated malignancy in different stages of hematopoietic development”

Ana Cachucho – João Barata Lab

May 18

“Strategies for anticancer peptide delivery”

Ítala Silva – Nuno Santos Lab

“RANKing a new driver of resistance to CDK4/6 inhibitors in luminal A Breast Cancer”

Inês Gomes – Luís Costa Lab

June 1

“What is hAPPening at the synapse: from development to Alzheimer’s Disease”

Joana Saraiva – Luísa Lopes Lab

“Statistical challenges of investigating a disease with a complex diagnosis”

João Malato – Luís Graça Lab

June 15

“Short-read metagenomic assembly: finding the best fit in a world of options”

Inês Mendes – Mário Ramirez Lab

“The interplay of B and T follicular cell subsets in Juvenile Idiopathic Arthritis”

Catarina Tomé – João Eurico da Fonseca Lab

September 28

“A key role for microRNAs in the development and functional differentiation of $\gamma\delta$ T cell subsets”

Daniel Inácio – Bruno Silva-Santos Lab

“Studying flavivirus capsid protein interaction with nucleic acids”

Nelly Silva – Nuno Santos Lab

October 12

“The fellowship between regulatory T cells and tissue-resident memory T cells”

Leandro Barros – Marc Veldhoen

“Unveiling the DNA damage response in multinucleated skeletal muscle cells”

Inês Faleiro – Sérgio de Almeida Lab

October 26

“Expansion of regulatory T cells for clinical translation in hematopoietic stem cell transplantation”

Carolina Pacini – João Lacerda Lab

“BDNF receptor cleavage promotes shedding of TrkB-ICD-containing extracellular vesicles in Alzheimer’s disease”

Tiago Coelho – Ana Sebastião Lab

November 23

“Synaptic regulation of chronic stress-induced miRs”

Beatriz Rodrigues – Centro de Neurociências e Biologia Celular (CNC), Universidade de Coimbra

“Establishing cellular models to investigate the role of LINE-1 elements in X-chromosome inactivation and genome stability”

Inês Dias – Sérgio de Almeida Lab

December 7

“Novel hybrid nanoparticles for Alzheimer’s disease theranostic: efficient overcoming of nanomaterials across the blood-brain-barrier”

Catarina Chaparro – Miguel Castanho Lab

“Phenotyping circulating monocytes and dendritic cells in SARS-COV-2 and HIV infections: unsupervised and supervised approaches to flow cytometry data analysis”

Guilherme Farias – Ana Espada de Sousa Lab

iMM Training Hub

The iMM is strongly committed to providing the best training for researchers to succeed in internationally competitive environments of academia, industry and clinical medicine. The Training Hub works closely with early-career researchers at iMM to maximize career prospects, ensuring the full running of ongoing Master, PhD and Postdoctoral Programs.

Team

Director of Studies: Domingos Henrique, PhD

Executive Manager: Filipa Nunes, PhD

Executive Committee: Leonor Saúde, PhD (Chair); Vanessa Morais, PhD; Claus M. Azzalin, PhD

Advanced Training in Numbers

	2021
Postdoctoral Fellows	132
Started in 2021	13
PhD Students	147
Started in 2021	25
MSc Students	134
Started in 2021	64

Together with Faculdade de Medicina da Universidade de Lisboa (FMUL) and with Hospital de Santa Maria (HSM), iMM is part of the Lisbon Academic Medical Center (CAML), a consortium that provides an integrated form of education and training in Biomedicine and Clinical Research, combining multidisciplinary and internationalization.

In pair with high-level research-centred training, our MSc/PhD students and Postdoctoral researchers benefit from a varied curricular offer organized into several Advanced Courses – scientific and transversal skills courses and workshops - distributed along each academic year.

In 2013, iMM was awarded FCT funding to create the Lisbon Biomedical and Clinical Research PhD Programme – **LisbonBioMed**. After 5 editions of the LisbonBioMed FCT PhD Programme, LisbonBioMed is now the iMM international PhD Program that integrates all PhD Students at iMM.

The majority of iMM PhD students belong to the CAML PhD Programme that runs in the campus since 2010. In addition, iMM also hosts students from other PhD programmes (e.g. GABBA) and Universities (e.g. University of Porto).

In 2021, iMM hosted **8 PhD students from other Institutions/Universities**: Universidade do Porto (1), Universidade de Coimbra (1), Universidade NOVA de Lisboa (1), Faculdade de Ciências da Universidade de Lisboa (1), Instituto Superior Técnico da Universidade de Lisboa (4).

iMM also hosted 3 PhD students from **3 Innovative Training Networks (ITN)** European Commission programme Marie Skłodowska-Curie Actions (MSCA), and 1 PhD student awarded with the “**la Caixa**” **Foundation INPhINIT – Incoming** doctoral fellowship.

In 2021, **15 iMM students concluded their PhD theses**, 13 of which were attributed by Faculdade de Medicina da Universidade de Lisboa (FMUL).

Advanced Courses

A total of 7 Advanced Courses were organized

5 Courses organized under the CAML PhD Programme in 2021

LisbonBioMed Course: Towards a Creative and Critical Mind

Organizer: Domingos Henrique

Date: April 19-30

The course aims to promote student integration, creates an informal welcoming, fosters team bonding, interaction with putative supervisors, introduces complementary skills training, and raises awareness to transversal competences needed for a successful scientific career.

Statistical Thinking for PhD Students

Organizer: Domingos Henrique

Date: 26th April to 14th June, every Monday (8 sessions of 3 h each; total: 24 h)

This is an introductory course to statistical methods applied to biological research, aimed at providing participants with basic concepts on statistics, and how these can be used in daily research activities, with particular emphasis on how to design experiments and how to deal with the limits of statistical methods. Participants are encouraged to bring their experimental questions to be discussed. This course provides the basis for further courses, aimed at more advanced statistical methods, targeted at specific needs from researchers at CAML.

Animate your Science: How to design an award-winning scientific poster (Online Workshop)

Organizer: Workshop group of the PhD Students Committee

Date: July 2

Speaker: Tulio Rossi, Animate your science, Adelaide, Australia

The aim of this workshop is for students to learn how to design a poster that is as innovative, intelligent and interesting as their scientific work. From choosing the appropriate software to mastering negative space, participants will learn how to take control of the reader’s experience. Following good design principles, students can shine a light on their work and stand out from the crowd of boring wall-of-text posters with an eye-catching, engaging and effective scientific poster.

Managing yourself through a PhD (Online Workshop)

Organizer: Workshop group of the PhD Students Committee

Date: November 24

Speaker: Desiree Dickerson, Spain

This workshop aims to help PhD students to optimize their productivity, increase their resilience to stress, anxiety and burnout, and enhance their well-being and work-life balance.

In this two-part workshop, participants: i) address self-critical and self-sabotaging thought processes that underlie perfectionism, imposter syndrome, worry, low motivation, and uncertainty and begin to reframe them; ii) begin to identify maladaptive coping strategies (e.g. avoidance and procrastination) that tend to reinforce unproductive thinking and behavioural patterns, and explore more effective (and healthier) short and long-term strategies.

Laboratory Animal Science Course for Functions A+D (former FELASA Category B) CONGENTO-harmonized program.

Organizers: Iolanda Moreira and Lara Carvalho

Date: September 1-30

The course was organized under the CONGENTO-harmonized programme and was targeted to Function A (former FELASA Category B) and D. The course provides theoretical and practical training for the use of animal models (rodents and fish) in scientific research. This course is a requirement to be able to work with animal models.

Other iMM Courses

Leadership and Management Skills Course for Postdocs (Online)

Organizer: Postdoctoral Association (PDA)

Date: January 11-28th (6 afternoons, 3.5h each)

Trainers: hfp consulting

Postdocs find themselves in a highly diverse and competitive research landscape. To successfully navigate their career paths, transferable skills in the areas of communication, (self)-organisation, and interpersonal relationships are essential. These skills can be acquired and developed. This workshop enables postdocs to productively deal with challenges related to the interpersonal aspects of doing science. Goals of the workshop:

- Advance communication, collaboration, and self-organisational skills
- Understand how to reach career goals more efficiently and effectively
- Learn and practice useful tools for career in science and beyond.

Portuguese Course (Foreign Language)

Organizer: Training Hub and Postdoctoral Association (PDA)

Dates: Levels A1 and B1/B2 (5th edition): November 2020 to June 2021 (45h, 1 class/level/week);
Levels A1 and B1/B2.2 (6th edition): November 2021 to June 2022 (45h, 1 class/level/week).

Teaching Staff: Linguagest - Escola de Línguas para Comunicação Empresarial, CRL

Other Events

Science Careers Sessions (Online)

“Science Careers” is a series of talks to get to know jobs in science beyond academia. During the sessions participants have the opportunity to know more about the daily work of the speakers, how they got there, the pros and cons of their work, and to ask questions about their path.

Organizer: Science Careers group of the PhD Students Committee

Date: January 14; May 25; June 15; October 14; November 16; December 15

Speakers: Rita Viana, Human Resources Department at Bial; Vitor Carmona, Rare Conditions Partner for Haemophilia at Roche; Eva Rodrigues, Research & Development department at Bial; Marie Bordone, Medical Science Liaison for Alzheimer's disease at Roche; Isa Matos, Key Account Manager at Tebu-bio; Luís Gomes, Scientific Editor at Cell Press.

Webinar: Bullying in Science

Organizer: Training Hub

Date: February 5th

Speaker: Morteza Mahmoudi, Michigan State University, USA

Webinar's Title and the Abstract:

“Filling the space: Integrative responding to academic incivility in higher education”

Academic incivility represents a serious issue that affects all disciplines and people of all levels of experience. To create a truly safe, productive and vibrant environment in academia requires coordinated and collaborative input and action of a variety of stakeholders including scholarly communities, funding agencies, and institutions. In this webinar, the speaker focused on a framework of integrated responding in which stakeholders as responsible and response-able parties could proactively collaborate and coordinate to reduce the incidence and consequences of academic incivility while building constructive academic cultures.

14th PhD Students (Virtual) Meeting

Organizer: PhD Meeting group of the PhD Students Committee

Date: May 5-7th

The annual PhD Students meeting is the place by excellence where students present their work to the iMM/CAML community. Moreover, it includes seminars from renowned scientists, and presentations from the João Lobo Antunes Merit PhD Thesis awardees. In 2021, the event included also a Graphical Abstract contest.

PostDoc Day (Online)

Organizer: Postdoctoral Association (PDA)

Date: May 27

The PostDoc Day is the opportunity for postdoctoral researchers to share their work with the iMM community. In 2021, the program included also a discussion panel on "Science Valorization and Intellectual Property" and a discussion panel on "Career Transition – From Academia to Industry".

Master's Day at iMM (for all iMM MSc students, Online)

Organizer: Training Hub and Master Students Committee 20/21

Date: 2nd June

Program:

- Awarding ceremony of the Best Master Thesis
- Keynote talk, by Maria Carmo-Fonseca: “My lifelong scientific quest”
- Roundtable discussion | What’s next?

Moderators: Master Students Committee 20/21

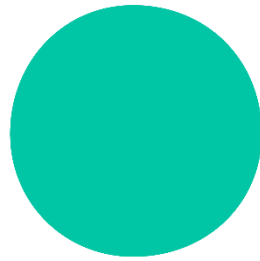
Guests:

PhD students: Eunice Paisana and Rui Rodrigues

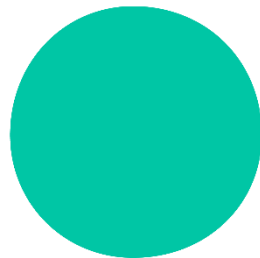
Postdoctoral researcher: Isaura Martins

Director of Studies: Domingos Henrique

Training Manager: Filipa Nunes



Research Activity



The mission of *Instituto de Medicina Molecular João Lobo Antunes* is to foster basic, clinical and translational biomedical research with the aim of contributing to a better understanding of disease mechanisms, developing novel predictive tests, improving diagnostics tools and developing new therapeutic approaches.

Research Labs:

Claus Azzalin Lab
João Barata Lab
Gonçalo Bernardes Lab
Maria Carmo-Fonseca Lab
Sérgio de Almeida Lab
Mamede de Carvalho Lab
Miguel Castanho Lab
Luís Costa Lab
Sérgio Dias Lab
Joaquim Ferreira Lab
José Ferro Lab
Luísa Figueiredo Lab
Paulo Filipe Lab
João Eurico da Fonseca Lab
Cláudio Franco Lab
Edgar Gomes Lab
Luís Graça Lab
João Lacerda Lab
Luísa Lopes Lab
Nuno Morais Lab
Vanessa Morais Lab
Maria Mota Lab
Joana Neves Lab
Miguel Prudêncio Lab
Mário Ramirez Lab
Miguel Remondes Lab
Nuno Santos Lab
Leonor Saúde Lab
Ana Sebastião Lab
Bruno Silva-Santos Lab
Pedro Simas Lab
Ana Espada de Sousa Lab
Marc Veldhoen Lab
Pedro Sousa-Victor Lab

Claus Azzalin Lab

Head of Laboratory: Claus Maria Azzalin, PhD, Group Leader

Team

Ana Beatriz Domingues Silva	Master Degree	PhD Student (Started April)
Bruno Adriano de Sousa Silva	PhD	Senior Postdoctoral Researcher
Joana Cristina Pedro Rodrigues	PhD	Postdoctoral Researcher
João Pedro Abreu Pessoa	PhD	Postdoctoral Researcher
Mariana Isabel Tavares Barroso	University Degree	Lab Technician (Started February)
Patrícia Alexandra Lona Abreu	Master Degree	PhD Student
Sara Barros Salgado	University Degree	MSc Student
Valentina Riva	PhD	Postdoctoral Researcher

Graphical Abstract

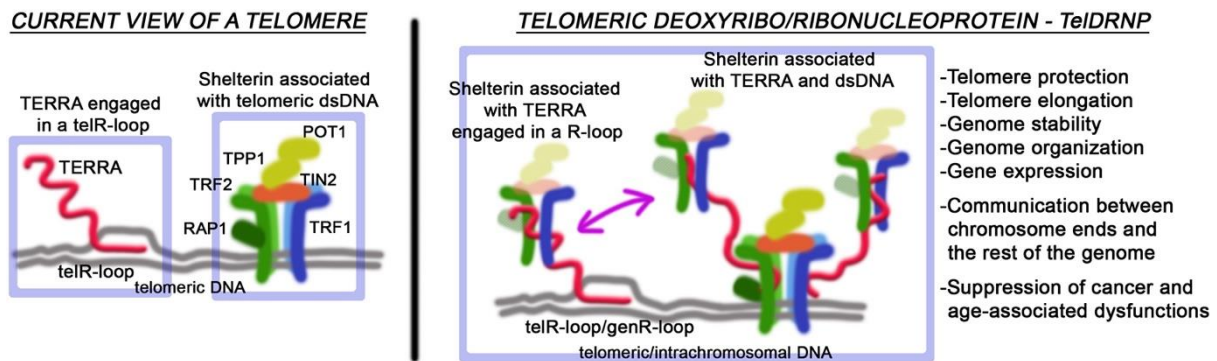


Image caption: Schematic representation of different views of telomeric chromatin organization. On the right, the working model of our lab is depicted; we propose that telomeres are dynamic DNA/RNA/particles - telomeric deoxyribo/ribonucleoproteins or telDRNPs – forming not only through protein/dsDNA interactions as in the current view (left), but also through multilayered RNA/protein and RNA/DNA interactions.

Lab Interests

Telomeres are nucleoprotein structures 'capping' the ends of linear eukaryotic chromosomes. Dysfunctional telomeres cause severe chromosome instability, which unleashes cellular reactions that are common hallmarks of human diseases including cancer and premature aging. We employ molecular biology, cell biology and biochemistry to understand how telomeres execute their protective functions and how telomeric dysfunctions are mechanistically linked to pathological conditions. In particular, we study how the telomeric long noncoding RNA TERRA regulates telomere structure and functions in both normal and diseased human cells. In 2021, our research largely focused on: i) how TERRA supports telomere maintenance in human cancer cells elongating their telomeres through the so-called 'Alternative Lengthening of Telomeres' (ALT) pathway; and ii) how TERRA regulates the proper assembly of the telomeric protective cap in telomerase-positive and primary human cells.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology

Major Scientific Achievements in 2021

We developed a novel cell biological tool for the suppression of telomere transcription in ALT cells. By employing this tool, we demonstrated that TERRA transcription is a major trigger of ALT activity; this answers a longstanding question in the field. Additionally, we discovered that TERRA inhibits the binding of the telomeric proteins TRF1 and TRF2 to telomeric double stranded DNA in vitro, suggesting a novel mechanism of nucleoprotein assembly regulated by noncoding RNAs. Indeed, over-expression of TERRA in human cells leads to a release of TRF1 and TRF2 from telomeres and to telomeric defects resembling the ones caused by mild depletion of the two proteins. We are currently testing the hypothesis that TERRA mediated eviction of TRF1 and TRF2 from telomeric chromatin might be involved in the repair of damaged telomeres.

Ongoing Projects in 2021

2021/2024: Regulatory RNA – protein interactions at telomeres in healthy cells and during malignant transformation. Coordinator: Claus Azzalin. Funding Agency: “la Caixa” Foundation. Reference: HR21-00077 – TELOTRANS. Amount: 495 792,00€. Total Amount: 495 792,00€.

2021/2024: Formação e funções da partícula telomérica desoxirribo/ribonucleoproteica de mamífero em extremidades cromossómicas e além - Assembly and functions of the mammalian telomeric deoxyribo/ribonucleoprotein particle at chromosome ends and beyond. Coordinator: Claus Azzalin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-MOL/6624/2020. Amount: 249 511,56€. Total Amount: 249 511,56€.

2021/2024: Estudo de mitigadores de stress replicativo telomérico associado ao alongamento alternativo dos telómeros – a abrir caminho para terapias inovadoras contra o cancro. Coordinator: Bruno de Sousa e Silva. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/7864/2020. Amount: 249 761,57€. Total Amount: 249 761,57€.

2021/2023: LIMM THERAPEUTICS. Coordinator: Claus Azzalin. Funding Agency: European Molecular Biology Organisation. Reference: EMBO - VALENTINA RIVA. Amount: 104 000,00€. Total Amount: 104 000,00€.

2020/2021: Tessellate Bio. Coordinator: Claus Azzalin. Funding Agency: Tessellate Bio. Reference: Tessellate Bio. Amount: 123 600,00€. Total Amount: 123 600,00€.

2018/2021: Alongamento dos telómeros mediado por TERRA e por telomerase: o desvendar de novas vias moleculares para o desenvolvimento de inovadoras abordagens terapêuticas contra o cancro. Coordinator: Claus Azzalin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-MOL/29352/2017. Amount: 239 789,17€. Total Amount: 239 789,17€.

2018/2021: Mecanismos de recombinação telomérica mediada por R-loops na via de alongamento alternativo de telómeros com vista ao desenvolvimento de novas terapias contra o cancro. Coordinator: Bruno de Sousa e Silva. Funding Agency: Fundação para a Ciência e a tecnologia. Reference: PTDC/MED-ONC/28282/2017. Amount: 239 854,03€. Total Amount: 239 854,03€.

2017/2021: TERRA and telomere transcription: towards therapies for healthy aging. Coordinator: Claus Azzalin. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG 3576. Amount: 200 000,00€. Total Amount: 200 000,00€.

2016/2021: TERRA and telomere transcription at the crossroads of cancer and aging. Coordinator: Claus Azzalin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01269/2015. Amount: 50 000,00€. Total Amount: 50 000,00€.

Scientific Impact

Academic Collaborations

Alexander Leitner, Department of Biology, Institute of Molecular Systems Biology, ETH Zurich

Anabelle Decottignies, Genetic and Epigenetic Alterations of Genomes, de Duve Institute, Université catholique de Louvain (UCLouvain)

Jack Griffith, Lineberger Comprehensive Cancer Center and Departments of Microbiology and Immunology, and Biochemistry and Biophysics, University of North Carolina at Chapel Hill

Jérôme Déjardin, Institute of Human Genetics, UMR 9002 CNRS and Université de Montpellier,

Maria Isabel Nogueira Cano, Department of Chemical and Biological Sciences, Biosciences Institute, São Paulo State University, UNESP

Saverio Brogna, School of Biosciences and Birmingham Centre of Genome Biology (BCGB), University of Birmingham

Sérgio de Almeida, Instituto de Medicina Molecular João Lobo Antunes

Silvia Bione, Institute of Molecular Genetics Luigi Luca Cavalli Sforza, National Research Council, Computational Biology Unit, Pavia, Italy

Selected Publications

Silva B, Pentz R, Figueira AM, Arora R, Lee YW, Hodson C, Wischnewski H, Deans AJ, Azzalin CM (2019). [FANCM limits ALT activity by restricting telomeric replication stress induced by deregulated BLM and R-loops](#). **Nature Communications** 10: e2253.

Relevance of the publication: We discovered that the human ATPase/translocase FANCM alleviates replication stress at ALT telomeres and ALT by counteracting aberrant R-loop accumulation and BLM activity. Also, depletion of FANCM leads to rapid and selective killing of ALT cells.

Lee YW, Arora R, Wischnewski H, Azzalin CM (2018). [TRF1 participates in chromosome end protection by averting TRF2-dependent telomeric R-loops](#). **Nature Structural & Molecular Biology** 25(2):147-153.

Relevance of the publication: We reported that TRF1 and TRF2 physically bind to TERRA and that TRF2 induces TERRA invasion of telomeric dsDNA, thus promoting telR-loop formation independently of ongoing transcription. TRF1 offsets TRF2-associated stimulation of telR-loop formation, thus safeguarding telomere integrity.

Moravec M, Wischnewski H, Bah A, Hu Y, Liu N, Lafranchi L, King MC, Azzalin CM (2016). [TERRA promotes telomerase-mediated telomere elongation in *Schizosaccharomyces pombe*](#). **EMBO Reports** 17(7):999-1012.

Relevance of the publication: We discovered that telomere shortening induces TERRA transcription in fission yeast. We also showed that TERRA recruits telomerase to telomeres thereby supporting telomere elongation.

Arora R, Lee YW, Wischnewski H, Brun CM, Schwarz T, Azzalin CM (2014). [RNaseH1 regulates TERRA-telomeric DNA hybrids and telomere maintenance in ALT tumour cells](#). **Nature Communications** 5: e5220.

Relevance of the publication: We discovered that human ALT telomeres produce elevated amounts of TERRA and are enriched in telR-loops. The endoribonuclease RNaseH1 binds to ALT telomeres and its inactivation leads to excessive telomeric replication stress and telomere instability specifically in ALT cells.

Azzalin CM, Reichenback P, Khoriauli L, Giilotto E, Lingner J (2007). [Telomeric Repeat Containing RNA and RNA surveillance factors at mammalian chromosome ends](#). **Science** 318(5851):798-801.

Relevance of the publication: We discovered that, contrarily to a longstanding dogma, mammalian telomeres are transcribed into the long noncoding RNA TERRA. TERRA associates with telomeric chromatin and this association is counteracted by RNA decay factors, which bind to human telomeres and support telomere stability.

2021 Publications in Peer-Reviewed Journals

De S, Edwards DM, Dwivedi V, Wang J, Varsally W, Dixon HL, Singh AK, Owuamalam PO, Wright MT, Summers RP, Hossain MN, Price EM, Wojewodzic MW, Falciani F, Hodges NJ, Saponaro M, Tanaka K, Azzalin CM, Baumann P, Hebenstreit D, Brogna S. (2021). [Genome-wide chromosomal association of Upf1 is linked to Pol II transcription in *Schizosaccharomyces pombe*](#). **Nucleic Acids Research** (Published online – December 20th 2021)

Morea EGO, Vasconcelos EJR, Alves CD, Giorgio S, Myler PJ, Langoni H, Azzalin CM, Cano MIN (2021). [Exploring TERRA during *Leishmania* major developmental cycle and continuous in vitro passages](#). **International Journal of Biological Macromolecules** 174:573-586

Silva B, Arora R, Bione S, Azzalin CM (2021). [TERRA transcription destabilizes telomere integrity to initiate break-induced replication in human ALT cells](#). **Nature Communications** 12:3760.

Viceconte N, Lorient A, Abreu PL, Scheibe M, Sola AF, Butter F, De Smet C, Azzalin CM, Arnoult N, Decottignies A (2021). [PAR-TERRA is the main contributor to telomeric repeat-containing RNA transcripts in normal and cancer mouse cells](#). **RNA** 27(1):106-121.

Pre-Print Publications

Sabino JC, Almeida MR, Abreu PL, Ferreira AM, Domingues MM, Santos NC, Azzalin CM, Grosso AR, de Almeida SF (2021). Epigenetic reprogramming by TET enzymes impacts co-transcriptional R-loops. bioRxiv. <https://doi.org/10.1101/2021.04.26.441414>

Invited Lectures and Seminars

Azzalin CM. The long noncoding RNA TERRA destabilizes telomere integrity in a subset of cancer cells to support telomere elongation and immortality. International Course “The Non-Coding Genome” 10th edition (virtual meeting). Institute Curie, Paris, France, February 3rd- February 10th, 2021.

Communications

Abreu PL, Lee YW, Azzalin CM. In vitro analysis of the physical interactions of TRF2 with the long noncoding RNA TERRA. Telomeres & Telomerase. Virtual meeting. December 14-17th 2021. Poster presentation. International conference.

Rodrigues J, Alfieri R, Bione S, Azzalin CM. The human telomeric transcriptome. Telomeres & Telomerase. Virtual meeting. December 14-17th 2021. Poster presentation. International conference.

Silva B, Arora R, Azzalin CM. TERRA transcription induces telomere loss in a Mus81-dependent manner in Alternative Lengthening of Telomeres cancer cells. Telomeres & Telomerase. Virtual meeting. December 14-17th 2021. Oral communication. International conference.

Organization of Conferences

Azzalin CM. Co-organizer. EMBO workshop ‘Telomere function and evolution in health and disease’, Tróia, Portugal, planned for 26th September – 1st October 2022.

Networks & Research Infrastructures

Azzalin CM. RiboMed. Co-PI. GA No. 857119 from H2020-WIDESPREAD-2018-2020.

Prizes & Honors in 2021

Azzalin CM is an invited referee for the journals: Nucleic Acid Research, Nature, Nature Structural and Molecular Biology, Nature Cell Biology, EMBO Journal, EMBO Reports; and the funding agencies: Cancer Research UK, EMBO (EMBO long term-fellowships).

Advanced Teaching

Azzalin CM. Lecture. Telomeres and Telomerase: from the discovery to the clinics. Mestrado Integrado em Medicina, 1^o ano, Módulo Biologia Molecular, Celular e do Desenvolvimento Humano e Genética, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Lecture recorded on November 2, 2021.

Azzalin CM. Lecture and practical course. FANCM functions in ALT cells. Curso livre experimental Introdução à investigação científica em biologia molecular da célula (unidade curricular optativa), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 13-17, 2021.

Azzalin CM, Silva B. Lecture. Telomeres and telomeric RNA. Lisbon BioMed PhD program, Towards a Creative and Critical Mind training module. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 29, 2021.

MSc Theses

Miguel Filipe Martins Louro Alves, 18/01/2021, TERRA Transcription Profiles in Human Cancer Cells, Instituto Superior Técnico. Supervisor: Claus M. Azzalin. Co-supervisor: Cláudia Silva. <https://fenix.tecnico.ulisboa.pt/departamentos/deec/dissertacao/846778572212732>

Beatriz Pedrosa Moleirinho, 12/01/2021, Novel Regulators of Telomerase-Independent Telomere Elongation in ALT Cancer Cells, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Claus M. Azzalin. Co-Supervisor: Rita Zilhão. <http://hdl.handle.net/10451/47971>

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Precision oncology company focused on telomere maintenance as a target, TessellateBio (Naarden, Netherlands; Azzalin CM is a co-founder and member of the Board of Directors), Contract Research

Intellectual Property Rights in 2021

Instituto de Medicina Molecular João Lobo Antunes, Children's Medical Research Institute. Azzalin CM, Pickett HA, Sobinoff AP. Treatment of ALT cancers. GB1907518.3 (28.05.2019) and AU2019901766 (24.05.2019). International application reference: PCT/PT2020/050021; National phases references (28.11.2021): European patent app.: EP2020754058; Chinese patent app.: CN1907518.3; Canadian patent app.: CA3141464; South Korea patent app.: KR1020217042352; United States patent app.: US17612547.

João Barata Lab

Head of Laboratory: João Pedro Taborda Barata, PhD, Group Leader and Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Patrícia Cebola Cachucho	Master Degree	PhD Student
Ana Rita Cascão Rodrigues	PhD	Senior Postdoctoral Researcher
Ana Rita Freitas Martins de Matos Fragoso	PhD	Staff Scientist
Bruno António Caetano Cardoso	PhD	Senior Postdoctoral Researcher (Left August)
Carlos Manuel Tavares da Custódia	Master Degree	PhD Student
Clara Lúcia Gonçalves Dias	PhD	Visiting Researcher (Started December)
Cláudia Maria Coelho de Faria	MD/PhD	Clinical Researcher
Daniel Filipe Silva Ribeiro	PhD	Postdoctoral Researcher (Left August)
Diana Filipa Pereira Vaz	Master Degree	Lab Manager (Left August)
Eunice Ribeiro João Silva Paisana	Master degree	PhD Student
João Luís Aguiar Martins Neto	PhD	Postdoctoral Researcher (Left August)
João Paulo Rita Fontela	University Degree	MSc Student (Started July)
Juliana Ronchi Corrêa	Master Degree	PhD Student (Started January. Left December)
Luís Pedro Dias Bernardo Maricoto Monteiro	Master Degree	PhD Student (Left July)
Mafalda dos Santos Dias Duque	Master Degree	PhD Student (Started January)
Marta Sofia Barbosa Fernandes	Master Degree	PhD Student
Patrícia Alexandra Martins Amaral	University Degree	MSc Student (Started July)
Rita Alexandra Nunes Rodrigues	High School Diploma	Trainee (Left December)
Sara Alexandra Barros da Gama	University Degree	MSc Student (Started July)
Susana Luisa dos Santos Costa Constantino Moleirinho	PhD	Senior Postdoctoral Researcher
Tatiana Vanessa Fernandes Araújo	University Degree	MSc Student

Lab Interests

Cancer Biology, Signal Transduction, Cellular and Molecular Biology, Rational Targeted Therapies, Leukemias (especially acute lymphoblastic leukemia), Brain Tumors.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Cancer biology

Major Scientific Achievements in 2021

In 2021 we have published two major findings. First, we showed that *IL7R* mutational activation can not only be a driver of B-cell acute lymphoblastic leukemia (i.e. an active player in promoting the disease) but actually be, in some cases, the initiating event of this malignancy (i.e. the event that triggers the whole process leading to leukemia development). We further demonstrated that B-cell leukemias arising from *IL7R* mutational activation can be treated with PI3K or sphingosine kinase pharmacological inhibitors (Almeida et al, Nature communications 2021). Second, we found that high levels of IL7R, even without any gain of function mutations, can be sufficient to drive the development of T-cell acute lymphoblastic leukemia and that several inhibitors of IL7R-mediated signaling can be used for therapeutic purposes to target the leukemic cells (Silva et al, Blood 2021). The quality of this work was highlighted by the 2021 Basic Research Pfizer Award from Sociedade de Ciências Médicas de Lisboa.

We were awarded a “la Caixa” Health Research grant to explore the potential oncogenic role of IL7R beyond the hematopoietic system, in lung cancer development and resistance to immune checkpoint inhibitors (a multidisciplinary project developed in partnership with groups in CNIO and Hospital 12 de October in Madrid, Spain).

Ongoing Projects in 2021

2021/2024: IL7R in lung cancer development, metastasis and resistance to immune checkpoint inhibitor therapy. Coordinator: João Barata. Funding Agency: “la Caixa” Foundation. Reference: HR18-00104, “ETERNITY”-“ENHANCING TISSUE RESIDENT. Amount: 489 158,00€. Total Amount: 489 158,00€.

2020/2021: Antibody-based IL-7R targeted therapies. Coordinator: João Barata. Funding Agency: European Commission. Reference: ERC-PoC-862545 - IL7RsignaTHER. Amount: 150 000,00€. Total Amount: 150 000,00€.

2018/2022: Descodificar a interação entre CK2, PI3K, e o relógio molecular circadiano para melhor compreender a biologia e maximizar respostas terapêuticas dirigidas contra leucemia de células T. Coordinator: João Barata. Funding Agency: Fundação para a Ciência e a Tecnologia. Amount: 239 640,12€. Total Amount: 239 640,12€.

2018/2021: Uso da genómica para a identificação de novas terapias alvo nas metástases cerebrais. Coordinator: Cláudia Faria. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/32222/2017. Amount: 238 740,32€. Total Amount: 238 740,32€.

2015/2021: IL-7/IL-7R signaling networks in health and malignancy. Coordinator: João Barata. Funding Agency: European Commission. Reference: ERC CoG-648455 - IL7sigNETure. Total Amount: 1 988 125,00€.

Other Projects

2021/2023: Liga Portuguesa Contra o Cancro. Coordinator: Ângela Afonso. Funding Agency: Liga Portuguesa contra o Cancro. Reference: LPCC – CFARIA. Amount: 20 060,00€. Total Coordinator: 20 060,00€.

Scientific Impact

Academic Collaborations

Ana Rita Grosso, Dept Ciências Vida - Universidade Nova de Lisboa

Ben Seddon, UCL Institute of Immunity & Transplantation

Jan Cools, KU Leuven

Jules Meijerink, Princess Maxima Ctr Pediat Oncol

Charles Mullighan, Dept Pathol, Hematol Malignancies Program St

J Andres Yunes, Boldrini Childrens Ctr

Nigel Pyne, Strathclyde Inst Pharm & Biomed Sci SIPBS

Vasco Barreto, CEDOC

David Langenau, Massachusetts Gen Res Inst

Selected Publications

Silva A, Almeida ARM, Cachucho A, Neto JL, Demeyer S, de Matos M, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT (2021). [Overexpression of wild-type IL-7R \$\alpha\$ promotes T-cell acute lymphoblastic leukemia/lymphoma](#). **Blood** 138(12):1040-1052.

Relevance of the publication: Published by our lab in the top journal in hematology, this is the first demonstration, that high levels of IL7R can lead to the development of T-cell leukemia, significantly expanding the understanding of how this cytokine receptor (which is essential for normal lymphoid development) can have an oncogenic role.

Barata JT, Durum SK, Seddon B (2019). [Flip the coin: IL-7 and IL-7R in health and disease](#). **Nature Immunology** 20: 1584–1593.

Relevance of the publication: This is a key review, commissioned by Nature Immunology to João T. Barata, on the multifaceted roles of interleukin 7 (IL-7) and its receptor (IL-7R) on the immune system, and how this critical axis is subverted in chronic inflammatory and autoimmune diseases and in cancer.

Zenatti PP, Ribeiro, Li, Zuurbier L, Silva MC, Paganin M, Tritapoe J, Hixon JA, Silveira AB, Cardoso BA, Sarmiento LM, Correia N, Toribio ML, Kobarg J, Horstmann M, Pieters R, Brandalise SR, Ferrando AA, Meijerink JP, Durum SK, Yunes JA, Barata JT (2011). [Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia](#). **Nature Genetics** 43:932-939

Relevance of the publication: We were the first to demonstrate, in this study, that the receptor for interleukin 7 (IL7R) is an oncogene. Patients with T-cell acute lymphoblastic leukemia often display gain-of-function mutations that lead to constitutive signaling and ensuing cellular transformation and in vivo tumor growth.

Henriques CM, Rino J, Nibbs RJ, Graham GG, Barata JT (2010). [IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R alpha in T cells](#). **Blood** 115:2724-2731.

Relevance of the publication: It was known that IL-7 leads to the transcriptional downregulation of its own receptor (IL7R). In this work, we showed that IL-7 also downregulates the surface expression of IL7R, with rapid receptor internalization and subsequent protein degradation, with kinetics that precede the impact on transcription. We also demonstrated that IL-7-mediated internalization of IL7R is actually

required for maximal IL-7-mediated signaling. In other words, we demonstrated that internalization of IL7R is essential for both optimal IL-7-mediated signaling and also for subsequent signaling shut down.

Silva A, Yunes JA, Cardoso BA, Martins LR, Jotta PY, Abecasis M, Nowill AE, Leslie NR, Cardoso AA, Barata JT (2008). [PTEN Posttranslational Inactivation and Hyperactivation of the PI3K/Akt Pathway Sustain Primary T Cell Leukemia Viability](#). **Journal of Clinical Investigation** 118:3762-3774.

Relevance of the publication: For many years, tumor suppressor genes were thought to be inactivated strictly by (epi)genetic mechanisms. This paradigm, supported by the Knudson two-hit hypothesis, was challenged by the realization that inactivation of both alleles is not required for the loss of tumor preventing activity of some tumor suppressors. Our work contributed to the demonstration that loss of function of the tumor suppressor PTEN can occur at a strictly post-translational level, without genetic deletion or mutation. We found that, in T-cell leukemia cells, PTEN is inactivated by phosphorylation and/or oxidation. Pharmacological reversion of these mechanisms promotes PTEN reactivation and elimination of leukemia cells.

2021 Publications in Peer-Reviewed Journals

Almeida ARM, Neto JL, Cachucho A, Euzébio M, Meng X, Kim R, Fernandes MB, Raposo B, Oliveira ML, Ribeiro D, Fragoso R, Zenatti PP, Soares T, de Matos MR, Corrêa JR, Duque M, Roberts KG, Gu Z, Qu C, Pereira C, Pyne S, Pyne NJ, Barreto VM, Bernard-Pierrot I, Clappier E, Mullighan CG, Grosso AR, Yunes JA, Barata JT (2021). [Interleukin-7 receptor \$\alpha\$ mutational activation can initiate precursor B-cell acute lymphoblastic leukemia](#). **Nature Communications** 12(1):7268.

Baroni LV, Sundaresan L, Heled A, Coltin H, Pajtler KW, Lin T, Merchant TE, McLendon R, Faria C, Buntine M, White CL, Pfister SM, Gilbert MR, Armstrong TS, Bouffet E, Kumar S, Taylor MD, Aldape KD, Ellison DW, Gottardo NG, Kool M, Korshunov A, Hansford JR, Ramaswamy V (2021). [Ultra high-risk PFA ependymoma is characterized by loss of chromosome 6q](#). **Neuro-Oncology** 23(8):1360-1370.

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, de Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu YH, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Barbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL (2021). [Allosteric Antagonist Modulation of TRPV2 by Piperlongumine Impairs Glioblastoma Progression](#). **ACS Central Science** 7(5): 868-881.

Donovan LK, Delaidelli A, Joseph SK, Bielamowicz K, Fousek K, Holgado BL, Manno A, Srikanthan D, Gad AZ, Van Ommeren R, Przelicki D, Richman C, Ramaswamy V, Daniels C, Pallota JG, Douglas T, Joynt ACM, Haapasalo J, Nor C, Vladioiu MC, Kuzan-Fischer CM, Garzia L, Mack SC, Varadharajan S, Baker ML, Hendrikse L, Ly M, Kharas K, Balin P, Wu XC, Qin L, Huang N, Stucklin AG, Morrissy AS, Cavalli FMG, Luu B, Suarez R, De Antonellis P, Michealraj A, Rastan A, Hegde M, Komosa M, Sirbu O, Kumar SA, Abdullaev Z, Faria CC, Yip S, Hukin J, Tabori U, Hawkins C, Aldape K, Daugaard M, Maris JM, Sorensen PH, Ahmed N, Taylor MD (2021). [Locoregional delivery of CAR T cells to the cerebrospinal fluid for treatment of metastatic medulloblastoma and ependymoma](#). **Nature Medicine** 26: 720-731.

Garcia EG, Veloso A, Oliveira ML, Allen JR, Loontjens S, Brunson D, Do D, Yan C, Morris R, Iyer S, Garcia SP, Iftimia N, Van Looche W, Matthijssens F, McCarthy K, Barata JT, Speleman F, Taghon T, Gutierrez A, Van Vlierberghe P, Haas W, Blackburn JS, Langenau DM (2021). [PRL3 enhances T-cell acute lymphoblastic leukemia growth through suppressing T-cell signaling pathways and apoptosis](#). **Leukemia** 35(3):679-690.

Kumar R, Smith KS, Deng M, Terhune C, Robinson GW, Orr BA, Liu APY, Lin T, Billups CA, Chintagumpala M, Bowers DC, Hassall TE, Hansford JR, Khuong-Quang DA, Crawford JR, Bendel AE, Gururangan S, Schroeder K, Bouffet E, Bartels U, Fisher MJ, Cohn R, Partap S, Kellie SJ, McCowage G, Paulino AC, Rutkowski S, Fleischhack G, Dhall G, Klesse LJ, Leary S, Nazarian J, Kool M, Wesseling P, Ryzhova M, Zheludkova O, Golanov AV, McLendon RE, Packer RJ, Dunham C, Hukin J, Fouladi M, Faria CC, Pimentel J, Walter AW, Jabado N, Cho YJ, Perreault S, Croul SE, Zapotocky M, Hawkins C, Tabori U, Taylor MD, Pfister SM, Klimo P, Boop FA, Ellison DW, Merchant TE, Onar-Thomas A, Korshunov A, Jones DTW, Gajjar A, Ramaswamy V, Northcott PA (2021). [Clinical Outcomes and Patient-Matched Molecular Composition of Relapsed Medulloblastoma](#). **Journal of Clinical Oncology** 39(7):807-821.

Martins EP, Gonçalves CS, Pojo M, Carvalho R, Ribeiro AS, Miranda-Gonçalves V, Taipa R, Pardal F, Pinto AA, Custódia C, Faria CC, Baltazar F, Sousa N, Paredes J, Costa BM (2021). [Cadherin-3 is a novel oncogenic biomarker with prognostic value in glioblastoma](#). **Molecular Oncology**.

Noronha C, Ribeiro AS, Taipa R, Castro DS, Reis J, Faria C, Paredes J (2021). [Cadherin Expression and EMT: A Focus on Gliomas](#). **Biomedicines** 9(10):1328.

Rocha S, Basto AP, Ijsselsteijn ME, Teles SP, Azevedo MM, Gonçalves G, Gullo I, Almeida GM, Maqueda JJ, Oliveira MI, Carneiro F, Barata JT, Graça L, de Miranda NFCC, Carvalho J, Oliveira C (2021). [Immunophenotype of Gastric Tumors Unveils a Pleiotropic Role of Regulatory T Cells in Tumor Development](#). **Cancers (Basel)** 13(3):241

Silva A, Almeida ARM, Cachucho A, Neto JL, Demeyer S, de Matos M, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT (2021). [Overexpression of wild-type IL-7R \$\alpha\$ promotes T-cell acute lymphoblastic leukemia/lymphoma](#). **Blood** 138(12):1040-1052.

Skowron P, Farooq H, Cavalli FMG, Morrissy AS, Ly M, Hendrikse LD, Wang EY, Djambazian H, Zhu H, Mungall KL, Trinh QM, Zheng TN, Dai SZ, Stucklin ASG, Vladioiu MC, Fong V, Holgado BL, Nor C, Wu XC, Abd-Rabbo D, Berube P, Wang YC, Luu B, Suarez RA, Rastan A, Gillmor AH, Lee JJY, Zhang XY, Daniels C, Dirks P, Malkin D, Bouffet E, Tabori U, Loukides J, Doz FP, Bourdeaut F, Delattre OO, Masliah-Planchon J, Ayrault O, Kim SK, Meyronet D, Grajkowska WA, Carlotti CG, de Torres C, Mora J, Eberhart CG, Van Meir EG, Kumabe T, French PJ, Kros JM, Jabado N, Lach B, Pollack IF, Hamilton RL, Rao AAN, Giannini C, Olson JM, Bogner L, Klekner A, Zitterbart K, Phillips JJ, Thompson RC, Cooper MK, Rubin JB, Liau LM, Garami M, Hauser P, Li KKW, Ng HK, Poon WS, Gillespie GY, Chan JA, Jung S, McLendon RE, Thompson EM, Zagzag D, Vibhakar R, Ra YS, Garre ML, Schuller U, Shofuda T, Faria CC, Lopez-Aguilar E, Zadeh G, Hui CC, Ramaswamy V, Bailey SD, Jones SJ, Mungall AJ, Moore RA, Calarco JA, Stein LD, Bader GD, Reimand J, Ragoussis

J, Weiss WA, Marra MA, Suzuki H, Taylor MD (2021). [The transcriptional landscape of Shh medulloblastoma](#). **Nature Communications** 12, 1749.

Invited Lectures and Seminars

João T. Barata. “IL-7R signaling as a therapeutic target in acute lymphoblastic leukemia?”, II ASPIC-ASEICA International Meeting – Current Trends in Precision Medicine in Cancer, 14-15 October 2021 (online meeting).

João T. Barata. “Diving into the dark side of IL-7 and IL-7R and their contribution to lymphoid leukemia development”, XLVI Annual Meeting of The Portuguese Society of Immunology (SPI), 20-21 May 2021 (Online meeting).

João T. Barata. “Signal Transduction and Cancer: IL-7 and leukemia”, XI Jornadas Nacionais de Ciências Biomédicas [XI National Meeting of Biomedical Sciences], 15 May 2021 (Online meeting).

Cláudia Faria. “Extended Endonasal Approaches”, Course – “Transsphenoidal endoscopic approach with 3D printed cranial models”, AHED – Advanced Health Education, Hospital Cuf Descobertas, Lisbon, Portugal, March 6th, 2021.

Cláudia Faria, “Identificação de alvos terapêuticos nos tumores cerebrais”, A Universidade de Lisboa à Procura de Respostas para o Cancro Webinar Rede Saúde da Universidade de Lisboa, Lisbon, Portugal, June 30th, 2021.

Cláudia Faria, “Neurocirurgiões-Investigadores: importância para os serviços hospitalares e para a academia”, 36º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia (SPNC), Porto, Portugal, September 9-11, 2021.

Cláudia Faria, “Médicos-cientistas: importância para os hospitais e para a academia”, 8º Congresso do Internato Médico Cuf, Hospital Cuf Descobertas, Lisbon, Portugal, October 8th, 2021.

Cláudia Faria, “Terapias moleculares dirigidas para o tratamento das metástases cerebrais”, A Universidade de Lisboa à Procura de Respostas para o Cancro, Webinar Rede Saúde da Universidade de Lisboa, Lisbon, Portugal, October 22nd, 2021.

Cláudia Faria, “The clinical implications of medulloblastoma molecular subtypes”, Webinar da Sociedade Espanhola de Neurocirurgia Pediátrica, Online, April 23rd, 2021.

Cláudia Faria, “BTG Young Investigators, training and education group & neurooncology curriculum”, 2nd Annual Meeting of the European Society of Pediatric Oncology, Virtual, April 30th, 2021.

Communications

Communications in National Conferences:

Cachucho A, Runchi J, Araújo T, Fernandes MB, Euzébio M, Almeida A, Yunes A, Barata JT. Characterizing the risk for IL-7R-mediated malignancy in different stages of hematopoietic development. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7th, 2021. Oral Presentation; National Conference.

Carlos Custódia, Rita Cascão, Eunice Paisana, Pedro Ruivo, José Pimentel, Rafael Roque, João T Barata and Cláudia C. Faria. Targeting the CCL2/CCR2 axis in metastatic medulloblastoma, XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7th, 2021. Oral Presentation; National Conference.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, Tânia Carvalho, Pedro Ruivo, Pedro Pereira, Rafael Roque, José Pimentel, Marc Remke, José Miguéns, João T. Barata, Cláudia C. Faria. Ubiquitin conjugating enzymes promote leptomeningeal dissemination and decrease survival in brain metastatic disease. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7th, 2021. Oral Presentation; National Conference.

Fernandes MB, Melão A, Almeida A, Cachucho A, Pyne S, Pyne NJ, Barata JT. Sphingosine Kinases are essential positive modulators of IL7/IL-7R signaling in Acute Lymphoblastic Leukemia. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7th, 2021. Oral Communication; National Conference.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, Tânia Carvalho, Pedro Ruivo, Pedro Pereira, Rafael Roque, José Pimentel, Marc Remke, José Miguéns, João T. Barata, Cláudia C. Faria. Ubiquitin Conjugating Enzymes promote aggressive metastatic brain disease and decrease patients' survival. 27th Porto Cancer Meeting – Stemness and metastasis: advances in research and clinical translation, Virtual, Porto, Portugal, May 20-21th, 2021. Oral Presentation; National Conference.

Rita Cascão, Eunice Paisana, Daniel Picard, Nuno Saraiva-Agostinho, Marc Remke, João T. Barata and Claudia C. Faria. Targeting therapeutic resistance in glioblastoma. IMM Postdoc Day, Virtual Meeting, Lisboa, Portugal, May 27th, 2021. Oral Presentation; National Conference.

Communications in International Conferences:

A. Almeida, J.L. Neto, A. Cachucho, M. Euzébio, X. Meng, R. Kim, M.B. Fernandes, B. Raposo, M.L. Oliveira, D. Ribeiro, R. Fragoso, P.P. Zenatti, T. Soares, M.R. de Matos, J. Ronchi Corrêa, M. Duque, K.G. Roberts, Z. Gu, C. Qu, S. Pyne, N.J. Pyne, V.M. Barreto, I. Bernard-Pierrot, E. Clappier, C.G. Mullighan, A.R. Grosso, J.A. Yunes, J.T. Barata (2021). *IL7R* gain-of-function mutation is sufficient to initiate B-cell acute lymphoblastic leukemia *in vivo* with features of PAX5 P80R and Ph-like ALL. European School of Hematology (ESH) Translational Research E-Conference ACUTE LYMPHOBLASTIC LEUKAEMIA, 7-9 May 2021. Oral Presentation; International Conference.

Almeida, J.L. Neto, A. Cachucho, M. Euzébio, X. Meng, R. Kim, M.B. Fernandes, B. Raposo, M.L. Oliveira, D. Ribeiro, R. Fragoso, P.P. Zenatti, T. Soares, M.R. de Matos, J. Ronchi Corrêa, M. Duque, K.G. Roberts, Z. Gu, C. Qu, S. Pyne, N.J. Pyne, V.M. Barreto, I. Bernard-Pierrot, E. Clappier, C.G. Mullighan, A.R. Grosso, J.A. Yunes, J.T. Barata (2021). IL7R mutational activation can initiate Ph- Like and Pax5 P80R precursor B-cell acute lymphoblastic leukemia. EHA 2021 - Online meeting of the European Hematology Association, 9-17 June 2021. Oral Presentation; International Conference.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, Pedro Pereira, Rafael Roque, José Pimentel, Marc Remke, José Miguéns, João T. Barata, Cláudia C. Faria. The Role of Ubiquitin Conjugating Enzymes in Brain Metastases. EACR 2021 Congress, Innovative Cancer Science: Better Outcomes through Research, Virtual Conference, June 9-12th, 2021. Poster Presentation; International Conference.

L.M. Sarmento, S.G. Pereira, F. Costa, A. Monteiro, J. Caldas, P. Ribeiro, J.T. Barata (2021). Checkpoint kinase 1 is overexpressed, by post-transcriptional regulation, in immature and monoblastic / monocytic acute myeloid leukemia. EHA 2021 - Online meeting of the European Hematology Association, 9-17 June 2021. Poster Presentation; International Conference.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, David Pauck, Tânia Carvalho, Pedro Ruivo, Pedro Pereira, Rafael Roque, José Pimentel, Marc Remke, José Miguéns, João T. Barata, Cláudia C. Faria. Ubiquitin Conjugating Enzymes promote leptomeningeal dissemination and decrease survival in patients with brain metastatic disease. Third Annual Conference on Brain Metastases, Virtual Conference, Toronto, Canada, August 19-20th, 2021. Poster Presentation; International Conference.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, Tânia Carvalho, Pedro Ruivo, Pedro Pereira, Rafael Roque, José Pimentel, Marc Remke, José Miguéns, João T. Barata and Cláudia C. Faria. Ubiquitin Conjugating Enzymes promote leptomeningeal dissemination and decrease survival in patients with brain metastatic disease. SNO 3rd Annual Conference on Brain Metastases (virtual), August 19-21, 2021. Poster Presentation; International Conference.

Cláudia Faria, “Monitoring the patient with severe traumatic brain injury”, European Association of Neurological Societies (EANS) Training Course, Functional Neurosurgery and Head Injury, Thessaloniki, Greece, August 22-25, 2021. Oral Presentation; International Conference.

Cláudia Faria, “Management of pediatric traumatic brain injury”, European Association of Neurological Societies (EANS) Training Course, Functional Neurosurgery and Head Injury, Thessaloniki, Greece, August 22-25, 2021. Oral Presentation; International Conference.

Cláudia Faria, “Break-out session on decompressive craniectomy”, European Association of Neurological Societies (EANS) Training Course, Functional Neurosurgery and Head Injury, Thessaloniki, Greece, August 22-25, 2021. Oral Presentation; International Conference.

Cláudia Faria, “How I do it: depressed skull fracture”, European Association of Neurological Societies (EANS) Training Course, Functional Neurosurgery and Head Injury, Thessaloniki, Greece, August 22-25, 2021. Oral Presentation; International Conference.

Cláudia Faria, “Patient-derived models of brain metastases: a tool for translational medicine”, European Association of Neurological Societies (EANS) Meeting 2021, Neurosurgery in Translation, Virtual, October 5th, 2021. Oral Presentation; International Conference.

Organization of Conferences

Cláudia Faria (co-organizer), EATRIS Summer School in Personalized Medicine, Online, June 14-18, 2021.

Cláudia Faria (co-organizer), 3rd European Combined Neuro-Oncology Course of the European Society for Pediatric, Oncology - Brain Tumour Group (SIOPE BTG), Online, June 18-19, 2021.

Cláudia Faria (co-organizer), II ASEICA-ASPIC International Meeting, Online, October 20-21, 2021.

Cláudia Faria (co-organizer), Dia da Investigação da Faculdade de Medicina da Universidade de Lisboa no âmbito do GAPIC, 10^a Edição, “Science is alive”, presencial e online, 15 de Dezembro de 2021.

Prizes & Honors in 2021

Marta B Fernandes received a merit award for the oral presentation entitled “Sphingosine Kinases are essential positive modulators of IL7/IL-7R signaling in Acute Lymphoblastic Leukemia” on the XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal. May 5-7th, 2021.

Claudia Faria received LPCC/LIONS Cancro Infantil 2021 Award - “Clinical validation of CCL2/CCR2 signaling pathway in metastatic medulloblastoma”. June 2021

João T Barata received Pfizer Award 2021 – Basic research for the publication entitled “Overexpression of wild-type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. November 18th 2021.

Advanced Teaching

R. Fragoso taught the topics “Wnt signaling pathway” and the “Notch signaling pathway” at the “Signal Transduction in Cancer” Course of the Masters in Oncobiology, Faculty of Medicine of Lisbon University, Lisbon Academic Medical Center (CAML), Lisbon, 19-20 January 2021.

Claudia Faria taught at the Course – “Transsphenoidal endoscopic approach with 3D printed cranial models” AHED – Advanced Health Education, Hospital Cuf Descobertas, March 6th, 2021 (postgraduate studies).

Claudia Faria presented the “Patient-derived xenografts of brain metastases – a tool for translational medicine”, Session bridging the gap, Programa Doutoral do CAML (Lisbon Biomed PhD Program) iMM, April 27th, 2020 (postgraduate studies).

João T. Barata taught at the “Cytokine signaling in healthy and malignant T cells”, Signalling & Techniques in Immunology Course (15 June – 6 July), Utrecht University, The Netherlands, 25 June. (via ZOOM online platform).

João T. Barata gave the lecture “Bridging – A integração da investigação básica na investigação clínica em Oncologia [Bridging – Integrating basic research into Clinical research in Oncology]”, at 3^a Edição do Curso de Investigação em Oncologia [3rd Edition of the Course on Research in Oncology], organized by Núcleo de Internos e Jovens Especialistas da SPO [Group of Interns and Young Specialists of the Portuguese Society of Oncology], 8-10 July 2021. (Online course)

Claudia Faria taught at the European Association of Neurological Societies (EANS) Training Course, Functional Neurosurgery and Head Injury, Thessaloniki, Greece, August 22-25, 2021 (postgraduate studies).

Claudia Faria taught at the “Médicos-cientistas: importância para os hospitais e para a academia”, 8^o congresso do Internato Médico Cuf, Hospital Cuf Descobertas, October 8th 2021 (postgraduate studies).

João T. Barata taught the Seminar “Signal transduction in cancer: towards precision medicine”, at Instituto de Investigação em Ciências da Vida e Saúde (ICVS), School of Health Sciences, University of Minho, Braga, Portugal, 26 October 2021.

Claudia Faria taught at the “Principles of Neurosciences – Neuroanatomy” class, Masters in Biomedical research, Faculdade de Medicina da Universidade de Lisboa, November 23rd, 2020 (postgraduate studies)

Claudia Faria taught at the PhD Advanced Course – Advances in Neuropharmaceutics, “Using Genomics for drug discovery in brain tumors – from patient samples to preclinical trials”, Faculdade de Farmácia da Universidade de Lisboa, Online, December 14th, 2021 (postgraduate studies).

MSc Theses

Brian Ringhofer, “The impact of IL-7 on metabolic reprogramming in T-cell acute lymphoblastic leukemia”, for the MSc in Biotechnology, Wien University, Austria. 25th February 2021. Supervisor: João T. Barata.

Valorization of Knowledge / Social and Economic Impact

Intellectual Property Rights in 2021

João T Barata and Rita Fragoso. PCT International Application filed on August 2021 "Genetic Construct". Ref: PCT/PT2021/050028

Science and Society in 2021

Luís Monteiro published the article “Leucemia linfoblástica aguda: rumo a um futuro mais auspicioso”, in which he explains, for a lay audience, the importance of studying IL-7-mediated signaling and its impact on metabolism for the potential treatment of acute lymphoblastic leukemia. This was published on the magazine “Saúde e Bem Estar” (number 316; May 2021).

Mafalda Duque participated in the “Job Shadowing for One Day” initiative from Núcleo de Engenharia Biológica do Instituto Superior Técnico de Lisboa. (December 2021)

Eunice Paisana participated as a volunteer in the event “Noite Europeia dos Investigadores 2021” on September 24th, a science communication event open to the whole public.

Gonçalo Bernardes Lab

Head of Laboratory: Gonçalo J. L. Bernardes, D.Phil., Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Associate Professor of Chemical Biology, University of Cambridge, UK

Team

Alexandra Isabel Freitas Rosa	PhD	Project Manager (Left February)
Ana Maria dos Santos Guerreiro	Master Degree	Project Manager
Ana Raquel Ligeiro Coelho	PhD	Postdoctoral Researcher (Started March)
Bárbara Beatriz da Costa Botelho Sousa	University Degree	PhD Student
Bruno Luís Jesus Pinto de Oliveira	PhD	Senior Postdoctoral Researcher
Carlos Diogo Labão Alpiarça Sousa de Almeida	Master Degree	PhD Student
Cláudia Filipa Martins Afonso	Master Degree	PhD Student
Cong Tang	PhD	Postdoctoral Researcher (Started May)
Eloah Latocheski	Master Degree	PhD Student (Left January)
João Daniel da Silva Seixas	PhD	Staff Scientist
Luís Miguel Afonso Ramos de Carvalho	PhD	Postdoctoral Researcher (Left September)
Maria Inês Sousa de Albuquerque	Master Degree	Project Manager (Left January)
Maria Sousa Rebelo	PhD	Postdoctoral Researcher
Marta Franco Coimbra Marques	PhD	Senior Postdoctoral Researcher
Marta Leal Bento Coelho	Master Degree	PhD Student (Started April)
Nicholas David Bossons	Master Degree	Visiting Researcher (Started September)
Pedro Miguel Saraiva Duarte Cal	PhD	Postdoctoral Researcher
Rafaela Carvalho Martins	University Degree	MSc Student
Ravikumar Govindan	PhD	Postdoctoral Researcher

Graphical Abstract

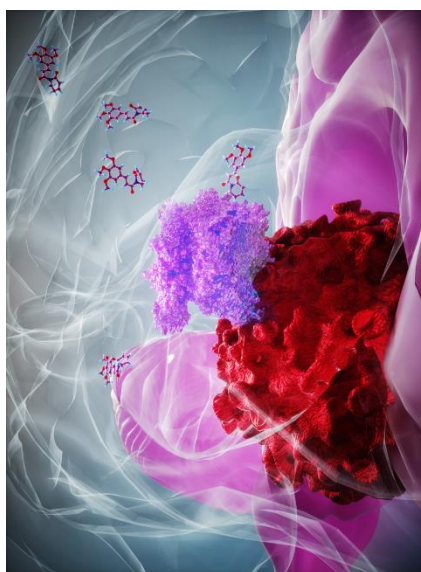


Image Caption: Allosteric antagonist modulation of TRPV2 by Piperlongumine impairs glioblastoma progression

Lab Interests

Our research uses chemical reactivity principles to develop drugs whose action is restricted to the tissue(s) where they maximise their therapeutic efficacy and reduce side-effects. Current examples of research topics we explore include:

- design new reagents for chemoselective and irreversible modification of proteins/antibodies with drugs, fluorophores, nucleic acids, or polymers to produce functional bioconjugates for imaging and drug-delivery;
- development of conceptually new bioorthogonal approaches — i.e. selective chemical reactions in cells and animals — to turn-on the activity of small-molecule drugs and antibodies/cytokines at specific tissues;
- recently we disclosed RNA-degraders — a novel class of small molecules that degrade RNA enabling, for instance, to edit and analyze RNA modifications

With a focus on translational research, we develop innovative strategies that bridge disciplines (organic and nucleic acid chemistry, chemical biology, genomics and cancer biology).

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Biotechnology and Biosystems Engineering

Major Scientific Achievements in 2021

My group's major scientific achievements in 2021 include:

- We discovered that allosteric antagonist modulation of TRPV2 by piperlongumine promotes remissions in mouse models of glioblastoma (*ACS Cent. Sci.* **2021**, 868) – these findings led me to co-found TargTex Lta, a new-company that explores targeted therapeutics to treat glioblastoma;
- We have developed an in vivo pretargeting based on cysteine-selective antibody modification with IEDDA 79iorthogonal handles for click chemistry (*Bioconjugate Chem.* **2021**, 121), one approach that we are extending to the targeting and masking of therapeutic antibodies and cytokines;
- We have demonstrated that biomolecules are subject to forces in vivo which can alter their conformation and reactivity by using microfluidics. The shear stress exposes buried residues of proteins, thereby selectively increasing the solvent accessible surface area of cysteines and altering their reactivity (*J. Am. Chem. Soc.* **2021**,16401);
- Finally, we reported RNA-degraders (*ACS Cent. Sci.* **2020**, 2196). The importance of this new tool can be likened to the development of siRNA or CRISPR/Cas13 systems. Degradation is induced by a small molecule without additional cofactors or pathways.

Ongoing Projects in 2021

2021/2024: Reversible Covalently Binding PROTACs Technology for Protein Degradation in Cancer Therapy. Coordinator: Gonçalo Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-QUI/1947/2020. Amount: 249 995,00€. Total Amount: 249 995,00€.

2021/2024: SRA - PROTERRIS - CARLOS LABÃO. Coordinator: Gonçalo Bernardes. Funding Agency: Proterris. Reference: SRA - PROTERRIS - CARLOS LABÃO. Amount: 38 160,00€. Total Amount: 38 160,00€.

2021/2023: E3-hijacking molecular glues of RNA binding protein IGF2BP1 in ovarian cancer. Coordinator: Gonçalo Bernardes. Funding Agency: European Commission. Reference: E3GLUERBP - H2020-WF-03-2020. Amount: 159 815,04€. Total Amount: 159 815,04€.

2020/2023: Ligand Directed NIR-based Theranostic Prodrugs for Prostate Cancer — ClickandTreatCancer. Coordinator: Gonçalo Bernardes. Funding Agency: European Commission. Reference: ClickToTreatCancer - GA891251- MSCA-H2020-ITN-2019. Amount: 238 356,36€. Total Amount: 3 554 499,69€.

2019/2022: Site-selective protein-modification chemistries for antibody-drug conjugates (ADCs). Coordinator: Bruno Oliveira. Funding Agency: European Commission. Reference: Twinning-SIMICA. Amount: 353 750,00€. Total Amount: 800 000,00€.

2018/2021: Entrega intracelular de fármacos usando conjugados entre pequenas células e fármacos para terapia do Cancro da Próstata. Coordinator: João Seixas. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-QUI/28764/2017. Amount: 239 960,32€. Total Amount: 239 960,32€.

2018/2021: Libertação controlada de agentes bioactivos por reacção química selectiva. Coordinator: Gonçalo Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: TzDD - LISBOA-01-0145-FEDER-028333. Amount: 238 166,90€. Total Amount: 238 166,90€.

2018/2021: Nanoparticle-Based Therapeutic Applications and Detection of Carbon Monoxide Releasing. Coordinator: Marta Marques. Funding Agency: European Commission. Reference: Twinning-ACORN. Amount: 353 750,00€. Total Amount: 1 000 000,00€.

Scientific Impact

Academic Collaborations

Francisco Corzana, La Rioja University

Vanessa Morais, Instituto de Medicina Molecular João Lobo Antunes

Nuno Morais, Instituto de Medicina Molecular João Lobo Antunes

Miguel Castanho, Instituto de Medicina Molecular João Lobo Antunes

Tia Kohs and Owen McCarty, Oregon Health & Science University

Cláudia Faria, Instituto de Medicina Molecular João Lobo Antunes and Centro Hospitalar Universitário Lisboa Norte

Selected Publications

Laserna V*; Abegg D; Afonso CF; Martin EM; Adibekian A; Ravn P; Corzana F; Bernardes GJL (2021) [Dichloro butendiamides as irreversible site-selective protein conjugation reagent](#). **Angew. Chem. Int. Ed.** 2021, 60, 23750–23755.

Relevance of the publication: Cláudia Afonso, a PhD from the lab performed some of the experiments reported in this paper. The method here described is important for site-selective protein modification, as new maleic-acid derivatives were described as robust cysteine-selective reagents for protein labelling. The synthetic accessibility of these reagents and the mild conditions required for fast and complete conjugation together with the superior stability of the conjugates make this strategy an important alternative to maleimides in bioconjugation.

Conde J; Pumroy RA; Baker C; Rodrigues T; Guerreiro A; Sousa BB; Marques MC; Almeida BP; Lee S; Leites EP; Picard D; Samanta A; Vaz SH; Sieglitz F; Langini M; Remke M; Roque R; Weiss T; Weller M; Liu Y; Han S; Corzana F; Morais VA; Faria CC; Carvalho T; Filippakopoulos P; Snijder B; Barbosa-Morais NL; Moiseenkova-Bell VY; Bernardes GJL (2021) [Allosteric antagonist modulation of TRPV2 by Piperlongumine impairs glioblastoma progression](#). **ACS Cent. Sci.** 2021, 7, 868–881.

Relevance of the publication: Several members of the group have performed experiments that led to this publication, namely João Conde (who developed the delivery method of piperlongumine for the *in vivo* models); Tiago Rodrigues (who developed the computational method that correlated PI with TRPV2), Charlotte Baker (as part of her PhD project), Ana Guerreiro (cell assays, western blots, qPCRs), Bárbara Sousa (protein assays), Marta Marques e Florian Sieglitz (calcium influx experiments). The importance of this work relies on the computational identification and experimental validation of TRPV2 as a target for piperlongumine and the establishment of a link between allosteric target engagement and impaired glioblastoma progression *in vivo*. Not only the use of these computational tools to identify biological targets of natural products with anticancer properties and unknown modes of action is gaining momentum but also the obtained results in GBM open up new possibilities for successful GBM therapies.

Hakala TA; Yates EV; Challa PK; Toprakcioglu Z; Nadendla K; Matak-Vinkovic D; Dobson CM; Martínez R; Corzana F*; Knowles TPJ*; Bernardes GJL* (2021) [Accelerating reaction rates of biomolecules by using shear stress in artificial capillary systems](#). **J. Am. Chem. Soc.** 2021, 143, 16401–16410.

2021 Publications in Peer-Reviewed Journals

António JPM, Carvalho JI, André AS, Dias JNR, Aguiar SI, Faustino H, Lopes RMRM, Veiros LF, Bernardes GJL, da Silva FA, Gois PMP* (2021). [Diazaborines are a versatile platform to develop ROS responsive antibody drug conjugates](#). **Angew. Chem.** 60, 25914–25921.

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu Y, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Barbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL (2021) [Allosteric antagonist modulation of TRPV2 by Piperlongumine impairs glioblastoma progression](#). **ACS Cent. Sci.** 2021, 7, 868–881.

Faidon Brotzakis Z, Lindstedt PR, Taylor RJ, Rinauro DJ, Gallagher NCT, Bernardes GJL, Vendruscolo M* (2021) [A structural ensemble of a Tau-microtubule complex reveals regulatory Tau phosphorylation and acetylation mechanisms](#). **ACS Cent. Sci.** 2021, 7, 1986–1995.

Ferhati X, Salas-Cubero M, Garrido P, García-Sanmartín J, Guerreiro A, Avenzoza A, Busto JH, Peregrina JM, Martínez A, Jiménez-Moreno E*, Bernardes GJL*, Corzana F (2021). [Bioorthogonal self-immolative linker based on Grob fragmentation](#). **Org. Lett.** 2021, 23, 8580–8584.

Ferreira VFC; Oliveira BL*; D'Onofrio A; Farinha CM; Gano L; Paulo A; Bernardes GJL*; Mendes F (2021) [In vivo pretargeting based on cysteine-selective antibody modification with IEDDA bioorthogonal handles for click chemistry](#). **Bioconjugate Chem.** 2021, 32, 121–132.

Hakala TA, Yates EV, Challa PK, Toprakcioglu Z, Nadendla K, Matak-Vinkovic D, Dobson CM, Martínez R, Corzana F*, Knowles TPJ*, Bernardes GJL* (2021) [Accelerating reaction rates of biomolecules by using shear stress in artificial capillary systems](#). **J. Am. Chem. Soc.** 2021, 143, 16401–16410.

Kiely-Collins H; Winter GE; Bernardes GJL* (2021) [The role of reversible and irreversible covalent chemistry in targeted protein degradation](#). **Cell Chem. Biol.** 2021, 28, 952–968. Review.

Kitowski A; Corzana F; Bernardes GJL* (2021) [Precise protein conjugation technology for the construction of homogenous glycovaccines](#). **Drug Discov. Today Technol.**

Konč J; Sabatino V; Jiménez-Moreno E; Latocheski E; Rodríguez Pérez L; Day J; Domingos JB; Bernardes GJL (2021). [Controlled in-cell generation of active palladium\(0\) species for bioorthogonal decaging](#). **Angew. Chem.** 60, 25905–25913.

Konč J, Brown J, Whiten DR, Zuo Y, Ravn P, Klenerman D, Bernardes GJL* (2021) [A platform for site-specific DNA-antibody bioconjugation by using benzoylacrylic-labelled oligonucleotides](#). **Angew. Chem.** 60, 25905–25913.

Laserna V; Istrate A; Kafuta K; Hakala TA; Knowles TPJ; Alcarazo M*; Bernardes GJL* (2021) [Protein conjugation by electrophilic alkynylation using 5-\(alkynyl\) dibenzothiophenium triflates](#). **Bioconjugate Chem.** 2021, 32, 1570–1575.

Laserna V*, Abegg D, Afonso CF, Martin EM, Adibekian A, Ravn P, Corzana F, Bernardes GJL* (2021) [Dichloro butenediamides as irreversible site-selective protein conjugation reagent](#). **Angew. Chem. Int. Ed.** 2021, 60, 23750–23755.

Lee K, Yang A, Lin Y-C, Reker D, Bernardes GJL, Rodrigues T (2021). [Combating small-molecule aggregation with machine learning](#). **Cell. Rep. Phys. Sci.** 2021, 2, 100573.

Lindstedt PR; Aprile FA; Sormanni P; Rakoto R; Dobson CM; Bernardes GJL*, Vendruscolo M (2021) [Systematic activity maturation of a single-domain antibody with non-canonical amino acids through chemical mutagenesis](#). **Cell Chem. Biol.** 2021, 28, 70–77.

Lindstedt PR; Taylor RJ; Bernardes GJL (2021) [Facile installation of post-translational modifications on the Tau protein via chemical mutagenesis](#). **ACS Chem. Neurosci.** 2021, 12, 557–561.

Neukirch K; Alsabil K; Dinh C-P; Bilancia R; Raasch M; Ville A; Cerqua I; Viault G; Bréard D; Pace S; Temml V; Brunner E; Jordan PM; Marques MC; Loeser K; Gollowitzer A; Permann S; Gerstmeier J; Lorkowski S; Stuppner H; Garscha U; Rodrigues T; Bernardes GJL; Schuster D; Séraphin D; Richomme P; Rossi A; Mosig AS; Roviezzo F; Werz O; Helesbeux J-J; Koeberle A (2021) [Exploration of long-chain vitamin E metabolites for the discovery of a highly potent, orally effective, and metabolically stable 5-LOX inhibitor that limits inflammation](#) **J. Med. Chem.** 2021, 64, 11496–11526.

Orellana EA, Liu Q, Yankova E, Pirouz M, De Braekeleer E, Zhang W, Lim J, Aspris D, Sendinc E, Garyfallos DA, Gu M, Ali R, Gutierrez A, Mikutis S, Bernardes GJL, Fischer ES, Bradley A, Vassiliou GS, Slack FJ, Tzelepis K, Gregory RI (2021) [METTL1-mediated m⁷G modification of Arg-TCT tRNA drives oncogenic transformation](#). **Molecular Cell** 2021, 81, 3323–3338.

Sousa BB; Sousa MFQ; Marques MC; Seixas JD; Brito JA; Matias PM; Bernardes GJL; Roldão A (2021) [A scalable insect cell-based production process of the human recombinant BMX for in-vitro covalent ligand high-throughput screening](#). **Bioprocess Biosyst. Eng.** 2021, 44, 209–215.

Zawada Z, Guo Z, Oliveira BL, Navo CD, Li H, Cal PMSD, Corzana F, Jiménez-Osés G*, Bernardes GJL* (2021) [Arylethynyltrifluoroborate dienophiles for on demand activation of IEDDA reactions](#). **Bioconjugate Chem.** 32, 1812–1822.

Invited Lectures and Seminars

KEYNOTE AND PRIZE LECTURES (Gonçalo Bernardes)

09/2021	International Symposium on Synthesis and Catalysis 2021 (ISySyCat2021), Évora, Portugal
08/2021	XXVI EFMC International Symposium on Medicinal Chemistry (EFMC-ISMC 2021), Basel, Switzerland
07/2021	Encontro Nacional da Sociedade Portuguesa de Química, Braga, Portugal Medalha Vicente de Seabra 2020
06/2021	2nd Meeting of the Group of Portuguese Chemists Abroad of the Portuguese Chemical Society
05/2021	Saúde: Construir o futuro, Conselho da Diáspora Portuguesa

INVITED SEMINARS

12/2021	Gonçalo Bernardes. Bringing Chemical Biology to Cancer Research, RSC Virtual Meeting
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- 11/2021 Gonalo Bernardes. NCCR Chemical Biology Lecture Series (Virtual seminar), Switzerland
- 05/2021 Gonalo Bernardes. Department of Genetics, University of Cambridge, UK – Host: Cambridge RNA club
- 2021 Marta Bento. Invited Speaker in NEDR - 1St RARO Symposium, Portugal, 2021. Theme: Substrate Reduction Therapies in Gaucher Disease, Eliglustat: The importance of a new oral treatment option confirmed by Real World Evidence.
- 2021 Marta Bento. Invited Speaker in “From Multiple Myeloma to Gaucher Meeting”, Takeda, Portugal, 2021. Theme: Gaucher Disease – Challenges from diagnosis to treatment outcomes.
- 2021 Marta Bento. Invited Speaker in “Simp3sio RARAS – Doenas Raras, sintomas comuns”, 8^a temporada, Portugal, 2021. Theme: Clinical Case of Gaucher Disease.

Communications

Ana Raquel Coelho. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: G4-RNA Degraders - A novel approach to target SARS-CoV-2 infection.

Ana Guerreiro. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: Novel MUC1-based glycoconjugate vaccines against cancer.

Ana Guerreiro **2-3rd Dec 2021** (Oral and Poster). Novel MUC1-based glycoconjugate vaccines against cancer. Bringing Chemical Biology to Cancer Research. 2021 RSC-BACR meeting.

Cong Tang. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: Potential of natural product—Piperlongumine against SARS-CoV-2.

Marta Bento. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: IGF2BP1 is required for maintaining leukemia cell survival by regulating mRNA stability in an m6 A-dependent manner.

Maria Rebelo. Antiviral NL-CVX1 efficiently blocks infection of SARS-CoV-2 viral variants of concern (VOC). IDWeek2021, San Diego, USA, 29 September 2021.

Maria Rebelo. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: Antiviral NL-CVX1 efficiently blocks infection of SARS-CoV-2 viral variants of concern (VOC).

Brbara B. Sousa. 2-3rd Dec 2021 (Oral and Poster). The importance of selectively target a cysteine in b-cell cancers. Bringing Chemical Biology to Cancer Research. 2021 RSC-BACR meeting.

Brbara B. Sousa. 7-9th July 2021 (Poster). From prostate to b-cell cancers: the importance of cysteine modification. Interfacing Chemical Biology and Drug Discovery SCT.

Bárbara B. Sousa. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: From prostate to b-cell cancers: the importance of cysteine modification.

Marta Marques. 1. 7th Iberian Biophysics Congress - virtual (June 2021)- poster and flash presentation. The potential role of GAPDH in cancer and metastasis.

Marta Marques. 45th FEBS Congress 2021-virtual (July 2021) - poster. The potential role of GAPDH in cancer and metastasis.

Marta Marques. 13-15 October 2021, ACORN summer school, Chemical Biology of Carbon Monoxide Symposium, flash talk session. Title: The potential role of GAPDH in cancer and metastasis.

Organization of Conferences

Bernardes GJL, Marques MC, Co-Organizer. Chemical Biology of Carbon Monoxide Symposium, Praia Verde, Algarve 13-15 October 2021.

Prizes & Honors in 2021

2021 Blavatnik Award for Young Scientist in the UK – Finalist in Chemistry (unrestricted £30,000 prize)

2021 Medalha Vicente de Seabra 2020, Sociedade Portuguesa de Química

2021 Advanced Contribution Supplement Award, University of Cambridge in recognition of Dr Bernardes exceptional trajectory

2021–To date Editorial Advisory Board, Bioconjugate Chem., ACS, US

Advanced Teaching

Bernardes GJL. 2019–To date. Visiting Professor, Farmacologia Clínica e Terapêutica da Faculdade de Medicina da Universidade de Lisboa, Portugal

Bernardes GJL. 2019–To date. Director of Studies in Chemistry at Trinity Hall College, Cambridge

Bernardes GJL. 2017–To date Supervisor of organic and biological chemistry courses at Trinity Hall College, Cambridge

Bernardes GJL. 2014–To date. Part III Course Internal Examiner, Univ. of Cambridge, UK

Bernardes GJL. 2014–To date. Lecturer - Chemical Biology & Drug Discovery - undergraduate course, Univ. of Cambridge, UK

Bernardes GJL. 2013–To date. Lecturer - Chemical Biology of Nucleic Acids - undergraduate course, Univ. of Cambridge, UK

Bernardes GJL. 2013–To date. Lecturer - Targeted Anti-Cancer Therapeutics - graduate course, Univ. of Cambridge, UK

Marques M. Biochemistry Practical Classes. Escola Superior de Ciências da Saúde, Lisbon, Portugal, September 2019-to date.

PhD Theses

Inês Albuquerque. "Unnatural glycopeptides and proteins and their use in antigen detection and immunization". 18/06/2021. Supervisor: Gonçalo Bernardes.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Partnership with Neoleukin Therapeutics (sponsored research) with the aim of testing new potential drugs against Sars-CoV-2. Project title: *Investigation of the in vivo activity and immune characterization of NL-CVX1 in a transgenic mouse model of SARS-CoV-2 infection*

Partnership with Proterris Inc (sponsored research), with the aim of investigating the roles of CO as immunomodulators in cancer. IP licensed to Proterris Inc.

Intellectual Property Rights in 2021

Production of Cross-reactive material 197 Fusion Proteins; Albuquerque I; Bernardes GJL. United Kingdom (GB) Patent Application No: 2108650.9; filled 17 June 2021. Status: Pending.

CRM197 Protein Carrier; Albuquerque I; Bernardes GJL. United Kingdom (GB) Patent Application No: 2108648.3; filled 17 June 2021. Status: Pending.

Ligand drug conjugates and modified BET inhibitors; Traquete R; Bernardes GJL. PCT/GB2021/050058; filled 11 January 2021. Status: Pending.

Treatment of Immunosuppressive Cancer; Labão–Almeida C; Bernardes GJL. GB Patent Application No: 2004514.2; filled 27 March 2020. PCT Application ref. PCT/EP2021/058146; filled 30 March 2021. Status: Pending.

Science and Society in 2021

During the summer of 2021, GBernardes lab received the visit of 4 high school students.

The work from the group originated 2 reports in media:

- 1- Público – Identificado potencial fármaco para tratamento do glioblastoma multiforme.
- 2- EurekAlert! – Ingredient in Indian long pepper shows promise against brain cancer in animal models.

Maria Carmo-Fonseca Lab

Head of Laboratory: Maria Carmo-Fonseca, MD, PhD, Group Leader and Full Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Adriana Andrade Vieira	Master Degree	Lab Technician (Started February)
Alípio Paulo Vasco Parreirão e Gomes	University Degree	MSc Student (Started March)
Ana Carolina Campos Pais	High School Diploma	Trainee (Started February)
Ana Catarina Cardoso Lopes	Master Degree	MSc Student (Left August)
Ana Cláudia Bernardino Raposo	Master Degree	PhD Student
Ana Margarida Inácio Veloso	University Degree	MSc Student (Started September)
Ana Pereira de Brito Líbano Monteiro	University Degree	MSc Student (Started September)
Beatriz Anjo Santos Lima	High School Diploma	Trainee
Beatriz Dias Gomes da Silva	Master Degree	PhD Student (Started June)
Beatriz Pinto Galvão	Master Degree	Lab Technician (Started March)
Carina Sofia Barradas Maranga	Master Degree	PhD Student
Carolina Lopes Gonçalves	University Degree	MSc Student (Started October)
Catarina Alves do Vale	Master Degree	Trainee
Catarina Fernandes Pereira Noronha Ribeiro	High School Diploma	Trainee
Célia da Conceição Vicente Carvalho	PhD	Staff Scientist
Christian Gomes da Silva Ramos	PhD	Senior Postdoctoral Researcher (Left November)
Dinora Levy	University Degree	Administrative Technician
Eunice de Melo Gomes Gonçalves	University Degree	MSc Student (Started March)
Evguenia Pavlovna Bekman	PhD	Senior Postdoctoral Researcher
Francisca do Sacramento Andrade Silva	University Degree	Trainee (Started January. Left July)
Inês Gonçalves Dias	University Degree	MSc Student (Started September)
João Tiago Alves Prior Proença	PhD	Senior Postdoctoral Researcher (Started January)
Laura Afonso Carepa Dias	University Degree	MSc Student (Started March)
Maria Joana Pinto Desterro	PhD	Staff Scientist
Maria João de Andrade Terras Arez	Master Degree	PhD Student (Started April)
Maria Teresa Tenório Figueiredo Carvalho Gonçalves	PhD	Staff Scientist
Marta de Jesus Ribeiro	PhD	Postdoctoral Researcher
Marta Isabel Brandão Furtado	Master Degree	PhD Student (Started February)
Marta Sousa Santos	High School Diploma	MSc Student (Started September)
Michelle Xavier Gonçalves Pereira	PhD	Lab Technician (Left December)
Noélia Maria Fernandes Custódio	PhD	Staff Scientist
Patrícia Alexandra Veloso Napoleão	PhD	Senior Postdoctoral Researcher
Paulo Jorge Varanda Bernardo	MD/Master Degree	Clinical Researcher
Pedro Galhardo Bak-Gordon	High School Diploma	Trainee
Pedro Santos Barbosa	Master Degree	PhD Student
Ricardo Carvalho Félix Almeida	University Degree	MSc Student (Started September)
Rosina Savisaar	PhD	Postdoctoral Researcher

Rui Gonçalo Viegas Russo da Conceição Martinho	PhD	Visiting Researcher
Rui Sérgio de Sousa Luís	Master Degree	PhD Student
Samantha Mancino	PhD	Postdoctoral Researcher (Left December)
Sandra Cristina Bento Penisga Martins	PhD	Senior Postdoctoral Researcher
Sandrina Nóbrega Pereira	PhD	Senior Postdoctoral Researcher (Left May)
Simão José Teixeira da Rocha	PhD	Staff Scientist
Teresa Maria Pereira da Silva	PhD	Senior Technician (Started June)
Thais Souza Cunha	University Degree	MSc Student

Graphical Abstract

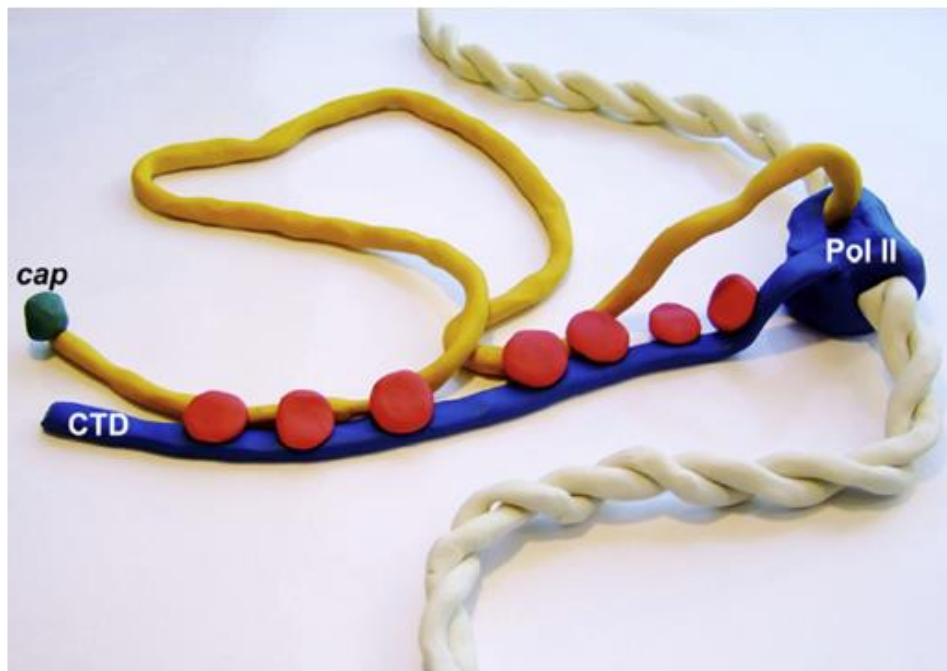


Image caption: RNA transcription and processing are tightly interwoven processes

Lab Interests

Gene regulation is central to all biology. RNA molecules, with their ability to both encode information and exert catalytic activities, play a key role in the regulation of gene expression. Our group aims to discover molecular pathways and mechanisms implicating RNA in human health and disease. More specifically, we study how the RNA splicing machinery influences the regulation of gene expression in genetic diseases including cancer, and we are exploring new therapeutic strategies targeting pre-mRNA splicing.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology

Major Scientific Achievements in 2021

Our lab is known for studies on RNA splicing using a combination of cutting-edge cell imaging and genome-wide approaches. In collaboration with the Proudfoot Lab in Oxford, we have pioneered genome-wide analysis of nascent RNA complexes using NET-seq (Nojima, Gomes, *et*

al., 2015; Nojima, Rebelo, *et al.*, 2018). More recently, our joint efforts led to the development of Polymerase Intact Nascent Transcript (POINT) technology (Sousa-Luis *et al.*, 2021). We further applied NET-seq to study early *Drosophila* development, and we found distinct patterns of transcription termination in early and late embryos, as well as highly heterogeneous splicing kinetics (Prudêncio, Savisaar, Rebelo *et al.*, 2021). In parallel, our lab is developing stem-cell derived cellular models to study the role of pre-mRNA splicing in disease (Silva *et al* 2021a, b, c; Ribeiro *et al* Patent application).

Ongoing Projects in 2021

2021/2021: NON-CODING BHF GRANT. Coordinator: M. Carmo-Fonseca. Funding Agency: University College London. Reference: NON-CODING BHF GRANT. Amount: 8 752,00€. Total Amount: 8 752,00€.

2020/2023: spliceHCM - RNA mis-splicing in hypertrophic cardiomyopathy: opportunities for diagnosis and therapy. Coordinator: M. Carmo-Fonseca. Funding Agency: “la Caixa” Foundation. Reference: HR20-00322 – spliceHCM. Amount: 573 796,50€. Total Amount: 986 964,00€.

2020/2022: From co-transcriptional splicing kinetics to the evolutionary impact of exon and intron definition. Coordinator: M. Carmo-Fonseca. Funding Agency: European Commission. Reference: EvolSpliceKinetics. Amount: 147 815,00€. Total Amount: 147 815,00€.

2020/2021: AbbVie Inc - Material Transfer Agreement. Coordinator: M. Carmo-Fonseca. Funding Agency: AbbVie Inc. Reference: AbbVie Inc - Material Transfer Agreement. Amount: 108 000,00€. Total Amount: 108 000,00€.

2020/2021: Exploring new therapeutic strategies for Angelman syndrome: A disease modelling approach based on 3D cerebellar organoids derived from patient iPSCs. Coordinator: Simão Teixeira da Rocha. Funding Agency: Fundação Amélia de Mello. Reference: Bolsa de Angelman da Fundação Amélia de Mello. Amount: 25 000,00€. Total Amount: 25 000,00€.

2020/2021: Assessing response to splicing inhibitor sulfonamides in cultured primary human AML cells. Coordinator: M. Carmo-Fonseca. Funding Agency: Gilead Sciences. Reference: Programa Gilead GÉNESE 2019. Amount: 26 500,00€. Total Amount: 26 500,00€.

2019/2022: RNA in disease — RiboMed. Coordinator: M. Carmo-Fonseca. Funding Agency: European Commission. Reference: RiboMed - GA 857119. Amount: 424 750,00€. Total Amount: 799 750,00€.

2018/2021: O papel dos RNAs não-codificantes longos (lncRNAs) na adaptação molecular e metabólica do cancro da mama. Coordinator: Bruno Jesus. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: RNAMETCANCER - LISBOA-01-0145-FEDER-028534. Amount: 238 213,92€. Total Amount: 238 213,92€.

2018/2021: As barreiras epigenéticas do envelhecimento na reprogramação celular. Coordinator: Simão Teixeira da Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-MOL/29320/2017. Amount: 239 555,22€. Total Amount: 239 555,22€.

2018/2021: BRCA_RNA: Organóides com edição génica para estudar o impacto funcional de mutações BRCA1 e BRCA2. Coordinator: M. Carmo-Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: BRCA_RNA LISBOA-01-0145-FEDER-029469. Amount: 237 261,63€. Total Amount: 237 261,63€.

2018/2021: CEREBREX: Desenvolvimento de organóides cerebelares para investigação de ataxias. Coordinator: M. Carmo-Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: CEREBREX - LISBOA-01-0145-FEDER-029298. Amount: 83 750,00€. Total Amount: 239 773,28€.

2017/2021: LysoMod: Genetic and small molecule modifiers of Lysosomal Function. Coordinator: M. Carmo-Fonseca. Funding Agency: European Commission. Reference: MSCA RISE 734825. Amount: 279 000,00€. Total Amount: 1 102 500, 00€.

Scientific Impact

Academic Collaborations

Nick Proudfoot, University of Oxford

Michael Gotthardt, MDC Berlin

Tony Futerman, Weizmann Institute of Science

Perry Elliott, St. Bartholomew's Centre for Inherited Cardiovascular Disease and UCL Centre for Heart Muscle Disease, London

Yvan Devaux, Luxembourg Institute of Health

Selected Publications

Nojima T, Rebelo K, Gomes T, Grosso AR, Proudfoot NJ, Carmo-Fonseca M (2018). [RNA Polymerase II phosphorylated on CTD Serine 5 interacts with the spliceosome during co-transcriptional splicing](#). *Molecular Cell* 72(2):369-379.

Relevance of the publication: Genome-wide analysis of nascent RNA complexes using NET-seq revealed unanticipated dynamic links between Pol II and the spliceosome. Contribution: our group is co-first author and co-corresponding author.

Bernardes de Jesus B, Matinho SP, Barros S, Sousa-Franco A, Alves-Vale C, Carvalho T, Carmo-Fonseca M (2018) [Silencing of the lncRNA Zeb2-NAT facilitates reprogramming of aged fibroblasts and safeguards stem cell pluripotency](#). *Nat Commun.* 9(1):94.

Relevance of the publication: This study highlights the physiological importance of antisense transcription in fine tuning the expression of a protein coding gene. We identified the transcription factor Zeb2 as a novel age-associated barrier to reprogramming. We show that forcing Zeb2 downregulation may help improve reprogramming efficiency, and we uncovered a long non-coding RNA that is overlapping and antisense to the Zeb2 locus as a target to achieve robust Zeb2 downregulation. Contribution: all authors are from our group.

Carvalho T, Martins S, Rino J, Marinho S, Carmo-Fonseca M. (2017) [Pharmacological inhibition of the spliceosome subunit SF3b triggers EJC-independent NMD](#). *J Cell Sci.* 130 (9): 1519-1531.

Relevance of the publication: This study not only shows that cytoplasmic pre-mRNAs evoke an EJC-independent NMD pathway response when splicing is blocked, but also provides insights into the effects of a set of potential anti-cancer drugs on the stability and transport of mRNAs. Contribution: all authors are from our group.

Vaz-Drago R, Custódio N, Carmo-Fonseca M, (2017) [Deep intronic mutations and human disease](#). *Hum Genet.* 136: 1093-1111.

Relevance of the publication: This review highlights the importance of studying variation in deep intronic sequence as a cause of monogenic disorders as well as hereditary cancer syndromes. Contribution: all authors are from our group.

Nojima T, Gomes T, Grosso AR, Kimura H, Dye MJ, Dhir S, Carmo-Fonseca M, Proudfoot N (2015). [Mammalian NET-seq reveals genome-wide nascent transcription coupled to RNA processing](#). *Cell* 161(3):526-540.

Relevance of the publication: This study provides the first genome-wide analysis of co-transcriptional RNA splicing at single-nucleotide resolution. Contribution: our group is co-first author and co-corresponding author.

2021 Publications in Peer-Reviewed Journals

Prudêncio P, Savaia R, Rebelo K, Martinho RG, Carmo-Fonseca M (2021) [Transcription and splicing dynamics during early Drosophila development](#). *RNA*, 28:1–23.

Silva TP, Pereira CA, Oliveira AR, Raposo AC, Arez M, Cabral JMS, Milagre I, Carmo-Fonseca M, and Rocha ST (2021). [Generation and characterization of induced pluripotent stem cells from a family carrying the BRCA1 mutation c.3612delA](#). *Stem Cell Research* 52: 102242.

Silva TP, Pereira CA, Raposo AC, Oliveira AR, Arez M, Cabral JMS, Milagre I, Carmo-Fonseca M, and Rocha ST (2021). [Generation and characterization of induced pluripotent stem cells heterozygous for the Portuguese BRCA2 founder mutation](#). *Stem Cell Research* 53:102364.

Silva TP, Sousa-Luís R, Fernandes TG, Bekman EP, Rodrigues CAV, Vaz SH, Moreira LM, Hashimura Y, Jung S, Lee B, Carmo-Fonseca M and Cabral JMS (2021). [Transcriptome profiling of human pluripotent stem cell-derived cerebellar organoids reveals faster commitment under dynamic conditions](#). *Biotechnology and Bioengineering* 118(7):2781-2803.

Silveira C, Sousa AC, Janeiro A, Malveiro S, Teixeira E, Brysch E, Pantarotto M, Felizardo M, Madureira R, Nogueira F, Guimarães C, Matos C, Canário D, Bruges-Armas, Carmo-Fonseca M (2021) [Detection and quantification of EGFR790M mutation in liquid biopsies by droplet digital PCR](#). *Transl. Lung Cancer Res.* 10(3):1200-1208.

Sousa-Luis R, Dujardin G, Zukher I, Kimura H, Carmo-Fonseca M, Proudfoot NJ, Nojima T (2021). [POINT Technology illuminates the processing of polymerase-associated intact nascent transcripts](#). *Molecular Cell* 81(9):1935-1950.

Invited Lectures and Seminars

Carmo-Fonseca M. Enabling Science's full impact on patients' needs and outcomes. How can EU lead the way? E-Conference "European Leadership in Health: to leave no one behind. April 7, 2021.

Carmo-Fonseca M. From co-transcriptional splicing to genome instability. 5th course on Post-Transcriptional Gene Regulation / 3rd course on Genome Instability and Human Disease, Institut Curie (Virtual). April 12, 2021.

Carmo-Fonseca M. Personalized Medicine. Innovations in Healthcare, Infarmed (Virtual). April 16, 2021.

Carmo-Fonseca M. O aumento da longevidade: o contexto biológico. Longevidade e seguros de saúde. AIDA (Associação Internacional de Direito dos Seguros). May 11, 2021.

Carmo-Fonseca M. Addressing the root cause of Spinal Muscular Atrophy: from the laboratory to the clinic. Symposium Novartis GTx at the Pediatric Neurology Portuguese Society Meeting, Virtual, May 13, 2021.

Carmo-Fonseca M. "My lifelong scientific quest". Keynote lecture at Master Students Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, June 2, 2021.

Carmo-Fonseca M. Fast or slow splicing? International Nucleome Consortium (INC) Academy, Virtual, June 17, 2021.

Carmo-Fonseca M. RNA de Interferência: De Prémio Nobel a estratégia terapêutica. Simpósio Alnylam, Congresso Nacional de Neurologia, Algarve. Outubro 28, 2021.

Carmo-Fonseca M. Modulação do fenótipo "BRCAness". Dia Mundial do Cancro do Pâncreas, Hospital da Luz, Lisboa. November 18, 2021.

Carmo-Fonseca M. Novos modelos de organização e investigação: da evidência à prática. Conferência APDH (Associação Portuguesa para o Desenvolvimento Hospitalar), Virtual, November 23, 2021.

Carmo-Fonseca M. Sessão plenária de abertura da 5ª Conferência Anual da rede Saúde "A Health Research Agenda towards 2030". Universidade de Lisboa, Lisboa. Novembro 30, 2021.

Carmo-Fonseca M. O que é a Medicina de Precisão? Webinar de divulgação organizado pela rede Saúde da Universidade de Lisboa. Dezembro 3, 2021.

Silva TP. Scalable generation of cerebellar organoids from human pluripotent stem cells. Virtual Workshop on Biochemistry of Ageing - Portuguese Biochemical Society. March 30, 2021.

Silva TP. Modelos para o Estudo do Cérebro e Implicações Bioéticas, Brain Gain - À descoberta das Neurociências. March 24, 2021.

Communications

Prudêncio P, Savisaar R, Rebelo K, Martinho RG, Carmo-Fonseca M. “Immediate” co-transcriptional splicing in *Drosophila* is associated to S5P of the Pol II CTD. Splicecon 2021 Symposium (Online). April 22-23, 2021. (Poster presentation). INTERNATIONAL CONFERENCE. Related to project LISBOA-01-0145-FEDER-016394; Marie Skłodowska-Curie Action No 842695; and RiboMed 857119.

Prudêncio P, Savisaar R, Rebelo K, Martinho RG, Carmo-Fonseca. The timing of co-transcriptional splicing in *Drosophila* embryos. The 26th Annual Meeting of the RNA Society - RNA 2021 (Online). May 25- June 5, 2021. (Poster presentation). INTERNATIONAL CONFERENCE. Related to project LISBOA-01-0145-FEDER-016394; Marie Skłodowska-Curie Action No 842695; and RiboMed 857119.

Ramos CG, Barbosa P, Lourenço DM, Xapelli S, Joseph T, Kaya E, Platt FM, Zanlungo S, Futerman AH, Carmo-Fonseca M. Alterations in pre-mRNA splicing associated with lysosomal storage diseases. The 26th Annual Meeting of the RNA Society - RNA 2021 (Online). May 25- June 5, 2021. (Poster presentation). INTERNATIONAL CONFERENCE. Related to project MSCA RISE 734825 (LysoMod) and RiboMed 857119.

Sousa-Luís R, Dujardin G, Zukher I, Kimura H, Weldon C, Savisaar R, Carmo-Fonseca M, Proudfoot NJ, Nojima T. Efficient co-transcriptional splicing suppresses premature transcription termination. The 26th Annual Meeting of the RNA Society - RNA 2021 (Online). May 25- June 5, 2021. (Oral presentation). INTERNATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017 and RiboMed 857119.

Sousa-Luís R, Dujardin G, Zukher I, Kimura H, Weldon C, Savisaar R, Carmo-Fonseca M, Proudfoot NJ, Nojima T. Polymerase-associated intact nascent transcripts reveal different kinetic classes of co-transcriptional splicing. Cold Spring Harbor virtual meeting “Eukaryotic mRNA processing”, August 24-27, 2021. (Oral presentation). INTERNATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017 and RiboMed 857119.

Silva TP, da Rocha ST, Milagre I, Pereira C, Cabral JMS, Carmo-Fonseca M. iPSC-derived mammary progenitors as a model to study the onset of malignant transformation triggered by BRCA mutations. Organoids: Advances and Applications, Virtual Conference from Wellcome Genome Campus – UK. September 28-30, 2021. (Poster presentation). INTERNATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017 and RiboMed 857119.

Lima B, Custódio N, Dias P, Sousa AB, Carvalho C, Carmo-Fonseca, M. Splicing modulation in patients carrying a mutation in the BRCA2 gene: therapeutic potential. ASPIC (Associação Portuguesa de Investigação em Cancro) international meeting. Porto, October 14-15, 2021. (Poster presentation). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Beatriz Gomes-Silva, Marta Ribeiro, Marta Furtado, Sandra Martins, Teresa Carvalho, Pedro Barbosa, Rosina Savisaar, Maria Carmo-Fonseca. Transcriptomic characterization of human iPSC-derived cardiomyocytes. 25th Annual Meeting of Sociedade Portuguesa de Genética Humana. November 18th, 2021. (Oral presentation). NATIONAL CONFERENCE. Related to project “La Caixa” HR20-00322.

Alves-Vale C, Galvão B, Silvestre AR, Custódio N, Borrvalho P, Carmo-Fonseca M. Morphologic and immunophenotypic analysis of patient-derived organoids from ovarian carcinoma and fallopian tube. 18º Congresso da Sociedade Portuguesa de Anatomia Patológica/21º Congresso da Sociedade Portuguesa de Citologia, Lisbon, Portugal, 19 November 2021 (Oral Communication). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Luís S, Furtado M and Carvalho T. Cardiomiopatia Hipertrófica e Base Editing: correção da variante c.2222A>G do gene ACTN2, associada a Cardiomiopatia Hipertrófica, através da tecnologia de Base Editing. Dia da Investigação GAPIC, Faculdade de Medicina da Universidade de Lisboa. December 15, 2021 (Poster Presentation). NATIONAL CONFERENCE. Related to project “La Caixa” HR20-00322.

Grilo M, Antunes R, Custódio N, Why does BRCA loss of function predisposes to tumors mainly in estrogen-related tissues? Dia da Investigação GAPIC, Faculdade de Medicina da Universidade de Lisboa. December 15, 2021 (Poster presentation). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Pais ACC, Carvalho C, Custódio N, Sousa AB, Dupont J, Carmo-Fonseca, M. Molecular and functional characterization of inherited intronic variants on BRCA1 and BRCA2 genes: aiming to reclassify variants of uncertain significance. Dia da Investigação GAPIC, Faculdade de Medicina da Universidade de Lisboa. December 15, 2021 (Poster presentation). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Ribeiro C, Carvalho C, Carmo-Fonseca, M. What is the mechanism by which lncRNA PCAT-1 affects BRCA2? Dia da Investigação GAPIC, Faculdade de Medicina da Universidade de Lisboa. December 15, 2021 (Poster presentation). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Lima B, Custódio N, Dias P, Sousa AB, Carvalho C, Carmo-Fonseca, M. Development of a new test based on CRISPR-Cas9 technology to assess the function of BRCA1 and BRCA2 proteins. Dia da Investigação GAPIC, Faculdade de Medicina da Universidade de Lisboa. December 15, 2021 (Poster and oral presentation). NATIONAL CONFERENCE. Related to project PTDC/MED-ONC/29469/2017.

Organization of Conferences

M. Carmo-Fonseca chaired a session at the Cold Spring Harbor virtual meeting “Eukaryotic mRNA processing”, August 24-27, 2021.

Prizes & Honors in 2021

In 2021, M. Carmo-Fonseca was:

President of Instituto de Medicina Molecular João Lobo Antunes
President of the Medical School “Conselho de Escola”
President of the international RNA Society
Editor for the Journal of Cell Science
Editor for the RNA Journal
Reviewed manuscripts submitted to Cell, Molecular Cell, Nature Structural and Molecular Biology, Nature Cell Biology, and Science Advances.
Member of the evaluation panel for ERC advanced grants.
Member of the review committee to assess the benefits of memberships of the Czech Republic in international R&D organizations (EMBC and EMBL).
Member of the jury for the Bial Award in Biomedicine.
Member of the jury for “Prémio Maria de Sousa 2021” (Ordem dos Médicos/Fundação Bial)
Member of the Advisory board for “Lusíadas Saúde”.
Member of the Advisory board on lung cancer for Janssen Pharmaceuticals.
Member of the Medical School “Conselho Científico”
Considered one of the “Most influential women in Portugal 2020” by the magazine Executiva
<https://executiva.pt/poder-da-influencia/>

Advanced Teaching

Carmo-Fonseca M. “Saving lives with RNA”. Ciclo de Formação (online) em Doenças Raras dedicado ao tema “Porfíria”, organizado pela Sociedade Portuguesa de Gastrenterologia. Abril 21, 2021.

Carmo-Fonseca M. Coordenação do programa NeuroP - Inside Gene Therapy, organizado pelo Instituto de Medicina Molecular João Lobo Antunes (iMM) com o objetivo de disponibilizar um treino avançado sobre os mecanismos moleculares e respostas imunitárias associadas à terapia genética, a toda a comunidade de neuropediatras em Portugal. Outubro 28 a Novembro 20, 2021.

Savisaar, R. Introduction to Data Analysis. Instituto de Medicina Molecular João Lobo Antunes, October 19 - December 10, 2021.

Alves-Vale C. The role of Pathology in Cancer Research. Translational and Clinical Oncology, NOVA Biomedical Research, NOVA Medical School, Universidade NOVA de Lisboa (virtual), 12 May 2021.

Alves-Vale C. The role of Pathology. Master in Oncobiology - Molecular Mechanisms in Cancer. Faculdade de Medicina e Ciências Biomédicas, Universidade do Algarve (virtual), 20 May 2021.

Prudêncio P. Splicing: astonishing facts and open questions. Mestrado em Biologia Molecular e Microbiana, Faculdade de Medicina e Ciências Biomédicas da Universidade do Algarve, Faro, Portugal, December 3, 2021.

Carvalho C. Tutoring Research Exchanges. Medical student: Melina Anthi Ntouchaniari; University of Ioannina, Greece. International Federation of Medical Students (IFMSA) - Associação de Estudantes da Faculdade de Medicina de Lisboa.

Carvalho C. Tutoring Research Exchanges. Medical student: Badder-Eddine Jou; Faculty of Medicine and Pharmacy of Rabat, Morocco. International Federation of Medical Students (IFMSA) - Associação de Estudantes da Faculdade de Medicina de Lisboa.

Sandra Martins and Teresa Carvalho. Tutoring Research Exchanges. Medical student: Avinindita Nura Lestari (Faculty of Medicine, Universitas Islam Bandung, Indonesia). International Federation of Medical Students (IFMSA) - Associação de Estudantes da Faculdade de Medicina de Lisboa. July 2-27, 2021.

Custódio N. Tutor in the curricular unit on Experimental Design in Research and Innovation, Master student Carolina Gonçalves. Master in Biopharmaceutical Sciences, Faculdade de Farmácia, Universidade de Lisboa. June 2021.

Custódio N. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical students Maria Grilo and Raquel Antunes. Why does BRCA loss of function predispose to tumor mainly in estrogen-related tissues? Faculdade de Medicina, Universidade de Lisboa.

Carvalho C. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student: Catarina Ribeiro. “What is the mechanism by which lncRNA PCAT-1 affects BRCA2 expression?”

Carvalho C. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student: Beatriz Lima. “Development of a new test based on CRISPR-Cas9 technology to assess the function of BRCA1 and BRCA2 proteins.”

Carvalho C. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student: Ana Carolina Campos Pais. “Molecular and functional characterization of inherited intronic variants on BRCA1 and BRCA2 genes: aiming to reclassify variants of uncertain significance.”

Martins, S. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student: Carlos Fernandes. “Assinatura molecular na cardiomiopatia hipertrófica – à descoberta de oportunidades de diagnóstico e terapêutica”.

Carvalho, T. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student: Sara Luís. “Correção da variante patogénica c.1987C>T do gene MYH7, associada a Cardiomiopatia Hipertrófica, através da tecnologia de base editing”.

MSc Theses

Eunice Gonçalves, 12/11/2021, iPSC-derived mammary epithelial cells as a model to study the onset of malignant transformation triggered by BRCA mutations. Master in Biological Engineering. Instituto Superior Técnico, Universidade de Lisboa. Supervisor: Teresa P. Silva

Ana Catarina Lopes, 06/09/2021, Patient-derived pancreatic cancer organoids for modeling drug response, Tecnologias Moleculares em Saúde (Master), Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa. Supervisor: Noélia Custódio.

Beatriz Galvão, 15/03/2021, Ovarian cancer organoids for modeling drug response and discovering novel BRCA biomarkers, Biologia Molecular e Genética (Master), Faculdade de Ciências, Universidade de Lisboa. Supervisor: Noélia Custódio.

Maria Inês Ribeiro, 07/06/2021, Expression profiles of BRCA1/2 and homologous recombination genes in ovarian cancer. Mestrado Integrado em Medicina. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Noélia Custódio and Co-Supervisor: Rosina Savisaar.

Pedro Bak-Gordon, 23/07/2021, Analysis of BRCA1 and BRCA2 mRNA levels in different cell types derived from BRCA germline mutation carriers. Mestrado Integrado em Medicina. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Carmo-Fonseca and Co-Supervisor: Célia Carvalho.

Thais Souza Cunha, 21/12/2021, The Role of CDKs in Co-Transcriptional Splicing through Phosphorylation of the RNA Pol II Carboxy-Terminal Domain, Mestrado em Ciências Biofarmacêuticas, Faculdade de Farmácia, Universidade de Lisboa. Supervisor: Pedro Prudêncio.

Carla Piqueras, 20/08/2021, Alternative splicing as an adaptive response to cardiac disease: an analysis of splicing events in patients with cardiomyopathy. “Magistere of Genetics”, Paris Diderot University, France. Supervisor: Sandra Martins.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Objectives: Investigate the efficacy of ABT-199 in combination with azacitidine and splicing inhibitors in cultured primary human AML cells.

Company: AbbVie

Type of partnership: Sponsored Research

Objetivo: disponibilizar um treino avançado sobre os mecanismos moleculares e respostas imunitárias associadas à terapia genética, a toda a comunidade de neuropediatras em Portugal.

Company: Novartis

Type of partnership: Sponsored Educational program

Intellectual Property Rights in 2021

Patent application: Unique ID: GB 2117642.5; United Kingdom Intellectual Property Office (UKIPO). Title: Methods of Cardiomyocyte Production. Inventors: Ribeiro M (Instituto Superior Técnico, IST), Martins S (iMM), Furtado M (iMM), Carvalho T (iMM), Carmo-Fonseca M (iMM), Diogo M (IST), Cabral J (IST). Date of filing: 07 December 2021.

Science and Society in 2021

Carmo-Fonseca M. As biotecnologias do século XXI. Thales Kick-Off 2021. February 3, 2021.

Carmo-Fonseca M. Será possível prevenir o cancro? Conferências do Chiado (organização CIDSENIOR). March 24, 2021.

Carmo-Fonseca M. Apresentação do livro “Como salvar um mundo doente” por Eduardo Paz Ferreira. July 6, 2021.

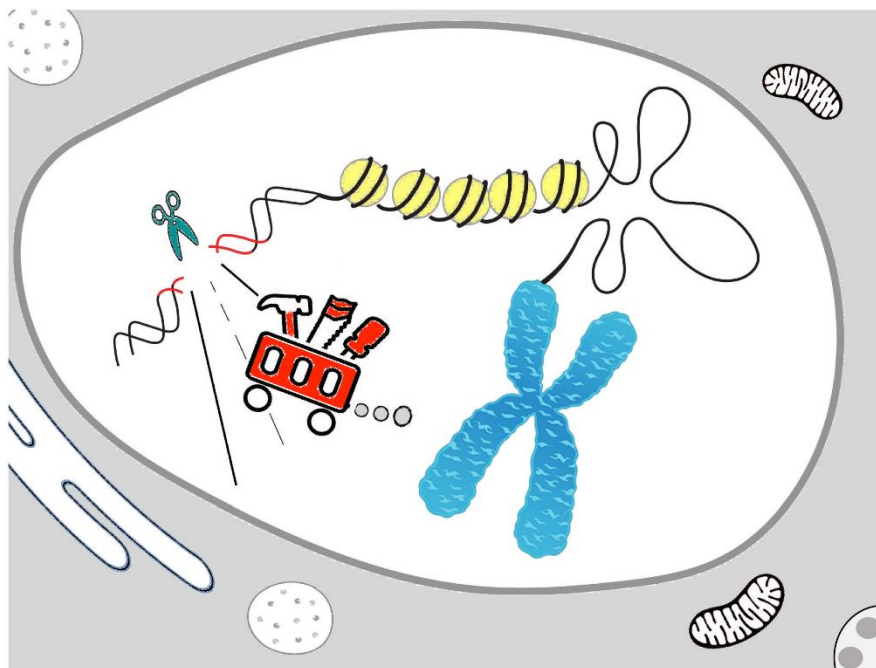
Sérgio de Almeida Lab

Head of Laboratory: Sérgio Fernandes de Almeida, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Rita Henriques Simões Marques	University Degree	MSc Student (Started September)
Anne-Valerie Gendrel	PhD	Senior Postdoctoral Researcher
Cristiana Marisa de Sousa Morgado	Master Degree	PhD Student
Eduardo Luís Correia Gameiro	Master Degree	Lab Technician (Left August)
Inês Cardial Mendes Dias	University Degree	MSc Student (Started February)
Inês Correia da Silva Pires Faleiro	Master Degree	PhD Student
João Maria Rodrigues Perlico da Cruz Sabino	Master Degree	PhD Student
Madalena Isabel Reto de Almeida	Master Degree	PhD Student
Maria João Rodrigues da Silva	PhD	Senior Postdoctoral Researcher (Left August)
Naike Salvador Moreno	PhD	Senior Postdoctoral Researcher
Robert Manfred Martin	PhD	Senior Postdoctoral Researcher

Graphical Abstract



Lab Interests

Research in our laboratory aims at understanding the mechanistic links between transcription and DNA damage and at deciphering their functional relevance. We seek to clarify the principles of the reciprocal interactions between transcription and DNA damage, focusing on the role of chromatin as a communication node between them.

To answer our questions, we follow a strong interdisciplinary experimental strategy that combines state-of-the-art molecular biology, genome editing, advanced single-molecule live-cell microscopy, and robust computational biology tools. Our long-term research goals are to elucidate the physiological relevance of DNA damage in the onset of age-related phenotypes and to scrutinize aspects of the DNA damage response that are compromised in cancer cells.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Physiology in Health, Disease and Aging

Major Scientific Achievements in 2021

During the last year, our lab has made important contributions to our research field. We spearheaded the development of a set of cutting-edge reporters that allow the direct visualization of break-induced transcription with single-molecule resolution upon the controlled induction of a unique DNA double-strand break (DSB) (de Almeida MR., et al 2021). We disclosed a novel epigenetic determinant of non-canonical DNA structures that are relevant for the regulation of gene expression programs in stem cells (Sabino JC., et al. 2021). Our collaboration with the Ronen lab in the Weizmann Institute in Israel revealed that reduced lamin A/C content compromises lung metastasis after extravasation but not the transendothelial migration capacity of metastatic cancer cells (Roncato F., et al. 2021).

Ongoing Projects in 2021

2021/2024: O Papel da Transcrição Induzida por Quebras do DNA no Envelhecimento - Decoding the Role of DNA Break-Induced Transcription in Ageing. Coordinator: Sérgio de Almeida. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-OUT/4301/2020. Amount: 249 925,00€. Total Amount: 249 925,00€.

2021/2022: Examine the contribution of “jumping genes” to Rett syndrome. Coordinator: Sérgio de Almeida. Funding Agency: Rett Foundation. Reference: INTERNATIONAL RETT FOUNDATION 2021 - ANNE VALERIE. Amount: 50 000,00€. Total Amount: 50 000,00€.

2018/2021: Papel fisiológico de inactivação seletiva de núcleos em células multinucleadas. Coordinator: Robert Martin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: ENUCLEATE - LISBOA-01-0145-FEDER-032271. Amount: 239 227,92€. Total Amount: 239 227,92€.

2018/2021: O papel determinante que lesões no DNA desempenham na transcrição e o seu impacto na diferenciação celular e em cancro. Coordinator: Sérgio de Almeida. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: BREAKandENTER - LISBOA-01-0145-FEDER-030438. Amount: 239 753,90€. Total Amount: 239 753,90€.

Scientific Impact

Selected Publications

Vítor AC, Sridhara SC, Sabino JC, Afonso AI, Grosso AR, Martin RM, de Almeida SF. (2019) [Single-molecule imaging of transcription at damaged chromatin](#) **Science Advances**, Jan 9, Vol 5, Issue 1.

Relevance of the publication: To investigate with unprecedented detail how DNA double-strand breaks (DSB) impact transcription, we established new reporters to visualize nascent RNA transcripts with high spatial precision and temporal resolution in live cells, upon the induction of a single DSB. Live-cell imaging of transcription of our reporter genes revealed that induction of a DSB rapidly suppresses pre-existing transcription regardless of the genomic location. However, while transcription is irreversibly suppressed upon a promoter-proximal DSB, DNA damage within the gene body drives the formation of a promoter-like nucleosome-depleted region and transcription initiation. Two-colour labelling of RNA transcripts at sequences flanking the DSB revealed bidirectional transcription initiating at broken DNA ends. Analysis of publicly available RNA-seq data further showed that DNA break-induced transcription initiation is a widespread feature associated with spontaneously occurring intragenic DSBs.

Sridhara SC, Carvalho S, Grosso AR, Gallego-Paez LM, Carmo-Fonseca M, de Almeida SF. (2017) [Transcription dynamics prevent RNA-mediated genomic instability through SRPK2-dependent DDX23 phosphorylation](#) **Cell Reports**, Jan 10; 18(2):334-343.

Relevance of the publication: Transcription poses important threats to genome stability. For instance, R-loops – a natural by-product of transcription – can cause DNA damage. R-loops are three-stranded nucleic acid structures formed when the nascent RNA invades the DNA duplex resulting in a DNA:RNA hybrid and a displaced single-stranded DNA sequence. In an attempt to elucidate mechanisms that sense, signal, and suppress R-loops, we asked whether changes in transcription dynamics, namely RNA polymerase II pausing, could act as R-loop-sensor. Indeed, we found that R-loops slow down RNA polymerase II complexes, driving SRPK2-dependent phosphorylation of the DDX23 helicase, which culminate in R-loop suppression. In agreement, we observed that knockdown of either *SRPK2* or *DDX23* drive R-loop-dependent genome instability and that mutations in these genes are frequent in cancer cells.

Grosso AR, Leite AP, Carvalho S, Matos MR, Martins FB, Vítor AC, Desterro JM, Carmo-Fonseca M, de Almeida SF. (2015) [Pervasive transcription read-through promotes aberrant expression of oncogenes and RNA chimeras in renal carcinoma](#) **eLife**, 2015 Nov 17, eLife.09214

Relevance of the publication: Widespread induction of long transcripts extending beyond the canonical poly(A) site is a phenomenon that we and others recently reported to naturally arise in response to different stimuli. While we observed the dramatic induction of transcription readthrough in human cancer cells, the Dolken and Steitz labs documented similar transcripts in cells infected with virus and under osmotic stress, respectively. In our study, we further identified epigenetic deregulation, namely mutations in the SETD2 histone methyltransferase, as a major driver of transcription read-through.

Carvalho S, Vitor A, Sridhara SC, Martins FB, Raposo AC, Desterro JM, Ferreira J, de Almeida SF (2014). [SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint](#), **eLife**, May 6;3:e02482.

Relevance of the publication: DSBs are repaired by two major pathways: non-homologous end joining (NHEJ) and homologous recombination (HR). NHEJ is rapid but error-prone (i.e. the repaired sequence is often mutated), whereas HR is slower but highly accurate. While mutations in the non-coding genome are probably less harmful than the persistence of a DSB, the same may not be true for protein-coding genes.

In particular mutations in tumour suppressors or oncogenes could lead to cancer. Consistently, we found that DSBs in protein-coding genes are preferentially repaired by the error-free HR pathway. We observed that the H3K36me3 histone modification (found in all transcribed chromatin) recruits homologous recombination factors to active genes. This study revealed a hitherto unknown segregation of DNA repair pathways that is determined by the transcriptional status of the damaged sequence. Mechanistically, we found that H3K36me3 is necessary for the formation of RAD51 microfilaments at resected DNA ends.

Carvalho S, Raposo AC, Martins FB, Grosso AR, Sridhara SC, Rino J, Carmo-Fonseca M, de Almeida SF. (2013) [Histone methyltransferase SETD2 coordinates FACT recruitment with nucleosome dynamics during transcription](#) **Nucleic Acids Research**, Mar 1;41(5):2881-93.

Relevance of the publication: In this study, we show that loss of the SETD2 chromatin modifying enzyme results in impaired definition of transcription start sites. This leads to the generation of RNA transcripts with truncated 5' sequences, which we found significantly enriched in cancer cells. Mechanistically, we show that SETD2 activity is necessary to recruit the FACT histone chaperone and maintain the nucleosome occupancy at active genes. When SETD2 is mutated, the formation of promoter-like nucleosome-depleted regions creates entry sites for RNA polymerase II (RNA pol II), driving intragenic transcription initiation.

2021 Publications in Peer-Reviewed Journals

Barreto VM, Kubasova N, Alves-Pereira CF, Gendrel AV. (2021) [X-chromosome inactivation and autosomal random monoallelic expression as "faux amis"](#). **Front Cell Dev Biol**. Sep 23;9:740937.

de Almeida MR, Gameiro E, de Almeida SF, Martin RM, (2021) [Live-cell imaging of transcriptional activity at DNA double-strand breaks](#), **Journal of Vis. Exp.** (175), e62968.

Gomes ER, de Almeida SF. (2021) [TREX1-dependent DNA damage links nuclear rupture to tumor cell invasion](#), **Developmental Cell**. Nov 22;56(22):3040-3041

Marion-Poll L., Foret B., Zielinski D., Massip F., Attia M., Carter AC., Syx L., Chang HY., Gendrel A-V., and Heard E. (2021) [Locus specific epigenetic modalities of random allelic expression imbalance](#). **Nat Commun**. Sep 9;12(1):5330.

Raposo AC, Casanova M, Gendrel AV, da Rocha ST. 2021. [The tandem repeat modules of Xist lncRNA: a swiss army knife for the control of X-chromosome inactivation](#). **Biochem Soc Trans**.

Roncato F, Regev O, Feigelson SW, Yadav SK, Kaczmarczyk L, Levi N, Drago-Garcia D, Ovadia S, Kizner M, Addadi Y, Sabino JC, Ovadya Y, de Almeida SF, Feldmesser E, Gerlitz G and Alon R. (2021) [Reduced Lamin A/C does not facilitate cancer cell transendothelial migration but compromises lung metastasis](#), **Cancers**, May 14;13(10):2383.

Silva-Navas J, Salvador N, Del Pozo JC, Benito C, Gallego FJ. (2021) [The rye transcription factor ScSTOP1 regulates the tolerance to aluminum by activating the ALMT1 transporter](#), **Plant Sci**. Sep;310:110951.

Pre-Print Publications

Sabino JC, de Almeida MR, Abreu PL, Ferreira AM, Domingues MM, Santos NC, Azzalin CM, Grosso AR, de Almeida SF*. (2021) [Epigenetic reprogramming by TET enzymes impacts co-transcriptional R-loops](#) **bioRxiv**.

Invited Lectures and Seminars

Gendrel AV. “Regulation of monoallelic expression: beyond X-chromosome inactivation.” Invited lecture for Institute of Genetics and Biophysics, Naples, Italy. May 31st, 2021.

Communications

Faleiro I, Moreno NS, Afonso AI, Lucas B, Gomes ER, Martin R, de Almeida SF. Unveiling the DNA damage response in multinucleated skeletal muscle cells. XIV PhD Students Meeting, 5th-7th May, Lisbon, Portugal, 2021. POSTER; NATIONAL CONFERENCE

Cristiana Morgado, Maria João Silva, Maria Luísa Alvarenga, de Almeida SF. Decoding R-Loops formation, function and relevance to cancer cells. XIV PhD Students Meeting, 5th-7th May, Lisbon, Portugal, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE

Organization of Conferences

Inês Faleiro and Madalena Almeida. Organizers. XIV PhD Students Meeting, 5th-7th May, Lisbon, Portugal, 2021.

Networks & Research Infrastructures

Ribomed – EU Twinning project.

Prizes & Honors in 2021

During 2021, Sérgio de Almeida and Anne Valerie Gendrel acted as invited grant reviewers for the European Commission.

Advanced Teaching

During 2021, the members of our lab coordinated curricular units in the following graduate courses:

- Lisbon BioMed PhD Program - Instituto de Medicina Molecular JLA/Faculty of Medicine of the University of Lisbon
- Masters in Biomedical Research - Instituto de Medicina Molecular JLA/Faculty of Medicine of the University of Lisbon
- Masters in Oncobiology - Faculty of Medicine of the University of Lisbon

MSc Theses

Eduardo Luís Correia Gameiro (No 83764), 15/01/2021, Designing novel tools to detect and quantify non-canonical DNA structures, Técnico Lisboa, Supervisor’s Name: Robert Martin.

Inês Cardial Mendes Dias (No 86710), 30/11 2021. Establishing cellular models to investigate the role of LINE-1 elements in X-chromosome inactivation and genome stability. Técnico Lisboa, Supervisor’s Name: Anne-Valerie Gendrel.

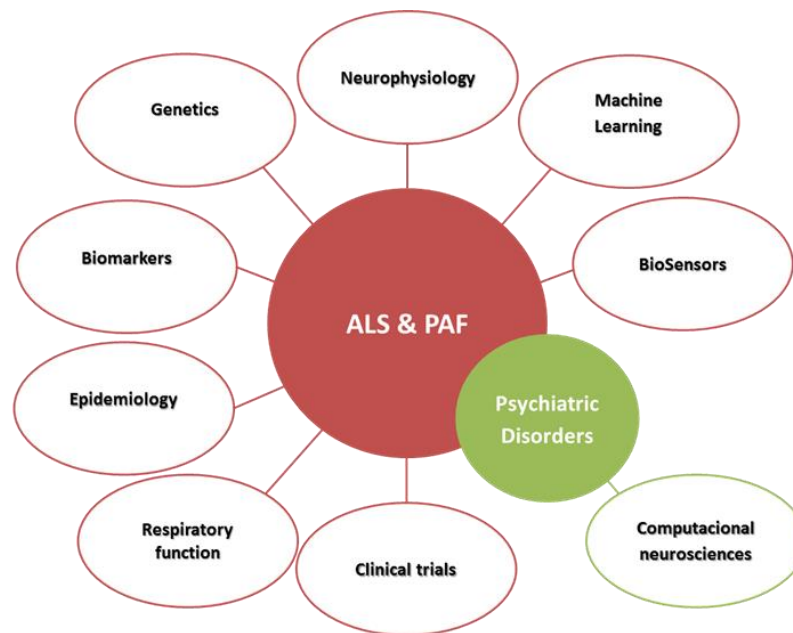
Mamede de Carvalho Lab

Head of Laboratory: Mamede Alves de Carvalho, MD, PhD, Group Leader and Full Professor of Physiology and Director of Physiology Institute and Vice-Dean of the Faculty of Medicine, Faculdade de Medicina da Universidade de Lisboa and Graduated Senior Consultant, Neurologist and Clinical Neurophysiologist of CHULN-HSM, head of the ALS Clinic of CHULN-HSM.

Team

Ana Catarina de Oliveira da Silva Pronto Laborinho	PhD	Clinical Researcher
Ana Catarina dos Santos Farinha	PhD	PhD Student (Left March)
Anabela Leuschner Fernandes Cardoso Pinto Noronha Sanches	MD/PhD	Clinical Researcher
Andreia Leitão Tavares Ribeiro dos Santos	University Degree	PhD Student
Ângelo Rodrigo Neto Dias	Master Degree	PhD Student
Anna Caroline Marques dos Anjos Braga	PhD	Clinical Researcher
Bruno André e Silva Miranda	PhD	Clinical Researcher
Bruno Daniel da Costa Gomes	PhD	Postdoctoral Researcher
Catarina Hoff Falcão de Campos	MD/Master Degree	Clinical Researcher (Started January)
Cristiano Torres Tavares dos Santos	Master Degree	Clinical Researcher
Diana Nicolau Candeias Monteiro Lopes	University Degree	MSc Student (Started December)
Fernando Manuel Pinto Ferreira Domingos	PhD	Clinical Researcher
Francisco José Correia Graça Almeida	Master Degree	Trainee
Gabriel Miltényi-Miltenberger	PhD	Staff Scientist
Inês Alexandra Ribeiro Lopes Alves	Master Degree	Lab Technician (Started April)
Isabel Maria dos Santos Conceição	University Degree	Clinical Researcher
Isabel Martins de Castro	University Degree	Technician
José Filipe Oliveira Castro	Master Degree	Senior Technician
Lena Helene Ernst	PhD	Postdoctoral Researcher
Leonel Almeida Luis	MD/PhD	Clinical Researcher
Mariana Fernandes Alves Pereira	Master Degree	PhD Student
Marta Luísa Gromicho Morgado da Silva	PhD	Senior Postdoctoral Researcher
Michael Swash	PhD	Clinical Researcher
Miguel Ângelo de Oliveira Santos	MD/Master Degree	Clinical Researcher (Started January)
Sofia Rita Cardoso Fernandes	PhD	Postdoctoral Researcher
Susana Cristina da Costa Pinto	PhD	Visiting Researcher
Tiago Vaz Maia	PhD	Staff Scientist
Vasco Manuel Aranha da Conceição	PhD	Postdoctoral Researcher (Left December)

Graphical Abstract



Lab Interests

This Unit aims to further develop the main areas where it has been highly competitive internationally. In particular: markers for early diagnosis, including wet biomarkers; epidemiology and treatment effectiveness/costs in hATTR amyloidosis; neurophysiology, phenotype-genotype, sensors and data mining in amyotrophic lateral sclerosis (ALS); clinical trials in hATTR amyloidosis and ALS; and computational models in behaviour and basal ganglia dysfunction. We intend to increment the progressive involvement in international projects associated with very productive centres located in Europe and USA, promoting scientific development and higher output in topics of this Unit expertise.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

Our Unit is involved in neuromuscular disorders, in particular amyotrophic lateral sclerosis (ALS) and hATTR amyloidosis, and in the nascent field of computational psychiatry. We have increased our output in the main areas of research, with important contributions published regarding the dopaminergic dysfunction in Tourette Syndrome, learning, modulation of the spinal cord and peripheral nerve on direct current stimulation, markers of diagnosis and progression in ALS, respiratory neurophysiology, novel treatments and its impact in hATTR amyloidosis, data mining and artificial intelligence, and sensors. Also, we published results on the genetic mutations, predictors and wet-biomarkers in ALS, clinical/neurophysiological features and epidemiology of

hATTR amyloidosis. Our participation in several competitive projects in ALS will promote additional future publications.

Ongoing Projects in 2021

2021/2024: AlpALS - Advanced learning models using Patient profiles and disease progression patterns for prognostic prediction in ALS. Participant: Mamede de Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CCI-CIF/4613/2020 - AIPALS. Amount: 30 832,50€. Total Amount: 30 832,50€.

2021/2024: Participant: Mamede de Carvalho. Funding Agency: Ono Pharm. Amount: 10 200,00€. Total Amount: 10 200,00€.

2021/2024: BrainTeaser. Local Coordinator: Mamede de Carvalho. Funding Agency: European Commission. Reference: SC1-DTH-02-2020 – BRAINTEASER. Amount: 315 690,00€. Total Amount: 315 690,00€.

2021/2023: Home-based monitoring of functional disability in amyotrophic lateral sclerosis with mobile sensing. Coordinator: Bruno André e Silva Miranda. Co-Coordinator: Mamede de Carvalho Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MEC-NEU/6855/2020 - HOME SENSE. Amount: 61 064,98€. Total Amount: 61 064,98€.

2018/2021: Avaliação detalhada de microRNA circulantes como biomarcadores de diagnóstico e prognóstico em Esclerose Lateral Amiotrófica. Coordinator: Mamede de Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MEC-NEU/31195/2017. Amount: 155 615,31€. Total Amount: 239 294,65€.

2018/2021: Investigação Síndrome Tourette. Coordinator: Tiago Maia. Funding Agency: Ampastta. Reference: Investigação Síndrome Tourette. Amount: 9 183,50€. Total Amount: 9 183,50€.

2017/2021: Computational Psychiatry Consulting on Pediatric Mental Illnesses. Coordinator: Tiago Maia. Funding Agency: National Institutes of Health (NIH). Reference: Computational Psychiatry Consulting on Pediatric Mental Illnesses. Amount: 30 903,27€. Total Amount: 30 903,27€.

Scientific Impact

Academic Collaborations

Amy Margolis, Columbia University

Carles Soriano-Mas, Institut d'Investigació Biomèdica de Bellvitge and University of Barcelona

Klaas Stephan, ETH and University of Zurich

Sara Madeira, LASIGE, Faculdade de Ciências da Universidade de Lisboa, Lisbon,

Julia Costa, Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa

Nuno Correia Santos e Filomena de Carvalho, Instituto de Bioquímica, Faculdade de Medicina da Universidade de Lisboa, Instituto de Medicina Molecular João Lobo Antunes

Hatice Tankisi, Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus, Denmark

Steve Vucic, The University of Sydney Westmead Clinical School, Sydney, NSW 2145, Australia
MiNE Project, Multicenter- International, Brainteaser Project – European, Multicenter

Hugo Gamboa, Fraunhofer Portugal

Pedro Miranda, IBEB, Faculdade de Ciências da Universidade de Lisboa, Lisbon

Sofia Fernandes, IBEB, Faculdade de Ciências da Universidade de Lisboa, Lisbon

Selected Publications

Maia TV, Frank MJ. [An integrative perspective on the role of dopamine in schizophrenia](#). **Biol Psychiatry** 2017;1;81(1):52-66.

Relevance of the publication: Taken together, then, these two disturbances explain many findings in schizophrenia. We review evidence supporting their co-occurrence and consider their differential implications for the treatment of positive and negative symptoms.

Conceição I, Miranda B, Castro J, de Carvalho M (2018). [Hereditary amyloidosis related to transthyretin V30M \(hATTR V30M\): disease progression in treated and untreated patients](#). **Eur J Neurol** 25, 1320-e115.

Relevance of the publication: Both liver transplantation and tafamidis therapy modified the natural history of hATTR V30M by reducing neuropathy progression.

Miltenberger-Miltenyi G, Conceição VA, Gromicho M, Pronto-Laborinho AC, Pinto S, de Carvalho M (2019). [C9orf72 expansion is associated with accelerated decline of respiratory function and decreased survival in amyotrophic lateral sclerosis](#). **J Neurol Neurosurg Psychiatry** 90(1):118-120.

Relevance of the publication: Our study shows that the C9orf72 expansion is independently associated with accelerated respiratory dysfunction and shorter survival in ALS.

Fernandes SR, Salvador R, Wenger C, de Carvalho M, Miranda PC (2018). [Transcutaneous spinal direct current stimulation of the lumbar and sacral spinal cord: a modelling study](#). **J Neural Eng** 15(3):036008.

Relevance of the publication: Computational modelling studies can provide detailed information regarding the electric field in the spinal cord during tsDCS. They are important to guide the design of clinical tsDCS protocols that optimize stimulation of application-specific spinal targets.

Gromicho M, Figueiral M, Uysal H, Grosskreutz J, Kuzma-Kozakiewicz M, Pinto P, Petri S, Madeira S, Swash M, de Carvalho M (2020). [Spreading in ALS: the relative impact of upper and lower motor neuron involvement](#). **Ann Clin Transl Neurol** 7:1181-1192. (IF: 3.930, Citation 8).

Relevance of the publication: Our results can best be fitted to a model of independent LMN and UMN degeneration, with regional progression of LMN degeneration mostly by contiguity. UMN lesion causes an acceleration of rostral-caudal LMN loss.

2021 Publications in Peer-Reviewed Journals

Adams D, Polydefkis M, González-Duarte A, Wixner J, Kristen AV, Schmidt HH, Berk JL, Losada López IA, Dispenzieri A, Quan D, Conceição IM, Slama MS, Gillmore JD, Kyriakides T, Ajroud-Driss S, Waddington-Cruz M, Mezei MM, Planté-Bordeneuve V, Attarian S, Mauricio E, Brannagan TH 3rd, Ueda M, Aldinc E, Wang JJ, White MT, Vest J, Berber E, Sweetser MT, Coelho T. Patisiran Global OLE study group. (2021). [Long-term safety and efficacy of patisiran for hereditary transthyretin-mediated amyloidosis with polyneuropathy: 12-month results of an open-label extension study](#). **Lancet Neurol.** 2021 Jan;20(1):49-59. Erratum in: *Lancet Neurol.* 2021 Feb;20(2):e2. PMID: 33212063

Caponetti AG, Rapezzi C, Gagliardi C, Milandri A, Dispenzieri A, Kristen AV, Wixner J, Maurer MS, Garcia-Pavia P, Tournev I, Planté-Bordeneuve V, Chapman D, Amass L; THAOS Investigators. (2021) [Sex-Related Risk of Cardiac Involvement in Hereditary Transthyretin Amyloidosis: Insights From THAOS](#). **JACC Heart Fail.** Oct;9(10):736-746. Epub 2021 Aug 11. PMID: 34391735.

Carvalho, J., Conceição, V. A., Mesquita, A., & Seara-Cardoso, A. (2021). [Acute stress impairs reward learning in men](#). **Brain and Cognition**, 147, 105657.

Carvalho, J., Conceicao, V. A., Mesquita, A., & Seara-Cardoso, A. (2021). [Acute stress blunts prediction error signals in the dorsal striatum during reinforcement learning](#). **Neurobiology of Stress**, 15, 100412.

Castro J, Miranda B, de Castro I, Conceição I. (2021). [Changes in nerve conduction studies predate clinical symptoms onset in early onset Val30Met hereditary ATTR amyloidosis](#). **Eur J Neurol.** Nov 9. PMID: 34751997.

Castro J, Swash M, de Carvalho M (2021). [The Cutaneous Silent Period in Motor Neuron Disease](#). **Clin Neurophysiol** 132:660-665.

Corcia C, Bede P, Pradat P-F, Couratier P, Vucic S, de Carvalho M (2021) [Split-hand and split-limb phenomena in Amyotrophic Lateral Sclerosis: pathophysiology, electrophysiology and clinical manifestations](#). **J Neurol Neurosurg Psychiatry**.

Corcia P, Lunetta C, Couratier P, Vourch P, Gromicho M, Desnuelle C, Soriani M, Pinto S, de Carvalho M (2021). [Familial clustering of PLS and ALS: A supplementary evidence for a continuum](#). **Eur J Neurol**.

Costa J, Gromicho M., Pronto-Laborinho A.C., Almeida C., Gomes R.A., Guerreiro A.C.L, Oliva A., Pinto S., de Carvalho M (2021). [Cerebrospinal fluid chitinases as biomarkers for amyotrophic lateral sclerosis](#). **Diagnostics**.

Damy T, Conceição I, García-Pavía P, Gillmore J, Jandhyala R, Sabbat J, Wixner J, Coelho T. [A simple core dataset and disease severity score for hereditary transthyretin \(ATTRv\) amyloidosis](#). **Amyloid.** Sep;28(3):189-198.

- de Carvalho M (2021). [Spiral of History: SARS-CoV-2 infection](#). **Clin Neurophysiol**.
- de Carvalho M, Swash M (2021). [Levosimendan for amyotrophic lateral sclerosis](#). **Lancet Neurol**.
- de Carvalho M., Gromicho M., Andersen PM, Grosskreutz J, Kuźma-Kozakiewicz M, Petri S, Uysal U, Pinto S (2021). [Peripheral neuropathy in ALS: phenotype association](#). **J Neurol Neurosurg Psychiatry** 92:1133-1134.
- Falcão de Campos C, Gromicho M, Uysal H, Grosskreutz J, Kuzma-Kozakiewicz M, Oliveira Santos M, Pinto S, Petri S, Swash M, de Carvalho M (2021). [Delayed diagnosis and diagnostic pathway of ALS patients in Portugal: where can we improve?](#) **Frontiers Neurol**.
- Farinha, A. C., & Maia, T. V. (2021). [People exert more effort to avoid losses than to obtain gains](#). **Journal of Experimental Psychology: General** 150(9), 1837–1853 (IF: 4.913).
- Fonseca AC, Almeida AG, Oliveira Santos M, Ferro JM (2021). [Neurological complications of cardiomyopathies](#). **Handb Clin Neurol** 177:91-109. Review.
- Ferro JM, Oliveira Santos M (2021). [Neurology of inflammatory bowel disease](#). **J Neurol Sci** 15;424: 117426. Review.
- Leão T, Madeira SC, Gromicho M, de Carvalho M, Carvalho AM (2021). [Learning dynamic Bayesian networks from time-dependent and time-independent data: unraveling disease progression in Amyotrophic Lateral Sclerosis](#). **J Biomed Inform** 117:103730.
- Martins AS, Gromicho M, Pinto S, de Carvalho M, Madeira SC (2021). [Learning Prognostic Models using Disease Progression Patterns: Predicting the Need for Non-Invasive Ventilation in Amyotrophic Lateral Sclerosis](#). **IEEE/ACM Trans Comput Biol Bioinform**.
- Moisse M, Zwamborn R, van Vugh J, van Rheenen W, Kenna B, van Eijk K, Kenna K, Corcia P, Couratier P, Hardiman O, McLaughlin R, Gotkine M, Drory V, Ticozzi N, Silani V, de Carvalho M, Pardina M, Povedano M, Andersen PM, Weber M, Badsak NA, Chen X, Eberle MA, Al-Chalabi A, Shaw C, Shaw PJ, Morrison KE, Landers JE, Glass JD, van Es M, van den Berg L, Veldink J, Van Damme P, on behalf of Project MinE Sequencing Consortium (2021). [The effect of SMN gene dosage on ALS risk and disease severity](#). **Ann Neurol** 89:686-97.
- Morgadinho, J.*, Pronto-Laborinho, A. C.*, Conceição, V. A.*, Gromicho, M., Pinto, S., Swash, M., & de Carvalho, M. (2021). [Plasma Creatinine Level Does Not Predict Respiratory Function in Amyotrophic Lateral Sclerosis](#). **Journal of Neuromuscular Diseases**, 8, 795-799.
- Montalvo A, Swash M, de Carvalho M (2021). [Benign Fasciculations: a follow-up study with electrophysiological studies](#). **Muscle Nerve**.

Muller M, Gromicho M, de Carvalho M, Madeira SC (2021). [Explainable Models of Disease Progression in ALS: Learning from Longitudinal Clinical Data with Recurrent Neural Networks and Deep Model Explanation](#). **Comput Methods Programs Biomed**.

Nunes Vicente B, Oliveira Santos M (2021). [Unexpected but successful non-instrumental vaginal delivery in a spinal muscular atrophy type II pregnant patient](#). **Neurol Sci** 42(9):3901-3902.

Oliveira Santos M, Castro I, Castro J, Gromicho M, de Carvalho M (2021). [Assessment of sympathetic sudomotor function in amyotrophic lateral sclerosis with electrochemical skin conductance](#). **Clin Neurophysiol**. 132(9):2032-2036.

Oliveira Santos M, Leal Rato M (2021). [Neurology of the acute hepatic porphyrias](#). **J Neurol Sci** 15;428:117605. Review.

Oliveira R, Ramalho Rocha F, Teodoro T, Oliveira Santos M (2021). [Acute non-traumatic tetraparesis – Differential diagnosis](#). **J Clin Neurosci** 87:116-124. Review.

Pereira M, Gromicho M, Henriques A, Pronto-Laborinho AC, Grosskreutz J, Kuźma-Kozakiewicz M, Petri S, Uysal H, Swash M, de Carvalho M. [Cardiovascular comorbidities in amyotrophic lateral sclerosis](#). **J Neurol Sci**. 2021 Feb 15;421:117292.

Pinto S, de Carvalho M (2021). [Phrenic nerve study as inclusion criterion and outcome in clinical trials for amyotrophic lateral sclerosis](#). **Amyotr Lat Scler Frontotemporal Degener** 22 (suppl 1):9-13.

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Portêlo, A., Shiban, Y., Maia, T. V. (2021). [Mathematical characterization of changes in fear during exposure therapy](#). **Biological Psychiatry: Cognitive Neuroscience and Neuroimaging** 6(11):1090-1099.

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Pugdahl K, Camdessanché JP, Cengiz B, de Carvalho M, Liguori R, Rossato C, Oliveira Santos M, Vacchiano V, Johnsen B (2021). [Gold Coast diagnosis criteria increase sensitivity in amyotrophic lateral sclerosis](#). **Clin Neurophysiol** 132(12):3183-3189.

Quintão C, Vigário R, Santos MM, Gomes AL, de Carvalho Pinto S, Gamboa H (2021). [Surface electromyography for testing motor dysfunction in amyotrophic lateral sclerosis](#). **Neurophysiol Clin**.

Rudnicki SA, Andrews JA, Bian A, Cockroft BM, Cudkowicz ME, Hardiman O, Malik FI, Meng L, Wolff AA, Shefner JM & ON BEHALF OF THE VITALITY-ALS STUDY GROUP (2021). [Noninvasive ventilation use by patients enrolled in VITALITY-ALS](#). **Amyotr Lat Scler Frontotemporal Degener.**

Santos M, Reimão S, de Carvalho M (2021). [Mimicking amyotrophic lateral sclerosis: a case of a spinal dural arteriovenous fistula](#). **Case Rep Neurol** 13:802–806. Q3

Shepherd SR, Parker MD, Cooper-Knock J, Verber NS, Tuddenham L, Heath PR, Beauchamp N, Place E, Sollars ESA, Project MinE ALS Sequencing Consortium, Turner MR, Malaspina A, Fratta P, Hewamadduma C, Jenkins TM, McDermott CJ, Wang D, Kirby J, Shaw PJ (2021). [Value of systematic genetic screening of patients with amyotrophic lateral sclerosis](#). **J Neurol Neurosurg Psychiatry** 92:510-8.

Silva CS, Oliveira Santos M, Gromicho M, Pinto P, Swash M, de Carvalho M (2021). [Electromyographic findings in primary lateral sclerosis during disease progression](#). **Clin Neurophysiol.**

Tankisi H, Nielsen C S-Z, Howells J, Cengiz B, Samusyte G, Koltzenburg M, Blicher J, Møller A, Pugdahl K, Fuglsang-Frederiksen A, de Carvalho M, Bostock H (2021). [Early diagnosis of amyotrophic lateral sclerosis by threshold tracking and conventional transcranial magnetic stimulation](#). **Eur J Neurol.**

Yarlas A, Lovley A, McCausland K, Brown D, Vera-Llonch M, Conceição I, Karam C, Khella S, Obici L, Waddington-Cruz M. (2021). [Early Data on Long-term Impact of Inotersen on Quality-of-Life in Patients with Hereditary Transthyretin Amyloidosis Polyneuropathy: Open-Label Extension of NEURO-TTR](#). **Neurol Ther.** Dec;10(2):865-886.

Pre-Print Publications

Muller TH, Butler JL, Veselic S, Miranda B, Behrens TEJ, Kurth-Nelson Z, Kennerley SW (2021). Distributional reinforcement learning in prefrontal cortex. bioRxiv. Jun;14.448422.

Invited Lectures and Seminars

de Carvalho, M., Motor Unit Potentials: its meaning for diagnosis. NATUS NEURO TRAINING ACADEMY. ONLINE, Março de 2021.

de Carvalho, M., Motor Neuron Diseases, NEURODEGENERATIVE DISEASES - Advanced Course. ONLINE, Março de 2021.

de Carvalho, M., Electrophysiology for monitoring progression in ALS. 25th CONGRESS of the MEDICAL-SCIENTIFIC ADVISORY BOARD of the GERMAN MUSCULAR DYSTROPHY SOCIETY (DGM). ONLINE, Março de 2021.

de Carvalho, M., Doença do Neurónio Motor, CICLO de PALESTRAS MEDICINA. ONLINE, Abril de 2021

de Carvalho, M., Avanços Terapêuticos na Esclerose Lateral Amiotrófica. III SIMPÓSIO INTERNACIONAL da ESCLEROSE LATERAL AMIOTRÓFICA. ONLINE, Abril de 2021.

de Carvalho, M., Neurophysiological Evaluation in ALS. 28º CONGRESS of the BRAZILIAN CLINICAL NEUROPHYSIOLOGY SOCIETY. Online. Dezembro de 2021.

de Carvalho, M., Motor Unit Potentials: its meaning for diagnosis, NATUS NEURO TRAINING ACADEMY. ONLINE, Março de 2021.

de Carvalho, M., Motor Neuron Diseases. NEURODEGENERATIVE DISEASES - Advanced Course. ONLINE, Março de 2021.

de Carvalho, M., Electrophysiology for monitoring progression in ALS 25th CONGRESS of the MEDICAL-SCIENTIFIC ADVISORY BOARD of the GERMAN MUSCULAR DYSTROPHY SOCIETY (DGM). ONLINE, Março de 2021.

de Carvalho, M., Doença do Neurónio Motor, CICLO de PALESTRAS MEDICINA. ONLINE, Abril de 2021.

de Carvalho, M., Avanços Terapêuticos na Esclerose Lateral Amiotrófica, III SIMPÓSIO INTERNACIONAL da ESCLEROSE LATERAL AMIOTRÓFICA. ONLINE, Abril de 2021.

de Carvalho, M., Marcadores Biológicos e Clínicos da ELA/DNM, XX SIMPÓSIO BRASILEIRO de ELA/DNM – ABrELA. ONLINE, Junho de 2021.

de Carvalho, M., Mesa Redonda: Clínica e Diagnóstico, DIA MUNDIAL DA ELA – APELA. ONLINE, Junho de 2021.

de Carvalho, M., Neurophysiological Evaluation in ALS. 28th BRAZILIAN CONGRESS of CLINICAL NEUROPHYSIOLOGY, Novembro de 2021.

Conceição, V.A., *Tourette syndrome from a computational perspective*. IDIBELL Seminars, Barcelona, Spain (but the seminar was remote/online), March 26th, 2021.

Pronto-Laborinho, A.C., "Biomarcadores moleculares na abordagem clínica na esclerose lateral amiotrófica", 3ª edição de Seminários do Mestrado em Tecnologias Moleculares em Saúde. (Webinar) Abril de 2021.

Pronto-Laborinho, A.C, BIOMARKERS IN ALS/MND, International Alliance of ALS/MND Associations " (Webinar), Julho 2021.

Conceição I., Establishing the diagnosis of ATTRv amyloidosis. 3rd European ATTR Amyloidosis meeting for Patients and Doctors (virtual). 2021.

Conceição I., Management of ATTR amyloidosis: The benefit of early diagnosis. (Virtual). Simposium Satélite no 7º Congresso da AEN, Junho 2021.

Conceição I., Highlights das Doenças Neuromusculares no 7º Congresso da EAN, 2021. (Virtual). Julho de 2021.

Conceição I., Precision Neurology in Neuromuscular Disorders: Spinal Muscular Atrophy. Congresso da Sociedade Portuguesa de Neurologia, 27-30, Albufeira, Portugal, Outubro 2021.

Conceição I., Management of ATTR amyloidosis: The benefit of early diagnosis. ATTR amyloidosis – navigating this multifaceted A Pfizer-sponsored satellite symposium at the 7th Congress of the European Academy of Neurology (Virtual), 19-22 Junho.

Communications

Santos Silva, C; Gromicho, M; Oliveira Santos, M; de Carvalho, M. Electromyographic findings in primary lateral sclerosis: a follow-up study. 7th CONGRESS of the EUROPEAN ACADEMY of NEUROLOGY. Virtual, Junho de 2021, Comunicação em “e-poster” INTERNATIONAL CONFERENCE.

Santos Silva, C; Oliveira Santos, M; Gromicho, M; Laborinho-Pronto, AC; de Carvalho, M. Phenotypic heterogeneity of C9orf72 gene expansion in a Portuguese family. 7th CONGRESS of the EUROPEAN ACADEMY of NEUROLOGY. Virtual, Junho de 2021, Comunicação em “e-poster” INTERNATIONAL CONFERENCE.

Fernandes, SR; Elbasiouny, S; Pereira, M; Dhaher, M; de Carvalho, M; Miranda, PC. Interplay between electrical conductivity of tissues and position of electrodes in transcutaneous spinal direct current stimulation (tsDCS). BRAIN and HUMAN MODELLING. Virtual, Agosto de 2021, ORAL COMMUNICATION, INTERNATIONAL CONFERENCE.

Costa, J; Laborinho-Pronto, AC; Pinto, S; Gromicho, M M; Bonucci, C; Tranfield, E; Correia, C; Alexandre, BM; Felgueiras, B; de Carvalho. Separation of extracellular vesicles from human cerebrospinal fluid, M. FIRST MEETING of the PORTUGUESE NETWORK on EXTRACELLULAR VESICLES. Porto, Setembro de 2021, ORAL COMMUNICATION, NATIONAL CONFERENCE.

Santos Silva, C; Gromicho, M; Oliveira Santos, M; Pinto, S; de Carvalho, M., Disfunção tiroideia em doentes Portugueses com esclerose lateral amiotrófica. 9º CONGRESSO PORTUGUÊS de DOENÇAS NEUROMUSCULARES – DOENÇAS NEUROMUSCULARES AUTOIMUNES. Online, Outubro de 2021, “e-poster” NATIONAL CONFERENCE.

Santos Silva, C; Oliveira Santos, Conceição I; de Carvalho, M., Esclerose lateral amiotrófica em três doentes assintomáticos portadores da mutação Val50Met no gene TTR. 9º CONGRESSO PORTUGUÊS de DOENÇAS NEUROMUSCULARES – DOENÇAS NEUROMUSCULARES AUTOIMUNES. Online, Outubro de 2021, “e-poster” NATIONAL CONFERENCE.

Vitor J, Dionisio JM, Campos C, Santos M, Cruz M, Castelo J, Castro J, Castro I, Santos M, Vale J, de Carvalho M, Conceição I. Incidência da Síndrome de Guillain-Barré durante a pandemia por SARS-CoV-2 - estudo retrospectivo multicêntrico, CONGRESSO DE NEUROLOGIA 2021. Santa Eulália, Outubro de 2021, ORAL COMMUNICATION, NATIONAL CONFERENCE.

Martins AS, Aidos H, Gromicho M, de Carvalho M, Madeira SC., Specialized prognostic models based on disease progression patterns: predicting non-invasive ventilation in ALS patients stratified by progression rate. CIBB 2021 COMPUTATIONAL INTELLIGENCE METHODS for BIOINFORMATICS and BIostatISTICS. Online, Novembro de 2021, ORAL COMMUNICATION, NATIONAL CONFERENCE.

Santos Silva, C; Oliveira Santos, M; Conceição I; de Carvalho, M. Amyotrophic lateral sclerosis in three asymptomatic Val50Met TTR gene carriers. 31th INTERNATIONAL SYMPOSIUM on ALS/MND (Online). Dezembro de 2021, E-poster Presentation; INTERNATIONAL CONFERENCE.

Santos Silva, C; Gromicho, M; Oliveira Santos, M; Pinto, S; de Carvalho, M. Thyroid disease in Portuguese amyotrophic lateral sclerosis patients: a case control study. 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online). Dezembro de 2021, E-poster Presentation; INTERNATIONAL CONFERENCE.

Pinto S, Gromicho M, Grosskreutz J, Kuzma-Kozakiewicz M, Petri S, Uysal H, Swash S, de Carvalho M. Spreading pattern in ALS patients with respiratory onset. 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online). Dezembro de 2021, E-poster Presentation; INTERNATIONAL CONFERENCE.

Alves, I; Gromicho, M; Pinto, Pinto; Oliveira Santos, M; de Carvalho, M. Clinical characteristics of a large motor neuron disease cohort in Portugal: exploring differences from 1994 to 2020. 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online), E-poster Presentation; INTERNATIONAL CONFERENCE.

Pronto Laborinho, A; Lopes C. Conceição, V; Gromicho, M; Santos, N; Carvalho, F; de Carvalho, M. Red cell distribution width (RDW) in ALS, 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online), E-poster Presentation; INTERNATIONAL CONFERENCE.

Rudnicki, SA; Shefner, JM; Cudkowicz, ME; Genge A; Hardiman, O; Al Chalabi, A; Andrews, JA; Chio, A; Corcia, P; Couratier, P; de Carvalho, M; Patterson, TH; Henderson, R; Ingre, C; Johnston, W; Ludolph, L; Maragakis, NJ; Miller, TM; Pardina, JSM; Petri, S; Simmons, Z; van den Berg, LH; Zinman, L; Kupfer, S; Malik, FI; Meng, L; Wei, J; Wolff AA. Update of COURAGE ALS: A Phase 3, Double Blind, Randomized, Placebo Controlled, Study to Evaluate Efficacy and Safety of Reldesemtiv in Patients with ALS. 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online), E-poster Presentation; INTERNATIONAL CONFERENCE.

Campos, C; Gromicho, M; Uysal, H; Grosskreutz, J; Kuzma-Kozakiewicz, M; Oliveira Santos, M; Pinto, S; S. Petri, S; Swash, M; de Carvalho; M. Delayed diagnosis and diagnostic pathway of ALS patients in Portugal: where can we improve? 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online), E-poster Presentation; INTERNATIONAL CONFERENCE.

Oliveira Santos, M; Gromicho, M; Pinto, S; Swash, M; de Carvalho, M. Is dysphagia a predictive factor for survival in amyotrophic lateral sclerosis patients with severe respiratory failure? 31th INTERNATIONAL SYMPOSIUM on ALS/MND (online), E-poster Presentation; INTERNATIONAL CONFERENCE.

Abdulrehman J, [...] [Miranda B](#), [...], Skeith L, Risk of recurrence after stopping anticoagulants in women with combined contraceptive-associated venous thromboembolism: a systematic review and meta-analysis. *63rd American Society of Hematology*. Atlanta (Estados Unidos da América), 11-14 de dezembro de 2021. ORAL COMMUNICATION, INTERNATIONAL CONFERENCE.

Madeira P, Carreiro A, Gamboa H, Malalasekera WM, Dayan P, Kennerley SW, Miranda B, Using eye-tracking data to study models of attention and decision-making, *XVII Meeting da Sociedade Portuguesa de Neurociências (SPN2021)*, Coimbra, 1-3 de dezembro de 2021. Poster; National Conference.

Organization of Conferences

Bruno Miranda. Organizer. Evento anual do projeto eMOTIONAL Cities, Reitoria da Universidade de Lisboa, 22 e 23 de novembro de 2021.

Networks & Research Infrastructures

Bruno Miranda, “Urban health cluster” da Comissão Europeia– coordenador do grupo de trabalho sobre determinantes de saúde e intervenções urbanas, Reitoria da Universidade de Lisboa, 22 e 23 de novembro de 2021.

Prizes & Honors in 2021

Prémio BIAL de Medicina Clínica 2021 pelo trabalho “A Paramiloidose em Portugal e no mundo: de doença fatal a doença crónica com qualidade de vida preservada” (Coelho M, Conceição I, Inês M, de Carvalho M, Costa J).

Prémio Melhor Comunicação do 8º Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares pelo trabalho “Spreading in ALS: the relative impact of upper and lower motor neuron involvement” (de Carvalho M, Gromicho M, Figueiral M, Uysal H, Grosskreutz J, Kuzma-Kozakiewicz M, Pinto P, Petri S, Madeira S, Swash M), em 2021.

Prémio “ENCALS POSTER AWARD 2021”, pelo trabalho “Dynamic Bayesian networks for stratification of disease progression in ALS” (Gromicho, M; Leão, T; Carvalho, A; Madeira, SC; de Carvalho, M), em 2021.

Segundo Prémio da Melhor Comunicação do 9º Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares pelo trabalho “Esclerose lateral amiotrófica em três doentes assintomáticos portadores da mutação Val50Met no gene TTR” (Silva CS, Oliveira Santos M, Conceição I, de Carvalho M), em 2021.

Advanced Teaching

Tiago Maia. Module Coordination. Computational neuroscience. Mestrado/Doutoramento em Neurociências, Faculdade de Medicina, Universidade de Lisboa, May 31 – June 8, 2021.

Tiago Maia. Lecture. Motor system. Mestrado em Investigação Biomédica, Instituto de Medicina Molecular João Lobo Antunes e Faculdade de Medicina, Universidade de Lisboa, November 25, 2021.

Isabel Conceição. Seminar - Evoked Potentials and Small Fibers Neurophysiology, Seminar and Lessons in Master Degree and Doctoral Presentation Program on Neurosciences 2021, University of Lisbon, Lisbon, Portugal, Feb 24th 2021. University of Lisbon, Lisbon, Portugal.

Isabel Conceição. Seminar - Neuropathies: Transthyretin-Related Hereditary Amyloidosis. Seminar and Lessons in Master Degree and Doctoral Presentation Program on Neurosciences 2021, University of Lisbon, Lisbon, Portugal, Feb 4th, 2021. University of Lisbon, Lisbon, Portugal.

Mamede de Carvalho, EMG, nerve conduction studies and DCS, Seminar and Lessons in Master Degree and Doctoral Presentation Program on Neurosciences 2021, University of Lisbon, Lisbon, Portugal.

MSc Theses

Tatiana Duque, 2021, *The Influence of TDP-43 in TGF- β Serum Levels in Amyotrophic Lateral Sclerosis (ALS)*. Mestrado Integrado de Medicina Aprovado. Supervisor: Mamede Alves de Carvalho.

André Castanheira, 2021, *Percutaneous Gastrostomy in Amyotrophic Lateral Sclerosis: a review*. Mestrado Integrado de Medicina. Aprovado, em 2021. Supervisor: Mamede Alves de Carvalho.

Pedro Alexandre da Silva Faria Tavares, Julho 2020, *Associação entre fadiga e tomada de decisão baseada nas vias de esforço-recompensa na esclerose múltipla*. Mestrado Integrado de Medicina. Supervisor: Bruno Miranda. Co-Supervisor: Prof. Doutor João de Sá.

Renata Bastos da Silveira Pereira da Cruz, Março 2021. *The role of the ventral telencephalon in collective motion*. Mestrado de Neurociências FMUL. Supervisor: Bruno Miranda. Co-Supervisor: Gonzalo de Polavieja.

Inês Alexandra Ribeiro Lopes Alves, Fevereiro 2021. *Episodic and semantic memories in cognitive planning: evidence from a two-stage decision task*. Mestrado de Neurociências (FMUL); Supervisor: Bruno Miranda.

PhD Theses

Ana Catarina Farinha, 12/03/2021, *Effort to Win versus Effort to Avoid Losing: Relation to Loss Aversion and Alterations in Attention-Deficit/Hyperactivity Disorder*, Faculdade de Medicina, Universidade de Lisboa. Supervisor: Tiago V. Maia.

Ana Portêlo, 05/02/2021, *Modeling of Anxiety Ratings during Behavior Therapy for Specific Phobia and Obsessive-Compulsive Disorder*, Faculdade de Medicina, Universidade de Lisboa. Supervisor: Tiago V. Maia.

Mónica Sofia Inácio Duarte Inês Mestre, CAML-FML, com o título *“Health Economics of Hereditary Transthyretin Amyloidosis Polyneuropathy”*, Abril de 2021, Supervisor: Orientador, Prof João P Costa. Co- Supervisor: Mamede de Carvalho - aprovada por unanimidade, distinção e louvor.

André Caetano, Neurociências-FMUL, com o título *“Changes in peripheral nerve excitability by transcutaneous direct currents - results with threshold tracking”*, em curso. Supervisor: Mamede de Carvalho.

Mariana Reis da Costa, Neurociências-FMUL, com o título *“Transcranial repetitive and static magnetic stimulation and somatosensory evoked high frequency oscillations to study cortical and subcortical sensory-motor interactions in normal subjects and in Amyotrophic Lateral Sclerosis patients”*, em curso. Supervisor: Mamede de Carvalho.

Lígia Sofia Ferreira, Neurociências-FML, com o título *“Predictors of successful treatment of Refractory Status Epilepticus”*, em curso. Supervisor: Carla Bentes. Co-Supervisor: Mamede de Carvalho.

Mariana Fernandes Alves Pereira, NeurULisbon-UL, com o título provisório *“Neuromodulação dos circuitos motores espinhais através de estimulação transcutânea por corrente directa: implicações na Esclerose Lateral Amiotrófica”*, agora iniciada. Supervisor: Mamede de Carvalho.

Valorization of Knowledge / Social and Economic Impact

Policy

Miranda B. “Urban health cluster” da Comissão Europeia– coordenador do grupo de trabalho sobre determinantes de saúde e intervenções urbanas. Reitoria da Universidade de Lisboa, 22 e 23 de novembro de 2021.

Science and Society in 2021

Our Unit has a strong interaction with the Portuguese Association of Amyotrophic Lateral Sclerosis, M de Carvalho has participated regularly in events including patients and caregivers to promote health education and their more active feedback. Working with patients and patient organizations can bring significant public health benefits.

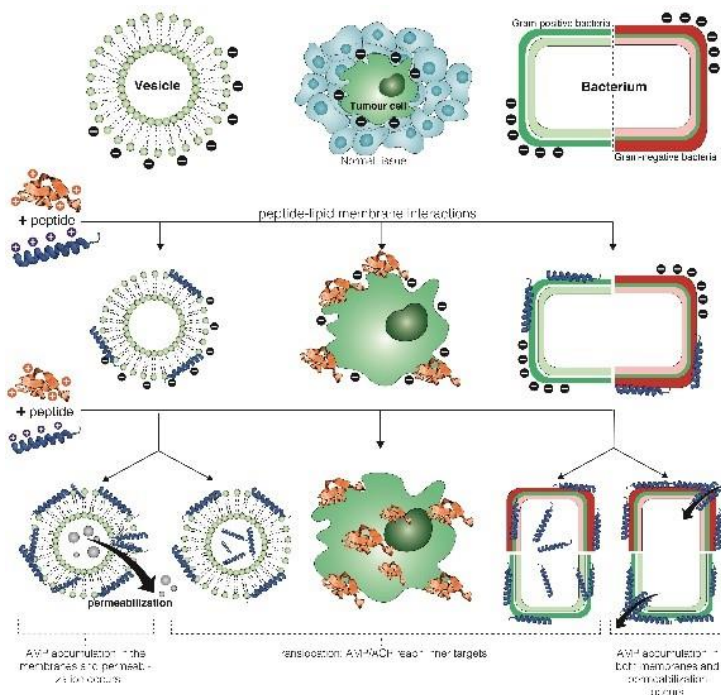
Miguel Castanho Lab

Head of Laboratory: Miguel A. R. B. Castanho, PhD, Group Leader and Full Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Carolina Carvalho Buga	University Degree	MSc Student
Ana Rosa Miranda dos Santos Silva Herdade	PhD	Postdoctoral Researcher
Ana Salomé Rocha do Nascimento Veiga	PhD	Staff Scientist
Beatriz Lopes Dias Vieira da Silva	University Degree	MSc Student
Carla Íris Cadima Couto	PhD	Senior Postdoctoral Researcher
Catarina de Jesus Pinto Gonçalves	Master Degree	PhD Student
Catarina Isabel Parente Chaparro	Master Degree	PhD Student
Christine Cruz Oliveira	PhD	Senior Postdoctoral Researcher
Daniel Gavino Leopoldino	Master Degree	Lab Technician
Diogo Alexandre de Mendonça	Master Degree	PhD Student
Filipa Dias de Oliveira	Master Degree	PhD Student
Iara Sofia Mota Lima da Silva	Master Degree	Lab Technician
Joana Azevedo Felice Lopes	University Degree	MSc Student
Liliana Faia Carvalho	Master Degree	Lab Manager
Marco Calvinho Cavaco	Master Degree	PhD Student
Patrícia Alexandra Branco Fraga	University Degree	MSc Student
Rita Isabel Pedro Aroeira	PhD	Project Manager
Susana Filipa Almeida Dias	Master Degree	PhD Student (Left October)
Vera Luísa Santos Neves	PhD	Senior Postdoctoral Researcher

Graphical Abstract



Lab Interests

There are many biological processes that depend on the interaction between peptides/proteins and membrane lipids, such as viral fusion, molecular translocation across epithelia or innate immune defense. Some of these may be inspiring to develop innovative therapeutic tools. Our goal is to unravel the physical principles that govern lipid-peptide interactions, with implications in viral fusion (HIV, SARS-CoV-2, Zika and Dengue viruses are of particular interest) and translocation of the blood-brain barrier, aiming at the development of anti-infective and antimetastatic cancer drugs. Towards this end, we discovered and developed our own proprietary drugs and drug carriers, and created our own spectroscopic and imaging methodologies, tailored to meet our research needs.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Biotechnology and Biosystems Engineering

Major Scientific Achievements in 2021

In 2021 we:

- Suggested guidelines for a proper discussion between experts in the peptide pharmacokinetics field on how to improve data readability so that peptide stability is adequately reported to take maximum advantage of it. Moreover, we deciphered intrinsic characteristics of peptide proteolytic susceptibility and were able to estimate peptide half-life in serum from tunable, sequence-related physicochemical properties.
- Tackled the synthesis of peptide–porphyrin conjugates capable of transpose the blood-brain barrier and with potential antiviral activity. Three of the peptide–porphyrin conjugates are able to reach the brain and effectively inhibit HIV infectivity *in vitro*.
- Discovered the anti-HIV-1 peptide pepRF1, a human serum-resistant peptide derived from the Dengue virus capsid protein. This peptide is specific for CXCR4-tropic strains, preventing viral entry into target cells by binding to the viral coreceptor CXCR4, acting as an antagonist of this receptor so one can also envisage its use as a novel therapeutic strategy for other CXCR4-related diseases.

Ongoing Projects in 2021

2021/2024: Protecting the brain from metastatic breast cancer. Coordinator: Miguel Castanho. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - BREAST-BRAIN-N-BBB - HR21-00605. Amount: 184 600,00€. Total Amount: 632 841,00€.

2021/2024: TRESPASS2TREAT: A novel approach in pharmacotherapies for breast cancer patients with brain metastasis. Coordinator: Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-BQM/5027/2020. Amount. 77 500,00€. Total Amount. 127 500,00€.

2021/2023: NOSTRESS: Novos alimentos funcionais para redução de efeitos do stress em aquacultura. Coordinator: Miguel Castanho. Funding Agency: Portugal 2020. Reference: NOSTRESS. Amount: 165 634,74€. Total Amount: 995 958,32€.

2020/2021: RIGHT-NOW-RIGHT-HERE: Evidence-based off-label application of porphyrin-based medicines to fight SARS-CoV-2. Coordinator: Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: Fundação para a Ciência e a Tecnologia COVID 2019. Amount: 40 000,00€. Total Amount: 40 000,00€.

2019/2023: "One size fits all" unique drug to eradicate multiple viral species simultaneously from the central nervous system of co-infected individuals - NOVIRUSES2BRAIN. Coordinator: Miguel Castanho. Funding Agency: European Commission. Reference: GA 828774 - H2020-FETOPEN-2018. Amount: 2 113 125,00€. Total Amount: 3 933 965,63€.

2018/2021: Selecção de fármacos líder anti-virus zika capazes de translocar as barreiras hemato-plantária e hemato-encefálica. Coordinator: Carla Couto. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-VIR/29495/2017. Amount: 239 302,82€. Total Amount: 239 302,82€.

Other Projects

2021/2022: LEO FARMACÊUTICOS - PFILIFE LAB. Co-Coordinator: Luís Costa. Funding Agency: Janssen - Cilag Farmacêutica, Lda. Reference: CIC- ESTUDO IMPA. Amount: 56 771,00€. Total Amount: 56 771,00€.

Scientific Impact

Academic Collaborations

Andrea Da Poian, Instituto de Bioquímica Médica Leopoldo de Meis, Federal University of Rio de Janeiro, UFRJ, Brazil.

Arnaldo Caruso, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy.

Charles Lawrie, Asociación Instituto Biodonostia.

David Andreu, Proteomics and Protein Chemistry Unit, Department of Experimental and Health Sciences, Pompeu Fabra. University, Barcelona, Spain.

Esmeralda Delgado, Faculdade de Medicina Veterinária, Universidade de Lisboa.

Frederico Aires da Silva, Centro de Investigação Interdisciplinar em Sanidade Animal (CIISA), Faculdade de Medicina Veterinária da Universidade de Lisboa, Portugal.

João D. G. Correia, Centro de Ciências e Tecnologias Nucleares and Departamento de Engenharia e Ciências Nucleares, Instituto Superior Técnico, Universidade de Lisboa, Bobadela, Portugal.

João Gonçalves, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal.

Jordi Llop, Asociación Centro de Investigación Cooperativa en Biomateriales, San Sebastián, Spain.

Luís Conceição, SPAROS, Faro, Portugal.

Mária A Deli, Department of Biophysics, Biological Research Centre, Hungarian Academy of Sciences, Szeged, Hungary.

Maria José Diógenes, Instituto de Farmacologia e Neurociências, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal.

Michael Burnet, Synovo GmbH, Tübingen, Germany.

Paula I P Soares and Joao P M R Borges, CENIMAT/I3N, Departamento de Ciência dos Materiais, Faculdade de Ciências e Tecnologia, FCT, Universidade Nova de Lisboa, Caparica, Portugal.

Pedro Ramos Cabrer, Center for Cooperative Research in Biomaterials (CIC biomaGUNE), Basque Research and Technology Alliance (BRTA), San Sebastián, Spain.

Selected Publications

Figueira TN, Mendonça DA, Gaspar D, Melo MN, Moscona A, Porotto M, Castanho MARB, Veiga AS. (2018). [Structure-stability-function mechanistic links in the anti-measles virus action of tocopherol-derivatized peptide nanoparticles](#). *ACS Nano*. 12(10):9855-9865.

Relevance of the publication: We have found the molecular determinants of self-assembly stability that determine *in vivo* efficacy of anti-measles peptide drugs. This work bridges biophysics studies at molecular scale to *in vivo* pharmacodynamics in a thorough interdisciplinary approach.

Skalska J, Andrade VM, Cena GL, Harvey PJ, Gaspar D, Mello ÉO, Henriques ST, Valle J, Gomes VM, Conceição K, Castanho MARB, Andreu D (2020). [Synthesis, structure, and activity of the antifungal plant defensin PvD1](#). *J Med Chem* 63(17):9391–9402.

Relevance of the publication: We created a process to synthesize PvD1, a plant defensin, and showed that its synthetic version retained the biological activity against four different *Candida* species and showed very low toxicity *in vivo*. Adding the high resistance of synthetic PvD1 to proteolytic degradation, we claim that conditions are now met to consider plant defensins druggable biologicals.

Mendonça DA; Bakker M; Cruz-Oliveira C; Neves V; Jiménez MA; Defaus S; Cavaco M; Veiga AS; Cadima-Couto I; Castanho MARB; Andreu D; Todorovski T. (2021). [Penetrating the blood-brain barrier with new peptide–porphyrin conjugates having anti-HIV activity](#). *Bioconjugate Chem.* (32): 1067–1077.

Relevance of the publication: We have tackled the synthesis of antiviral peptide–porphyrin conjugates capable of transposing the blood-brain barrier. Three peptide–porphyrin conjugates are potentially able to reach the brain and inhibit HIV infectivity.

Cadima-Couto I; Tauzin A; Freire JM; Figueira TN; Silva RD; Pérez-Peinado C; Cunha-Santos C; Bártolo I; Taveira N; Gano L; Correia JDG; Goncalves J; Mammano F; Andreu D; Castanho MARB; Veiga AS. (2021) [Anti-HIV-1 activity of pepRF1, a proteolysis-resistant CXCR4 antagonist derived from Dengue virus capsid protein](#). *ACS Infect Dis*. 7(1):6-22.

Relevance of the publication: We discovered the anti-HIV-1 peptide pepRF1, a human serum-resistant peptide derived from the Dengue virus capsid protein. This peptide is specific for CXCR4-tropic strains, preventing viral entry into target cells. Acting as an antagonist of the viral coreceptor CXCR4, one can also envisage its use as a novel therapeutic strategy for other CXCR4-related diseases.

Cavaco M; Andreu D; Castanho MARB. (2021). [The challenge of peptide proteolytic stability studies: scarce data, difficult readability, and the need for harmonization](#). *Angew Chem Int Ed Engl*. 60(4):1686-1688.

Relevance of the publication: We suggested guidelines for a proper discussion between experts in the field on how to improve data readability so that peptide stability, an often-missing parameter in older literature, is adequately reported to take maximum advantage of it.

2021 Publications in Peer-Reviewed Journals

Aguiar S; Dias JNR; Andre A; Cavaco M; Correia JDG; Neves V; Aires-da-Silva F. (2021). [Highly Specific Blood-Brain Barrier Transmigrating Single-Domain Antibodies Selected by an In Vivo Phage Display Screening](#). **Pharmaceutics**. 13(10): 1598.

Cadima-Couto I; Tauzin A; Freire JM; Figueira TN; Silva RD; Pérez-Peinado C; Cunha-Santos C; Bártolo I; Taveira N; Gano L; Correia JDG; Goncalves J; Mammano F; Andreu D; Castanho MARB; Veiga AS. (2021) [Anti-HIV-1 activity of pepRF1, a proteolysis-resistant CXCR4 antagonist derived from Dengue virus capsid protein](#). **ACS Infect Dis**. 7(1):6-22.

Cavaco M; Andreu D; Castanho MARB. (2021). [The Challenge of Peptide Proteolytic Stability Studies: Scarce Data, Difficult Readability, and the Need for Harmonization](#). **Angew Chem Int Ed Engl**. 60(4):1686-1688.

Cavaco M; Fraga P; Valle J; Andreu D; Castanho MARB; Neves V. (2021). [Development of Breast Cancer Spheroids to Evaluate Cytotoxic Response to an Anticancer Peptide](#). **Pharmaceutics**. 13(11):1863.

Cavaco M; Frutos S; Oliete P; Castanho MARB; Vila-Perelló M; Neves V. (2021). [Conjugation of a Blood Brain Barrier Peptide Shuttle to an Fc Domain for Brain Delivery of Therapeutic Biomolecules](#). **ACS Med. Chem. Lett**. 12(11):1663–1668.

Cavaco M; Valle J; Flores I; Andreu D; Castanho MARB. (2021). [Estimating peptide half-life in serum from tunable, sequence-related physicochemical properties](#). **Clin Transl Sci**. 14(4):1349–1358.

Farber PL; Dias A; Freitas T; Pinho AC; Viggiano D; Saldanha C; Silva-Herdade AS. (2021) [Evaluation of hemorheological parameters as biomarkers of calcium metabolism and insulin resistance in postmenopausal women](#). **Clin Hemorheol Microcirc**. 77(4):395-410.

Gallo M; Moreno E; Cavaco M; Neves V; Castanho MARB; Andreu D. (2021). [Orally active peptide vector allows using cannabis to fight pain while avoiding side effects](#). **J Med Chem**. 64(10):6937-6948.

Lacerda JF; Lagos AC, Carolino E; Silva-Herdade AS; Silva M; Guerreiro CS. (2021) [Functional food components, intestinal permeability and inflammatory markers in patients with inflammatory bowel disease](#). **Nutrients**, 13(2):642.

Martins DB; Fadel V; Oliveira FD; Gaspar D; Alvares DS; Castanho MARB; Cabrera MPDS (2021). [Protonectin peptides target lipids, act at the interface and selectively kill metastatic breast cancer cells while preserving morphological integrity](#). **J Colloid Interface Sci**. 601:517-530.

Mendonça DA; Bakker M; Cruz-Oliveira C; Neves V; Jiménez MA; Defaus S; Cavaco M; Veiga AS; Cadima-Couto I; Castanho MARB; Andreu D; Todorovski T. (2021). [Penetrating the blood-brain barrier with new peptide–porphyrin conjugates having anti-HIV activity](#). **Bioconjugate Chem.** (32): 1067–1077.

Mink C; Strandberg E; Wadhvani P; Melo MN; Reichert J; Wacker I; Castanho MARB; Ulrich AS. (2021). [Overlapping Properties of the Short Membrane-Active Peptide BP100 With \(i\) Polycationic TAT and \(ii\) \$\alpha\$ -helical Magainin Family Peptides](#). **Front Cell Infect Microbiol.** 11:609542.

Oliveira FD; Castanho MARB; Neves V. (2021). [Exosomes and Brain Metastases: A Review on Their Role and Potential Applications](#). **Int J Mol Sci.** 22(19):10899.

Woods B; Silva RDM; Schmidt C; Wragg D; Cavaco M; Neves V; Ferreira VFC; Gano L; Morais TS; Mendes F; Correia JDG; Casini A. (2021). [Bioconjugate Supramolecular Pd²⁺ Metallacages Penetrate the Blood Brain Barrier In Vitro and In Vivo](#). **Bioconjug Chem**, 32(7), 1399–1408.

Invited Lectures and Seminars

Diogo A. Mendonça. How to prepare a perfect pizza... oh sorry, develop trans-BBB antiviral conjugates? Pizza Seminar, Virtual event, January 25, 2021.

Vera Neves. Peptide shuttles for receptor independent transport across the BBB. Models of the Blood-Brain Barrier (BBB) Scientific Tools to Target the Brain. Faculdade de Farmácia, Universidade de Lisboa, Lisbon, Portugal. Virtual event, March 18-20, 2021.

Miguel Castanho. Drug conjugation as a tool to overcome the BBB. Models of the Blood-Brain Barrier (BBB) Scientific Tools to Target the Brain. Faculdade de Farmácia, Universidade de Lisboa, Lisbon, Portugal. Virtual event, March 18-20, 2021.

Miguel Castanho. Uma Universidade multifacetada e “poliglota”: entre a complexidade e a identidade. VI Edição dos Estados Gerais, Universidade de Lisboa, virtual event. March 21, 2021.

Miguel Castanho. A mensagem técnica em modo simples. Ética e Comunicação em Ciência: a incerteza e a complexidade. Instituto Nacional de Saúde Dr Ricardo Jorge. Virtual event. April 6, 2021.

Miguel Castanho. Diffusion-lysis coupling of antimicrobial peptides in biofilms of *S. aureus*. 7th European joint theoretical / experimental meeting on membranes (EJTEMM 2021). Virtual event. April 7-9, 2021.

Miguel Castanho. From Zika virus to SARS-CoV-2 - Developing drugs to fight viruses in the brain. XII Biochemistry Day. Universidade de Aveiro, Aveiro, Portugal. April 14, 2021.

Miguel Castanho. From Zika virus to SARS-CoV-2 - Developing drugs to fight viruses in the brain. XIII Jornadas de Genética e Biotecnologia / III Jornadas Ibéricas de Genética y Biotecnologia (UTAD). Virtual event. April 15, 2021.

Miguel Castanho. COVID-19: como viver a nova realidade. 2nd meeting TAS 2021. Virtual event. April 22, 2021.

Miguel Castanho. SARS-CoV-2: Inovação em vacinas. TechCare. Universidade de Aveiro, Aveiro, Portugal. April 24, 2021.

Miguel Castanho. 33^a edição da Jobshop AEIST. Virtual event. May 4, 2021.

Miguel Castanho. Vacinação contra a COVID-19 em Portugal: Ponto de Situação. Virtual event. May 13, 2021.

Miguel Castanho. Pandemia: saberes e práticas. VIII Congresso Luso-Espanhol de Estudantes de Enfermagem. Virtual event. May 17, 2021.

Miguel Castanho. Novas vacinas contra COVID-19: uma perspetiva molecular. IV Dia do Bioanalista. Faculdade de Farmácia da Universidade de Coimbra. Coimbra, Portugal. May 31, 2021.

Miguel Castanho. Pursuing innovative peptide drugs with biophysical approaches: why, what, what for? 7th International Iberian Biophysics Congress, Coimbra, Portugal, June 14-16, 2021.

Miguel Castanho. A perceção pública da Ciência em tempos de pandemia. XXVII Encontro Nacional da Sociedade Portuguesa de Química. Virtual event. July 15, 2021.

Miguel Castanho. Experimentar o Futuro: as novas tecnologias e os desafios de inovação em Neurociências. Ciclo de Conversas VectorB2B. Virtual event. July 22, 2021.

Miguel Castanho. Chapter “Ciência - Saúde – Comunicação – Política: os vértices de um quadrado (ainda mais) complexo em tempo de pandemia” of the book “Complexidade: Implicações e políticas globais” (ISBN 978-989-53277-4-4). Encontros da Complexidade – Arrábida, Setúbal, Portugal. September 27-29, 2021.

Miguel Castanho. Vacinas: onde estamos e para onde vamos? – uma perspetiva de investigação. COVID-19 – O papel das novas terapêuticas na resposta global e concertada à pandemia. Virtual event. October 6, 2021.

Miguel Castanho. Developing drugs to fight viruses in the brain – the NOVIRUSES2BRAIN project. III Simpósio em Bioquímica Aplicada. Universidade do Minho, Braga, Portugal. October 1-7, 2021.

Miguel Castanho. Desafios de natureza molecular na compreensão da COVID-19: o papel da bioquímica presente e futuro. XXI National Congress of Biochemistry “Tuning Biochemistry with Life and Society” Évora, Portugal. October 14-16, 2021.

Miguel Castanho. Comunicação de ciência: uma perspetiva. I Curso Breve de Comunicação, Ciência e Saúde. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 3, 2021.

Miguel Castanho. As revelações da pandemia de COVID-19: uma perspetiva de investigação. Instituto de Ciências Sociais, Universidade de Lisboa. Lisbon, Portugal. November 11, 2021.

Miguel Castanho. O Papel da Universidade no combate à pandemia de COVID-19. I Congresso Iuso-brasileiro de Divulgação Científica e Resiliência Universitária. Virtual event, December 1-4, 2021.

Catarina Chaparro. Novel hybrid nanoparticles for Alzheimer’s disease theranostic: efficient overcoming of nanomaterials across the blood-brain barrier. Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 7, 2021.

Communications

Vera Neves. Dual-active Peptides for the Treatment of Brain Metastases. 26th Annual Blood-Brain Barrier Consortium Meeting "Cultivating the Next Generation of Translational Scientists" Virtual meeting, March 11-12, 2021. Poster Communication, International Conference.

Diogo A. Mendonça, Lorena O. Fernandes-Siqueira, Christine Cruz-Oliveira, Vera Neves, Iris Cadima-Couto, Sira Defaus, Ana Salomé Veiga, Toni Todorovski, David Andreu, Andrea T. Da Poian, Miguel A.R.B. Castanho. Novel peptide-porphyrin conjugates efficiently translocate a cellular model of the blood-brain barrier and inactivate ZIKV *in vitro*. XIV Annual CAML PhD Students’ Scientific Meeting • IV NeurULisboa Meeting, Lisboa, Portugal, May 5-7, 2021. Online Poster Communication; National Conference.

Marco Cavaco. The use of a selective and nontoxic dual-active peptide to eliminate brain metastasis. XIV Annual CAML PhD Students’ Scientific Meeting • IV NeurULisboa Meeting, Lisboa, Portugal, May 5-7, 2021. Oral Communication; National Conference.

Carolina C. Buga, Mariana Valério, Alexandra Balola, Ana S. Ferreira, Ana M. Sequeira, Miguel Rocha, João B. Vicente, Miguel A. R. B. Castanho, Cláudio M. Soares, Ana S. Veiga, Diana Lousa. Molecular determinants of the SARS-CoV-2 fusion peptide activity. Bioinformatics Open Days. Braga, Portugal. May 5-8, 2021. Poster communication; National conference.

Filipa D. Oliveira, Marco Cavaco, Tiago N. Figueira, Javier Valle, Patrícia Napoleão, Vera Neves, David Andreu, Diana Gaspar, and Miguel A. R. B. Castanho. vCPP2319 is a cell-penetrating peptide that selectively targets breast cancer cells and interacts with cells’ derived exosomes.

XIV CAML · IV NeurULisboa PhD Students Virtual Meeting/Online, May 6, 2021. Oral Communication; National Conference.

Susana A. Dias, Sandra N. Pinto, Ana S. Silva-Herdade, Marco Cavaco, Vera Neves, Manuela Oliveira, Ana Coutinho, Miguel A.R.B. Castanho, Ana Salomé Veiga. A novel viral-derived peptide with potent activity against *Staphylococcus aureus* in the planktonic and biofilm forms. 7th International Iberian Biophysics Congress, Online format, June 14-16, 2021. Poster Communication; International Conference.

Diogo A. Mendonça, Lorena O. Fernandes-Siqueira, Christine Cruz-Oliveira, Vera Neves, Iris Cadima-Couto, Sira Defaus, Ana Salomé Veiga, Toni Todorovski, David Andreu, Andrea T. Da Poian, Miguel A.R.B. Castanho. Novel peptide-porphyrin conjugates efficiently translocate a cellular model of the blood-brain barrier and inactivate ZIKV *in vitro*. 7th International Iberian Biophysics Congress, Coimbra, Portugal, June 14-16, 2021. Online Oral Communication; International Conference.

Filipa D. Oliveira, Marco Cavaco, Tiago N. Figueira, Javier Valle, Patrícia Napoleão, Vera Neves, David Andreu, Diana Gaspar, and Miguel A. R. B. Castanho. The cell-penetrating peptide vCPP2319 selectively targets breast cancer cells and interacts with breast cancer cells' derived exosomes. 7th International Iberian Biophysics Congress/Online, June 15, 2021. Poster Communication; International Conference.

Catarina Chaparro, Vera Neves, João Paulo Borges, Paula Soares. Novel hybrid nanoparticles for Alzheimer's disease theranostic: efficient overcoming of nanomaterials across the blood-brain barrier. 4th Doctoral Congress in Engineering/Virtual meeting, June 28, 2021. Poster Communication; National Conference.

Diogo A. Mendonça, Tiago N. Figueira, Manuel N. Melo, Olivia Harder, Stefan Niewiesk, Anne Moscona, Matteo Porotto, Miguel A.R.B. Castanho, Ana Salomé Veiga "The efficacy of designed anti-measles virus peptides depends on the stability of self-assembled clusters." 45th FEBS Congress, Ljubljana, Slovenia, July 3-8, 2021. Online Poster Communication; International Conference.

Catarina Chaparro, Vera Neves, João Paulo Borges, Paula Soares. Novel hybrid nanoparticles for Alzheimer's disease theranostic: efficient overcoming of nanomaterials across the blood-brain barrier. 31st Conference of the European Society for Biomaterials/ Virtual Meeting, September 6, 2021. Oral Communication, International Conference.

Ana Salomé Veiga. Anti-HIV-1 activity and mode of action of pepRF1, a viral-derived CXCR4 antagonist. XXI National Congress of Biochemistry "Tunning Biochemistry with Life and Society", Évora, Portugal, October 14-16, 2021. Oral Communication; National Conference.

Vera Neves. Development of a Blood Brain Barrier Peptide Shuttle and its conjugation to an Fc domain for brain delivery of therapeutic biomolecules. XXI National Congress of Biochemistry

“Tuning Biochemistry with Life and Society” Évora, Portugal. October 14-16, 2021. Oral Communication; National Conference.

Catarina Chaparro, Vera Neves, João Paulo Borges, Paula Soares. Novel hybrid nanoparticles for Alzheimer’s disease theranostic: efficient overcoming of nanomaterials across the blood-brain barrier. NanoMedicine International Conference and Exhibition, Milan, Italy, October 21, 2021. Oral Communication; International Conference.

Catarina Gonçalves. Anticancer activity of a mini body against triple negative breast cancer brain metastasis. EMBO – Biomolecular interaction analysis 2021. Virtual meeting, October 25-29, 2021. Poster Communication; International Conference.

Carolina C. Buga, Mariana Valério, Diogo A. Mendonça, João B. Vicente, Miguel A. R. B. Castanho, Cláudio M. Soares, Ana S. Veiga, Diana Lousa. Molecular determinants of the SARS-CoV-2 fusion peptide activity. Encontro de Jovens Investigadores em Biologia Computacional Estrutural. Coimbra, Portugal. December 20, 2021. Poster Communication; National Conference.

Organization of Conferences

Vera Neves. Co-organizer. Summer School entitled “Trends and Challenges in Epilepsy Research”, Lisbon, Portugal, September 27th to October 1st, 2021.

Prizes & Honors in 2021

Diogo A Mendonça - Nzytech Award for the Poster “Novel peptide-porphyrin conjugates efficiently translocate a cellular model of the blood-brain barrier and inactivate ZIKV in vitro.” at XIV Annual CAML PhD Students’ Scientific Meeting • IV NeurULisboa Meeting, Lisboa, Portugal, May 5-7, 2021.

Advanced Teaching

Vera Neves. Lecture. Blood Brain Barrier: Challenges to develop new therapeutic tools to act in the brain. PhD and MSc in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. September 15, 2021.

Miguel Castanho. Lecture. MSc in Biopharmaceutical Sciences, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal. November 9, 2021.

Miguel Castanho. Round Table. PhD Advanced Course – Advances in Neuropharmaceutics. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal. December 13-17, 2021.

MSc Theses

Patricia Fraga, 12/11/2021, Development of a brain metastasis co-culture cellular model for drug testing. Faculdade de Farmácia da Universidade de Lisboa. Supervisor: Vera Neves. Co-Supervisor: Miguel Castanho.

PhD Theses

Julia Michalina Skalska, 21/05/2021, Biophysical and functional studies to unravel the biomedical potential of plant defensin PvD₁, Online. Supervisor: Miguel Castanho.

Eva Cunha, 14/12/2021, Periodontal disease in dogs: an experimental approach towards prevention using antimicrobial peptides, Faculdade de Medicina Veterinária, Universidade de Lisboa. Supervisor: Manuela Oliveira. Co-Supervisor: Ana Salomé Veiga.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Collaboration to provide highly qualified services of drug discovery and development from the bench to bedside, VectorB2B, a Drug Developing Association for Research in Biotechnology (<http://vectorb2b.com/>) (Collaborative Research).

Intellectual Property Rights in 2021

Vicent Casado Burillo, Estefania Moreno Guillén, Rafael Maldonado López, David Andreu Martínez, Maria Gallo, Leonardo Pardo Carrasco, Miguel Castanho, Vera Neves, Marco Cavaco. Peptide compounds for reducing side effects of CB1 receptor agonists. WO2021064165A1. April 8, 2021.

Fabrizio Mammano, Alexandra Tauzin, Miguel Castanho, Ana Salomé Veiga, Carla Iris Couto, João Freire, David Andreu Martinez, Clara Perez-Peinado, Javier Valle Garcia, João Gonçalves. C-X-C motif chemokine receptor 4 antagonist. WO2021156451A1. August 12, 2021.

Policy

Miguel Castanho. Member of Conselho Consultivo do Hospital Distrital de Santarém.

Science and Society in 2021

- Rita Aroeira. O que te passa pela cabeça? Como fazemos investigação em neurociências? Seminar to Escola Secundária de Águas Santas. - Brain Awareness Week 2021, March 19, 2021.

- Rita Aroeira and Vera Neves. Como é que os cientistas estudam o cérebro? Como é que os medicamentos chegam ao cérebro? Seminar to Centro de Reabilitação e Integração de Fátima (Zoomas-me uma história). - Brain Awareness Week 2021, March 30, 2021.

- Miguel Castanho. Vacinas contra a COVID-19: ir na torrente ou na contracorrente? - 60 minutos de Ciência, Museu Nacional de História Natural e da Ciência, Lisboa, April 7, 2021.

- Vera Neves. Como é que os cientistas estudam o cérebro? Como é que os medicamentos chegam ao cérebro? Seminar to Santa Casa da Misericórdia Fátima-Ourém. - World Environmental Day, June 4, 2021.

- Miguel Castanho. Em que ponto estamos na pandemia? – uma perspetiva de investigação científica. Escola Mem Ramires, Santarém, Portugal. October 12, 2021.

- Miguel Castanho. À conversa - Estamos (quase) todos/as vacinados/as. E agora? November 17, 2021

- Marco Cavaco. "Pura Vida" from Canal Saúde+, December, 2021 (<https://www.saudemais.tv/video/259885--t07-e013-02-1>)

- Miguel Castanho. Chapter "Ciência - Saúde – Comunicação – Política: os vértices de um quadrado (ainda mais) complexo em tempo de pandemia" of the book "Complexidade: Implicações e políticas globais" (ISBN 978-989-53277-4-4).

- Development of a video related to the book "Integrative Human Biochemistry" by Miguel Castanho and Andrea Da Poian, May, 2021.

- Participation in several media communication events, from which we highlight:
 - "Cancro da mama: proteger o cérebro das metástases", Observador, December 6, 2021. (<https://observador.pt/2021/12/06/cancro-da-mama-protoger-o-cerebro-das-metastases/>)
 - "VIH. Portugueses criam moléculas que ajudam a tratar distúrbios neurocognitivos", E=MC², Observador, December 13, 2021. (<https://observador.pt/programas/e-mc2/vih-portugueses-criam-moleculas-que-ajudam-a-tratar-disturbios-neurocognitivos/>)

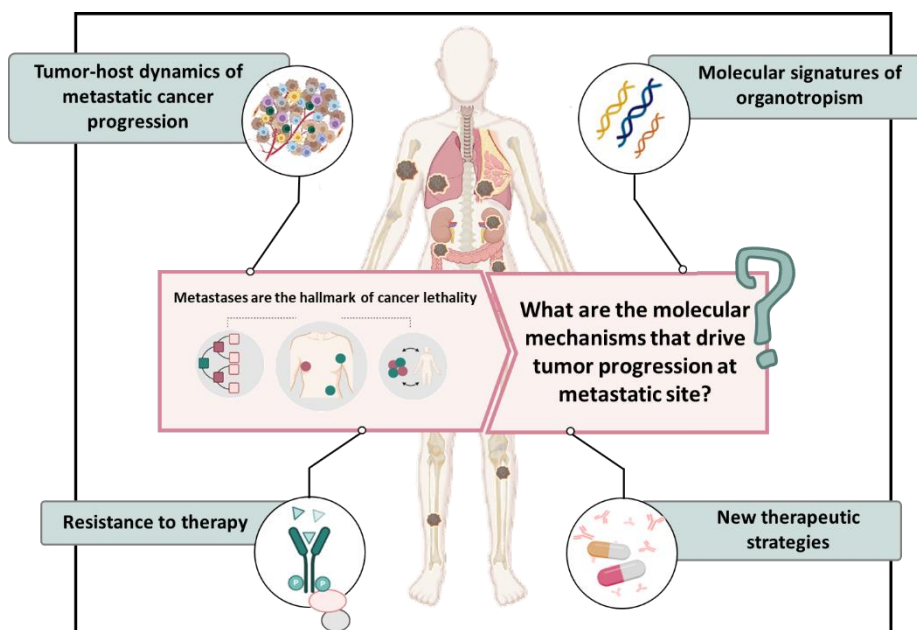
Luís Costa Lab

Head of Laboratory: Luis António Marques da Costa, MD, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa and Director of Serviço de Oncologia do Hospital de Santa Maria – Centro Hospitalar Universitário Lisboa Norte.

Team

Ana Cláudia Martins Cavaco	PhD	Postdoctoral Researcher
Ana Margarida Fernandes Rodrigues	University Degree	MSc Student (Left May)
André Miguel Branco Mansinho	MD/Master Degree	Clinical Researcher
Francisco de Aguiar António Baptista	High School Diploma	Trainee (Left June)
Inês Fernandes Gomes	Master Degree	PhD Student
Isabel Cristina Ferreira Fernandes Borges da Costa	MD/PhD	Clinical Researcher
Laura Teixeira Castro	Master Degree	Trainee (Left December)
Maria Miguel Evans Seguro	MD/PhD	Trainee
Marta Sofia Alves Martins	University Degree	Staff Scientist
Miguel Maria Escoval Lopes Esperança Martins	PhD	PhD Student
Patrícia Borges Alves	Master Degree	Trainee (Left December)
Patrícia Isabel Martins Corredeira	Master Degree	Lab Technician
Raquel Sofia Cruz Duarte	Master Degree	PhD Student
Rúben Duarte Dos Santos Vilela	Master Degree	MSc Student (Started September)
Sandra Cristina Cara de Anjo Casimiro	University Degree	Staff Scientist
Sandra Kucharczak	PhD	MSc Student (Started September)
Sara Daniela Botelho Rosa	University Degree	Trainee (Started May)
Sara Miguel Jesus da Silva	Master Degree	MSc Student
Soraia Lobo de Lourdes Martins	University Degree	Clinical Researcher
Teresa Raquel Duarte Pacheco	MD/Master Degree	Senior Post-Doctoral Researcher
Tito Miguel Palmela Leitão	PhD	Clinical Researcher

Graphical Abstract



Lab Interests

Metastases are the hallmark of cancer lethality. They represent a unique and complex phenomenon, associated not only with genomic alterations in cancer cells, but also with a heterotypic signaling between cancer cells and host tissues. Our main goal is to better understand the molecular mechanisms driving tumor progression at the metastatic site (using bone metastases as a paradigm); and to unravel molecular signatures of organotropism through identification of “leader gene signatures” common to the primary tumor and corresponding metastasis (using colorectal cancer (CRC) as a model). We also focus in the identification of the mechanisms involved in resistance to therapy in the metastatic setting, as well as in finding new therapeutic strategies to overcome such resistance. It is also our objective to interpret the dynamics of metastatic cancer progression by comprehensive analysis of clonal evolution and host immune and humoral response.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

During 2021, we have established a new collaborative project with Illumina Inc. untitled Multi-Cancer Profile Project- MCPP, where breast, endometrial and lung cancers and sarcomas, will be DNA and RNA sequenced. Results from this collaboration are expected to bring new insights into the field, with the potential to generate novel approaches in the management and treatment of these diseases. Moreover, taking advantage of the MCPP breast cancer cohort and the Oncodynamics Biobanking project (ODB), a clinically annotated prospective collection of liquid biopsies, aiming to characterize both the host immune response and tumor clonal evolution of metastatic cancer progressing under therapy, we received the Pfizer Global Medical Grant - Metastatic Breast Cancer, to study predictive biomarkers for CDK4/6i plus ET therapy. We also submitted for the National phase the international patent on RANK pathway inhibitors in combination with CDK4/6 inhibitors (WO2020/222668A1).

Ongoing Projects in 2021

2021/2025: ALS PROJECT - ONO PHARMA. Coordinator: Luís Costa. Funding Agency: Pfizer. Reference: CDKI. Amount: 15 000,00€. Total Amount: 15 000,00€.

2020/2023: MCPP- Illumina. Coordinator: Luís Costa. Funding Agency: Illumina. Reference. MCPP-Illumina. Amount: 36 000,00€. Total Amount: 36 000,00€.

2020/2021: Fisiopatologia e implicações clínicas da mutação RANK c.1386C>T (R450W) em doentes com cancro da mama. Coordinator: Sandra Casimiro. Funding Agency: Fundação para a

Ciência e a Tecnologia. Reference: PTDC/MED-ONC/28636/2017. Amount: 234 615,31€. Total Amount: 234 615,31€.

2018/2021: Inervação patológica em metástases ósseas: OSTEOLASTOS, o que estão a fazer? Coordinator: Sandra Casimiro. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: POCI-01-0145-FEDER-030158. Amount: 6 250,00€. Total Amount: 239 504,80€.

Scientific Impact

Academic Collaborations

Lorena Dieguez, International Iberian Nanotechnology Laboratory, RUBYnanomed Lda, Portugal.

Marília Antunes, FCUL

Ana Rita Grosso, FCT-NOVA

Susana Vinga, INESC-ID, Instituto Superior Técnico, Universidade de Lisboa

Luis Moita, IGC

Bruno Silva-Santos, iMM

Nuno Barbosa-Morais, iMM

Ricardo Ferreira, Instituto Superior de Agronomia

Meriem Lamghari, i3S

Sérgio J. Dias, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa

Daniela Macedo, Medical Oncology Department, Hospital Lusíadas Lisboa

Joaquim Soares do Brito, Orthopedics and Traumatology Department, Centro Hospitalar Universitário Lisboa Norte – Hospital de Santa Maria; Faculdade de Medicina da Universidade de Lisboa.

Hugo Vasques, General Surgery Department, Instituto Português de Oncologia de Lisboa Francisco Gentil; Faculdade de Medicina da Universidade de Lisboa.

Marc Veldhoen, Immune Regulation Laboratory, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa; Faculdade de Medicina da Universidade de Lisboa.

Selected Publications

Coleman RE, Croucher PI, Padhani AR, Clézardin P, Chow E, Fallon M, Guise T, Colangeli S, Capanna R, Costa L. (2020) Bone metastases. **Nature Reviews Disease Primers**. 6(1):83.

Relevance of the publication: This PrimeView, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, describes the epidemiology, pathophysiology and clinical features of metastatic bone disease, and highlights the specific treatment approaches to prevent and treat bone metastases from solid tumours as well as myeloma bone disease.

Gomes I, de Almeida BP, Dâmaso S, Mansinho A, Correia I, Henriques S, Cruz-Duarte R, Vilhais G, Félix P, Alves P, Corredeira P, Barbosa-Morais N, Costa L, Casimiro S (2020). Expression of receptor activator of NFκB (RANK) drives stemness and resistance to therapy in ER+HER2- breast cancer. **Oncotarget**. 11 (19):1714-1728.

Relevance of the publication: This is an original research from our Lab where it was reported for the first time the role of RANK pathway in Luminal breast cancer, opening new therapeutic possibilities in this setting.

Costa L, Ferreira AR (2017). Adjuvant zoledronic acid to treat breast cancer: not for all. **Lancet Oncology** 18(11):1437-1439.

Relevance of the publication: This Letter published in the prestigious Lancet Oncology was written by the expert in the biology and clinics of bone metastases Dr. Costa with Dr. Ferreira, and discusses the results from pivotal clinical trials aiming to assess if adjuvant bisphosphonates will represent a benefit for all breast cancer patients.

Body JJ, Casimiro S, Costa L (2015). Targeting bone metastases in prostate cancer: improving clinical outcome. **Nature Reviews Urology** 12: 340-56. Review

Relevance of the publication: This Review, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, describes the latest developments in the treatment of bone metastases in prostate cancer, and is an important tool for clinicians and scientists in the field.

Henry D, Costa L, Goldwasser F, Hirsh V, Hungria V, Prausova J, Scagliotti GV, Sleeboom H, Spencer A, Vadhan-Raj S, von Moos R, Willenbacher W, Woll PJ, Wang J, Jiang Q, Jun S, Dansey R, Yeh H (2011). A randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma. **Journal of Clinical Oncology** 9(9):1125-1132

Relevance of the publication: This paper, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, reported the results of the pivotal clinical trial which has demonstrated that Denosumab was a potential novel treatment option with the convenience of subcutaneous administration and no requirement for renal monitoring or dose adjustment.

2021 Publications in Peer-Reviewed Journals

Alpuim Costa D, Nobre JG, Batista MV, Ribeiro C, Calle C, Cortes A, Marhold M, Negreiros I, Borralho P, Brito M, Cortes J, Braga SA, Costa L (2021) [Human Microbiota and Breast Cancer-Is There Any Relevant Link?-A Literature Review and New Horizons Toward Personalised Medicine Front Microbiol.](#) 12: 584332. Review.

Batista MV, Ulrich J, Costa L, Ribeiro LA (2021). Multiple Primary Malignancies in Head and Neck Cancer: A University Hospital Experience over a Five-Year Period. **Cureus.** 2021 Aug 21;13(8):e17349.

Bjartell A, Lumen N, Maroto P, Paiss T, Gomez-Veiga F, Birtle A, Kramer G, Kalinka E, Spaëth D, Feyerabend S, Matveev V, Lefresne F, Lukac M, Wapenaar R, Costa L, Chowdhury S.(2021) Real-World Safety and Efficacy Outcomes with Abiraterone Acetate Plus Prednisone or Prednisolone as the First- or Second-Line Treatment for Metastatic Castration-Resistant Prostate Cancer: Data from the Prostate Cancer Registry. **Target Oncol.** 2021 May;16(3):357-367.

Borges da Ponte C, Leitão TP, Miranda M, Polido J, Alvim C, Fernandes I, Braga T, Pena B, de Almeida JM, Costa L, Dos Reis JP. [Prostate Ewing Sarcoma/PNET: A case of long survival in a highly aggressive malignancy.](#) **Urology.** 2021 May 16:S0090-4295(21)00396-4. Case report.

Casimiro S, Vilhais G, Gomes I, Costa L (2021) [The Roadmap of RANKL/RANK Pathway in Cancer](#). *Cells* 10(8):1978. Review.

Costa L, Alexandre MTA, Mansinho AR, Teixeira Sousa AR, Pereira Vieira DM, Bell E, Swales O, Hughes R, Nagda N, Lucherini S, Roediger A, Araujo A (2021). [113P Health outcomes and budget impact projection of the anti-PD-\(L\) 1 class in cancer care in Portugal](#). *Annals of Oncology*. Volume 32. Pages S1424-S1425

Esperança-Martins, M., Evangelista, V., Fernandes, S., Almeida, R. [Vasculitis and breast cancer: mind the hint](#). *Case Rep Oncol*. 2021; 14:550-560. Case Report.

Esperança-Martins, M., Fernandes, I., Soares do Brito, J., Macedo, D., Vasques, H., Serafim, T., Costa, L., Dias, S. Sarcoma Metabolomics: [Current Horizons and Future Perspectives](#). *Cells*. 2021; 10: 1432. Review.

Fernandes, I., Melo-Alvim, C., Lopes-Brás, R., Esperança-Martins, M. [Osteosarcoma Pathogenesis Leads The Way to New Target Treatments](#). *Int. J. Mol. Sci*. 2021; 22(2): 813. Review

Ferreira RA, Ferreira S, Lambertini M, Maurer C, Martel S, **Costa L**, Ponde N, de Azambuja E. [Association between pertuzumab-associated diarrhoea and rash and survival outcomes in patients with HER2-positive metastatic breast cancer: Exploratory analysis from the CLEOPATRA trial](#). *Eur J Cancer*. 2021 144:351-359.

Leitão, T. P., Miranda, M., Polido, J., Morais, J., Corredeira, P., Alves, P., ... & Costa, L. (2021). [Circulating tumor cell detection methods in renal cell carcinoma: A systematic review](#). *Critical Reviews in Oncology/Hematology*, 161, 103331. Review.

Lobo-Martins S, Pais HL, Soares-de-Almeida L, **Costa L**, Mansinho A, Teixeira de Sousa R. BRAF L597K mutation: an opportunity to treat. *Dermatol Online J*. 2021 Jan 15;27(1):13030/qt18k3573s. Case report.

Mahdi Golkaram, Michael Salmans, Shannon Kaplan, Raakhee Vijayaraghavan, Marta Martins, Nafeesa Khan, Cassandra Garbutt, Aaron Wise, Joyee Yao, Sandra Casimiro, Catarina Abreu, Daniela Macedo, Ana Lúcia Costa, Cecília Alvim, André Mansinho, Pedro Filipe, Pedro Marques da Costa, Afonso Fernandes, Paula Borralho, Cristina Ferreira, Fernando Aldeia, João Malaquias, Jim Godsey, Alex So, Traci Pawlowski, Luis Costa, Shile Zhang, and Li Liu (2021) [HERVs establish a distinct molecular subtype in stage II/III colorectal cancer with poor outcome](#). *npj Genomic Medicine* 6:13.

Mansinho A, Nejo P, Leitão T, Casimiro S, Costa L (2021) [Management of bone metastases in renal cell carcinoma: Bone-targeted treatments, systemic therapies, and radiotherapy](#). *J Cancer Metastasis Treat*. 7:44. Review.

Lobo Martins S, Corredeira P, Alves PB, Antunes M, Rodrigues A, Quintela A, Mansinho A, Filipe P, Ribeiro L, Teixeira de Sousa R, Pinto C, Abreu C, Gordino G, Ribot J, Serre K, Martins M, Cavaco

A, Casimiro S, Silva-Santos B, Costa L (2021). Abstract PS17-37: [Immune cell populations in peripheral blood of metastatic breast cancer patients under CDK4/6 inhibitors](#). **American Association for Cancer Research**. Volume 81. Issue 4 Supplement. Abstract publication.

Lopes C, Piairo P, Chícharo A, Abalde-Cela S, Pires LR, Corredeira P, ... & Diéguez L (2021). [HER2 Expression in Circulating Tumour Cells Isolated from Metastatic Breast Cancer Patients Using a Size-Based Microfluidic Device](#). **Cancers**, 13(17), 4446.

Neto JP, Alho I, Costa L, Casimiro S, Valério D, Vinga S (2021). [Dynamic modeling of bone remodeling, osteolytic metastasis and PK/PD therapy: introducing variable order derivatives as a simplification technique](#). **J Math Biol**. 2021 Sep 22;83(4):39

Esperança-Martins M, Gonçalves L, Soares-Pinho I, Gomes A, Serrano M, Blankenhaus B, Figueiredo-Campos P, Catarina-Marques A, Castro-Barbosa A, Cardoso A, Antunes-Meireles P, Atalaia-Barbacena H, Gaspar P, Howell-Monteiro P, Pais-de-Lacerda A, Mota C, Veldhoen M (2021) [Humoral Immune Response of SARS-CoV-2-Infected Patients with Cancer: Influencing Factors and Mechanisms](#). **The Oncologist**. 2021; 26: 1-14.

Pais HL, Luz P, Martins SL, Mansinho A, Sousa R, Luís R, Presa D, Gomes D, Costa L, Teixeira de Sousa R (2021). [Immunotherapy in Metastatic Mucosal Melanoma with Disseminated Intravascular Coagulation: A Case of Success](#). **Case Reports in Immunology**. Volume 2021. Case report.

Gordino G, Costa-Pereira S, Corredeira P, Alves P, Costa L, Gomes AQ, Silva-Santos B, Ribot JC. [MicroRNA-181a restricts human \$\gamma\delta\$ T cell differentiation by targeting Map3k2 and Notch2](#). **EMBO Rep**. 2021 Nov 24:e52234.

Yekelchik M, Madan E, Wilhelm J, Short KR, Palma AM, Liao L, Camacho D, Nkadori E, Winters MT, Rice ES, Rolim I, Cruz-Duarte R, Pelham CJ, Nagane M, Gupta K, Chaudhary S, Braun T, Pillappa R, Parker MS, Menter T, Matter M, Haslbauer JD, Tolnay M, Galior KD, Matkowskyj KA, McGregor SM, Muller LK, Rakha EA, Lopez-Beltran A, Drapkin R, Ackermann M, Fisher PB, Grossman SR, Godwin AK, Kulasinghe A, Martinez I, Marsh CB, Tang B, Wicha MS, Won KJ, Tzankov A, Moreno E, Gogna R (2021). [Flower lose, a cell fitness marker, predicts COVID-19 prognosis](#). **EMBO Molecular Medicine**, 13(11):e13714.

Invited Lectures and Seminars

Inês Gomes. RANKL/RANK pathway blockade: an opportunity to overcome resistance to CDK4/6 inhibitors in breast cancer. Oncobiology Club, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 17 2021.

Luis Costa. How host and tumor microenvironment relate to tumor heterogeneity?. Tumour Heterogeneity and Ecosystem Retreat. ITMO Cancer - France. March 17, 2021

Gomes I. RANKing a new driver of resistance to CDK4/6 inhibitors in luminal A Breast Cancer. Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 18 2021.

Raquel Cruz-Duarte. The controversial role of PLCy1 across different tumor types. Oncobiology Club, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 23, 2021.

Luis Costa. Liquid Biopsy in Cancer. Rede de Saúde da Universidade de Lisboa. Virtual event, October 10, 2021

Sandra Casimiro. RANKL-RANK pathway in hormone-dependent breast cancer. II ASPIC-ASEICA International Meeting, October 14, 2021. Virtual event.

Luis Costa. Bone Protection in Metastatic Breast Cancer. Breast Cancer Tumor Board Meeting, Rede D'or, Brasil. Virtual event, November 4, 2021

Isabel Fernandes. Terapêuticas sistémicas em neoplasia neuroendócrinas. 1º Curso de neoplasia neuroendócrinas do Grupo Português de Tumores Neuroendócrinos. Online event. November 5, 2021.

Isabel Fernandes. Cabozantinib e nivolumab e primeira linha do carcinoma do rim. Curso do Grupo Português de Génito-Urinário (GPGU) - imunoterapia em Uro-oncologia. Lisbon, Portugal, November 11, 2021.

Isabel Fernandes. Terapêuticas sistémicas dos tumores neuroendócrinos torácicos. 18º Congresso Nacional de Oncologia. Online event. November 18, 2021.

Sandra Casimiro. RANK pathway blockade in combination with CDK4/6 inhibitors as a therapeutic approach for hard-to-treat metastatic breast cancers: what we know and the (nearby) future. Oncobiology Club, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 24, 2021.

Isabel Fernandes. Tumores neuroendócrinos gastroenteropancreáticos. Reunião da associação de doentes Europacolón. Lisbon, Portugal, November 25, 2021.

Isabel Fernandes. Sarcomas de tecidos moles. Congresso da SPCCTV (Sociedade Portuguesa de Cirurgia Cardiorácica). Albufeira, Portugal, November 27, 2021.

Communications

Sara Dâmaso, Raquel Lopes Brás, Rita Paiva, Daniela Macedo, Isabel Fernandes, Luis Costa. Clinical features and management of paragangliomas in a university hospital. ENETS 2021. Virtual event. February 25-27, 2021. POSTER; INTERNATIONAL CONFERENCE.

Atalaia Barbacena, H., Gaspar, P., Dias, M., Esperança Martins, M., Mendes, C., Serrazina, J., Cunha, F., Mendonça Freitas, J.V., Duarte, L., Almeida Soares, R., Madeira Lopes, J., Howell Monteiro, P., Pais de Lacerda A. HIV and SARS-CoV-2 coinfection: Can HIV be a protective factor associated with a better clinical outcome? 19th European Congress of Internal Medicine. Virtual Edition. March 18-20, 2021. POSTER; INTERNATIONAL CONFERENCE

Atalaia Barbacena, H., Esperança Martins, M., Dias, M., Duarte, L., Serrazina, J., Mendes, C., Cunha, F., Mendonça Freitas, J.V., Almeida Soares, R., Madeira Lopes, J., Howell Monteiro, P., Pais de Lacerda, A. Bone Marrow Involvement in SARS-CoV-2 infection: A case report. 19th European Congress of Internal Medicine. Virtual Edition. March 18-20, 2021. POSTER; INTERNATIONAL CONFERENCE

Atalaia Barbacena, H., Dias, M., Serrazina, J., Esperança Martins, M., Duarte, L., Mendes, C., Cunha, F., Mendonça Freitas, J.V., Almeida Soares, R., Madeira Lopes, J., Howell Monteiro, P., Pais de Lacerda, A. Drug Induced Hepatitis in a Young COVID-19 Patient. 19th European Congress of Internal Medicine. Virtual Edition. March 18-20, 2021. POSTER; INTERNATIONAL CONFERENCE

V. Dias, M., Atalaia Barbacena, H., Serrazina, J., Esperança Martins, M., Duarte, L., Mendes, C., Serrazina, J., Cunha, F., Madeira Lopes, J., Howell Monteiro, P., Pais de Lacerda, A. Multiple Sclerosis Diagnosis and SARS-CoV-2 Infection. 19th European Congress of Internal Medicine. Virtual Edition. March 18-20, 2021. POSTER; INTERNATIONAL CONFERENCE

Gomes I, Costa L, Casimiro S. RANK signalling pathway: a new driver of resistance to CDK4/6 inhibitors in breast cancer. XIV CAML. IV NeurULisboa Virtual meeting, Lisbon, Portugal, May 5-7 2021. (POSTER COMMUNICATION / NATIONAL CONFERENCE)

Raquel Cruz-Duarte, Luís Costa, Marta Martins. PLC γ 1 Confers Resistance to Cetuximab by Triggering SHP2 Mediated RAS Activation in Colorectal Cancer. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisbon, Portugal, May 5-7, 2021. POSTER; NATIONAL CONFERENCE.

Gomes I, Costa L, Casimiro S. RANKL-blockade is effective against RANK-mediated resistance to chemo and hormone therapy in Luminal breast cancer. 27th PORTO CANCER MEETING Stemness & Metastasis: Advances in Research and Clinical Translation, Porto, Portugal, May 20-21 2021. (POSTER COMMUNICATION / INTERNATIONAL CONFERENCE)

Martins Cavaco, A. C. & Costa, M. et al. Biological effect of type I procollagen carboxyterminal propeptide in breast cancer tumour microenvironment. 27th PORTO CANCER MEETING Stemness & Metastasis: Advances in Research and Clinical Translation, Porto, Portugal, May 20-21 2021. (POSTER COMMUNICATION / INTERNATIONAL CONFERENCE)

Dâmaso, S., Paiva, R., Pinho, I., Esperança Martins, M., Lopes Brás, R., Costa, A.L., Quintela, A., Pinto, C., Costa, L. Índice de Resposta Inflamatória Sistémica Prediz Benefício de Quimioterapia de Primeira Linha à Base de Platino em Doentes com Adenocarcinoma do Pâncreas Irressecável.

Encontros da Primavera 2021. Virtual Edition. May 20-22, 2021. POSTER; NATIONAL CONFERENCE

Dâmaso, S., Willumsen, N., Cavaco, A. C. M., Corredeira, P., Pacheco, T. R. D., Costa, A. L., ... & Costa, L. Association of serum brain-specific protein fragments and brain metastases in patients with metastatic breast cancer. ASCO Annual Meeting, Chicago, EUA, 4th-8th June 2021. POSTER; INTERNATIONAL CONFERENCE.

David Gonçalves Ferreira, André Spranger, Paulo Almeida, Dolores Presa, Isabel Fernandes, Joaquim Brito. Telangiectasic Osteosarcoma Arising In Osteogenesis Imperfecta. Virtual EFORT Congress. June 30 to July 2, 2021. POSTER; INTERNATIONAL CONFERENCE.

Sardinha, M., Simão, D., Reis, A., Spencer, A., Parmanande, A., Saraiva, R., Calinas, F., Filipe, F., Winckler, P., da Luz, R., Martins, M., Gramaça, J., Ramos, M., Cadavez, E., Moura, M., Gil, L., Presa, J., Carrola, P., Pinho, I., Carvalho, S. Real-world data of nivolumab in advanced hepatocellular carcinoma: A multi-centric and retrospective study. ESMO World Congress on Gastrointestinal Cancer 2021. June 30 – July 3, 2021. Virtual Edition. July POSTER; INTERNATIONAL CONFERENCE

Dâmaso, S., Lopes Brás, R., Pinho, I., Esperança Martins, M., Paiva R., M. Alvim, C., L.Costa, A., Costa, L. A score combining CA19-9 and SIRI as a prognostic tool in metastatic pancreatic ductal adenocarcinoma. II ASPIC-ASEICA International Meeting. Virtual Edition. October 14-15, 2021. POSTER; INTERNATIONAL CONFERENCE

Luz, P, Fernandes, I., Lopes Brás, R., Soares de Pinho, I., Patel, V., Esperança Martins, M., Gonçalves, L., Diaz Acedo, R., Gamez Casado, S., Baena Cañada J., Costa, L., Sousa, R., Gregório, J., G. Costa, J., S. Fernandes, A. Occurrence of relapse after neoadjuvant treatment with trastuzumab and pertuzumab in HER2+ breast cancer patients: preliminar results from a Iberic cohort. 11^º Congresso Nacional de Senologia. Porto, Portugal, October 29-30, 2021. ORAL; NATIONAL CONFERENCE

Gordino G, Costa-Pereira S, Corredeira P, Alves P, Costa L, ... & Ribot JC. MicroRNA-181a Restricts Human $\gamma\delta$ T Cell Functional Differentiation by Targeting Map3k2 and Notch2. The 9th International $\gamma\delta$ T Cell Conference, Beijing, China, 5th-8th November 2021. POSTER; INTERNATIONAL CONFERENCE

Carolina Peixoto; Marta Lopes; Martins, Marta; Luis Costa; Susana Vinga. Biomarker selection in survival colorectal cancer data using correlation based regularization. EMBL Conference Cancer Genomics/ Virtual, Nov 22 - 24, 2021. POSTER; INTERNATIONAL CONFERENCE.

Lopes Brás, R., Lopéz, D., Esperança Martins, M., Melo-Alvim, C., Costa, L., Fernandes, I. Genomic Profile of Sarcomas as a New Approach to Targeted Therapies. 18^º Congresso Nacional de Oncologia. Virtual Edition. November 18-20, 2021. ORAL; NATIONAL CONFERENCE

Lopes Brás, R., Tomás, T., Lopéz, D., Esperança Martins, M., Melo-Alvim, C., Soares do Brito, J., Portela, J., Branquinho, A., Costa, L., Fernandes, I. Next Generation Sequencing Opens New Therapeutic Options in Sarcomas – A case series. 18^o Congresso Nacional de Oncologia. Virtual Edition. November 18-20, 2021. POSTER; NATIONAL CONFERENCE

Neves, M.E., Esperança Martins, M., Domingues, T.D., Simas, M., Ulrich, J., Abrunhosa-Branquinho, A., Pina, M.F. Radioterapia adjuvante vs. Vigilância em meningiomas grau I: estudo observacional retrospectivo. 18^o Congresso Nacional de Oncologia. Virtual Edition. November 18-20, 2021. POSTER; NATIONAL CONFERENCE

Organization of Conferences

Isabel Fernandes. Co-organizer. Reunião nacional do Grupo Português de Estudo de Sarcomas GPES. Monte Real, Portugal, April 10 (online) and September 27, 2021.

Prizes & Honors in 2021

Isabel Fernandes, Miguel Esperança Martins e Luis Costa. Best Medical Oncology poster. Occurrence of relapse after neoadjuvant treatment with trastuzumab and pertuzumab in HER2+ breast cancer patients: preliminar results from an Iberic cohort. 11^o Congresso Nacional de Senologia. Porto, Portugal, October 29-30, 2021.

Marta Martins. Guest Associate Editor in Molecular and Cellular Oncology of Frontiers in Oncology. 2021

Sandra Casimiro. Invited referee for IPO Lisboa funding grants.

Sandra Casimiro. Invited referee for KWF Kankerbestrijding – Dutch Cancer Society funding grants.

Sandra Casimiro. Topical Advisory Panel Member of Cancers. 2021

Sandra Casimiro. Guest Associate Editor in Molecular and Cellular Oncology of Frontiers in Oncology. 2021

Advanced Teaching

André Mansinho. Novos desenhos de RCTs. Oncobiology MSc, Lisbon, Portugal, April 2021

André Mansinho. Phase II Clinical Trials. Drug Discovery and Development in Oncology. Oncobiology MSc, Lisbon, Portugal, April 2021

Isabel Fernandes. Coordination of Curricular Unit. Clinical Governance. Masters in Health Services Management. ISCTE-INDEG. 2021

Isabel Fernandes. Lecture. Ethical dilemmas. Senior management program of health institutions – PADIS. Portugal, June 1, 2021.

Luis Costa. Relevância dos dados genómicos em oncologia - CURSO PÓS-GRADUADO DE GENÉTICA E GENÓMICA PARA CLINICOS 2ª EDIÇÃO, Nova Medical School. Online event, November 20, 2011

Luis Costa. Coordination of Curricular Unit. Cancer Therapeutics. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Luis Costa. Coordination of Curricular Unit. Drug Discovery in Oncology. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Luis Costa. Coordination of Curricular Unit. Seminars in Oncology. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Sandra Casimiro. Coordination of Curricular Unit. Journal Club. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Sandra Casimiro. Coordination of Curricular Unit. Laboratory Rotations. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Sandra Casimiro. Executive Coordination. Masters in Oncobiology, FMUL. Lisbon, Portugal, 2021.

Sandra Casimiro. Lecture. Preclinical Identification of Therapeutic Targets. Masters in Oncobiology, FMUL. Lisbon, Portugal, April 27 2021.

Sandra Casimiro. Lecture. Principles of Cancer Biology: The tumor microenvironment, Masters in Biomedical Research, IMM. Lisbon, Portugal, October 12, 2021.

MSc Theses

Guilherme Vilhais, 23/3/2021, Tackling the mystery of the “small xenografts”: RANK-pathway activation in RANK overexpressing breast cancer xenografts in an immune deficient mouse host, Integrated Masters in Medicine, Lisbon Medical School, University of Lisbon, Supervisor: Sandra Casimiro

Mariana Barroso, 14/5/2021, Establishment of pancreatic cancer zebrafish xenografts and therapies, Masters in Oncobiology, Lisbon Medical School, University of Lisbon, Supervisor’s Name: Rita Fior Co-Supervisor: Sandra Casimiro

Alexandre Afonso, 16/6/2021, Transcriptomic analysis of cancer cells with winner and loser behaviour, Masters in Oncobiology, Lisbon Medical School, University of Lisbon, Supervisor’s Name: Ana Queirós Co-Supervisor: Sandra Casimiro

Neuza Bacalhau, 17/6/2021, Tradução independente de cap da proteína humana up-frameshift 1 (UPF1) e cancro, Masters in Oncobiology, Lisbon Medical School, University of Lisbon, Supervisor’s Name: Luisa Romão Co-Supervisor: Sandra Casimiro

Francisco Batista, 28/6/2021, Effect of long-term RANK pathway blockade with OPG-Fc in RANK-overexpressing Luminal breast cancer cells, Integrated Masters in Medicine, Lisbon Medical School, University of Lisbon, Supervisor: Sandra Casimiro

Margarida Rodrigues, 07/07/2021, Circulating Tumour Cells Detection in Renal Cell Carcinoma, Instituto de Medicina Molecular João Lobo Antunes, Lisboa. Supervisor's Name: Tito Palmela Leitão. Co-Supervisor: Cláudia Lobato da Silva.
<https://fenix.tecnico.ulisboa.pt/cursos/mebiol/dissertacao/283828618790566>

Joana Jesus, 16/7/2021, Ikaros and C14ORF143-dependent Cell Competition on Basal Cell Carcinoma, Masters in Oncobiology, Lisbon Medical School, University of Lisbon, Supervisor's Name: Eduardo Moreno Co-Supervisor: Sandra Casimiro

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Study of Sarcomas' metabolomics. PharmaMar. Sponsored Research.
ONCODYNAMICS. Astellas, Merck Sharp & Dhome, Merck SA, Servier, Novartis, Roche, Bayer. Sponsored Research
MCPP - Multi-Cancer Profile Project. Illumina, Inc. Collaborative Research
MCPP - Multi-Cancer Profile Project. BMS, Roche. Sponsored Research
IFN-mediated immune response in patients with metastatic breast cancer under CDK4/6 inhibitors (CDK4/6i) plus endocrine therapy (ET). Pfizer. Competitive grant.
Rank Pathway Inhibitors in Combination with CDK Inhibitors. Amgen, Inc. Collaborative Research

Intellectual Property Rights in 2021

Instituto de Medicina Molecular. Sandra Cristina Cara de Anjo Casimiro and Luis António Marques da Costa. Rank Pathway Inhibitors in Combination with CDK Inhibitors. 115483 30.04.2019 PT, 62/840,810 30.04.2019 US. PCT/PT2020/050017. National phase 2021.

Science and Society in 2021

Luis Costa. Cancro. É preciso reativar rastreios e travar aumento de casos avançados. Interview. Radio Renascença. May 14 2021

Miguel Esperança Martins. Invited columnist for Portuguese newspaper "Observador".

Miguel Esperança Martins. Interview for the Portuguese newspaper "Diário de Notícias", published on the July 13th 2021 edition.

Miguel Esperança Martins. Interview for the Portuguese television channel "RTP", transmitted on July 13th 2021

Sérgio Dias Lab

Head of Laboratory: Sérgio Jerónimo Rodrigues Dias, PhD, Group Leader Associate Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Ana Luísa Ferro Espadanal Torres Magalhães	PhD	Senior Postdoctoral Researcher
Daniela Alexandra Silva Botinas	University Degree	MSc Student (Started September)
Diogo da Silva Coutinho	University Degree	MSc Student (Started July)
Emanuel Estevez de Oliveira	High School Diploma	MSc Student (Left May)
Mara Santiago Rodrigues	University Degree	MSc Student (Started October)
Miguel Maria Escoval Lopes Esperança Martins	Master Degree	PhD Student
Pedro Miguel da Silva Marreiros	University Degree	MSc Student (Left September)
Sofia Andreia Mata da Nazaré Pinheiro Esteves	High School Diploma	Trainee (Left July)
Teresa Laura Mendes Serafim	PhD	Senior Postdoctoral Researcher (Left June)

Lab Interests

We study cancer as a systemic disease, and our main focus is to understand how cancers communicate with their "host". In detail, we study the role of blood vessels and the importance of metabolic systemic signals in cancer onset and progression.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Physiology in Health, Disease and Aging
- Immunity and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

We established a novel line of research at iMM, focused on cancer metabolism and its importance for cancer onset and progression in 2017. In 2021, we further developed our projects dealing with breast cancer metabolism and the importance of vascular mimicry as a mechanism favouring metastatic dissemination of solid tumors (2 manuscripts, submitted). Importantly, in 2021 we launched a novel project in sarcoma metabolomics, in collaboration with Universidade de Aveiro and the Oncology Department of Hospital Santa Maria (Isabel Fernandes and Luís Costa) which will be the basis for a PhD Project of Dr Miguel Esperança-Martins. As a result, we published our first paper reviewing the state of the art in Sarcoma Metabolism. We also had the chance to present our findings in National and International Conferences, reinforcing our role as leaders in this particular topic of cancer research. In addition to our ongoing International (David Lyden, Cornell University, USA) and National (Rita Fior, Champalimaud Foundation; Iola Duarte, Universidade de Aveiro) collaborations, we established fruitful collaborations with several Labs at iMM, including Vanessa Morais, Edgar Gomes and Luís Costa.

Ongoing Projects in 2021

2018/2021: Como o colesterol promove a metastização em cancro de mama. Coordinator: Sérgio Dias. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/30436/2017. Amount: 190 615,32€. Total Amount: 190 615,32€.

Scientific Impact

Selected Publications

Rodrigues NV, Correia DV, Mensurado S, Nóbrega-Pereira S, deBarros A, Kyle-Cezar F, Tutt A, Hayday AC, Norell H, Silva-Santos B, Dias S (2018). [Low-density lipoprotein uptake inhibits the activation and antitumor functions of human V \$\gamma\$ 9V \$\delta\$ 2 T cells](#). **Cancer Immunology Research** 6(4):448-457.

Nóbrega-Pereira S, Caiado F, Carvalho T, Matias I, Graça G, Gonçalves LG, Silva-Santos B, Norell H, Dias S (2018). [VEGFR-2-mediated reprogramming of mitochondrial metabolism regulates the sensitivity of acute myeloid leukemia to chemotherapy](#). **Cancer Research** 78(3):731-741.

dos Santos CR, Domingues G, Matias I, Matos J, Fonseca I, de Almeida JM, Dias S (2014). [LDL-cholesterol signaling induces breast cancer proliferation and invasion](#). **Lipids in Health and Disease** 13:16.

Caiado F, Carvalho T, Rosa I, Remedio L, Costa A, Matos J, Heissig B, Yagita H, Hattori K, da Silva JP, Fidalgo P, Dias Pereira A, Dias S (2013). [Bone marrow-derived CD11b+Jagged2+ cells promote epithelial to mesenchymal transition and metastization in colorectal cancer](#). **Cancer Research** 73(14):4233-46.

2021 Publications in Peer-Reviewed Journals

Esperança-Martins M, Fernandes I, Soares do Brito J, Macedo D, Vasques H, Serafim T, Costa L, Dias S. [Sarcoma Metabolomics: Current Horizons and Future Perspectives](#). **Cells**. 8;10(6):1432 (2021). Review.

Matias I., Dias S., Carvalho T. (2020) Modulating the Metabolic Phenotype of Cancer Microenvironment. In: Serpa J. (eds) [Tumor Microenvironment](#). **Advances in Experimental Medicine and Biology**, vol 1219. Springer, Cham. Book chapter.

Invited Lectures and Seminars

Dias S. Lipids and Metabolic Shifts in Cancer. CEDOC (Universidade NOVA, Lisbon) Lecture Series. 28 April 2021.

Communications

Goodbye Flat Biology: Next Generation Cancer Models virtual meeting organized by the European Association for Cancer Research (EACR). Oct 2021.

NanoTME: Nanomedicine meets the tumor microenvironment virtual Meeting organized by the International Cancer Microenvironment Society and the University of Twente, The Netherlands. Sept 2021.

Advanced Teaching

Dias S. Coordinator. Development and Cancer, Module of the Master Program in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Dias S. Coordinator. Oncobiology, module of the LisbonBiomed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Lecturer at the following PhD Programs:

- PhD Program (“Programa de Doutoramento em Ciências Químicas, Biológicas e Engenharia”) (ITQB, Nova Universidade de Lisboa).
- PhD Program (“Programa Doutoral em Biologia Experimental e Biomedicina (Universidade de Coimbra”).
- PhD Program (“Programa de Doutoramento em Medicina (FCM, Nova Universidade de Lisboa”).

And of the following Master Programs:

- Master Degree (“Mestrado em Biologia Humana e Ambiente” (Faculdade de Ciências, Universidade de Lisboa).
- Master Degree (“Mestrado em Ciências Biomédicas”, Universidade do Algarve).

MSc Theses

Emanuel Oliveira. Master Degree in Medicine from Faculdade de Medicina da Universidade de Lisboa. “Molecular mechanisms that regulate the effect of low density lipoprotein in breast cancer transendothelial migration: the roles of Her2 and LDLR”. April 2021.

Sofia Esteves. Master Degree in Medicine from Faculdade de Medicina da Universidade de Lisboa. “The impact of nutritional availability in the microenvironment on metabolic remodeling and aggressiveness of breast cancer cells”. Junho 2021.

Valorization of Knowledge / Social and Economic Impact

Science and Society in 2021

Lecture on “Cancer and the environment”. European Researchers Night (“Noite Europeia dos Investigadores”). Monsaraz, 24th September 2021.

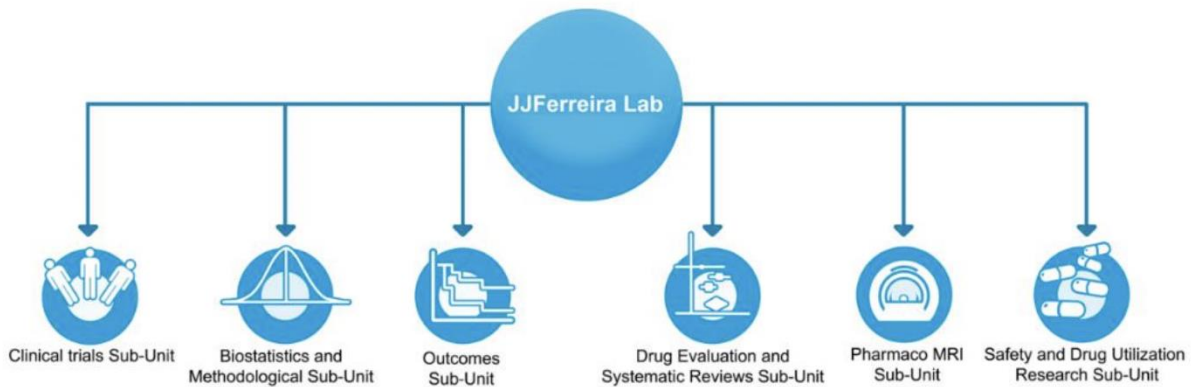
Joaquim Ferreira Lab

Head of Laboratory: Joaquim Ferreira, MD/PhD, Group Leader and Neurologist, Associate Professor, Faculdade de Medicina Universidade de Lisboa (FMUL), Head of Laboratory of Clinical Pharmacology and Therapeutics (FMUL) and Head of CNS - Campus Neurológico Sénior

Team

Ana Cristina Brito Almeida Sampaio Cruz	MD/Agregação	Clinical Staff Scientist
Ana Patrícia Silva Pita Lobo	MD/Master Degree	Clinical Researcher
Ana Paula Caldas Gomes	University Degree	Clinical Researcher (Started November)
Ana Raquel Duque Gonçalves Fernandes	Master Degree	Clinical Researcher
Ana Teresa Martins Sousa Santos	Master Degree	Lab Manager
Anabela Ferreira Valadas	MD/University Degree	Clinical Researcher
Carla Filipa Pestana Leão Guerreiro	MD/Master Degree	Clinical Researcher
Catarina Filipa Severiano e Sousa	Master Degree	PhD Student
Cláudio Virgílio Antunes David	MD/Master Degree	Clinical Researcher
Constança Maria Abecasis Jalles	MD/Master Degree	Clinical Researcher
Daisy Andreina Vieira de Abreu	PhD	Clinical Researcher
Daniel Gomes Caldeira	MD/PhD	Clinical Researcher
Daniela Marina Dias Guerreiro	University Degree	Trainee
Fátima Vanessa Santos Carvalho	MD/Master Degree	Clinical Researcher
Inês Marques de Matos Dias	Master Degree	Lab Technician
Isabel Cristina Ramos Peixoto Guimarães	PhD	Clinical Researcher
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Clinical Researcher
Luís António Garcez Duarte da Costa Ferreira	Master Degree	Clinical Researcher
Margarida de Fátima Palma Faria Borges	MD/University Degree	Clinical Researcher
Margherita Fabbri	MD/PhD	Clinical Researcher
Maria Isabel Boaventura de Atouguia	University Degree	Clinical Researcher
Maria João Bettencourt Pereira Forjaz	PhD	Clinical Researcher
Maria Leonor Brito de Arriaga Correia Guedes Möller Miranda	MD/PhD	Clinical Researcher
Mariana da Cruz Alves	MD/PhD	Clinical Researcher
Mário Miguel Coelho da Silva Rosa	MD/PhD	Clinical Researcher
Miguel Vilhena Soares Coelho	MD/PhD	Clinical Researcher
Raquel de Queirós Bouça Ribeirinho Machado	PhD	Postdoctoral Researcher
Raquel José Ladeira Lobo	Master Degree	Lab Technician
Ricardo Miguel Ribeiro Marques Cunha Fernandes	MD/PhD	Clinical Researcher
Sofia Cristina Pereira Coutinho Reimão	MD/PhD	Clinical Researcher
Tiago Alexandre Mestre	MD/PhD	Clinical Researcher
Tiago Heleno Mendes	Master Degree	Clinical Researcher
Tiago Rodrigues Teodoro	MD/Master Degree	Clinical Researcher
Vanda Viseu Filipa Cândido de Freitas	Master Degree	Clinical Researcher
Verónica Candeias Caniça	University Degree	Clinical Researcher

Graphical Abstract



Lab Interests

Parkinson's disease, Huntington Disease, Movement Disorders, Neuropharmacology, Clinical trials, Systematic reviews.

Research Field

-Neuroscience and Disorders of the Nervous System

Major Scientific Achievements in 2021

During 2021, our research group managed to produce important clinical pharmacology information, namely clinical trials' design and factors related with the efficacy and safety of therapeutic management of COVID-19. In parallel, there was a clear increase in scientific output and impact on the topics of non-pharmacological therapeutic interventions and objective and functional outcome measures.

Ongoing Projects in 2021

2021/2022: Rostock International Parkinson's Disease Study. Coordinator: Joaquim Ferreira. Funding Agency: CENTOGENE GmbH. Reference: ROPAD 01-2019. Amount: 8 000,00€. Total Amount: 8 000,00€.

2019/2025: IDEA-FAST: Identifying Digital Endpoints to Assess FATigue, Sleep and acTivities in daily living in Neurodegenerative disorders and Immune-mediated inflammatory diseases. Coordinator: Joaquim Ferreira. Funding Agency: European Commission. Reference: JTI-IMI2 853981. Amount: 289 500,0€. Total Amount: 20 997 522,50€.

2015/2021: Fair-ParK-II: Conservative iron chelation as a disease-modifying strategy in Parkinson's disease: a multicentric, parallel-group, placebo-controlled, randomized clinical trial of deferiprone. Coordinator: Joaquim Ferreira. Funding Agency: European Commission. Reference: SC3 633190. Amount: 187 083,00€. Total Amount: 5 998 994,00€.

Scientific Impact

Academic Collaborations

Gonçalo Nuno da Silva Duarte, Univ Lisbon, Lab Clin Pharmacol & Therapeut, Fac Med, Lisbon, Portugal, Univ Lisbon, Fac Med, Ctr Estudos Med Baseada Evidencia, Lisbon, Portugal, Ctr Hosp Univ Lisboa Norte, Lisbon, Portugal.

Joana Maria Rasteiro de Menezes de Alarcão, Univ Lisbon, Ctr Estudos Med Baseada Evidencia, Fac Med, Lisbon, Portugal, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Tiago Luís Gonçalves Neves Machado, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Beatrice Mainoli, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Luisa Maria Russo Prada, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Rita Avó Baião, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Catarina Dias Santos, Univ Lisbon, Lab Farmacol Clin & Therapeut, Fac Med, Lisbon, Portugal.

Ana Rita Simões Cardoso Valente, CNS Campus Neurol, P-2560280 Torres Vedras, Portugal.

Inês Chendo, Hosp Santa Maria, CHULN, Dept Neurosci & Mental Hlth, Neurol, Ave Prof Egas Moniz MB, P-1649028 Lisbon, Portugal, Faculty of Medicine, University of Lisbon, Institute of Molecular Medicine.

Filipe Brogueira Rodrigues, UCL, UCL Queen Sq Inst Neurol, UCL Huntingtons Dis Ctr, London, England.

Nilza Karina Gonçalves, Univ Lisbon, Lab Clin Pharmacol & Therapeut, Fac Med, Lisbon, Portugal.

Olga Sofia de Oliveira Caetano, Univ Lisbon, Lab Clin Pharmacol & Therapeut, Fac Med, Lisbon, Portugal.

Selected Publications

Ferreira JJ, Rodrigues FB, Duarte GS, Mestre TA, Bachoud-Levi AC, Bentivoglio AR, Burgunder JM, Cardoso F, Claassen DO, Landwehrmeyer GB, Kulisevsky J, Nirenberg MJ, Rosser A, Roth J, Seppi K, Slawek J, Furr-Stimming E, Tabriz, SJ, Walker FO, Wandenberghe W, Costa J, Sampaio C (2022). [A MDS Evidence-Based Review on Treatments for Huntington's Disease](#), **Movement Disorders**, 37(1): 25-35. Review.

Bouca-Machado R, Pona-Ferreira F, Leitao M, Clemente A, Vila-Vicosa D, Kauppila LA, Costa RM, Matias R, Ferreira JJ (2021). [Feasibility of a mobile-based system for unsupervised monitoring in Parkinson's Disease](#). **Sensors**, 21(15): 4972.

Mainoli B, Machado T, Duarte GS, Prada L, Goncalves N, Ferreira JJ, Costa J (2021). [Analysis of clinical and methodological characteristics of early COVID-19 treatment clinical trials: so much work, so many lost opportunities](#). **BMC Medical Research Methodology**, 21(1:42).

Costa J, Alarcao J, Araujo F, Ascencao R, Caldeira D, Fiorentino F, Gil V, Gouveia M, Lourenço F, Silva AME et al., (2021). [The burden of atherosclerosis in Portugal](#). **European Heart Journal-Quality of Care and Clinical Outcomes**, 7(2): 154-162.

Abrams EM, McGill G, Bhopal SS, Sinha I, Fernandes RM (2020). [COVID-19, asthma, and return to school](#), **Lancet Respiratory Medicine**, 8(9): 847-849. Editorial Material.

2021 Publications in Peer-Reviewed Journals

Abrams E M., Shaker M., Greenhawt M., Fernandes RM., Sinha, I. (2021). [Treatment of mild-to-moderate asthma in childhood and adolescence in 2021](#). **The Lancet. Respiratory Medicine**, 9(5), 443–445. Editorial Material.

Abrantes AM., Garcia AB., Alves M., Teixeira D., Brito D., Pinto FJ., Caldeira D. (2021). [Low dose colchicine in coronary artery disease: systematic review with meta-analysis](#). **Circulation Reports**, 15;3(8):457-464. Original article.

Abreu D., Ware J., Georgiou-Karistianis N., Leavitt BRR., Fitzer-Attas CJ., Cheryl J., Lobo R., Fernandes AR., Handley O., Anderson KEE., Stout JCC., Sampaio C., (et al). (2021). [Utility of Huntington's Disease Assessments by Disease Stage: Floor/Ceiling Effects](#). **Frontiers in Neurology**, 12: 595679. Original article.

Ahmed M., Marín M., Bouça-Machado R., How D., Judica E., Tropea P., Bentlage E., Brach M. (2021). [Investigating Users' and Other Stakeholders' Needs in the Development of a Personalized Integrated Care Platform \(PROCare4Life\) for Older People with Dementia or Parkinson Disease: Protocol for a Mixed Methods Study](#). **JMIR Research Protocols**, 10(1): e22463. Original article.

Alberto S., Cabral S., Proença J., Pona-Ferreira F., Leitão M., Bouça-Machado R., Kauppila LA., Veloso AP., Costa RM., Ferreira JJ., Matias R. (2021). [Validation of quantitative gait analysis systems for Parkinson's disease for use in supervised and unsupervised environments](#). **BMC NEUROLOGY**, 21(1): 331. Original article.

Aleksovska K., Bassetti CLA., Berger T., Carvalho V., Costa J., Deuschl G., Frederiksen KS., Jaarsma J., Kobulashvili T., Leone MA., Pavlakova L., Romoli M., Vignatelli L. (et al). (2021). [Guidelines should be guidelines: Time to leave the terms "consensus" and "position" for other purposes](#). **European Journal of Neurology**, 28(8):2461-2466. Editorial material.

Alonso J., Vilagut G., Mortier P., Ferrer M., Alayo I., Aragón-Peña A., Aragonès E., Campos M., Cura-González ID., Emparanza JI., Espuga M., Forjaz M.J, González-Pinto A., Haro JM., López-Fresneña N., Salázar ADM., Molina JD., Ortí-Lucas RM., Parellada M., Pelayo-Terán JM., Pérez-Zapata A., Pijoan JI., Plana N., Puig MT., Rius C., Rodríguez-Blázquez C., Sanz F., Serra C., Kessler RC., Bruffaerts R., Vieta E., Pérez-Solà V. MINDCOVID Working group (2021). [Mental health impact of the first wave of COVID-19 pandemic on Spanish healthcare workers: A large cross-sectional survey](#). *Revista de Psiquiatria y Salud Mental*, (Engl Ed). 4(2):90-105. Original article.

Alves M., Abrantes AM., Portugal G., Cruz MM., Reimão S., Caldeira D., Ferro JM., Ferreira JJ. (2021). [Does Parkinson's Disease Increase the Risk of Atrial Fibrillation? Insights from Electrocardiogram and Risk Scores from a Case-Control Study](#). *Frontiers in Neurology*, 12(652424). Original article.

Alves M., Fernandes MA., Bahat G., Benetos A., Clemente H., Grodzicki T., Martínez-Sellés M., Mattace-Raso F., Rajkumar C., Ungar A., Werner N., Strandberg T.; EuGMS Special Interest Group in Cardiovascular Medicine. (2021). [Protecting older patients with cardiovascular diseases from COVID-19 complications using current medications](#). *European Geriatric Medicine*, 12(4):725-739. Original article.

Alves., Lobo PP., Kauppila LA., Rebordão L., Cruz MM., Manuela M., Soares F., Cruz J., Tornada A., Caldeira D., Reimão S., Oliveira V., Ferro JM., Ferreira JJ. (2021). [Cardiovascular and cerebrovascular risk markers in Parkinson's disease: Results from a case-control study](#). *European Journal of Neurology*, 28(8): 2669-2679. Original article.

Alves M., Lobo PP., Kauppila L., Rebordão ML., Cruz MM., Reimão S., Ferro JM., Ferreira JJ. (2021). [Neuroimaging cerebrovascular biomarkers in Parkinson's disease](#). *Neuroradiology Journal*, 19714009211059118. Original article.

Alves M., Prada L., Costa J., Ferreira JJ., Pinto FJ., Caldeira D. (2021). [Effect of oxygen supply on mortality in acute ST-elevation myocardial infarction: systematic review and meta-analysis](#). *European Journal of Emergency*, 28(1): 11-18. Review.

Alves M., Macedo I., Távora C., Freitas Silva J., Fonseca T. (2021). [Sleep disturbances management in elderly hospitalized patients](#). *Journal of Pharmacy Practice*, 08971900211053287.

Alves M., Távora C., Freitas Silva J., Gomez N., Fonseca T. (2021). [To How Much Noise Are We Exposing Hospitalized Elderly Patients During Sleep?](#) *Acta Médica Portuguesa*, 34(10):707-716. Letter.

Amaral R., Jácome C., Almeida R., Pereira AM., Alves-Correia M., Mendes S., Rodrigues JCC., Carvalho J., Araújo L., Costa A., Silva A., Teixeira MF., Ferreira-Magalhães M., Alves RR., Moreira AS., Fernandes RM., Ferreira R., Pinto P.L, Neuparth N., Bordalo D., Bom AT., Cálix MJ., Ferreira T., Gomes J., Vidal C., Mendes A., Vasconcelos MJ., Silva PM., Ferraz J., Morête A., Pinto CS., Santos N., Loureiro CC., Arrobas A., Marques ML., Lozoya C., Lopes C., Cardia F., Loureiro CC.,

Câmara R., Vieira I., Silva Sd., Silva E., Rodrigues N., Fonseca JÁ. (2021). [Profiling Persistent Asthma Phenotypes in Adolescents: A Longitudinal Diagnostic Evaluation from the INSPIR ERS Studies](#). **International Journal of Environmental Research and Public Health**, 18(3):1015. Original article.

António JP., Carvalho JI., André AS., Dias JN., Aguiar SI., Faustino H., Gois, P. M. (2021). [Diazaborines are a versatile platform to develop ROS-responsive antibody drug conjugates](#). **Angewandte Chemie International Edition**, 60(49), 25914-25921. Original article

Antunes MM., Alves M., Pinto FJ., Agnelli G., Caldeira D. (2021). [The high-risk bleeding category of different scores in patients with venous thromboembolism: systematic review and meta-analysis](#). **European Journal of Internal Medicine**, 94: 45-55. Review.

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Vila-Viçosa D., Clemente A., Pona-Ferreira F., Leitão M., Bouça-Machado R., Kauppila L., Costa RM., Matias R., Ferreira JJ. (2021). [Unsupervised walking activity assessment reveals COVID-19 impact on Parkinson's disease patients.](#) *Movement Disorders*, 36(3):531-532. Letter.

Vives-Cases C., Sanz-Barbero B., Ayala A., Pérez-Martínez V., Sánchez-SanSegundo M., Jaskulska S., Antunes das Neves AS., Forjaz MJ., Pyżalski J., Bowes N., Costa D., Waszyńska K., Jankowiak B., Mocanu V., Davo-Blanes MC. (2021). [Dating Violence Victimization Among Adolescents in Europe: Baseline Results from the Lights4Violence Project.](#) *International Journal of Environmental Research and Public Health*, 18, 1414. Original article.

Vouga Ribeiro N., Gouveia Melo R., Guerra NC., Nobre Â., Fernandes R M., Pedro L M., Costa J., Pinto FJ., Caldeira, D. (2021). [Fluoroquinolones Are Associated with Increased Risk of Aortic Aneurysm or Dissection: Systematic Review and Meta-analysis.](#) *Seminars in Thoracic and Cardiovascular Surgery*, 33(4), 907–918. Review.

Pre-Print Publications

M Byrne L., Schultz J., B Rodrigues F., van der Plas E., Langbehn D., Nopoulos P., J Wild E. (2021). [Neurofilament light protein as a blood 2 biomarker for Huntington's disease in 3 children.](#) medRxiv. <https://doi.org/10.1101/2021.02.02.21251000>.

Domenighetti, C., Sugier, P. E., Ashok Kumar Sreelatha, A., Schulte, C., Grover, S., Mohamed, O., ... & Comprehensive Unbiased Risk Factor Assessment for Genetics and Environment in Parkinson's Disease (Courage-PD) Consortium. (2022). Dairy Intake and Parkinson's Disease: A Mendelian Randomization Study. *Movement Disorders*. <https://doi.org/10.1002/mds.28902>.

Chendo, I., Silva, C., Duarte, G. S., Prada, L., Voon, V., & Ferreira, J. J. (2021). Frequency and Characteristics of Psychosis in Parkinson's Disease: A Systematic Review and Meta-Analysis. *Journal of Parkinson's Disease*, (Preprint), 1-10. <https://doi.org/10.3233/JPD-212930>. Article. (IF: -, Citations: 0. Source: Thomson Reuters.

Invited Lectures and Seminars

Reimão S. Workshop Clinical Cases - Differential Diagnosis: DISH + CPPD, Novartis Virtual Symposium. 17 de dezembro de 2021. (online).

Ferreira, JJ. Doença de Parkinson Avançada (HY = IV - V) - o que eu faço? 12º Encontro Nacional de Distúrbios do Movimento, Centro de Hotel Majestic Palace - Florianópolis, SC, 25 -27 de novembro de 2021.

Ferreira, JJ. Doença de Parkinson: novas drogas disponíveis. 12º Encontro Nacional de Distúrbios do Movimento, Centro de Hotel Majestic Palace - Florianópolis, SC, 25 -27 de novembro de 2021.
Ferreira, JJ. Casos clínicos com vídeo: doença em fase inicial. Curso de Doenças do Movimento em Medicina Geral e Familiar, 20 de novembro de 2021. (online).

Ferreira, JJ. What happens now? The Medical Education in a Post-Covid Er. 8ª edição do Congresso de Educação Médica da FMUL, Faculdade de Medicina da Universidade de Lisboa, 20 de novembro de 2021.

Reimão S (Moderador). Sessão de Casos Clínicos SILAN - virtual, 19 de novembro de 2021.

Guimarães, I. How to develop and validate health instruments. Master in Speech therapy, Health School of Sciences, Instituto Politécnico do Porto, 6th November 2021. (online).

Reimão S. Predicción imagenológica del TCE: Microhemorragias. Congresso SILAN virtual, 4 de novembro de 2021.

Ferreira, JJ. Doenças do Movimento. Moderador de Sessão de Comunicações Orais, Congresso de Neurologia 2021, Moderador, Centro de Congressos Real Santa Eulália & Hotel Real Bellavista, 28 de outubro de 2021.

Ferreira, JJ. Microbioma intestinal e doenças neurológicas. Congresso de Neurologia 2021, Moderador, Centro de Congressos Real Santa Eulália & Hotel Real Bellavista, 28 de Outubro de 2021.

Reimão S. Neurological markers of a flourishing mind and emotional system, Symposium on “Biological Markers of human flourishing: extent and challenges”, Angelicum – Pontificia Università S. Tommaso D’Aquino and University of Birmingham, Roma, 23 de outubro de 2021.

Reimão S. Biomarcadores na Doença de Alzheimer: Ressonância Magnética. Curso de Biomarcadores na Doença de Alzheimer da Sociedade Portuguesa de Neurologia, Figueira da Foz, 18 de outubro de 2021.

Reimão S. Trans-humanismo De *homo sapiens* a *homo ciborgue*? Congresso da Associação de Médicos Católicos Portugueses, Sintra, 9 de outubro de 2021.

Ferreira, JJ. Tremor e Doença de Parkinson. IX Curso Anual de Atualização em Geriatria e Gerontologia, Hotel VIP Executive Entrecampos Hotel & Conference, Lisboa, 5 de outubro de 2021.

Reimão S. Multi-modal MRI in Parkinson’s Disease: More Information, More Knowledge? MDS virtual congress, 19 de setembro de 2021.

Fernandes RM. Como proceder. Eosinófilos na Asma e Infecções Virais. Anjos ou Demónios? 9º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica (SPAP), 18th September 2021.

Fernandes RM. A importância dos guidelines. 9º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica (SPAP), 18th September 2021.

Guimarães, I. Speech and Swallowing Assessment in Parkinson's Disease. 4th Allied Health Rehabilitation Course for Parkinson's Disease. International Parkinson and Movement Disorders Society Asian & Oceanian Section. Dubai, August 25, 2021. (online).

Guimarães, I. Speech Therapy in Parkinson's Disease. 4th Allied Health Rehabilitation Course for Parkinson's Disease. International Parkinson and Movement Disorders Society Asian & Oceanian Section. Dubai, August 25, 2021. (online).

Mariana Alves. Workshop - Upon Arrival Training. International Federation of Medical Students' Associations. Lisbon, Portugal, August 4th, 2021

Alves, M. Equators. Introdução à avaliação de risco de viés e qualidade de estudos clínicos. Lisbon, Portugal, July 14th, 2021.

Ferreira, JJ. Experimentar o futuro: as novas tecnologias e os desafios da inovação em Neurociências. Ciclo de Conversas Vector B2B, Auditório da Incubadora de Lisboa, 22 de julho de 2021.

Fernandes RM. Biológicos nos Endótipos. Como proceder. SPAP DIGITAL 2021, Sociedade Portuguesa de Alergologia Pediátrica (SPAP), 29th May 2021.

Ferreira, JJ. New developments on COMT inhibitors for the management of Parkinson disease. web advisory meeting of ONgentys/Opicapone _ONO Pharma, 12 de Abril de 2021.

Ferreira, JJ. A doença de Parkinson começa no intestino. Reunião da SPDMOV, 10 de abril de 2021. (videoconferência).

Guimarães I. Os sons da Fala e suas perturbações [Speech sounds and its disorders]. 4rd Course on Language. ISPA (Instituto Superior de Psicologia Aplicada), Lisbon, 17 February. (online).

Ferreira, JJ. Covid-19 e incerteza: lições da encefalite letártigica 100 anos depois. Ciclo de Conferências, 28 de Janeiro de 2021. (videoconferência).

Communications

Martins ME., Lopes AA., Santos HF., Rosado M.L, Guimarães I., Paquete P., Almeida P., Lopes AF., Carrillo E., Vilaró J., Järvinen STS., Kozakiewicz M., Kędziora-Kornatowska K., Hoxha A., Pekarić J., Gruneberg C. Projeto SIENHA – Rede europeia estratégica e inovadora para a educação no envelhecimento saudável [SIENHA-Strategic Innovative Educational Network for Healthy Ageing]. 4^a Reunião Internacional da Rede Académica das Ciências da Saúde da Lusofonia, Benguela, Angola, 25-27th November, 2021. (poster presentation). International conference.

Nogueira P., Forjaz M.J, Rodriguez-Blazquez C., Diaz-Franco A., Unim B., Palmieri L., Carcaillon-Bentata L., Makovski T., Feteira-Santos R. Research methodologies to assess the impact of COVID-19. 14th European Public Health Conference, 10-12 Nov 2021. (Oral communication). International conference.

Nascimento D., Carmona J., Mestre T., Ferreira JJ., Guimarães I. Characteristics and validity of rating scales for the assessment of drooling in Parkinson's disease: A systematic review. European Society for Swallowing disorders. 4-6th November 2021. (Online) (Poster presentation). International conference.

Amaral, R., Jácome, C., Almeida, R., Pereira, A., Alves-Correia, M., Mendes, S., Rodrigues, J. C., Carvalho, J., Araújo, L., Costa, A., Silva, A., Teixeira, M. F., Ferreira-Magalhães, M., Rodrigues-Alves, R., Moreira, A. S., Fernandes, R., Ferreira, R., Leiria-Pinto, P., (et al). (2021). Phenotypes of persistent asthma in adolescents revealed different patterns in longitudinal asthma-related outcomes. *European Respiratory Journal*, 58(suppl 65), OA2566, ERS International Congress, in session "Prediction of exacerbations in patients with COPD". International conference.

Prada L. Guerra I., Rodrigues A., Fernandes RM., Ferreira, JJ. (2021, October). Review of Medical Devices for Pediatric Cough. 21^a Congresso Nacional de Pediatria, Braga, Portugal, October 27-29, 2021 (Poster presentation). National conference.

Pires MJ., Cavaco J., Alves M., Bessa F., Gomes AC., Coimbra E., Oliveira A. Uma causa rara de Choque Hemorrágico – Caso clínico. 27^o Congresso Nacional Medicina Interna, Out 2021 (poster presentation). National conference.

Alves M., Caldeira D., Ferro JM., Ferreira. JJ. Blood pressure variability and asymptomatic end-organ damage in Parkinson's disease patients – case control study. 17th EuGMS Congress, Athens, Greece, 13 Oct 2021. (Poster). International conference.

Marques Macedo I., Alves M., Távora C., Gómez N., Freitas Silva J., Nunes Da Silva G., Fonseca T. Wakeup call: to how much nighttime noise are we exposing our elderly hospitalized patients? 17th EuGMS Congress, Athens, Greece, 13 Oct 2021. (Poster presentation). International conference.

Fontes L., Guimarães I. Funcionamento oromotor e articulatorio na criança traqueotomizada [Oromotor functioning and verbal articulation in tracheotomized children]. II International Congress «Communicating science», Portuguese Society of Speech Therapy, 22-26th September 2021. (Oral communication). International conference.

Pós de Mina S., Martins F., Guimarães I. Motricidade oral em crianças em idade pré-escolar com Perturbação dos Sons da Fala: Estudo preliminar. [Oromotor performance in preschool children with speech sound disorders]. II International Congress «Communicating science», Portuguese Society of Speech Therapy, 22-26th September 2021 (Oral communication). International conference.

Ascensão M., Grilo M., Guimarães I. Desempenho oromotor em crianças dos seis aos nove anos de idade. [Oromotor performance in children aged six to nine years old]. II International Congress «Communicating science», Portuguese Society of Speech Therapy, Lisbon, 23th September 2021. (Oral communication). International conference.

Pereira N., Coutinho M., Lima C., Almeida J., Guimarães I. Protocolo de Avaliação da Disfagia Neurogénica: Dados preliminares da disfagia no AVC. [Neurogenic dysphagia assessment: preliminar data for dysphagia in Cerebral Vascular Accident]. II International Congress «Communicating science», Portuguese Society of Speech Therapy, 22-26th September 2021. (Oral communication). International conference.

Capucho C., Guimarães I., Lá F. (2021). Novas abordagens à (re)habilitação vocal dos cantores [New approaches to Singers' vocal rehabilitation]. 68th Nacional Congresso for the Portuguese Society of Ear Nose & Throat (ENT) & XVIII ENT Luso-Spanish Congress, Viseu, 17th September (oral presentation). National Conference.

Falcón M., Rodríguez-Blázquez C., Fernández-Gutiérrez M., Romay-Barja M., Bas-Sarmiento P., Forjaz MJ. Propiedades psicométricas del cuestionario COVID-19 Health Literacy en España. XXXIX Reunión Anual de la Sociedad Española de Epidemiología (SEE) y XVI Congresso da Associação Portuguesa de Epidemiologia (APE). León, 7-10 sept 2021. Abstract publicado en Gac Sanitaria 2021; 5 Supl Congr: 67. (Oral communication). International conference.

Beca Martínez T., Romay Barja M., Falcón Romero M., Rodríguez Blázquez M., Forjaz MJ. Factores asociados al cumplimiento de las principales medidas de prevención frente a la covid-19 en España. XXXIX Reunión Anual de la Sociedad Española de Epidemiología (SEE) y XVI Congresso da Associação Portuguesa de Epidemiologia (APE). León, 7-10 sept 2021. Abstract publicado en Gac Sanitaria 2021; 5 Supl Congr: 175. (poster presentation). International conference.

Rodríguez-Blázquez C., Falcón M., Romay-Barja M., Forjaz MJ. Evaluación de la fatiga pandémica ante COVID-19 y factores asociados en población general española. XXXIX Reunión Anual de la Sociedad Española de Epidemiología (SEE) y XVI Congresso da Associação Portuguesa de Epidemiologia (APE). León, 7-10 sept 2021. Abstract publicado en Gac Sanitaria 2021; 5 Supl Congr: 206. (Poster presentation). International conference.

Machado T., Caldeira D., Ferreira, JJ, Fernandes R. Data Monitoring Committees in Paediatrics: a review of randomised clinical trials registered in ClinicalTrials.gov. The European Society for Developmental, 18th European Society for Developmental Perinatal and Paediatric Pharmacology Congress, Liverpool, England. June 29-30, 2021 (Poster presentation).

Guerra I., Prada L., Rodrigues A., Fernandes RM., Ferreira JJ. Review of Medical Devices for Pediatric Cough. 18th European Society for Developmental Perinatal and Paediatric Pharmacology Congress, Liverpool, England. June 29-30, 2021 (Poster presentation). International conference.

Stocchi F., Ferreira JJ., Klepitskaya, O., Magalhães D., Rocha, JF, Soares-da-Silva P. Efficacy of Opicapone in the Reduction of ON-time with Troublesome Dyskinesia in Parkinson's Disease Patients with Motor Fluctuations and Troublesome Dyskinesia. Presented virtually at the XXVI World Congress on Parkinson's disease and Related Disorders, May, 1-4, 2021. (Poster presentation). International conference.

LeWitt P., Stocchi F., Ferreira JJ., Klepitskaya O, Shah C., Magalhães D., Rocha JR, Soares-da-Silva P. Efficacy of Opicapone at Different Levodopa Regimens up to a Threshold of 600 mg/day Levodopa in Parkinson's Disease Patients with Motor Fluctuations. Presented virtually at the XXVI World Congress on Parkinson's disease and Related Disorders, May,1-4, 2021. (poster presentation). International conference.

Hauser RA., Isaacson S., Ferreira JJ., Serbin M.,Farahmand K., Olson K., Klepitskaya O., Rocha F., Soares-Da-Silva P. (et al). Efficacy of opicapone in Parkinson's patients with motor fluctuations and ON Hoehn & Yahr 2.5: post hoc analysis of BIPARK-1. Presented virtually at the XXVI World Congress on Parkinson's disease and Related Disorders, May, 1-4, 2021. New Number: A 201 (poster presentation). International conference.

Hauser RA. Lew MF., Comella CL., Poewe W., Rascol O., Ferreira JJ., Olson K., Farahmand K., Shah C., Rocha JF., (et al). Nighttime and morning OFF improvements with opicapone in patients with Parkinson's Disease and motor fluctuations. Presented virtually at the XXVI World Congress on Parkinson's disease and Related Disorders, May, 1-4, 2021. New Number: A 187. (poster presentation). International conference.

Ferreira JJ. Manifestações neurológicas associadas a pandemias. 3º Congresso CNS, "COVID-19 e doenças neurológicas: do confinamento ao pós-pandemia", 24 de Abril de 2021. (Oral communication). National conference

Ferreira JJ. As doenças neurológicas são critério de prioridade para vacinação? 3º Congresso CNS, "COVID-19 e doenças neurológicas: do confinamento ao pós-pandemia", 24 de Abril de 2021. (Oral communication). National conference.

Prada, L., Prada, A., Antunes, M.M., Fernandes, R.M., Costa, J., Ferreira, J.J., & Caldeira, D. Systematic reviews and meta-analyses published in indexed Portuguese medical journals: time trends and critical appraisal. 51st Meeting of the Portuguese Society of Pharmacology, 39th Meeting of the Clinical Pharmacology and 20th Meeting of the Toxicology, at the Faculty of Pharmacy, Universidade de Lisboa. February 17-19, 2021. (Oral communication). National conference.

Graça Rodrigues TE., Cunha N., Silvério António P., Couto Pereira P., Valente Silva B., Alves Da Silva P., Brito J., David C., Pinto FJ., Almeida AG. (2021). Hypertensive response in exercise-a tool to predict stroke risk? *European Journal of Preventive Cardiology*, 28, S1. (Meeting Abstract). International conference.

Cunha NPD., Rodrigues T., Silvério António P., Couto Pereira S., Morais P., Alves Da Silva P., Valente Silva B., Brito J., David C., Pinto FJ., Almeida AG. (2021). Hypertensive response to exercise-to treat or not to treat? *European Journal of Preventive Cardiology*, 28, S1. (Meeting Abstract). International conference.

Lima C., Coutinho M., Pereira N., Almeida J., Guimarães I. (2021) Protocolo de Avaliação da Disfagia Neurogénica: Contributo para o estudo da aplicabilidade, sensibilidade dos itens e fidedignidade. [Neurogenic dysphagia assessment: Contribution for its applicability, itens sensibility and reliability] 15th Congress of Cerebral Vascular Stroke, 4-6th February. (Oral communication). National conference.

Esquenazi A., Jorge, J., FERREIRA JJ. et al. (2021). Patient experiences of symptom –emergence_ finding from 2 online patient surveys in spasticity and cervical dystonia, *Toxicon*, 190, S23-S24:1. (Meeting Abstract). International conference.

Esquenazi A., Ferreira, JJ., Jacinto J, Lysandropoulos A., Comella C. (2021). Management of symptom re-emergence in patients living with spasticity and cervical dystonia: findings from 2 online patient surveys, *Toxicon*, 190, S23-S23:1. (Meeting Abstract). International conference.

Cunha NPD., Rigueira J., Santos R., Nunes-Ferreira A., Rodrigues T., António P., Pereira S., Morais P., Silva P., Brito J., Silva B., Plácido R., David C., Pinto FJ., Almeida AG. (2021). Mitral annulus disjunction: is it a marker of ominous prognosis? *European Heart Journal-Cardiovascular*, 22, S1. (Meeting Abstract). International conference.

Silvério António P., Rodrigues T., Santos R., Nunes-Ferreira A., Cunha N., Couto Pereira S., Morais PS., Alves Da Silva P., Valente Silva B., Brito J., Plácido R., David C., Pinto FJ., Almeida AG. (2021). Mitral valve prolapse-it" s possible to stratify prognosis in these patients? *European Heart Journal-Cardiovascular Imaging*, 22, S1. (Meeting Abstract). International conference.

Organization of Conferences

Guimarães I. President of the scientific committee. II International Congress «Communicating science», Portuguese Society of Speech Therapy, 22-26th September, 2021.

Ferreira JJ. 3^o Congresso CNS, "COVID-19 e doenças neurológicas: do confinamento ao pós-pandemia", 24 de Abril de 2021.

Prizes & Honors in 2021

Guimarães, I. Scientific merit award [2017-2020]. Portuguese Society of Speech Therapy, Lisbon, Portugal, 24th September 2021.

Távora C., Alves M., Gómez N., Marques Macedol., Freitas Silva J., Nunes Da Silva G., Fonseca T. 3^o Prémio - Prémio Popular, 23^o Congresso Nacional da Ordem dos Médicos, "Ruído diurno e noturno numa enfermaria de medicina interna", agosto 2021.

Lima, C., Coutinho, M., Pereira, N., Almeida. J., Guimarães, I. Multiprofessional award by the Portuguese Society of AVC on behalf of the oral presentation Protocolo de Avaliação da Disfagia Neurogénica: Contributo para o estudo da aplicabilidade, sensibilidade dos itens e fidedignidade [Neurogenic dysphagia assessment: Contribution for its applicability, itens sensibility and reliability] 15th Congress of Cerebral Vascular Stroke, 4-6th February (online).

Mendes Pedro D., Ribeiro Narciso M., Alves M., Fonseca T. Prémio risco cardiovascular Dr Pedro Marques da Silva 2021: “Neutrophil-to-lymphocyte ratio: The role of adding a biomarker to a predictive post-stroke pneumonia score”, Lisboa, Portugal, 2021.

Advanced Teaching

Guimarães, I. Lecturing «Research methods» at ESSAlcoitão-SCML, Estoril, Portugal Master in Speech Therapy specialization in oral motor function and swallowing: 9th edition (2020-2022), 10th edition (2021-2023).

Guimarães, I. Master in Occupational Therapy specialization in Sensory Integration, 9th edition at ESSAlcoitão-SCML, Estoril, Portugal 2021.

Fernandes RM. Curso pós-graduado, Curso de Formação Contínua em Pediatria. Módulo de Alergologia. Alegria respiratória, fenótipos e tratamento. Sociedade Portuguesa de Pediatria. 10th December 2021.

Ferreira, JJ. 12º Encontro Nacional de Distúrbios do Movimento, Florianópolis, SC, 25-27 de novembro de 2021.

Fernandes RM. Pós-Graduação em Gestão Saúde Baseada na Evidência. Introdução as revisões sistemáticas. ISEG. 23-24th November 2021.

Ferreira, JJ. Casos clínicos com vídeo: doença em fase inicial, Curso de doenças do Movimento em Medicina geral e Familiar: Parkinson, SPDMov, 20 de Novembro de 2021. (online).

Reimão S. “Ressonância Magnética na Doença de Parkinson: prática clínica e investigação”? - Seminário do 2º ano da Unidade Curricular “Neurociências e Neuromodulação” do Mestrado em Engenharia Biomédica e Biofísica da Faculdade de Ciências da Universidade de Lisboa, 18 de Novembro de 2021.

Fernandes RM. Mestrado de Investigação Clínica. Outcomes e instrumentos de avaliação clínica. FMUL. 6th November 2021.

Fernandes RM. Curso Básico de Revisões Sistemáticas, 3rd ISBE 8th Cochrane 4th CWP Annual event. Course co-coordinator, and lecturer - Wrap-up with an expert, and the future of systematic reviews. Ordem dos Médicos, Lisboa. 26th October 2021.

Ferreira, JJ. Tremor e Doença de Parkinson: dicas práticas na avaliação e tratamento, IX Curso Anual de Atualização em Geriatria e Gerontologia, Auditório do Centro Ismaili, Lisboa, 16 de outubro de 2021.

Fernandes RM. Mestrado de oncobiologia. Introdução às revisões sistemáticas de intervenções terapêuticas, Faculdade de Medicina da Universidade de Lisboa. 8th April 2021. (online).

Ferreira, JJ. Desenvolvimento pré-clínico, Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 12 de março de 2021. (online).

Rosa, MM. Desenvolvimento clínico, Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 12 de março de 2021. (online).

Fernandes, R. Instrumentos de avaliação e outcomes, Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 12 de março de 2021. (online).

Duarte G. Avaliação da qualidade de ensaios clínicos, Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 12 de março de 2021. (online).

Ferreira, JJ. Desenho de ensaios e elaboração de protocolo (em grupos de trabalho), Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 13 de março de 2021. (online).

Ferreira, JJ. Desenho de ensaios e elaboração do protocolo (em grupos de trabalho), Módulo V, Ensaio clínicos, Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina de Lisboa, 13 de março de 2021. (online).

Ferreira, JJ. Parkinson's disease: clinical presentation and current therapeutics, Curso Avançado – Doenças Neurodegenerativas, Faculdade de Medicina da Universidade Nova de Lisboa, 27 de fevereiro de 2021. (online).

Fernandes RM. Postgraduate course. Como escolher os parâmetros de avaliação e instrumentos de avaliação? ABC de Investigação Clínica para Internos de Neurologia. 29th-30th January 2021. (Online).

MSc Theses

Bárbara Ribeiro de Sousa, 22 de Abril de 2021, Mild traumatic brain injury: a systematic review on brain MRI changes and correlation with neuropsychological outcomes. Faculdade de Medicina da Universidade de Lisboa (FMUL). Supervisor: Sofia Reimão. Co-Supervisor: Carla Guerreiro.

Manuel Lucas, 22 de abril de 2021, Brainstem MRI measurements in Parkinsonian syndromes: which is the best? FMUL. Supervisor: Sofia Reimão. Co-Supervisor: Carla Guerreiro.

Bárbara Rodrigues, 22 de abril de 2021, Imagem do Acidente Vascular Cerebral agudo: Tomografia Computorizada ou angio-TC – qual o melhor preditor de enfarte? Supervisor: Sofia Reimão. Co-Supervisor: Lia Neto.

Afonso Gonçalves, 19 de abril de 2021, Mapeamento funcional da linguagem na avaliação pré-operatória de neoplasias primárias do sistema nervoso central: a propósito de um caso clínico. Supervisor: Sofia Reimão.

Teresa Santana, 12 de maio de 2021, Post-operative imaging findings in deep brain stimulation: a retrospective study? Supervisor: Sofia Reimão.

PhD Theses

Mariana Cruz Alves, 29/10/2021, *Fatores de risco cardiovasculares associados à Doença de Parkinson*. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

Raquel Bouça Machado, 21/9/2021, *Functional Mobility in Parkinson's Disease*, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

Valorization of Knowledge / Social and Economic Impact

Science and Society in 2021

Ferreira, JJ. Entrevista. Dia Mundial da Doença de Parkinson. Bom dia Portugal, RTP 1, 12 de abril de 2021.

Guimarães I. Conference moderator: *Who should we treat using research findings to make clinical decisions on who to treat and what approach to use for children with speech sound disorder*. Speaker: Yvonne Wren, PhD. Portuguese Society of Speech Therapy, 22-26th September 2021. (Online).

Guimarães, I. Co-coordination of the Web App "ReageCOVID" to promote self-management at short and long term in COVID.19 context [Voice & Swallowing]. ESSAlcoitão, oficial presentation in July 2021.

Fernandes RM. Stand4kids, supporting pediatric trials. Semana da Epilepsia, Associações de doentes com Epilepsia, Online. 13th March 2021.

Ferreira JJ. Entrevista: Vacinação contra a COVID-19 em Portugal, SIC Notícias, 12 de Fevereiro de 2021.

José Ferro Lab

Head of Laboratory: José M Ferro, MD, PhD, Group Leader and Honorary Full Professor of Neurology, Faculdade de Medicina Universidade de Lisboa

Team

Alcina Amparo Fraga Luz	High school Diploma	Administrative Technician
Alexandre Valério de Mendonça	PhD with Habilitation	Clinical Staff Scientist (Left December)
Ana Catarina Gaspar Fonseca	MD/PhD	Clinical Researcher
Ana Isabel Figueira Verdelho	PhD	Clinical Staff Scientist
Carla Cristina Paulo Gabriel Bentes	PhD	Clinical Researcher
Carolina Pires Maruta	PhD	Clinical Researcher
Diana de Aguiar Dias de Sousa	MD/PhD	Clinical Researcher
Dina Lúcia Gomes da Silva	PhD	Visiting Researcher (Left December)
Elisa Cristina Leal Martins de Nunes	Master Degree	Lab Technician (Left December)
Frederico Simões Oliveira Fernandes do Couto	PhD	Clinical Researcher (Left December)
Inês Gomes de Cabaço	Master Degree	Trainee (Started June)
José Manuel Borges Fonseca	PhD	Senior Technician
Lara Isabel Pires Melo Caeiro	PhD	Clinical Researcher
Maria Gabriela Mariano Leal	University Degree	Lab Technician (Left June)
Maria Isabel Segurado Pavão Martins Catarino Petiz	PhD	Clinical Staff Scientist
Maria Luísa Mendonça Correia Pires	High School Diploma	Administrative Technician
Maria Luísa Reis e Sousa de Abreu e Albuquerque	MD/University Degree	Clinical Researcher (Left December)
Maria Manuela Gil Guerreiro	PhD	Clinical Staff Scientist (Left December)
Mariana Durão Borges	Master Degree	Lab Technician (Left December)
Mário Rui Jesus Santos Rodrigues	Master Degree	Lab Technician (Left December)
Marisa Marina Fatuda Costa	High School Diploma	Administrative Technician
Marta Almeida e Silva Granadeiro	Master Degree	Psychologist (Started January)
Patrícia Martins Canhão	PhD	Clinical Staff Scientist
Pedro Miguel Nascimento Alves	MD/Master Degree	Clinical Researcher
Sandra Maria Dias Cardoso	Master Degree	Lab Technician
Teresa Maria de Pinho e Melo Pereira Marques	University Degree	Clinical Researcher

Graphical Abstract

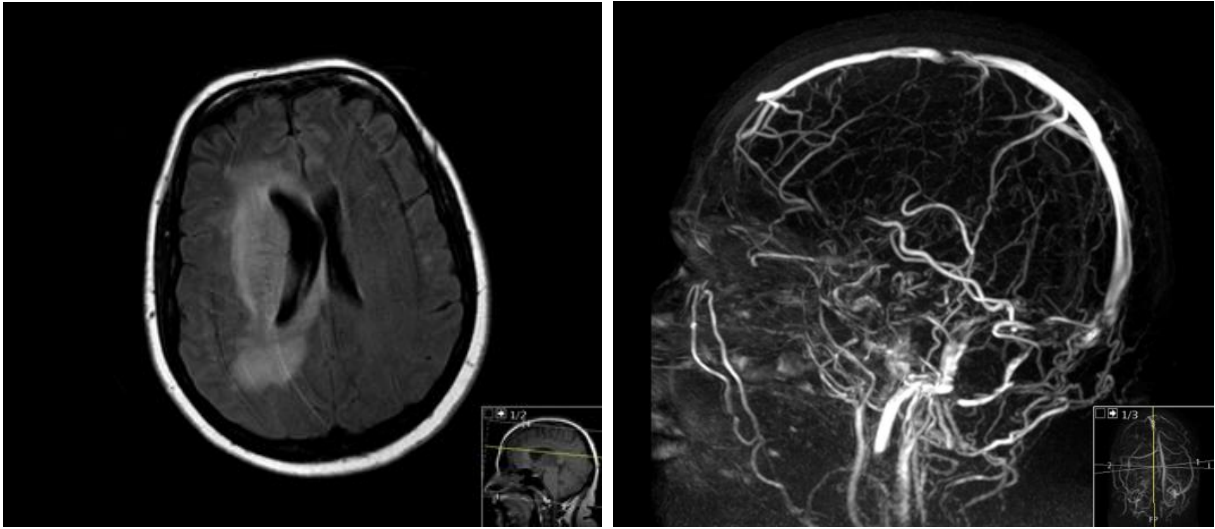


Image caption: Brain lesions caused by a cerebral venous thrombosis in a young woman

Lab Interests

We study the prevention and treatment of the cerebrovascular diseases using clinical investigation methodologies, clinical genetics, advanced statistical methods, neuropsychology, artificial intelligence, biomarkers and advanced neuroimaging. The researchers of the Unit conduct observational and experimental studies on the clinical impact of different interventions, in multinational efforts to get new targeted and personalized treatments for these common and disabling brain disorders.

Main topics of interest:

Cerebral venous thrombosis: mechanisms of disease and treatment

Identification of hidden causes of cryptogenic stroke

Use of artificial intelligence to improve the prediction of stroke outcome

Spatial navigation and orientation in stroke patients

Interventions to improve aphasia after stroke

Role of physical exercise in the prevention and treatment of vascular cognitive impairment

Research Field

- Neuroscience and Disorders of the Nervous System

Major Scientific Achievements in 2021

Identification and description of the clinical, imaging and laboratorial features and of the natural history of cerebral venous thrombosis associated with anti-SARS-CoV-2 ADN vector-based vaccines; production of international guidelines for the management of this new clinical entity.

Leading role on the production of European clinical guidelines for acute stroke management (IV thrombolysis, dual antiplatelet treatment), TIAs and vascular cognitive impairment (management of cerebrovascular disease, epilepsy and post-stroke cognitive impairment).

Ongoing Projects in 2021

2018/2021: Biomarcadores imagiológicos multimodais ao longo do ciclo da enxaqueca e tratamento preventivo personalizado por neurofeedback. Coordinator: Isabel Pavão Martins. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EMD-EMD/29675/2017. Amount: 7 500,00€. Total Amount: 238 761,32€.

Other Projects

Randomised interventional prospective study of the effect of physical activity in vascular cognitive impairment. Coordinator: Ana Isabel Verdelho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-DES/3706/2014. Amount: 199 588,00€. Total Amount: 199 588,00€.

2016/2021: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: M. Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: 1 199 140,10€. Total Amount: 2 499 827,92€.

Spatial navigation and orientation after stroke. Coordinator: Pedro Nascimento Alves. Orientation: Isabel Pavão Martins, Ana Catarina Fonseca. Laboratório de Estudos de Linguagem, Faculty of Medicine, University of Lisbon. Bolsa de Investigação em Doença Vasculiar Cerebral, Sociedade Portuguesa do AVC e Prémio João Lobo Antunes 2018, Santa Casa da Misericórdia de Lisboa.

Cognition and brain amyloid deposition in transthyretin-related familial amyloid polyneuropathy. PI: Pedro Nascimento Alves. Coordination: Isabel Pavão Martins, Isabel Conceição. Sub-investigators: Vanda Freitas, Durval Costa. Laboratório de Estudos de Linguagem, Faculty of Medicine, University of Lisbon. 13.ª Bolsa de Investigação Fundação Astrazeneca / Faculdade de Medicina da Universidade de Lisboa and Pfizer Investigator Initiated Research grant.

2020/2024: eMOTIONAL Cities: Mapping the cities through the senses of those who make them. Coordinator: Bruno Miranda. Funding Agency: H2020-SC1-BHC-29 - European Commission. Reference: SC1-BHC-29-2020-945307. Faculdade de Medicina da Universidade de Lisboa.

DECOMPRESS2. Prospective registry of decompressive neurosurgery for patients with cerebral venous thrombosis. Coordinator: José Ferro.

EXCOA-CVT. EXtending oral antiCOAgulant treatment after Cerebral Vein and Dural Sinus Thrombosis (EXCOA-CVT). Prospective study with a cluster randomised allocation design that aims to compare a policy of short (3 to 6 months) versus long term (12 months) oral anticoagulation in the prevention of VTEs after an episode of CVT. Principal Investigators. Bruno Miranda and José Ferro.

Scientific Impact

Academic Collaborations

Jonathan Coutinho, University of Amsterdam Academic Medical Center, Netherlands
 Jukka Putaala, University of Helsinki, Finland
 Arlindo Oliveira, Instituto Superior Técnico, Universidade de Lisboa
 Helena Santa Clara, Faculdade de Motricidade Humana, Universidade de Lisboa
 Michel Thiebaut de Schotten, Groupe d'Imagerie Neurofonctionnelle, University of Bordeaux, Bordeaux ; Brain Connectivity and Behaviour Laboratory, Sorbonne Universities, Paris, France
 Charlotte Cordonnier, Hôpital Salengro CHU Lille, Lille, France

Selected Publications

Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F; ISCVT Investigators. (2004) [Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis \(ISCVT\)](#). *Stroke*. Mar;35(3):664-70.

Relevance of the publication: Descriptive study of a large global cohort of patients with cerebral venous thrombosis. This publication became the “standard” reference for the clinical characteristics, causes and outcome of patients with cerebral venous thrombosis.

Ferro JM, Coutinho JM, Dentali F, Kobayashi A, Alasheev A, Canhão P, Karpov D, Nagel S, Posthuma L, Roriz JM, Caria J, Frässdorf M, Huisman H, Reilly P, Diener HC; RE-SPECT CVT Study Group. [Safety and Efficacy of Dabigatran Etxilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis: A Randomized Clinical Trial](#). *JAMA Neurol*. 2019 Dec 1;76(12):1457-1465.

Relevance of the publication: A global randomised controlled trial (RCT) showing that a direct anticoagulant (dabigatran) and warfarin have similar efficacy and safety for preventing recurrences after cerebral venous thrombosis. It also showed that RCTs are feasible in rare diseases.

Aguiar de Sousa D, Canhão P, Crassard I, Coutinho J, Arauz A, Conforto A, Béjot Y, Giroud M, Ferro JM; ISCVT-2-PREGNANCY Investigators. [Safety of Pregnancy After Cerebral Venous Thrombosis: Results of the ISCVT \(International Study on Cerebral Vein and Dural Sinus Thrombosis\)-2 PREGNANCY Study](#). *Stroke*. 2017 Nov;48(11):3130-3133.

Relevance of the publication: A long (>10 years) follow up of women in fertile age included in ISCVT (publication 1) showing that pregnancy is safe after a cerebral venous thrombosis, and should not be contraindicated.

Fonseca AC, Marto JP, Pimenta D, Guimarães T, Alves PN, Inácio N, Viana-Baptista M, Pinho E Melo T, Pinto FJ, Ferro JM, Almeida AG. [Undetermined stroke genesis and hidden cardiomyopathies determined by cardiac magnetic resonance](#). *Neurology*. 2020 Jan 7;94(1):e107-e113.

Relevance of the publication: A national multicentre study showing that in patients with stroke of unknown cause, cardiac MRI reveals cardiomyopathies, not diagnosed by other imaging and electrophysiological methods.

Alves PN, Fonseca AC, Silva DP, Andrade MR, Pinho-E-Melo T, Thiebaut de Schotten M, Martins IP. [Unravelling the Neural Basis of Spatial Delusions After Stroke](#). **Ann Neurol**. 2021 Jun;89(6):1181-1194.

Relevance of the publication: Using sophisticated neuroimaging analysis, this publication describes in a large case-control study, the connectomes that have a role in the abnormal spatial-emotional binding and in the defective updating of spatial representations underlying reduplicative paramnesia. The study also disentangles the pathophysiology of the different delusional syndromes after stroke.

2021 Publications in Peer-Reviewed Journals

Aguiar de Sousa D. (2021) A Ph.D. degree can be started during the Neurology Training. **Eur J Neurol**. 2021 Jun 28;54-54 Supplement 1SPS08-2. Opinion.

Aguiar de Sousa D, Katan M (2021) Promising Use of Automated Electronic Phenotyping: Turning Big Data Into Big Value in Stroke Research. **Stroke**. 2021 Jan;52(1):190-192.

Aguiar de Sousa D, Pereira-Santos MC, Serra-Caetano A, Lucas Neto L, Sousa AL, Gabriel D, Correia M, Gil-Gouveia R, Oliveira R, Penas S, Carvalho Dias M, Correia MA, Carvalho M, Sousa AE, Canhão P, Ferro JM (2021) Blood biomarkers associated with inflammation predict poor prognosis in cerebral venous thrombosis: a multicenter prospective observational study. **Eur J Neurol**. 2021 Jan;28(1):202-208.

Aguiar de Sousa D, Pereira-Santos MC, Serra-Caetano A, Neto LL, Sousa AL, Gabriel D, Correia M, Gil-Gouveia R, Oliveira R, Penas S, Carvalho Dias M, Correia MA, Carvalho M, Sousa AE, Canhão P, Ferro JM (2021). Matrix Metalloproteinase-9 Levels are Associated with Brain Lesion and Persistent Venous Occlusion in Patients with Cerebral Venous Thrombosis. **Thromb Haemost**. 2021 Nov;121(11):1476-1482.

Aguiar de Sousa D (2021) Cerebral Venous Thrombosis: What's New? **Hamostaseologie**. 2021 Feb;41(1):25-30. Review.

Alves M, Abrantes AM, Portugal G, Cruz MM, Reimão S, Caldeira D, Ferro JM, Ferreira JJ. (2021) Does Parkinson's Disease Increase the Risk of Atrial Fibrillation? Insights from Electrocardiogram and Risk Scores from a Case-Control Study. **Front Neurol** 2021;12:633900.

Alves M, Pita Lobo P, Kauppila LA, Rebordão L, Cruz MM, Soares F, Cruz J, Tornada A, Caldeira D, Reimão S, Oliveira V, Ferro JM, Ferreira JJ (2021). Cardiovascular and cerebrovascular risk markers in Parkinson's disease: Results from a case-control study. **Eur J Neurol** 2021;28:2669-2679.

Alves PN, Fonseca AC, Silva DP, Andrade MR, Pinho-E-Melo T, Thiebaut de Schotten M, Martins IP (2021). Unravelling the Neural Basis of Spatial Delusions After Stroke. **Ann Neurol**. 2021 Jun;89(6):1181-1194.

Arnold M, Sandset EC, Aguiar de Sousa D, Demchuk AM (2021). Transitioning From Mentee to Mentor: How and When to Start Developing the Skills Needed to Support Others? **Stroke**. 2021 Dec;52(12):e848-e851. Opinion.

Baduro Y, Ferro JM (2021). Cerebral Venous Thrombosis in Sub-Saharan Africa: A Systematic Review. **J Stroke Cerebrovasc Dis** 2021;30:105712.

Baldini T, Asioli GM, Romoli M, Carvalho Dias M, Schulte EC, Hauer L, Aguiar De Sousa D, Sellner J, Zini A. (2021) Cerebral venous thrombosis and severe acute respiratory syndrome coronavirus-2 infection: A systematic review and meta-analysis. **Eur J Neurol**. 2021 Oct;28(10):3478-3490.

Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C, de la Ossa NP, Strbian D, Tsvigoulis G, Turc G (2021). European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. **Eur Stroke J**. 2021 Mar;6(1):I-LXII. Guideline.

Coelho P, Schön M, Alves PN, Fonseca AC, Pinho E Melo T (2021). An image is not always worth a thousand words: an image mimic of transient global amnesia. **Neurol Sci**. 2021 Jun;42(6):2515-2517.

Cortes-Figueiredo F, Carvalho FS, Fonseca AC, Paul F, Ferro JM, Schönherr S, Weissensteiner H, Morais VA (2021). From Forensics to Clinical Research: Expanding the Variant Calling Pipeline for the Precision ID mtDNA Whole Genome Panel. **Int J Mol Sci**. 2021 Nov 6;22(21):12031.

Dawson J, Merwick Á, Webb A, Dennis M, Ferrari J, Fonseca AC (2021) European Stroke Organisation. European Stroke Organisation expedited recommendation for the use of short-term dual antiplatelet therapy early after minor stroke and high-risk TIA. **Eur Stroke J**. 2021 Jun;6(2):VI. Guideline.

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Dourado Sotero F, Calçada A, Aguiar de Sousa D, Dias M, Fonseca AC, Pinho E Melo T, Canhão P (2021) Mean Platelet Volume is a Prognostic Marker in Acute Ischemic Stroke Patients Treated with Intravenous Thrombolysis. **J Stroke Cerebrovasc Dis**. 2021 Jun;30(6):105718.

Ferreira-Atuesta C, Döhler N, Erdélyi-Canavese B, Felbecker A, Siebel P, Scherrer N, Bicciato G, Schweizer J, Sinka L, Imbach LL, Katan M, Abaira L, Santamarina E, Álvarez-Sabín J, Winklehner M, von Oertzen TJ, Wagner JN, Gigli GL, Serafini A, Janes F, Merlini G, Valente M, Gregoraci G, Conrad J, Evers S, Lochner P, Roell F, Brigo F, Bentes C, Peralta AR, Melo TPE, Keezer MR, Duncan

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Ferreira-Brito F, Ribeiro F, Aguiar de Sousa D, Costa J, Caneiras C, Carriço L, Verdelho A (2021) Are Video Games Effective to Promote Cognition and Everyday Functional Capacity in Mild Cognitive Impairment/Dementia Patients? A Meta-Analysis of Randomized Controlled Trials. **J Alzheimers Dis.** 2021;84(1):329-341.

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Ferro JM, Infante J. (2021) Cerebrovascular manifestations in hematological diseases: an update. **J Neurol** 2021;268:3480-3492.

Ferro JM, Oliveira Santos M. (2021) Neurology of inflammatory bowel disease. **J Neurol Sci.** 2021;15;424:117426. Review.

Ferro JM. (2021) Improving outcomes and decreasing costs of neurological diseases: Mind the gap. **Eur J Neurol.** 2021;28(2):361-362. Editorial.

Fonseca AC, Almeida AG, Santos MO, Ferro JM. (2021) Neurological complications of cardiomyopathies. **Handb Clin Neurol** 2021;177:91-109. Review.

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Fonseca AC, Ferro JM, Almeida AG. (2021) Cardiovascular magnetic resonance imaging and its role in the investigation of stroke: an update. **J Neurol** 2021;268:2597-2604. Review.

Fonseca AC, Merwick Á, Dennis M, Ferrari J, Ferro JM, Kelly P, Lal A, Ois A, Olivot JM, Purroy F. (2021) European Stroke Organisation (ESO) guidelines on management of transient ischaemic attack. **Eur Stroke J.** 2021 Jun;6(2):CLXIII-CLXXXVI. Guideline.

Fonseca AC, Silva DP, Infante J, Ferro JM. (2021) Cerebrovascular Complications of Anemia. **Curr Neurol Neurosci Rep.** 2021 Sep 3;21(10):51. Review.

Fonseca AC. (2021) The dawn of precision medicine in stroke. **Eur J Neurol.** 2021 Nov;28(11):3548-3549. Editorial.

Fonseca, AC. (2021) Future applications. **Eur J Neurol**. 2021 Jun; 28, 30-30 Suppl 1. Editorial.

Fonseca J, Miranda F, Leal G, Melo TPE, Martins IP. (2021) Aphasia assessment: impact of material on naming performance. **Arq Neuropsiquiatr**. 2021 Sep;79(9):774-780.

Galovic M, Ferreira-Atuesta C, Abaira L, Döhler N, Sinka L, Brigo F, Bentes C, Zelano J, Koepp MJ. (2021) Seizures and Epilepsy After Stroke: Epidemiology, Biomarkers and Management. **Drugs Aging**. 2021 Apr;38(4):285-299. Review.

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Valério D, Santana I, Aguiar de Sousa D, Schu G, Leal G, Pavão Martins I, Almeida J (2021) Knowing how to do it or doing it? A double dissociation between tool-gesture production and tool-gesture knowledge. **Cortex.** 2021 Aug;141:449-464.

Verdelho A, Biessels GJ, Chabriat H, Charidimou A, Duering M, Godefroy O, Pantoni L, Pavlovic A, Wardlaw J (2021) Cerebrovascular disease in patients with cognitive impairment: A white paper from the ESO dementia committee - A practical point of view with suggestions for the management of cerebrovascular diseases in memory clinics. **Eur Stroke J.** 2021 Jun;6(2):111-119. Guideline.

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Webb AJS, Fonseca AC, Berge E, Randall G, Fazekas F, Norrving B, Nivelles E, Thijs V, Vanhooren G (2021) Stroke Working Group of the European Brain Council Value of Treatment initiative. [Value of treatment by comprehensive stroke services for the reduction of critical gaps in acute stroke care in Europe.](#) **Eur J Neurol.** 2021 Feb;28(2):717-725.

Tsivgoulis G, Kargiotis O, De Marchis G, Kohrmann M, Sandset EC, Karapanayiotides T, de Sousa DA, Sarraj A, Safouris A, Psychogios K, Vadikolias K, Leys D, Schellinger PD, Alexandrov AV (2021) Off-label use of intravenous thrombolysis for acute ischemic stroke: a critical appraisal of randomized and real-world evidence. **Ther Adv Neurol Disord.** 2021 Feb 26;14:1756286421997368. Review.

Invited Lectures and Seminars

Aguiar de Sousa D

1. Lecture, "Cerebral venous thrombosis – an update", 65th Annual Meeting of the Society of Thrombosis and Hemostasis Research – GTH 2021, February 2021
2. Co-Chair, Scientific session "State of the Art: Neurology", 65th Annual Meeting of the Society of Thrombosis and Hemostasis Research – GTH 2021, February 2021
3. Lecture, "Management of ischemic stroke during pregnancy", European Stroke Organisation Conference 2021, September 2021
4. Co-Chair, Scientific session "Young Stroke Physicians and Researchers Research Design Workshop for Studies in Development", European Stroke Organisation Conference 2021, September 2021
5. Lecture, "Vaccine induced immune thrombosis and thrombocytopenia syndrome", Garmisch Stroke Science Workshop 2021, November 2021

Alves PN. Topographic memory and spatial delusions: unraveling the neural basis of reduplicative paramnesia. Workshop Memory and Attention in Healthy and Pathological Ageing: Theories and Applications, online. Faculdade de Psicologia da Universidade de Lisboa, Portugal, May 17-18, 2021.

Ferro JM

1. Lecture: ABC da investigação clínica. Sociedade Portuguesa de Neurologia, reunião virtual, January 2021

2. Seminar, with Dias M, Aguiar de Sousa D, Fonseca AC. COVID and Neurology. Neuroses meeting, IMM JLA, March 2021
3. Lecture: Cerebral venous thrombosis: clinical trials in adults and pediatric patients. Boehringer Ingelheim Symposium, 7th ESOC, virtual, 1st September 2021
4. Lecture: Cerebral venous thrombosis. XIII Congresso da Sociedade Paulista de Neurologia, virtual, 27-29th May 2021
5. Lecture: Poststroke anxiety, apathy and depression. 13th World Stroke Organization Congress, 29th October 2021
6. Lecture: Cerebral venous thrombosis: un update. XIII Congresso Brasileiro de Doença Cerebrovascular-AVC 2021 e II Jornadas Alagoanas de Neurologia, virtual, 11-14th November, 2021
7. Lecture: Cerebral venous thrombosis. World Stroke Day – Mexico; Mexico city, virtual, November 2021

Fonseca AC

1. Cardiomiopatias – onde não se sabe a causa do AVC onde procurar. 15^o Congresso SPAVC. Porto, Portugal. February 4, 2021; National Conference.
2. AVC criptogénico – critérios de diagnóstico e algoritmo. CPC 2021. Virtual congress, May 2, 2021; National conference
3. COVID-19 e doença neurológica: estado da arte. Congresso da ordem dos médicos. Coimbra, June 2, 2021; National conference
4. Specific risk factors in women. Seventh National Congress of the Bulgarian Society of Neurosonology and Cerebral Hemodynamics. October 2, 2021. International Conference
5. Close that PFO STAT – Size matters. AHA sessions 21. Boston, November 13, 2021; International Conference.
6. Abordagem do doente com AIT. Congresso de Neurologia 2021. October 30, 2021; National Conference

Martins IP. Language symptoms and testing, in aging, aphasia and cognitive decline. European Academy of Neurology Congress 2021. Focused workshop on new developments in understanding disorders of language. 19 June, 2021

Communications

International:

Alves PN. Unravelling the neural basis of spatial delusions after stroke. Congress of the European Academy of Neurology online, June 19, 2021. (Oral presentation)

Miranda F. Análise micro e macrolinguístico do discurso. Workshop 7. II Congresso Internacional de Terapia da fala online. September, 22-26, 2021. (oral presentation)

Miranda F, Fonseca J, Leal G. Teclado vs Manual - um estudo de caso. II Congresso Internacional de Terapia da fala online. September, 22-26, 2021. (poster presentation)

Fonseca J. Tipologia de erros na nomeação intraoperatória. II Congresso Internacional de Terapia da fala online. September, 22-26, 2021. (oral presentation)

Aaron S, Sanchez Van Kammen M, Conforto A, Arauz A, Carvalho M, Masjuan J, Sharma V, Uyttenboogaart M, Werring D, Bazan R, Mohindra S, Putaala J, Weber J, Ferreira J, Aguiar De Sousa D, Canhão P, Coert B, Kirubakaran P, Singh P, Coutinho J, Ferro J. Decompressive neurosurgery for patients with severe cerebral venous thrombosis. Final results of the DECOMPRESS2 STUDY. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Sanchez Van Kammen M, Lindgren E, De Winter M, Krzywicka K, Hiltunen S, Heldner M, Mansour M, Aguiar De Sousa D, Barboza M, Arauz A, Arnold M, Putaala J, Leker R, Spratt N, Garcia-Esperon C, Rodrigues M, Ekizoglu E, Punter M, Ghiasian M, Alasheev A, Yesilot N, Guisado-Alonso D, Aridon P, Simaan N, Arnao V, Silva E, Sezgin M, Canhão P, Ferro J, Tatlisumak T, Jood K, Coutinho J. Prediction of late seizures after cerebral venous thrombosis. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Lindgren E, Sanchez Van Kammen M, De Winter M, Krzywicka K, Heldner M, Hiltunen S, Aguiar De Sousa D, Mansour M, Canhão P, Ekizoglu E, Rodrigues M, Silva E, Garcia-Esperon C, Spratt N, Arnao V, Aridon P, Simaan N, Sezgin M, Alasheev A, Smolkin A, Guisado-Alonso D, Yesilot N, Barboza M, Ghiasian M, Leker R, Ferro J, Arauz A, Putaala J, Arnold M, Tatlisumak T, Coutinho J, Jood K. Prediction of poor outcome and mortality after cerebral venous thrombosis. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication
 Aguiar De Sousa D, Aaron S, Arauz A, Bazan R, Canhão P, Carvalho M, Coert B, Conforto A, Ferreira J, Kirubakaran P, Masjuan J, Mohindra S, Putaala J, Sharma V, Sanchez Van Kammen M, Singh P, Uyttenboogaart M, Weber J, Werring D, Coutinho J, Ferro J. Predictors of mortality in patients treated with decompressive neurosurgery due to severe cerebral venous thrombosis – Results of the DECOMPRESS2 STUDY. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Sanchez Van Kammen M, Aguiar De Sousa D, Aaron S, Conforto A, Arauz A, Carvalho M, Masjuan J, Sharma V, Werring D, Bazan R, Mohindra S, Putaala J, Weber J, Ferreira J, Canhão P, Coert B, Kirubakaran P, Singh P, Coutinho J, Ferro J. Seizures in patients with severe cerebral venous thrombosis treated with decompressive surgery. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Sanchez Van Kammen M, Heldner M, Brodard J, Scutelnic A, Silvis S, Schroeder V, Kremer Hovinga J, Middeldorp S, Levi M, Hiltunen S, Lindgren E, Mansour M, Arauz A, Barboza M, Zuurbier S, Aguiar De Sousa D, Ferro J, Fischer U, Field T, Jood K, Tatlisumak T, Putaala J, Arnold M, Coutinho J. Frequency of thrombocytopenia and platelet factor 4/heparin antibodies in cerebral venous thrombosis in the pre-COVID-19 era. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Oliveira R, Correia M, Carvalho Dias M, Marto JP, Lucas Neto L, Aguiar De Sousa D. Reocclusion after successful endovascular treatment in acute ischemic stroke due to large vessel occlusion –

Systematic review and meta-analysis. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Oral Communication

Marto JP, Kauppila L, Jorge C, Faustino P, Sargento Freitas J, Pereira L, Galego S, Dias R, Castro P, Melo TP, Fonseca AC. Acute myocardial infarction after intravenous thrombolysis for acute ischemic stroke: case series and systematic review. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication

Vitor J, Bonifácio G, Fonseca AC. Frequency of atrial fibrillation in young patients with ischemic stroke: a systematic review and meta-analysis. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication

Gorjão M, Fonseca AC. Palliative care in the stroke unit – awareness and training. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication

Gorjão M, Fonseca AC. Palliative care in the stroke unit – access and referral. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication

Rodrigues S, Biscoito L, Fonseca AC. Sinus venous stenosis caused by a giant arachnoid granulation. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication;

Paula A, Alves P, Dias M, Fonseca AC, Melo TP. HIV infection and vascular disease – a complex interplay. 7th European Stroke Organisation Conference – Virtual, September1-3, 2021. Poster Communication

Vazão A, Rosário M, Nunes E, Melo TP, Ferro J, Fonseca AC. Evaluation of blood pressure control post-stroke in a cohort of ischemic stroke patients. 7th Congress of the European Academy of Neurology – Virtual 2021, June 19-22, 2021. Oral Communication

Leal Rato M, Peralta A, Bentes C, Aguiar de Sousa D, Franco, Melo TP. Acute symptomatic seizures in patients with recurrent ischemic stroke: a retrospective cohort study. 7th Congress of the European Academy of Neurology – Virtual 2021, June 19-22, 2021. Oral Communication

Coelho P, Amado J, Nascimento Alves P, Fonseca AC. Time perception dysfunction in stroke patients: a systematic review 7th Congress of the European Academy of Neurology – Virtual 2021, June 19-22, 2021. Oral Communication

National:

Alves PN, Fonseca AC, Silva DP, Andrade MR, Pinho-e-Melo T, de Schotten MT, Martins IP. Unravelling the Neural Basis of Spatial Delusions after Stroke. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting – May 5-7, 2021. (oral presentation)

Martins IP. Cérebro e cognição. Reunião da Secção de Neurologia do Comportamento- Formato Híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021. (Oral presentation)

Martins IP. “Why are we here?” Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 28, 2021. (oral presentation)

Alves PN, Fonseca AC, Pinho-e-Melo T, Martins IP. Característica clinicas e correlações antomo-funcionais dos delírios de espaço após acidente vascular cerebral. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 28, 2021. (oral presentation)

Coelho P, Dias M, Alves PN, Fonseca AC, Pinho-e-Melo T. Complicações neurológicas da endocardite: a importância do diagnóstico precoce. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27-30, 2021. (poster presentation)

Maruta C. Reserva e falência cognitiva durante o envelhecimento normal. 9th International Congress of Educational Sciences and Development, Outubro 20-22, 2021, online.

Organization of Conferences

Aguiar de Sousa D

1. Member of the organizing committee, ESO-GAINS-WSO Early Career Investigators Trials and Cohorts Workshop, 2021
2. Co-chair, Garmisch Stroke Science Workshop 2021, November 2021
3. Member of the Programme Committee, European Stroke Organization Conference (ESOC) 2021

Fonseca AC. World Stroke Organization. World Stroke Congress 2021. Virtual congress. October 28-29 2021. Co-chair of the scientific committee co-organizer, Scientific Organizing Committee World Stroke Congress

Fonseca J. II Congresso Internacional de Terapia da fala online. September, 22-26, 2021.

Maruta C, Alves PN. Curso de Atualização em Funções Nervosas Superiores, Reunião Anual da Secção de Neurologia do Comportamento, formato híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021.

Patrícia Canhão. Co-Organizer:

1. Reunião da Unidades de AVC, virtual, 24 September, 2021
2. Reunião Anual da Sociedade Portuguesa do AVC, Virtual. 19-20 October, 2021
3. Congresso da Sociedade Portuguesa do AVC, virtual, 3-5 February 2021.

Networks & Research Infrastructures

Aguiar de Sousa, D

1. Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillation (ELAN)", Member of the Steering Committee and national coordinator (2020 -)
2. Direct Oral Anticoagulants for the treatment of Cerebral Venous Thrombosis (DOAC-CVT) Member of the Steering Committee and National coordinator (2020 -)
3. SECRET trial (Multicentre, prospective randomized open label, blinded-endpoint (PROBE) controlled trial of anticoagulation with rivaroxaban versus standard of care in determining safety at 365 days in symptomatic cerebral venous thrombosis) Member of the Data Safety Monitoring Board (2020 -)
4. the MOSES-study (Midregional proatrial natriuretic peptide to guide Secondary Stroke prevention) Member of the Clinical Event Committee (2019 -)

Bentes C & Ferro JM

International Post Stroke Epilepsy Research Consortium (IPSERC): A consortium to accelerate discoveries in preventing epileptogenesis after stroke.

Ferro JM

1. Extended anticoagulation for cerebral venous thrombosis EXCOA-CVT. Principal Investigator. Funding JFerro, Lab, IMM JLA
2. Prospective registry of decompressive surgery in cerebral venous thrombosis DECOMPRESS 2 Principal Investigator. Funding JFerro, Lab, IMM JLA
3. Direct Oral Anticoagulants for the treatment of Cerebral Venous Thrombosis (DOAC-CVT) Member of the Steering Committee
4. Edoxaban for IntraCranial Hemorrhage Survivors with Atrial Fibrillation (ENRICH-AF). Member of the Steering Committee and National coordinator (2019 -)
5. Proper Dosing and Safety of the Oral FXIIa Inhibitor BAY 2433334 in Patients Following Acute Non-Cardioembolic Ischemic Stroke (PACIFIC-STROKE) Member of the Steering Committee and National coordinator (2019 -)

Fonseca AC

1. Colchicine for Prevention of Vascular Inflammation in Non-cardio Embolic Stroke CONVINCE, member of the Steering Committee.
2. International Multicenter Patent for Ramen Oval & stroke (IMPROVE) Registry (IMPROVE), member of the writing Committee, investigator
3. International multicenter study aiming to evaluate accurately risk factors, mechanisms, and prognosis of cryptogenic ischemic stroke in young adults aged under 50 years SECRETO, Principal investigator of Lisbon center
4. Cardiac imaging in undetermined stroke Junior CAIUS-JUNIOR, principal investigator

Martins IP & Fonseca J

REhabilitation and recovery of people with Aphasia after Stroke (RELEASE) Collaborators

Prizes & Honors in 2021

Aguiar de Sousa D. João Lobo Antunes Merit PhD Thesis Award, Instituto de Medicina Molecular, 2021.

Alves PN. Unravelling the neural basis of spatial delusions after stroke. Runner-up in the Tournament: Clinical 2021. 7th Congress of the European Academy of Neurology - Virtual 2021. (oral presentation).

Alves PN, Fonseca AC, Silva DP, Andrade MR, Pinho-e-Melo T, de Schotten MT, Martins IP. Unravelling the Neural Basis of Spatial Delusions after Stroke. 1st Experts prize of the XIV CAML · XIV CAML · IV NeurULisboa PhD Students Virtual Meeting – May 5th to 7th 2021 (oral presentation).

Ferro JM. World Expert in venous thrombosis. Expertscape. October 2021.

Ferro JM. Louvor e agradecimento. Conselho de Administração do Centro Hospitalar Universitário Lisboa Norte. 21th October 2021.

Ferro JM. Medalha de Homenagem. Lição de Jubilação. Faculdade de Medicina, Universidade de Lisboa, 14th December 2021.

Fonseca AC. Recognized as part of the cohort “Mulheres da Ciência 2021” by Ciência Viva.

Fonseca AC. Award for the second best oral communication at the 15^o Congresso da SPAVC.

Fonseca AC. 15th Programa Educação pela Ciência - Bolsa CHULN/FMUL - Antiplatelet therapy and its role on reducing ischemic events in patients with giant cell arteritis: a systematic review and meta-analysis.

Scientific boards:

Aguiar de Sousa D. Member of Board of Directors, European Stroke Organization.

Aguiar de Sousa D. Member of the Steering Committee for the implementation of the European Stroke Action Plan.

Aguiar de Sousa D. Member at Large, Executive Committee, European Stroke Organisation (ESO).

Aguiar de Sousa D. Chair, Young Stroke Physicians and Researchers Committee in European Stroke Organisation.

Aguiar de Sousa D. Member of the Clinical Research Subcommittee, American Academy of Neurology.

Aguiar de Sousa D. Secretary, Steering Committee, Portuguese Stroke Society, since February.

Fonseca AC. Portuguese Institutional Delegate of the Scientific Stroke Panel of the European Academy of Neurology.

Fonseca AC. Member of the Research Committee of the World Stroke Organization.

Fonseca AC. Member of the Congress Planning Committee of the World Stroke Organization.

Editorial positions:

Aguiar de Sousa D. Assistant Editor, Stroke (Journal of the American Heart Association/American Stroke Association), since 2020.

Aguiar de Sousa D. Editorial Board member, Stroke (Journal of the American Heart Association/American Stroke Association), since 2019.

Aguiar de Sousa D. Editorial Board member, European Stroke Journal (Journal of the European Stroke Organization), since 2019.

Aguiar de Sousa D. Review Editor for Stroke, Frontiers in Neurology, since 2018.

Aguiar de Sousa D. Invited associated editor for topic proposal “Cerebral Venous Thrombosis, Frontiers in Neurology, 2021.

Aguiar de Sousa D. Editor of Scientific Content on the European Stroke Organisation blog (<https://eso-stroke.org/blog>), since 2017.

Ferro JM. Editorial Board Member: “Stroke”, “European Stroke Journal”, “Journal of Neurology”, “European Journal of Neurology”, “Cerebral Circulation -Cognition & Behaviour”.

Fonseca AC. Associate Editor for “BMC neurology” and “Frontiers in Stroke”.

Fonseca AC. Invited Editor – “Frontiers in Cardiovascular Medicine”.

Fonseca AC. Editorial Board member – “Stroke”, “BMC neurology”.

Referee for funding agencies:

Aguiar de Sousa D. Grant review, American Academy of Neurology, 2021.

Ferro JM. Member of Jury: Prémios Santa Casa Neurociências Montero Belard e Melo e Castro, 2021.

Ferro JM. Member of Jury: Prémios da revista SINAPSE, Sociedade Portuguesa de Neurologia, 2021.

Ferro JM. External evaluator of grant progress: Treat Small Vessel Disease - RHU TRT_cSVD Hôpital Lariboisière – APHP, Inserm, Université Paris Diderot. – Third General Assembly, virtual, June 14th, 2021.

Ferro JM. Evaluator: Dossiers de projet de recherche sur les AVC, Fondation pour la Reserche sur les AVC, Paris, França.

Ferro JM. Grant reviewer: Netherlands Organisation for Scientific Research (NWO/ZonMw) VIDI program, Netherlands.

Advanced Teaching

Curso de Introdução à Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa

Ferro JM – Co- Director

Aguiar de Sousa D. Module IV Causation studies. Multivariate analysis. 26th February 2021

Alves PN. Module VII Prognostic Studies. Online format 14th May, 2021

Ferro JM. Module IV Coordination of Module. Causation studies 26-27th February 2021

Fonseca AC. Module VII. Coordination of module. Prognostic studies 14-15th May 2021

Master/Doctoral Programme in Neurosciences, Faculdade de Medicina da Universidade de Lisboa

Martins IP – Co-Director

1. Aguiar de Sousa D. Seminar: “Systematic Reviews of observational data”.2021
2. Alves PN. Right hemisphere syndromes, Lisboa, Edifício Egas Moniz, May 13, 2021.
3. Ferro JM. Chronic disorders of consciousness. Curricular Unit: Neuro-ethics
4. Ferro JM. Case-control studies. Curricular Unit: Clinical research
5. Martins IP. Functional organization of the mind, Methods in Cognitive assessment. Lisboa, Edifício Egas Moniz, May 4, 2021.
6. Maruta C. Assessment of memory systems. Lisboa, Edifício Egas Moniz, May 11, 2021.
7. Maruta C. Executive functions and the frontal lobes. Lisboa, Edifício Egas Moniz, May 18, 2021.
8. Canhão P. Coordinator, Curricular Unit Clinical Research

Alves PN. Right hemisphere syndromes. Curso Neurodegenerative Diseases – Advanced Course V – Session – Symposium on Brain, language and cognition, Ahed – Advanced Health Education, NOVA Medical School, March, 6, 2021, online.

Fonseca J. Avaliação da afasia. Curso Neurodegenerative Diseases – Advanced Course V – Session – Symposium on Brain, language and cognition, Ahed – Advanced Health Education, NOVA Medical School, March, 6, 2021, online.

Martins IP. Linguagem ao longo da vida. Curso Neurodegenerative Diseases – Advanced Course V – Session – Symposium on Brain, language and cognition, Ahed – Advanced Health Education, NOVA Medical School, March, 6, 2021, online.

Alves PN. Desatento, desorientado e sem saber para onde ir: Síndromes do Hemisfério direito. Curso de Atualização em Funções Nervosas Superiores, Reunião Anual da Secção de Neurologia do Comportamento, formato híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021.

Martins IP. Cérebro e Cognição. Curso de Atualização em Funções Nervosas Superiores, Reunião Anual da Secção de Neurologia do Comportamento, formato híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021.

Maruta C. Guardei tão bem as minhas memórias que agora não as encontro: A memória. Curso de Atualização em Funções Nervosas Superiores, Reunião Anual da Secção de Neurologia do Comportamento, formato híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021.

Miranda F. (2021) Eles falam, falam, mas não percebo nada: a linguagem. Curso de Atualização em Funções Nervosas Superiores, Reunião Anual da Secção de Neurologia do Comportamento, formato híbrido. Congresso Nacional de Neurologia. Neurologia de Precisão. Sociedade Portuguesa de Neurologia. October, 27, 2021.

Testes de diagnóstico. Mestrado/Doutoramento Neurociências. Faculdade de Medicina de Lisboa. Abril 15, 2021.

Fonseca AC. Estudos observacionais. Mestrado Investigação Clínica, Faculdade de Medicina de Lisboa. Lisboa, Portugal, novembro 5, 2021.

Fonseca AC. Curso de Investigação da Sociedade Portuguesa de Neurologia. Virtual, Janeiro 29-30 2021.

Fonseca AC. Workshop Precision medicine in stroke – future applications. 7th Congress of the European Academy of Neurology 2021. June 20, 2021.

Fonseca AC. Teaching course. Posterior circulation – life and health after Stroke. ESOC 2022. Virtual, September 3 2021.

Fonseca AC. DTC no vasospasmo da HSA e SVCR. Curso de neurosonologia. Sociedade Portuguesa de Neurologia. October 27, 2021.

Fonseca AC. Webinar Women in Stroke, primary prevention in women. World Stroke Organization. June 30 2021.

Fonseca AC. Webinar Specific stroke risk factors in women – primary prevention in women. European Academy of Neurology. November 23, 2021.

MSc Theses

Mariana Silva, 12/02/21, Relação entre Fístulas arteriovenosas durais e trombose venosa cerebral: Revisão Sistemática, FMUL. Isabel Pavão Martins.

Luis Cotrim, 19/03/2021, Os parâmetros do hemograma na predição da recorrência vascular precoce após AIT, FMUL. Patrícia Canhão.

Rita Tomás. 21/04/2021, Autoperceção das alterações do gosto pós-AVC, FMUL. Patricia Canhão.

Mariana Santana, 21/04/2021, AF and Stroke or Stroke and AF?, FMUL. Ana Catarina Fonseca.
Adriana Silva, 15/06/2021, NIHs underestimates right hemisphere stroke injury: raising and old issue with a new cognitive approach. FMUL. Isabel Pavão Martins.

Maria Cristina Fialho Biomarkers for the identification of atrial fibrillation in ischemic stroke: Atrial Natriuretic Peptide versus N-terminalpro Brain Natriuretic Peptide, FMUL. Ana Catarina Fonseca.

Ana Catarina Correia, 15/06/2021, Trombose associada a anemia ferropénica como causa de AVC isquémico, FMUL. Ana Catarina Fonseca.

Daniel Araújo, 17/07/2021, ABCD2 score: Análise de recorrências vasculares em doentes com AIT e score ABCD2 <4, FMUL. Patrícia Canhão.

PhD Theses

Mariana Cruz Alves. Cardiovascular risk factors associated with Parkinson's disease; Universidade de Lisboa, Lisboa, Portugal. 20.10.2021. Supervisor: Joaquim Ferreira; Co-Supervisor: José Ferro.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

PACIFIC Clinical trial, Bayer, Contract Research

Stroke collection of the Biobanco IMM, Daiichi-Sankyo sponsorship

Policy

Aguiar de Sousa D. Member of the working group for the update of the Methodology for Health Technology Assessment in Portugal, INFARMED - National Authority of Medicines and Health Products, Portugal

Aguiar de Sousa D. Member of the Medicines Evaluation Commission, INFARMED - National Authority of Medicines and Health Products, Portugal

Ferro JM. External ad-hoc adviser for the neurological side-effect of SARS-CoV-2 vaccines, European Medicine Agency, March 2021

Ferro JM. Member of the “Comissão Técnica de Vacinação contra a COVID-19, (role: Neurology consultant)

Fonseca AC. Member of the expert panel “Norma DGS – Abordagem diagnóstica e terapêutica do doente com fibrilhação auricular” of the Direção Geral da Saude

Fonseca AC. Portuguese national coordinator of the “Stroke Action Plan Europe”

Melo TP. Member of the coordinating group: Tratamento endovascular do AVC agudo, Urgência Metropolitana de Lisboa. ARSLVT, Ministério da Saúde

Science and Society in 2021

General public:

Aguiar de Sousa D. Diário de Notícias. <https://www.dn.pt/sociedade/estudo-de-trombose-venosa-cerebral-confirma-seguranca-das-vacinas-contr-a-covid-19-14432922.html>

Aguiar de Sousa D. <https://www.facebook.com/jornalexpresso/videos/277191397001790>
RTP. https://www.rtp.pt/play/p8271/e535678/sociedade-civil?fbclid=IwAR0xKrSqvF-dWGBr2_O-QSYR0pssBYN9V0Q-nWQu_JAVg-yUSAaMBc_Tvww

Fonseca AC. Participation in an educational section “SINOPSE” with videos of the Portuguese Neurological Society that aims to explain neurological diseases to the general public.

Fonseca AC. Participation in an event “Mulheres na Ciência” organized by the Nucleo de Nanotecnologia da Faculdade de Ciências e tecnologia da Universidade Nova de Lisboa” in 13 March 2021 that aimed to debate women’ participation in science to the general public.

Martins IP, Alves N. (2021) Cérebro. Revista Visão Saúde. Nº 19, pp 16-24, Agosto/Setembro.

Verdelho A, Santa-Clara H. Toca a mexer! O seu cérebro agradece. Exercícios para melhorar a sua saúde mental. Lidel, Lisboa, 2021.

Patients/families/caregivers/patients associations:

Ferro JM. Member of the Scientific Advisory Board. Associação Portugal AVC.

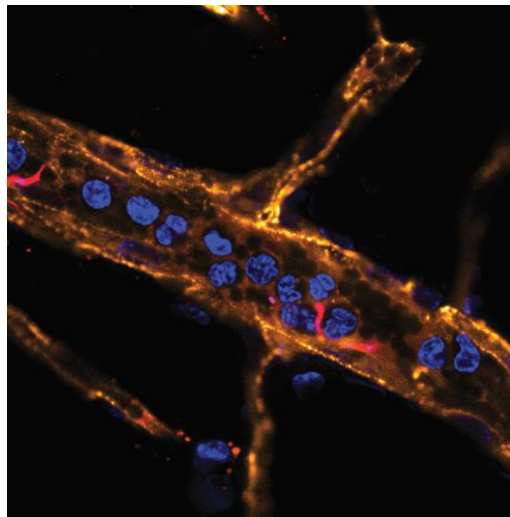
Luísa Figueiredo Lab

Head of Laboratory: Luísa Figueiredo, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Adriana Beatriz Oliveira Temporão	Master Degree	PhD Student
Ana Raquel Santos Pereira	Master Degree	MSc Student
Fabien Marc Guegan	PhD	Senior Postdoctoral Researcher
Henrique Pedro Pereira da Silva Amaral Machado	Master Degree	Lab Technician
Idálio de Jesus Contreiras Viegas	Master Degree	PhD Student
Lara López Escobar	Master Degree	PhD Student
Leonor Duarte Pinho	Master Degree	Lab Manager
Lúcia Branco Serra	Master Degree	PhD Student (Started March)
Mariana Isabel De Niz Hidalgo	PhD	Postdoctoral Researcher (Left June)
Marta Valido Narciso	University Degree	MSc Student (Started October)
Martha Catalina Alvarez Meneses	PhD	Postdoctoral Researcher (Started September. Left December)
Sandra Isabel Gonçalves Trindade	PhD	Senior Postdoctoral Researcher
Sara Silva Pereira	PhD	Postdoctoral Researcher

Graphical Abstract



Lab Interests

The African trypanosome is a single-celled parasite responsible for a fatal disease in humans (sleeping sickness) and a chronic disease in cattle (Nagana). Our group is interested in understanding the disease mechanisms caused by two species of African trypanosomes (*Trypanosoma brucei* and *Trypanosoma congolense*).

TISSUE TROPISM - We have recently discovered that adipose tissue is an important reservoir of parasites in mouse infection and that the parasites adapt functionally to the tissue. Now we are studying how parasites interact with host vasculature to sequester or invade tissues, the consequences of parasite heterogeneity and the impact of tissue tropism on immune evasion and host metabolism.

POST-TRANSCRIPTIONAL GENE REGULATION - We are interested in understanding the importance of RNA modifications and non-coding RNAs in the regulation of genes in African trypanosomes.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy

Major Scientific Achievements in 2021

Our group acts in two new research lines. First, in collaboration with Claudio Franco, we are studying the importance of the vasculature in Trypanosome infections. Second, we have developed a new animal model to study cerebral trypanosomiasis caused by *T. congolense*.

Ongoing Projects in 2021

2021/2024: TrypM6A: Mechanism and function of epitranscriptomic poly(A) tail modifications in African trypanosomes. Coordinator: Luísa Figueiredo. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - TRYPM6A - HR20-00361 – LFIGUEIREDO. Amount: 499 400,00€. Total Amount: 499 400,00€.

2019/2023: Cell2Cell: What makes a successful pathogen? Understanding the impact of cell-to-cell heterogeneity in chromatin structure on infection and adaptation. Coordinator: Luísa Figueiredo. Funding Agency: European Commission. Reference: MSCA-ITN 860675. Amount: 228 720,24€. Total Amount: 228 720,24€.

2019/2021: HFSP fellowship - Human Frontier Science European Commission Program. Coordinator: Mariana De Niz. Funding Agency: Human Frontier Science Program. Reference: HFSP fellowship - Human Frontier Science European Commission Program. Amount: 69 120,00€. Total Amount: 69 120,00€.

2019/2021: TRYPTISSUE: Characterising Trypanosoma tissue tropism: new perspectives for variant surface glycoproteins. Coordinator: Luísa Figueiredo. Funding Agency: European Commission. Reference: MSCA-IF 839960. Amount: 159 815,04€. Total Amount: 159 815,04€.

2018/2022: FatTryp: Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease. Coordinator: Luísa Figueiredo. Funding Agency: European Commission. Reference: ERC- FATTRYP – 771714. Amount: 2 000 000,00€. Total Amount: 2 000 000,00€.

2018/2021: FatReservoir: Importância dos Reservatórios de Parasitas Extravasculares em Gado e Modelos Laboratoriais de Ratinhos. Coordinator: Sandra Trindade. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-029161. Amount: 231 666,35€. Total Amount: 239 970,42€.

Scientific Impact

Academic Collaborations

Claudio Franco, Instituto de Medicina Molecular

Samie Jaffrey, Weill Cornell Medicine

Shulamit Michaeli, The Bar-Ilan University

Catarina Gadelha, University of Nottingham

Selected Publications

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Henao Misikova L, Franco CA, Figueiredo LM (2021). [Organotypic endothelial adhesion molecules are key for *Trypanosoma brucei* tropism and virulence](#). *Cell Reports* 21;36(12):109741.

Relevance of the publication: We showed that *T. brucei* distributes differentially across the blood vasculature of the mammalian host, preferring some blood networks to others. This work also revealed that *T. brucei* relies on organotypic vascular endothelial receptors to establish extravascular reservoirs, including ICAM2, CD36 and P/E selectins.

Aresta-Branco F, Sanches-Vaz M, Bento F, Rodrigues JA, Figueiredo LM (2019). [African trypanosomes expressing multiple VSGs are rapidly eliminated by the host immune system](#). *Proceedings of the National Academy of Sciences* 116 (41):20725-20735.

Relevance of the publication: This work helped understanding that parasites that express multiple VSGs at the cell surface through the overexpression of a high mobility group protein (TDP1) are more vulnerable to the elimination by the host's immune system compared to wild-type parasites that present a homogeneous VSG coat. As such, future therapeutics that induce parasites to express multiple VSGs should be considered.

Rijo-Ferreira F, Carvalho T, Afonso C, Sanches-Vaz M, Costa RM, Figueiredo LM, Takahashi JS (2018). [Sleeping sickness is a circadian disorder](#). *Nature Communications* 9(62).

Relevance of the publication: Behavioral, tissue and molecular circadian analysis of the host reveals that sleeping sickness infection accelerates the host circadian clock. As a result, a mouse infected by *T. brucei* is constantly jet-lagged.

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais NL, Takahashi JS, Figueiredo LM (2017). [Trypanosoma brucei metabolism is under circadian control](#). *Nature Microbiology* 2(6):17032.

Relevance of the publication: Analysis of the circadian transcriptome of *T. brucei* in culture, in the absence of host and environmental signals identified an underlying parasite molecular rhythm. This circadian rhythm controls parasite metabolism, which has implications in drug resistance.

Trindade S & Rijo-Ferreira F, Carvalho T, Pinto-Neves D, Guegan F, Aresta-Branco F, Bento F, Young SA, Pinto A, Van Den Abbeele J, Ribeiro RM, Dias S, Smith TK, Figueiredo LM (2016). [Trypanosoma brucei parasites occupy and functionally adapt to the adipose tissue in mice](#). **Cell Host & Microbe** 19(6):837-848.

Relevance of the publication: This work revealed for the first time that *T. brucei* preferentially accumulates in the adipose tissue. In this tissue, *T. brucei* adapts its metabolism to catabolize fatty acids.

2021 Publications in Peer-Reviewed Journals

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Henao Misikova L, Franco CA, Figueiredo LM (2021). [Organotypic endothelial adhesion molecules are key for Trypanosoma brucei tropism and virulence](#). **Cell Reports** 21;36(12):109741.

Luzak V, López-Escobar L, Siegel TN, Figueiredo LM (2021). [Cell-to-Cell Heterogeneity in Trypanosomes](#). **Annual Reviews Microbiology** 8;75: 107-128.

Machado H, Bizarra-Rebello T, Costa-Sequeira M, Trindade S, Carvalho T, Rijo-Ferreira F, Rentroia-Pacheco B, Serre K, Figueiredo LM (2021). [Trypanosoma brucei triggers a broad immune response in the adipose tissue](#). **PLoS Pathogens** 15;17(9):e1009933.

Silva Pereira S, Jackson AP, Figueiredo LM (2021). [Evolution of the variant surface glycoprotein family in African trypanosomes](#). **Trends in Parasitology** 38(1):23-36.

Temporão A, Sanches-Vaz M, Luís R, Nunes-Cabaço H, Smith TK, Prudêncio M, Figueiredo LM (2021). [Excreted Trypanosoma brucei proteins inhibit Plasmodium hepatic infection](#). **PLoS Neglected Tropical Diseases** 15(10): e0009912.

Pre-Print Publications

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Franco CA, Figueiredo LM (2021). Organotypic endothelial adhesion molecules are key for *Trypanosoma brucei* tropism and virulence. **bioRxiv**. DOI: <https://doi.org/10.1101/2021.02.26.433042>

Silva Pereira S, De Niz M, Serre K, Ouarné M, Franco CA, Figueiredo LM (2021). Immunopathology and parasite sequestration cause severe cerebral trypanosomiasis in animals. **Research Square**. DOI: [10.21203/rs.3.rs-1050698/v1](https://doi.org/10.21203/rs.3.rs-1050698/v1)

Trindade S, De Niz M, Costa-Sequeira Bizarra-Rebello T, Bento F, Dejung M, Ferreira J, Butter F, Bringaud F, Gjini E, Figueiredo LM (2021). Persistence behavior in African trypanosomes during adipose tissue colonization. **Research Square**. Doi: [0.21203/rs.3.rs-499897/v1](https://doi.org/10.21203/rs.3.rs-499897/v1)

Invited Lectures and Seminars

Luisa M. Figueiredo. Poly(A) tail methylation stabilizes VSG transcripts. EMBO YIP meeting. Instituto de Medicina Molecular, Lisboa, Portugal. July 2th, 2021.

Luisa M. Figueiredo. Poly(A) tail methylation stabilizes key virulence transcripts in African trypanosomes. Online Meeting on Epigenetics in the Biology of Parasites. Israeli Society for Parasitology, Protozoology and Tropical Diseases, Israel. June 17th, 2021.

Luisa M. Figueiredo. Tissue tropisms in the mammalian host. Swiss TPH Virtual. Bern, Switzerland. April 20th, 2021.

Communications

Adriana Temporão. Can *Trypanosoma brucei* be a new ally in the fight against malaria? 32nd Molecular Parasitology Meeting. Marine Biological Laboratory, Woods Hole, MA, USA, October 9th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease (FatTryp).

Fabien Guegan. Grumpy long non-coding RNA controls trypanosome differentiation via a smaller nucleolar RNA. 32nd Molecular Parasitology Meeting. Marine Biological Laboratory, Woods Hole, MA, USA, October 9th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease (FatTryp).

Idálio Veigas. Poly(A) methylation of VSG genes inhibits deadenylation and increases mRNA stability. 32nd Molecular Parasitology Meeting. Marine Biological Laboratory, Woods Hole, MA, USA, October 8th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease (FatTryp).

Sara Silva Pereira. Immunopathology and parasite sequestration cause severe cerebral animal African trypanosomiasis. 32nd Molecular Parasitology Meeting. Marine Biological Laboratory, Woods Hole, MA, USA, October 9th, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Mechanism and function of epitranscriptomic poly(A) tail modifications in African trypanosomes (TrypM6A).

Networks & Research Infrastructures

Luisa M. Figueiredo. ITN Cell2Cell - Challenging trypanosome antigenic variation paradigms using natural systems (UNS39799). Group Leader.

2019/2023 – *Marie Curie Innovative Training Network* - € 2 055 000

Luisa M. Figueiredo. COBALT - Challenging trypanosome antigenic variation paradigms using natural systems (UNS39799). Participant.

2017/2021 - Wellcome Trust Collaborative Award in Science - £ 2 021 766

Prizes & Honors in 2021

Sara Silva Pereira has received the Maria de Sousa Award (first edition, 2021) on November 24th in 2021. The award recognizes out-of-the-box projects by early-career scientists and includes

funding for a short internship in an international research center of excellence. The project funded aims to identify biomarkers of trypanosomiasis disease severity by combining infection, molecular, computational approaches and clinical data from infected livestock.

Luisa M. Figueiredo has been appointed Associate Editor at PLoS Pathogens and has acted as peer-reviewer of Cell Reports (2), eLIFE (1), iSCIENCE (1), Nat Comm (1), Plos NTD (1), PLOS Pathogens (2), Review Commons (1).

Advanced Teaching

Idálio Viegas. Master in Biomedical Research. Principles of Infection and Immunity. Instituto de Medicina Molecular, Lisboa, Portugal, November 28th, 2021.

PhD Theses

Margarida Sanches-Vaz (12/04/2021), *Understanding how African trypanosomes impair a subsequent Plasmodium infection*, Instituto de Medicina Molecular, Lisboa, Portugal. Supervisor's Name: Miguel Prudêncio Co-Supervisor: Luisa M. Figueiredo. <http://hdl.handle.net/10451/10014>

Valorization of Knowledge / Social and Economic Impact

Science and Society in 2021

Scientific dissemination at FIC.A / Oeiras. A journey into the world of science and technology where we will celebrate knowledge, curiosity and creativity through an innovative and free program.

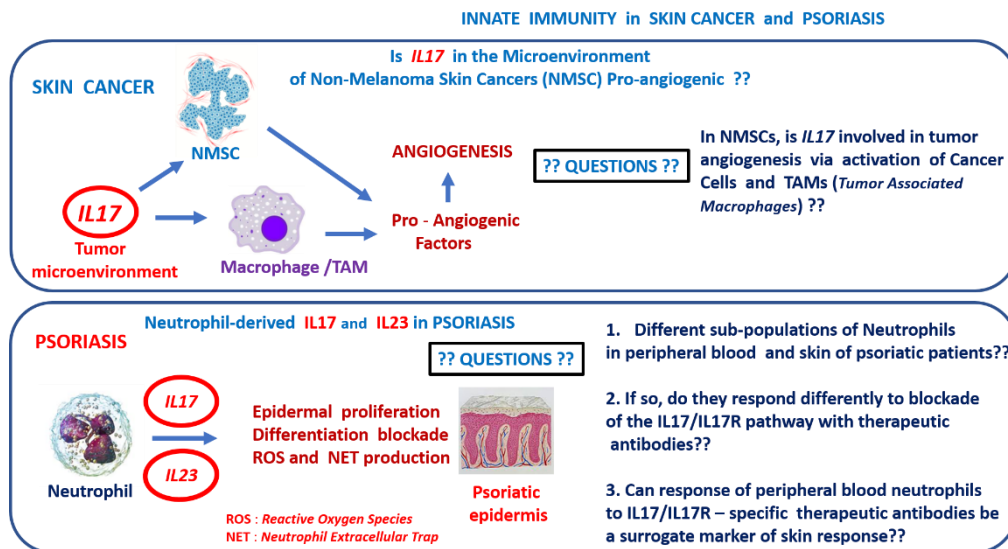
Paulo Filipe Lab

Head of Laboratory: Paulo Filipe, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Associate Professor at Faculdade de Medicina da Universidade de Lisboa, Director of the Department of Dermatology at Centro Hospitalar Universitário Lisboa Norte – Hospital Santa Maria.

Team

Ana Daniela Casimiro Cunha	University Degree	PhD Student
David José Roxo Botequim	PhD	Postdoctoral Researcher (Started December)
João António Augusto Ferreira	PhD	Staff Scientist
João Borges da Costa	University Degree	Clinical Researcher
João Nuno Maia Rodrigues da Silva	PhD	Clinical Researcher
Luís Miguel dos Santos Reis Soares de Almeida	University Degree	Clinical Researcher
Maria Clara Gomes da Fonseca Pedro Bicho	PhD	Clinical Researcher
Miguel Duarte Botas Alpalhão	Master Degree	Trainee

Graphical Abstract



Lab Interests

1. To study T cell-mediated host immune responses against Non-Melanoma Skin Cancers (NMSCs), namely Basal Cell carcinomas and Squamous Cell carcinomas. Also, how host innate immune cells (namely macrophages) impact the tumor microenvironment to promote tumor growth and angiogenesis.
2. To understand how another innate immune cell – the neutrophil – is involved in the pathogenesis of psoriasis namely through participation in the *IL-17* and *IL-23*-dependent pathways. Also, in psoriasis we are currently testing to what extent Factor H, a cell-protective

factor during activation of immune responses, may serve as a biomarker of therapeutic response and disease recurrence.

3. To implement methodologies of cell cycle analysis that could be applied to human skin diseases associated with cellular hyperproliferation, namely psoriasis and skin cancers. These methods may provide useful readouts of the efficacy of targeted therapies.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

1. We have characterized the T-cell infiltrate of two types of high incidence skin cancers namely Basal Cell Carcinomas (BCCs) and Squamous Cell Carcinomas (SCCs). We found a Th1-predominant anti-tumoral response, counterbalanced by an increased pro-tumoral response highlighted by an enrichment in regulatory T cells (Tregs) and reduced levels of $\gamma\delta$ T cells relative to normal, control skin. Importantly, BCCs (but not SCCs) featured an increase in Th17 cells, suggesting interleukin17 as a putative therapeutic target in clinically advanced BCCs.

2. We have developed an innovative methodology that allows, through single imaging (one shot), the assessment of both the cell cycle stage at which non-synchronous cells were exposed to genotoxic stimuli and the cell cycle stage upon cell collection. This complements a series of technological developments aimed at improving analysis of the cell cycle in hyperproliferative skin conditions, namely psoriasis and skin cancers.

Ongoing Projects in 2021

2021/2022: LIMM THERAPEUTICS. Coordinator Paulo Filipe. Funding Agency: Leo Farmacêutica. Reference: LEO FARMACÊUTICOS - PFILIFE LAB. Amount: 81 000,00€. Total Amount: 81 000,00€.

2020/2023: Apoio Janssen. Coordinator: Paulo Filipe. Funding Agency: Janssen - Cilag Farmacêutica, Lda. Reference: Acordo Janssen. Amount: 67 928,40€. Total Amount: 67 928,40€.

2019/2022: Study of changes in human skin microbiome induced by phototherapy treatment in AD. Coordinator: Paulo Filipe. Funding Agency: Sanofi. Reference: Microbiome in Atopic Dermatitis. Amount: 18 171,65€. Total Amount: 18 171,65€.

2019/2021: The IL-23/IL-17 axis and angiogenesis in non-melanoma skin Cancer. Coordinator: Daniela Cunha. Funding Agency: Almirall, S.A. Reference: Almirall. Amount: 88 000,00€. Total Amount: 88 000,00€.

2018/2021: Apoio Novartis. Coordinator: Paulo Filipe. Funding Agency: Novartis Consumer Health SA. Reference: Apoio Novartis. Amount: 5 000,00€. Total Amount: 5 000,00€.

2017/2021: Vascular patterns in non-melanoma skin cancer assessed by reflectance confocal microscopy and 3D imaging. Coordinator: Paulo Filipe. Funding Agency: Sociedade Portuguesa de Dermatologia e Venerologia and Several Laboratories. Reference: Angiogenesis PFilipe. Amount: 19 850,00€. Total Amount: 19 850,00€.

2016/2021: Th9-IL9R axis: a role in tissue memory in plaque-type psoriasis? Coordinator: Paulo Filipe. Funding Agency: Novartis. Reference: Novartis PFilipe. Amount: 30 400,00€. Total Amount: 30 400,00€.

Scientific Impact

Academic Collaborations

Joana Marques Marto, Faculty of Pharmacy, University of Lisbon

Fernando António da Costa Ferreira, Faculty of Veterinary Medicine, University of Lisbon

René Claude Santus, Museum national d'Histoire naturelle, Paris

Heinz Kutzner, Institute of Dermatopathology, Friedrichshafen, Germany

Selected Publications

Queirós C, Filipe P, Soares-Almeida L (2020). [Cutaneous metastases from solid neoplasms in the 21st century: A retrospective study from a Portuguese tertiary care centre](#). *J Eur Acad Dermatol Venereol*. 34(6):1218-1224. Original article.

Relevance of Publication: This retrospective study comprises one of the largest published analyses on the topic of cutaneous metastasis from solid tumours (n= 164 patients). The Authors found that melanoma and breast cancer comprise the most frequent sources of cutaneous metastases, followed by lung cancer. This study consolidated the clinical landscape on this relevant topic. Our group was the exclusive contributor to this piece of research.

Alpalhão M, Filipe P. (2021). [Herpes Zoster following SARS-CoV-2 vaccination - a series of four cases](#). *J Eur Acad Dermatol Venereol*., 35(11): e750-e752. Letter.

Relevance of Publication: In this Letter, a clinical state of immunodepression following SARS-CoV-2 vaccination was revealed by reactivation of Herpes Zoster in a small cohort of elderly patients. The data suggests that immune reactivity against the viral SARS-Cov2 Spike-protein may be involved. Clearly, these relevant findings warrant further research to identify susceptible individuals. Our group was the exclusive contributor to this work.

Pereira PD, Serra-Caetano A, Cabrita M, Bekman E, Braga J, Rino J, Santus R, Filipe PL, Sousa AE, Ferreira JA (2017). [Quantification of cell cycle kinetics by EdU \(5-ethynyl-2'-deoxyuridine\)-coupled-fluorescence-intensity analysis](#). *Oncotarget* 8:40514-40532. Original Article.

Relevance of Publication: We described a novel technology of cell cycle analysis that, in contrast to precedent flow cytometric methodologies, allows the determination of both relative and absolute durations of all the cell cycle stages. Our group is the main contributor to this research, with collaborations from the groups of René Santus (Museum national d'Histoire naturelle Paris, France) and Ana Espada-Sousa (iMM-JLA, Lisbon, Portugal). This research was very welcome within the scientific community working on the cell cycle, resulting in an invitation to contribute to the prestigious monographic series "*Methods in Molecular Biology*" (cf item 2021 publications, below).

Teixeira A, Morlière P, Ferreira J, Conte MA, Galmiche A, Mazière JC, Santus R, Filipe P (2016). [Interplay between membrane lipid peroxidation and photoproduct formation in the Ultraviolet A-induced phototoxicity of Vemurafenib in skin keratinocytes](#). *Toxicological Sciences* 154:289-295. Original Article.

Relevance of Publication: Vemurafenib, a BRAF-inhibitor, remains mainstay of treatment of advanced (BRAF V600-mutant) melanoma. However, Vemurafenib may cause serious secondary effects namely induction on non-melanoma cutaneous malignancies and photosensitization. In this research the Authors show that both membrane photosensitization (lipid peroxidation) and formation of photoproducts synergize to induce Vemurafenib-dependent cell phototoxicity. Our group was the main contributor to this research, conducted in collaboration with the team of René Santus (Museum national d'Histoire naturelle, Paris, France), a long-term collaborator with our group.

Nascimento C, Urbano AC, Gameiro A, Ferreira J, Correia J, Ferreira F (2020). [Serum PD-1/PD-L1 levels, tumor expression and PD-L1 somatic mutations in HER2-positive and triple negative normal-like feline mammary carcinoma subtypes](#). *Cancers* 12(6):1386-1401. Original Article.

Relevance of Publication: The mammary gland is a major skin appendage (or adnexa) and a prominent source of pathology in the oncology setting. The tumour inflammatory infiltrate has recently attracted much attention due to its ability to regulate distinct immune checkpoints, and thus orchestrate tumour progression. Herein, we addressed the expression of main immune checkpoint regulators, PD-1 (Programmed cell Death protein-1) and its ligand, PD-L1, in cats with mammary carcinoma. It was found that both serum and tumour levels of PD-1 and PD-L1 were significantly higher in cats with HER2-positive mammary carcinomas. Future research shall address whether this translates to human breast cancers. Our group collaborated in this research mainly conducted at the Faculty of Veterinary Sciences, University of Lisbon, Lisbon.

2021 Publications in Peer-Reviewed Journals

Alpalhão M, Maia-Silva J, Filipe P (2021). [Severe Acute Respiratory Syndrome Coronavirus 2 vaccines and cutaneous adverse reactions: A review](#). *Dermatitis*, 32(3):133-139. Review.

Alpalhão M, Filipe P (2021). [Herpes Zoster following SARS-CoV-2 vaccination - a series of four cases](#). *J Eur Acad Dermatol Venereol.*, 35(11): e750-e752. Letter.

Brazão C, Alpalhão M, Aguado-Lobo M, Antunes J, Soares-de-Almeida L, Filipe P (2021). Is there a link between Guttate psoriasis and SARS-CoV-2? A series of three cases. *An Bras Dermatol.*, S0365-0596(21)00316-0. (Online ahead of print; Dec 30). Original article.

Correia C, Bouceiro-Mendes R, Sanches M, Fernandes S, Borges-Costa J, Soares-de-Almeida L, Filipe P (2021). [A unique presentation of papulonodular secondary syphilis in an elderly patient](#). *Int J Dermatol.*, 60(8): e304-e306.

Correia C, Fernandes S, Soares-de-Almeida L, Filipe P (2021). [Bullous pemphigoid probably associated with pembrolizumab: a case of delayed toxicity](#). *Int J Dermatol.* (Online ahead of print; Jul 21). Original article.

Correia C, Fernandes S, Soares-de-Almeida L, Filipe P (2021). [Exuberant lichenoid eruption after Oxford–AstraZeneca COVID-19 vaccine: a singular case](#). *J Eur Acad Dermatol Venereol*. (Dec 16; Online ahead of print). Original article.

Correia C, Mendes R, Filipe P (2021). [Quiz your knowledge! Three violet plaques in an immunocompromised patient](#). *Eur J Dermatol.*, 31(4):595-597. Original article.

Ferreira JA, Neves M, Alpalhão M, Pereira P, Cunha D, Ferreira F, Santus R, Sousa AE, Filipe PL (2021). [EDU \(5-ethynyl-2'-deoxyuridine\)-coupled-fluorescence-intensity analysis – Determining absolute parameters of the Cell Cycle](#). *Methods in Molecular Biology (Cell Cycle Oscillators)*, 2329: 165-177.

Garrido PM, Pimenta R, Viana I, Kutzner H, Filipe P, Soares-Almeida L (2021). [Cutaneous mucormycosis mimicking pancreatic panniculitis](#). *J Cutan Pathol.*, 48(8):1007-1009. Original article.

Leitão TP, Miranda M, Polido J, Morais J, Corredeira P, Alves P, Oliveira T, Pereira e Silva R, Fernandes R, Ferreira J, Reis JP, Lopes T, Costa L (2021). [Circulating tumor cell detection methods in renal cell carcinoma: A systematic review](#). *Critical Reviews in Oncology/Hematology*, 161: 103331.

Mendes RB, Alpalhão M, Filipe P (2021). [UVB phototherapy in the treatment of vitiligo: State of the art and clinical perspectives](#). *Photodermatol Photoimmunol Photomed.*, (online ahead of print; Oct 09). Review.

Nascimento C, Gameiro A, Ferreira J, Correia J, Ferreira F (2021). [Diagnostic Value of VEGF-A, VEGFR-1 and VEGFR-2 in feline mammary carcinoma](#). *Cancers*, 13(1): 117. Original article.

Queirós C, Casinhas-Santos M, Pimenta R, Tapadinhas C, Filipe P (2021). [Transient cutaneous alterations of the newborn](#). *Eur Medical J.*, 6(1):97-106. Review.

Queirós C, Filipe P, Soares-de-Almeida L (2021). [Cutaneous leiomyosarcoma: a 20-year retrospective study and review of the literature](#). *An Bras Dermatol.*, 96(3):278-283. Original article.

Queirós C, Silva L, Miroux-Catarino A, Labareda J, Catorze G, Viana I (2021). [Topical imiquimod as neoadjuvant therapy before Mohs micrographic surgery for basal cell carcinoma in the head and neck region: findings from a large retrospective study](#). *Br J Dermatol.*, 185(4):851-853.

Sirakanyan S, Arabyan E, Hakobyan A, Hakobyan T, Chiligaryan G, Sahakyan H, Sargsyan A, Arakelov G, Nazaryan K, Izmailyan R, Abroyan L, Karalyan Z, Arakelova E, Hakobyan E, Hovakimyan A, Serobian A, Neves M, Ferreira J, Ferreira F, Zakaryan H (2021). [A new microtubule-stabilizing agent shows potent antiviral effects against African swine fever virus with no cytotoxicity](#). *Emerging Microbes and Infections*, 10(1): 783-796. Original article.

Torres T, Gonçalo M, Lopes MJP, Claro C, Ramos L, Selores M, Bastos P, Rocha J, Carvalho R, Mota A, Filipe P (2021). [Portuguese recommendations for the treatment of atopic dermatitis with biologic therapy and JAK inhibitors in adult patients](#). *Drugs Context*, 10:2021-9-5.

Vilardouro AS, Ferreira J, Alpalhão M, Neves M, Gonçalo-Marques J, Filipe P (2021). [A Case Report of Mycetoma and Cranial Osteomyelitis by Nocardia nova](#). *J Pediatr Infect Dis.*, 16(06): 303-306. Original article.

Invited Lectures and Seminars

Ferreira J. Skin Basal Cell Carcinomas and Squamous Cell Carcinomas Share a Th1-dominant Microenvironment. 8th International Meeting on Cancer and Radiology, Prague Czech Republic, October 25, 2021. (Keynote presentation). Oral Communication / International Conference.

Communications

ORAL COMMUNICATIONS

INTERNATIONAL:

Queirós C, Silva L, Miroux-Catarino A, Labareda J, Catorze G, Viana I. Topical imiquimod as neoadjuvant therapy before Mohs micrographic surgery for basal cell carcinoma in the head and neck region: findings from a large retrospective study. 30th European Academy of Dermatology and Venereology (EADV) Congress (virtual), September 29 -October 2, 2021. Oral Communication / International Conference.

Ferreira J. Skin Basal Cell Carcinomas and Squamous Cell Carcinomas Share a Th1-dominant Microenvironment. 8th International Meeting on Cancer and Radiology, Prague Czech Republic, October 25, 2021. (Keynote presentation). Oral Communication / International Conference.

NATIONAL:

Correia C, Fernandes S, Soares-de-Almeida L, Filipe P. Micose fungóide poiquilodérmica. 3^a Academia de Dermatologia Almirall, Figueira da Foz, Portugal, junho 26-27, 2021. Oral Communication / National Conference.

Garrido PM, Soares-Almeida L, Filipe P. Líquen plano hipertrófico associado a hepatite B crónica. 3^a Academia de Dermatologia Almirall, Figueira da Foz, Portugal, junho 26-27, 2021. Oral Communication / National Conference.

Antunes-Duarte S, Bouceiro-Mendes R, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Adalimumab no tratamento de pioderma gangrenoso em idade pediátrica. Reunião da Primavera (SPDV), Centro Cultural e de Congressos, Aveiro, Portugal, julho 9-10, 2021. Oral Communication / National Conference.

Antunes-Duarte S, Lopes L, Fernandes S, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Penfigóide bolhoso sem bolhas. Reunião da Primavera (SPDV), Centro Cultural e de Congressos, Aveiro, Portugal, julho 9-10, 2021. Oral Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Lopéz-Presa D, Soares-de-Almeida L, Filipe P. Exuberante metastização cutânea de adenocarcinoma gástrico, 20 anos após o seu diagnóstico primário Penfigoide bolhoso sem bolhas. Reunião da Primavera (SPDV), Centro Cultural e de Congressos, Aveiro, Portugal, julho 9-10, 2021. Oral Communication / National Conference.

Correia C, Alpalhão M, Guerreiro N, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Tapadinhas C, Soares-de-Almeida L, Filipe P. Pênfigo vulgar na idade pediátrica – uma entidade rara. Reunião da Primavera (SPDV), Centro Cultural e de Congressos, Aveiro, Portugal, julho 9-10, 2021. Oral Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Alves D, Soares-de-Almeida L, Filipe P. Pápulas nas arcadas supraciliares – uma manifestação inaugural rara de leucemia linfocítica crónica de células B. Reunião da Primavera (SPDV), Centro Cultural e de Congressos, Aveiro, Portugal, julho 9-10, 2021. Oral Communication / National Conference.

Correia C, Cunha M, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Soares-de-Almeida L, Filipe P. Infecção cutânea por *Mycobacterium marinum* num doente sob adalimumab. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Soares-de-Almeida L, Borges-Costa J, Filipe P. Sífilis maligna num doente imunocompetente – um caso raro e exuberante a não esquecer. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Correia T, Soares-de-Almeida L, Filipe P. Reações cutâneas exuberantes associadas à vacinação anti-SARS-CoV-2: série de casos. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Garrido P, Alpalhão M, Esteves-Caldeira E, Correia I, Correia T, Filipe P. Dermatite de contacto alérgica aos elásticos das máscaras FFP2. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Brazão C, Matias-Lopes I, Santos-Cunha F, Campaniço S, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P. Penfigoide bolhoso e hemofilia A adquirida: uma associação rara de doenças autoimunes. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Antunes-Duarte S, Roda A, Queirós C, Cunha M, Marques T, Soares-de-Almeida L, Filipe P. Reação lepromatosa tipo 1 em contexto de Síndrome Inflamatória de Reconstituição Imunológica. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

Antunes-Duarte S, Fraga A, Soares-Almeida L, Filipe P. Consulta de Patologia Ungueal num Hospital Terciário: Estudo retrospectivo de 3 anos. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Oral Communication / National Conference.

POSTER COMMUNICATIONS

INTERNATIONAL:

Correia C, Roda A, Fernandes S, Cravo M, Soares-de-Almeida L, Filipe P. Cutaneous epithelioid angiosarcoma in the elderly: treatment challenges. 10th World Congress of Melanoma (Interactive Virtual Meeting), April 15-17, 2021. Poster Communication / International Conference.

Mancha D, Sanches M, Brazão C, Sun L, Soares-de-Almeida, Filipe P. Tattoo-Associated Sarcoidosis Related to Targeted Therapies in Melanoma. 10th World Congress of Melanoma (Interactive Virtual Meeting), April 15-17, 2021. Poster Communication / International Conference.

Correia C, Antunes-Duarte S, Aguado-Lobo M, Fernandes S, Filipe P, Kutzner H, Soares-de-Almeida L. A rare case of cutaneous metastases of chondrosarcoma of the distal phalanx. European Academy of Dermatology and Venereology Spring Symposium (Virtual Meeting), May 6-7, 2021. Poster Communication / International Conference.

Correia C, Bouceiro-Mendes R, Aguado-Lobo M, Fernandes S, Alves D, Soares-de-Almeida L, Filipe P. Multiple translucent papules on eyebrows: the presenting sign of chronic lymphocytic leukemia. European Academy of Dermatology and Venereology Spring Symposium (Virtual Meeting), May 6-7, 2021. Poster Communication / International Conference.

Antunes-Duarte S, Correia C, Bouceiro-Mendes R, Espinosa-Lara P, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Ciprofloxacin-induced localized bullous drug reaction. European Academy of Dermatology and Venereology Spring Symposium (Virtual Meeting), May 6-7, 2021. Poster Communication / International Conference.

Brazão C, Mendonça-Sanches M, Mancha D, Sun L, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Primary cutaneous diffuse large B cell lymphoma leg type of the face. European Academy of Dermatology and Venereology Spring Symposium (Virtual Meeting), May 6-7, 2021. Poster Communication / International Conference.

Antunes-Duarte S, Correia C, Bouceiro-Mendes R, Espinosa-Lara P, Aguado-Lobo M, Soares-Almeida L, Filipe P. Secondary syphilis in a tattooed man. European Academy of Dermatology and Venereology Spring Symposium (Virtual Meeting), May 6-7, 2021. Poster Communication / International Conference.

Antunes-Duarte S, Correia C, Lopes L, Fernandes S, Filipe P. Pyoderma gangrenosum associated with Crohn's disease successfully treated with adalimumab. 20th European Society of Pediatric Dermatology (ESPD) Annual Meeting (Virtual Meeting), Vienna, Austria, May 12-14, 2021. Poster Communication / International Conference.

Correia C, Roda A, Mendes R, Ramos F, Fernandes S, Soares-de-Almeida L, Filipe P. Cutaneous calcinosis in pediatric age: how to act. 20th European Society of Pediatric Dermatology (ESPD) Annual Meeting (Virtual Meeting), Vienna, Austria, May 12-14, 2021. Poster Communication / International Conference.

Correia C, Bouceiro-Mendes R, Antunes-Duarte S, Aguado-Lobo M, Fernandes S, Soares-de-Almeida L, Filipe P. Atypical presentation of herpes-simplex associated to recurrent erythema multiforme in an infant. 20th European Society of Pediatric Dermatology (ESPD) Annual Meeting (Virtual Meeting), Vienna, Austria, May 12-14, 2021. Poster Communication / International Conference.

Correia C, Bouceiro-Mendes R, Sanches M, Fernandes S, Borges-Costa J, Soares-de-Almeida L, Filipe P. A unique presentation of papulonodular secondary syphilis in an elderly patient. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Antunes-Duarte S, Correia C, Fraga A, Filipe P. Disseminated tinea incognito in a patient with psoriasis. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Mancha D, Aguado-Lobo M, Pimenta R, Soares-de-Almeida L, Filipe P. Galli-Galli disease: a case report. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Correia C, Duarte S, Aguado-Lobo M, Fernandes S, Soares-de-Almeida L, Filipe P. Tungiasis: a neglected ectoparasitosis. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Correia C, Espinosa-Lara P, Aguado-Lobo M, Fernandes S, Soares-de-Almeida L, Filipe P. Rivaroxaban-induced leukocytoclastic vasculitis. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Garrido P, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P. The impact of peripheral blood and tissue eosinophil levels on the phenotype of bullous pemphigoid: a retrospective study. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Brazão C, Pimenta R, Aguado-Lobo M, Kutzner H, Soares-de-Almeida L, Filipe P. Lupus Panniculitis: a challenging differential diagnosis of localized acquired Lipodystrophy. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

Alpalhão M, Correia C, Antunes J, Soares-de-Almeida L, Filipe P. Rosacea fulminans – a case report. 30th Anniversary Congress of the European Academy of Dermatology and Venereology, Lugano, Switzerland, September 29-October 2, 2021. Poster Communication / International Conference.

NATIONAL:

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Soares-de-Almeida L, Filipe P. Penfigóide não-bolhoso - um diagnóstico clínico e histológico nem sempre fácil. XXXIII Fórum de Dermatologia, Centro de Congressos da Alfândega do Porto, Porto, Portugal, novembro 5-6, 2021. Poster Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Soares-de-Almeida L, Filipe P. Fibrofolículos: uma pista para o diagnóstico da síndrome de Birt-Hogg-Dubé. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Correia C, Aguado-Lobo M, Espinosa-Lara P, Fernandes S, Soares-de-Almeida L, Filipe P. Úlceras cutâneas disseminadas causadas pelo metotrexato: um efeito adverso raro. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Garrido P, Lacerda A, Fernandes I, Soares-de-Almeida L, Filipe P. Leiomiossarcoma cutâneo: diagnóstico e tratamento durante a pandemia COVID-19. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Mancha D, Roda A, Queirós C, Garrido P, Filipe P. O papel do dermatologista no apoio ao doente internado: análise retrospectiva da urgência interna de Dermatologia de um centro hospitalar terciário. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Mancha D, Roda A, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P, Borges-Costa J. Vitiligo no local da vacina mRNA contra a COVID-19: consequência ou coincidência? XX

Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Brazão C, Mendonça-Sanches M, Lozada A, Soares-de-Almeida L, Filipe P. Endometriose cutânea primária: um desafio diagnóstico. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Brazão C, Esperança-Martins M, Sun L, Mendonça-Sanches M, Fernandes I, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P. Eritrodisestesia associada a Doxorrubicina. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Antunes-Duarte S, Sun L, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P. Múltiplas úlceras cutâneas causadas por *Serratia marcescens*: uma apresentação exuberante. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Antunes-Duarte S, Alpalhão M, Garrido P, Maia-Silva J, Filipe P. Reconstrução de um grande defeito cirúrgico do nariz com combinação de retalhos cutâneos. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Antunes-Duarte S, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Filipe P. Miopericitoma subungueal doloroso. XX Congresso Nacional de Dermatologia e Venereologia (SPDV), Convento de São Francisco, Coimbra, Portugal, novembro 26-28, 2021. Poster Communication / National Conference.

Brazão C, Alpalhão M, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Psoríase *gutata* após vacina de mRNA contra o SARS-CoV-2. Reunião de Primavera da Sociedade Portuguesa de Dermatologia e Venereologia 2021, Centro Cultural e de Congressos de Aveiro, Aveiro, Portugal, julho 9-10, 2021. Poster Communication / National Conference.

Alpalhão M, Duarte S, Antunes J, Soares-de-Almeida L, Filipe P. Carcinogénese associada aos inibidores da *Janus Kinase* – a propósito de um caso clínico. Brazão C, Alpalhão M, Aguado-Lobo M, Soares-de-Almeida L, Filipe P. Psoríase *gutata* após vacina de mRNA contra o SARS-CoV-2. Reunião de Primavera da Sociedade Portuguesa de Dermatologia e Venereologia 2021, Centro Cultural e de Congressos de Aveiro, Aveiro, Portugal, julho 9-10, 2021. Poster Communication / National Conference.

Organization of Conferences

Filipe P (Organizer). 5.as Jornadas de Dermatologia do Hospital de Santa Maria -CHULN, Hospital de Santa Maria, Lisboa, Portugal, novembro 11-12, 2021.

Was this conference included as dissemination activity in an active project? (YES/NO): NO

Networks & Research Infrastructures

João Maia Silva. *Ser4Skin - Serotonergic-based therapies to decrease the impact of moderate to severe psoriasis: translation of fundamental research into industry*. Collaborator. Fundação para a Ciência e a Tecnologia (FCT, Portugal; PTDC/MEC-DER/30198/2017; total funding: € 206,231).

Prizes & Honors in 2021

Paulo Filipe has served as invited referee for the following Journals: *British Journal of Dermatology, Journal of Dermatology, Journal of European Academy of Dermato-Venereology, Molecular Diagnosis & Therapy, Photochemical and Photobiological Sciences, Rheumatology, Wound Repair and Regeneration*.

João Ferreira has served as invited referee for the following Journals: *Veterinary Sciences, Frontiers in Immunology, Molecular Biology Reports, Journal of Pharmacy and Pharmacology*.

Advanced Teaching

Ferreira J. Lecture. Micoses superficiais. Mestrado em Análises Clínicas, Faculdade de Farmácia, Universidade de Lisboa, Lisboa, Portugal, julho 6, 2021.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Postdoctoral Fellowship (ref., IMM/BIPD/18-2021), JANSSEN – CILAG Farmacêutica Lda., Portugal, Sponsored Research.

Elucidate the effects of *Brodalumab* on neutrophils in psoriasis, LEO Farmacêuticos Lda., Portugal, Sponsored Research.

Elucidate the role of IL-23/IL-17 axis in skin cancer angiogenesis, ALMIRALL, S.A., Barcelona, Spain, Sponsored Research.

Policy

Paulo Filipe serves as regular Senior Consultant to *INFARMED* – Autoridade Nacional do Medicamento e Produtos de Saúde, I.P., Portugal, more specifically on the area of dermatological pharmaceuticals.

João Eurico da Fonseca Lab

Head of Laboratory: João Eurico da Fonseca, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full professor, Vice President Scientific Council, Director Instituto de Semiotica Clínica and of Clínica Universitária de Reumatologia at Faculdade de Medicina da Universidade de Lisboa, Diretor of the Rheumatology Department and Vice-Diretor of Centro de Investigação Clínica at Rheumatology Department, Centro Hospitalar Universitário Lisboa Norte (CHULN) Hospital de Santa Maria.

Team

Alexandre Figueiredo Brito	University Degree	MSc Student
Ana Filipa Brojo Lopes de Oliveira Ramos Cordeiro	MD/University Degree	PhD Student
Ana Patrícia Costa Reis	MD/PhD	Postdoctoral Researcher
Ana Rita da Cruz Machado	MD/Master Degree	Clinical Researcher
Ângelo Miguel Silva Calado	PhD	Senior Postdoctoral Researcher
Bruno Miguel Costa Vidal	PhD	Postdoctoral Researcher
Catarina Sofia Melo Tomé	Master Degree	PhD Student
Cristina Dias Botelho da Ponte	University Degree	PhD Student
Elsa Cristina Vieira de Sousa	MD/PhD	Clinical Researcher
Estela Leite Nogueira	MD/University Degree	Clinical Researcher (Started October)
Fernando Manuel Diamantino Saraiva	MD/University Degree	Clinical Researcher
Inês de Almada Correia	University Degree	MSc Student
Joaquim Miguel Polido Pereira	MD/University Degree	PhD Student
Manuel Quaresma Jorge Silvério António	MD/Master Degree	Clinical Researcher
Maria Catarina Nobre Semedo Tenazinha	Master Degree	Clinical Researcher
Maria Helena Regalo da Fonseca	University Degree	Senior Postdoctoral Researcher
Maria José Parreira dos Santos	PhD	Clinical Staff Scientist
Matilde José Sousa Bandeira	MD/Master Degree	Clinical Researcher (Started September)
Miguel Batista Lyon de Castro	University Degree	MSc Student
Mónica da Silva	University Degree	MSc Student
Neide Fernanda Meireles da Silva	University Degree	MSc Student
Nikita Khmelinskii	Master Degree	Clinical Researcher
Patrícia Godinho Bexiga Martins	MD/Master Degree	Clinical Researcher
Pedro Manuel Ávila Ribeiro	Master Degree	PhD Student
Raquel Patrícia Campanilho Marques Ruivo	Master Degree	Clinical Researcher
Rita Alexandra Pedra Aguiar de Moura	PhD	Senior Postdoctoral Researcher
Rui Pedro Lourenço Teixeira	MD/Master Degree	PhD Student
Sofia Carvalho Fernandes Barreira	MD/Master Degree	Clinical Researcher
Susana Paula Leonardo Dias Abreu Capela	University Degree	Clinical Researcher
Vasco Madeira Crispim Romão	MD/PhD	Clinical Researcher

Lab Interests

The Rheumatology Research Unit (RRU) results from a partnership between the IMM/FMUL and the Rheumatology Department of the Santa Maria Hospital, CHULN. Basic scientists and clinicians closely work together to promote translational research and clinical excellence in the field of Rheumatology. Our research objective is the study of inflammatory joint diseases (such as Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Spondyloarthritis (SpA) and Systemic Lupus Erythematosus (SLE)) in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies. The long-term objective of the RRU is to achieve recognition as a European League against Rheumatism Centre of Excellence in Rheumatology.

Research Fields

- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

- Definition of the clinical and biological phenotype of polyarticular and extended oligoarticular juvenile idiopathic arthritis (JIA), differentiating it from persistent oligoarticular JIA and aligning it with the pattern of rheumatoid arthritis.
- Early diagnosis and use of ultrasound in giant cell arteritis, with major contribution for the European and American Classification Criteria.
- Implementation of ultrasound synovial tissue biopsy for patient stratification. International training centre for this technique, as a EULAR centre for excellence in imaging.
 - Silvério-António M, Khmelinskii N, Fonseca JE. Efficacy of intravenous immunoglobulin in shrinking lung syndrome associated with mixed connective tissue disease: a case report. *Aceite na revista Clinical and Experimental Rheumatology.*

Ongoing projects in 2021

2021/2023: CP – VASCULARITIES. Coordinator: João Eurico da Fonseca. Funding Agency: Vários. Reference: CP – VASCULARITIES. Amount: 5 000,00€. Total Amount: 5 000,00€.

2021/2023: MB – VASCULARITIES. Coordinator: João Eurico da Fonseca. Funding Agency: Vários. Reference: MB – VASCULARITIES. Amount: 500,00€. Total Amount: 500,00€.

2021/2023: IIS EARLY JAKI. Coordinator: João Eurico da Fonseca. Funding Agency: AbbVie Inc. Reference: IIS EARLY JAKI – ABBVIE. Amount: 27 422,05€. Total Amount: 27 422,05€.

2019/2026: Identification of the Molecular Mechanisms of non-response to Treatments, Relapses and Remission in Autoimmune, Inflammatory, and Allergic Conditions. Coordinator: João Eurico da Fonseca. Funding Agency: European Commission. Reference: 3TR. Amount: 290 996,25€. Total Amount: 40 273 191,50€.

Scientific Impact

Academic Collaborations

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Selected Publications

Vieira-Sousa E, Alves P, Rodrigues AM, Teixeira F, Tavares-Costa J, Bernardo A, Pimenta S, Pimentel-Santos FM, Gomes JL, Aguiar R, Pinto P, Videira T, Catita C, Santos H, Borges J, Sequeira G, Ribeiro C, Teixeira L, Ávila-Ribeiro P, Martins FM, Canhão H, McInnes IB, Ribeiro RM, Fonseca JE. GO-DACT: a phase 3b randomised, double-blind, placebo-controlled trial of GOLimumab plus methotrexate (MTX) versus placebo plus MTX in improving DACTylitis in MTX-naive patients with psoriatic arthritis. **Ann Rheum Dis.** 2020 Apr;79(4):490-498.

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Moura RA, Weinmann P, Pereira PA, Caetano-Lopes J, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Graça L, Fonseca JE Alterations on peripheral blood B-cell subpopulations in very early arthritis patients. *Rheumatology (Oxford).* 2010 Jun;49(6):1082-92.

Moura RA, Cascão R, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2011). Cytokine pattern in early Rheumatoid arthritis favors B cell activation and survival. *Rheumatology*. **Rheumatology** 50(2), 278-82.

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Barreira SC, Melo AT, Ponte C, Khmelinskii N. (2021) [Macaroni sign and carotid occlusion in Takayasu's arteritis](#). *Rheumatology (Oxford)*.;60(4):2029-2030. Letters (clinical vignettes).

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Brito-Zerón P, Acar-Denizli N, Romão VC, Armagan B, Seror R, Carubbi F, Melchor S, Priori R, Valim V, Retamozo S, Pasoto SG, Trevisani VFM, Hofauer B, Szántó A, Inanc N, Hernández-Molina G, Sebastian A, Bartoloni E, Devauchelle-Pensec V, Akasbi M, Giardina F, Bandeira M, Sisó-Almirall A, Ramos-Casals M; Sjögren Big Data Consortium (2021) [Post-COVID-19 syndrome in patients with primary Sjögren's syndrome after acute SARS-CoV-2 infection](#). *Clin Exp Rheumatol*. 39 Suppl 133(6):57-65. Original article.

Carmona-Fernandes, D, Barreira, SC, Leonardo, N, Casimiro, RI, Castro, AM, Santos, PO, Fernandes, AN, Cortes-Figueiredo, F, Gonçalves, CA, Cruz, R, Fernandes, ML, Ivo, M, Pedro, LM, Canhão, H, Fonseca, JE, Santos, MJ (2021). [Atherosclerosis and Bone Loss in Humans-Results From Deceased Donors and From Patients Submitted to Carotid Endarterectomy](#). *Front. Med* 8: 672496. Original article.

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Cunha RN, Monteiro M, Tenazinha C, Khmelinskii N, Ponte C (2021). [Prospective clinical and ultrasonographic assessment of the temporal artery in a patient with giant cell arteritis](#). *Rheumatology (Oxford)*. Online ahead of print. Original article.

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Nemcova D, Patwardhan A, Santos MJ, Sawhney S, Schonenberg-Meinema D, Battagliotti C, Berntson L, Bica B, Brunner J, Costa-Reis P, Eleftheriou D, Harel L, Horneff G, Kaiser D, Kallinich T, Lazarevic D, Minden K, Nielsen S, Nuruzzaman F, Uziel Y, Helmus N, Torok KS. [Differences sustained between diffuse and limited forms of juvenile systemic sclerosis in expanded international cohort.](#) www.juvenile-scleroderma.com. **Arthritis Care Res.**

Foessler I, Bassett JHD, Bjørnerem Å, Busse B, Calado Â, Chavassieux P, Christou M, Douni E, Fiedler IAK, Fonseca JE, Hassler E, Högl W, Kague E, Karasik D, Khashayar P, Langdahl BL, Leitch VD, Lopes P, Markozannes G, McGuigan FEA, Medina-Gomez C, Ntzani E, Oei L, Ohlsson C, Szulc P, Tobias JH, Trajanoska K, Tuzun Ş, Valjevac A, van Rietbergen B, Williams GR, Zekic T, Rivadeneira F, Obermayer-Pietsch B. (2021) [Bone Phenotyping Approaches in Human, Mice and Zebrafish - Expert Overview of the EU Cost Action GEMSTONE \("GEnomics of MusculoSkeletal traits Translational Network"\).](#) **Front Endocrinol** (Lausanne). 12: 720728. Review.

Fogaça da Mata M, Rebelo M, Sousa HS, Rocha A, Miguel P, Oliveira Ramos F, Costa-Reis P. (2021) [Sinus node dysfunction in an adolescent with systemic lupus erythematosus.](#) **Lupus** 30(2): 342-346.

Fontes T, Silvério-António M, Macieira C, Fonseca JE, Polido-Pereira J. (2021) [An unusual cause of shoulder pain in a young woman with systemic sclerosis: isolated intra-articular calcinosis](#) **Rheumatology (Oxford)**. 13: keab645. Clinical vignette.

Freitas AT, Calhau C, Antunes G, Araújo B, Bandeira M, Barreira S, Bazenga F, Braz S, Caldeira D, Santos SCR, Faria A, Faria D, Fraga M, Nogueira-Garcia B, Gonçalves L, Kovalchuk P, Lacerda L, Lopes H, Luís D, Medeiros F, Melo AMP, Melo-Cristino J, Miranda A, Pereira C, Pinto AT, Pinto J, Proença H, Ramos A, Rato JPR, Rocha F, Rocha JC, Moreira-Rosário A, Vazão H, Volovetska Y, Guimarães JT, Pinto FJ. (2021) [Vitamin D-related of COVID-19 disease severity.](#) **Sci Rep.** 11(1):20837. Original article.

Freitas R, Martins P, Dourado E, Santiago T, Guimarães F, Fernandes B, Garcia S, Samões B, Pinto A, Gonçalves N, Lourenço M, Costa E, Rocha M, Couto M, Duarte A, Araújo F, Cordeiro I, Godinho F, Resende C, Salvador M, Cordeiro A, Santos MJ (2021). [Gender differences in clinical features and outcomes of systemic sclerosis.](#) **Clinical Rheumatology** (online ahead of print). Original article.

Grayson PC, Ponte C, Suppiah R, Robson JC, Craven A, Judge A, Khalid S, Hutchings, Luqmani RA, Watts RA, Merkel PA. (2021) American College of Rheumatology / European League Against Rheumatism Classification Criteria for Eosinophilic Granulomatosis with Polyangiitis. **Arthritis Rheumatol.**

Janeiro J, Barreira SC, Martins P, Ninitas P, Campos J and Fonseca JE (2021) [Ultrasound features associated with shoulder complaints: Calcifications larger than 6 mm in young patients and positive doppler are associated with pain.](#) **Front. Med.** 8:715423. Original article.

Kaushik M, Ponte C, Mollan SP (2021). Current advances in giant cell arteritis. **Curr Opin Neurol.** 34:133-141.

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Leal I, Romão VC, Mano S, Khmelinskii N, Campanilho-Marques R, Ponte C, Macieira C, Oliveira-Ramos F, Vieira-Sousa E, Rosa CM, Rodrigues W, Abegão Pinto L, Marques-Neves C, Fonseca JE. [A non-infectious uveitis multidisciplinary clinic in a tertiary referral center: clinical impact and added value.](#) **J Multidiscip Healthc.** 14: 695-704. Original article.

Lindström U, Di Giuseppe D, Delcoigne B, Glintborg B, Möller B, Ciurea A, Pombo-Suarez M, Sanchez-Piedra C, Eklund K, Relas H, Gudbjornsson B, Love TJ, Jones GT, Codreanu C, Ionescu R, Nekvindova L, Závada J, Atas N, Yolbas S, Fagerli KM, Michelsen B, Rotar Ž, Tomšič M, Iannone F, Santos MJ, Avila-Ribeiro P, Ørnbjerg LM, Østergaard M, Jacobsson LT, Askling J, Nissen MJ (2021). [Effectiveness and treatment retention of TNF inhibitors when used as monotherapy versus comedication with csDMARDs in 15 332 patients with psoriatic arthritis. Data from the EuroSpA collaboration.](#) **Ann Rheum Dis.** 80(11): 1410-1418. Original article.

Makhzoum JP, Grayson PC, Ponte C, Robson J, Suppiah R, Watts RA, Luqmani RA, Merkel PA, Pagnoux C; DCVAS collaborators (2021) [Pulmonary involvement in primary systemic vasculitides.](#) **Rheumatology (Oxford).** 31:keab325.

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Ali Mobasheri, João Eurico Fonseca, Oreste Gualillo, Yves Henrotin, Raquel Largo, Gabriel Herrero-Beaumont, Francisco Airton Castro Rocha. (2021) [Editorial: Inflammation and biomarkers in osteoarthritis](#). **Front Med (Lausanne)**. 8:727700.

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Pre-Print Publications

Mills J, Ponte C, Robson J, Verhoeven P. Improving Knowledge in ANCA-Associated Vasculitis: What Do Patients and Doctors Think? Interviews with Two Opinion Leaders and Two Patient Representatives *EMJ Rheumatol*. 2021;8: 2-11. Disponível em: <https://emj.emg-health.com/wp-content/uploads/sites/2/2021/10/EMJ-Rheumatology-8-Supplement-4-2021.pdf>

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Invited Lectures and Seminars

Ana Margarida Monteiro. Curso Dor – MGF ANALGESIA E ANTINFLAMATÓRIOS NA PRÁTICA CLÍNICA (Online). November 11th, 2021.

Ana Teresa Melo. "IX Practical essentials; Clinical Maneuvers: Physical examination"; Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 23rd, 2021.

Eduardo Dourado, Ana Teresa Melo, Elsa Vieira Sousa. "Metrologia do envolvimento axial, da artrite periférica, da entesite e da dactilite nas espondilartrites." Curso metrologia SpA 2021, Lisbon, Portugal, April 15th, 2021.

Ana Teresa Melo. "Patologia loco-regional. Módulo V – Casos clínicos". Workshop prático de dor, Lisbon, Portugal, November 18th, 2021.

Augusto Silva. O papel dos canabinóides no tratamento farmacológico da dor músculo-esquelética. Curso de Dor, organizado pelo Serviço de Reumatologia do CHLN-HSM, online. Caso clínico interativo sobre fratura vertebral osteoporótica. Curso de Dor, organizado pelo Serviço de Reumatologia do CHLN-HSM, October 2021, online.

Augusto Silva. Highlights das apresentações no Congresso Português de Reumatologia. Fórum da Liga Portuguesa Contra as Doenças Reumáticas, online. November 2021.

Carolina Zinterl. "Tratamento farmacológico da dor músculo-esquelética: Relaxantes musculares - quando usar?", November 11st, 2021.

Carolina Zinterl, Matilde Bandeira "Dor músculo-esquelética - Casos clínicos interativos: Gota", November 18th, 2021.

Catarina Tenazinha. Polimialgia Reumática. Curso da Dor, online, Nov 18th, 2021.

Ponte C. Investigation of Systemic Vasculitis. Simpósio de Inflamação Ocular - 64º Congresso Português de Oftalmologia/Vilamoura / e-meeting; December 9-11, 2021.

Ponte C. The Role of Ultrasound in the Diagnosis, Classification and Monitoring of Giant Cell Arteritis. Reunião do Serviço de Reumatologia do Centro Hospitalar e Universitário de Coimbra; Virtual, September 21st, 2021.

Ponte C. Arterite de células gigantes: Uma nova classificação, importância da ecografia e intervenção selectiva com biológicos. 23º Congresso Nacional da Ordem dos Médicos; Coimbra, May 31st to June 3rd, 2021.

Ponte C. The long-term prognostic role of a quantitative ultrasound assessment in giant cell arteritis. PMR GCA work group virtual meeting; E-meeting, November 8th, 2021.

Ponte C. Imaging in secondary LV vasculitis in rheumatoid arthritis and other rheumatic diseases. European Large Vessel Vasculitis Imaging Course 2021; E-meeting; October 14, 2021.

Ponte C OMERACT GCA ultrasound score - training sessions. OMERACT ultrasound task-force on LVV meeting; E-meeting. October 6, 12 and 26, 2021.

Ponte C. New ACR-EULAR classification criteria for large vessel vasculitis. The 38th Scandinavian Congress of Rheumatology; Alesund – Noruega, September 1-4, 2021.

Ponte C. Ultrasound in the diagnosis of giant cell arteritis. Early-stage Vasculitis Group; E-meeting, March 30th, 2021.

Eduardo Dourado. Urgências reumatológicas e dor no SU. Curso Básico de Urgência CHULN, Lisbon, Portugal, January 15th, 2021.

Eduardo Dourado. Osteoartrose: o sofrimento é opcional. Curso em patologias com dor, Espinho, Portugal, January 30th, 2021.

Eduardo Dourado. Exame físico da coluna cervical e membros superiores. Bial Active Learning, Lisbon, Portugal, March 3rd, 2021.

Eduardo Dourado, Matilde Bandeira, João Eurico Fonseca. Clinical reasoning in Rheumatology. Annual International (bio)Medical Students Meeting (AIMS Meeting), Lisbon, Portugal, March 18th, 2021.

Eduardo Dourado. Exame físico da coluna lombar e anca. Bial Active Learning, Lisbon, Portugal, April 14th, 2021.

Eduardo Dourado. Metrologia do envolvimento axial, da artrite periférica, da entesite e da dactilite nas espondilartrites. Curso metrologia SpA 2021, Lisbon, Portugal, April 15th, 2021.

Eduardo Dourado. Reumatologia e envelhecimento. Curso Intensivo em Geriatria. Online, June 5th, 2021.

Eduardo Dourado. Dor em doenças reumáticas. Curso intensivo da Dor, online, September 16th, 2021.

Eduardo Dourado. Tratamento das doenças reumáticas inflamatórias. Workshop prático de dor, Lisbon, Portugal, November 11th, 2021.

Eduardo Dourado. Reumatologia nos cuidados de saúde primários. Curso MGF 2.0 (online), Porto, Portugal, November 13th, 2021.

Eduardo Dourado, Filipe Cunha-Santos, Carla Macieira. Fibromialgia. Workshop prático de dor, Lisbon, Portugal, November 18th, 2021.

Carolina Zinterl, Matilde Bandeira, Eduardo Dourado. Sessão de casos clínicos: artrite gotosa. Workshop prático de dor, Lisbon, Portugal, November 18th, 2021.

Vieira-Sousa E. Escalas de monitorização e atividade da doença. IV Curso de internos do 2º ano da Sociedade Portuguesa de Reumatologia (online), February 25th, 2021.

Vieira-Sousa E. Psoriatic Disease and guselkumab. Formação Janssen, Portugal (online), March 8th, 2021.

Vieira-Sousa E. Psoriatic Disease. Formação Serviço de Reumatologia, Hospital do Divino Espírito Santo, Portugal (online), March 17th, 2021.

Dourado E, Melo AT, Vieira-Sousa E. Avaliação axial, de articulações periféricas, enteses e dactilite. 2º Curso de Metrologia nas Espondiloartrites (online), April 15th, 2021.

Vieira-Sousa E. João Lobo Antunes Merit PhD Thesis Award. New perspectives on tumor necrosis factor inhibition for the treatment of Psoriatic Arthritis. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting (online), May 4 -5, 2021.

Vieira-Sousa E. Gestão da lombalgia pela Medicina Geral e Familiar. Programa AAP - Atualização em Medicina Geral e Familiar 2021, May 25 (Lisbon) and June 23 (Évora), 2021.

Vieira-Sousa E. Chair of Poster Tours session - Fine-tuning strategies (beyond treatments) to reduce the impact of PsA. European League against Rheumatism Annual Congress Virtual Congress (online), June 2-5, 2021.

Vieira-Sousa E. Psoriatic arthritis. Pharmaexperts Course 2021 (online), July 20, 2021.

Vieira-Sousa E. Guselkumab: are we closer to sustained remission? XXIII Congresso Português de Reumatologia, E-Congresso, Portugal, October 13-16, 2021.

Vieira-Sousa E and Reimão S. Workshop Clinical Cases (Differential Diagnosis)– DISH + CPPD. MRI in axSpA – Update (online), December 16-17, 2021.

Vieira-Sousa E. Escalas de monitorização e atividade da doença. IV Curso de internos do 2º ano da Sociedade Portuguesa de Reumatologia (online), February 25, 2021.

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Dourado E, Melo AT, Vieira-Sousa E. Avaliação axial, de articulações periféricas, enteses e dactilite. 2º Curso de Metrologia nas Espondiloartrites (online), April 15, 2021.

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Vieira-Sousa E and Reimão S. Workshop Clinical Cases (Differential Diagnosis) – DISH + CPPD. MRI in axSpA – Update (online), December 16-17, 2021.

Filipa Ramos - Consulta de transição. Fórum Art & Treat, online, March 17, 2021.

Filipa Ramos - 1º Fórum Nacional de Apoio às Famílias ANDAI, online, March 20, 2021.

Filipa Ramos - Seguimento e manutenção de cuidados nas doenças reumáticas em idade pediátrica em tempo de pandemia. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13-16, 2021.

Inês Leal - Sessão de Inflamação Ocular “Widefield Imaging”, Reunião Conjunta dos Grupos Oftalmologia Pediátrica e Estrabismo, Ergoftalmologia e hipovisão e Inflamação Ocular, Online, May 15, 2021.

Inês Leal - Instrutora no workshop “Skills of Ophthalmology”, AIMS Meeting, Faculdade de Medicina de Lisboa, Lisboa March 15-18, 2021.

Inês Leal - Regime Geral de Protecção de Dados_ o hospital público, a clínica privada, a investigação, as publicações, as bases de dados, as páginas web”.

Carla Barbosa, Rufino Silva, Fernando Trancoso Vaz, Lilianne Duarte, Bernardete Pessoa, Nuno Campos, Manuel Falcão, Inês Leal, Carlos Marques-Neves. Quartas da SPO, online December 1st, 2021

Inês Leal - Chair “Onde a retina encontra a inflamação ocular”. Grupo Português de Retina e Vítreo, Coimbra, Portugal October 15-16, 2021.

João E. Fonseca. Artrite Reumatoide em 2021: O que os inibidores da JAK trazem de novo? Formação em Terapêutica da Artrite Reumatóide February 25, 2021.

João E. Fonseca. Casos clinicos. Workshop AIMS. March 18, 2021.

João E. Fonseca. Issues related to the management of rCTDs treatment plans in the COVID era - what we already know? Clinical challenges on the management of treatment of rCTDs patients in the COVID era – ERN ReCONNET multi-stakeholder workshop March 25, 2021.

João E. Fonseca. Imunodepressão e imunomodulação. Liga contra as doenças Reumáticas. May 21, 2021.

João E. Fonseca. Glucosamina e Condroitina na osteoartrite: analgesia, condroproteção e redução de mortalidade. Evento Ache May 22, 2021.

João E. Fonseca. Medicamentos orais- iJAK. XXI Jornadas ANDAR. September 30, 2021.

João E. Fonseca. Tratamento da Artrite Reumatoide: O que mudou e o que vai mudar? 25 anos Jornadas Patient Care. October 7, 2021.

João E. Fonseca. Integração de cuidados na Artrite Reumatoide. Congresso Portugues de Reumatologia, Herdade dos salgados, October 13-16, 2021.

João E. Fonseca. Growing Evidence on the safety profile. Congresso Portugues de Reumatologia, Herdade dos salgados, October 13-16, 2021.

João E. Fonseca. Guselkumab- redefinir o tratamento da artrite psoriática- introdução. Congresso Portugues de Reumatologia, Herdade dos salgados, October 13-16, 2021.

João E. Fonseca. Baricitinib – update de eficácia e segurança. Congresso Portugues de Reumatologia, Herdade dos salgados. October 13-16, 2021.

João E. Fonseca. Tofacitinib in current treatment strategies. Congresso Portugues de Reumatologia, Herdade dos salgados. October 13-16, 2021.

João E. Fonseca. Carreiras médicas alternativas: Investigação Clínica. VIII Congresso Nacional de Estudantes de Medicina. October 31, 2021.

João E. Fonseca. Currículo à Medida, Case Study: reforma anos clínicos FMUL. VII Call me. November 14, 2021.

João E. Fonseca. Chassing the treatment of Arthritis. 5a Conferência Anual da rede SAÚDE. A Health Research Agenda towards 2030. November 30, 2021.

João E. Fonseca. À Procura da Cura da Artrite: A Artrite Reumatoide como exemplo. Webinar Medicina de Precisão Rede Saúde. December 3, 2021.

João E. Fonseca. O Papel da Indústria Farmacêutica na Formação pós-Graduada da classe médica. December 9, 2021.

Eduardo Dourado, Matilde Bandeira, João Eurico Fonseca. Clinical reasoning in Rheumatology. Annual International (bio)Medical Students Meeting (AIMS Meeting), Lisbon, Portugal, March 18, 2021.

Matilde Bandeira. Artrite e síndromes reumáticas inflamatórias. Sessões de Aprendizagem Relacional do grupo 54o de internos de MGF do ACeS Almada-Seixal, Lisbon, Portugal, August 24, 2021.

Matilde Bandeira. Principais doenças reumáticas seguidas nos cuidados de saúde primários. Sessões de Aprendizagem Relacional do grupo 54o de internos de MGF do ACeS Arrábida, Lisbon, Portugal, September 28, 2021.

Matilde Bandeira. Principais doenças reumáticas seguidas nos cuidados de saúde hospitalares – o papel dos cuidados de saúde primários. Sessões de Aprendizagem Relacional do grupo 54o de internos de MGF do ACeS Arrábida, Lisbon, Portugal, October 19, 2021.

Matilde Bandeira. Papel dos opióides na dor musculoesquelética. Workshop prático de dor, Lisbon, Portugal, November 11th, 2021.

Carolina Zinterl, Matilde Bandeira, Eduardo Dourado. Sessão de casos clínicos: artrite gotosa. Workshop prático de dor, Lisbon, Portugal, November 18, 2021.

Pedro Ávila Ribeiro. "Diagnosis with just a touch" – musculoskeletal physical examination. PET/T4PE 2021 – AEFML, Lisboa, Portugal, May 1, 2021.

Raquel Campanilho Marques. Difficult Juvenile Dermatomyositis case – Case-based Session. Pediatric Rheumatology European Society e-Conference. September 19, 2021.

Susana Capela - Abordagem geral. As várias dimensões da dor - da teoria à prática. Abordagem da dor musculoesquelética. Como avaliar a dor?, 2021.

Susana Capela - A dor nas diferentes doenças reumáticas, 2021.

Susana Capela - Medidas não farmacológicas no tratamento da dor: Introdução. Fadiga nas doenças reumáticas, 2021.

Susana Capela - Medidas farmacológicas no tratamento da dor. Avaliação holística do doente, 2021.

Susana Capela - Casos clínicos: Discussão, 2021.

Susana Capela - I Curso Monotematico de Dor do Serviço de Reumatologia do HSM/IMM, October-November, 2021.

Communications

Ana Margarida Duarte-Monteiro, Fernando Saraiva, JE Fonseca. A case of Rhupus diagnosed in pregnancy in a patient with rheumatoid arthritis and antiphospholipid syndrome. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Ana Margarida Duarte-Monteiro, Joana Martins-Martinho, Ryan Costa Silva, Lígia Peixoto, Joana Lobato, Catarina Abreu, Nikita Khmelinskii, José Carlos Romeu, Cristina Ponte. Granulocyte Colony-Stimulating Factor related Large Vessel Vasculitis - a rare diagnosis. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Ana Margarida Duarte-Monteiro, Eduardo Dourado, Ana Ortins-Pina, Ana Valido. Psoriasis and psoriatic arthritis: a stellar response to ustekinumab. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Ana Margarida Duarte-Monteiro, Eduardo Dourado, JE Fonseca. Tophaceous gout: the natural evolution of a common disease. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER (Clinical image); NATIONAL CONFERENCE.

Ana Margarida Duarte-Monteiro, Eduardo Dourado, Ana Ortins-Pina, Ana Valido. Psoríase e artrite psoriática - de uma cama para a vida. Janssen Clinical iChallenge, Setúbal, Portugal. November, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ana Margarida Monteiro. Severe Cutaneous Involvement in Psoriatic Arthritis. ACR Convergence 2021 (Image Competition), Online, November 1st, 2021. POSTER; INTERNATIONAL CONFERENCE.

Sofia Charneca, Margarida Ferro, João Vasques, Eduardo Dourado, Catarina Sousa Guerreiro, João Eurico Fonseca. Adherence to the Mediterranean Diet is associated with patient-reported functional status in Rheumatoid Arthritis. 2021 European Society for Clinical Nutrition and Metabolism (ESPEN) Congress, Online, September 9th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Margarida Ferro, Sofia Charneca, João Vasques, Eduardo Dourado, Ana Margarida Duarte-Monteiro, Joana Martins Martinho, Catarina Sousa Guerreiro, João Eurico Fonseca. Adesão à dieta mediterrânica em doentes com artrite reumatoide: relação com a atividade da doença, capacidade funcional e impacto global. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Sofia Charneca, Margarida Ferro, João Vasques, Eduardo Dourado, Joana Martins Martinho, Ana Margarida Duarte-Monteiro, Catarina Sousa Guerreiro, João Eurico Fonseca. Ângulo de fase na artrite reumatoide – uma nova variável com valor prognóstico? XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Ana Teresa Melo, Miguel Bernardo, Filipe Pinheiro, Mariana Rodrigues, Rita Torres, Ana Filipa Mourão, Sónia Carvalho, João Nascimento, Maria José Santos, Catarina Soares, Marta Cabral, Raquel Campanilho Marques, Patrícia Costa-Reis, Filipa Oliveira Ramos. “Assessment of the impact of SARS-CoV-2 infection in a Portuguese pediatric population with rheumatic diseases”. XXIX Jornadas Virtuais Internacionais do Instituto Português de Reumatologia, edição virtual. 26th November 2021. - ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Miguel Bernardo, Ana Teresa Melo, Filipe Pinheiro, Mariana Rodrigues, Rita Torres, Ana Filipa Mourão, Sónia Carvalho, João Nascimento, Maria José Santos, Catarina Soares, Marta Cabral, Raquel Campanilho Marques, Patrícia Costa-Reis, Filipa Oliveira Ramos. “Infeção SARS-COV-2 numa série de doentes pediátricos com doença reumática.” XXI Congresso Nacional de Pediatria. Braga, Portugal, 27th October 2021, - ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ana Teresa Melo, Joana Martins Martinho, Patrícia Martins, Rui Ferreira, Patrícia José, Sofia Mano, Inês Leal, Patrícia Costa Reis, Filipa Oliveira Ramos, João Eurico Fonseca, Raquel Campanilho Marques. “Predictive factors of uveitis and its complications in a cohort of 302 JIA patients” XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 15th, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Francisca Guimarães, Manuel António, Joana Martinho, Ana Teresa Melo, Daniela Oliveira, Jorge Lopes, André Saraiva, Ana Gago, Margarida Correia, Ana Lúcia Fernandes, Sara Dinis, Rafaela Teixeira, Susana Silva, Carlos Costa, Tiago Beirão, Carolina Furtado, Pedro Abreu, Carmo Afonso, Daniela Peixoto. “Clinical and immunological features of a Portuguese cohort of Mixed Connective Tissue Disease”. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 15th, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Filipa Oliveira-Ramos, Ana M. Rodrigues, Fernando Martins, Ana Melo, Francisca Aguiar, Luisa Brites, Soraia Azevedo, Ana C Duarte, José Melo-Gomes, Carolina Furtado, Ana Filipa Mourão, Graça Sequeira, Inês Cunha, Ricardo Figueira, Maria J. Santos, João E. Fonseca. “Health-related quality of life and function in adults with Juvenile Idiopathic Arthritis – comparison with adult-onset Rheumatic Diseases” XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ana Teresa Melo, Catarina Tenazinha, Filipa Oliveira Ramos, Patrícia Costa Reis, João Eurico Fonseca, Raquel Campanilho Marques “Bone fragility risk factors in a pediatric rheumatology department - data from a single-center.” 27th European Paediatric Rheumatology e-Congress, Online, 19th September, 2021 POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Ana Teresa Melo, Catarina Tenazinha, Filipa Oliveira Ramos, Patrícia Costa Reis, João Eurico Fonseca, Raquel Campanilho Marques “Bone fragility risk factors in a pediatric rheumatology department - data from a single-center.” Virtual Young Investigators Meeting, Online, 18th September, 2021 POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Ana Teresa Melo, Inês Cordeiro, Oana Moldovan, Sónia Melo Gomes, Raquel Campanilho Marques. “Not just another calcinosis clinical case...”. 27th European Paediatric Rheumatology e-Congress, Online, 19th September, 2021 POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Filipa Oliveira-Ramos, Ana M. Rodrigues, Fernando Martins, Ana Melo, Francisca Aguiar, Luisa Brites, Soraia Azevedo, Ana C Duarte, José Melo-Gomes, Carolina Furtado, Ana Filipa Mourão, Graça Sequeira, Inês Cunha, Ricardo Figueira, Maria J. Santos, João E. Fonseca. “Health-related quality of life and function in adults with juvenile idiopathic arthritis – comparison with adult-onset rheumatic diseases.” 27th European Paediatric Rheumatology e-Congress, Online, 19th September, 2021 POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Patrícia Martins, Eduardo Dourado, Ana Teresa Melo, Beatriz Samões, Marlene Sousa, Raquel Freitas, Maria Helena Fernandes Lourenco, Bruno Miguel Fernandes, Emanuel Costa, Hugo Parente, Frederico Rajao Martins, Joao Eurico Fonseca, Vasco C Romão, Nikita Khmelinskii, Raquel Campanilho-Marques, Inês Cordeiro. Clinical characterization of Portuguese patients with Antisynthetase syndrome. EULAR 2021, Online, June 2nd, 2021. POSTER; INTERNATIONAL CONFERENCE.

Patrícia Martins, Eduardo Dourado, Ana Teresa Melo, Beatriz Samões, Marlene Sousa, Raquel Freitas, Maria Helena Fernandes Lourenco, Bruno Miguel Fernandes, Emanuel Costa, Hugo Parente, Frederico Rajao Martins, Joao Eurico Fonseca, Vasco C Romão, Nikita Khmelinskii, Raquel Campanilho-Marques, Inês Cordeiro. Clinical characterisation of Portuguese patients with antisynthetase syndrome. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Ana Teresa Melo, E. Dourado, P. Martins, N. Khmelinskii, J. E. Fonseca, I. Cordeiro, R. Campanilho-Marques. First clinical analysis of myositis patients registered at Reuma.pt/Myositis protocol: data from a single-center. EULAR 2021, online, June 2nd, 2021. ABSTRACT; INTERNATIONAL CONFERENCE.

Ines Leal, Patricia Jose, Rafael Barão, Sofia Mano, Ana Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Dinis, Filipe Cunha Santos, Henrique Fernandes, Nikita Khmelinskii, Carlos Marques-Neves, Elsa Vieira de Sousa, João Eurico Fonseca. Vision-related quality of life in spondyloarthritis patients with history of acute anterior uveitis under treatment with golimumab: preliminary results of the GO-VISION observational study. European Association for Vision and Eye Research (EVER) 2021 Virtual Congress, Online, October 2nd, 2021. POSTER; INTERNATIONAL CONFERENCE.

Ines Leal, Patricia Jose, Rafael Barão, Sofia Mano, Ana Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Dinis, Filipe Cunha Santos, Henrique Fernandes, Nikita Khmelinskii, Carlos Marques-Neves, Elsa Vieira de Sousa, João Eurico Fonseca. Vision-related quality of life in spondyloarthritis patients with history of acute anterior uveitis under treatment with golimumab: preliminary results of the GO-VISION observational study.

XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Carolina Ochôa Matos, Filipe Cunha Santos, Augusto Silva, Miguel Alpalhão, Paulo Filipe, João Eurico Fonseca, Carlos Miranda Rosa, Joana Antunes, Elsa Vieira-Sousa. Multidisciplinary Rheumatology and Dermatology Clinic for Psoriatic Arthritis: first report of the experience in a tertiary center. XXIII Congresso Português de Reumatologia, Herdade dos Salgados, outubro de 2021. POSTER; NATIONAL.

Augusto Silva, Tomás Fontes, Maria João Saavedra, João Eurico Fonseca. Ultrasound ability in early diagnosis of stress fractures. XXIX Jornadas Internacionais do Instituto Português de Reumatologia, november 2021, online. POSTER, NATIONAL.

Augusto Silva, Nikita Khmelinskii, Catarina Queirós, Maria João Saavedra, João Eurico Fonseca. Cutaneous subacute lupus erythematosus in a patient with primary Sjögren Syndrome. XXIII Congresso Português de Reumatologia, Herdade dos Salgados, October 2021. IMAGE. NATIONAL.

Augusto Silva, Maria João Saavedra, João Eurico Fonseca. Long-lasting Calcinosis cutis. XXIX Jornadas Internacionais do Instituto Português de Reumatologia, november 2021, online. IMAGE. INTERNATIONAL.

Augusto Silva, Maria João Saavedra, João Eurico Fonseca. Enchondroma - a frequent incidental finding. XXIX Jornadas Internacionais do Instituto Português de Reumatologia, november 2021, online. IMAGE. INTERNATIONAL.

Catarina Tenazinha, Rita Barros, Vasco C. Romão. Candida albicans tenosynovitis of the hand. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, Oct, 2021. POSTER; NATIONAL CONFERENCE.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Campanilho-Marques, Ana F. Mourão, Sandra Sousa, Ana P. Martins, Patrícia C. Reis, Ana T. Melo, Rui L. Teixeira, Miroslava Gonçalves, Maria J. Santos, Luis Graca, João E. Fonseca, Rita A. Moura. Children with Juvenile Idiopathic Arthritis have alterations in B and T follicular cell subsets in peripheral blood. 12 Topics in Rheumatology, 3rd Edition. Virtual Meeting, Lisbon, Portugal. October 30-2nd, 2021. ORAL. NATIONAL CONFERENCE.

Catarina Tomé, Luís Graça, JEFonseca, Rita A. Moura. The interplay of B and T Follicular cell subsets in Juvenile Idiopathic Arthritis. Pizza Seminar. Lisboa, Portugal. June 15th, 2021. ORAL. NATIONAL CONFERENCE.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Campanilho-Marques, Ana F. Mourão, Sandra Sousa, Ana P. Martins, Patrícia C. Reis, Ana T. Melo, Rui L. Teixeira, Miroslava Gonçalves, Maria J. Santos, Luis Graca, João E. Fonseca, Rita A. Moura. Children with Juvenile Idiopathic Arthritis

have alterations in B and T follicular cell subsets in peripheral blood. XIV Annual CAML | IV NeurULisboa PhD Students Virtual Meeting. Virtual Meeting, May 5-7th, 2021. ORAL. NATIONAL.

Catarina Tomé, Luís Graça, JEFonseca, Rita A. Moura. The interplay of B and T Follicular cell subsets in Juvenile Idiopathic Arthritis. Immunology Club. Lisboa, Portugal. February 10th, 2021. ORAL. NATIONAL.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Campanilho-Marques, Ana F. Mourão, Sandra Sousa, Ana P. Martins, Patrícia C. Reis, Ana T. Melo, Rui L. Teixeira, Miroslava Gonçalves, Maria J. Santos, Luis Graca, João E. Fonseca, Rita A. Moura. Children with Juvenile Idiopathic Arthritis have alterations in B and T follicular cell subsets in peripheral blood. XXIII Congresso Português de Reumatologia, Palácio de Congressos do Algarve, Algarve, Portugal. October 13-16th, 2021. POSTER. NATIONAL CONFERENCE.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Campanilho-Marques, Ana F. Mourão, Sandra Sousa, Ana P. Martins, Patrícia C. Reis, Ana T. Melo, Rui L. Teixeira, Miroslava Gonçalves, Maria J. Santos, Luis Graca, João E. Fonseca, Rita A. Moura. Children with Juvenile Idiopathic Arthritis have alterations in B and T follicular cell subsets in peripheral blood. PRES European Paediatric Rheumatology Congress, Virtual Meeting. September 19-21th, 2021. POSTER INTERNATIONAL.

Trivioli G, Canzian A, Maritati F, Fenoglio R, Pillebout E, Urban ML, Mohammad AJ, Nogueira E, Silvestri E, Eriksson P, Segelmark M, Novikov P, Harris H, Smitienko I, Moiseev S, Farisogullari B, O'Sullivan D, Ponte C, Lamprecht P, Hocevar A, Karadag O, Little M, Emmi G, Jayne D, McAdoo S, Roccatello D, Vaglio A. Renal outcome after rituximab in adult-onset IgA Vasculitis and crescentic IgA Nephropathy. A multicenter study. 58th ERA-EDTA Congress; e-congress, June 5-8th, 2021. ORAL. INTERNATIONAL.

Ponte C, Monti S, Scirè CA, Delvino P, Khmelinskii N, Milanesi A, Teixeira V, Brandolino F, Saraiva F, Montecucco C, Fonseca JE, Schmidt WA, Luqmani RA Ultrasound halo sign as a potential monitoring tool for patients with giant cell arteritis: a prospective analysis. EULAR Annual Meeting 2021; e-meeting, June 2nd, 2021. ORAL. INTERNATIONAL.

José P, Mano S, Vaz-Pereira S, Cruz-Machado R, Ponte C, Capela S, Macieira C, Teixeira F, Leal I. Vasculite retiniana e síndrome oculo-isquémico como manifestações da arterite de Takayasu. 64º Congresso Português de Oftalmologia; Vilamoura, December 9-11th, 2021. POSTER. NATIONAL CONFERENCE.

Cunha RN, Monteiro M, Tenazinha C, Khmelinskii N, Ponte C. Prospective clinical and ultrasonographic assessment of the temporal artery in a patient with giant cell arteritis. XXIII Congresso Português de Reumatologia; Albufeira, October 13-16th 2021. POSTER. NATIONAL CONFERENCE.

Quinn KA, Alessi H, Ponte C, Rose E, Ahlman MA, Redmond C, Luo Y, Bolek EC, Langford CA, Merkel PA, Grayson PC. Use of 18F-fluorodeoxyglucose Positron Emission Tomography to Standardize Clinical Trial Recruitment in Takayasu's Arteritis Submitted to the 20th International

Vasculitis and ANCA Workshop; e-congress / Dublin – Irlanda, April 3-6th 2022. POSTER. INTERNATIONAL.

Martins-Martinho J, Bandeira M, Barreira SC, Dourado E, Cruz-Machado AR, Teixeira V, Macieira C, Khmelinskii N, Fonseca JE, Ponte C. Differences in giant cell arteritis manifestations according to the ultrasound pattern of disease involvement. Submitted to the 20th International Vasculitis and ANCA Workshop; e-congress / Dublin – Irlanda, April 3-6th 2022. POSTER. INTERNATIONAL.

Quinn KA, Alessi H, Rose E, Ahlman MA, Redmond C, Luo Y, Bolek EC, Langford CA, Ponte C, Merkel PA, Grayson PC. Using 18F-fluorodeoxyglucose Positron Emission Tomography to Standardize Clinical Trial Recruitment in Takayasu’s Arteritis. ACR Convergence 2021; e-congress, November 5-9th, 2021. POSTER. INTERNATIONAL.

Matilde Bandeira, Eduardo Dourado, Carina Oliveira Dias, Mileta Gomes, Joana Silva-Dinis, João Eurico Fonseca. Projeto GAP - um plano integrado de apoio aos doentes com gota. XLI Curso de Reumatologia: Ciência na Prática Clínica 2021, Coimbra, Portugal, February 25th, 2021. POSTER; NATIONAL CONFERENCE.

Eduardo Dourado, Inês Cordeiro. Neither arms NOR legs were feeling well: myositis in a NOR-90+ systemic lupus erythematosus patient. 10th Lupus Academy Annual Meeting. Online, April 17th, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Eduardo Dourado, Filipe Cunha-Santos, Carla Macieira. Mialgias – das gerais às proximais: um caso de dermatomiosite hipomiopática associada ao anti-TIF1γ. Webinar de Fibromialgia (SPR). Online, May 22nd, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Sofia Charneca, Margarida Ferro, João Vasques, Eduardo Dourado, Catarina Sousa Guerreiro, João Eurico Fonseca. Índice de Massa Corporal e Composição Corporal na Artrite Reumatoide: qual a relação com a capacidade funcional e o impacto da doença? Congresso da Associação Portuguesa de Nutrição Entérica e Parentérica, Lisbon, Portugal, May 28th, 2021. POSTER; NATIONAL CONFERENCE.

Raquel Freitas, Patrícia Martins, Eduardo Dourado, Maria Joao Salvador, Tânia Santiago, Inês Cordeiro, Bruno Miguel Fernandes, Francisca Guimarães, Salomé Garcia, Beatriz Samões, Nuno Gonçalves, Maria Helena Fernandes Lourenco, Ana Sofia Pinto, Margarida Rocha, Maura Couto, Emanuel Costa, Filipe Araújo, Catarina Resende, Fátima Godinho, Ana Cordeiro, Maria Jose Santos. Clinical features and outcome of 1054 patients with Systemic Sclerosis: an analysis of the Portuguese Reuma.pt registry for Scleroderma (Reuma.pt/SSc). EULAR 2021, Online, June 2nd, 2021. POSTER; INTERNATIONAL CONFERENCE.

Margarida Ferro, Sofia Charneca, João Vasques, Eduardo Dourado, Catarina Sousa Guerreiro, João Eurico Fonseca. Is bioelectrical phase angle associated with functional status and disease impact in patients with Rheumatoid Arthritis?. EULAR 2021, Online, June 2nd, 2021. POSTER; INTERNATIONAL CONFERENCE.

Matilde Bandeira, Eduardo Dourado, Carina Oliveira, João Eurico Fonseca. Projeto GAP - Gouty Arthritis Pathway. 13^o Curso de Reumatologia Prática em Cuidados de Saúde Primários, Lisboa, Portugal, September 23rd, 2021. POSTER; NATIONAL CONFERENCE.

Eduardo Dourado, Filipe Cunha Santos, Inês Cordeiro. Neither arms NOR legs were feeling well: a case of anti-NOR-90 lupus myositis. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Eduardo Dourado, Sofia Barreira. Jaccoud's arthropathy. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER (Clinical Images); NATIONAL CONFERENCE.

Eduardo Dourado, Ana Sofia Pinto, Anabela Oliveira, Nikita Khmelinskii. Axial ochronotic arthropathy. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER (Clinical Images); NATIONAL CONFERENCE.

Martins P, Dourado E, Fonseca JE, Romão V, Resende C. The safety and persistence of intravenous iloprost in systemic sclerosis. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Matilde Bandeira, Eduardo Dourado, João Eurico Fonseca. Chronic Chikungunya disease: a case of virus-induced erosive and deforming polyarthritis. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Matilde Bandeira, Eduardo Dourado, Filipe Lopes, Sofia C. Barreira. Reactive arthritis as a rare complication of intravesical bacillus Calmette–Guérin treatment. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER; NATIONAL CONFERENCE.

Eduardo Dourado, Ana Silva Martins, Inês Cordeiro, João Eurico Fonseca. Hoarseness as the presentation of IgG4-related disease with vocal cord and mediastinal infiltration. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 14th, 2021. POSTER (with oral presentation); NATIONAL CONFERENCE.

Raquel Freitas, Patrícia Martins, Eduardo Dourado, Maria Joao Salvador, Tânia Santiago, Inês Cordeiro, Bruno Miguel Fernandes, Francisca Guimarães, Salomé Garcia, Beatriz Samões, Nuno Gonçalves, Maria Helena Fernandes Lourenco, Ana Sofia Pinto, Margarida Rocha, Maura Couto, Emanuel Costa, Filipe Araújo, Catarina Resende, Fátima Godinho, Ana Cordeiro, Maria Jose Santos. Gender differences in clinical features and outcomes of Systemic Sclerosis. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 15th, 2021. POSTER (with oral presentation); NATIONAL CONFERENCE.

Eduardo Dourado, Raquel Freitas, Patrícia Martins, Liliana Saraiva, Tânia Santiago, Francisca Guimarães, Emanuel Costa, Diogo Esperança Almeida, Sara Dinis, Ana Sofia Pinto, Alexandra Daniel, Inês Genrinho, Maura Couto, Marília Rodrigues, Maria João Salvador, Ana Catarina Duarte, Ana Cordeiro, Maria José Santos, João Eurico Fonseca, Catarina Resende, Inês Cordeiro.

Prevalence and clinical associations of different autoantibodies in the Reuma.pt systemic sclerosis cohort: is it all really set in stone? XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 16th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Eduardo Dourado. Butterfly Rash in Systemic Lupus Erythematosus Patient with Lupus Myositis. ACR Convergence 2021 (Image Competition), Online, November 1st, 2021. POSTER; INTERNATIONAL CONFERENCE.

Martins P, Dourado E, Fonseca JE, Romão V, Resende C. The safety and persistence of intravenous iloprost in systemic sclerosis. ACR Convergence 2021, Online, November 6th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Raquel Freitas, Patrícia Martins, Eduardo Dourado, Maria Joao Salvador, Tânia Santiago, Inês Cordeiro, Bruno Miguel Fernandes, Francisca Guimarães, Salomé Garcia, Beatriz Samões, Nuno Gonçalves, Maria Helena Fernandes Lourenco, Ana Sofia Pinto, Margarida Rocha, Maura Couto, Emanuel Costa, Filipe Araújo, Catarina Resende, Fátima Godinho, Ana Cordeiro, Maria Jose Santos. Gender differences in clinical features and outcomes of Systemic Sclerosis: analysis of Reuma.pt/SSc registry. ACR Convergence 2021, Online, November 6th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Eduardo Dourado, Ana Silva Martins, João Eurico Fonseca. Hoarseness as the rare presentation of a rare rheumatic disease. ACR Convergence 2021, Online, November 9th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Carina Oliveira Dias, Mileta Gomes, Matilde Bandeira, Eduardo Dourado. Projeto GAP - um projeto iniciado em tempos pandémicos. Jornadas Internacionais do IPR 2021, Lisboa, Portugal, November 25th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Vieira-Sousa E, Vidal B, Silva SP, Sofio AR, Lopes IP, Canhão H, Fonseca JE. Phenotypic, histologic and imagiologic characterization of transmembrane tumor necrosis factor transgenic mice. 12th International Congress on Spondyloarthropathies, Gent, Belgium (online), September 9-11th, 2021 ORAL. INTERNATIONAL

Carvalho PD, Vieira-Sousa E, Marreiros A, Machado PM. Determinants of quality of life in rheumatoid arthritis and spondyloarthritis: how do they interact from a hierarchical perspective? XXIII Congresso Português de Reumatologia, Algarve, 13-16 Outubro 2021. ORAL. NATIONAL.

Patrícia Martins, Patrícia Nero, Jorge Pestana Lopes, Rui Lourenço Teixeira, Inês Silva, Maria José Santos, JE Fonseca, Elsa Vieira-Sousa. New biologic and targeted synthetic disease modifying antirheumatic drugs for the treatment of psoriatic arthritis. How are they positioned in clinical practice? 12th International Congress on Spondyloarthropathies, Gent, Belgium, September 9-11th, 2021. POSTER. INTERNATIONAL.

Vieira-Sousa E, Vidal B, Silva SP, Sofio AR, Lopes IP, Canhão H, Fonseca JE. Phenotypic, histologic and imagiologic characterization of transmembrane tumor necrosis factor transgenic mice. XXIII Congresso Português de Reumatologia, E-Congresso, Portugal, October 13-16th, 2021. POSTER. INTERNATIONAL.

Carolina Ochôa Matos, Joana Antunes, Carlos Miranda Rosa, João Eurico Fonseca, Elsa Vieira-Sousa. A severe, deforming case of juvenile psoriatic arthritis. XXIII Congresso Português de Reumatologia, E-Congresso, Portugal, October 13-16th, 2021. POSTER. INTERNATIONAL.

Ávila-Ribeiro P, Saraiva F, Martins P, Fonseca JE, Vieira-Sousa E “Effectiveness of a biologic tapering protocol for axial spondyloarthritis and psoriatic arthritis (TaPSpA)” XXIII Congresso Português de Reumatologia (comunicação oral) Herdade dos Salgados - October 13-16th, 2021. POSTER. NATIONAL.

Ana Dias Curado, Carolina Amaro Gonçalves, Filipa Afonso Ferreira, Catarina Salgado, Maria João Palaré, Filipa Oliveira Ramos, Anabela Ferrão. ISQUÉMIA AGUDA DO MEMBRO INFERIOR - APRESENTAÇÃO DE SÍNDROME DE ANTICORPOS ANTIFOSFOLÍPIDOS EM PEDIATRIA, 21º Congresso Nacional de Pediatria, Braga, Portugal, October, 27-29th 2021 POSTER. NATIONAL.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Marques, Ana Filipa Mourão, Sandra Sousa, Patrícia Costa Reis, Maria Teresa Melo, Rui Teixeira, Maria José Santos, Luis Graca, João Eurico Fonseca, Rita A. Moura. Children with extended oligoarticular and polyarticular Juvenile Idiopathic Arthritis have alterations in B cell subpopulations and T follicular cell subsets in blood. PRoS 2021, online, September 19-21st 2021. POSTER. INTERNATIONAL.

Miguel Bernardo, Raquel Campanilho Marques, Patrícia Costa-Reis, Filipa Oliveira Ramos., LÚPUS ERITEMATOSO SISTÉMICO JUVENIL - CARACTERIZAÇÃO E AVALIAÇÃO DE DANO NUMA SÉRIE DE DOENTES. 21º Congresso Nacional de Pediatria, Braga, Portugal, October, 27-29th 2021. POSTER. NATIONAL.

Carolina Amaro Gonçalves, Ana Dias Curado, Filipa Ferreira, Catarina Salgado, Maria João Palaré, José Gonçalo Marques, Filipa Oliveira Ramos, Anabela Ferrão Síndrome febril prolongado, esplenomegalia e pancitopenia – será sarcoidose? 21º Congresso Nacional de Pediatria, Braga, Portugal, October, 27-29th 2021. POSTER. NATIONAL.

Filipa Oliveira Ramos, Ana Rodrigues, Fernando Magalhaes Martins, Ana Teresa Melo, Francisca Aguiar, Luisa Brites, Soraia Azevedo, Ana Catarina Duarte, Carolina Furtado, Ana Filipa Mourão, Graça Sequeira, Inês Cunha, Ricardo Figueira, Jose Antonio Melo Gomes, Maria Jose Santos, Joao Eurico Fonseca. Health-related quality of life and disability in adults with juvenile idiopathic arthritis: comparison with adult-onset rheumatic diseases. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13, 2021. POSTER. NATIONAL.

Filipe Cunha Santos. “Avaliação de macrocitose – com ou sem anemia”, apresentado nas XXIX Jornadas Virtuais Internacionais do Instituto Português de Reumatologia, November, 25 – 26th, 2021. POSTER. INTERNATIONAL.

Cruz-Machado AR, Barreira SC, Veldhoen M, Bandeira M, Duarte C, Rato M, Fernandes BM, Garcia S, Pinheiro F, Bernandes M, Madeira N, Miguel C, Torres R, Silva AB, Pestana J, Almeida D, Mazedo C, Santos FC, Pinto P, Sousa M, Parente H, Sequeira G, Santos MJ, Fonseca JE, Romão VC, “Risk factors for infection, predictors of severe disease and antibody response to COVID-19 in patients with rheumatic diseases in Portugal – a multicentre, nationwide study”, XXIII Congresso Português de Reumatologia, October 13-16th, 2021; POSTER, NATIONAL.

“Sessão de Casos Clínicos”, Dourado E, Santos FC, Macieira C, Curso de Dor, November 18th, 2021. ORAL. NATIONAL.

Santos, FC; Vieira-Sousa, E; Pinto, AS; Dinis, SP; Madeira, N; Ferreira, JF; Vaz, CC; “A união não faz força: anquilose total dos ossos do carpo na artrite reumatoide”, aceite nas XXIX Jornadas Virtuais Internacionais do Instituto Português de Reumatologia, November 25 -26th, 2021. POSTER. INTERNATIONAL.

Inês Leal, Patrícia José, Rafael Barão, Sofia Sousa Mano, Ana Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Paiva Dinis, Filipe Cunha Santos, Henrique Fernandes, Nikita Khmelinskii, Carlos Marques-Neves, Elsa Vieira-Sousa, JE Fonseca. Vision-related quality of life in spondyloarthritis patients with history of acute anterior uveitis under treatment with golimumab: preliminary results of the go-vision observational study rheumatology XXIII Congresso Português de Reumatologia, Salgados, Portugal 13th October 2021. POSTER. NATIONAL.

Polido-Pereira J. Corticoterapia e outras opções anti-inflamatórias. 2nd Shoulder and Elbow Congress (Sociedade Portuguesa de Ombro e Cotovelo), Tomar, Portugal, November 19th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, EULAR 2021 virtual congress. June 2nd-5th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Tenazinha MC, Romão VC, Polido-Pereira J, Khmelinskii N, Barros R, Saraiva F, Fonseca JE. “Performance of Major Salivary Gland Ultrasound for the Diagnosis of Sjogren Syndrome in Clinical Practice” EULAR 2021 virtual congress. June 2nd-5th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, Swiss Society of Rheumatology (SSR 2021), Lausanne, Switzerland. September 2-3, 2021. POSTER COMMUNICATION (POSTER TOUR); NATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, PANLAR 2021, August 12th-15th, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, XXIII Congresso Português de Reumatologia. October 15th, 2021. POSTER COMMUNICATION (PRESENTING AUTHOR); NATIONAL CONFERENCE.

Garcia S, Silva A, Zinterl C, Polido-Pereira J, Maduro AI, Duarte C, Soares C, Santos-Faria D, Silva S, Nóvoa T, Dinis S, Araújo F, Tavares-Costa J, Meirinhos T, Cruz M, Bernardes M. Rheumatic Disease Comorbidity Index as a Predictor of Clinical Response to the First Biological Agent in Portuguese Patients with Rheumatoid Arthritis: A Multicenter Cohort Study. XXIII Congresso Português de Reumatologia. October 15th-18th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Fontes T, Silvério-António M, Macieira C, Fonseca JE, Polido-Pereira J. An unusual cause of shoulder pain in a young woman with systemic sclerosis: isolated intra-articular calcinosis. XXIII Congresso Português de Reumatologia. October 15th-18th, 2021. IMAGE POSTER; NATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, ACR Convergence 2021. November 8th, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Kavanaugh A, Szekanecz Z, Keystone EC, Rubbert-Roth A, Hall S, Xavier R, Polido-Pereira J, Song IH, Martin N, Song Y, Anyanwu S, Nash P “Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity among Upadacitinib-treated Patients with Rheumatoid Arthritis”, Societa Italiana di Reumatologia - LVIII Congresso Nazionale (SIR 2021), Rimini, Italy. November 24th-27th, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Silvério-António M, Khmelinskii N, Fonseca JE. “Efficacy of intravenous immunoglobulin in shrinking lung syndrome associated with mixed connective tissue disease”. XXIII Congresso Português de Reumatologia, Algarve, Portugal, October 13-16th, 2021. POSTER. NATIONAL.

Matilde Bandeira, Ana Rita Cruz-Machado, Sofia C. Barreira, et al. Risk Factors for SARS-CoV-2 infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide Study. XXIII Congresso

Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER (with oral presentation); NATIONAL CONFERENCE.

Ana Rita Cruz-Machado, Sofia C. Barreira, Marc Veldhoen, et al. Antibody response after SARS-CoV-2 Infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 16th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Sofia C. Barreira, Ana Rita Cruz-Machado, Matilde Bandeira, et al. Clinical Course and Risk Factors for Severe/Critical COVID-19 in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 16th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Sofia C. Barreira, Ana Rita Cruz-Machado, Matilde Bandeira, et al. Clinical Course and Risk Factors for Severe/Critical COVID-19 in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. ACR 2021, November, 2021. POSTER (with oral presentation); INTERNATIONAL CONFERENCE.

Ana Rita Cruz-Machado, Sofia C. Barreira, Marc Veldhoen, et al. Antibody response after SARS-CoV-2 Infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. ACR 2021, November, 2021. POSTER (with oral presentation); INTERNATIONAL CONFERENCE.

Carina Oliveira Dias, Mileta Gomes, Matilde Bandeira, Eduardo Dourado. Projeto GAP - um projeto iniciado em tempos pandémicos. Jornadas Internacionais do IPR 2021, Lisboa, Portugal, November 25th, 2021. POSTER; INTERNATIONAL CONFERENCE.

Ávila-Ribeiro P, Saraiva F, Martins P, Fonseca JE, Vieira-Sousa E. Effectiveness of a biologic tapering protocol for rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis. XXIII Congresso Português de Reumatologia, Albufeira, October 13-16th, 2021- POSTER. NATIONAL.

Martins P, Dourado E, Fonseca JE, Romão VC, Resende C. Safety and Persistence of Monthly Intravenous Iloprost in Systemic Sclerosis. ACR Convergence, Online, November, 3-10th 2021. POSTER. INTERNATIONAL.

Ávila-Ribeiro P., Saraiva, F., Martins, P., Fonseca, J.E., Vieira-Sousa, E., on behalf of the TaPSpA team. Effectiveness of a biologic tapering protocol for axial spondyloarthritis and psoriatic arthritis (TaPSpA). 12th International Congress on Spondylarthritides, Ghent, Belgium, September 9-11th 2021. POSTER; INTERNATIONAL CONFERENCE.

Rita Cunha, Elsa Vieira-Sousa, Nikita Khmelinskii, Pedro Ávila Ribeiro, Couto M, Maria Inês Seixas, Nádia Martins, Miguel Bernardes, Ana Martins, Ana Bento da Silva, Maria Helena Lourenço, Cláudia Miguel, Paula Valente, José Tavares-Costa, João Rovisco, Renata Aguiar, Anabela Barcelos. Are there gender differences in axial spondyloarthritis: data from a Portuguese spondyloarthritis cohort. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, from October 13-16, 2021. POSTER; NATIONAL CONFERENCE.

Ana Teresa Melo, Catarina Tenazinha, Filipa Oliveira Ramos, Patrícia Costa Reis, João Eurico Fonseca, Raquel Campanilho Marques. Bone fragility risk factors in a pediatric rheumatology department - data from a single-center. September 19- 21th, 2021 XXIII Congresso Português de Reumatologia. Salgados. Outubro de 2021 – POSTER. NATIONAL.

Miguel Bernardo, Ana Teresa Melo, Filipe Pinheiro, Mariana Rodrigues, Rita Torres, Ana Filipa Mourão, Sónia Carvalho, João Nascimento, M^a José Santos, Catarina Soares, Marta Cabral, Raquel Campanilho-Marques, Patrícia Costa-Reis, Filipa Oliveira Ramos. Infecao SARS-COV-2 numa série de doentes pediátricos com doença reumática. Congresso Português de Pediatria. Braga – October 27- 29th, 2021 – ORAL. NATIONAL.

Miguel Bernardo, Ana Teresa Melo, Filipe Pinheiro, Mariana Rodrigues, Rita Torres, Ana Filipa Mourão, Sónia Carvalho, João Nascimento, M^a José Santos, Catarina Soares, Marta Cabral, Raquel Campanilho-Marques, Patrícia Costa-Reis, Filipa Oliveira Ramos. Infecao SARS-CoV-2 numa série de doentes pediátricos com doença reumática. XXIX Jornadas Internacionais do Instituto Português de Reumatologia a realizar em Lisboa – November 25- 26th, 2021 – ORAL. NATIONAL.

Martins P, Dourado E, Melo AT, Samões B, Sousa M, Freitas R, Lourenço M, Fernandes BM, Costa E, Parente H, Martins F, Fonseca JE, Romão V, Khmelinskii N, Campanilho-Marques R, Cordeiro I. Clinical characterization of Portuguese patients with antisynthetase syndrome. XXIII Congresso Português de Reumatologia. Salgados. October, 2021 – POSTER. NATIONAL.

AS Pinto, FC Santos, AT Melo, E Dourado, T Carneiro, R Campanilho-Marques, JF Ferreira, CC Vaz. Impact of rheumatic diseases: an eight-item questionnaire. XXIII Congresso Português de Reumatologia. Salgados. October, 2021 – POSTER. NATIONAL.

Catarina Tomé, Filipa Oliveira-Ramos, Raquel Campanilho-Marques, Ana F. Mourão, Sandra Sousa, Ana P. Martins, Patrícia C. Reis, Ana T. Melo, Rui L. Teixeira, Miroslava Gonçalves, Maria J. Santos, Luis Graca, João E. Fonseca, Rita A. Moura. Children with juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood. Virtual Young Investigators Meeting 2021 – POSTER. INTERNATIONAL.

Ana Rita Cruz-Machado, Sofia C Barreira, Marc Veldhoen, Matilde Bandeira, Catarina Duarte, Maria Rato, Bruno Miguel Fernandes, Salomé Garcia, Filipe Pinheiro, Miguel Bernardes, Nathalie Madeira, Cláudia Miguel, Rita Torres, Ana Bento Silva, Carolina Mazedo, Filipe Cunha Santos, Marlene Sousa, Hugo Parente, Maria José Santos, João Eurico Fonseca, Vasco C Romão. On behalf of the COVID-Reuma.pt study group. Antibody response after SARS-COV-2 infection in patients with rheumatic diseases: a multicenter, nationwide study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October, 2021. ORAL. NATIONAL.

Catarina Tomé, Luis Graca, João E. Fonseca, Rita A. Moura. The interplay of B and T follicular cell subsets in Juvenile Idiopathic Arthritis. 12 Topics in Rheumatology, 3rd Edition, CEDOC - Chronic Diseases Research Center, NOVA Medical School, September 30th- October 2nd, 2021. ORAL. NATIONAL.

Felice Rivellese, Elena Pontarini, Liliane Fossati-Jimack, Rita A. Moura, Vasco C. Romão, João Eurico Fonseca, Alessandra Nerviani, Cankut Cubuk, Katriona Goldmann, Michele Bombardieri, Myles Lewis, Costantino Pitzalis. Integration of flow and digital cytometry in early treatment-naïve rheumatoid arthritis identifies distinct immunophenotypes in peripheral blood and disease tissue. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Virtual Congress, June 2-5th, 2021 ORAL. INTERNATIONAL.

Teixeira RL. Towards a holistic approach to early arthritis patients: Does mental health relate with disease activity? Congresso Português de Reumatologia 2021. Albufeira, October 2021. POSTER. NATIONAL.

Matilde Bandeira, Ana Rita Cruz-Machado, Sofia C. Barreira, et al. Risk Factors for SARS-CoV-2 infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide Study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 13th, 2021. POSTER (with oral presentation); NATIONAL CONFERENCE.

Ana Rita Cruz-Machado, Sofia C. Barreira, Marc Veldhoen, et al. Antibody response after SARS-CoV-2 Infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 16th, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ana Rita Cruz-Machado, Sofia C. Barreira, Marc Veldhoen, et al. Antibody response after SARS-CoV-2 Infection in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. ACR 2021, November, 2021. POSTER (with oral presentation); INTERNATIONAL CONFERENCE.

Organization of Conferences

Raquel Campanilho-Marques. Co-organizadora do Young Investigator Meeting da Paediatric Rheumatology European Society (PReS). Virtual, September 18th, 2021.

Raquel Campanilho-Marques. Co-organizadora da Juvenile Dermatomyositis Working Party do PReS – Virtual, September 21st, 2021.

Ponte C. moderadora de discussão nas cinco *Vasculitis Hub Sessions*. ACR Convergence 2021, e-meeting, November 5-9th, 2021;

Ponte C. Comissão científica, escolha de temas e responsável pela revisão de *abstracts* submetidos. 20th International Vasculitis and ANCA Workshop, Dublin – Irlanda, April 3-6th, 2022;

Ponte C. responsável pela elaboração do programa, selecção e distribuição de convites a palestrantes, realização de questões relacionadas com os temas e moderação de cinco sessões. ACR Convergence 2021 - Vasculitis Hub Sessions, e-meeting, November 5-9th, 2021;

João Eurico Fonseca - Organizador do 3^o Curso de Internos de Reumatologia, Lisboa, Portugal. March 4th, 2021.

Networks & Research Infrastructures

Ana Margarida Monteiro. Reuma.pt. Active member.

Ana Margarida Monteiro. European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET). Active member.

Ana Teresa Melo. Reuma.pt. Active member.

Ana Teresa Melo. European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET). Active member.

Ana Teresa Melo. Grupo de trabalho de estudos de Reumatologia Pediátrica. Active member.

Ana Teresa Melo. Emerging EULAR NETWORK (EMEUNET). Active member.

Eduardo Dourado. Reuma.pt. Active member.

Eduardo Dourado. European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET). Active member.

Eduardo Dourado. Grupo de trabalho de estudos de doenças reumáticas sistémicas da Sociedade Portuguesa de Reumatologia (GEDRESIS). Active member.

Eduardo Dourado. International Myositis Society (iMyoS). Member.

Eduardo Dourado. Grupo de trabalho de estudos da dor da Sociedade Portuguesa de Reumatologia (GTDor). Member.

Inês Leal, Ibertinu Clínicas, Gestão e Prognóstico do Síndrome TINU (Nefrite tubulo-intersticial e uveíte) em Espanha e Portugal – Estudo IBERTINU, responsável pelo pólo de colaboração do CHULN. No funding

Inês Leal- GO-VISION - PI Prospective observational study to examine the change of vision-related quality of life in subjects with spondyloarthritis during treatment with monthly subcutaneous injections of golimumab 50 mg according to EU label. MSD

Matilde Bandeira. Reuma.pt. Active member.

Matilde Bandeira. European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET). Active member.

Matilde Bandeira. Grupo de trabalho de estudos de doenças reumáticas sistémicas da Sociedade Portuguesa de Reumatologia (GEDRESIS). Active member.

Matilde Bandeira. Grupo de trabalho de Estudo das Espondilartrites (GESPA). Active member.

Ângelo Calado and João Eurico Fonseca. GEMSTONE (Genomics of musculoskeletal traits translational network) COST Action. GEMSTONE members.

Sofia C. Barreira. Reuma.pt. Active member.

Sofia C. Barreira. European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET). Active member.

Sofia C. Barreira. European Reference Network on Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases (RITA). Active member.

Sofia C. Barreira. Grupo de Estudos das Espondilartrites (GESPA). Active member.

Sofia C. Barreira. Grupo de trabalho de estudos de doenças reumáticas sistémicas da Sociedade Portuguesa de Reumatologia (GEDRESIS). Active member.

Raquel Campanilho-Marques. ReConnect – European Reference Network. Clinical management team.

Raquel Campanilho-Marques. RITA - European Reference Network. Clinical management team.

Raquel Campanilho-Marques. Juvenile Dermatomyositis Working Party of the Pediatric Rheumatology European Society (PReS). Education/Training pillar responsible.

Raquel Campanilho-Marques. PReS EMERging RheumatoloGists and rEsearchers (PReS EMERGE). Responsible for Education and Training.

PONTE C. Membro da European Vasculitis Study Group (EUVAS) desde 2015

PONTE C. Membro do OMERACT Ultrasound Large-Vessel Vasculitis Subtask Force desde 2015

PONTE C. Membro da EMEUNET - EMERging EUlar NETwork group desde 2014

PONTE C. Membro da Grupo de trabalho de imagem músculo-esquelética – GoTIME (pertencente à Sociedade Portuguesa de Reumatologia) desde 2014

PONTE C. Membro da Grupo de estudos das Doenças Reumáticas Sistémicas – GEDRESIS (pertencente à Sociedade Portuguesa de Reumatologia) desde 2013

Prizes & Honors in 2021

João Eurico Fonseca – Associated Editor of Acta Reumatológica Portuguesa.

João Eurico Fonseca - Associated Editor of Arthritis Research and Therapy.

João Eurico Fonseca - Associated Editor of RMD.

João Eurico Fonseca – Chief Section Editor (Rheumatology) *Frontiers in Medicine*

João Eurico Fonseca – Reviewer for award applications at Rheumatology Greek Society.

Sofia C. Barreira, Ana Rita Cruz-Machado, Matilde Bandeira, et al. Clinical Course and Risk Factors for Severe/Critical COVID-19 in Patients with Rheumatic Diseases – a Multicenter, Nationwide study. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 16th, 2021. Prémio melhor comunicação oral.

Teixeira RL, Martins P, et al. 2nd Award Sociedade Portuguesa de Reumatologia Jakie. Dr. Robert Martins. Project: Comparative effectiveness of tofacitinib and interleukin (IL)23/IL17 inhibitors in PsA patients registered in the Rheumatic Diseases Portuguese Register.

Catarina Tomé, Luis Graca, João E. Fonseca, Rita A. Moura. The interplay of B and T follicular cell subsets in Juvenile Idiopathic Arthritis. *12 Topics in Rheumatology*, 3rd Edition, CEDOC - Chronic Diseases Research Center, NOVA Medical School, September 30th- October 2nd, 2021. Best Clinical Basic Research Award.

João Eurico Fonseca - Reumeritus 2021- Career prize Sociedade Portuguesa de Reumatologia.

João Eurico Fonseca - Prémio de Mérito Pedagógico João Gomes Pedro 2021, Faculdade de Medicina, Universidade de Lisboa.

Silvério-António M - Projeto “Is ultrasound a good surrogate marker for remission in Rheumatoid Arthritis? - validation of Contrast-enhanced Doppler ultrasound as a useful tool to detect minimal inflammation in RA patients in remission - 2.^ª Bolsa Instituto de Medicina Molecular - João Lobo Antunes/Faculdade de Medicina de Lisboa (2020).

Ines Leal, Patricia Jose, Rafael Barão, Sofia Mano, Ana Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Dinis, Filipe Cunha Santos, Henrique Fernandes, Nikita Khmelinskii, Carlos Marques-Neves, Elsa Vieira de Sousa, João Eurico Fonseca. “Vision-related quality of life in spondyloarthritis patients with history of acute anterior uveitis under treatment with golimumab: preliminary results of the GO-VISION observational study”. European Association for Vision and Eye Research (EVER) 2021 Virtual Congress, Online, October 2nd, 2021. Best contribution on the field of Immunology.

Francisca Guimarães, Manuel António, Joana Martinho, Ana Teresa Melo, Daniela Oliveira, Jorge Lopes, André Saraiva, Ana Gago, Margarida Correia, Ana Lúcia Fernandes, Sara Dinis, Rafaela Teixeira, Susana Silva, Carlos Costa, Tiago Beirão, Carolina Furtado, Pedro Abreu, Carmo Afonso, Daniela Peixoto. “Clinical and immunological features of a Portuguese cohort of Mixed Connective Tissue Disease”. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 14th, 2021. Melhor poster original – menção honrosa.

Best Oral Presentation of Basic Science at *12 Topics in Rheumatology*, 3rd Edition. CEDOC – Chronic Diseases Research Centre, NOVA Medical School, Lisbon, Portugal. October 1-2nd, 2021.

Matilde Bandeira, Eduardo Dourado, Carina Oliveira Dias, Mileta Gomes, Joana Silva-Dinis, João Eurico Fonseca. Projeto GAP - um plano integrado de apoio aos doentes com gota. XLI Curso de Reumatologia: Ciência na Prática Clínica 2021, Coimbra, Portugal, February 25th, 2021. Prémio “Pérolas da Reumatologia” (5 melhores posters).

Eduardo Dourado, Inês Cordeiro. Neither arms NOR legs were feeling well: myositis in a NOR-90+ systemic lupus erythematosus patient. 10th Lupus Academy Annual Meeting. Online, April 17th, 2021. 3rd best clinical case.

Sofia Charneca, Margarida Ferro, João Vasques, Eduardo Dourado, Catarina Sousa Guerreiro, João Eurico Fonseca. Adherence to the Mediterranean Diet is associated with patient-reported functional status in Rheumatoid Arthritis. 2021 European Society for Clinical Nutrition and Metabolism (ESPEN) Congress, Online, September 9th, 2021. Best abstract from a young researcher.

Matilde Bandeira, Eduardo Dourado, Carina Oliveira, João Eurico Fonseca. Projeto GAP - Gouty Arthritis Pathway. 13^o Curso de Reumatologia Prática em Cuidados de Saúde Primários, Lisboa, Portugal, September 23rd, 2021. Melhores projetos - 2^o lugar.

Eduardo Dourado, Ana Silva Martins, Inês Cordeiro, João Eurico Fonseca. Hoarseness as the presentation of IgG4-related disease with vocal cord and mediastinal infiltration. XXIII Congresso Português de Reumatologia, Albufeira, Portugal, October 14th, 2021. Melhor caso clínico.

Elsa Vieira-Sousa “New perspectives on tumor necrosis factor inhibition for the treatment of Psoriatic Arthritis”. Prémio João Lobo Antunes Merit PhD Thesis Award 2021

Ines Leal, Patricia José, Rafael Barão, Sofia Mano, Ana Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Dinis, Filipe Cunha Santos, Henrique Fernandes, Nikita Khmelinski, Carlos Marques-Neves, Elsa Vieira de Sousa, João Eurico Fonseca. Vision-related quality of life in spondyloarthritis patients with history of acute anterior uveitis under treatment with golimumab: preliminary results of the GO-VISION observational study Rheumatology. RAPID FIRE AWARD, European Vision & Eye Research (Ever) Virtual Congress, October 2, 2021

Elsa Sousa - Revisora de Abstracts. European League against Rheumatism Annual Congress Virtual Congress (online), 2-5 Junho 2021. Faculty. Tópico. Psoriatic arthritis - clinical aspects (other than treatment).

Elsa Sousa - Revisora de abstracts. XXIII Congresso Português de Reumatologia. Outubro 2021.

Elsa Sousa - Revisora abstracts de investigação básica. 3rd Edition 12 Topics in Rheumatology, 31 Setembro – 2 Outubro 2021, Lisboa, Nova Medical School.

Elsa Sousa - Revisora de Candidaturas Prémios Pfizer 2021, Sociedade de Ciências Médicas de Lisboa, Outubro 2021

Elsa Sousa - Membro do Comité Executivo da Fundação para a Investigação em Reumatologia (FOREUM) (desde Junho 2021)

Elsa Sousa - Presidente Júri Bolsa Sociedade Portuguesa de Reumatologia/Pfizer Dr. Robert Martins. 24 Novembro de 2021.

Elsa Sousa - Juri Tese Mestrado - Catarina Ferreira Duarte Clinical Course and Predictors of Severe Coronavirus Disease 19 Among Patients with Rheumatic Diseases

Elsa Sousa - Juri Tese Mestrado - Ana Rita da Silva Vieira Artrite inicial - caracterização da evolução clínica e de patient reported outcomes. 2021

Ponte C, Martins-Martinho J, Branco C, Khmelinskii N, Godinho I, Pereira M, Macieira C, Resina C, Jorge S, Lopes J, Fonseca JE, Nogueira EL. Clinical characteristics and predictors of poor outcomes in Portuguese patients with ANCA associated vasculitis. Bolsa Sociedade Portuguesa de Reumatologia / Roche 2021 – 5000€

Cunha RN, Monteiro M, Tenazinha C, Khmelinskii N, Ponte C. Prospective clinical and ultrasonographic assessment of the temporal artery in a patient with giant cell arteritis. Prémio melhor imagem em Reumatologia - 1º Lugar - XXIII Congresso Português de Reumatologia October 14th, 2021 –500 €

Inês Leal, Patrícia José, Rafael Barão, Sofia Mano, Teresa Melo, Eduardo Dourado, Catarina Tenazinha, Cláudia Vaz, Joana Fonseca Ferreira, Sara Dinis, Filipe Cunha Santos, Telma Carneiro, Henrique Fernandes, Nikita Khmelinski, Carlos Marques-Neves, Elsa Vieira de Sousa, João Eurico Fonseca. Prospective observational study to examine the change of vision-related quality of life in subjects with spondyloarthritis under treatment with golimumab 50 mg monthly according to EU label: 6 months results of the GO-VISION Study. EVER Conference 2021. Best Poster Immunology/Microbiology section

Pedro Ávila Ribeiro - Invited referee for Acta Reumatológica Portuguesa.

Filipa Ramos - Moderator in the Young Investigators Meeting (YIM) of PReS, virtual, September 18th, 2021.

Advanced Teaching

Calado, A. “Metabolismo Glicídico”. Master in Metabolic Diseases and Feeding Behavior (2021-22). Faculdade de Medicina, Universidade de Lisboa. December 2021.

Calado, A. “Respostas metabólicas à hiperglicemia e à hipoglicémia”. Master in Metabolic Diseases and Feeding Behavior (2020-21). Faculdade de Medicina, Universidade de Lisboa. January 2021.

Calado, A. “Metabolismo Glicídico”. Master in Metabolic Diseases and Feeding Behavior (2020-21). Faculdade de Medicina, Universidade de Lisboa. January 2021.

Polido-Pereira J. Lecture. “Exames auxiliares essenciais”, Curso de Internos (Sociedade Portuguesa de Reumatologia). Online, Portugal. February 28th 2021

Silvério-António M - Professor of Academia da Especialidade (2018 – presente). Lectures of Rheumatology to prepare to Portuguese Medical Licensing Examination. Lisbon, Portugal, 2021.

Silvério-António M - Coordinator and Lecturer of the Project “Reumatologia nos Cuidados de Saúde Primários – a formação como estratégia para a melhoria dos cuidados aos doentes reumáticos”. Lectures of rheumatology to family’s physicians. Lisbon (online), Portugal, 2021.

Sofia Barreira. Lecture. Doenças difusas do tecido conjuntivo. Academia da Especialidade – Módulo Medicina – Reumatologia. Covilhã, Portugal, December 2021

Sofia Barreira. Lecture. Casos Clínicos. Academia da Especialidade – Módulo Medicina – Reumatologia. Covilhã, Portugal, December 2021

Susana Capela - Course organization and lecturing. I Curso Monotemático de Dor do Serviço de Reumatologia/IMM, Online, Portugal, October- November, 2021.

Ponte C. Simpósio de Inflamação Ocular - Congresso da Sociedade Portuguesa de Oftalmologia - December 9-11 de 2021; Vilamoura - Portugal / e-meeting.

Ponte C. Fairvasc plenary session – December 7th, 2021; e-meeting.

Ponte C. ACR Convergence 2021 - November 5-9th 2021; e-meeting.

Ponte C. Vasculitis Investigators Meeting 2021 - October 30, 2021; e-meeting

Ponte C. OMERACT Halo Score GCA Training sessions - Reliability exercise – October 6 and 12, 2021; e-meeting

Ponte C. EUVAS Scientific Council Meeting Meeting – October 1st, 2021; Lund e virtual.

Ponte C. The 38th Scandinavian Congress of Rheumatology 2021 - 1 a 4 de Setembro de 2021; Alesund-Noruega.

Ponte C. EULAR 2021 Virtual Congress – June 2 – 5th, 2021; e-meeting.

Ponte C. CAML Rheumatology Series - Carl Orr – What can synovial tissue research teach us about preventing arthritis? – June 1st, 2021; e-meeting.

Ponte C. Early-sate Vasculitis Group – March 30th, 2021; e-meeting.

Ponte C. Art&Treat – March 17-19th, 2021; e-meeting.

Ponte C. Simpósio de Inflamação Ocular - Congresso da Sociedade Portuguesa de Oftalmologia - December 9-11 de 2021; Vilamoura - Portugal / e-meeting.

Ponte C. Fairvasc plenary session – December 7th, 2021; e-meeting.

Ponte C. ACR Convergence 2021 - November 5-9th 2021; e-meeting.

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Ponte C. OMERACT Halo Score GCA Training sessions - Reliability exercise – October 6 and 12, 2021; e-meeting

Ponte C. EUVAS Scientific Council Meeting Meeting – October 1st, 2021; Lund e virtual.

Ponte C. The 38th Scandinavian Congress of Rheumatology 2021 - 1 a 4 de Setembro de 2021; Alesund-Noruega.

Ponte C. EULAR 2021 Virtual Congress – June 2 – 5th, 2021; e-meeting.

Ponte C. 23º Congresso Nacional da Ordem dos Médicos: A Ciência em Tempo de Pandemia – May 31st to June 3rd, 2021; e-meeting.

Ponte C. Early-sate Vasculitis Group – March 30th, 2021; e-meeting.

Ponte C. Art&Treat – March 17-19th, 2021; e-meeting.

Ponte C. European Large Vessel Vasculitis Imaging Course 2021 – October 14th, 2021; e-meeting.

João Eurico Fonseca - Grandes síndromes em Reumatologia. Terceiro Curso de Internos de Reumatologia. March 4th 2021

João Eurico Fonseca - A evolução das recomendações terapêuticas da artrite reumatoide nos últimos 20 anos. I Encontro de Internos de Reumatologia. September 25th 2021

João Eurico Fonseca - Reuma.pt: 13 anos de evolução. Curso Reuma.pt, XXIII Congresso Português de Reumatologia, Herdade dos salgados Albufeira, Portugal, October 13rd, 2021

Rita Moura - Invited for a teaching class entitled “B cells, autoantibodies and cytokines in Rheumatoid Arthritis”, Curso livre: Mecanismos fisiopatológicos das doenças reumáticas da autoinflamação à autoimunidade, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, in May 20th and September 23rd 2021

Rita Moura - Graduation examiner of student Hugo Mateus for a licentiate degree in Biochemistry, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal in January 2021

Rita Moura - Supervision of undergraduate students José Guilherme Nobre, Maria Beatriz Santos e João Pedro Marques during a research internship GAPIC (Gabinete de Apoio à Investigação Científica, Tecnológica e Inovação) - Programa “Educação pela Ciência”, Faculdade de Medicina da Universidade de Lisboa, developed at Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal from January 2019 – December 2021

Rita Moura - Supervision of undergraduate student João Carço Fernandes Pedro during a research internship GAPIC (Gabinete de Apoio à Investigação Científica, Tecnológica e Inovação) - Programa “Educação pela Ciência”, Faculdade de Medicina da Universidade de Lisboa, developed at Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal from January 2019 – December 2021

MSc Theses

Ana Rita Vieira da Silva, 06/2021. Clinical evolution and Patient-reported outcomes in a cohort of early arthritis. Supervisor: João Eurico da Fonseca. Co-Supervisor: Rui Teixeira.

Maria João Antero da Silva, 14/05/2021. A Oxigenioterapia Hiperbárica no Controlo Sintomático da Fibromialgia. Virtual meeting. Supervisor: Raquel Campanilho-Marques. Co-Supervisor: João Eurico da Fonseca.

PhD Theses

Cristina Dias Botelho da Ponte, "The role of ultrasound as a predictor of disease activity and response to therapy in Giant Cell Arteritis". Supervisor: João Eurico da Fonseca. Co-Supervisor: Helena Cristina Matos de Canhão.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Inês Leal - GO-VISION STUDY, MSD, Sponsored Research.

Partnership iMM-Pfizer – Webcasts.

Joaquim Polido Pereira - Internal education on AbbVie – Lecture on Rheumatoid arthritis treatment with special focus on JAK inhibitors and IL6 inhibition.

Rui Teixeira - Investigator -Initiated Study. Abbvie. Collaborative Research. The role of JAK-1 signaling pathway in early arthritis.

Immune response to Hepatitis B and Influenza vaccines in rheumatic patients under biological therapies – Novartis.

Post-transcriptional regulation of response to Etanercept in patients with rheumatoid arthritis – Pfizer.

Ensaio clínico de mesoterapia – Bial.

MILES STUDY – Mesotherapy in Lateral Epicondylitis, a prospective randomized controlled Study - Fundação Grünenthal.

Prospective observational study to examine the change of vision-related quality of life in patients with spondyloarthritis during treatment with monthly subcutaneous injections of golimumab 50 mg according to EU label - Merck Sharp & Dohme.

Is ultrasound a good surrogate marker for remission in RA? (Association of ultrasound and histological synovitis in rheumatoid arthritis patients in clinical remission) – Pharmakern.

Autoinflammatory Diseases: analysis based on The Rheumatic Diseases Portuguese Register – Novartis.

Loss of follow up dos doentes sob biológicos – Novartis.

Linking Biomechanics, Inflammation and Bone Formation in Psoriatic Arthritis - UCB Pharma.

Golimumab as first line DMARD therapy in MTX naive psoriatic arthritis - a 24 weeks efficacy and safety study focussing on dactylitis and enthesitis - Merck Sharp & Dohme - Merck Sharp & Dohme.

LESS - Lisbon Enthesitis Sonographic Score – Novartis.

EARLY_JAKi: JAK-STAT signaling pathway as key to chronic arthritis onset – Abbvie.

Clinical course and predictors of severe coronavirus disease 19 among patients with rheumatic diseases in Portugal – a multicentre, observational, nationwide study - Merck Sharp & Dohme.

Policy

Joaquim Polido Pereira and João Eurico Fonseca - Member of Colégio de Especialidade de Reumatologia da Ordem dos Médicos.

Science and Society in 2021

Filipa Ramos - Member of the board of patients association ANDAI (Associação Nacional de Doentes com artrites e outros reumatismos infância).

Podcast presentation by Raquel Campanilho-Marques about “Myositis Specific Antibodies” requested by PReS, resulting from a collaboration between the JDM Working Party from PReS and Bath Institute for Rheumatic Diseases – BIRD available on <https://anchor.fm/birdbathcharity>.

Susana Capela - Vice-president of the Portuguese League against Rheumatic Diseases, participating in different educational forums with patients, including a Gout educational Program



that is now available online. Educatinal hangout about the Rheumatic Diseases Internacional Day, for HSM.

Cláudio Franco Lab

Head of Laboratory: Claudio Areias Franco, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Raquel Martins Figueiredo Fonseca	PhD	Postdoctoral Researcher
André Brás Gonçalves	PhD	Postdoctoral Researcher
Andreia Alexandra Santos de Areosa Pena	Master Degree	PhD Student
Catarina Gonçalves Fonseca	Master Degree	PhD Student
Cátia Alexandra da Silva Janota	PhD	Postdoctoral Researcher (Left October)
Daniela Maria Grou Ramalho	Master Degree	PhD Student (Started January)
Francisca Ferreira de Vasconcelos	PhD	Postdoctoral Researcher
Hemaxi Narotamo	Master Degree	PhD Student (Started February)
Ilaria Ferrarotto	University Degree	Trainee (Started March. Left September)
João Manuel Coelho Carreira	Master Degree	PhD Student
Lenka Henao Mišíková	Master Degree	Lab Technician
Maria Clara Barreto Carromeu Gomes	Master Degree	Lab Technician
Marie Ouarné	PhD	Postdoctoral Researcher
Marta Filipa Alves Fidalgo	Master Degree	Lab Technician (Left August)
Pedro Jorge Sequeira Costa de Jesus Campinho	PhD	Senior Postdoctoral Researcher
Pedro Miguel Branco Barbacena	PhD	Postdoctoral Researcher (Left January)
Samuel Filipe Moreira Carvalho	High School Diploma	Trainee (Started February)
Tiago Magalhães Nascimento Plácido Costa	University Degree	MSc Student (Started December)

Graphical Abstract

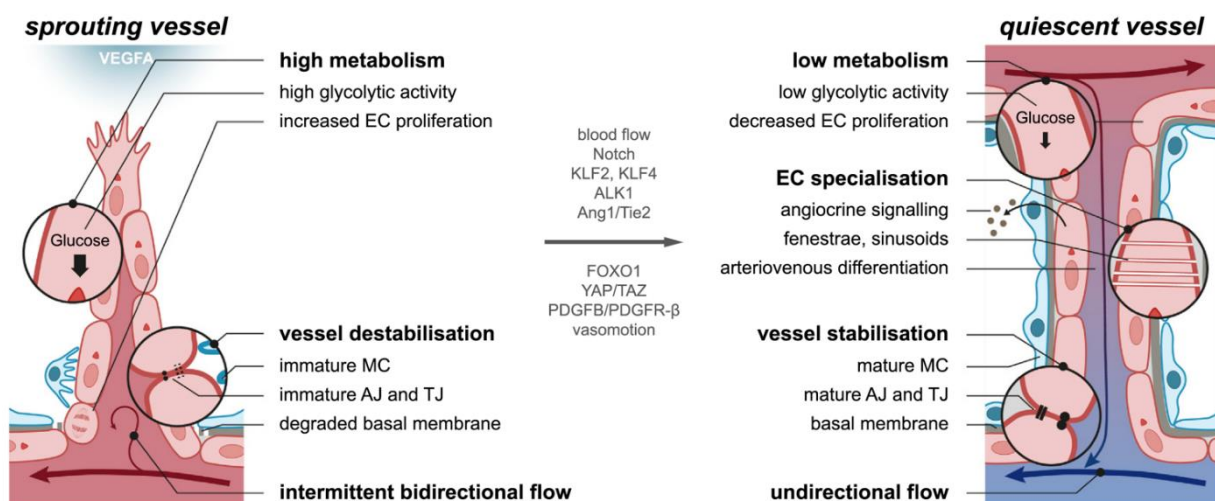


Image caption: Schematic representation of the main different topics the laboratory investigates: the changes in the biological activity of endothelial cells during the transition between sprouting angiogenesis and vascular remodeling.

Lab Interests

Appropriate blood supply in multicellular organisms is essential for development, growth and regeneration. Several diseases arise from dysfunction of blood vessels, e.g. diabetic retinopathy, stroke, or tumor angiogenesis. The formation of a functional vascular network requires two distinct processes – sprouting angiogenesis (which expands the network) and vascular remodeling (which generates a hierarchical network) – both driven by endothelial rearrangements.

Our Lab has the aim to understand the molecular mechanisms regulating coordinated endothelial cell behavior. We want to uncover:

- Novel regulators of endothelial cell migration;
- Molecular regulation of endothelial cell polarity;
- Effects of haemodynamic forces in vascular patterning;
- Novel anti-angiogenic therapies

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

We described how endothelial cells (ECs), the cells lining the interior of blood vessels, invade into tissues to form new vessels through sprouting angiogenesis. We found that ECs use a unique membrane protrusion for invasion, which we termed dactylopodia. Our work lays the foundations for drug discovery targeting sprouting angiogenesis. Moreover, we established the cellular, mechanical and molecular principles that define the competitive nature between blood flow and VEGFA, the two main organizers of blood vessel formation.

In addition, we had fruitful collaborations. In collaboration with L. Figueiredo's group, we showed how blood vessels affect *T. brucei* tissue tropism and the relevance of EC surface adhesion molecules for sleep disease severity. Alongside, in collaboration with A. Eichman's group, we proved that our original concept of flow-migration coupling is a key mechanism involved in the aetiology of arteriovenous malformations, a severe vascular anomaly.

Ongoing Projects in 2021

2021/2024: Mecanismos de arteriogénese dependentes da migração endotelial - Migration-based mechanisms of arteriogenesis. Coordinator: Cláudio Franco. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ANM/7695/2020. Amount: 249 950,00€. Total Amount: 249 950,00€.

2019/2021: ADAPT2FLOW: Adaptive and maladaptive endothelial European Commission dynamics. Coordinator: Marie Ourné. Funding Agency: European Commission. Reference: MSCA-IF 842498. Amount: 147 815,04€. Total Amount: 147 815,04€.

2018/2022: ATTRACT: Arterial flow as attractor for endothelial European Commission migration. Coordinator: Cláudio Franco. Funding Agency: Fondation Leducq. Reference: ATTRACT. Amount: 25 424,99€. Total Amount: 5 000 000,00€.

2018/2021: Invasiveness: Identify the mechanisms of endothelial tip European Commission invasive behavior in order to inhibit physiological and pathological sprouting angiogenesis. Coordinator: Cláudio Franco. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-European Commission/32180/2017. Amount: 238 685,33€. Total Amount: 238 685,33€.

2018/2021: Flow(in)DR: Deregulated Endothelial Blood Flow Response as a cause of Diabetic Retinopathy. Coordinator: Francisca Vasconcelos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-PAT/31639/2017. Amount: 235 365,31€. Total Amount: 235 365,31€.

2016/2021: AXIAL.EC: Principles of Axial Polarity-Driven Vascular Patterning. Coordinator: Cláudio Franco. Funding Agency: European Commission. Reference: ERC StG 679368. Amount: 1 618 750,00€. Total Amount: 1 618 750,00€.

Scientific Impact

Selected Publications

Jakobsson L, Franco CA, Bentley K, Collins RT, Ponsioen B, Aspalter IM, Rosewell I, Busse M, Thurston G, Medvinsky A, Schulte-Merker S, Gerhardt H (2010). [Endothelial cells dynamically compete for the tip cell position during angiogenic sprouting](#). *Nat Cell Biol.* Oct;12(10):943-53.

Relevance of the publication: Demonstrates that endothelial cells compete for the position of leaders of new vascular sprouts (tip cells) via Notch signaling. This publication also established the models for genetic competition *in vivo*, now currently used in the community.

Bentley K, Franco CA, Philippides A, Blanco R, Dierkes M, Gebala V, Stanchi F, Jones M, Aspalter IM, Cagna G, Weström S, Claesson-Welsh L, Vestweber D, Gerhardt H (2014). [The role of differential VE-cadherin dynamics in cell rearrangement during angiogenesis](#). *Nat Cell Biol.* Apr;16(4):309-21.

Relevance of the publication: Demonstrates that endothelial cell rearrangements within vascular sprouts depends on dynamic regulation of adherens junctions (VE-cadherin). This publication also established the integration of the cellular Potts model and the memAgent-spring model into a hybrid computational model to study vascular biology.

Franco CA, Jones ML, Bernabeu MO, Geudens I, Mathivet T, Rosa A, Lopes FM, Lima AP, Ragab A, Collins RT, Phng LK, Coveney PV, Gerhardt H. (2015). [Dynamic endothelial cell rearrangements drive developmental vessel regression](#). *PLoS Biol.* Apr 17;13(4): e1002125.

Relevance of the publication: Demonstrates that vessel regression in physiological conditions is mediated by cell migration and not cell death, changing the paradigm in the field. It also establishes that endothelial cells migrate against the flow direction, a feature now recognized as essential for artery formation and the development of vascular malformations.

Carvalho JR, Fortunato IC, Fonseca CG, Pezzarossa A, Barbacena P, Dominguez-Cejudo MA, Vasconcelos FF, Santos NC, Carvalho FA, Franco CA (2019). [Non-canonical Wnt signaling regulates junctional mechanocoupling during angiogenic collective cell migration](#). *eLife*. Jun 27;8: e45853.

Relevance of the publication: Identifies for the first time that non-canonical Wnt signaling regulates collective cell migration by regulating the strength of adhesion of adherens junctions. Moreover, it establishes the fundamentals of collective cell migration of endothelial cells in vessel sprouting.

2021 Publications in Peer-Reviewed Journals

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Henao Misikova L, Franco CA, Figueiredo LM (2021). [Organotypic endothelial adhesion molecules are key for *Trypanosoma brucei* tropism and virulence](#). *Cell Rep*. Sep 21;36(12):109741.

Edgar LT, Franco CA, Gerhardt H, Bernabeu MO (2021). [On the preservation of vessel bifurcations during flow-mediated angiogenic remodelling](#). *PLoS Comput Biol*. Feb 4;17(2):e1007715.

Figueiredo AM, Barbacena P, Russo A, Vaccaro S, Ramalho D, Pena A, Lima AP, Ferreira RR, Fidalgo MA, El-Marjou F, Carvalho Y, Vasconcelos FF, Lennon-Duménil AM, Vignjevic DM, Franco CA (2021). [Endothelial cell invasion is controlled by dactylopodia](#). *Proc Natl Acad Sci U S A*. May 4;118(18): e2023829118.

Narotamo H, Ouarne M, Franco CA, Silveira M (2021). [Joint Segmentation and Pairing of Nuclei and Golgi in 3D Microscopy Images](#). *Annu Int Conf IEEE Eng Med Biol Soc*. Nov; 2021:3017-3020.

Ouarné M, Pena A, Franco CA (2021). [From remodeling to quiescence: The transformation of the vascular network](#). *Cells Dev*. Aug 21:203735.

Park H, Furtado J, Poulet M, Chung M, Yun S, Lee S, Sessa WC, Franco CA, Schwartz MA, Eichmann A (2021). [Defective flow-migration coupling causes arteriovenous malformations in hereditary hemorrhagic telangiectasia](#). *Circulation*. Sep 7;144(10):805-822.

Pena A, Ouarné M, Franco CA (2021). [Methods to quantify endothelial cell front-rear polarity in vivo and in vitro](#). *Curr Opin Hematol*. May 1;28(3):208-213.

Savulescu AF, Brackin R, Bouilhol E, Dartigues B, Warrell JH, Pimentel MR, Beaume N, Fortunato IC, Dallongeville S, Boule M, Soueidan H, Agou F, Schmoranzler J, Olivo-Marin J-C, Franco CA, Gomes ER, Nikolski M, Mhlanga MM (2021). [Interrogating RNA and protein spatial subcellular distribution in smFISH data with DypFISH](#). *Cell Reports Methods*, Sep 21;36(12):109741.

Pre-Print Publications

Barbacena P, Dominguez-Cejudo M, Fonseca CG, Zarkada G, Faure L, Pena A, Pezzarossa A, Giarratano Y, Ouarne M, Barata D, Fortunato I, Mauldin I, Ramalho D, Carvalho Y, Roca-Cusachs P, Eichmann A, Bernabeu MO, Franco CA (2021). As Competition for endothelial cell polarity drives vascular morphogenesis. DOI: 10.1101/2021.11.23.469704. November 23, 2021.

Invited Lectures and Seminars

Franco CA. New Insights on Vascular Biology. IMM internal seminar series – Instituto de Medicina Molecular, Lisboa, Portugal, April 28, 2021.

Franco CA. Reading and interpreting the endothelial compass. EVBO-ESM Summer School, Virtual event, July 13, 2021.

Franco CA. The different shapes of tip cells. NAVBO webinar, Virtual event, August 17, 2021.

Franco CA. Mechanisms regulating adaptation (and maladaptation) of vascular networks. INSERM U1034 «Biology of Cardiovascular Diseases», Bordeaux (virtual), France, October 12, 2021.

Franco CA. OIR-induced arteriovenous shunts. LeDucq annual meeting, Phoenix (virtual), USA, October 28, 2021.

Franco CA. Flow-migration coupling and cerebral vascular malformations, University of Lisbon, Lisbon, Portugal, November 9, 2021.

Pena A. Unveiling the effects of Myh9 in pericytes during sprouting angiogenesis. IMM Pizza seminar, Instituto de Medicina Molecular, Lisbon, Portugal, February 9, 2021.

Marie Ouarné. Competition for endothelial cell polarity drives vascular morphogenesis. 2021 Leducq ATTRACT network summer symposium, online, June 22nd, 2021.

Communications

Franco CA. Mechanisms regulating adaptation (and maladaptation) of vascular networks. EMBO Vascular Malformations Workshop - EMBO, Barcelona, Spain, October 7, 2021. Oral communication; International Meeting.

Narotamo H, Ouarné M, Franco CA, Silveira M. Joint Segmentation and Pairing of Nuclei and Golgi in 3D Microscopy Images. 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Guadalajara, Mexico, November 1-5, 2021. Oral communication; International Meeting.

Pena A. Unveiling the effects of Myh9 in pericytes during sprouting angiogenesis, XIV CAML - IV NeurULisboa PhD Students, Virtual Meeting, Instituto de Medicina Molecular, Lisbon, Portugal, May 5-7, 2021. Oral communication; National Meeting.

Daniela Ramalho, Pedro Barbacena, Rui Benedito and Cláudio Franco. Mechanisms of cell migration in Arteriogenesis. IMM PhD meeting, Lisbon, Portugal, May 6th, 2021.

Catarina Fonseca. Unveiling new regulators of flow-dependent endothelial cell polarization. INESC-MN Seminar Series. Lisbon, Portugal. November 25, 2021.

Prizes & Honors in 2021

- Elected as a Council Member to the European Vascular Biology Organization (EVBO).
- Elected Vice-president of the Portuguese Society for Developmental Biology (SPBD).
- Invited to participate in the pilot EMBO Journal Catalysts program.

Advanced Teaching

Franco CA. Vascular Morphogenesis: how to make vessels. PhD course Molecular Biology of the Cell - Institut Pasteur (virtual), Paris, France, February 2, 2021.

Franco CA. Advances techniques in biomedical research - II. Biomedical Master course – Faculty of Medicine of the University of Lisbon/Instituto de Medicina Molecular, Lisbon, Portugal, March 1-12, 2021.

Franco CA. Retinal vasculature: a polarising perspective! Advanced Course in Vision Sciences, Visual Systems and Associated Pathologies - University of Coimbra, Coimbra (virtual), Portugal, March 11, 2021.

Franco CA. Principles of Vascular Biology: how to make vessels. Mestrado integrado em Medicina - Faculty of Medicine of the University of Lisbon, Lisbon, Portugal, April 6, 2021.

Franco CA. Principles of Vascular Biology. Biomedical Master course – Faculty of Medicine of the University of Lisbon/Instituto de Medicina Molecular, Lisbon, Portugal, November 8-19, 2021.

Franco CA. Principles of Vascular Biology: how to make vessels. Mestrado integrado em Medicina - Faculty of Medicine of the University of Lisbon, Lisbon, Portugal, November 30, 2021.

Samuel Carvalho, 15/12/2021, O papel dos filopodia na migração de células endoteliais durante a angiogénese por brotação, Faculdade de Medicina da Universidade de Lisboa. Orientação: Cláudio Franco. Co-orientação: Ana Figueiredo.

MSc Theses

Ilaria Ferrarotto, 15/10/2021, Unravelling the biomechanics driving dorsal aorta extension in the zebrafish embryo. University of Torino / Instituto de Medicina Molecular João Lobo Antunes. Co-Supervisor: Pedro Campinho.

Edgar Gomes Lab

Head of Laboratory: Edgar R. Gomes, PhD, Group Leader and Associate Professor and Director of Instituto de Histologia e Biologia do Desenvolvimento, Faculdade de Medicina Universidade de Lisboa

Team

Afonso de Botelho Ferreira Braga Malheiro	PhD	Postdoctoral Researcher (Started June)
Ana Margarida da Rosa Soares	PhD	Postdoctoral Researcher
Ana Raquel Ramos Pereira	PhD	Postdoctoral Researcher
Bruno Filipe Gonçalves Freitas	Master Degree	Lab Technician (Left April)
Catarina Antunes Sequeira	Master Degree	PhD Student (Started January)
Cátia Alexandra da Silva Janota	PhD	Postdoctoral Researcher
David Miguel Baião Barata	PhD	Postdoctoral Researcher
Francisco Javier Calero Cuenca	PhD	Postdoctoral Researcher
Graciano da Silva Leal	PhD	Senior Postdoctoral Researcher (Left November)
Helena Alexandra Ribeiro de Carvalho Pinheiro	Master Degree	PhD Student
Hélia Cristina de Oliveira Neves	PhD	Senior Postdoctoral Researcher
Inês Isabel Baltazar Belo Martins	Master Degree	Lab Technician
Isabel da Conceição Alves Alcobia Príncipe Henriques	PhD	Senior Postdoctoral Researcher
Joana Marques Pinto Monteiro	University Degree	MSc Student (Started March)
João Pedro Nunes Paulo da Silva Martins	Master Degree	PhD Student
Katharina Hennig	PhD	Postdoctoral Researcher
Luís Manuel Farinha Bernardino de Oliveira	Master Degree	Lab Technician (Left February)
Maria Judite Sousa da Costa	PhD	Lab Manager
Sara Sofia Gasalho Ferreira	University Degree	Lab Technician
Thomas Matthew Huckaba	PhD	Visiting Researcher (Started January. Left July)
William Roman	PhD	Postdoctoral Researcher

Graphical Abstract

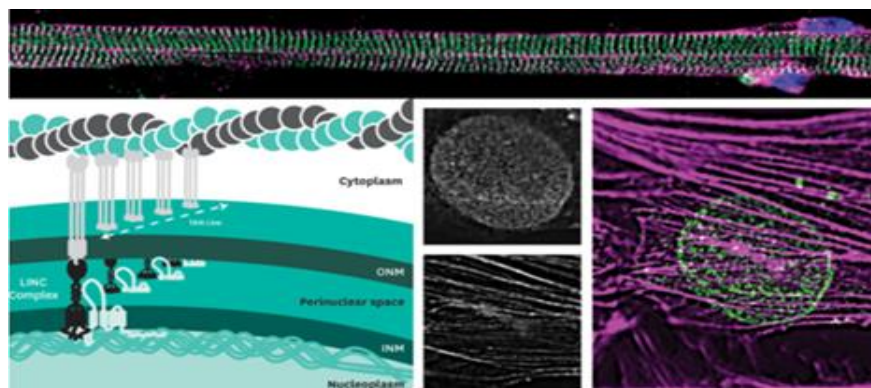


Image caption:

Top: differentiated muscle cell with peripheral nuclei

Bottom left: scheme of interaction between nuclear envelope proteins and cytoskeleton

Bottom right: fluorescent image of nuclei in green and actin in purple

Lab Interests

The cell nucleus is linked to the cytoskeleton and this connection is relevant for multiple cellular processes. Disruption of these connections result in several pathologies. Nuclear positioning within cell cytoplasm requires the connection between the nucleus and the cytoskeleton. We are interested in understanding the processes involved in these connections and the role for nuclear positioning in cell function. We study cell migration and skeletal myofiber formation, which involves the connection between the nucleus and the cytoskeleton and precise nuclear positioning. We also study the formation and maintenance of muscle triads, membrane structures that comprise the connection of a plasma membrane tubule with two sarcoplasmic reticulum cisternae, contiguous with the nuclear envelope. We use different molecular and cellular approaches in combination with time-lapse imaging analysis to address these questions.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Biotechnology and Biosystems Engineering

Major Scientific Achievements in 2021

We have successfully differentiated iPSCs into motor neurons and co-culture them with primary muscle myofibers. We generated microdevices for the organization of endothelial cells into large vessels and for muscle attachment. In addition, we differentiated iPSCs from ALS patients into motor neurons for future in silico disease modelling. (Myochip FET-OPEN project, in collaboration with CFranco Lab).

We found that mRNAs are differentially distributed within multinucleated muscle cells, depending on their size. We also found that transcription regulates mRNA localization (Pinheiro et al. 2021).

We found a complex between a nuclear envelope phosphatase (Ctdnep1) and an actin binding protein (Eps8L2) that is involved in nuclear movement (Calero-Cuenca et al. Current Biol 2021).

We found a mechanism of self-repair of muscle fibers involving nuclear movement and local translation at the site of injury (Roman et al. Science 2021).

Ongoing Projects in 2021

2021/2022: STARTHEALTH@ULISBOA. Coordinator: Edgar Gomes. Funding Agency: Universidade de Lisboa. Reference: PRÉMIO 3ª EDIÇÃO STARTHEALTH@ULISBOA. Amount: 1 000,00€. Total Amount: 1 000,00€.

2021/2021: PRESTAÇÃO DE SERVIÇOS - SARA FERREIRA. Coordinator: Geral. Funding Agency: Geral. Reference: PRESTAÇÃO DE SERVIÇOS - SARA FERREIRA. Amount: 6 000,00€. Total Amount: 6 000,00€.

2019/2025: ArpComplexity: Defining the role of Arp2/3 complex diversity at multiple scales of biology. Coordinator: Edgar Gomes. Funding Agency: European Commission. Reference: ERC SyG 810207. Amount: 3 207 935,00€. Total Amount: 10 715 153,00€.

2018/2022: MyoChip: Building a 3D innervated and irrigated muscle on a chip. Coordinator: Edgar Gomes. Funding Agency: European Commission. Reference: MyoChip 801423. Amount: 1 266 861,25€. Total Amount: 3 153 553,74€.

2018/2021: Posicionamento do núcleo das células musculares esqueléticas. Coordinator: Edgar Gomes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 031075/2017. Amount: 239 999,86€. Total Amount: 239 999,86€.

Scientific Impact

Academic Collaborations

Bruno Cadot, Institut Myologie

Stephanie Decroix, Institut Curie, IPGG

Miguel Bernabeu, University of Edinburgh

Fluigent, Fluigent - SME

Michael Way, The Francis Crick Institute

Carolyn Moores, The Francis Crick Institute

Pura Muñoz, Department of Experimental & Health Sciences, University Pompeu Fabra, CIBERNED

Sérgio Almeida, Instituto de Medicina Molecular João Lobo Antunes

Selected Publications

Calero-Cuenca FJ, Osorio DS, Carvalho-Marques S, Sridhara SC, Oliveira LM, Jiao Y, Diaz J, Janota CS, Cadot B, Gomes ER. [Ctdnep1 and Eps8L2 regulate dorsal actin cables for nuclear positioning during cell migration](#). *Curr Biol*. (2021) Feb 9:S0960-9822(21)00040-3.

Relevance of the publication: We found a complex between a nuclear envelope phosphatase (Ctdnep1) and an actin binding protein (Eps8L2) that is involved in nuclear movement.

Roman, W., Pinheiro, H., Pimentel, M.R., Segalés, J., Oliveira, L.M., García-Domínguez, E., Gómez-Cabrera, M.C., Serrano, A.L., **Gomes, E.R.**, and Muñoz-Cánoves, P. (2021). [Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction](#). *Science*, 374, 355–359.

Relevance of the publication: We found a mechanism of self-repair of muscle fibers involving nuclear movement and local translation at the site of injury.

Gimpel P, Lee YL, Sobota RM, Calvi A, Koullourou V, Patel R, Mamchaoui K, Nédélec F, Shackleton S, Schmoranzler J, Burke B, Cadot B, Gomes ER (2017). [Nesprin-1 \$\alpha\$ -Dependent Microtubule Nucleation from the Nuclear Envelope via Akap450 Is Necessary for Nuclear Positioning in Muscle Cells](#). *Current Biology*.

Relevance of the publication: We identified Nesprin-1 as the nuclear envelope protein required for the nucleation of microtubules from the nuclear envelope. Nesprin-1 recruits Akap450, a centrosomal protein that is necessary for microtubule nucleation and nuclear position.

Roman W, Martins J, Carvalho FA, Voituriez R, Abella JVG, Santos NC, Cadot B, Way M, Gomes ER (2017). [Myofibril contraction and cross-linking drive nuclear movement to the periphery of skeletal muscle](#). *Nature Cell Biology*, 1189–1201.

Relevance of the publication: We identify the mechanism of nuclear positioning at the periphery of skeletal muscle fibers. We found that nuclei are squeezed to the periphery and this process requires skeletal muscle contraction, myofiber crosslinking and activation of specific arp 2/# and actin isoforms.

Pinheiro, H., Pimentel, M.R., Sequeira, C., Oliveira, L.M., Pezzarossa, A., Roman, W., and **Gomes, E.R.** (2021). [mRNA distribution in skeletal muscle is associated with mRNA size](#). *Journal of Cell Science* 134.

Relevance of the publication: We found that mRNAs are differentially distributed within multinucleated muscle cells, depending on their size. We also found that transcription regulates mRNA localization.

2021 Publications in Peer-Reviewed Journals

Gomes, ER, deAlmeida, SF (2021) [TREX1-dependent DNA damage links nuclear rupture to tumor cell invasion](#), *Developmental Cell* 56(22): 3040-3041.

Calero-Cuenca FJ, Osorio DS, Carvalho-Marques S, Sridhara SC, Oliveira LM, Jiao Y, Diaz J, Janota CS, Cadot B, Gomes ER. [Ctdnep1 and Eps8L2 regulate dorsal actin cables for nuclear positioning during cell migration](#). *Curr Biol.* (2021) Feb 9:S0960-9822(21)00040-3.

Pinheiro, H., Pimentel, M.R., Sequeira, C., Oliveira, L.M., Pezzarossa, A., Roman, W., and **Gomes, E.R.** (2021). [mRNA distribution in skeletal muscle is associated with mRNA size](#). *Journal of Cell Science* 134.

Roman, W., Pinheiro, H., Pimentel, M.R., Segalés, J., Oliveira, L.M., García-Domínguez, E., Gómez-Cabrera, M.C., Serrano, A.L., **Gomes, E.R.**, and Muñoz-Cánoves, P. (2021). [Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction](#). *Science* 374, 355–359.

Savulescu, A.F., Brackin, R., Bouilhol, E., Dartigues, B., Warrell, J.H., Pimentel, M.R., Beaume, N., Fortunato, I.C., Dallongeville, S., Boulle, M., et al. (2021). [Interrogating RNA and protein spatial subcellular distribution in smFISH data with DypFISH](#). *Cell Reports Methods*

Invited Lectures and Seminars

Myofiber development and differentiation, New Directions in Biology and Disease of muscle, New York, USA, 28-01/07/2021

Role of nuclear positioning during myofiber formation, iim Meeting, Interuniversity Institute of Myology, Assisi, Italy, 17-20/10/2021

Networks & Research Infrastructures

MyoChip, a FetOpen project. Instituto de Medicina Molecular João Lobo Antunes (iMM), Institut Curie, University of Edinburgh, Fluigent (SME). iMM is the Coordinator.

ArpComplecity is a ERC Synergy Grant. The Francis Crick Institute (Host), Birkbeck College - University of London, iMM (Beneficiary).

Advanced Teaching

LisbonBioMed PhD Program, Lisbon, Portugal. Subject: Cytoskeleton, cell migration, stem cell differentiation, muscle development, muscle regeneration, neuromuscular disorders.

Gulbenkian Institute PhD course, Oeiras, Portugal. Subject: muscle development and regeneration.

Master of Biomedical Research - lecture "Lab rotations II", Coordinator of CU Project design, and Member of the scientific commission.

MSc Theses

Joana Monteiro, 26/11/2021, "Studying cancer cell migration under confinement and with correlative microscopy", Instituto Superior Técnico. Supervisor: **Edgar Gomes**.

PhD Theses

Helena Pinheiro, 17/12/2021, Unravelling the role of mRNA localization mechanisms in the establishment of myofiber nuclear domains, Instituto de Medicina Molecular João Lobo Antunes/Faculdade de Medicina da Universidade de Lisboa. Supervisor: **Edgar Gomes**.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021


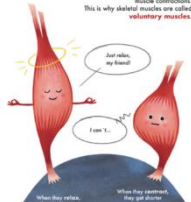
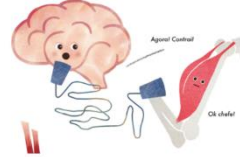

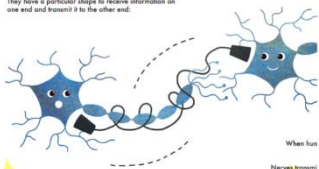
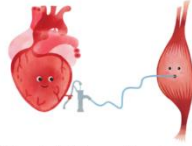
Build a 3D human skeletal muscle irrigated by vasculature and innervated by neurons, **Fluigent**, Myochip Consortium.

Policy

Substitute Member of the School Council of the Faculdade de Medicina da Universidade de Lisboa.

Science and Society in 2021

We have designed and printed a Booklet about muscle. We will distribute them to schools and the general public in collaboration with "Ciência Viva", "Pavilhão do Conhecimento" and "Programa Nacional de Promoção do Sucesso Escolar" of "Ministério de Educação".

<p>How muscles move your body</p> 	<p>Muscles are elastic - just like a rubber band. They lengthen and shorten to move the heavy and rigid bones inside your body.</p> <p>You can actively control muscle contractions. This is why skeletal muscles are called voluntary muscles.</p> 	<p>O cérebro é o maestro de todos os movimentos do corpo.</p> <p>O chefe do teu corpo é o teu cérebro. O cérebro envia mensagens a todos os órgãos para lhes dizer o que devem fazer. Para te moverem o cérebro diz aos nossos músculos quando relaxar e quando contrair.</p> 
<p>Como os músculos movem o teu corpo</p> 	<p>Neurons - the cells of our brain</p> <p>As every organ, the brain is also made out of cells. The cells of the brain are called neurons.</p> <p>Neurons can be very long. Like spaghetti! They have a particular shape to receive information on one end and transmit it to the other end.</p>  <p>When two Nerves transmit</p>	<p>O sistema circulatório fornece energia ao corpo todo</p>  <p>O sistema circulatório é composto pelo coração, vasos sanguíneos por onde circula sangue, transportando nutrientes e oxigénio até aos diferentes órgãos do teu corpo. É desta forma que os teus músculos recebem o que precisam para conseguirem contrair.</p>

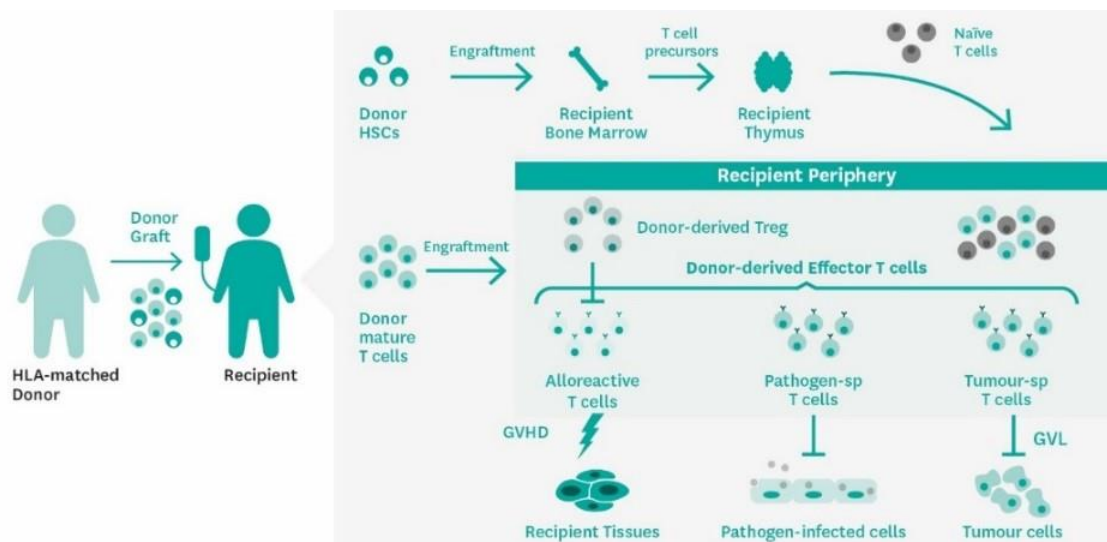
João Lacerda Lab

Head of Laboratory: João Forjaz de Lacerda, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full Professor at Faculdade de Medicina da Universidade de Lisboa, Senior Attending, Hematology and Bone Marrow Transplant Service at Hospital Santa Maria, President, Ethics Committee, Vice-President, Clinical Research Center at Lisbon Academic Medical Center

Team

Ana Catarina Vagos Gomes Rodrigues da Mata	MD/Master Degree	PhD Student (Started April)
Ana Cristina Frazão Lopes Alho	MD/Master Degree	PhD Student
Ana Teresa da Silva Pais	Master Degree	Lab Technician (Started June)
Carolina Paulino Pacini	Master Degree	PhD Student
Diogo Gomes da Silva	PhD	Postdoctoral Researcher
Eduardo Lima da Silva Espada	MD/Master Degree	PhD Student
Inês Amendoeira Cabral	Master Degree	Lab Technician (Left May)
Joana Brioso Infante	MD/Master Degree	PhD Student
Maria Godinho Alves Vieira Duarte Soares	PhD	Senior Postdoctoral Researcher
Mariana Torres Goulart Peixoto Maurício	High School Diploma	MSc Student (Left July)
Rita Isabel Silva de Azevedo	PhD	Senior Postdoctoral Researcher (Left August)

Graphical Abstract



Lab Interests

Our group focuses on the period that follows Hematopoietic Stem Cell Transplantation (HSCT), aiming to identify immunological risk factors and mechanisms involved in the most common complications, namely Graft-versus-Host Disease (GVHD), infection, and malignancy relapse. We are studying the clinical benefits of infusing donor-derived regulatory T cell (Treg) in patients with steroid-resistant GVHD.

At the same time, we also monitor tissue regeneration markers and immunological parameters following Treg infusion. Ongoing projects further aim to improve Treg therapies by using antigen-specific Treg to treat GVHD whilst retaining leukemia-specific responses. We also study virus-specific T cell responses after HSCT, and are involved in studies dissecting the pattern of genetic propensities for the emergence of invasive fungal infections. In order to tackle disease relapse, we have initiated new projects with Chimeric antigen T Cell Receptor (CAR-T) therapies that target cancer-specific proteoglycans.

Research Fields

- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

In 2021 we published the manuscript entitled “Suppression by allogeneic-specific regulatory T cells is dependent on the degree of HLA compatibility” in *ImmunoHorizons*. This paper addresses a major hurdle in cellular therapies using Treg, which is the issue of specificity.

Treg therapies using polyclonal populations may result in unwanted suppression of T cell responses. Hence, in our lab we aim to generate and expand Treg in vitro that specifically target antigens involved in GVHD. Although this remains an area of further research in our lab, the data presented in the article show that the development of antigen-specific Treg in vitro for clinical use is feasible and paves the way for novel approaches to the use of Treg in the treatment of GVHD.

The TREGeneration project, coordinated by our team, has officially finished in December 2021. We are now working together with all partners to analyze the data resulting from the clinical trials and prepare the publications resulting from this work.

Ongoing Projects in 2021

2020/2021: In vitro expansion of recipient-specific regulatory T cells for the treatment of chronic graft versus host disease after hematopoietic stem cell transplantation. Coordinator: João Lacerda. Funding Agency: Gilead Sciences. Reference: Programa Gilead GÉNESE 2019. Amount: 39 125,00€. Total Amount: 39 125,00€.

2020/2021: CMV infection and CMV-specific T-cell reconstitution in unrelated donor allo-HSCT after in vivo T-cell depletion with ATG. Coordinator: João Lacerda. Funding Agency: Merck Sharp & Dohme. Reference: Projecto MSD. Amount: 95 083,00€. Total Amount: 95 083,00€.

2020/2021: Prémio SPH. Coordinator: João Lacerda. Funding Agency: Sociedade Portuguesa de Hematologia. Reference: Prémio SPH. Amount: 25 000,00€. Total Amount: 25 000,00€.

2020/2021: Development of a novel chimeric antigen receptor T-cell therapy using B-cell activating factor, for triple targeting of B-cell specific receptors for multiple myeloma and other mature B cell neoplasms. Coordinator: Diogo Silva. Funding Agency: Associação Portuguesa contra a Leucemia. Reference: Bolsa em Neoplasias B Células Maduras. Amount: 15 000,00€. Total Amount: 15 000,00€.

2020/2021: Evolução dos Linfócitos T Reguladores ao Longo do Tratamento em Doentes com Leucemia Mielóide Aguda e sua Associação com Recaída. Coordinator: Joana Infante. Funding Agency: Sociedade Portuguesa de Hematologia. Reference: Bolsa de Investigação. Amount: 9 200,00€. Total Amount: 9 200,00€.

2019/2022: Apoio Doutoral Inphinit Incoming. Coordinator: Carolina Pacini. Funding Agency: “la Caixa” Foundation. Reference: Bolsas de Doutoramento ‘La Caixa’ Inphinit – Incoming em Centros de Investigação de Excelência de Espanha e Portugal. Amount: 115 092,00€. Total Amount: 115 092,00€.

2015/2021: TREGeneration: Repair of tissue and organ damage in refractory chronic graft versus host disease after hematopoietic stem cell transplantation by infusion of purified allogeneic donor regulatory T lymphocytes. Coordinator: João Lacerda. Funding Agency: European Commission. Reference: SC3 643776. Amount: 1 886 979,18€. Total Amount: 5 899 250,00€.

Scientific Impact

Academic Collaborations

Jerome Ritz, Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA

Matthias Edinger, Universitaetsklinik, Regensburg, Germany.

Frederic Baron, Laboratory of Cell and Gene Therapy, CHU Sart-Tilman, Liege, Belgium.

Mario Arpinatti, Department of Hematology “Seragnoli”, University Hospital S. Orsola-Malpighi, Bologna, Italy.

Marie-Laure Yaspo, Max Planck Society, Max Planck Institute for Molecular Genetics, Berlin, Germany.

Hans Lehrach, Alacris Theranostics GmbH, Berlin, Germany.

Marta Garcia-Finana, Department of Biostatistics, Faculty of Health & Life Sciences, University of Liverpool, UK.

José Antonio Pérez-Simón, Unidad de Hematología y Hemoterapia, Hospital Universitario Virgen del Rocío, Seville, Spain and University of Seville, Spain.

Jerome Ritz, Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA.

Agostinho Carvalho, Universidade do Minho

Selected Publications

Minskaia E, Saraiva BC, Soares MV, Azevedo RI, Ribeiro RM, Kumar SD, Vieira AIS, Lacerda JF (2018). [Molecular markers distinguishing T Cell subtypes with TSDR strand-bias methylation.](#)

Frontiers in Immunology 9: 2540. Original article.

Relevance of the publication: This study was performed entirely by members of the JLacerda lab and describes a previously unreported strand-bias hemimethylation pattern in FOXP3 promoter and TSDR that may prove to be instrumental in correctly defining Treg subsets in health and in disease.

Soares MV, Azevedo RI, Ferreira IA, Bucar S, Ribeiro AC, Vieira A, Pereira PNG, Ribeiro RM, Ligeiro D, Alho AC, Soares AS, Camacho N, Martins C, Lourenço F, Moreno R, Ritz J, Lacerda JF (2019).

[Naive and stem cell memory T Cell subset recovery reveals opposing reconstitution patterns in CD4 and CD8 T cells in chronic graft vs host disease.](#) **Frontiers in Immunology** 6(10):334. Original article.

Relevance of the publication: This study was performed almost entirely by members of the JLacerda lab, with the contribution of Dario Ligeiro (IPST Lisboa). The work involved a strong partnership with clinicians indicated the author list in addition to a collaboration with Jerome Ritz from the Dana Farber, USA who was involved in the initial planning of the project that led to this study. In this article we provide evidence to suggest that certain subsets of CD8 T lymphocytes, namely Naive, SCM and EMRA CD8 T cells play a role in the emergence of chronic GVHD, a frequent complication occurring after hematopoietic stem cell transplantation. These findings may pave the way to novel approaches to tackle this disease which is significantly hampered by the success of this therapy.

Azevedo RI, Minskaia E, Fernandes-Platzgummer A, Vieira AIS, da Silva CL, Cabral JMS, Lacerda JF (2020). [Mesenchymal stromal cells induce regulatory T cells via epigenetic conversion of human conventional CD4 T cells *in vitro*.](#)

Stem Cells 38(8):1007-1019. Original article.

Relevance of the publication: This study was performed entirely by members of the JLacerda lab and dissects the mechanisms by which MSC promote regulatory T cell expansion. This was a gap in the literature, and we describe for the first time that MSC recruit conventional CD4+ cells that assume a regulatory T cell phenotype and immunosuppressive function.

Alho AC, Kim HT, Chammas MJ, Reynolds CG, Matos TR, Forcade E, Whangbo J, Nikiforow S, Cutler CS, Koreth J, Ho VT, Armand P, Antin JH, Alyea EP, Lacerda JF, Soiffer RJ, Ritz J (2016).

[Unbalanced recovery of regulatory and effector T cells after allogeneic stem cell transplantation contributes to chronic GVHD.](#) **Blood** 127(5):646-657. Original article.

Relevance of the publication: This Paper dissects the kinetics of T-cell recovery after hematopoietic stem cell transplantation, with a focus on the development of chronic GVHD.

Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Löffler M, Maertens JA, Bell AS, Almeida B, Sousa PS, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano I, Lupi M, Garlanda C, Mantovani A, Velardi A, Romani L, Carvalho A (2014). [Genetic PTX3 deficiency and aspergillosis in stem-cell transplantation.](#)

The New England Journal of Medicine 370(5): 421-432. Original article.

Relevance of the publication: This paper dissects the genetics associated with invasive fungal disease after hematopoietic stem cell transplantation.

Stappers MHT, Clark AE, Amanianda V, Bidula S, Reid DM, Asamaphan P, Hardison SE, Dambuza IM, Valsecchi I, Kerscher B, Plato A, Wallace CA, Yucel R, Hebecker B, Sousa MGT, Cunha C, Liu

Y, Feizi T, Brakhage AA, Kwon-Chung KJ, Gow NRJ, Zanda M, Piras M, Zanato C, Jaeger M, Netea MG, Van De Veerdonk FL, Lacerda JF, Campos A, Carvalho A, Willment JA, Latgé JP, Brown GD (2018). Recognition of DHN-melanin by a C-type lectin receptor is required for immunity to *Aspergillus*. **Nature** 555:382-386. Original article.

Relevance of the publication: This paper dissects the genetics associated with invasive fungal disease after hematopoietic stem cell transplantation.

2021 Publications in Peer-Reviewed Journals

Bianchi J, Vieira AIS, Ligeiro D, Azevedo RI, Lacerda JF (2021). Suppression by Allogeneic-Specific Regulatory T Cells Is Dependent on the Degree of HLA Compatibility. **Immunohorizons** 5(5):307-321. Original article.

Doni A, Parente R, Laface I, Magrini E, Cunha C, Colombo FS, Lacerda JF, Campos A Jr, Mapelli SN, Petroni F, Porte R, Schorn T, Inforzato A, Mercier T, Lagrou K, Maertens J, Lambris JD, Bottazzi B, Garlanda C, Botto M, Carvalho A, Mantovani A (2021). [Serum amyloid P component is an essential element of resistance against *Aspergillus fumigatus*](#). **Nature Communications** 12(1):3739. Original article.

Gonçalves SM, Antunes D, Leite L, Mercier T, Horst RT, Vieira J, Espada E, Pinho Vaz C, Branca R, Campilho F, Freitas F, Ligeiro D, Marques A, van de Veerdonk FL, Joosten LAB, Lagrou K, Maertens J, Netea MG, Lacerda JF, Campos A Jr, Cunha C, Carvalho A (2021). [Genetic variation in PFKFB3 impairs antifungal immunometabolic responses and predisposes to invasive pulmonary Aspergillosis](#). **mBio** 12(3): e0036921. Original article.

Invited Lectures and Seminars

João Lacerda “Estado da Arte – Avanços terapêuticos em leucemias agudas”, hybrid, 16^o Congresso Brasileiro de Clínica Médica 2021, São Paulo, Brasil, October 10 2021

João Lacerda “Regulatory T cells in hematopoietic stem cell transplantation”, Portuguese Society for Immunology Annual Meeting, Online Meeting, May 20 2021.

João Lacerda “Investigação Clínica e Ensaio Clínicos: a evolução e novos desafios”, Encontro Ciência 21, Lisboa, Portugal, June 30 2021.

João Lacerda “Transplante haploidêntico e progenitores hematopoiéticos”, Reunião Anual da Sociedade Portuguesa de Hematologia 2021, hybrid, Espinho, Portugal), November 13 2021.

João Lacerda, “Regulatory T cells in graft versus host disease”, 5^a Conferência Anual Rede Saúde Universidade de Lisboa, Session on Personalized Medicine; Lisboa, November 30 2021.

Advanced Teaching

João Lacerda Lecture at PhD Program “CAR T cell Therapy”, Universidade de Coimbra, Portugal, April 13 2021.

MSc Theses

Mariana Maurício, 13/07/2021, “Dendritic cell reconstitution in allogeneic hematopoietic stem cell transplantation: implications for chronic graft-versus-host disease development”, Faculdade de Medicina da Universidade de Lisboa. Supervisor: João Forjaz de Lacerda. Co-Supervisor: Maria Soares.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Investigate CMV infection and CMV-specific T-cell reconstitution in unrelated donor allo-HSCT after *in vivo* T-cell depletion with ATG in a comparative study of prophylaxis with letermovir *versus* standard of care preemptive treatment; MSD; Sponsored Research.

Luísa Lopes Lab

Head of Laboratory: Luísa V. Lopes, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Inês Marques Morgado	Master Degree	PhD Student
Catarina Candeias Ferreira	University Degree	MSc Student
Cátia Cristina Peixinho Reis	PhD	Postdoctoral Researcher
Joana Fernandes Esteves Soares Coelho	PhD	Senior Postdoctoral Researcher
Joana Gomes Ribeiro	Master Degree	PhD Student
Joana Isabel Rajão Saraiva	Master Degree	PhD Student
João Baptista Moreira	Master Degree	PhD Student
João Pedro Cláudio Agapito	University Degree	MSc Student
Nicolas Andres Morgenstern	PhD	Postdoctoral Researcher
Pedro Filipe Duarte Pereira Batista	MD/Master Degree	Clinical Researcher
Raquel Lagoa Madruga da Costa	University Degree	MSc Student
Rui Artur Paiva Loureiro Gomes	PhD	Senior Postdoctoral Researcher

Graphical Abstract

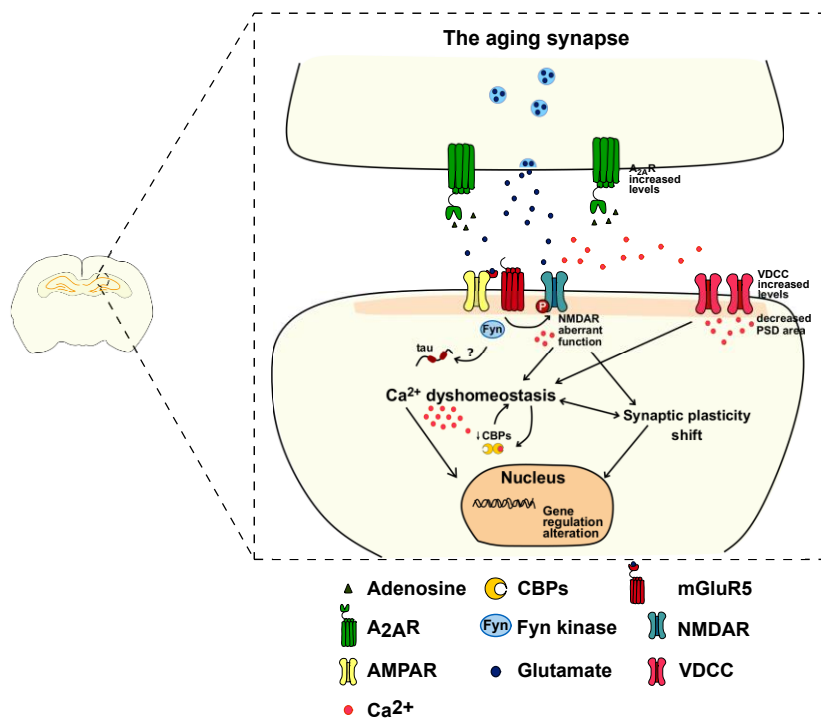


Image caption: The aged glutamatergic synapse in the hippocampus. Adenosine A_{2A}R increased levels are associated with post-synaptic impairments, such as a mGluR5-dependent NMDAR activation, possibly through Fyn Kinases. NMDAR aberrant activation and VDCC increased expression trigger an increase in Ca²⁺ influx.

Associated with a dysfunction of calcium binding proteins, this mechanism shifts Ca²⁺-dependent induction mechanism. Ca²⁺ imbalance and the associated synaptic plasticity shift impairs gene regulation, further exacerbating synaptic dysfunction. Our work has provided clues to the comprehension of these mechanisms, which are of crucial importance to understand the age-related cognitive decline. *Abbreviations: CBPs, calcium binding proteins; VDCC, voltage-dependent calcium channels.*

Lab Interests

We run a neuroscience research program aimed at understanding the mechanisms inducing the "early-aging" of cognitive function, focusing on hippocampal circuitry and related behavior in rodent models. Our current focus is to create better translational aging models, through the use of age-equivalent equivalent human-derived neurons. We focus our research on the mechanisms underlying early synaptic dysfunction in order to understand the resilience versus vulnerability in cognitive aging.

Research Fields

- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System

Major Scientific Achievements in 2021

- ***Catalyst Award 'Cholinergic Input in Fast versus Slow Cognitive Decline upon Aging' Healthy Longevity Global Challenge Award - National Academy of Medicine***

As people age, some maintain the cognitive function, while others suffer from rapid cognitive decline. It is thought that the cholinergic circuit gradually degenerates with aging, resulting in impaired cholinergic function and memory impairment. However, the lack of a method to measure acetylcholine release in vivo with high resolution has hampered subsequent studies. This grant will fund our proposal of using a combination of state-of-the-art in vivo photometry, with wireless technology and human-derived neurons to study the temporal and functional characteristics of cholinergic dysfunction. The identification of the cholinergic input which is dysfunctional in age-impairment will add knowledge to the field and hopefully provide novel clues to interfere or delay memory decline upon aging. PIs: Luisa Lopes (iMM, Lisbon, Portugal); Yusuke Tsuno, Kanazawa University, Japan; Ulkuhan Guler, Worcester Polytechnic, USA. Competition Sponsor: Japan Agency for Medical Research and Development; <https://healthylongevitychallenge.org/winners/cholinergic-input-in-fast-versus-slow-cognitive-decline-upon-aging/>

- ***IL-17 promotes early synaptic dysfunction in Alzheimer's disease onset independently of Aβ and tau pathology***

In a previous paper, in collaboration with Julie Ribot and Bruno Silva-Santos (Ribeiro et al, 2019), we described a distinctive population of Vγ6+ γδ T cells in the mouse meninges but not in the brain parenchyma, involved in synaptic plasticity and short-term spatial memory acquisition. However, the question of whether these meningeal-resident γδ IL-17 producing T cells have a role in a chronic neuroinflammatory setting such as Alzheimer's disease remained unexplored. In this new neuroimmunology paper (Brigas et al, Cell Reports, 2021), using the 3xTg-AD model, we report an accumulation of interleukin-17 (IL-17)-producing cells, mostly γδ T cells, in the brain and the meninges of female, but not male, mice, concomitant with the onset of cognitive decline. Critically, IL-17 neutralization into the ventricles is sufficient to prevent short-term memory and synaptic plasticity deficits at early stages of disease. These effects precede blood-

brain barrier disruption and amyloid-beta or tau pathology, implying an early involvement of IL-17 in AD pathology.

When IL-17 is neutralized at later stages of disease, the onset of short-memory deficits and amyloidosis-related splenomegaly is delayed. Altogether, our data support the idea that cognition relies on a finely regulated balance of "inflammatory" cytokines derived from the meningeal immune system.

- ***Development of a novel surgical method to access deep regions of the rodent midline brain while causing minimal damage and avoiding major vessels***

Stereotaxic access to brain areas underneath the superior sagittal sinus (SSS) is notoriously challenging. As a major drainage vessel, covering the whole extension of the sagittal fissure, the SSS impedes direct bilateral access to underlying regions for recording and stimulation probes, drug-delivery cannulas, and injection devices. Our team, together with Miguel Remondes', now describe a new method for transection and retraction of the SSS in rats (Dias, Marques-Morgado et al., eNeuro, 2021) that allows the accurate placement of microinjection devices, or chronic electrode probes, while avoiding hemorrhage and the ensuing deleterious consequences for local structures, animal health, and behavior. To demonstrate the feasibility of this approach we evaluated its consequences acutely during surgery, and thereafter during surgical survival, recovery, behavioral testing, as well as postmortem analysis of histologic impact in the related brain structures of male rats. This method provides a new approach enabling direct access for manipulation and recording of activity in brain areas previously obstructed by the SSS.

Ongoing Projects in 2021

2021/2024: SRA - PROTERRIS - CARLOS LABÃO. Coordinator: Luísa Lopes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/3890/2020. Amount: 218 050,00€. Total Amount: 218 050,00€.

2019/2021: Mechanistic insight on Alzheimer's using novel aging-based models. Coordinator: Luísa Lopes. Funding Agency: Santa Casa da Misericórdia de Lisboa. Reference: Prémio Santa Casa Mantero Belard (MB-07-2018) – Luísa Lopes. Amount: 175 000,00€. Total 175 000,00€.

2019/2021: NeuroSeS: NeuroscienEuropean Commission Seminar Series. Coordinator: Luísa Lopes. Funding Agency: Roche Farmacêutica. Reference: NeuroSeS: NeuroscienEuropean Commission Seminar Series. Amount: 3 200,00€. Total Amount: 3 200,00€.

2019/2021: The physiological role of circadian rhythms in memory. Coordinator: Luísa Lopes. Funding Agency: Fundação BIAL. Reference: BIAL L Lopes. Amount: 45 000,00€. Total Amount: 45 000,00€.

Scientific Impact

Academic Collaborations

Julie Ribot/Bruno Silva-Santos, iMM; FML, Lisbon

Miguel Remondes, iMM; FML, Lisbon

Paula Pousinha, Univ Côte d'Azur, Nice, France

Alexandre de Mendonça, iMM; FML, Lisbon

Ana Oliveira, Heidelberg Univ, Germany

Chun- Li Zhang, Soutwestern Uni. USA

David Blum, INSERM, Lille, France

Freg Gage & Jerome Mertens, Salk Institute, USA and Innsbruck Univ., Austria

Luís Pereira de Almeida, CNC, Coimbra

Michael Bader, MDC, Berlin

Miguel Castelo-Branco, ICNAS, Coimbra

Ulkuhan Guler, Worcester Uni, USA

Yusuke Tsuno, Kanazawa Univ, Japan

Selected Publications

Mariana Temido-Ferreira, Diana G. Ferreira, Vânia L. Batalha, Inês Marques-Morgado, Joana E. Coelho, Pedro Pereira, Rui Gomes, Andreia Pinto, Sara Carvalho, Paula M. Canas, Laetitia Cuvelier, Valerie Buée-Scherrer, Emilie Faivre, Younis Baqi, Christa E. Müller, José Pimentel, Serge N. Schiffmann, Luc Buée, Michael Bader, Tiago F. Outeiro, David Blum, Rodrigo A. Cunha, Hélène Marie, Paula A. Pousinha and Luísa V. Lopes (2020) [Age-related shift in LTD is dependent on neuronal adenosine A2A receptors interplay with mGluR5 and NMDA receptors](#), **Molecular Psychiatry**, 25(8):1876-1900.


Relevance of the publication Synaptic dysfunction plays a central role in Alzheimer's Disease (AD), since it drives the cognitive decline. An association between a polymorphism of the adenosine A2A receptor (A2AR) encoding gene - ADORA2A, and hippocampal volume in AD patients was recently described. In this study, we report, for the first time, a significant overexpression of A2AR in hippocampal neurons of aged humans, which is aggravated in AD patients. A similar profile of A2AR overexpression in rats was sufficient to drive age-like memory impairments in young animals and to uncover a hippocampal LTD-to-LTP shift. This is a consequence of an A2AR-induced increase in postsynaptic Ca²⁺ influx via NMDAR, which is dependent on mGluR5 activation. We confirmed the same plasticity shift in memory-impaired aged rats and APP/PS1 mice modelling AD, which was rescued upon A2AR blockade. This A2AR/mGluR5/NMDAR interaction might prove a suitable alternative for regulating aberrant mGluR5/NMDAR signaling in AD without disrupting their constitutive activity. n

Diana G. Ferreira, Mariana Temido-Ferreira, Hugo Vicente Miranda, Vânia L. Batalha, Joana E. Coelho, Éva M. Szegő, Inês Marques-Morgado, Sandra H. Vaz, Jeong Seop Rhee, Matthias Schmitz, Inga Zerr, Luísa V. Lopes* and Tiago F. Outeiro* (2017) [α-Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B](#). **Nature Neuroscience** 20(11):1569-1579.

Relevance of the publication Synucleinopathies, such as Parkinson's disease (PD) and dementia with Lewy bodies, are neurodegenerative disorders characterized by the accumulation of a-synuclein (aSyn) in intracellular inclusions. The main finding of this study is that aSyn oligomeric species physically interact with PrPC through mGluR5, activating SFK kinases and, subsequently, NMDAR2B, leading to neuronal calcium imbalance. We found for the first time, that genetic or antibody-mediated inactivation of PrPC prevented the toxic effects of aSyn on synaptic function. Finally, we confirmed the importance of this mechanism in vivo, by rescuing synaptic and cognitive deficits following blockade of mGluR5- evoked phosphorylation of NMDARs, in a mouse model overexpressing human aSyn. Together, these data support the hypothesis that a receptor-mediated mechanism, independent of pore formation and membrane leakage, is sufficient to trigger early synaptic damage induced by extracellular aSyn, which could occur as part of the normal biology of the protein or during the spreading of pathology in PD and other synucleinopathies.

Blum D, Lopes LV (2021) [Stabilizing synapses](#). *Science*. doi: 10.1126/science.abm3902

Relevance of the publication Compelling evidence from our group and others demonstrates that the synaptic and neuronal up-regulation of adenosine A2AR in aging and neurodegeneration is instrumental to the decline of synaptic function and degeneration, presumably through neuron-glia dialog. Hereby, we put into the context the mechanism uncovered for synaptogenesis by Gomez-Castro (2021, *Science*) which may have broader implications—e.g., that of adenosine possibly playing a more general role as an activity detector, regulating synaptic dynamics and presumably synaptic loss, in the aged and diseased brain. Adenosine and A2AR would then regulate the fate of particular synapses in extreme stages of the brain life cycle. This supports a prime role for adenosine in synaptic allostasis (i.e., during brain adaptation to challenges), the controlling of brain network wiring, and cognitive function and emphasizes our contribution to this important physiological mechanism.

VL. Batalha, JM. Pego B Fontinha, AR Costenla, J Valadas, Y Baqi, H Radjainia, C E. Müller, AM. Sebastião and Luísa V. Lopes (2013) [Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation](#). *Mol. Psychiatry*, 18, 320-331. 

Relevance of the publication While the hippocampus is best known for its role in memory and spatial navigation, it's also extremely important in emotional responses. Neuronal growth in the hippocampus can come from enriched environments or chronic antidepressants, and death of those neurons can come from chronic stress. Chronic stress also disrupts the hypothalamic-pituitary-adrenal axis (the HPA axis). There are compelling evidences for a role of hippocampal adenosine A2AR in stress-induced modifications related to cognition. We assessed the therapeutic potential of a blocker of A2A receptors in stress-impaired animals and found that it reverted the behavior, electrophysiological and morphological impairments induced by stress. This mechanism is associated with restoration of the HPA-axis activity, as both the plasma corticosterone levels and hippocampal glucocorticoid receptor expression pattern returned to physiological-like status after the treatment. These results reveal that the HPA-axis dysfunction, as well as the long-lasting synaptic and behavioral effects of stress are associated to overactivation of A2A receptors. These findings provide a novel evidence for the use of adenosine A2A receptor antagonists as potential therapy against psychopathologies.

2021 Publications in Peer-Reviewed Journals

Blum D, Lopes LV (2021) [Stabilizing synapses](#). *Science*. doi: 10.1126/science.abm3902.

Brigas HC, Ribeiro M, Coelho JE, Gomes R, Gomez-Murcia V, Carvalho K, Faivre E, Costa-Pereira S, Darrigues J, de Almeida AA, Buée L, Dunot J, Marie H, Pousinha PA, Blum D, Silva-Santos B, Lopes LV, Ribot JC (2021) [IL-17 triggers the onset of cognitive and synaptic deficits in early stages of Alzheimer's disease](#). *Cell Rep*. doi: 10.1016/j.celrep.2021.109574.

Dias M, Marques-Morgado I, Coelho JE, Ruivo P, Lopes LV, Remondes M. (2021) [Transection of the superior sagittal sinus enables bilateral access to the rodent midline brain structures](#). *eNeuro*. ENEURO.0146-21.2021.

Korman M, Tkachev V, Reis C, Komada Y, Kitamura S, Gubin D, Kumar V, Roenneberg T. (2021) [Outdoor daylight exposure and longer sleep promote wellbeing under COVID-19 mandated restrictions](#). *Journal of Sleep Research*, e13471.

Loock,AS, Sullivan AK, Reis C, Paiva T, Ghotbi N, Pilz LK, Biller AM, Molenda C, Vuori-Brodowski M, Roenneberg T, Winnebeck EC. (2021) [Validation of the Munich Actimetry Sleep Detection Algorithm for estimating sleep-wake patterns from activity recordings](#). **Journal of Sleep Research**, 2021;00:e13371.

Madeira SG, Reis C, Paiva T, Moreira CS, Nogueira P, Roenneberg T. (2021) [Social Jetlag is associated with high cardiovascular risk in blue-collar workers under permanent atypical work schedules](#). **Journal of Sleep Research**, 2021;00:e13380.

Paiva T, Reis C, Feliciano A, Canas-Simião H, Machado MA, Gaspar T, Tomé G, Branquinho C, Silva MR, Ramiro L, Gaspar S, Bentes C, Sampaio F, Pinho L, Pereira C, Carreiro A, Moreira S, Luzeiro I, Pimentel J, Videira G, Fonseca J, Bernarda A, Vaz Castro J, Rebocho S, Almondes K, Canhão H, Matos MG. (2021) [Sleep and awakening quality during COVID-19 confinement: complexity and relevance for health and behavior](#). **International Journal of Environmental Research and Public Health**. 2021 Mar 28;18(7):3506.

Reis C, Tecedeiro M, Pellegrino P, Paiva T, Marôco J.(2021) [Psychometric Properties of the Oldenburg Burnout Inventory \(OLBI\) in a Portuguese sample of Aircraft Maintenance Technicians](#). **Frontiers in Psychology**, 12:725099.

Invited Lectures and Seminars

Luísa Lopes. 'Age-based models to study Alzheimer's disease' Neurodegenerative Course, FM/UNL, Lisboa, March 2021.

Luísa Lopes. Bridging research in academia and in a private company. EIT Health, Coimbra, May 2021.

Luísa Lopes. Lost in translation? Fundamental neuroscience with clinical significance, I3S, Porto, July 2021.

Luísa Lopes. 'Towards assessing human synaptic aging - new models' Bordeaux Neurocampus, Univ. Bordeaux, Sept 2021.

Luísa Lopes. 'Caffeine and adenosine receptors in the aging hippocampus' Bordeaux Neurocampus, Univ. Bordeaux, Sept 2021.

Luísa Lopes. 'Circadian rhythms – it is about time' Univ Côte d'Azur, Oct 2021.

Inês Marques-Morgado. Mapping the interactions between circadian rhythms and memory; Invited lecture for the Master in Applied Neuropsychology at Universidade Lusófona de Humanidades e Tecnologias; 1st June 2021.

Cátia Reis. Ahed - Advanced Health Education "Diagnostic work up of sleep rythm" - Cuf Saúde.

Cátia Reis. 1º Seminário em Sono na Infância e Adolescência da ESSCVP – Lisboa "O ritmo circadiano e a sua influencia no sono" - Escola Superior Saúde Cruz Vermelha Portuguesa.

Cátia Reis. Webinar - O Adolescente do Século XXI – “O sono do adolescente” - Escola Superior Saúde Cruz Vermelha Portuguesa.

Cátia Reis Webinar O impacto da desregulação do sono ao longo da vida – “Ritmos circadianos, sono, saúde e envelhecimento”; CNS – Campus Neurológico Sénior.

Communications

Joana Ribeiro “Brain maps of drug-related memories” Short pre-recorded ORAL presentation: XIV CAML - IV NeurULisboa PhD Students Virtual Meeting | May 2021 |

Joana Ribeiro “Memory traces of a drug-led life” ORAL presentation: Seminar for the FMUL Neuroscience Seminars Series – via zoom | November 2021 |

Joana Ribeiro “Chasing the trace of opioid addiction in the memory system” POSTER presentation: XVII Meeting of the Portuguese Society for Neurosciences 2021 (Coimbra, Portugal) | December 2021 |

Marques-Morgado I, Dias M, Coelho JE, Ribeiro JG, Remondes M, Dawson N, Lopes LV; Adaptive changes in memory-related brain regions upon chronic circadian manipulation; POSTER presentation at the XVII Meeting of the Portuguese Society for Neuroscience, 1st December 2021;

Marques-Morgado I, Dias M, Coelho JE, Ribeiro JG, Remondes M, Dawson N, Lopes LV; Mapping the interactions between circadian rhythms and memory; Oral presentation at the XIV Annual CAML PhD Students' Meeting, 5th May 2021;

Joana Rajão-Saraiva. Amyloid precursor protein regulation of glutamatergic synapses in early development. 15th International Conference on Alzheimer’s and Parkinson’s Diseases, POSTER March 2021 (Online)

Joana Rajão-Saraiva, What is hAPPening at the synapse: from development to Alzheimer’s Disease. XVII Meeting of the Portuguese Society for Neuroscience, POSTER December 2021 (Coimbra, Portugal)

Joana Rajão-Saraiva, What is hAPPening at the synapse: from development to Alzheimer’s Disease. 35ª Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demência, ORAL July 2021 (Online)

Joana Rajão-Saraiva, Joana E. Coelho, Mariana Temido-Ferreira, Hélène Marie, Luísa V. Lopes, Paula A. Pousinha. What is hAPPening at the synapse: from development to Alzheimer’s Disease. ORAL XIV CAML PhD Students' Meeting, May 2021 (Online)

Organization of Conferences

Luísa Lopes. Director. Cajal Course on Ageing Cognition, Bordeaux School of Neuroscience, Bordeaux, France, September-Oct 2021.

Luisa Lopes (with Cláudia Faria) NeuroSeS: Neuroscience Seminar Series, CAML, 2021.

Prizes & Honors in 2021

Catalyst Award 'Cholinergic Input in Fast versus Slow Cognitive Decline upon Aging' (Healthy Longevity Global Challenge Award - National Academy of Medicine) to the team of Luisa Lopes, Yusuke Tsuno and Ulkuhan Guler.

Advanced Teaching

PhD

Luisa Lopes, LisbonBiomed PhD program, IMM Lisbon

Luisa Lopes, PhD in Neurosciences, Univ. Lisbon

Cátia Reis, Advanced methods in research (Statistical analysis); Doctoral Program in Communication Studies – Catholic Lisbon University

MSc

Luísa Lopes, Master in Biomedical Research, IMM, Lisbon, November 2021

Luisa Lopes, Master in Neurosciences, Univ Côte d'Azur, Nice, France, October 2021

Luisa Lopes, Master in Neurosciences, Univ Lisbon, Portugal, October 2021

Cátia Reis. Thematic seminars (Sleep and work); Master's in Psychology in Business and Economics – Catholic Lisbon University, 2021

BSc

Cátia Reis. Cognitive Psychology I, Introduction to Statistics, Psychosomatics; Universidade Católica Portuguesa; Lisbon, Portugal, 2021

Post-graduation

Luisa Lopes, FENS-Cajal Training program 'Cognitive Ageing', Bordeaux, France Sept 2021

Cátia Reis. Post-Graduation in Sleep Psychology (Circadian Rhythms, Circadian Rhythms Sleep-Wake Disorders, Sleep and work, Adolescence)

Cátia Reis. Workshop in Programs in Sleep interventions; Universidade Católica Portuguesa; Lisbon, Portugal

Cátia Reis. Advance Sleep training course (circadian rhythm disorders, actigraphy: analyses and interpretation); Medical Faculty – Universidade Católica Portuguesa

MSc Theses

Raquel Lagoa Madruga da Costa, Editing of the ADORA2A gene by CRISPR/Cas9, Master in Neurosciences FMUL, April 8 2021, Supervisor: Luisa Lopes, co-supervisor: Simão Rocha.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Design, create and test anti-sense A2AR oligonucleotides, Ionis USA, Collaborative Research

Science and Society in 2021

Luisa Lopes. Brain Gain 2021, Brain Awareness Week, Coimbra, March 2021.

Luisa Lopes, Fronteiras XXI 'Demências: conseguimos preveni-las?', RTP, April 14, 2021.

Luisa Lopes, Round table 'Longevidade e Neurociências' Feira do Livro de Lisboa, September 8, 2021.

Luisa Lopes, A pandemia de COVID-19 e a nossa saúde - Final Meeting EXCELLtoINNOV, June 17, 2021.

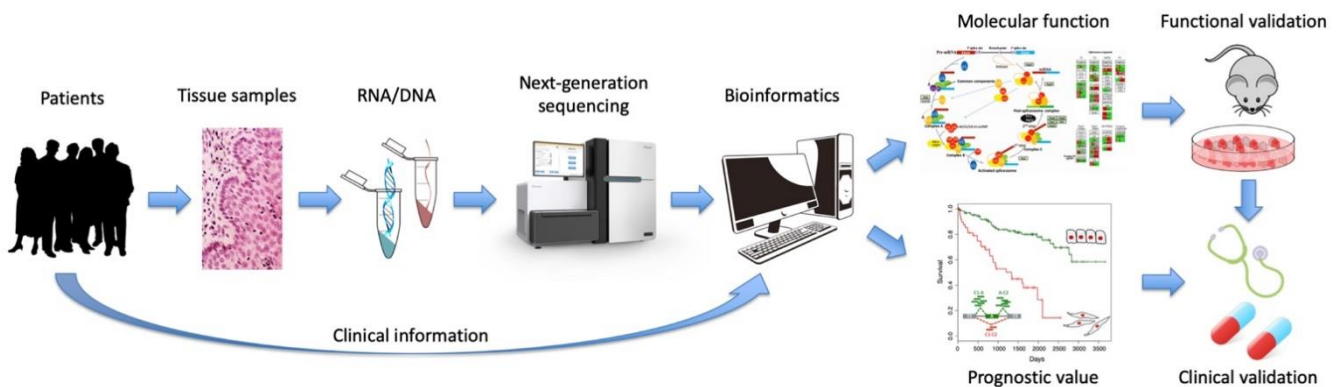
Nuno Morais Lab

Head of Laboratory: Nuno Luís Barbosa Morais, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Ana Marta Fernandes Bica	Master Degree	PhD Student (Started May)
José Cândido de Oliveira Alves Ferrão	Master Degree	MSc Student
Mariana da Ascensão Ferreira	Master Degree	PhD Student
Nuno Daniel Saraiva Agostinho	Master Degree	PhD Student
Rita Alexandra Figueira Belo	Master Degree	PhD Student (Started May. Left November)

Graphical Abstract



Lab Interests

We have a long-term interest in the systems-level transcriptional regulation underlying mammalian cell specification, often perturbed in disease. We aim to understand how RNA-level (transcription initiation, splicing, etc.) changes in (mostly) human tissues increase proneness to diseases, namely cancer, neurodegenerative disorders and other ageing-related pathologies. We thereby aim to identify molecular targets for functional exploration *in vitro* and *in vivo*. We also combine molecular and clinical information for the unveiling of novel candidate prognostic factors and therapeutic targets. Along the way, we develop some tools for assisting non-computational scientists in their analyses of transcriptomic data.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

We have launched a website (<https://compbio.imm.medicina.ulisboa.pt/>) that harbours all the bioinformatics web applications developed in the lab, making them available to the scientific community. These include the already published *pischomics* and beta versions of *voyAGER* (analysis of age-related gene expression changes in human tissues) and *cTRAP* (identification of candidate causal perturbations from differential gene expression data).

Our collaborations with the labs of George Garinis (FORTH Crete), on the role of splicing factor *XAB2* for R-loop processing, and Gonçalo Bernardes (iMM), on piperlongumine in glioblastoma therapeutics, were published in *Nature Communications* and *ACS Central Science*, respectively.

The very first PhD student in the lab, Marie Bordone, successfully defended her thesis.

Ongoing Projects in 2021

2020/2022: Protocolo Limm. Coordinator: Nuno Morais. Funding Agency: Limm Therapeutics. Reference: Protocolo Limm. Amount: 79 896,00€. Total Amount: 79 896,00€.

2017/2021: GENOME Portugal. Coordinator: Nuno Morais. Funding Agency: Portugal 2020. Reference: PINFRA/22134/2016. Amount: 123 711,00€. Total Amount: 826 226,00€.

2015/2021: Transcriptomic landscapes of cancer. European Commission: studying the transcriptional etiology of metastization and its implications on personalized therapeutics. Coordinator: Nuno Morais. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG NMorais. Amount: 250 000,00€. Total Amount: 250 000,00€.

Other Projects

2019/2022: Inovação de GWAS em cancro da mama através da integração de genómica funcional. Coordinator: Joana Xavier. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: Intergen. Amount: 500,00€. Total Amount: 236 221,43€.

Scientific Impact

Academic Collaborations

Jesús Gil, MRC London Institute of Medical Sciences, UK
 Karine Serre, Instituto de Medicina Molecular João Lobo Antunes
 Mónica Bettencourt-Dias, Instituto Gulbenkian de Ciência, Portugal
 Simão Rocha, Instituto de Medicina Molecular João Lobo Antunes

Selected Publications

Bordone MC, Barbosa-Morais NL (2020). [Unraveling Targetable Systemic and Cell-Type-Specific Molecular Phenotypes of Alzheimer's and Parkinson's Brains with Digital Cytometry](#). *Frontiers in Neuroscience* 14:607215.

Relevance of the publication: Alzheimer's and Parkinson's diseases are the two most common neurodegenerative disorders. Their progression is characterized by a loss of neurons in the brain but most research on those disorders' underlying mechanisms does not consider the differences in the number of

neurons and cell of other types between healthy and diseased brains. As such, we developed a computational approach that considers cell type composition in the identification of molecular changes in Alzheimer's and Parkinson's brains, enabling to associate those changes with the type of cell in which they occur. We also computationally identified small molecules potentially targeting those changes, thereby fostering the research of novel therapeutic approaches for those disorders.

Munkley J, Li L, Krishnan SRG, Hysenaj G, Scott E, Dalgliesh C, Oo HZ, Maia TM, Cheung K, Ehrmann I, Livermore KE, Zielinska H, Thompson O, Knight B, McCullagh P, McGrath J, Crundwell M, Harries LW, Daugaard M, Cockell S, Barbosa-Morais NL*, Oltean S*, Elliott DJ*. (2019). [Androgen-regulated transcription of ESRP2 drives alternative splicing patterns in prostate cancer](#). *eLife* 8:e47678.

Relevance of the publication: This article describes a regulatory circuit involving ESRP-regulated epithelial splicing switches in prostate cancer. We found that these switches can be triggered by changes in expression of ESRP2 induced by androgens, thus linking hormonal/transcription control to isoform changes. Our group led the alternative splicing analyses, including its integration with clinical information.

de Almeida BP, Vieira AF, Paredes J, Bettencourt-Dias M, Barbosa-Morais NL (2019). [Pan-cancer association of a centrosome amplification gene expression signature with genomic alterations and clinical outcome](#). *PLoS Computational Biology* 15(3):e1006832.

Relevance of the publication: To bypass the technical difficulties in characterising centrosome amplification, known to induce cancer, in patient samples, we looked at the expression of genes known to cause it and analysed its incidence in thousands of tumours of different types of cancer and in normal tissue samples from the same patients. We observed that such signature is present only in tumour samples and is more prevalent in aggressive forms of cancer, being associated with a lower survival rate in different types of cancer. Using drug sensitivity studies, we also identified selective compounds for cells with centrosome amplification that could specifically target cancer cells, not affecting the healthy cells of patients. Additionally, the samples that we have analysed are characterised at the levels of their DNA sequence and the expression of thousands of genes. This means that the integration of these data allows us to better understand the causes and molecular consequences of centrosome amplification.

Saraiva-Agostinho N, Barbosa-Morais NL (2019). [psichomics: graphical application for alternative splicing quantification and analysis](#). *Nucleic Acids Research* 47(2):e7.

Relevance of the publication: Cancer cells are characterised by perturbations in the regulation of genes and, in particular, by alterations in alternative splicing, a process by which the same gene can originate different proteins. Some of those alterations are associated with different malignant features of cancer and its resistance to treatment but vary from tumour to tumour. We developed a new software for the analysis of large databases with clinical and splicing information for thousands of tumours that allows the detection of patterns of similarities between different cases and the identification of molecular alterations associated with prognosis and resistance to therapy of different types of cancer. In practice, the interactive program allows to quickly convert a lot of genome-wide data into biological information with clinical potential. With it, we identified a possible mechanism of resistance to chemotherapy in colorectal cancer and a new prognostic marker in breast cancer that we are now investigating.

Gallego-Paez LM, Bordone MC, Leote AC, Saraiva-Agostinho N, Ascensão-Ferreira M, Barbosa-Morais NL (2017). [Alternative splicing: the pledge, the turn, and the prestige: The key role of alternative splicing in human biological systems](#). *Human Genetics* 136(9):1015-1042.

Relevance of the publication: This well accepted and well cited review on human alternative splicing was a collective effort by the lab, with writing and illustration tasks evenly shared by most of its members,

irrespectively of their seniority. We therein describe mechanisms and regulation of alternative splicing in several systems and tissues of the human body, from neurodevelopment to the interactions with the human microbiome, discussing, on one hand, its essential role in assuring tissue function, diversity, and swiftness of response in these systems or tissues, and on the other hand, what goes wrong when its regulatory mechanisms fail. We also focus on the possibilities that splicing modulation therapies open for the future of personalized medicine, along with the leading techniques in this field.

2021 Publications in Peer-Reviewed Journals

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, de Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu Y, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Barbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL (2021). [Allosteric Antagonist Modulation of TRPV2 by Piperlongumine Impairs Glioblastoma Progression](#). *ACS Central Science* 7(5):868-881.

Goulielmaki E, Tsekrekou M, Batsiotos N, Ascensão-Ferreira M, Ledaki E, Stratigi K, Chatzinikolaou G, Topalis P, Kosteas T, Altmüller J, Demmers JA, Barbosa-Morais NL, Garinis GA (2021). [The splicing factor XAB2 interacts with ERCC1-XPF and XPG for R-loop processing](#). *Nature Communications* 12(1):3153

Invited Lectures and Seminars

Nuno Barbosa Morais. *Bioinformatic analyses of human transcriptomes made intelligible to biologists*. iBiMED - Institute of Biomedicine, University of Aveiro, Portugal, November 19, 2021. (Virtual)

Nuno Barbosa Morais. *Computational biology in the translation of disease 'omics'*. Department of Bioengineering, Instituto Superior Técnico, Lisbon, Portugal, May 25, 2021. (Virtual)

Nuno Barbosa Morais. *Making biological big data intelligible to yourself and others*. Kiel Evolution Center, University of Kiel, Germany, April 21, 2021. (Virtual)

Communications

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. 6th International Cell Senescence Association (ICSA) Conference/Osaka International Convention Center, Osaka, Japan, December 12-15, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE. (Hybrid conference, virtual attendee).

Ascensão-Ferreira M, Barbosa-Morais NL. Intuitive visualisation of differential alternative splicing. 2nd Genome PT Symposium (Virtual), July 7, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Ascensão-Ferreira M, Barbosa-Morais NL. Intuitive visualisation of differential alternative splicing. VIZBI 2021 – EMBL Conference: Visualizing Biological Data/EMBL Advanced Training Centre (Virtual), March 24-26, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. XIV CAML Annual PhD Students' Meeting/Faculdade de Medicina da Universidade de Lisboa (Virtual), Lisbon, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Belo RF. AD/PD 2021 – The 15th International Conference on Alzheimer's & Parkinson's Diseases (Virtual), March 9-14, 2021. ONLY ATTENDEE; INTERNATIONAL CONFERENCE.

Belo RF, Bica M, Silva RM, Schneider A, Barbosa-Morais NL. Bioinformatics Matters: more than a cause, an action! 2nd Genome PT Symposium (Virtual), July 7, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Silva RM, Barbosa-Morais NL. Unravelling gene signatures of aging human astrocytes with single-cell transcriptomics. 2nd Genome PT Symposium (Virtual), July 7, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Bica M, Serre K, Barbosa-Morais NL. Single-cell transcriptomics in unravelling the cellular diversity and molecular signature governing anti-tumour functions of myeloid cells. 2nd GenomePT Symposium, (Virtual). July 7, 2021. POSTER; NATIONAL CONFERENCE.

Bica M, Serre K, Barbosa-Morais NL. Single-cell transcriptomics in unravelling the complexity of the breast tumour microenvironment. XIV CAML Annual PhD Students' Meeting/Faculdade de Medicina da Universidade de Lisboa (Virtual), Lisbon, Portugal, May 5-7, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Indi JA, Barbosa-Morais NL, Eyras E. Reference-free identification of open reading frames and encoded proteins from nanopore transcriptomic long reads. 2nd GenomePT Symposium, (Virtual). July 7, 2021. POSTER; NATIONAL CONFERENCE.

Belo RF, Bica M, Silva RM. Bioinformatics Matters: more than a cause, an action! iMM Post-Doc Day (Virtual), May 27, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Saraiva-Agostinho N, Almeida BP, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. 2nd Genome PT Symposium (Virtual), July 7, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Saraiva-Agostinho N, Almeida BP, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. VIZBI 2021 – EMBL Conference: Visualizing Biological Data/EMBL Advanced Training Centre (Virtual), March 24-26, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Saraiva-Agostinho N, Almeida BP, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. XIV CAML Annual PhD Students' Meeting/Faculdade de Medicina da Universidade de Lisboa (Virtual), Lisbon, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Organization of Conferences

Ascensão-Ferreira M. Co-Organizer. XIV CAML Annual PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 5-7, 2021.

Belo RF. Co-Organizer. XIV CAML Annual PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 5-7, 2021.

Networks & Research Infrastructures

Nuno Barbosa Morais. GenomePT - National Laboratory for Genome Sequencing and Analysis. Local PI, work package leader, and member of the Executive Committee. Funding: POCI-01-0145-FEDER-022184, supported by COMPETE 2020 - Operational Programme for Competitiveness and Internationalisation (POCI), Lisboa Portugal Regional Operational Programme (Lisboa2020), Algarve Portugal Regional Operational Programme (CRESC Algarve2020), under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF), and by Fundação para a Ciência e a Tecnologia (FCT) [FPJ001062] - €125,322.

Nuno Barbosa Morais. Horizon 2020 Twinning: "RiboMed: RNA in disease". Co-PI and work package leader (PI: Maria Carmo-Fonseca). Funding: H2020-WIDESPREAD-2018-2020/H2020-WIDESPREAD-2018-03, grant agreement 857119 supported by the European Commission's Research Executive Agency - €424,750.

Prizes & Honors in 2021

Nuno Barbosa Morais refereed manuscripts for *BMC Cancer*, *Frontiers in Medicine*, *Genome Biology*, *Genome Research*, *Nature Communications*, *NPJ Genomic Medicine*, *Nucleic Acids Research*, *PLoS Computational Biology*, and the *RNA Journal*. Mariana Ascensão Ferreira and Nuno Saraiva Agostinho shared some of those reviews.

Ana Marta Bica refereed a manuscript for *BMC Bioinformatics*.

Nuno Barbosa Morais refereed grant applications for Worldwide Cancer Research (WWCR) and UK Research and Innovation - Biotechnology and Biological Sciences Research Council (BBSRC).

Nuno Barbosa Morais refereed PhD research studentship applications for Fundação para a Ciência e a Tecnologia (FCT).

Nuno Barbosa Morais refereed abstract applications for iMED Conference 13.0.

Rita Silva was selected for the 2022 Class of iMM's LisbonBioMed International PhD Program.

Nuno Barbosa Morais was honoured with the medal of Citizen of Merit by the Municipality of Viana do Castelo.

Advanced Teaching

Nuno Barbosa Morais. Lectures and Co-coordination of Curricular Unit. Computational Biology Course. Masters in Biomedical Engineering, Instituto Superior Técnico, Lisbon, Portugal, October - November, 2021.

Nuno Barbosa Morais. Lectures and Coordination of Curricular Unit. Bioinformatics Course. Masters in Oncobiology and Biomedical Research, Faculty of Medicine of the University of Lisbon, Portugal, January - February, 2021.

Nuno Barbosa Morais. Lecture and Tutorial. *Big Data in Ageing*. CAJAL advanced neuroscience course in Ageing Cognition, Bordeaux School of Neuroscience, France, September 30 - October 8, 2021.

Nuno Barbosa Morais. Lecture. *Perspectives in Computational Biology - What transcriptomic data tell us about ageing*. Masters in Computational Biology & Bioinformatics, ITQB NOVA Lisbon, Oeiras, Portugal, November 19, 2021.

Nuno Barbosa Morais. Lecture. *Bioinformatics - Computational biology in the translation of cancer 'omics'*. Masters in Biomedical Research, NOVA Medical School, Lisbon, Portugal, October 12, 2021.

Nuno Barbosa Morais. Lecture. *Computational biology and what transcriptomes tell us about disease*. LisbonBioMed PhD Program, Instituto de Medicina Molecular, Lisbon, Portugal, April 26, 2021.

Nuno Barbosa Morais. Lecture. *Computational biology in the translation of disease 'omics'*. Masters in Biopharmaceutical Sciences and Integrated Masters in Pharmaceutical Sciences, Faculty of Pharmacy of the University of Lisbon, Portugal, March 15, 2021.

Nuno Barbosa Morais. Lecture. *What transcriptomes tell us about diseases*. PhD Program in Molecular Biosciences, ITQB NOVA Lisbon, Oeiras, Portugal, February 9, 2021.

MSc Theses

Rita Silva (16/11/2021), Profiling ageing-associated gene expression alterations in human astrocytes using single cell transcriptomics, Instituto de Medicina Molecular João Lobo Antunes / Instituto Superior Técnico. Supervisor: Nuno Luís Barbosa Morais.

PhD Theses

Marie Bordone, (26/03/2021), The transcriptional landscape of Alzheimer's and Parkinson's diseases, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Nuno Luís Barbosa Morais.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Molecular characterization of innate lymphoid cells, LiMM Therapeutics, Sponsored Research

Science and Society in 2021

Ascensão-Ferreira M. Volunteer speaker. [Conversas com Cientistas - Décadas de Ciência para Dias de Vacinas](#). April, 2021. Ciência Viva initiative for the clarification of doubts on the scientific knowledge supporting COVID-19 vaccine development to school kids and the general public (online events).

Bica M, Silva RM, Ascensão-Ferreira M. Volunteer collaboration with twelfth grade students from Escola Secundária de Mem Martins. The goal of the project was to introduce students to massive parallel sequencing technologies, focusing on RNA-sequencing, as well as R programming language and RStudio. The students also acquired theoretical and practical knowledge of single-cell RNA-sequencing data analysis methods and participated in the development of an application that enables the exploration of cell type composition of human brain tissue from their pre-processed bulk transcriptomes.

Vanessa Morais Lab

Head of Laboratory: Vanessa A. Morais, PhD, Group Leader and Associate Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Ana Beatriz Marta Ferreira Madeira Ramos	Master Degree	Lab Technician (Started April)
Andreia Sofia Faria Pereira	Master Degree	PhD Student
Bernardo Cetra Antunes	Master Degree	PhD Student
Carlos Eduardo Cardanho dos Ramos	Master Degree	PhD Student
Elvira Pequeno Leites	Master Degree	PhD Student
Filipa Alexandra Barroso Gonçalves	Master Degree	PhD Student
Filipe Carlos Pereira dos Reis Cortes Figueiredo	Master Degree	PhD Student
Isa Fernandes Mota	University Degree	MSc Student (Started September)
Renata Lopes Familiar Couto	PhD	Postdoctoral Researcher
Rúben Filipe Alves Simões	High School Diploma	MSc Student (Started April)

Graphical Abstract

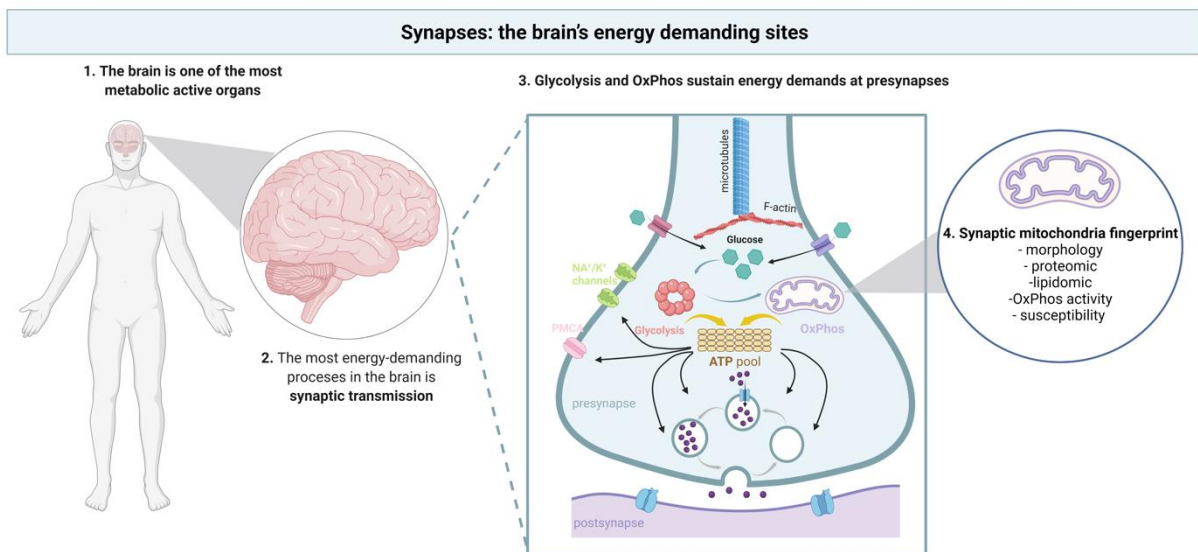


Image caption: Synapses: the brain's energy demanding sites. Faria-Pereira, A; Morais, V.A. (submitted).

Lab Interests

Our overarching goal is to clarify the intimate crosstalk between the host cell – the neuron – and the powerhouse organelle – the mitochondria.

Mitochondria at the synapse have a pivotal role in neurotransmitter release, but almost nothing is known about synaptic mitochondria composition or specific functions. Synaptic mitochondria compared to mitochondria in other cells, need to cope with increased calcium load, more oxidative stress, and high energy demands that sustain neurotransmitter release and synaptic plasticity.

Our research interests aim at deciphering the intrinsic properties of synaptic mitochondria and to scrutinize their relevance for the healthy brain. For this, we aim to assess the protein fingerprint, the metabolic profile and fuel preference of synaptic mitochondria; the mitochondrial clearance and biogenesis rates at synapse, as well as the contribution of mitochondrial dynamics to neural stem cell fate. Ultimately, we intend to unveil how disruption of these synapse-specific mechanisms contribute to neurodegeneration.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

A proper mitochondrial function is of utmost importance in neurons. However, little is known about mitochondrial biology and brain homeostasis.

At present, we have unraveled the protein fingerprint that will allow the discrimination between synaptic and non-synaptic mitochondria, and we are now scrutinizing the metabolic fuel preference of mitochondria at synapse. Additionally, we have observed that mitochondrial dynamics play a crucial role in neural stem cell fate. We have also developed a new open-source research tool (variant level determination algorithm) that will enable us to analyze mitochondrial DNA genome using a very limited amount of sample. This research tool will facilitate the assessment of mitochondria DNA in clinical samples where metabolic and neurological disorders may be at stake.

Our research findings are yielding promising molecular targets that will enable us to unravel the importance of mitochondrial function for synapse biology, and overall brain homeostasis.

Ongoing Projects in 2021

2021/2024: Função mitocôndrial em Esclerose Múltipla: abordagens para prever progressão da doença e promover remielinização. Coordinator: Vanessa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: MITOCHONDRIALMS - PTDC/MED-NEU/7976/2020. Amount: 249 987,50€. Total Amount: 249 987,50€.

2018/2021: Mecanismos moleculares que mantêm a Homeostase Mitocondrial no Cérebro. Coordinator: Vanessa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/31230/2017. Amount: 239 998,20€. Total Amount: 239 998,20€.

2016/2021: SynapticMitochondria: Quality Control and Maintenance of Synaptic Mitochondria. Coordinator: Vanessa Morais. Funding Agency: European Commission. Reference: ERC StG 679178. Amount: 1 300 000,00€. Total Amount: 1 300 000,00€.

Scientific Impact

Academic Collaborations

Bart de Strooper, VIB, Belgium
 Jeffrey Savas, North Western University, Chicago USA
 Friedemann Paul, Charité | MDKZ, Berlin, Germany
 Christine Klein, University Luebeck, Germany

Selected Publications

Soares R, Ribeiro FF, Lourenço DM, Rodrigues RS, Moreira JB, Sebastião AM, Morais VA, Xapelli S (2020) [Isolation and expansion of neurospheres from postnatal \(P1–3\) mouse neurogenic niches](#). **Journal of Visualized Experiments**, 159: e60822.

Relevance of the publication: A methods paper with visual-aid that clearly shows how mouse neurosphere cultures from neural stem cell niches can be obtained and maintained, and enabling cell-based assays and neural differentiation.

Aerts L, Craessaerts K, De Strooper B, Morais VA (2015). [PINK1 kinase catalytic activity is regulated by phosphorylation on serines 228 and 402](#). **The Journal of Biological Chemistry** 290:2798-811.

Relevance of the publication: In this work we show that the Parkinson's disease gene PINK1 modulates its specificity towards its substrates by autophosphorylation modifications.

Morais VA*, Haddad D, Craessaerts K, De Bock P, Swerts J, Vilain S, Aerts L, Overbergh L, Grünewald A, Seibler P, Klein C, Gevaert K, Verstreken P, De Strooper B* (2014). [PINK1 loss of function mutations affect mitochondrial complex I activity via Ndufa10 ubiquinone uncoupling](#). **Science** 344:203-7. *shared corresponding authors.

Relevance of the publication: Here we show that PINK1 mediates the phosphorylation of an electro-transport chain Complex I subunit, thereby regulating the coupling of Complex I to ubiquinone.

Haddad D, Vilain S, Vos M, Esposito G, Matta S, Kalscheuer V, Craessaerts K, Leyssen M, Morais VA*, Verstreken P* (2013). [Mutations in the intellectual disability gene Ube2a cause neuronal dysfunction and impair parkin-dependent mitophagy](#). **Molecular Cell** 50:831-41. *shared corresponding authors.

Relevance of the publication: In intellectual disability patients we found mutations in the E2 conjugase Ube2a and showed that it acts with the E3 ligase Parkin to mediate mitophagy.

Morais VA, Verstreken P, Roethig A, Smet J, Snellinx A, Vanbrabant M, Haddad D, Frezza C, Mandemakers W, Vogt-Weisenhorn D, Van Coster R, Wurst W, Scorrano L, De Strooper B (2009). [Parkinson's disease mutations in PINK1 result in decreased Complex I activity and deficient synaptic function](#). **EMBO Molecular Medicine** 1:99-111.

Relevance of the publication: A landmark paper that has changed the PINK1 field: PINK1 loss-of-functions causes reduced mitochondrial Complex I activity.

2021 Publications in Peer-Reviewed Journals

Cardanho-Ramos C. and Morais VA (2021). [Mitochondrial Biogenesis in Neurons: How and Where](#). **International Journal of Molecular Sciences**, 22(23): 13059.

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, de Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu Y, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Barbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL (2021). [Allosteric Antagonist Modulation of TRPV2 by Piperlongumine Impairs Glioblastoma Progression](#). **ACS Cent Sci** 7(5):868-881.

Cortes-Figueiredo F, Carvalho FS, Fonseca AC, Paul F, Ferro JM, Schönherr S, Weissensteiner H, Morais VA (2021) [From forensics to clinical research: expanding the variant calling pipeline for the precision ID mtDNA whole genome panel](#). **International Journal of Molecular Sciences** 22(21): 12031.

El Manaa W, Duplan E, Goiran T, Lauritzen I, Vaillant Beuchot L, Lacas-Gervais S, Morais VA, You H, Qi L, Salazar M, Ozcan U, Chami M, Checler F, Alves da Costa C. (2021) [Transcription- and phosphorylation-dependent control of a functional interplay between XBP1s and PINK1 governs mitophagy and potentially impacts Parkinson disease pathophysiology](#). **Autophagy**, 17(12):4363-4385.

Gonçalves FB, Morais VA. (2021 Apr 21) [PINK1: A Bridge between Mitochondria and Parkinson's Disease](#). **Life** (Basel).;11(5):371.

Leites EP, Morais VA. (2021) [The PINK1-Mediated Crosstalk between Neural Cells and the Underlying Link to Parkinson's Disease](#). **Cells** 10(6):1395

Soares R, Ribeiro FF, Lourenço DM, Rodrigues R S, Moreira J B, Sebastião A M, Morais V A, Xapelli S (2021) [The neurosphere assay: an effective in vitro technique to study neural stem cells](#). **Neural Regeneration Research** 16(11):2229-2231

Invited Lectures and Seminars

Morais VA. Mitochondrial Bioenergetics in Neurodegeneration. 17th International Symposium SPDM (Virtual Meeting), Lisbon, Portugal, 8 to 10 Set 2021.

Communications

Cardanho-Ramos C, Morais VA. Mitochondrial biogenesis at the synapse requires local protein synthesis. XVI CAML PhD students' meeting. IMM, Lisbon, Portugal. ORAL COMMUNICATION. NATIONAL.

Cortes-Figueiredo, F, Morais VA. Multiple Sclerosis and mitochondrial DNA mutations - is there a link?. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting, Lisbon, Portugal, May 5–7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: modulator of adult neural stem cell fate. XVII Meeting of the Portuguese Society for

Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Investigating Mitochondrial Dynamics as regulator of adult neural stem cell differentiation. V Symposium Portuguese Glial Network – Glial cells at the crossroad of health and disease, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics as modulator of adult neural stem cell fate, XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE

Leites EP, Morais VA. Brain homeostasis in Parkinson's disease: Role of PINK1 in neurons, astrocytes and microglia. XIV CAML – IV NeuroULisboa PhD Students, Lisbon, Portugal, May 7th, 2021. ORAL PRESENTATION; NATIONAL CONFERENCE.

Bernardo Antunes. The Metabolic Profile of Synaptic Mitochondria. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL PRESENTATION; NATIONAL CONFERENCE.

Prizes & Honors in 2021

PRIZES:

Cardanho-Ramos C. Fifth Best Oral Presentation – XIV CAM-IV NeurULisboa PhD Students Meeting, May 5-7, 2021.

Soares R. Mobility grant from Horizon 2020 SIMICA project to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Antunes B. Second best oral presentation (beginner's panel). XIV CAM-IV NeurULisboa PhD Students Meeting; National Conference, May 5-7, 2021.

BOARD MEMBER:

Morais VA. Member of the E-mit European mitochondrial society network.

INVITED REFEREE:

Morais VA. Member of the evaluation panel for the Portuguese Science Foundation FCT PhD fellowships, Biochemistry and Experimental Biology panel.

Morais VA. Ad-hoc Reviewer for Grant Evaluations panels of the ERC Synergy Grant, EMBO, GAPIC fellowships, Pfizer prize.

Morais VA. Ad hoc Reviewer to Journals: Molecular Cell, JBC, JCB, PLoS Biology, PLoS One, eLIFE, EMBO Mol Cell, EMBO, Neuron, Mitochondria.

Advanced Teaching

Morais VA. Member of the Scientific Advisory Board of the Instituto de Medicina Molecular João Lobo Antunes Training Hub.

Morais VA. Lecture for 1st year medical students – Molecular and Cellular Biology Discipline, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

Morais VA. Lecture in Master Program - Biochemistry of Neurodegeneration Course. Faculty of Science University of Lisbon FCUL, Lisbon, Portugal.

Morais VA. Lecture in Master Program – Biochemistry for Health, ITQB, UNL, Oeiras, Portugal

Morais VA. Lecture in PhD Program – Towards a Creative and Critical mind, LisbonBioMed PhD Programme, iMM, Lisbon, Portugal.

Morais VA. Lecture in Master Program: Advanced Techniques II, MIB – Master Integrated Biomedicine, iMM- JLA Master Programme, iMM, Lisbon, Portugal.

Antunes B, Morais VA. **Student tutoring for the Bachelor in Nutrition Sciences (course unit Estágio de Iniciação à Investigação)**. Do Synaptic Mitochondria have a different metabolic profile when compared with Non-Synaptic Mitochondria? October 2021, FMUL/iMM Lisbon, Portugal.

Valorization of Knowledge / Social and Economic Impact

Science and Society in 2021

Cortes-Figueiredo, F. Conversations with Scientists — decades of Science for days of Vaccines (“Conversas com Cientistas — Décadas de Ciência para Dias de Vacinas”) — Campaign aiming to communicate to the general population the scientific process behind the COVID-19 vaccines. April 22 and 29, 2021.

Cortes-Figueiredo, F. Science without closets (“Ciência sem Armários”), by SciDoArmário — Initiative aiming to promote, represent, and bring visibility to LGBTIQ individuals in the STEM (Science, Technology, Engineering, and Mathematics) community. May 18, 2021.

VMorais Lab Members. Organization and participation in the “European Researchers' Night” event, held in the National Museum of Natural History and Science, in Lisbon, Portugal. This involved assembling a mitochondria-related game for everyone to play with: from 3 to 99 years old and for people with or without any scientific background, where mitochondrial concepts were very smoothly introduced, as well as, the impact that fundamental biomedical research can have in better diseases diagnosis and treatments.

Maria Mota Lab

Head of Laboratory: Maria M. Mota, PhD, Group Leader and Executive Director of Instituto de Medicina Molecular João Lobo Antunes

Team

Ana Filipa Caetano Parreira	University degree	Lab Technician
Ana Margarida Aires Alves Vigário	PhD	Visiting Researcher
Ângelo António Ferreira Chaves do Rosário Chora	PhD	Senior Postdoctoral Researcher
Aparajita Lahree	PhD	PhD Student (Left September)
Bárbara Daniela Araújo Pinheiro Teixeira	Master degree	PhD Student (Started May)
Cristina Fernández Arias	PhD	Visiting Researcher
Debanjan Mukherjee	Master degree	PhD Student
Inês Fernandes Bento	PhD	Senior Postdoctoral Researcher
Maria Inês Moreira Oliveira Leite Marreiros	Master degree	PhD Student
Marta Sofia Martinez Barata	University degree	MSc Student
Nuno Miguel Valente Leal	University degree	MSc Student
Sara de Jesus Santos Baptista	Master degree	PhD Student
Sofia Pinto Guia Marques	PhD	Lab Manager
Sónia Maria Leite Pereira	Master degree	PhD Student
Soraia Cristina Marques Caetano	PhD	Postdoctoral Researcher (Left December)
Vanessa Alexandra Zuzarte Luís	PhD	Senior Postdoctoral Researcher (Left March)
Yash Girish Pandya	PhD	Postdoctoral Researcher
Yvonne Azasi	PhD	Postdoctoral Researcher

Graphical Abstract

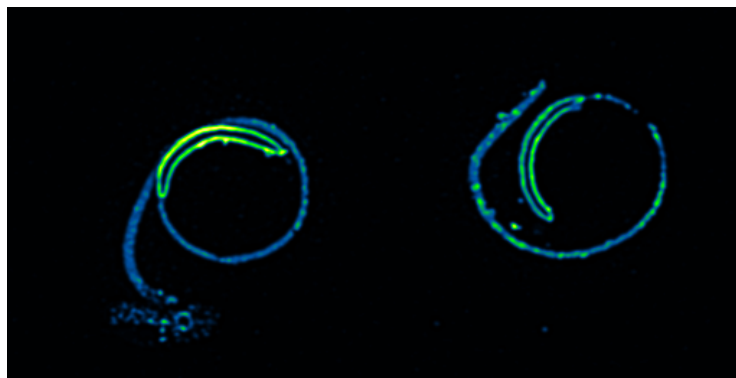


Image caption: *Plasmodium berghei* sporozoites gliding on glass, stained for the parasite Circumsporozoite protein (by Sara Baptista).

Lab Interests

Malaria, caused by *Plasmodium* parasites, still kills a child every minute. Disease combat, impaired by a poor understanding of the factors that dictate the onset and outcome of infection, is more pressing than ever.

Indeed, the COVID-19 pandemic has resulted in unprecedented challenges to health systems worldwide, including in malaria services, which led to a marked increase in cases and deaths.

We aim to elucidate some of the most fundamental and conceptually innovative questions of Host-Plasmodium interactions by pursuing two long-lasting questions: (i) What is so special about the liver that allow *Plasmodium* to achieve an extraordinary rate of replication? & (ii) Why do people die of malaria? Through the process of answering these broad questions and testing our hypotheses, we are making pivotal contributions to unravel the molecular components and functions behind the intricate Host-*Plasmodium* interactions paving the way for new intervention strategies against this deadly disease.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

Eukaryotes have canonical pathways for responding to amino acid (AA) availability. Under AA-limiting conditions, the TOR complex is repressed, while the sensor kinase GCN2 is activated. While these pathways have been highly conserved throughout evolution, malaria parasites are a rare exception. *Plasmodium*, although auxotrophic for most AA, does not have neither a TOR complex nor the GCN2 downstream transcription factors. How these organisms detect and respond to AA-fluctuations in the absence of these pathways remains elusive. Our most recent data identify a previously unknown set of parasite heterogeneous responses mediated by an AA-sensing mechanism that is critical for modulating parasite cell cycle and survival under AA fluctuations.

Ongoing Projects in 2021

2018/2021: Hepatic metabolism driving Plasmodium replication. Coordinator: Maria Mota. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-030751. Amount: 239 886,62€. Total Amount: 239 886,62€.

2018/2021: Plasmodium Iron regulatory Network: the need to sense, acquire and detoxify. Coordinator: Vanessa Zuzarte-Luís. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-MOL/30112/2017. Amount: 239 761,60€. Total Amount: 239 761,60€.

2018/2021: Plasmodium cross-stage interplay modulates Severe Malaria pathology. Coordinator: Ângelo Chora. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/28664/2017. Amount: 239 058,69€. Total Amount: 239 058,69€.

2018/2021: Plasmodium Exploitation of Liver-specific Methionine Metabolism. Coordinator: Maria Mota. Funding Agency: “la Caixa” Foundation. Reference: PoEMM: La Caixa. Amount: 499 950,00€. Total Amount: 499 950,00€.

2018/2021: Sanofi - Institut Pasteur Awards 2018. Coordinator: Maria Mota. Funding Agency: Institut Pasteur. Reference: Sanofi - Institut Pasteur Awards 2018. Amount: 150 000,00€. Total Amount: 150 000,00€.

2018/2021: Prémio Lóreal. Coordinator: Inês Bento. Funding Agency: L'oréal Paris. Reference: PRÉMIO LOREAL. Amount: 13 500,00€. Total Amount: 13 500,00€.

Scientific Impact

Academic Collaborations

Shalev Itzkovitz, Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel.

William R. Heath, Department of Microbiology and Immunology, Peter Doherty Institute for Infection and Immunity, University of Melbourne, Melbourne, VIC 3000, Australia.

Ann T. Tate, Department of Biological Sciences, Vanderbilt University, Nashville, TN, USA.

Mara K N Lawniczak, Parasites and Microbes Programme, Wellcome Sanger Institute, Hinxton, UK.

Björn Kafsack, Department of Microbiology and Immunology, Weill Cornell Medical College, NY, USA.

Catherine Merrick, Department of Pathology, University of Cambridge.

Ian Cheeseman, Host-Pathogen interactions program at Texas Biomedical Research Institute.

Selected Publications

Mello-Vieira J, Enguita FJ, de Koning-Ward TF, Zuzarte-Luís V, Mota MM (2020). [Plasmodium translocon component EXP2 facilitates hepatocyte invasion](#). **Nature Communications** 11(1):5654.

Relevance of the publication: *Plasmodium* parasites possess a translocon that exports parasite proteins into the infected erythrocyte. The different translocon components are also expressed during the liver stage of infection but their function remains unexplored. A combination of genetic and chemical assays revealed that the translocon component Exported Protein 2 (EXP2) is critical for parasite invasion of hepatocytes; and not later, when parasite is developing inside the hepatocyte, surrounded by a parasitophorous vacuole membrane, and where translocon molecules are expected to play their role. Activity of EXP2 - a pore-forming protein that is secreted from the invading parasite upon contact with the host cell milieu - induces hepatocyte membrane repair, which is key for parasite invasion. Overall, our findings propose an active participation of the host cell in *Plasmodium* invasion, challenging the current view of the establishment of liver stage infection.

Real E, Rodrigues L, Cabal GG, Enguita FJ, Mancio-Silva L, Mello-Vieira J, Beatty W, Vera IM, Zuzarte-Luís V, Figueira TN, Mair GR, Mota MM (2018). [Plasmodium UIS3 sequesters host LC3 to avoid elimination by autophagy in hepatocytes](#). **Nature Microbiology** 3(1):17-25.

Relevance of the publication: Our work shows that *Plasmodium berghei* parasites infecting hepatic cells rely on a parasite protein – UIS3 – that resides at the parasitophorous vacuole membrane to avoid elimination by host-cell-mediated autophagy. UIS3 acts as a bona fide autophagy inhibitor by competing with host LC3-interacting proteins for LC3 binding. We propose that the protein-protein interaction between UIS3 and host LC3 represents a target for antimalarial drug development.

Zuzarte-Luís V, Mello-Vieira J, Marreiros IM, Liehl P, Chora ÂF, Carret CK, Carvalho T, Mota MM (2017). [Dietary alterations modulate susceptibility to *Plasmodium* infection](#). **Nature Microbiology** 2:600-1607.

Relevance of the publication: By showing that administration of a high-fat diet to mice for a period as short as 4 days impairs *Plasmodium* liver infection by over 90%, our data reveal that acute and transient dietary alterations markedly impact the establishment of a *Plasmodium* infection and disease outcome.

Mancio-Silva L, Slavic K, Grilo Ruivo MT, Grosso AR, Modrzynska KK, Vera IM, Sales-Dias J, Gomes AR, MacPherson CR, Crozet P, Adamo M, Baena-Gonzalez E, Tewari R, Llinás M, Billker O, Mota MM (2017). [Nutrient sensing modulates malaria parasite virulence](#). **Nature** 13:213-216.

Relevance of the publication: This study shows that *Plasmodium* blood-stage parasites actively respond to host dietary calorie alterations through rearrangement of their transcriptome accompanied by substantial adjustment of their multiplication rate. A kinome analysis combined with chemical and genetic approaches identified KIN as a critical regulator that mediates sensing of nutrients and controls a transcriptional response to the host nutritional status. KIN shares homology with SNF1/AMPK α , and yeast complementation studies suggest that it is part of a functionally conserved cellular energy-sensing pathway. Overall, these findings reveal a key parasite nutrient-sensing mechanism that is critical for modulating parasite replication and virulence.

Liehl P, Zuzarte-Luís V, Chan J, Zillinger T, Baptista F, Carapau D, Konert M, Hanson KK, Carret C, Lassnig C, Müller M, Kalinke U, Saeed M, Chora AF, Golenbock DT, Strobl B, Prudêncio M, Coelho LP, Kappe SH, Superti-Furga G, Pichlmair A, Vigário AM, Rice CM, Fitzgerald KA, Barchet W, Mota MM (2014). [Host-cell sensors for *Plasmodium* activate innate immunity against liver-stage infection](#). **Nature Medicine** 20:47-53.

Relevance of the publication: Before they infect red blood cells and cause malaria, *Plasmodium* parasites undergo an obligate and clinically silent expansion phase in the liver that is has been thought to be undetected by the host. In this study, we have challenged this dogma by showing that the liver has sensor mechanisms for *Plasmodium* that mediate a functional antiparasite response driven by type I IFN.

2021 Publications in Peer-Reviewed Journals

Arias, C. F., Herrero, M. A., Bertocchini, F., Acosta, F. J., & Fernandez-Arias, C. (2021). [Modeling the Dependence of Immunodominance on T Cell Dynamics in Prime-Boost Vaccines](#), **Mathematics**, 9(1), 28.

Canto E Castro L, Pereira AHG, Ribeiro R, Alves C, Veloso L, Vicente V, Alves D, Domingues I, Silva C, Gomes A, Serrano M, Afonso Â, Veldhoen M, de Sousa MJR, de Sousa JGR, de Sousa G, Mota MM, Silva-Santos B, Ribeiro RM. [Prevalence of SARS-CoV-2 Antibodies after First 6 Months of COVID-19 Pandemic, Portugal](#). **Emerg Infect Dis**. 2021 Nov;27(11):2878-2881.

Veldhoen M, Zuzarte-Luis V. [Academic labs supporting COVID-19 diagnostics](#). **Eur J Immunol**. 2021 Jan;51(1):13-16.

Pre-Print Publications

Viriato M'Bana, Aparajita Lahree, Sofia Marques, Ksenija Slavic and Maria Manuel Mota (2021) *Plasmodium* Parasitophorous Vacuole Membrane-Resident Protein UIS4 Manipulates Host Cell Actin to Avoid Parasite Elimination. SSRN. <http://dx.doi.org/10.2139/ssrn.3921345>

Amichay Afriat, Vanessa Zuzarte-Luís, Keren Bahar Halpern, Lisa Buchauer, Sofia Marques, Aparajita Lahree, Ido Amit, Maria M. Mota, Shalev Itzkovitz. (2021) A spatiotemporally resolved single cell atlas of the *Plasmodium* liver stage. bioRxiv. <https://doi.org/10.1101/2021.12.03.471111>

Invited Lectures and Seminars

Ângelo Chora, 'Plasmodium cross-stage interplay dictates malaria outcome'. New Voices in Infection Biology, Max Planck Institute for Infection Biology, Berlin, Germany, 15th of December 2021 (virtual).

Maria Mota, "The Hepatocyte as a Household for *Plasmodium* Parasites", November 18th 2021, 30th Irwin Arias Symposium.

Maria Mota, "The classical epidemiological triad in malaria infections", October 21st 2021, Institut Pasteur Seminar.

Maria Mota, "The classical epidemiological triad in malaria infections". September 23rd 2021, Johns Hopkins University.

Sofia Marques, Unveiling Host-Parasite interactions: *Plasmodium* and the Liver. June 17th 2021 - CiiEM congress. Online event.

Inês Bento, 'Cycling is all that matters: Malaria parasite is governed by different biological rhythms'. New Voices in Infection Biology, Max Planck Institute for Infection Biology, Berlin, Germany, 9th of June 2021 (virtual).

Communications

Yvonne Azasi, "Complement C1s cleaves PfEMP1 at interdomain conserved sites inhibiting *Plasmodium falciparum* cytoadherence" West African Centre for Cell Biology of Infectious Pathogens Research Conference, Legon, Ghana. 21st -23rd July, 2021. (Oral presentation)

Aparajita Lahree, gRABing the APPLE : *Plasmodium* hijacks a host endosomal adaptor during liver stage development. EMBL conference - BioMalPar XVII: Biology and Pathology of the Malaria parasite (25-27 May 2021 -Virtual, EMBL.

Advanced Teaching

Anastasia Selivanova. 'Estágio de Iniciação à Investigação - How does *Plasmodium* sense and respond to altered nutrient availability?' FMUL. September - November 2021. Supervisor: Yash Pandya.

Rute Alves. 'Estágio de Iniciação à Investigação - How does *Plasmodium* sense and respond to altered nutrient availability?' FMUL. September - November 2021. Supervisor: Yash Pandya.

Catarina Mendonça. 'Programa Co-Labs - Understanding the mechanisms of *Plasmodium* liver stage schizogony'. IST. March – June 2021. Supervisor: Inês Bento.

Maria Martelo. 'Projeto em Biologia Celular e Molecular - Understanding the mechanisms of *Plasmodium* liver stage schizogony'. FCT NOVA. March – June 2021. Supervisor: Inês Bento.

MSc Theses

Marta Barata, 25/11/2021, Immune-independent control mechanisms of *Plasmodium* parasite virulence, Instituto Superior Técnico da Universidade de Lisboa, Supervisor: Ângelo Ferreira Chora.

PhD Theses

Aparajita Lahree, 30/07/2021, "Endosomal dynamics at the Host-*Plasmodium* interface through liver-stage parasite development" – Instituto Superior Técnico, Universidade de Lisboa. Supervisor: Maria Manuel Mota. Co-Supervisor: Gabriel Monteiro.

Valorization of Knowledge / Social and Economic Impact

Intellectual Property Rights in 2021

International application, INSTITUTO DE MEDICINA MOLECULAR JOÃO LOBO ANTUNES, Maria Mota, Sonali Setua, Francisco Enguita, Varadharajan Sundaramurthy, Harish Ranga-Prasad. ANTI-MALARIAL COMPOUNDS. US 63/117,743 (17.11.2020) No: PCT/PT2020/050021 (17.11.2021).

Science and Society in 2021

Sofia Marques, Inês Bento. "Mosquito Lab - Malaria", 8ª ed. AIMS Masterclasses, 6 Novembro 2021.

Inês Bento. 'F.I.C.A. – Festival Internacional de Ciência', 12-17 Outubro 2021.

Inês Bento. 'Noite europeia dos investigadores', 24 Setembro 2021.

Maria Mota. Encontro Ciência 2021, Investigar na Europa com o Horizonte Europa – Pilar 1 e o ERC; laCaixa iMM - da investigação à sociedade & A Ciência e economia, recuperação e resiliência, 28 e 29 Junho 2021.

Maria Mota. 19º Café de Ciência no Parlamento, 5 Maio 2021.

Maria Mota. UNICEF Portugal Semana Mundial da Imunização, 30 Março 2021.

Maria Mota. Embaixada de França - Igualdade entre mulheres e homens em tempo de pandemia - mundo da investigação, 25 Março 2021.

Maria Mota. Liderança no Feminino na UL- Estados Gerais VI, Associação Académica da UL, 21 Março 2021.



Sofia Marques, Aparajita Lahree. “Mosquito Lab - Malaria”, 7ª ed. AIMS Masterclasses, 20 Março 2021.

Maria Mota. As Mulheres na Ciência (núcleo nano FCT/UNL). 13 Março 2021.

Joana Neves Lab

Head of Laboratory: Joana Neves, PhD, Group Leader

Team

Ana Cristina Costa Sousa	University Degree	MSc Student (Started September)
Bárbara de Ferreira Pimenta Mouta e Pereira	High School Diploma	Trainee (Started March)
Débora Alexandra Prata Pinheiro de Castro	University Degree	MSc Student (Started August)
Júlia Garrido Fernandes	University Degree	Trainee
Mariana Simas Faria	Master Degree	Trainee (Started June. Left November)

Graphical Abstract

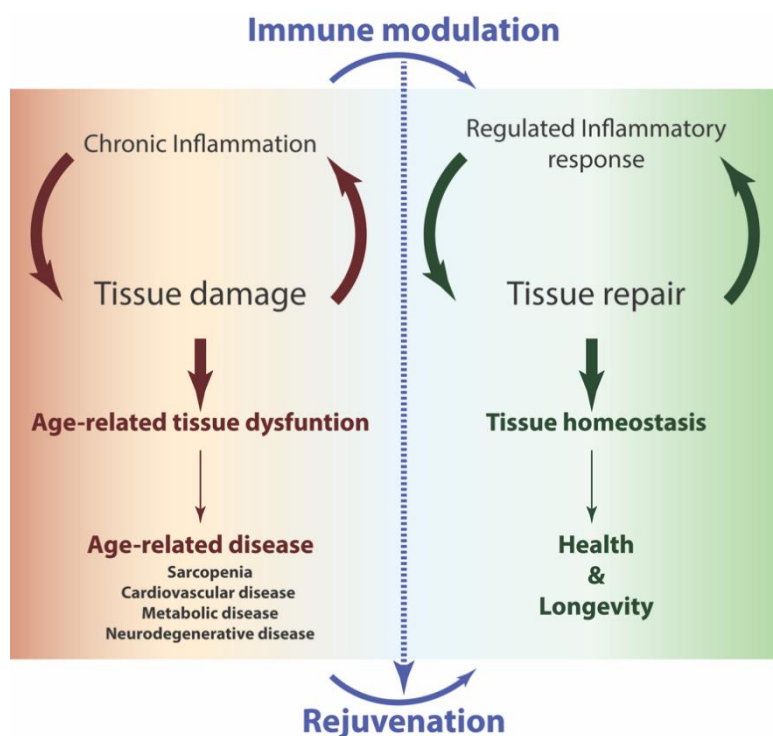


Image caption: Chronic inflammation as a target for anti-aging interventions. In young healthy organisms (right, green) optimal tissue repair capacity and a regulated inflammatory response sustain tissue homeostasis and maintain organismal health. During aging (left, red), chronic inflammation and tissue damage create an auto amplifying loop that drives tissue dysfunction, leading to disease. Immune modulatory interventions that restore a regulated inflammatory response promote tissue repair and could be envisioned as rejuvenating interventions (blue arrows) for several age-related diseases.

Lab Interests

Tissue repair processes have evolved as mechanisms of healing damaged organs. We are interested in harnessing the potential of tissue repair to promote organ rejuvenation. We use skeletal muscle regeneration as a paradigm of tissue repair to understand the molecular and cellular basis of the immune modulatory component of tissue regeneration and how its

dysregulation in ageing and disease can be targeted to optimize stem cell-based therapies. Our goal is to identify pathways that are used by immune cells to modulate the inflammatory tone of the tissue environment, with the goal of identifying new molecules with immune modulatory properties and therapeutic potential in regenerative medicine applied to old patients. The Neves lab is part of the Ageing & Tissue Repair joint lab, running two independent, complementary and cooperative research programs focused on biology of stem cell aging and the age-associated changes in the immune environment.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy

Major Scientific Achievements in 2021

This year we explored the mechanisms through which MANF controls the repair-associated myeloid response and how they are impacted in aging. We discovered that aging leads to a delay in the emergence of pro-repair macrophages during tissue repair that can be linked to a specific autocrine function of MANF in macrophages. Through a combination of transcriptome analysis and electron microscopy on macrophages we uncovered defects in lysosomal-associated lytic vesicles and ultrastructural alterations in vesicular compartments consistent with defects in the phagocytic pathway. Using mass spectrometry analysis we have also uncovered an unexpected interaction between MANF, catalase, peroxisomal and redox proteins *in vivo*. We are now using genetic manipulations in *Drosophila* to uncover the cross-talk between MANF and the peroxisomal pathways and mouse models to understand the link between MANF signaling, impairments in phagocytic activity and loss of pro-repair capacity of macrophages in aging.

Ongoing Projects in 2021

2020/2021: MANF role in bone marrow hematopoiesis. Coordinator: Joana Neves and Pedro Sousa-Victor. Funding Agency: Genentech, Inc.. Reference: MANF ROLE IN BONE MARROW HEMATOPOIESIS. Amount: 42 200,00€. Total Amount: 42 200,00€.

Scientific Impact

Academic Collaborations

Heinrich Jasper, Genentech
Deepak Lamba, University of California, San Francisco

Selected Publications

Neves J, Zhu J, Sousa-Victor P, Konjikusic M, Riley R, Chew S, Qi Y, Jasper H, Lamba DA (2016). [Immune modulation by MANF promotes tissue repair and regenerative success in the retina.](#) *Science* 353(6294):aaf3646.

Relevance of the publication: This work characterized a new evolutionarily conserved mechanism of tissue repair based the immune modulatory activity of MANF and showed that this activity is necessary for MANF's pro-repair function *in vivo*. We showed that MANF therapy is sufficient to delay retinal degeneration and to improve the integration efficiency of transplanted photoreceptors and improvement

of visual function. These findings provided a proof of principle for the use of immune modulators in improving the success of regenerative therapies.

Sousa-Victor P*, Neves J*, Cedron-Craft W, Ventura PB, Liao CY, Riley RR, Soife I, van Bruggen N, Kolumam GA, Villeda SA, Lamba DA, Jasper H (2019). [MANF regulates metabolic and immune homeostasis in ageing and protects against liver damage](#). *Nature Metabolism* 1(2):276–290.

Relevance of the publication: This work provides the first demonstration that MANF (Mesencephalic Astrocyte-derived Neurotrophic Factor) is a systemic regulator of organismal homeostasis that declines during ageing and a proof of principle for the use of MANF as a treatment for age related diseases. We found that MANF levels are systemically down-regulated during ageing in flies, mice and humans and we used genetic manipulations in flies and mice to demonstrate that MANF is necessary to limit inflammation and maintain tissue homeostasis in young organisms. Moreover, using genetic and pharmacologic interventions, we showed that MANF is an effective therapy to reverse several hallmarks of tissue ageing in older organisms and extend lifespan in flies. This work described the potential of immune modulators to prevent or delay age-related tissue dysfunction and described an important model of chronic inflammation that can be used in subsequent studies to isolate the inflammatory component of the ageing process.

Neves J**, Chirco KR, Cedron-Craft W, Chew S, Zhu J, Jasper H, Lamba DA** (2020). [MANF delivery improves retinal homeostasis and cell replacement therapies in ageing mice](#). *Experimental Gerontology* 134:110893.

Relevance of the publication: This work identified age-related alterations in retinal homeostasis, leading to age-related retinal inflammation and damage susceptibility. We showed that MANF loss in the aged choroid is associated with increased densities of activated macrophages, limited homeostatic capacity after damage imposed by light exposure and reduced engraftment efficiency of exogenously supplied photoreceptors. We further showed that supplementation of MANF recombinant protein can improve retinal homeostasis and repair capacity, correlating with reduced numbers of activated macrophages in the old retina. This work provides the first demonstration that aging alone imposes a limitation to the repair capacity in the retina that can be ameliorated with MANF.

Neves J*, Sousa-Victor P*, Jasper H (2017). [Rejuvenating Strategies for Stem Cell-Based Therapies in Aging](#). *Cell Stem Cell* 20(2):161-175.

Relevance of the publication: In this review we discuss the major roadblocks imposed by aging to regenerative medicine. We highlight studies that have identified a growing number of promising rejuvenating interventions and propose a strategy to improve stem cell-based therapies through the simultaneous targeting of stem cell intrinsic limitations and niche dysregulations.

Neves J**, Sousa-Victor P** (2020). [Regulation of inflammation as an anti-ageing intervention](#). *FEBS Journal* 287(2020):43–52.

Relevance of the publication: In this perspective we discuss the rejuvenation potential of interventions that target chronic inflammation. We specifically highlight studies pointing to research strategies that could be used in the identification of new targets to improve tissue repair in aged organs based on the modulation of inflammatory pathways.

2021 Publications in Peer-Reviewed Journals

Kramer J, Neves J, Koniikusic M, Jasper H, Lamba DA (2021) [Dpp/TGFβ-superfamily play a dual conserved role in mediating the damage response in the retina](#). *PLoS One* 16 (10), e0258872.

Advanced Teaching

Joana Neves (Lecture). Ageing and Tissue Repair. Lisbon BioMed PhD Program seminar series “Towards a Creative and Critical Mind”, University of Lisbon, Lisbon, Portugal, April 29, 2021.

Joana Neves (Lecture). Immune modulatory interventions in ageing and tissue repair. Seminar for Histology Class – 2nd year Medical Students, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 2nd, 2021.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Characterize the role of MANF in bone-marrow hematopoiesis, Genentech, Sponsored Research/Collaborative Research.

Science and Society in 2021

Joana Neves was an invited speaker at JorTEC Biologia 2021, an event organized by students from the Faculty of Sciences and Technology from Nova University. February 18th 2021. Target Audience: BSc students.

Joana Neves was interviewed for the Portuguese Newspaper “Publico” about career path and direction of aging research. January 18th 2021. Target Audience: General Public.

Miguel Prudêncio Lab

Head of Laboratory: Miguel Prudêncio, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Adriana Beatriz Oliveira Temporão	Master Degree	PhD Student
Américo José dos Santos Alves	Master Degree	PhD Student
Ana Catarina Freire Fraga	University Degree	MSc Student (Started September)
Ana Filipa Gonçalves Teixeira	Master Degree	Lab Technician (Left April)
António Manuel Barbeiro Mendes	PhD	Senior Postdoctoral Researcher
Bárbara Daniela Araújo Pinheiro Teixeira	Master Degree	PhD Student (Started March)
Carla Sofia Bastos Oliveira	University Degree	Lab Technician (Started February)
Catarina Maria Vicente Rôla	University Degree	MSc Student
Daniela Cristina de Henriques Brás	University Degree	PhD Student
Denise Rodrigues Francisco	Master Degree	Lab Technician (Left June)
Diana Alves Moita	Master Degree	PhD Student
Diana Marisa Pinto Freire Fontinha	PhD	Postdoctoral Researcher
Francisca de Andrade Maria Terras Arez Durisic	Master Degree	PhD Student
Helena Isabel Marques Nunes Cabaço	PhD	Senior Postdoctoral Researcher
Isabel Margarida Meneses Moules	University Degree	MSc Student
Jorge Henrique Ferreira Grilo	Master Degree	PhD Student (Left February)
Luciano Gonçalo Nogueira Seabra Pereira	University Degree	MSc Student
Madalena Soares Ferreira de Jesus Carvalho	University Degree	MSc Student
Patrícia dos Santos Meireles	PhD	Postdoctoral Researcher (Left November)
Pedro Gil Gameiro Eloy Sena Rego	Master Degree	PhD Student
Raquel Alves de Azevedo	Master Degree	PhD Student
Rita Mateus Lopes	University Degree	MSc Student (Started September)
Soraia Cristina Marques Caetano	PhD	Postdoctoral Researcher (Started December)
Tiago Alexandre Pena Santos	Master Degree	Lab Technician (Started August. Left October)
Viriato M´Bana	PhD	Postdoctoral Researcher (Started April)

Graphical Abstract

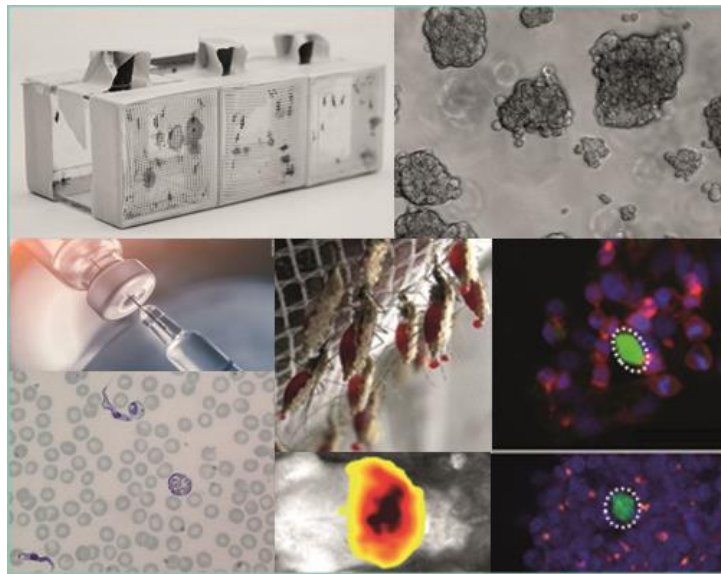


Image caption: The various facets of research at the Prudêncio Lab. Clockwise from top-left image: Experimental administration of the PbVac vaccine; Hepatic cell spheroids; Immunofluorescence microscopy images of *Plasmodium*-infected hepatic cells; Live imaging of infected mouse liver by bioluminescence; Trypanosoma and *Plasmodium* parasites; The goal of a multi-stage vaccine against malaria; Centre: Infection of *Anopheles* mosquitoes by membrane feeding on *P. falciparum*-infected blood.

Lab Interests

Research at the Prudêncio Lab focuses on the liver stage of infection by *Plasmodium* parasites, the causative agents of malaria, with a clear aim to harness its potential for the development of antimalarial strategies. The Lab's research lines include the assessment of the antiplasmodial activity of novel and repurposed compounds, an understanding of co-infections between *Plasmodium* and other infectious agents present in malaria-endemic regions, the development of new experimental tools and methodologies to study infection by *Plasmodium* parasites, and the establishment of an effective strategy for vaccination against malaria. The lab also has a clear interest on the parasite's transmission stages and on the development of transmission-blocking interventions. Our research is markedly translational and aims to deliver new tools that may ultimately contribute to an effective combat against this devastating disease.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

In spite of the impact of the COVID-19 pandemic on scientific research activities in general, the lab delivered several important achievements in 2021. Among them is the evaluation of the activity of several antiplasmodial compounds, including novel ivermectin derivatives with

possible major impacts on malaria control, and a novel drug that exerts potent antiviral and antiparasitic activities. We also reported on the impact of proteins excreted by *Trypanosoma* parasites, the causative agents of sleeping sickness, on liver infection by *Plasmodium*, the malaria parasites. Significant progress has also been made with regards to the development of a novel vaccine against malaria, an endeavor that met with further impetus as a result of a recently awarded grant by the La Caixa Foundation. Finally, the laboratory published two landmark reviews on the topics of drug repurposing to fight *Plasmodium* parasites and on the state-of-the-art of methodologies employed to investigate human immune responses in the context of malaria vaccination.

Ongoing Projects in 2021

2021/2024: Whole-organism vaccines against *P. falciparum* and *P. vivax* malaria with enhanced efficacy and scope. Coordinator: Miguel Prudêncio. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - MALVAX+ - HR21-00848. Amount: 758 082,50€. Total Amount: 758 082,50€.

2020/2023: AMAZING – toxinas de serpentes da AMAZónia: INvestiGação na valorização de biorrecursos. Coordinator: Miguel Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: CIRCNA/BRB/0281/2019. Amount: 74 615,00€. Total Amount: 234 214,63€.

2018/2021: Uma estratégia multialvo para atuar em todas as fases do ciclo de vida do *Plasmodium*. Coordinator: Miguel Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-QUI/30021/2017. Amount: 25 000,00€. Total Amount: 239 873,31€.

2018/2021: Estratégias para o desenvolvimento e melhoramento de vacinas de organismos inteiros contra a malária. Coordinator: Miguel Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: SporoMalVac LISBOA-01-0145-FEDER- 029550. Amount: 215 464,63€. Total Amount: 234 214,63€.

Scientific Impact

Academic Collaborations

Chris Janse & Blandine Franke-Fayard, Leiden University Medical Centre, Leiden, The Netherlands.

Maria-José Lafuente-Monsaterio, GSK Diseases for the Developing World, Tres Cantos, Madrid, Spain.

Paula Gomes, Universidade do Porto, Porto, Portugal.

Catarina Brito & Paula Alves, Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal.
Miguel Rodrigues, Smartfreez, Lisbon, Portugal.

Kamaljit Singh, Guru Nanak Dev University, Amristar, India.

Zrinka Rajic, University of Zagreb, Zagreb, Croatia.

Ellen Bushell, Umea University, Umea, Sweden.

Luísa Figueiredo, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal

Maria M. Mota, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal.

Selected Publications

I.J. Reuling, A.M. Mendes, G.M. de Jong GM, A. Fabra-García, H. Nunes-Cabaço, G.J. van Gemert, W. Graumans, L.E. Coffeng, S.J. de Vlas, A.S.P. Yang, C.K. Lee, Y. Wu, A.J. Birkett, C.F. Ockenhouse, R. Koelewijn, J.J. van Hellemond, P.J.J. van Genderen, R.W. Sauerwein, M. Prudêncio (2020) [Safety and efficacy of a genetically modified rodent malaria parasite against *Plasmodium falciparum* malaria: an open-label randomized phase 1/2a trial](#), **Science Transl. Med.**, 12, eaay2578.

Relevance of the publication: We now report the clinical evaluation of the biological activity of a transgenic *P. berghei* sporozoite immunization platform expressing *P. falciparum* circumsporozoite protein (PbVac) against controlled human malaria infection (CHMI). This first-in-human trial shows that PbVac is safe and well tolerated, when administered by a total of similar to 300 PbVac-infected mosquitoes per volunteer. Although protective efficacy evaluated by CHMI showed no sterile protection at the tested dose, significant delays in patency (2.2 days, $P = 0.03$) and decreased parasite density were observed after immunization, corresponding to an estimated 95% reduction in Pf liver parasite burden (confidence interval, 56 to 99%; $P = 0.010$). PbVac elicits dose-dependent cross-species cellular immune responses and functional PfCSP-dependent antibody responses that efficiently block Pf sporozoite invasion of liver cells in vitro. This study demonstrates that PbVac immunization elicits a marked biological effect, inhibiting a subsequent infection by the human Pf parasite, and establishes the clinical validation of a new paradigm in malaria vaccination.

P. Meireles, D. Brás, D. Fontinha, A.F. Chora, K. Serre, A.M. Mendes, M. Prudêncio (2020) [Elimination of Hepatic Rodent *Plasmodium* Parasites by Amino Acid Supplementation](#), **iScience**, 23, 101781.

Relevance of the publication: We show that dietary supplementation of mice employing a combination of arginine (R) with two additional amino acids, lysine (K) and valine (V), termed RKV, significantly decreases *Plasmodium* liver infection. RKV supplementation results in the elimination of parasites at a late stage of their development in the liver. Our data employing genetic knockout mouse models and *in vivo* depletion of specific cell populations suggest that RKV supplementation boosts the host's overall innate immune response, and that parasite elimination is dependent on MyD88 signaling in immune cells. The immunostimulatory effect of RKV supplementation opens a potential role for dietary supplementation as an adjuvant for prophylaxis or immunization strategies against *Plasmodium* infection.

M. Sanches-Vaz, A. Temporão, R. Luis, H. Nunes-Cabaço, A.M. Mendes, S. Goellner, T. Carvalho, L.M. Figueiredo*, M. Prudêncio* (2019) [Trypanosoma brucei infection protects mice against malaria](#), **PLoS Pathogens**, 15, e1008145.

Relevance of the publication: We observed that a primary infection by *T. brucei* significantly attenuates a subsequent infection by the malaria parasite, protecting mice from experimental cerebral malaria and prolonging host survival. We further observed that an ongoing *T. brucei* infection leads to an accumulation of lymphocyte-derived IFN-gamma in the liver, limiting the establishment of a subsequent hepatic infection by *P. berghei* sporozoites. Thus, we identified a novel host-mediated interaction between two parasitic infections, which may be epidemiologically relevant in regions of *Trypanosoma/Plasmodium* co-endemicity.

F. Arez, S. Rebelo, D. Fontinha, D. Simão, T.R. Martins, M. Machado, C. Fischli, C. Oeuvray, L. Badolo, M. J. T. Carrondo, M. Rottmann, T. Spangenberg, C. Brito, B. Greco*, M. Prudêncio*, P.M. Alves* (2019) [Flexible 3D cell-based platforms for the discovery and profiling of novel drugs targeting *Plasmodium hepatic infection*](#), *ACS Infect. Dis.*, 5, 1831-1842.

Relevance of the publication: Using stirred tank culture systems, spheroids of human hepatic cell lines were generated, sustaining a stable hepatic phenotype over 4 weeks of culture. Spheroids were employed in the establishment of 3D *Plasmodium berghei* infection platforms that relied on static or dynamic culture conditions. *P. berghei* invasion and development were recapitulated in the hepatic spheroids, yielding blood infective merozoites. The translational potential of the 3D platforms was demonstrated by comparing the *in vitro* minimum inhibitory concentration of M5717, a compound under clinical development, with *in vivo* plasma concentrations that clear liver stage *P. berghei* in mice. Our results show that the 3D platforms are flexible and scalable and can predict the efficacy of antiplasmodial therapies, constituting a powerful tool for integration in drug discovery programs.

R. Azevedo, M. Markovic, M. Machado, B. Franke-Fayard, A.M. Mendes, M. Prudêncio (2017) [A bioluminescence method for in vitro screening of *Plasmodium* transmission-blocking compounds](#), *Antimicrob. Agents Chemother.*, 61, 202699-16.

Relevance of the publication: We describe a methodology that simplifies the in vitro screening of much-needed transmission-blocking (TB) compounds employing a bioluminescence-based method to monitor the in vitro development of sporogonic stages of the rodent malaria parasite *Plasmodium berghei*. Our proof-of-principle assessment of the in vitro TB activity of several commonly used antimalarial compounds identified cycloheximide, thiostrepton, and atovaquone as the most active compounds against the parasite's sporogonic stages. The TB activity of these compounds was further confirmed by in vivo studies that validated our newly developed in vitro approach to TB compound screening.

2021 Publications in Peer-Reviewed Journals

N.G. Alves, I. Bártolo, A.J.S. Alves, D. Fontinha, D. Francisco, S.M.M. Lopes, M.I.L. Soares, C. J.V. Simões, M. Prudêncio, N. Taveira, T.M.V.D. Pinho e Melo (2021) [Synthesis and structure-activity relationships of new chiral spiro-b-lactams highly active against HIV-1 and *Plasmodium*](#), *Eur. J. Med. Chem.*, 219, 113439.

I Bártolo, B.S. Santos, D. Fontinha, M. Machado, D. Francisco, B. Sepodes, J. Rocha, H. Mota-Filipe, R. Pinto, M.E. Figueira, H. Barroso, T. Nascimento, A.P.A. de Matos, A.J.S. Alves, N.G. Alves, C.J.V. Simões, M. Prudêncio, T.M.V.D. Pinho e Melo, N. Taveira (2021) [Spiro- \$\beta\$ -lactam BSS-730A displays potent activity against HIV and *Plasmodium*](#), *ACS Infectious Diseases*, 7, 2, 421-434.

M. Fonte, N. Tassi, D. Fontinha, I. Bouzón-Arnáiz, R. Ferraz, M.J. Araújo, X. Fernández-Busquets, M. Prudêncio, P. Gomes, C. Teixeira (2021) [4,9-diaminoacridines and 4-aminoacridines as antiplasmodial hits](#). *ChemMedChem*, 16, 799-792.

M. Marinović, G. Poje, I. Perković, D. Fontinha, M. Prudêncio, J. Held, L.P. Carvalho, T. Tandarić, R. Vianello, Z. Rajić (2021) [Further investigation of harmicines as novel antiplasmodial agents: Synthesis, structure-activity relationship and insight into the mechanism of action](#), *Eur. J. Med. Chem.*, 224, 113687.

D. Moita, H. Nunes-Cabaço, A.M. Mendes, M. Prudêncio (2021) [A guide to investigating immune responses elicited by whole-sporozoite pre-erythrocytic vaccines against malaria](#), **FEBS J.**, doi:10.1111/febs.16016.

M. Prudêncio (2021) [Portugal's prominence in malaria research](#), **EMBO Reports**, e51692.

C.S. Pereira, H.C. Quadros, D.R.M. Moreira, W. Castro, Silva R.I.S.D.S., M.B.P. Soares, D. Fontinha, M. Prudêncio, V. Schmitz, H.F. Santos, M. Gendrot, I. Fonta, J. Mosnier, B. Pradines, M. Navarro (2021) [A novel hybrid of chloroquine and primaquine linked by gold\(i\): multitarget and multiphase antiplasmodial agent](#), **ChemMedChem**, 16, 662-678.

H.C. Quadros, A. Çapcı, L. Herrmann, S. D'Alessandro, D. Fontinha, R. Azevedo, W. Villarreal, N. Basílico, M. Prudêncio, S.B. Tsogoeva, D.R.M. Moreira (2021) [Studies of potency and efficacy of an optimized dihydroartemisinin-quinoline hybrid against multiple stages of the *Plasmodium* life cycle](#), **Pharmaceuticals**, Nov 6;14(11):1129.

A.T. Silva, I.S. Oliveira, J. Gomes, L. Aguiar, D. Fontinha, D. Duarte, F. Nogueira, M. Prudêncio, E.F. Marques, C. Teixeira, R. Ferraz, P. Gomes (2021) [Drug-derived surface-active ionic liquids: a cost-effective way to expressively increase blood-stage antimalarial activity of primaquine](#), **ChemMedChem**, Dec 9;e202100650.

T.A. Tavella, N.S.M. Silva, N. Spillman, A.C.A.V.K., G.C. Cassiano, A.A. Vasconcelos, A.P. Camargo, D.C.B. Silva, D. Fontinha, L.C.S. Alvarez, L.T. Ferreira, K.C.P. Tomaz, B.J. Neves, L.D. Almeida, D.Y. Bargieri, M.V.G. Lacerda, P.V.L. Cravo, P. Sunnerhagen, M. Prudêncio, C.H. Andrade, S.C.P. Lopes, M.F. Carazzolle, L. Tilley, E. Bilsland, J.C. Borges, F.T.M. Costa (2021) [Violacein-induced chaperone system collapse underlies multistage antiplasmodial activity](#), **ACS Infect. Dis.**, 7, 759-776.

A. Temporão, M. Sanches-Vaz, R. Luís, H. Nunes-Cabaço, T.K. Smith, M. Prudêncio, L. Figueiredo (2021) [Excreted *Trypanosoma brucei* proteins inhibit *Plasmodium* hepatic infection](#), **PLoS Negl. Trop. Dis.** Oct 29;15(10): e0009912.

Invited Lectures and Seminars

Prudêncio M. "Further development of P. berghei-based malaria vaccines", International PfSPZ Consortium Meeting, Rockville, MD, USA, December 9-10, 2021.

Prudêncio M. 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Round Table: Vaccines and Vaccination, Reitoria da Universidade de Lisboa, November 30, 2021.

Prudêncio M. "Disease prevention through vaccination", 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, November 30, 2021.

Prudêncio M. "Generation, characterization and in vivo evaluation of a novel live malaria vaccine", 10th Anniversary Symposium of the Tres Cantos OpenLab Foundation, November 17-24, 2021, Online.

Prudêncio M. "Vacinação contra a COVID-19. O que conseguimos e os novos desafios", 37º Congresso da Sociedade Portuguesa de Pneumologia, Albufeira, Portugal, November 11-13, 2021.

Prudêncio M. SymbNET Career Development Events, SymbNET virtual career development event for PhD students, Instituto Gulbenkian de Ciência, Oeiras, Portugal, October 28 2021.

Prudêncio M. Lisbon Living+, 2nd Annual Conference: The COVID-19 Pandemic - The Day After, Round Table: Future perspectives for technological and data-based innovation, Universidade Nova de Lisboa, Portugal, October 22, 2021.

Prudêncio M. Round Table "Vamos falar de vacinas!", Festival Internacional de Ciência de Oeiras (FIC.A) 2021, Oeiras, Portugal, October 14, 2021.

Round Table "ULisboa nos Trópicos | Os desafios da saúde global nas regiões tropicais: seres humanos, animais e ambiente", Festival Internacional de Ciência de Oeiras (FIC.A) 2021, Round Table, Oeiras, Portugal, October 13, 2021.

Prudêncio M. "Vaccinating the World Against COVID-19 - How Science Will Return Normality To Our Lives", National Model United Nations (MUN) Conference, LisboMUN Association, Lisbon, Portugal, July 10, 2021.

Prudêncio M. "Pre-clinical and clinical evaluation of a P. berghei-based vaccine against human malaria" (Plenary Session), BioMalPar XVII: Biology and Pathology of the Malaria Parasite, EMBL, Heidelberg, Germany (Virtual), May 25-27, 2021.

Prudêncio M. "Vacinação contra a COVID-19 em Portugal: Ponto de situação", Webinar Sociedade Portuguesa de Pneumologia, Lisbon, Portugal, May 13, 2021.

Prudêncio M. "Desafios à investigação biomédica em Portugal", Encontro: mais saúde para vencer a crise - Vacinas, investigação e produção, Lisbon, Portugal, May 2, 2021.

Prudêncio M. "COVID-19, the next chapter: The road to the vaccine and its role from now on", Oporto Biomedical Summit, Porto, Portugal, April 9-11, 2021.

Prudêncio M. "The role of biotechnology in combating pandemics and the evolution of science in the context of COVID-19", XII Symposium on Bioengineering, Porto, Portugal. Full Symposim available here (click on the session name to watch it), March 26-28, 2021.

Prudêncio M. Webinar: "COVID-ZERO - COVID-19, O que Preocupa as Empresas: 2021 e Agora? - Testagem e Vacinação", Trivalor, January 20, 2021.

Prudêncio M. Webinar: "Challenges and Opportunities in Tropical Research and Cooperation", Colégio Tropical Universidade de Lisboa, January 15, 2021.

Communications

POSTER. A. Fraga, A. Temporão, A. Mósca, P. Simas, M. Prudêncio “The impact of SARS-CoV-2 on a subsequent infection by malaria parasites”, 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, 30 November 2021.

POSTER. R. Azevedo, M. Carvalho, P. Meireles, B. Franke-Fayard, A.M. Mendes, C.J. Janse, M. Prudêncio “Development of a multi-stage vaccine against malaria”, 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, 30 November 2021.

POSTER. D. Moita, T. Maia, M. Duarte, A.M. Mendes, M. Prudêncio, “Characterization of a new malaria vaccine candidate against Plasmodium vivax using genetically modified rodent malaria parasites”, 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, 30 November 2021.

POSTER. S.S. Mendes, J.T. Marques, D. Fontinha, D. Moita, C.C. Romão, M. Prudêncio, L.M. Saraiva, "Carbon monoxide releasing molecules and infectious diseases", Microbiotec '21, 23-26 November 2021, Universidade Nova de Lisboa, Portugal.

POSTER. D.R. Moreira, H. Quadros, A Çapci, L. Herrmann, S. d'Alessandro, D. Fontinha, R. Azevedo, W. Villareal, N. Basilico, M. Prudêncio, S. Tsogoeva, "Studies of potency and efficacy of an optimized dihydroartemisinin-quinoline hybrid against multiple stages of the Plasmodium life cycle", 7th International Electronic Conference on Medicinal Chemistry, 1-30 November 2021, Online.

POSTER. M. Fonte, N. Tassi, D. Fontinha, I. Bouzón-Arnáiz, R. Ferraz, M.J. Araújo, X. Fernández-Busquets, M. Prudêncio, P. Gomes, C. Teixeira, "4,9-Diaminoacridines as antiplasmodial dual-stage hits", 7th International Electronic Conference on Medicinal Chemistry, 1-30 November 2021, Online.

POSTER. P.A.F. Pacheco, V. Barcherini, D. Fontinha, J. Legac, P.J. Rosenthal, M. Prudêncio, M.M.M. Santos, "Synthesis and structure-activity relationship of novel indolizinoindolones with in vitro antimalarial activity", 7th International Electronic Conference on Medicinal Chemistry, 1-30 November 2021, Online.

POSTER. A. Temporão, M. Sanches-Vaz, R. Luís, T.K. Smith, M. Prudêncio, L.M. Figueiredo, "Can Trypanosoma brucei be a new ally in the fight against malaria?", Molecular Parasitology Meeting 2021, 5-9 October 2021, Woods Hole, USA.

POSTER. H. Nunes-Cabaço, D. Moita, C. Rôla, A.M. Mendes, M. Prudêncio, “Impact of protein deficiency on the immunogenicity and efficacy of malaria vaccination”, BioMalPar XVII: Biology and Pathology of the Malaria Parasite, 25-27 May 2021, EMBL, Heidelberg, Germany (Virtual).

POSTER. A. Temporão, M. Sanches-Vaz, R. Luís, T.K. Smith, L.M. Figueiredo, M. Prudêncio, “Trypanosoma brucei proteins: new allies in the fight against malaria?”, BioMalPar XVII: Biology and Pathology of the Malaria Parasite, 25-27 May 2021, EMBL, Heidelberg, Germany (Virtual).

POSTER. D. Moita, T. Maia, M. Duarte, A.M. Mendes, M. Prudêncio, “Characterization of a new malaria vaccine candidate against Plasmodium vivax using genetically modified rodent malaria parasites”, BioMalPar XVII: Biology and Pathology of the Malaria Parasite, 25-27 May 2021, EMBL, Heidelberg, Germany (Virtual).

POSTER. G. Nogueira, D. Moita, D. Fontinha, M. Prudêncio, A.M. Mendes, “Effect of antiretroviral therapy on liver stage development of Plasmodium parasites and whole-organism vaccination against malaria”, BioMalPar XVII: Biology and Pathology of the Malaria Parasite, 25-27 May 2021, EMBL, Heidelberg, Germany (Virtual).

POSTER. R. Azevedo, M. Markovic, B. Franke-Fayard, A.M. Mendes, M. Prudêncio, “Drug repurposing for malaria control: Impact on mosquito and transmission stages”, BioMalPar XVII: Biology and Pathology of the Malaria Parasite, 25-27 May 2021, EMBL, Heidelberg, Germany (Virtual).

POSTER. H. Nunes-Cabaço, D. Moita, C. Rôla, A.M. Mendes, M. Prudêncio, “Impact of protein deficiency on the immunogenicity and efficacy of malaria vaccination”, XLVI Meeting of Portuguese Society for Immunology (SPI’46), 20-21 May 2021, Portugal.

POSTER. D. Moita, T. Maia, M. Duarte, C.M. Andrade, A. Dwivedi, J.C. Silva, L. González-Céron, C.J. Janse, S.M. Khan, A.M. Mendes, M. Prudêncio, “Characterization of a new malaria vaccine candidate against Plasmodium vivax using genetically modified rodent malaria parasites”, XIV CAML | IV NeurULisboa PhD Students Virtual Meeting, 5-7 May 2021, Lisboa, Portugal.

POSTER. R. Azevedo, M. Carvalho, P. Meireles, B. Franke-Fayard, A.M. Mendes, C.J. Janse, M. Prudêncio, “Development of a multi-stage Plasmodium vaccine”, XIV CAML | IV NeurULisboa PhD Students Virtual Meeting, 5-7 May 2021, Lisboa, Portugal.

POSTER. A. Temporão, M. Sanches-Vaz, R. Luís, T.K. Smith, M. Prudêncio, L.M. Figueiredo, “Trypanosoma brucei proteins: new allies in the fight against malaria?”, XIV CAML | IV NeurULisboa PhD Students Virtual Meeting, 5-7 May 2021, Lisboa, Portugal.

Organization of Conferences

5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, 30 November 2021.

Advanced Teaching

PhD COURSE: "Correlates of protection in whole-organism vaccination against malaria", Advanced PhD Course, Molecular Biomarkers and Technologies, Faculdade de Farmácia, Universidade de Lisboa, 22 September 2021, Lisboa, Portugal.

MASTER’S COURSE: "Malaria: the quest for an effective vaccine", Frontiers of Research in Biology - Masters in Molecular Biology and Genetics, Fac. Ciências Univ. Lisboa, 26 March 2021.

MASTER'S COURSE: "Vaccination against malaria - Development and clinical evaluation of a new vaccine", Masters in Biochemistry / Masters in Molecular Genetics and Biomedicine / Masters in Bioorganic Chemistry, Fac. Ciências e Tecnologia, Univ. Nova Lisboa, 2 June 2021.

MASTER'S COURSE: "Basic principles of writing a scientific article", Masters in Molecular Biology and Genetics, Fac. Ciências Univ. Lisboa, 29 September / 1 October 2021.

MASTER'S COURSE: "Malaria - The quest for an effective vaccine", Masters in Biomedical Research, Fac. Medicina Univ. Lisboa, 26 October 2021.

MSc Theses

Gonçalo Pereira - "Effect of Antiretroviral Therapy on Liver Stage Development of Plasmodium Parasites and Whole Organism Vaccination Against Malaria", Fac. Ciências, Univ. Lisboa, 2021. Supervisor's Name: António Mendes; Co-Supervisor: Miguel Prudêncio.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Objectives: Development of a 3D hepatic cell platform for the evaluation of compound activity against *Plasmodium*; Company: Merck; Type of partnership: Sponsored Research.

Objectives: Evaluation and characterization of new vaccine candidates against malaria; Company: GSK; Type of partnership: Sponsored Research.

Intellectual Property Rights in 2021

"Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine" (WO 2013156949 A1, also published as CN104302313A, EP2838554A1, US20150071966).

"Infected cell cultures", European Patent Office application EP 17 160 277.4, filed on 10.03.2017. PCT application number PCT/EP2018/055717 (8 March 2018).

"Novel spiro-lactam compounds, process and uses thereof", Pub. No.: WO/2018/207165, International Application No.: PCT/IB2018/053357, International Filing Date: 14.05.2018, Publication Date: 15.11.2018.

Science and Society in 2021

WEBINARS AND CONFERENCES:

5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Round Table: Vaccines and Vaccination, Reitoria da Universidade de Lisboa, 30 November 2021.

"Disease prevention through vaccination", 5ª Conferência da redeSAÚDE - A Health Research Agenda towards 2030, Reitoria da Universidade de Lisboa, 30 November 2021.

Round Table "Vamos falar de vacinas!", Festival Internacional de Ciência de Oeiras (FIC.A) 2021, 14 October 2021, Oeiras, Portugal.

Round Table "ULisboa nos Trópicos | Os desafios da saúde global nas regiões tropicais: seres humanos, animais e ambiente", Festival Internacional de Ciência de Oeiras (FIC.A) 2021, Round Table, 13 October 2021, Oeiras, Portugal.

Webinar: "COVID-ZERO - COVID-19, O que Preocupa as Empresas: 2021 e Agora? - Testagem e Vacinação", Trivalor, 20 January 2021.

Webinar: "Challenges and Opportunities in Tropical Research and Cooperation", Colégio Tropical Universidade de Lisboa, 15 January 2021.

OPINION ARTICLES AND ESSAYS:

M. Prudêncio, "Se não agora, quando?", Diário de Notícias, 9 October 2021.

M. Prudêncio, "Desconfinar as escolas", Público, 30 September 2021.

M.A. Macedo, M. Prudêncio, "Covid-19: as infeções no verão das vacinas", Público, 9 September 2021.

M.M. Mota, M. Prudêncio (2021) "O tempo em biologia / Time in biology", Ministério da Ciência, Tecnologia e Ensino Superior, Lisboa, Portugal.

L. Graça, M. Prudêncio, "É tempo de celebrar as vacinas!", Expresso, 30 April 2021.

M. Prudêncio, "Malária: um exemplo de sucesso da investigação científica portuguesa", Público, 25 April 2021.

MEDIA APPEARANCES:

> 500 presences or references on TV, radio, and printed and online press.

OTHERS:

Cartas Com Ciência – A program for letter exchanges between scientists and children from Portuguese-speaking countries.

Mário Ramirez Lab

Head of Laboratory: Mário Ramirez, PhD, Group Leader and Associate Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Ana Catarina da Silva e Costa	PhD	Senior Postdoctoral Researcher
Ana Isabel de Aquino Friães	PhD	Senior Postdoctoral Researcher
Ana Margarida Pires Lavado de Sousa Modesto	Master Degree	Trainee (Started September)
Ana Sofia de Sousa Soares	High School Diploma	Trainee (Left December)
Ana Sofia Duarte Correia	Master Degree	PhD Student (Started February)
Andreia Isabel Pais Santos	University Degree	MSc Student
Beatriz Vicente dos Santos	University Degree	MSc Student
Bruno Brandão de Capistrano	University Degree	MSc Student
Bruno Filipe Ribeiro Gonçalves	Master Degree	PhD Student
Catarina Inês Marques de Sousa Mendes	Master Degree	PhD Student
Elisabete Raquel Ferreira Martins	PhD	Senior Postdoctoral Researcher
Fábio Alexandre Súbtil Limpo	University Degree	MSc Student
Filipe Barbosa Valcovo	University Degree	MSc Student (Started September)
Inês Pereira Blum	University Degree	MSc Student (Started September)
Inês Vicente de Almeida	University Degree	MSc Student (Started September)
Joana Filipa Gomes da Silva	Master Degree	Lab Technician
José Augusto Gamito Melo Cristino	PhD	Clinical Staff Scientist
Lúcia de Lurdes Ferreira	Master Degree	Administrative Technician
Marcos Daniel Caetano Borges de Pinho	PhD	Senior Postdoctoral Researcher
Maria Guilhermina de Oliveira Firmino	University Degree	MSc Student
Melissa Neiva de Sousa	University Degree	MSc Student (Left November)
Milani Sibell Rodrigues	High School Diploma	MSc Student
Mykyta Forofontov	Bachelor Degree	MSc Student (Started September)
Pedro Rafael Vila Cerqueira	Master Degree	Lab Technician (Started January. Left June)
Rafael Fresca Mamede	Master Degree	PhD Student (Started January)
Rita Alexandra Marinheiro Melão	University Degree	MSc Student
Sara Mateus Mahomed	High School Diploma	Trainee
Thomas Hanscheid	PhD with Habilitation	Clinical Staff Scientist
Tomás Filipe Reis Gonçalves	High School Diploma	Trainee (Left November)
Yara de Sousa Lobo Almeida	University Degree	MSc Student
Yenine Telma Santos Martins	University Degree	MSc Student

Lab Interests

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations. By exploring the relationships between commensal and disease-causing populations of the same bacterial pathogen, we hope to identify particularly virulent clones as well as successful colonizers for further characterization. A strong

bioinformatics effort in microbial genomics, microbial typing data sharing, data analysis and visualization tools is ongoing.

The development of novel laboratory methodologies for the diagnosis of infectious diseases, with a special interest in malaria, is also an active area of research.

Research Fields

- Integrative Biology: From Genes and Genomes to Systems
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Environmental Biology, Ecology and Evolution

Ongoing Projects in 2021

2018/2021: Ferramentas para análise filogenética em larga escala. Coordinator: João Carriço. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CCI-BIO/29676/2017. Amount: 33 324,50€. Total Amount: 237 827,12€.

Scientific Impact

Selected Publications

van der Linden M, Mamede R, Levina N, Helwig P, Vila-Cerqueira P, Carriço JA, Melo-Cristino J, Ramirez M, Martins ER. (2020). [Heterogeneity of penicillin-non-susceptible group B streptococci isolated from a single patient in Germany](#). *J Antimicrob Chemother*. 75:296–299. Original article.

Relevance of the publication: First description of a penicillin-non-susceptible *Streptococcus agalactiae* isolated from a patient in Europe. Potential in vivo development of penicillin resistance under therapy. Our group performed the phenotypic and genomic analysis of the isolates.

Pinho MD, Foster G, Pomba C, Machado MP, Baily JL, Kuiken T, Melo-Cristino J, Ramirez M, Portuguese Group for the Study of Streptococcal Infections (2019). [Streptococcus canis are a single population infecting multiple animal hosts despite the diversity of the universally present M-like protein SCM](#). *Front Microbiol* 10:631. Original article.

Relevance of the publication: Confirmation that *Streptococcus canis* constitute a single population infecting a large diversity of hosts, including humans, reptiles and both land and sea mammals.

Silva-Costa C, Brito MJ, Pinho MD, Friães A, Aguiar SI, Ramirez M, Melo-Cristino J, Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society (2018). [Pediatric complicated pneumonia caused by Streptococcus pneumoniae serotype 3 in 13-valent pneumococcal conjugate vaccinees, Portugal, 2010-2015](#). *Emerging Infectious Diseases* 24:1307–1314. Original article.

Relevance of the publication: Data showing the need to use molecular methods in the diagnosis of pediatric complicated pneumonia for the identification of its etiology. Evidence of complicated pneumonias in fully vaccinated children indicating breakthrough infections with serotype 3 suggesting the benefits of vaccination in preventing infection against this serotype may not be as significant as against other serotypes.

Silva M, Machado MP, Silva DN, Rossi M, Moran-Gilad J, Santos S, Ramirez M, Carriço JA. (2018). [chewBBACA: A complete suite for gene-by-gene schema creation and strain identification](#). **Microb Genom** 4:000166. Original article.

Relevance of the publication: Creation of a software application facilitating the use of genomic information in outbreak investigation and surveillance of bacterial pathogens.

Hanscheid T, Hardisty DW (2018). [How "resistant" is artemisinin resistant malaria? - The risks of ambiguity using the term "resistant" malaria](#). **Travel Medicine and Infectious Disease** 24:23-24. Editorial.

Relevance of the publication: Discussion of the importance of properly using the term resistance in the malaria field.

2021 Publications in Peer-Reviewed Journals

Elias R, Melo-Cristino J, Lito L, Pinto M, Gonçalves L, Campino S, Clark TG, Duarte A, Perdigão J. 2021. Klebsiella pneumoniae and colistin susceptibility testing: performance evaluation for broth microdilution, agar dilution and minimum inhibitory concentration test strips and impact of the “skipped well” phenomenon. **Diagnostics** 11:2352. Original article.

DOI: [10.3390/diagnostics11122352](https://doi.org/10.3390/diagnostics11122352)

Adegbite BR, Edoa JR, Ndzebe Ndoumba WF, Dimessa Mbadinga LB, Mombo-Ngoma G, Jacob ST, Rylance J, Hänscheid T, Adegnika AA, Grobusch MP. 2021. A comparison of different scores for diagnosis and mortality prediction of adults with sepsis in Low-and-Middle-Income Countries: a systematic review and meta-analysis. **EClinicalMedicine** 42:101184. Review.

DOI: [10.1016/j.eclinm.2021.101184](https://doi.org/10.1016/j.eclinm.2021.101184)

Freitas AT, Calhau C, Antunes G, Araújo B, Bandeira M, Barreira S, Bazenga F, Braz S, Caldeira D, Santos SCR, Faria A, Faria D, Fraga M, Nogueira-Garcia B, Gonçalves L, Kovalchuk P, Lacerda L, Lopes H, Luís D, Medeiros F, Melo AMP, Melo-Cristino J, Miranda A, Pereira C, Pinto AT, Pinto J, Proença H, Ramos A, Rato JPR, Rocha F, Rocha JC, Moreira-Rosário A, Vazão H, Volovetska Y, Guimarães J-T, Pinto FJ. 2021. Vitamin D-related polymorphisms and vitamin D levels as risk biomarkers of COVID-19 disease severity. **Sci Rep** 11:20837. Original article.

DOI: [.1038/s41598-021-99952-z](https://doi.org/10.1038/s41598-021-99952-z)

Baeringsdottir B, Erlendsdottir H, Bjornsdottir ES, Martins ER, Ramirez M, Haraldsson A, Thorkelsson T. 2021. Group B streptococcal infections in infants in Iceland: clinical and microbiological factors. **J Med Microbiol** 70:001426. Original article.

DOI: [10.1099/jmm.0.001426](https://doi.org/10.1099/jmm.0.001426)

Silva-Costa C, Gomes-Silva J, Prados L, Ramirez M, Melo-Cristino J, on behalf of the Portuguese Group for the Study of Streptococcal Infections, the Portuguese Study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society. 2021. Pediatric invasive pneumococcal disease three years after PCV13 introduction in the national immunization plan - The continued importance of serotype 3. 7. **Microorganisms** 9:1428. Original article.

DOI: [10.3390/microorganisms9071428](https://doi.org/10.3390/microorganisms9071428)

Hernández-García M, García-Fernández S, García-Castillo M, Pássaro L, Cantón R, STEP study group. 2021. In vitro characterization of *Pseudomonas aeruginosa* recovered in Portugal from low respiratory tract infections in ICU patients (STEP Study). **FEMS Microbiol Lett** 368:fnab099. Original article.

DOI: [10.1093/femsle/fnab099](https://doi.org/10.1093/femsle/fnab099)

Grobusch MP, Schnyder J, Garcia-Garrido HM, Wisman JJ, Stijnis C, Goorhuis A, Häscheid T, de Jong HK. 2021. Delayed large local reaction to the adenovirus-vectored (ChAdOx1) vaccine. *Travel Med Infect Dis* 43:102093. Letter.

DOI: [10.1016/j.tmaid.2021.102093](https://doi.org/10.1016/j.tmaid.2021.102093)

Silva L, Queirós C, Borges-Costa J, Barreto R, Filipe P, Melo-Cristino J. 2021. Chlamydia trachomatis Infections in a Tertiary Care Portuguese Hospital: An 11-Year Retrospective Study. **Actas Dermosifiliogr** 112:528–533. Original article.

DOI: [10.1016/j.ad.2021.01.002](https://doi.org/10.1016/j.ad.2021.01.002)

Silva-Costa C, Gomes-Silva J, Teodoro I, Ramirez M, Melo-Cristino J, on behalf of the Portuguese Group for the Study of Streptococcal Infections. 2021. Invasive Pneumococcal Disease in Adults in Portugal: The Importance of Serotypes 8 and 3 (2015–2018). 5. **Microorganisms** 9:1016. Original article.

DOI: [10.3390/microorganisms9051016](https://doi.org/10.3390/microorganisms9051016)

Mäesaar M, Mamede R, Elias T, Roasto M. 2021. Retrospective Use of Whole-Genome Sequencing Expands the Multicountry Outbreak Cluster of *Listeria monocytogenes* ST1247. **Int J Genomics** 2021:6636138. Original article.

DOI: [10.1155/2021/6636138](https://doi.org/10.1155/2021/6636138)

Grobusch MP, Häscheid T. 2021. Dracunculiasis X in Vietnam: Emerging public health threat or exotic gem? **Int J Infect Dis** 105:416–417. editorial

DOI: [10.1016/j.ijid.2021.02.063](https://doi.org/10.1016/j.ijid.2021.02.063)

Mendes Pedro D, Mendes Pedro MM, Valadas E, Häscheid T. 2021. SARS-CoV-2 and Cancer: Beyond Immunosuppression. **Acta Med Port** 34:237. letter

DOI: [10.20344/amp.15640](https://doi.org/10.20344/amp.15640)

Hernández-García M, García-Fernández S, García-Castillo M, Melo-Cristino J, Pinto MF, Gonçalves E, Alves V, Costa E, Ramalheira E, Sancho L, Diogo J, Ferreira R, Silva T, Chaves C, Pássaro L, Paixão L, Romano J, Cantón R, STEP study group. 2021. Confronting ceftolozane-tazobactam susceptibility in multidrug-resistant Enterobacterales isolates and whole-genome sequencing results (STEP Study). **Int J Antimicrob Agents** 57:106259. Original article.

DOI: [10.1016/j.ijantimicag.2020.106259](https://doi.org/10.1016/j.ijantimicag.2020.106259)

Hernández-García M, García-Castillo M, García-Fernández S, Melo-Cristino J, Pinto MF, Gonçalves E, Alves V, Vieira AR, Ramalheira E, Sancho L, Diogo J, Ferreira R, Silva T, Chaves C,

Bou G, Cercenado E, Delgado-Valverde M, Oliver A, Pitart C, Rodríguez-Lozano J, Tormo N, Romano J, Pássaro L, Paixão L, López-Mendoza D, Díaz-Regañón J, Cantón R, STEP and SUPERIOR study groups. 2021. Distinct epidemiology and resistance mechanisms affecting ceftolozane/tazobactam in *Pseudomonas aeruginosa* isolates recovered from ICU patients in Spain and Portugal depicted by WGS. **J Antimicrob Chemother** 76:370–379. Original article.

DOI: [10.1093/jac/dkaa430](https://doi.org/10.1093/jac/dkaa430)

Mamede R, Vila-Cerqueira P, Silva M, Carriço JA, Ramirez M. 2021. Chewie Nomenclature Server (chewie-NS): a deployable nomenclature server for easy sharing of core and whole genome MLST schemas. **Nucleic Acids Res** 49:D660–D666. Original article.

DOI: [10.1093/nar/gkaa889](https://doi.org/10.1093/nar/gkaa889)

Queirós C, Borges da Costa J, Lito L, Filipe P, Melo-Cristino J. 2020. Gonorrhoea in a tertiary care Portuguese hospital: a 10-year retrospective study of the evolution of cases and drug resistance of the isolates. **Actas Dermosifiliogr** 111:761–767. Original article.

Barros Pinto MP, Marques G, Melo-Cristino J. 2021 Promastigotes of *Leishmania* spp. developing in human bone marrow in vitro. **Br J Haematol** 192:7. Editorial.

DOI: [10.1111/bjh.17078](https://doi.org/10.1111/bjh.17078)

Invited Lectures and Seminars

Ramirez M. Adventures with Streptococci: the surprises in phage release and challenging the correlation between antibiotic consumption and resistance. Carnegie Mellon invited talk. Virtual. May 19, 2021

Mendes CI. 2021. Comparing and reporting AMR results using hAMRnization. (Invited Lecture). [Public Health Alliance for Genomic Epidemiology \(PHA4GE\) and the Joint Programming Initiative on Antimicrobial Resistance \(JPIAMR\) Workshop on Antimicrobial Resistance](#). October 15.

Communications

Firmino MO, Silva AV, Louro RO, Ramirez M, Paquete CM. 2021. Proposing a new *Shewanella* species causing human infections (Poster 376). Microbiotec 21, 2021, November 23-26 - Virtual.

Martins ER, Melo-Cristino J, Ramirez M. 2021. Colonization as a reservoir for *Streptococcus agalactiae* infections – lessons from non-pregnant adults (Poster). 2nd International Symposium on *Streptococcus agalactiae* Disease (ISSAD 2021) 3-5 November, London, UK.

Firmino MO, Silva AV, Louro RO, Ramirez M, Paquete CM. 2021. Unraveling genetic and pathogenic characteristics of infectious *Shewanella* (Poster 7750). XXI SPB National Congress of Biochemistry. October 14-16, Évora, Portugal.

Mendes CI, Vila-Cerqueira P, Motro Y, Moran-Gilad J, Carriço JA, Ramirez M. 2021. LMAS: Evaluating metagenomic de novo assembly methods through defined communities. (Poster). ICCMg, 2021, 21-22 October.

Lapidot R, Ramirez M, Lee D, Scully I, Gessner B, Pelton S. 2021. Serotype 3 pneumococci evade activation of the classical complement pathway (Poster 1000). IDWeek 2021. Sept. 29-Oct. 3, virtual. [Open Forum Infectious Diseases 8:S591].

Correia AD, Ramirez M, Francisco AP, Vaz C. 2021. PHYLOViZ - Phylogenetic data analysis and visualization. (Poster). 2nd GenomePT Symposium. July 7.

Mamede R, Vila-Cerqueira P, Friães A, Ramirez M. 2021. Towards a framework for the definition of publicly available whole-genome multilocus sequence typing schemas - the example of *Streptococcus pyogenes*. (Poster). 2nd GenomePT Symposium, 2021, July 7.

Mendes CI, Vila-Cerqueira P, Motro Y, Moran-Gilad J, Carriço JA, Ramirez M. 2021. Evaluating de novo methods of genome assembly in metagenomics with LMAS. (Poster). 2nd GenomePT Symposium, 2021, July 7.

Aguiar S, Gaspar MM, Silva M, Ferreira M, Martins D, André A, Dias JN, Neves V, Gano L, Correia JDG, Carriço J, Ramirez M, Melo-Cristino J, Gonçalves J, Castanho M, Aires-Da-Silva F. 2021. Novel treatment for pneumococcal meningitis: an innovative brain-targeted immunoliposome for antimicrobial drug delivery. (Oral 2596). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Mendes CI, Vila-Cerqueira P, Motro Y, Moran-Gilad J, Carriço JA, Ramirez M. 2021. Short-read metagenomic assembly: finding the best fit in a world of options. (Oral 3410). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Würdig Riche CV, Mamede R, Falci D, Carrico J, Ramirez M, Dias C. 2021. Methicillin-resistant *Staphylococcus aureus* (MRSA) invasive infections: epidemiology and risk-factors for mortality in bacteraemic patients in Porto Alegre, Brazil. (Poster 3650). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Faria NA, Touret T, Simões AS, Pinto M, Melo-Cristino J, Ramirez M, Toscano C, Gonçalves E, Martins F, Bispo AS, Palos C, Pereira P, Correia AB, Gonçalves L, Serrano M, De Lencastre H, Duarte A, Carriço JA, Sá-Leão R, Miragaia M. 2021. Successful dissemination of KPC-3 and OXA-181 carbapenemases in different genetic backgrounds of *Klebsiella pneumoniae* from Portuguese hospitals. (Poster 4305). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Vila-Cerqueira P, Mamede R, Friães A, Ramirez M. 2021. Defining publicly available whole genome multilocus sequence typing schemas: the example of *Streptococcus pyogenes*. (Poster 4265). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Mamede R, Vila-Cerqueira P, Ramirez M. 2021. Fast, faster, fastest: improving an allele calling algorithm for whole genome multilocus sequence typing (wgMLST). (Poster 4175). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Mendes Pedro D, Eduardo Paulo S, Bruschy Fonseca A, Marques Lito L, Melo Cristino J, Ayres Pereira A. 2021. Extensively drug-resistant *Pseudomonas aeruginosa*: the experience of a large Portuguese university hospital. (Poster 4966). 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), 9-12 July 2021.

Mendes CI, Manuele A, Fornika D, Tausch SH, Le-Viet T, Raphenya AR, Alcock B, Culp E, McArthur AG, Feldgarden M, Tyson GH, Campos J, Witney AA, Aanensen DM, Black A, Hodcroft E, Katz LS, Oluniyi PE, Olawoye IB, Timme RE, Vasconcelos ATR, MacCannell DR, Griffiths EJ, Page AJ, Maguire F. hAMRonization: Parsing multiple AMR tool outputs into a common data structure with PHA4GE's AMR Gene Detection Specification (P56). Applied Bioinformatics & Public Health Microbiology 2021 (ABPHM21). 2021, May 5-7.

Mendes CI, Vila-Cerqueira P, Motro Y, Moran-Gilad J, Carriço JA, Ramirez M. LMAS: Last (meta)genomic assembler standing (P57). Applied Bioinformatics & Public Health Microbiology 2021 (ABPHM21). 2021, May 5-7.

Mendes CI, Vila-Cerqueira P, Motro Y, Moran-Gilad J, Carriço JA, Ramirez M. LMAS: Last (meta)genomic assembler standing (31I6). XIV CAML - IV NeurULisboa PhD Students Virtual Meeting. 2021, May 5-7.

Organization of Conferences

Mario Ramirez. Programme Committee. European Congress of Clinical Microbiology and Infectious Diseases, Virtual, July 9-12, 2021.

Advanced Teaching

(Lecture) Ramirez M. Doença invasiva pneumocócica: o que conseguimos, os desafios e as novas vacinas. 5º Curso básico de vacinas, Centro Hospital e Universitário de Coimbra. December 15, 2021.

(Lectures/Coordination of Curricular Unit) Ramirez M, Silva-Costa C, Pinho M, Friães A, Hänscheid T. Microbiologia Médica. Mestrado em Microbiologia, Universidade de Lisboa, 2021.

(Lecture) Ramirez Genomics in Microbiology. Mestrado em Investigação Biomédica Faculdade de Medicina, Universidade de Lisboa. 2021.

MSc Theses

Melissa Neiva de Sousa, 30/11/2021, "Exploring the reasons underlying *Streptococcus pneumoniae* serotype 8 capsular variants". Mestrado em Microbiologia, Instituto Superior Técnico, Universidade de Lisboa. Supervisor: Catarina Silva-Costa Co-Supervisor: Nuno Mira.

Sara Mateus Mahomed (2021) "Large interindividual variations of *Plasmodium falciparum* growth in in-vitro cultures: Investigation of underlying factors especially related to red blood cells". Trabalho Final, MIM, FMUL. Supervisor: Thomas Hanscheid.

Valorization of Knowledge / Social and Economic Impact

Policy

FAO. 2021. Risk profile - Group B Streptococcus (GBS) / Streptococcus agalactiae sequence type (ST) 283 in freshwater fish. Bangkok. (<https://www.fao.org/3/cb5067en/cb5067en.pdf>).

Miguel Remondes Lab

Head of Laboratory: Miguel C. P. Remondes, DVM PhD, Group Leader and Invited Assistant Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Catarina Nobre Mesquita	University Degree	MSc Student (Started June)
Ana Inês Marques Morgado	Master Degree	PhD Student
Ana Sofia Carvalho Cruz	Master Degree	PhD Student
Bárbara Pinto Correia	Master Degree	PhD Student
Gonçalo Aires de Oliveira	PhD	Postdoctoral Researcher
Joana Gomes Ribeiro	Master Degree	PhD Student
Jorge Miguel Claro Cardoso	Master Degree	PhD Student
Marcelo Francisco Vieira Dias	University Degree	PhD Student
Marta Filipa Leite Luís	University Degree	MSc Student (Started March)
Patrícia Morais Caldeira Rodrigues Bernardo	University Degree	MSc Student
Sara Filipa Agostinho da Cruz	University Degree	MSc Student

Graphical Abstract

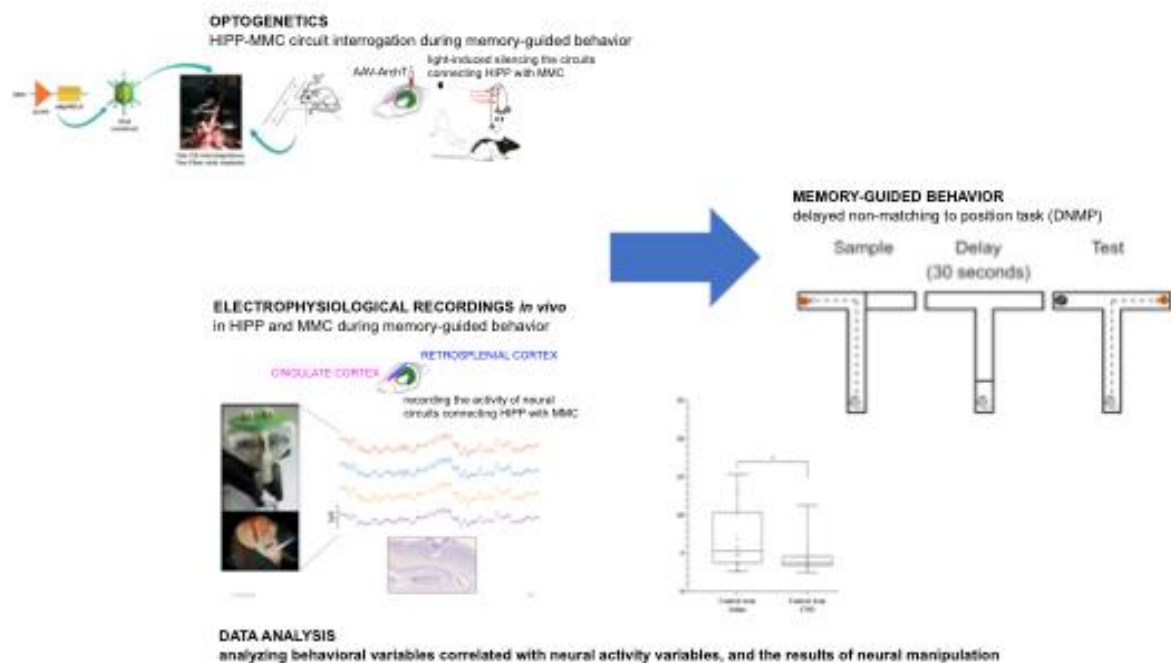


Image caption:

In the lab, we measure electrical signals from the brain of rodents, to analyse the activity of individual neurons and populations thereof, while animals execute tasks involving sensory perception, memory, decision-making, and switch between distinct rules when faced with unexpected contingencies and conflicting choices, performing economic decisions. While we correlate neural activity with cognitive function, we reversibly manipulate such neural activity using molecular techniques, optogenetics and chemogenetics, to either silence or activate

specific groups of neurons we hypothesize to be involved in such behaviours, thus causally dissecting neural mechanisms of brain function.

Lab Interests

The ability of guiding our behaviour according to knowledge stored previously in memory lies at the heart of adaptive behaviour and is essential for survival. However, we must also be ready to adapt such behaviour to unexpected changes in context, often contrary to what would be warranted by previous knowledge.

Our work consists of measuring electrical signals from the brain areas responsible for mediating spatial cognition and memory, occipital secondary cortex (Oc2M), hippocampus (HIPPO), retrosplenial cortex (RSC), during decisional behaviour. All the while we use molecular tools to manipulate the activity of neurons and dissect mechanisms behind such complex behavior.

The neural circuit we focus on is affected in Autism Spectrum Disorders (ASD). We presently use the Valproate (VPA) ASD rodent model, study the dysfunctional connectivity in the HIPPO-RSC-Oc2M-CG during innate and adaptive behaviour, and explore the combined use of behavioural sensory stimulation, pharmacology, and neural manipulation, to attempt revert circuit malfunctions, and possibly behavioural symptoms.

Research Field

- Neuroscience and Disorders of the Nervous System

Major Scientific Achievements in 2021

In a collaboration with Prof Teresa Garcia-Marques, we published these interesting results showing that you make less mistakes the harder the task you're doing. In other works, in a numeric Stroop Task, rendering the characters dysfluent (by using a font that is hard to read, for instance) increases performance in incongruent trials, suggesting increased activation of cognitive control mechanisms.

In another work, we joined behavior, neuro electrophysiology and chemogenetic neural manipulation in rodents, and developed a memory task in which animals learn to count time accurately to receive a reward. We demonstrated that reversibly silencing medial entorhinal cortex excitatory neurons significantly decreases performance in a timing memory task.

We have developed a novel method to access previously inaccessible midline brain structures allowing their targeting for recording, cannulation, manipulation, and drug delivery.

Ongoing Projects in 2021

2018/2021: Coordenação hipocampo-cortical e mecanismos cognitivos: a formação e recuperação de memórias episódicas durante o comportamento decisional. Coordinator: Miguel Remondes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/29325/2017. Amount: 239 421,20€. Total Amount: 239 421,20€.

Scientific Impact

Academic Collaborations

Luisa Lopes, Instituto de Medicina Molecular João Lobo Antunes

Neil Dawson, University of Lancaster

Miguel Castelo-Branco, Universidade de Coimbra

Vanessa Morais, Instituto de Medicina Molecular João Lobo Antunes

Selected Publications

Oliveira GA^{1,2*}, Remondes M², Garcia - Marques T¹ (2022) [Bad after bad is good: Previous trial disfluency reduces interference promoted by incongruence](#) **Psychological Research**

Relevance of the publication: In a collaboration with Prof Teresa Garcia-Marques, we published these interesting results showing that you make less mistakes the harder the task you're doing. In other works, in a numeric Stroop Task, rendering the characters dysfluent (by using a font that is hard to read, for instance) increases performance in incongruent trials, suggesting increased activation of cognitive control mechanisms.

Dias M*, Ferreira R, Remondes M * (2021). [Medial entorhinal cortex is necessary for estimation of elapsed time](#) **Journal of Neuroscience** 20 October 2021, JN-RM-0750-21

Relevance of the publication: This recent work joined behavior, neuro electrophysiology and chemogenetic neural manipulation, and developed a memory task in which animals learn to count time accurately to receive a reward. Our experiments thus probe cortico-hippocampal brain circuits for the mechanisms of memory for time. Once this task was developed, we tested the role of one strong candidate for temporal coding in memory – medial entorhinal cortex – and demonstrated that reversibly silencing medial entorhinal cortex excitatory neurons significantly decreases performance in a timing memory task.

Ferreira - Fernandes E, Pinto - Correia B, Quintino C and **Remondes M *** (2019). [A gradient of hippocampal inputs to the medial mesocortex](#). **Cell Reports** 29, pp. 3266

Relevance of the publication: This article uses multiple in vitro and in vivo techniques, among which electrophysiology, to study the nature of anatomical and functional connections between hippocampus and medial mesocortex (CG, MCC and RSC), filling a critical gap in our understanding of hippocampal-cortical circuits and mechanisms supporting memory-guided behaviors (Cell Rep., 2019).

2021 Publications in Peer-Reviewed Journals

Dias M*, Ferreira R, Remondes M * (2021). [Medial entorhinal cortex is necessary for estimation of elapsed time](#). **Journal of Neuroscience** 20 October 2021, JN-RM-0750-21; DOI:

Dias M, Marques - Morgado I, Coelho J, Ruivo P, Lopes LV, **Remondes M *** (2021). [Transection of the superior sagittal sinus enables bilateral access to the rodent midline brain structures](#). **eNeuro** 1 July 2021, DOI: ENEURO.0146-21.2021.

Networks & Research Infrastructures

H2020 Twinning Grant "EpiEpiNet - Epileptogenesis and Epilepsy Network: from genes, synapses and circuits to pave the way for novel drugs and strategies". Jan 2021 - 2023 €900,000.00, Partner

Advanced Teaching

Cajal School on Neurobiology of Cognitive Ageing Consortium, Neurocentre Magendie UMR 1215, Université de Bordeaux, (<http://cajal-training.org/on-site/ageing-cognition/>)
September 2021

PhD Program in Biomedical Sciences (<https://www.medicina.ulisboa.pt/en/biomedical-research>)
iMM - JLA, University of Lisbon Medical School, Portugal,
2015 – Present **Synapses Circuits, Learning and Memory (Co-organizer and teacher)**

PhD Program in Neuroscience
University of Lisbon Medical School, Portugal,
2020 – Present **Neuronal Circuits (Lecture)**

International PhD in Biomedicine – Nova Medical School
2016 – Present **Core Skills in Research (Lecture)**

Doctoral Program in Experimental Biology and Biomedicine
Instituto de Neurociências e Biologia Celular, Universidade de Coimbra
2015 - Present **Circuits and Behavior (Lecture)**

Master Programs:

MSc Program in Biomedical Sciences (<https://www.medicina.ulisboa.pt/en/biomedical-research>)
iMM - JLA, University of Lisbon Medical School, Portugal,
2020 – Present **Synapses Circuits, Learning and Memory (Co-organizer and teacher)**

Nova Biomedical Research Master Program (NBR),
Nova Medical School, Universidade Nova de Lisboa
2017 - Present **Nuclear Competences in Research (Lecture)**

MSc Program Neuramus ERASMUS Mundus Program
(from 2016 fused with the MIT - Portugal PhD Program in BioEngineering)
Instituto de Neurociências e Biologia Celular, Universidade de Coimbra
2015 - Present **Circuits and Behavior (Lecture)**

MSc Theses

Sara Cruz, BSc, in the **CNC University of Coimbra MSc Program in Cell and Molecular Biology Cruz, S** *The role of cingulate cortex in working memory*, **Master Thesis, University of Coimbra Medical School, Lisbon, Portugal. (18/20)**

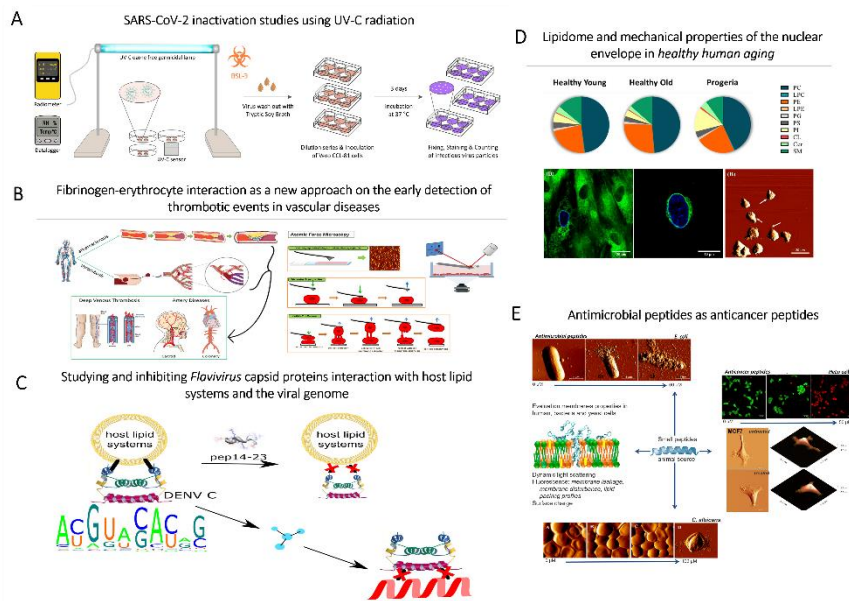
Nuno Santos Lab

Head of Laboratory: Nuno Fernando Duarte Cordeiro Correia dos Santos, PhD, Group Leader and Associate Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Ana de Souto Martins	Master Degree	PhD Student
Ana Luísa Regatão Tomás	PhD	Postdoctoral Researcher
André Ribeiro de Oliveira	University Degree	MSc Student (Left December)
Anna Reichel	PhD	Postdoctoral Researcher
Catarina Andreia Baptista Matos	University Degree	MSc Student
Catarina Isabel de Sousa Lopes	Master Degree	PhD Student
Filomena Maria Dias Almeida Carvalho Arede	PhD	Staff Scientist
Guilherme Ribeiro da Silva	University Degree	MSc Student (Left September)
Inês de Andrade Matos Gonçalves Saraiva	Master Degree	PhD Student (Started October)
Ítala Cristine Silva	Master Degree	PhD Student
Ivo Cristiano da Rocha Martins	PhD	Staff Scientist
José Miguel Fernandes Bento	University Degree	MSc Student (Started September)
Marcin Makowski	Master Degree	PhD Student
Marco André Manso Domingues	PhD	Senior Postdoctoral Researcher
Maria Constança Gomes Redinha Pais do Amaral	Master Degree	PhD Student
Maria Inês Pinto Coelho da Silva	University Degree	MSc Student (Left December)
Maria João Martins Sarmiento	PhD	Postdoctoral Researcher
Maria Teresa Damásia Freitas Santos	High School Diploma	Lab Technician
Nelly Marine Carreira da Silva	University Degree	PhD Student
Nilton Maciel Mangueira	PhD	Visiting Researcher (Started November)
Patrícia Isabel Duarte Montês Carvalho	Master Degree	PhD Student
Patrícia Morgado da Silva	Master Degree	PhD Student
Pedro Miguel Soares Castro	PhD	Postdoctoral Researcher (Started October)
Raquel Ventura Rebordão Gouveia	High School Diploma	Trainee (Left March)
Sónia Gonçalves Abreu	PhD	Staff Scientist

Graphical Abstract



Lab Interests

Biochemical and biophysical processes occurring in membranes of human cells, as well as of their viral, fungal and bacterial pathogens. Study of the infection cycle and strategies for the inactivation of enveloped viruses, namely SARS-CoV-2, HIV-1, dengue, West Nile, Zika and pediatric respiratory viruses. Study of the binding of fibrinogen to erythrocytes as a risk determinant in different cardiovascular diseases. Pre-clinical evaluation of the membrane activity and mechanism of action of antimicrobial (AMP) and anticancer (ACP) peptides, both by themselves and combined with metal nanoparticles. Also on the Nanomedicine area, we are interested in the development of biosensor systems using innovative protein-ligand interactions (nanoparticles and amyloid-based biosensors).

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Biotechnology and Biosystems Engineering

Major Scientific Achievements in 2021

Among the major scientific achievements of the lab in 2021, the work conducted on the context of the SARS-CoV-2/COVID-19 pandemic is worth of notice. This new research line led to the hiring of new researchers, enabling the work with the isolated virus at the IMM Biosafety Level 3 (BSL-3) facility. This work opened the way for new partnerships and projects, both with academic collaborators and with private companies from 3 different continents for the testing of their product candidates currently under development.

The work conducted in 2021 with SARS-CoV-2 included the testing of different surfaces with antiviral activity, antiviral compounds, viral inactivation strategies based on the use of UV light on different porous and non-porous materials / surfaces, and evaluation of different air-sampling methods for viral load quantification in patients' rooms.

In parallel, lab research on other viruses, membrane-active peptides and cardiovascular diseases was maintained, including also new strategies at the lipidomics and other omics levels.

Ongoing Projects in 2021

2021/2024: Fibrinogen-erythrocyte interaction as a new approach on the early detection of thrombotic events in vascular diseases. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EMD-TLM/7289/2020. Amount: 181 950,00€. Total Amount: 181 950,00€.

2021/2023: SRA - PROTERRIS - CARLOS LABÃO. Coordinator: Nuno Santos. Funding Agency: European Commission. Reference: LIPLAGE - MSCA - ITN - 892321 - H2020. Amount: 148 090,04€. Total Amount: 148 090,04€.

2020/2021: UVtizer – Multifunctional sanitizer. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 15/SI/2020 (P2020) – UVTIZER. Amount: 82 195,00€. Total Amount: 250 000,00€.

2018/2021: iDNArT - Intelligent DNA nanostructures aimed at brain therapeutics. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/NAN-MAT/30898/2017. Amount: 7 812,00€. Total Amount: 239 894,05€.

2018/2021: When the host Cell is not so cosy anymore? A drop off in energy or an increase in toxicity? Coordinator: Filomena Aréde. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/28456/2017. Amount: 47 064,00€. Total Amount: 232 779,88€.

Other Projects

2019/2023: SAFE-N-MEDTECH – Safety Testing in the life cycle of nanotechnology-enabled medical technologies for health. Coordinator: Pedro Silva. Funding Agency: European Commission. Reference: GA 814607 – SAFE-N-MEDTECH. Amount: 714 815,00€. Total Amount: 14 588 286,50€.

Scientific Impact

Academic Collaborations

Ana Paula Pêgo, Instituto de Engenharia Biomédica (INEB) / Instituto de investigação e Inovação em Saúde (i3S), Universidade do Porto, Portugal.

Benhur Lee, Department of Microbiology, Mount Sinai School of Medicine, Nova York, Estados Unidos da América.

Doutor Cláudio M. Soares, Instituto de Tecnologia Química e Biológica António Xavier (ITQB), Universidade Nova de Lisboa, Oeiras, Portugal.

Doutora Ana Paula Arez, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Portugal.

Eulália Pereira, Departamento de Química, Faculdade de Ciências da Universidade do Porto, Portugal.

Gandhi Rádis-Baptista, Laboratório de Bioquímica e Biotecnologia, Instituto de Ciências do Mar, Universidade Federal do Ceará, Fortaleza, Brasil

Graça Soveral, Faculdade de Farmácia da Universidade de Lisboa, Portugal.

José Roberto Leite, Faculdade de Medicina, Universidade de Brasília, Brasil. Collaborator 1

Luís Mendes Pedro, Serviço de Cirurgia Vasculard, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Portugal.

Maria do Rosário Domingues, Universidade de Aveiro, Portugal.

Matteo Porotto, Department of Pediatrics, Columbia University Medical Center, Nova York, Estados Unidos da América.

Octavio L. Franco, Universidade Católica de Brasília / Universidade Católica Dom Bosco, Campo Grande, Brasil.

Robert A. S. Ariëns, Division of Cardiovascular and Diabetes Research, Leeds Institute for Genetics, Health and Therapeutics, University of Leeds, Reino Unido.

Rui Travasso, Departamento de Física, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, Portugal.

Sebastian Maurer-Stroh, Bioinformatics Institute (BII), Agency for Science, Technology and Research (A*STAR), Singapura.

Sónia Mendo, Universidade de Aveiro, Portugal.

Teresa Gonçalves, CNC e Faculdade de Medicina da Universidade de Coimbra, Portugal.

Selected Publications

Vigant F, Santos NC, Lee B (2015). Broad-spectrum antivirals against viral fusion. **Nature Reviews Microbiology** 13:426-437.

Guedes AF, Carvalho FA, Malho I, Lousada N, Sargento L, Santos NC (2016). Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients. **Nature Nanotechnology** 11:687-692.

Guedes AF, Carvalho FA, Moreira C, Nogueira JB, Santos NC (2017). Essential arterial hypertension patients present higher cell adhesion forces, contributing for fibrinogen-dependent cardiovascular risk. **Nanoscale** 9:14897-14906.

Gomes B, Augusto MT, Felício MR, Hollmann A, Franco OL, Gonçalves S, Santos NC (2018). Designing improved active peptides for therapeutic approaches against infectious diseases. **Biotechnology Advances** 36:415-429.

Martins AS, Carvalho FA, Faustino AF, Martins IC, Santos NC (2019). West Nile virus capsid protein interacts with biologically relevant host lipid systems. **Frontiers in Cellular and Infection Microbiology** 9:8.

2021 Publications in Peer-Reviewed Journals

Alves, M.M.S., Araújo, J.M.M., Martins, I.C., Pereira, A.B., Archer, M. (2021). [Insights into the interaction of Bovine Serum Albumin with Surface-Active Ionic Liquids in aqueous solution.](#) **Journal of Molecular Liquids**, 322:114537.

Borges-Araújo, L., Domingues, M.M., Fedorov, A., Santos, N.C., Melo, M.N., Fernandes, F. (2021) [Acyl-chain saturation regulates the order of phosphatidylinositol 4,5-bisphosphate nanodomains.](#) **Comm. Chem.**, 4, 164.

Carvalho, P.M., Makowski, M., Domingues, M.M., Martins, I.C., Santos, N.C. (2021) [Lipid membrane-based therapeutics and diagnostics.](#) **Arch. Biochem. Biophys.**, 704, 108858.

Cruz, T.B., Carvalho, F.A., Matafome, P.N., Soares, R.A., Santos, N.C., Travasso, R.D., Oliveira, M.J. (2021) [Mice with type 2 diabetes present significant alterations in their tissue biomechanical properties and histological features.](#) **Biomedicines**, Epub ahead of print 28 December 2021.

De Falco, L., Silva, N.M., Santos, N.C., Huber, R.G., Martins, I.C. (2021) [The pseudo-circular genomes of flaviviruses: structures, mechanisms, and functions of circularization.](#) **Cells**, 10(3):642.

Dematei, A., Nunes, J.B., Moreira, D.C., Jesus, J.A., Laurenti, M.D., Mengarda, A.C.A., Vieira, S.M., do Amaral, C.P., Domingues, M.M., de Moraes, J., Passero, L.F.D., Brand, G., Bessa, L.J., Wimmer, R., Kuckelhaus, S.A.S., Tomás, A.M., Santos, N.C., Plácido, A., Eaton, P., Leite, J.R.S.A. (2021) [Mechanistic insights into the leishmanicidal and bactericidal activities of batroxidin, a cathelicidin-related peptide from a South American viper \(*Bothrops atrox*\).](#) **J. Nat. Prod.**, 84(6): 1787-1798.

Domingues, M.M., Gomes, B., Hollmann, A., Santos, N.C. (2021) [25 Hydroxycholesterol effect on membrane structure and mechanical properties.](#) **Int. J. Mol. Sci.**, 2(5):2574.

Felício, R.F., Silveira, G.G.O.S., Oshiro, K.G.N., Meneguetti, B.T., Franco, O.L., Santos, N.C., Gonçalves, S. (2021) [Polyalanine peptide variations may have different mechanisms of action against multidrug-resistant bacterial pathogens.](#) **J. Antimicrob. Chemother.**, 76(5):1174–1186.

Ferreira, S., Raimundo, A., Menezes, R., Martins, I.C. (2021). [Islet amyloid polypeptide & amyloid beta peptide roles in Alzheimer's disease: Two triggers, one disease.](#) **Neural Regeneration Research**, 16(6):1127–1130.

Mancini, G., Gonçalves, L.M.D., Marto, J., Carvalho, F.A., Simões, S., Ribeiro, H.M., Almeida, A.J. (2021) [Increased Therapeutic Efficacy of SLN Containing Etofenamate and Ibuprofen in Topical Treatment of Inflammation.](#) **Pharmaceutics**; 13(3):328.

Mendes, R.M., Francisco, A.P., Carvalho, F.A., Dardouri, M., Costa, B., Bettencourt, A.F., Costa, J., Gonçalves, L., Costa, F., Ribeiro, I.A.C. (2021) [Fighting *S. aureus* catheter-related infections](#)

[with sophorolipids: Electing an antiadhesive strategy or a release one?](#) **Colloids Surf B Biointerfaces**; 208:112057.

Pronto-Laborinho, A.C., Lopes, A.S., Conceição, V.A., Gromicho, M., Santos, N.C., de Carvalho, M., Carvalho, F.A. (2021) [\$\gamma\$ fibrinogen as a predictor of survival in amyotrophic lateral sclerosis](#). **Front. Cardiovasc.**, 8, 715842.

Silva, P.M., Augusto, M.T., Porotto, M., Santos, N.C. (2021) [The pH-sensitive action of cholesterol-conjugated peptide inhibitors of influenza virus](#). **Biochim. Biophys. Acta**, 1863(12), 183762.

Barbosa, J.C., Silva, I.C., Caetano, T., Mösker, E., Seidel, M., Lourenço, J., Süßmuth, R.D., Santos, N.C., Gonçalves, S., Mendo, S. (2021) [Assessing the potential of the two-peptide lantibiotic lichenicidin as a new generation antimicrobial](#). **World J. Microbiol. Biotechnol.**, in press.

Barbosa, J.C., Gonçalves, S., Makowski, M., Silva, I.C., Caetano, T., Schneider, T., Mösker, E., Süßmuth, R.D., Santos, N.C., Mendo, S. (2021) [Insights into the mode of action of the two-peptide lantibiotic lichenicidin](#). **Colloids Surf. B – Biointerfaces**, in press.

Alves, L.S., Marques, A.R.A., Padrão, N., Carvalho, F.A., Ramalho, J., Lopes, C.S., Soares, M.I.L., Futter, C.E., Pinho e Melo, T.M.V.D., Santos, N.C., Vieira, O.V. (2021) [Cholesteryl hemiazelate causes lysosome dysfunction impacting vascular smooth muscle cells homeostasis](#). **J. Cell Sci.**, in press.

Domingues, M.M., Carvalho, F.A., Santos, N.C. (2021) [Nanomechanics of blood clot and thrombus formation](#). **Annu Rev. Biophys.**, in press.

Invited Lectures and Seminars

Nuno C. Santos. Caracterização de sistemas biológicos e nanoestruturados por microscopia de força atómica e espectroscopia de força. Escola de Síntese de Caracterização de Sistemas Biológicos e Nanoestruturados, Sociedade Brasileira de Biofísica, online, March 15-19, 2021.

Nuno C. Santos. Avaliação de propriedades biomecânicas e adesão célula-célula por AFM em doenças cardiovasculares e oncologia. VI Congresso Regional da Sociedade Brasileira de Biofísica, online, March 22-25, 2021.

Nuno C. Santos. Nanomedicina na avaliação da interação fibrinogénio-eritrócito e risco cardiovascular. Centro Cardiovascular da Universidade de Lisboa (CCUL), Lisbon, Portugal May 27, 2021.

Bárbara Gomes, Giusepinna Sanna, Silvia Madeddu, Sónia Gonçalves, Axel Hollmann, Nuno C. Santos. Characterization of enveloped virus inhibition by 25-hydroxycholesterol at the membrane level. 7th International Iberian Biophysics Congress, online, June 14-16, 2021.

Luís Borges-Araújo, Marco M. Domingues, Alexander Fedorov, Nuno C. Santos, Manuel N. Melo, Fábio Fernandes. Acyl-chain saturation regulates the order of phosphatidylinositol 4,5-bisphosphate nanodomains. Encontro Ciência '21, online, June 28-30, 2021.

Maria J. Sarmento. The impact of the glycan headgroup on the nanoscopic segregation of gangliosides. XXI SPB National Congress of Biochemistry, Évora, Portugal, October 15, 2021.

Catarina S. Lopes, Ryan Gouveia e Melo, Ana Filipa Guedes, Luís Mendes Pedro, Filomena A. Carvalho, Nuno C. Santos. Atomic force microscopy as a nanotool for the assessment of cardiovascular patients. NanoMed (NanoMedicine) 2021 / Sensors 2021 / SMS (Smart Materials and Surfaces) 2021 / EGF (European Graphene Forum) 2021 Joint International Conferences and Exhibition, Milan, Italy, October 20-22, 2021.

Catarina S. Lopes, Ryan Gouveia e Melo, Teresa Freitas, Sofia Nabais, Ana Rita Gaspar, Ana Mara Fonseca, Ana Filipa Guedes, Filomena A. Carvalho, Luís Mendes Pedro, Nuno C. Santos. Microscopia de força atómica na avaliação da doença carotídea. Reunião do Núcleo de Biologia Vasculard da SPACV (Sociedade Portuguesa de Angiologia e Cirurgia Vasculard), Lisbon, Portugal, November 20, 2021.

Nuno C. Santos. Atomic force microscopy-based assessment of cardiovascular risk. XLIX Reunión Anual de la Sociedad Argentina de Biofísica, online, December 1-3, 2021.

Nuno C. Santos. AFM-based assessment of cardiovascular risk. Webinar AFM Applications in Biomedical Research and Diagnostics, online, December 15, 2021.

Communications

Sedrine, N.B., Silva, P.G., Epalanga, J., Guinho, R., Frias, R., Tomás, A.L., Reichel, A., Silva, P.M., Pinto, J., Calado, I., Campos, J., Silva, A.I., Machado, V., Laranjeira, R., Santos, N.C., Abreu, P., Mendes, P. Novel solution for efficient and simultaneous air and surface disinfection using UV-C technology. 2021 IUVA (International Ultraviolet Association) World Congress, online, June 7-8, 2021. Oral communication; international conference.

Curty, J., Lopes, C.S., Hernández-Machado, A., Carvalho, F., Santos, N.C., Travasso, R.D.M. Fibrinogen-mediated erythrocyte adhesion. 55th Annual Scientific Meeting of ESCI (European Society for Clinical Investigation), online, June 9-11, 2021. Oral communication; international conference.

Curty, J., Lopes, C.S., Hernández-Machado, A., Carvalho, F., Santos, N.C., Travasso, R.D.M. Fibrinogen-mediated erythrocyte adhesion. SMB (Society for Mathematical Biology) 2021 Annual Meeting, online, June 13-17, 2021. Oral communication; international conference.

do Amaral, C.P., Plácido, A., Teixeira, C., Gomes, P., Leite, J.R.S.A., Santos, N.C., Eaton, P. Short bioactive peptides from European amphibian skin secretions. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Silva, I.C., de Almeida, M.P., Pereira, E., Franco, O.L., Santos, N.C., Gonçalves, S. Improving the anticancer activity of PaMAP1.9-conjugated star-shaped nanoparticles. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Lopes, C.S., Gouveia e Melo, R., Nabais, S., Freitas, T., Gaspar, A.R., Fonseca, A.M., Guedes, A.F., Pedro, L.M., Santos, N.C., Carvalho, F.A. Relevance of fibrinogen-erythrocyte binding in carotid artery disease. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Martins, A.S., Carvalho, F.A., Faustino, A.F., Nascimento, A.R., Enguita, F.J., Santos, N.C., Martins, I.C. Zika virus capsid protein does not bind host lipid systems. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Silva, N.M., Martins, A.S., Karguth, N., Enguita, F.J., Huber, R.G., Santos, N.C., Martins, I.C. Studying flavivirus capsid proteins interactions with viral RNA. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Silva, P.M., da Silva, I.V., Sarmento, M.J., Carvalho, F.A., Soveral, G., Santos, N.C. Effects of aquaporin-3 and aquaporin-5 silencing on pancreatic cancer cell biomechanics and cell-cell adhesion. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Borges-Araújo, L., Domingues, M.M., Fedorov, A., Santos, N.C., Melo, M.N., Fernandes, F. Acyl-chain saturation regulates the order of phosphatidylinositol 4,5-bisphosphate nanodomains. 7th International Iberian Biophysics Congress, online, June 14-17, 2021. Poster communication; international conference.

Martins, A.S.G., Reis, S.D., Baboi, R., Cortinhas, J., Domingues, M.M., Santos, N.C., Santos, S.D., Pêgo, A.P., Moreno, P.M.D. Aptamer-functionalized tetrahedral DNA nanostructures aiming at neuronal targeting. 1st Symposium on Oligonucleotide Technologies and Therapeutics@Portugal – OTP2021, online, July 8-9, 2021. Poster communication; national conference.

Tomás, A.L., Reichel, A. Silva, P.M., Sedrine, N.B., Silva, P.G., Pinto, J., Calado, I., Campos, J., Silva, I., Machado, V., Laranjeira, R., Abreu, P., Mendes, P., Santos, N.C. Effective use of UV-C irradiation as an inactivation tool for SARS-CoV-2 on porous and non-porous surfaces. 31st ECCMID (European Congress of Clinical Microbiology and Infectious Diseases), online, July 9-12, 2021. Poster communication; international conference.

Martins, A.S.G., Reis, S.D., Baboi, R., Cortinhas, J., Domingues, M.M., Santos, N.C., Santos, S.D., Pêgo, A.P., Moreno, P.M.D. Nucleic acid-based nanostructures functionalized with neurotrophin-mimetic aptamer aiming at neuronal targeting. ESB 2021 – 31st Conference of the European Society of Biomaterials, together with the 43rd Annual Congress of the Iberian Society

of Biomechanics and Biomaterials (SIBB), online, September 5-9, 2021. Oral communication; international conference.

Plácido, A., do Amaral, C.P., Teixeira, C., Nogueira, A., Brango-Vanegas, J., Barbosa, E.A., Moreira, D.C., Silva-Carvalho, A.É., Gloria, M., Nascimento, J., Albuquerque, P., Saldanha-Araújo, F., Lima, F.C.D.A., Batagin-Neto, A., Kuckelhaus, S., J. Bessa, L.J., Freitas, J., Brand, G.D., Santos, N.C., Relvas, J.B., Gomes, P., Leite, J.R.S.A., Eaton, P. A novel antioxidant peptide identified in the skin secretion of *Pelophylax perezii*. XVI Congresso Luso-Espanhol de Herpetologia, online, September 6-17, 2021. Oral communication; international conference.

Silva, I.C., de Almeida, M.P., Pereira, E., Franco, O.L., Santos, N.C., Gonçalves, S. Peptide-conjugated silver nanoparticles as anticancer agent. IUPAB (International Union for Pure and Applied Biophysics) Young Scientist Program webinar series: Drug Discovery and Delivery, online, September 15, 2021. Oral communication; international conference.

Silva, I.C., de Almeida, M.P., Pereira, P., Tranfeld, E.M., Franco, O.L., Santos, N.C., Gonçalves, S. Enhancing anticancer activity of antimicrobial peptide by silver nanostars functionalization. MFS2021 – Microscopy at the Frontier of Science Conference, online, September 29-October 1, 2021. Oral communication; international conference.

Sarmento, M.J., Silva, M.I., do Amaral, C.P., Carvalho, F.A., Santos, N.C. Deciphering the lipidome of the human nuclear envelope during healthy age progression. I PhasAGE International Conference “Phase Transitions in Aging and Age-related Diseases, online, October 12-14, 2021. Oral communication; international conference.

do Amaral, C.P., Plácido, A., Teixeira, C., Gomes, P., Leite, J.R.S.A., Santos, N.C., Eaton, P. The possible anticancer role of bioactive peptides from European amphibian skin secretions. 20th IUPAB (International Union for Pure and Applied Biophysics) Congress, online, October 4-8, 2021. Poster communication; international conference.

Silva, I.C., de Almeida, M.P., Pereira, E., Franco, O.L., Santos, N.C., Gonçalves, S. Peptide-conjugated silver nanoparticles as anticancer agent. 20th IUPAB (International Union for Pure and Applied Biophysics) Congress, online, October 4-8, 2021. Poster communication; international conference.

Silva, N.M., Martins, A.S., Karguth, N., Enguita, F.J., Huber, R.G., Santos, N.C., Martins, I.C. Studying flavivirus capsid proteins interactions with viral RNA. 20th IUPAB (International Union for Pure and Applied Biophysics) Congress, online, October 4-8, 2021. Poster communication; international conference.

Silva, P.M., da Silva, I.V., Sarmento, M.J., Carvalho, F.A., Soveral, G., Santos, N.C. AQP3 and AQP5 silencing promotes changes in cell-cell adhesion and biomechanical properties of pancreatic cancer cells. 20th IUPAB (International Union for Pure and Applied Biophysics) Congress, online, October 4-8, 2021. Poster communication; international conference.

Lopes, C.S., Gouveia e Melo, R., Nabais, S., Freitas, T., Gaspar, A.R., Fonseca, A.M., Guedes, A.F., Pedro, L.M., Santos, N.C., Carvalho, F.A. Changes on fibrinogen-erythrocyte binding in carotid artery disease. SPB (Sociedade Portuguesa de Bioquímica) 2021 – XXI Congresso Nacional de Bioquímica, online, October 14-16, 2021. Oral communication; national conference.

Silva, N.M., Martins, A.S., Karguth, N., Enguita, F.J., Huber, R.G., Santos, N.C., Martins, I.C. Unravelling dengue virus capsid protein interaction with viral genome. SPB (Sociedade Portuguesa de Bioquímica) 2021 – XXI Congresso Nacional de Bioquímica, online, October 14-16, 2021. Oral communication; national conference.

do Amaral, C.P., Plácido, A., Teixeira, C., Gomes, P., Leite, J.R.S.A., Santos, N.C., Eaton, P. Bioactive peptides isolated from European amphibian skin secretions with possible anticancer effect. SPB (Sociedade Portuguesa de Bioquímica) 2021 – XXI Congresso Nacional de Bioquímica, online, October 14-16, 2021. Oral communication; national conference.

Da Silva, I.V., Silva, P.M., Santos, N.C., Soveral, G. Peroxiporins and pancreatic cancer: new roles for aquaporin-3 and aquaporin-5 in tumor biology. SPB (Sociedade Portuguesa de Bioquímica) 2021 – XXI Congresso Nacional de Bioquímica, online, October 14-16, 2021. Oral communication; national conference.

Lopes, C.S., Gouveia e Melo, R., Nabais, S., Freitas, T., Gaspar, A.R., Fonseca, A.M., Guedes, A.F., Pedro, L.M., Santos, N.C., Carvalho, F.A. Relevance of fibrinogen-erythrocyte binding in carotid artery disease. ESVB 2021 – European Symposium on Vascular Biomaterials, Strasbourg, France, November 4-6, 2021. Oral communication; international conference.

Organization of Conferences

Nuno C. Santos. Member of the scientific committee. SPB (Sociedade Portuguesa de Bioquímica) 2021 – XXI Congresso Nacional de Bioquímica, Évora, Portugal, October 14-16, 2021.

Nuno C. Santos. Member of the scientific and organizing committees. 7th International Iberian Biophysics Congress, online, June 14-16, 2021.

Networks & Research Infrastructures

Maria J. Sarmiento. EpiLipidNet COST Action (CA19105 – Pan-European Network in Lipidomics and EpiLipidomics). WG4 & WG5 (dissemination) member, ECI committee member.

Nuno C. Santos. Sociedade Portuguesa de Biofísica (SPBf). President (until November/2021) and Secretary (from November 2021).

Nuno C. Santos. European Peptide Society. National representative.

Nuno C. Santos. European Biophysical Societies' Association (EBSA). Executive Committee member.

Nuno C. Santos. Initiative for Science in Europe (ISE). EBSA representative (until February 2021).

Nuno C. Santos. Biophysical Society (U.S.A). Ambassador.

Prizes & Honors in 2021

Nuno C. Santos. Associate editor of Peptide Science;

Nuno C. Santos. Referee in international journals (ACS Nano, Analytica Chimica Acta, Analytical Chemistry, Antimicrobial Agents and Chemotherapy, Antiviral Chemistry and Chemotherapy, Applied Surface Science, Biochemistry, Biochimica et Biophysica Acta, Biomacromolecules, Biophysical Chemistry, Biophysical Reviews, Biopolymers – Peptide Science, Biotechnology Advances, Blood, Chemical Communications, Chemistry and Biology, Clinical Hemorheology and Microcirculation, Colloids and Surfaces B: Biointerfaces, Critical Care, Current Medicinal Chemistry, Current Pharmaceutical Design, Current Protein & Peptide Science, Disease Markers, Drug Discovery Today, Enzyme and Microbial Technology, European Biophysics Journal, European Journal of Medicinal Chemistry, FEBS Journal, Frontiers in Microbiology, Frontiers in Pharmacology, Fungal Biology Reviews, International Journal of Nanomedicine, Journal of Biomedicine and Biotechnology, Journal of Fluorescence, Journal of Innovative Optical Health Sciences, Journal of Medicinal Food, Journal of Molecular Recognition, Journal of Molecular Structure, Journal of Photochemistry and Photobiology, Journal of Physical Chemistry, Journal of Peptide Science, Journal of the American Chemical Society, Journal of the Royal Society – Interface, Langmuir, Leukemia Research, mBio, Molecular Membrane Biology, Nanoscale, Nanomedicine (NBM), Organic & Biomolecular Chemistry, Peptides, PLoS ONE, Recent Patents on Anti-Infective Drug Discovery, Retrovirology, Scientific Reports, and Small).

Nuno C. Santos. Portuguese Biophysical Society (SPBf). President (until November/2021) and Secretary (from November 2021).

Nuno C. Santos. European Peptide Society. National representative.

Nuno C. Santos. European Biophysical Societies' Association (EBSA). Executive Committee member.

Nuno C. Santos. Initiative for Science in Europe (ISE). EBSA representative (until February 2021).

Nuno C. Santos. Biophysical Society (U.S.A). Ambassador.

Ítala C. Silva. Best oral communications prize at MFS2021 – Microscopy at the Frontier of Science Conference, online, September 29-October 1, 2021.

Advanced Teaching

Nuno C. Santos. M2B-PhD – Medical Biochemistry and Biophysics PhD program. Faculdade de Medicina da Universidade de Lisboa, Faculdade de Farmácia da Universidade de Lisboa, Instituto Superior Técnico (Universidade de Lisboa), Faculdade de Farmácia da Universidade de Coimbra, Faculdade de Ciências da Universidade do Porto. Since April, 2016.

Nuno C. Santos. Coordination of the Curricular Units Metabolismo Geral and Bioquímica. Mestrado em Doenças Metabólicas e Comportamento Alimentar. Faculdade de Medicina da Universidade de Lisboa. Since September, 2015.

Nuno C. Santos. Coordination of the Curricular Unit. Advanced Techniques in Biomedical Research I. Mestrado em Investigação Biomédica. Faculdade de Medicina da Universidade de Lisboa / Instituto de Medicina Molecular. Since September, 2020.

Nuno C. Santos. Lecture. Atomic force microscopy. Molecular Biosciences (MolBioS) PhD program. ITQB (Instituto de Tecnologia Química e Biológica), IBET (Instituto de Biologia Experimental Tecnológica), REQUIMTE (Rede de Química e Tecnologia), CREM (Centro de Recursos Microbiológicos), IGC (Instituto Gulbenkian de Ciência). Oeiras. January 28, 2021.

Nuno C. Santos. Lecture. Molecular interactions probed by AFM-based force spectroscopy. Farmácia PhD program. Faculdade de Farmácia da Universidade de Lisboa. Lisboa. March 17, 2021.

Nuno C. Santos. Lecture. Fibrinogen-erythrocyte interaction as a cardiovascular risk. Ciências da Saúde PhD program. Faculdade de Medicina da Universidade de Coimbra. Coimbra. April 9, 2021.

Nuno C. Santos. Lecture. Atomic force microscopy. Biologia estrutural master course. Instituto Superior Técnico, Universidade de Lisboa. Lisboa. April 16, 2021.

Nuno C. Santos. Lecture. Biological and biomedical applications of atomic force microscopy. Bioquímica master course. Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica. April 30, 2021.

Nuno C. Santos. Lecture. Biomembranes and the assessment of the interaction with membrane-active molecules. Ciências farmacêuticas master course. Faculdade de Farmácia da Universidade de Lisboa, Lisboa. September 29, 2021.

MSc Theses

Maria do Carmo Valentina Greier, 18/02/2021, Metabolic stress and epithelial-mesenchymal transition in head and neck cancer, Mestrado em Doenças Metabólicas e do Comportamento Alimentar, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Nuno C. Santos.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

On the context of the SARS-CoV-2/COVID-19 pandemic, in 2021 several contracts were established with companies, both from Portugal and from abroad, to quantify in vitro, in the

iMM BSL-3 facility, the anti-SARS-CoV-2 activity of potential drugs, surface coatings, UV irradiation, pre-treated face masks and pre-treated carpets.

Intellectual Property Rights in 2021

Patent 1

Patent Applicants: Instituto de Medicina Molecular João Lobo Antunes (iMM, Lisbon, PT), Ivo Martins

Inventors: Ivo C. Martins, Gabriela Guerra, Patrícia Carvalho

Title of the invention: Biomaterials.

Priority reference (if applicable): 10 February 2020, 20 February, 2020.

Filing date: 10 February 2021.

Publication date: 10 August 2021.

Application number: PCT/EP2021/053235

Application reference (if applicable): International publication number WO 2021/160688 A1

Science and Society in 2021

Nuno C. Santos. Conversas com Cientistas – Décadas de Ciência para Dias de Vacinas. Agrupamento de Escolas de Vila Verde, Vila Verde, Portugal, April 22, 2021.

Nuno C. Santos. Conversas com Cientistas – Décadas de Ciência para Dias de Vacinas. Colégio São João de Brito, Lisbon, Portugal, April 22, 2021.

Nuno C. Santos. Conversas com Cientistas – Décadas de Ciência para Dias de Vacinas. Escola Profissional de Educação para o Desenvolvimento, Caparica, Portugal, April 29, 2021.

Nuno C. Santos. Conversas com Cientistas – Décadas de Ciência para Dias de Vacinas. Externato Ribadouro, Porto, Portugal, April 29, 2021.

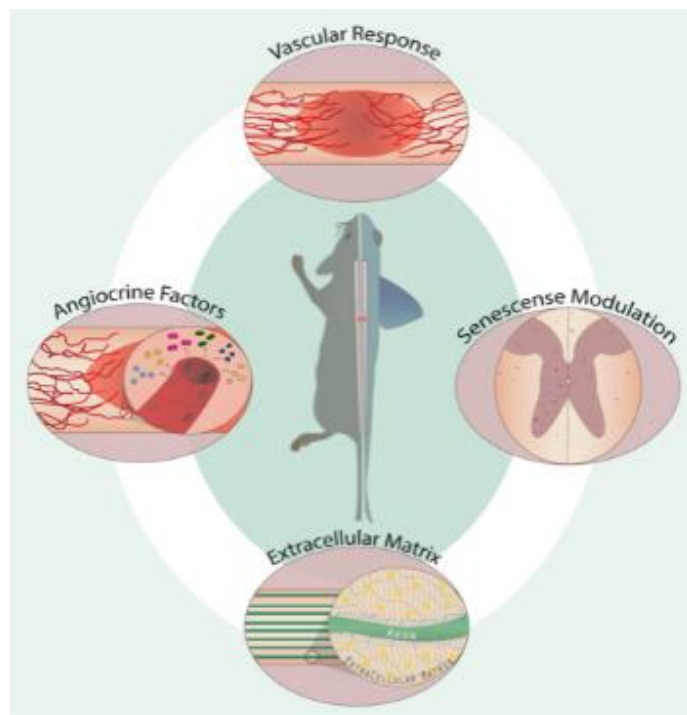
Leonor Saúde Lab

Head of Laboratory: Leonor Saúde, PhD, Group Leader and Invited Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Ana Catarina Esteves Ribeiro	PhD	Senior Postdoctoral Researcher
Ana Filipa Carvalho Marques Dias	PhD	Postdoctoral Researcher
Ana Filipa Pombinho Isidro	Master Degree	PhD Student
Ana Paula Lopes Martins	University Degree	Trainee (Left July)
Ana Raquel Dias Quitéria	Master Degree	Lab Manager
Carmen de Sena Tomás	PhD	Senior Postdoctoral Researcher
Dalila Maria Neves Silva	Master Degree	PhD Student
Daniel Filipe Silva Ribeiro	PhD	Postdoctoral Researcher (Started October)
Isaura Vanessa Antunes Martins	PhD	Postdoctoral Researcher
Maria Leonor Rebola Lameira	University Degree	MSc Student
Mariana Antão Ventura Monteiro	High School Diploma	MSc Student (Started September)
Mariana Antas Rebocho da Costa	Master Degree	PhD Student
Patrícia Naique Taborda	University Degree	MSc Student (Started September)

Graphical Abstract



Lab Interests

We want to understand the molecular and cellular mechanisms controlling fundamental regenerative processes activated in the context of a spinal cord injury.

Research Fields

- Cellular, Developmental and Regenerative Biology
- Neuroscience and Disorders of the Nervous System

Major Scientific Achievements in 2021

- We published our working on the role of senescent cells in the context of a spinal cord injury in mammals (Paramos-de-Carvalho D. et al. Cell Reports, 2021).
- We published our views on the role of senescent states in diverse physiological contexts (Paramos-de-Carvalho D. et al. Elife, 2021).
- We were awarded the 2021 Pfizer Award in Basic Research

Ongoing Projects in 2021

2019/2022: Targeting induced-senescent cells: a novel approach to promote spinal cord regeneration in mammals Acronym: SENSE. Coordinator: Leonor Saúde. Funding Agency: “la Caixa” Foundation. Reference: Initiative i4b (HR18-00187). Amount: 444 048,00€. Total Amount: 444 048,00€.

2018/2021: Modulação da reparação vascular durante a regeneração da medula espinal. Coordinator. Ana Catarina Ribeiro. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-BID/28572/2017. Amount: 239 365,16€. Total Amount: 239 365,16€.

2018/2021: A função das células senescentes induzidas na regeneração da medula espinal. Coordinator: Leonor Saúde. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/30428/2017. Amount: 239 340,72€. Total Amount: 239 340,72€.

Scientific Impact

Academic Collaborations

António Jacinto, CEDOC-NMS, Lisbon, PT
Caetano Reis e Sousa, Francis Crick Institute, London, UK
Lino Ferreira, CNC-UC, Coimbra, PT
Nuno Barbosa-Morais, IMM, Lisbon, PT
César Mendes, CEDOC-NMS, Lisbon, PT
Rune Matthiesen, CEDOC-NMS, Lisbon, PT
Hans C. Beck, CCP, Odense, Denmark

Selected Publications

Paramos-de-Carvalho D., Martins, I. Cristóvão A.M., Dias A.F., Pereira T., Chapela D., Farinho A., Neves-Silva D., Jacinto A. and Saúde L. (2021). [Targeting senescent cells improves functional recovery after spinal cord injury](#). *Cell Reports* 36(1):109334.

Relevance of the publication: The L. Saúde lab was the coordinator of this study. The main relevance of this study was to show the detrimental effect of induced-senescent cells in the repair outcome in the context of spinal cord injuries in mammals.

Chapela D, Sousa S, Martins I, Cristóvão AM, Pinto P, Corte-Real S, Saúde L (2019). [A zebrafish drug screening platform boosts the discovery of novel therapeutics for spinal cord injury in mammals](#). **Scientific Reports** 9(1):10475.

Relevance of the publication: The L. Saúde lab was the coordinator of this study. The main relevance of this study was to show that zebrafish larvae can be successfully used as screening platforms for drug repositioning for spinal cord injury indications.

Ribeiro A, Monteiro JF, Certal AC, Cristóvão AM, Saúde L (2017). [Foxj1a is expressed in ependymal precursors, controls central canal position and is activated in new ependymal cells during regeneration in zebrafish](#). **Open Biology** 7(11):170139.

Relevance of the publication: The L. Saúde lab was the coordinator of this study. We contributed to establish the similarity between spinal cord neural stem cells (NSCs) that exist in the ependymal canal in zebrafish and mice. These ependymal cells share several transcription factors, one of such factors is Foxj1. It was shown that foxj1 is expressed by ependymal cells in mammals including humans and, in our laboratory, we have shown that foxj1a positive cells are also present in the zebrafish ependymal canal. The Foxj1 NSCs were shown to react to an injury by engaging in a proliferative state in mammals and again we have demonstrated that also in zebrafish these cells are the first ones to activate a proliferative program after injury.

Mendes RV, Martins GG, Martins AM, Saúde L (2014). [N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells](#). **Developmental Cell** 30(3):353-60.

Relevance of the publication: The L. Saúde lab was the coordinator of this study. We showed that a cell-cell adhesion mechanism mediated by N-cadherin terminates the leftward movements of Left-Right organizer cells, thus locking the Left-Right asymmetries established earlier in the embryo. Furthermore, we provided evidence that this locking of Left-Right asymmetries in the Left-Right organizer is essential for the proper asymmetric looping of the developing heart.

Azevedo AS, Grotek B, Jacinto A, Weidinger G, Saúde L (2011). [The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations](#). **PLoS ONE** 6(7):e22820.

Relevance of the publication: The L. Saúde lab was the coordinator of this study. In this study, we challenged to the limit the regenerative capacity of the zebrafish and showed that this small vertebrate, through a process of de-differentiation, has an almost unlimited capacity to regenerate its caudal fin.

2021 Publications in Peer-Reviewed Journals

Estronca L., Francisco V., Pitrez, P., Honório I., Carvalho L., Vazão H., Blerish J., Rai A., Nissan X., Simon, U. Grãos M., Saúde L. and Ferreira L. (2021). [Induced pluripotent stem cell-derived vascular networks to screen nano-bio interactions](#). **Nanoscale Horizons** 6(3):245-259

Paramos-de-Carvalho D., Jacinto A. and Saúde L. (2001). [The right time for senescence](#). **eLife** 10:e72449

Paramos-de-Carvalho D., Martins, I. Cristóvão A.M., Dias A.F., Pereira T., Chapela D., Farinho A., Neves-Silva D., Jacinto A. and Saúde L. (2021). [Targeting senescent cells improves functional recovery after spinal cord injury](#). **Cell Reports** 36(1):109334.

Invited Lectures and Seminars

Martins I. Improving spinal cord repair: from targeting senescence to endothelial cells and beyond. UC-Biotech, Coimbra, Portugal, December 2021.

Saúde L. Spinal cord regeneration: what can we learn from zebrafish? XXIII Encontro Nacional de Estudantes de Biologia (ENEB), Online, Portugal, March 28, 2021.

Saúde L. Zebrafish in Biomedical Research Workshop. Annual International (Bio)Medical Students Meeting, Online, Portugal, March 20, 2021.

Saúde L. Bridging the (re)generation gap: insights from the zebrafish. VI Semana de Bioengenharia do Instituto Superior Técnico, Online, Portugal, March 9, 2021.

Saúde L. Spinal cord repair & regeneration. JorTec Biologia 2021, Online, Portugal, February 18, 2021.

Communications

Neves-Silva, D. Mimicking the Zebrafish Extracellular Matrix Profile in Mammals to Promote Spinal Cord Repair. XVII Meeting of the Portuguese Society for Neuroscience (SPN2021), Coimbra, Portugal, December 1-3, 2021. POSTER; NATIONAL CONFERENCE.

Martins, I. Targeting senescent cells improves functional recovery after spinal cord injury. XVII Meeting of the Portuguese Society for Neuroscience (SPN2021), Coimbra, Portugal, December 1-3, 2021. POSTER; NATIONAL CONFERENCE.

Neves-Silva, D. Using the regenerative potential of zebrafish extracellular matrix to promote spinal cord repair in mammals. 3rd NMS Symposium on Chronic Diseases and Translational Science, Lisboa, Portugal, October 11-13, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE - ONLINE.

Lameira, L. Modulation of neutrophil dynamics after spinal cord injury influences regeneration in zebrafish. Lisbon iMed Conference, Lisbon, Portugal, October 6-10, 2021. POSTER; NATIONAL CONFERENCE.

de Sena-Tomás, C. Activation of Nkx2.5 transcriptional program is required for adult myocardial repair. 16th International Zebrafish Conference. June 16-22, 2021. POSTER; INTERNATIONAL CONFERENCE - ONLINE.

Ribeiro, A. Vascular repair after spinal cord injury in zebrafish. Poster presentation. 16th International Zebrafish Conference. June 16-22, 2021. POSTER; INTERNATIONAL CONFERENCE - ONLINE.

Rebocho da Costa, M.. Role of macrophages in angiogenesis and vessel remodeling during spinal cord regeneration in zebrafish. XIV CAML - IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE - ONLINE.

Neves-Silva, D. Using the regenerative potential of zebrafish extracellular matrix to promote spinal cord repair in mammals. XIV CAML - IV NeurULisboa PhD Students Virtual Meeting, Lisboa, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE - ONLINE.

Prizes & Honors in 2021

Saúde, L. 2021 Pfizer Award in Basic Research, Portugal.

Lameira, L. Basic Research Award for Best Oral Communication. AstraZeneca Foundation Innovative Competition at the iMED Conference 13.0, Portugal.

Neves-Silva, D. Rising Star Award at 3rd NMS Symposium on Chronic Diseases and Translational Science, Portugal.

Saúde, L. Grant reviewer. GAPIC-FMUL, Portugal.

Saúde, L. Grant reviewer. Liliane Bettencourt Prize for Life Sciences. Fondation Bettencourt Schueller, France.

Saúde, L. Manuscript reviewer. Nature Communications.

Saúde, L. Manuscript reviewer. Review Commons.

Saúde, L. Manuscript reviewer. PloS Genetics.

Saúde, L. Review Editor, Frontiers in Cell and Developmental Biology.

Saúde, L. Associate Editor, BMC Developmental Biology.

Advanced Teaching

Ana Ribeiro. Lecture. Spinal cord regeneration in zebrafish. Master in Evolution and Developmental Biology, FCUL, Lisbon, Portugal, December 7, 2021

Leonor Saúde. Lecture. Zebrafish in Research. IGC PhD Programme in Integrative Biology and Biomedicine, IGC, Oeiras, Portugal, October 25, 2021

MSc Theses

Ana Paula Martins, 01/June/2021, Can an injury-activated molecular program correct a defective developmental program? Faculdade de Medicina da Universidade de Lisboa. Leonor Saúde.

Valorization of Knowledge / Social and Economic Impact

Intellectual Property Rights in 2021

Applicants: TechnoPhage, SA & iMM. Inventors: Chapela, D., Côrte-Real, S., Saúde, L., Martins, I., Sousa, S. Eletriptan Hydrobromide for treatment of spinal cord injury and improvement of locomotor function. PCT/IB2020/062306 (20/01/2021).

Science and Society in 2021

Leonor Saúde. “Ciência é luz. Mesmo quando os holofotes se apagam”. Entrevista ao Expresso, November 20, 2021.

Leonor Saúde. “As lesões na coluna deixarão de ser irreversíveis?” Podcast Mentres Brilhantes do Observador, November 27, 2021.

<https://observador.pt/programas/mentres-brilhantes/as-lesoes-na-coluna-deixarao-de-ser-irreversiveis/>

Leonor Saúde. “Regenerar lesões na medula espinhal? Estes peixes podem ajudar”. Entrevista ao Observador, September 6, 2021.

<https://observador.pt/2021/09/06/regenerar-lesoes-na-medula-espinhal-estes-peixes-podem-ajudar/>

Leonor Saúde. “Paraplégicos e tetraplégicos podem ter esperança”. Entrevista ao jornal O Figueirense, Janeiro 29, 2021.

Ana Sebastião Lab

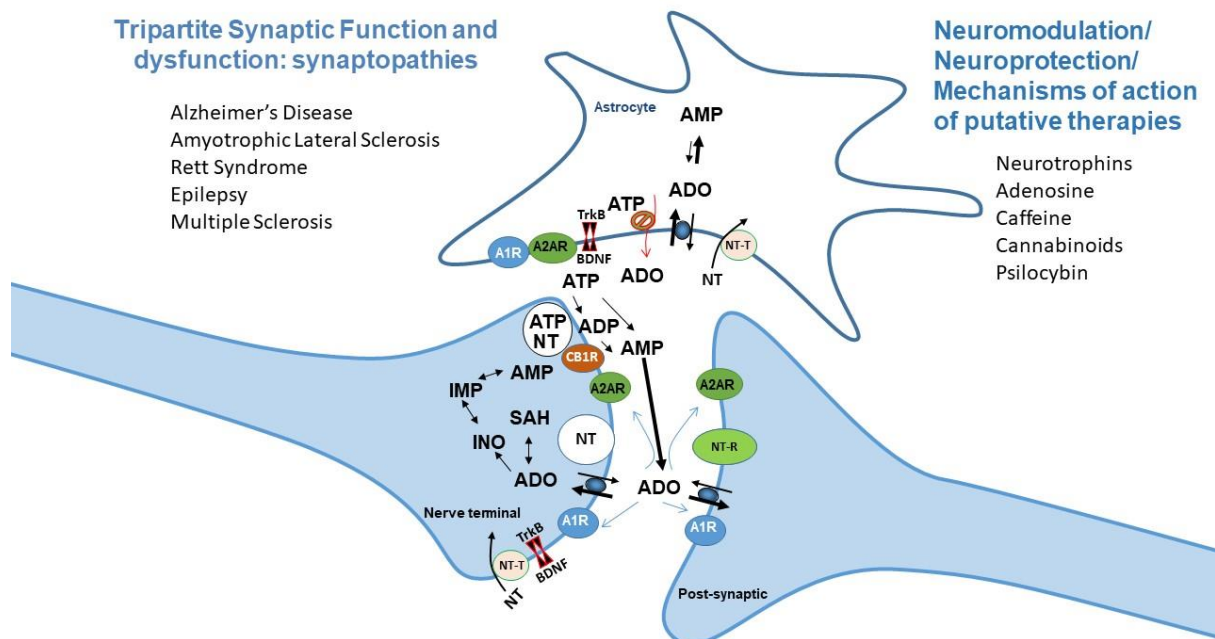
Head of Laboratory: Ana M Sebastião, PhD, Group Leader and Full Professor and Director of Instituto de Farmacologia e Neurociências and Vice-Dean of Faculdade de Medicina da Universidade de Lisboa

Team

Ana Filipa Ferreira da Cunha Ribeiro	PhD	Postdoctoral Researcher
Ana Rita Carreira Baptista Gomes	Master Degree	PhD Student
Anwesh Ghosh	Master Degree	PhD Student
Carolina de Almeida Borlido	University Degree	Trainee
Catarina Beatriz Silva Ferreira	Master Degree	PhD Student
Catarina Miranda Lourenço	Master Degree	PhD Student
Céline Felicidade Freitas	University Degree	MSc Student
Cláudia Alexandra dos Santos Valente de Castro	PhD	Senior Postdoctoral Researcher
Cristina Maria de Oliveira Varandas	High School Diploma	Administrative Technician
Daniela Cristina Melo Magalhães	Master Degree	PhD Student
Daniela Sofia da Costa Abreu	University Degree	MSc Student
Diana Sousa Correia	High School Diploma	MSc Student
Diogo André Mendonça Dias	Master Degree	MSc Student (Started January. Left March)
Diogo Miguel da Palma Lourenço	Master Degree	PhD Student
Diogo Miguel Santos Rombo	PhD	Postdoctoral Researcher
Élia Marília da Fonte Mota	PhD	Postdoctoral Researcher (Started January. Left March)
Francisco José Gonçalves Meda	University Degree	MSc Student (Started January)
Gonçalo Valentim André da Costa	University Degree	MSc Student (Started September)
Hugo Rafael Marques Simões	University Degree	MSc Student
Isa Fernandes Mota	University Degree	MSc Student (Started September)
Jacinta Manuel de Oliveira Manta	Master Degree	Trainee (Started May. Left December)
Joana Filipa Gonçalves Ribeiro	Master Degree	PhD Student
Joana Moura Mateus	Master Degree	PhD Student
Joana Simão Correia Nunes	High School Diploma	MSc Student
João Baptista Moreira	Master Degree	PhD Student (Started January)
João Frederico Nóbrega Carvalho	High School Diploma	MSc Student (Started January)
Joaquim Alexandre Ribeiro	PhD	Staff Scientist
Jorge Miguel Farinha Ferreira	Master Degree	PhD Student
José António Matos Silva	High School Diploma	MSc Student (Started March)
Leonor Pedro Oliveira Ribeiro Rodrigues	Master Degree	PhD Student
Lia Marta Barreira Fernandes	University Degree	MSc Student (Started October)
Mafalda Cagica Pinto de Carvalho	Master Degree	MSc Student (Started January. Left March)
Mafalda Ferreira Manso	Master Degree	Trainee (Started March)
Maria Alexandra Pereira Botelho	High School Diploma	Administrative Technician
Maria Filipa Soares Mila Porfírio	High School Diploma	MSc Student
Maria José de Oliveira Diógenes Nogueira	PhD	Staff Scientist
Mariana Fernandes Van Zeller da Silva Campos	University Degree	MSc Student (Started January)

Mariana Serra de Sequeira Neuparth Sottomayor	University Degree	MSc Student
Mariana Silva Pires Crespo Vendeirinho	University Degree	MSc Student (Started February)
Miranda Mele	PhD	Postdoctoral Researcher (Started March. Left June)
Nuno Alemã Serrano Patriarca Ramalho	High School Diploma	MSc Student (Started January)
Oksana Savchak	High School Diploma	MSc Student
Pedro Guilherme Alves Dias	High School Diploma	MSc Student
Ricardo Silva dos Santos Viais	PhD	Project Manager
Rita Abrunhosa Soares	Master Degree	PhD Student
Rita Alexandra Figueira Belo	Master Degree	PhD Student (Started December)
Rita Soares Branco Cardoso do Amaral	High School Diploma	MSc Student (Started January)
Rui Miguel Silva Rodrigues	Master Degree	PhD Student
Sandra Cristina Henriques Vaz	PhD	Senior Postdoctoral Researcher
Sara Alves Xapelli	PhD	Staff Scientist
Sara Filipa Castro da Costa Pinto	Master Degree	PhD Student
Sara Inteiro de Oliveira	University Degree	MSc Student
Sara Luísa Ramalho Tanqueiro	Master Degree	PhD Student
Sara Raquel Landeira Nabais do Paulo	University Degree	PhD Student
Sodikdzhon Kodirov	PhD	Senior Postdoctoral Researcher
Svitlana Zavalko	University Degree	MSc Student
Tatiana Pinto Morais	Master Degree	PhD Student
Tiago Miguel Garcia Ferreira	University Degree	MSc Student (Started May)
Tiago Rodrigo da Costa Coelho	University Degree	MSc Student

Graphical Abstract



Lab Interests

Understanding how synaptic activity is controlled and how to correct its abnormal function are major challenges to Neurosciences, with impact in the fight against neurologic and psychiatric diseases. Our team aims to elucidate how the neuronal and glial components of the tripartite synapse are fine-tuned under normal and dysfunctional situations. How endogenous modulators affect synaptic signaling, neuronal excitability, neuronal and glial maturation, degeneration, renewal and repair, are our current goals of research. We focus on neurotrophic factors, on adenosine and on endocannabinoids, as major endogenous neuromodulators. As exogenous substances we focus on psychoactive drugs (caffeine, cannabinoid receptor ligands, psilocybin and other serotonergic receptor ligands) aiming to know how they influence endogenous neuromodulation at synapses. As disease models we have been interested on those involving neurodegeneration and/or dysregulated excitability, from newborn to aging.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

Neurodegeneration; neuroprotection and regeneration:

- 1) High caloric diet is a risk factor for ageing-related diseases
- 2) Astrocytic dysfunction in an animal model of ALS can be corrected by pharmacological immunoregulatory interventions
- 3) Glial cells are dysfunctional in ARSACS
- 4) A2ARs promote neural stem cell self-renewal, protect committed neuronal cells from death and are essential for BDNF-mediated increase in neuronal differentiation

Novel therapies and their mechanisms:

- 1) Glioblastoma: Tumour glioblastoma cells adapt against antiproliferative properties of extracellular adenosine through overexpression of adenosine kinase. Piperlongumine, an anticancer agent, binds to TRPV2 channel to inhibit calcium influx and glioblastoma proliferation.
- 2) Psychiatric dysfunctions: 5-HTR function is affected by DBS, an emerging anxiolytic therapy. BDNF signalling and LTP are impaired in the prefrontal cortex in a model of schizophrenia. Synaptic plasticity mechanisms differ at different ages.

Ongoing Projects in 2021

2021/2023: CSL BEHRING-IMM. Coordinator: Ana Sebastião. Funding Agency: International Society for Neurochemistry. Reference: ISN CAREER DEVELOPMENT GRANT. Amount: 6 607,20€. Total Amount: 6 607,20€.

2020/2023: Twinning - EpiEpeNet - Epileptogenesis and Epilepsy Network: from genes, synapses and circuits to pave the way for novel drugs and strategies. Coordinator: Ana Sebastião. Funding Agency: European Commission. Reference: Twinning EpiEpinet - Grant number: 952455. Amount: 587 500,00€. Total Amount: 900 000,00€.

2018/2021: Controlo mecanístico e optogénico da astrogliia para reparação neuronal. Coordinator: Ana Sebastião. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/31417/2017. Amount: 21 250,00€. Total Amount: 239 884,80€.

2018/2021: Titanic- CYP46A1 as new Therapeutic Target in Niemann-Pick Type-C disease. Coordinator: Maria José Diógenes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/29455/2017- TITANIC. Amount: 12 500,00€. Total Amount: 237 017,12€.

2018/2021: Regulação da homeostase e polarização pró-inflamatória da microglia Rac1. Coordinator: Ana Sebastião. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: POCI-01-0145-FEDER-031318. Amount: 15 000,00€. Total Amount: 224 179,81€.

2018/2021: Na procura do mecanismo de ação de um novo e seletivo fármaco antiepiléptico. Coordinator: Ana Sebastião. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-FAR/30933/2017. Amount: 239 867,80€. Total Amount: 239 867,80€.

2018/2021: Astrossomas: Astrócitos Artificiais como reguladores da comunicação neuronal. Coordinator: Sandra Vaz. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BTM-SAL/32147/2017. Amount: 239 667,82€. Total Amount: 239 667,82€.

2018/2021: Restabelecimento dos níveis de Adenosina: nova abordagem para o tratamento da Síndrome de Rett. Coordinator: Maria José Diógenes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: AdoRett - LISBOA-01-0145-FEDER-031929. Amount: 208 541,35€. Total Amount: 239 791,35€.

Scientific Impact

Academic Collaborations

Eleonora Palma, Department of Physiology and Pharmacology, Uni Rome La Sapienza

Eleonora Aronica, Department of Pathology, Academic Medical Center, University of Amsterdam

Merab Kokaia, Epilepsy Center, University of Lund

Neil Dawson, Division of Biomedical and Life Sciences, Faculty of Health and Medicine, Lancaster University, UK.

Michele Simonato, School of Medicine, Vita-Salute San Raffaele University: Milan

Zsolt Lenkei, Institute of Psychiatry and Neuroscience, INSERM, Paris

Tomáš Páleníček, National Institute of Mental Health, Czech Republic

Karl Jacobson, National Institute of Health, Bethesda, USA

José Francisco Cascalheira, Departamento de Química, Centro de Investigação em Ciências da Saúde, Universidade da Beira Interior

Gilberto Alves, Universidade da Beira Interior
 Bruno Manadas, CNC, Universidade de Coimbra
 Rui Pinto, Faculdade de Farmácia da Universidade de Lisboa
 Paulo Paixão, Faculdade de Farmácia da Universidade de Lisboa
 Nuno Silva, Faculdade de Farmácia da Universidade de Lisboa
 Margarida Diogo, Instituto Superior Técnico
 Joana Loureiro, Faculdade de Engenharia da Universidade do Porto
 Maria do Carmo Pereira, Faculdade de Engenharia da Universidade do Porto
 Alexandre Valério de Mendonça, Faculdade de Medicina da Universidade de Lisboa
 Ruy Ribeiro, Faculdade de Medicina da Universidade de Lisboa
 Kerensa Broersen, University of Twente, The Netherlands
 Mikko Hiltunen, Institute of Biomedicine, School of Medicine, University of Eastern Finland, Finland
 Eero Castrén, Neuroscience Center, University of Helsinki, Helsinki, Finland
 Hugo Vicente Miranda, CEDOC, Chronic Disease Research Centre, NOVA Medical School | Faculdade de Ciências Médicas, Universidade NOVA de Lisboa,
 Tiago Outeiro, Department of Experimental Neurodegeneration, Center for Biostructural Imaging of Neurodegeneration, University Medical Center Göttingen, Germany
 Max Planck Institute for Experimental Medicine, Göttingen, Germany
 Carlos Fitzsimons, University of Amsterdam, The Netherlands
 Helena Mira, IBV-CSIC, Valencia, Spain
 Jorge Valero, Institute for Neuroscience of Castilla y León. University of Salamanca, Spain
 Susana Solá, Faculty of Pharmacy, University of Lisbon
 Vincenzo Crunelli, University of Cardiff, UK
 Brigitte Städler, University of Aarhus, Denmark
 Alfonso Araque, University of Minnesota, USA
 Gareth Miles, University St Andrews, UK
 Nicole Deglon, Faculty of Biology and Medicine, Center for Research in Neuroscience, Université de Lausanne
 João Relvas, I3S, Porto, Portugal
 Graham Sheridan, School of Life Sciences, University of Nottingham

Selected Publications

Rei N, Rombo DM, Baqi Y, Müller CE, Ribeiro JA, Sebastião AM, Vaz SH (2020). [Neuronal Plasticity changes in non-motor synapses of an Amyotrophic Lateral Sclerosis mouse model \(SOD1G93A\) along disease progression](#). *Neuropharmacology*. 171:108106.

Relevance of the publication: Amyotrophic Lateral Sclerosis is a neurodegenerative disease that affects motor neurons. However, patients may also have other comorbidities, as cognitive impairment. In this study, we clearly identified synaptic dysfunctions at the hippocampus of a genetic model of ALS, therefore that exist beyond the motor control areas. Importantly also, these dysfunctions are biphasic, with enhanced excitability at a prodromic disease phase and decreased synaptic plasticity at later disease stages. Both changes involve over-activation of adenosine A2A receptors from early disease stages.

Mouro FM, Rombo DM, Dias RB, Ribeiro JA, Sebastião AM (2018). [Adenosine A2A receptors facilitate synaptic NMDA currents in CA1 pyramidal neurons](#). *British Journal of Pharmacology* 175:4386-4397.

Relevance of the publication: Adenosine A2A receptors are known as excitotoxic exacerbating neurodegeneration. However, much less is known about the role of these receptors in young healthy subjects. We clearly show that in young healthy rodents these receptors facilitate NMDA receptor activity, in clear contrast with what is known to occur under neurodegenerative conditions. Importantly, this action mainly involves synaptic rather than extrasynaptic NMDA receptors. Therefore, under non-pathological conditions A2A receptors likely contribute to shift the dual role of NMDA receptors towards enhancement of synaptic plasticity. We thus put into evidence a mechanism for the facilitatory action of adenosine A2A receptors upon synaptic plasticity in young subjects.

Magalhães DM, Pereira N, Rombo DM, Beltrão-Cavacas C, Sebastião AM, Valente CA (2018). [Ex vivo model of epilepsy in organotypic slices-a new tool for drug screening](#). **Journal of Neuroinflammation** 15:203.

Relevance of the publication: In vivo models of epilepsy are time consuming and pose ethical issues. We developed an ex vivo model, organotypic slice cultures gradually deprived of serum, and clearly showed that under such conditions they mimic the epileptic-like activity, as well as the inflammatory events associated with in vivo epilepsy. We thus developed a new tool to explore the interplay between neuroinflammation and epilepsy and to screen potential drug candidates, within the inflammatory cascades, to reduce/halt epileptogenesis

Ferreira FF, Ribeiro FF, Rodrigues RS, Sebastião AM, Xapelli S (2018) [Brain-Derived Neurotrophic Factor \(BDNF\) Role in Cannabinoid-Mediated Neurogenesis](#). **Front Cell Neurosci**. 2018 Nov 28;12:441. doi: 10.3389/fncel.2018.00441. eCollection 2018

Relevance of the publication: Post-natal neurogenesis is under control of several neuromodulators but little is known on how different neuromodulators interact to influence neurogenesis. In this study, we concluded that endogenous BDNF is crucial for the cannabinoid-mediated effects on SVZ and DG neurogenesis. On the other hand, cannabinoid receptor signalling is also determinant for BDNF actions upon neurogenesis. These findings provide support for an interaction between BDNF and endocannabinoid signalling to control neurogenesis at distinct levels, further contributing to highlight novel mechanisms in the emerging field of brain repair.

Jerónimo-Santos A, Vaz SH, Parreira S, Rapaz-Lérias S, Caetano AP, Buée-Scherrer V, Castrén E, Valente CA, Blum D, Sebastião AM, Diógenes MJ (2015). [Dysregulation of TrkB Receptors and BDNF Function by Amyloid- \$\beta\$ Peptide is Mediated by Calpain](#). **Cerebral Cortex** 25:3107-3121.

Relevance of the publication: This work is part of a pioneer line of research initiated by the Unit that clearly identified a yet unknown mechanism operated by beta-amyloid peptide (A β) to promote neuronal death. A β leads by promoting calcium entry through NMDA receptors activates calpains, which cleave the receptor for the neuroprotective agent, BDNF, leading to loss of BDNF function. These results opened a promising line of research targeting prevention of BDNF receptor cleavage to mitigate neuronal loss in Alzheimer's disease.

2021 Publications in Peer-Reviewed Journals

Barbosa M, Gomes C, Sequeira C, Gonçalves-Ribeiro J, Pina CC, Carvalho LA, Moreira R, Vaz SH, Vaz AR, Brites D. (2021) [Repair of defective miR-146a in ALS cortical astrocytes reverts cell aberrancies and prevents paracrine pathogenicity on microglia and motor neurons](#). **Frontiers in Cell and Developmental Biology**. 9:634355.

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, de Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu Y, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Marbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL. (2021) [Allosteric Antagonist Modulation of TRPV2 by Piperlonguemin Impairs Glioblastoma Progression](#). **ACS Central Science**. 7(5):868-881.

Diógenes MJ, Guimas Almeida C, Xapelli S (2021) [Editorial: Meeting of the Portuguese Society for Neurosciences SPN2019](#). **Front Mol Neurosci**. 7;14:753500. Editorial.

do Vale FM, Diógenes MJ, Barbacena HA (2021). [Controversies about the cardiovascular effects of OM3FA. Did inappropriate placebos skew clinical trial results?](#) **Pharmacol Res**. 164:105368.

Ferreira CB, Marttinen M, Coelho JE, Paldanius KMA, Takalo M, Makinen P, Leppanen L, Miranda-Loureço C, Fonseca-Gomes J, Tanqueiro SR, Vaz SH, Belo RF, Sebastião AM, Leinonen V, Soininen H, Pike I, Haapasalo A, Lopes LV, de Mendonça A, Diógenes MJ, Hiltunen M (2021). [S327 phosphorylation of the presynaptic protein SEPTIN5 increases in the early stages of neurofibrillary pathology and alters the functionality of SEPTIN5](#). **Neurobiology of disease** 163:105603.

Gomes JI, Farinha-Ferreira M. Rei N, Gonçalves-Ribeiro, Ribeiro JA, Sebastião AM, Vaz SH. (2021) [Of adenosine and the blues: the adenosinergic system in the pathophysiology and treatment of major depressive disorder](#). **Pharmacological Research**. 163:105363. Review.

Lattaa L, Figueiredo FC, Ashery-Padand R, Collinsone JM, Daniels J, Ferrarig S, Szentmárya N, Soláh S, Shalom-Feuersteini R, Lako M, Xapelli S, D. Aberdamm D, and N. Lagalio N (2021) [Pathophysiology of aniridia-associated keratopathy: developmental aspects and unanswered questions](#). **Ocular Surface** 22:245-266. Review.

Marcelino, H., Carvalho, T., Tomás, J., Teles, F. I., Honório, A. C., Rosa, C. B., Costa, A. R., Costa, B. M., Santos, C., Sebastião, A. M., & Cascalheira, J. F. (2021). [Adenosine Inhibits Cell Proliferation Differently in Human Astrocytes and in Glioblastoma Cell Lines](#). **Neuroscience**, 467, 122–133.

Murtinheira F, Mafalda Migueis, Ricardo Letra-Vilela, Mickael Diallo, Andrea Quezada, Cláudia A. Valente, Abel Oliva, Carmen Rodriguez, Vanesa Martin, Federico Herrera (2022). [Sacsin Deletion Induces Aggregation of Glial Intermediate Filaments](#). **Cells** 11(2): 299.

Paulo SL, Miranda-Lourenço C, Belo RF, Rodrigues RS, Fonseca-Gomes J, Tanqueiro SR, Galdes V, Rochal, Sebastião AM, Xapelli, Diógenes MJ (2021). [High caloric diet induces memory impairment and disrupted synaptic plasticity in aged rats](#). **Current Issues in Molecular Biology** 18; 43(3):2305-2319.

Paulo SL, Ribeiro-Rodrigues L, Rodrigues RS, Mateus JM, Fonseca-Gomes J, Soares R, Diógenes MJ, Solá S, Sebastião AM, Ribeiro FF, Xapelli S (2021). [Sustained hippocampal neural plasticity](#)

[questions the reproducibility of an amyloid- \$\beta\$ -induced Alzheimer's disease model](#). **J. Alzheimers Dis.** 82(3):1183-1202.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Pedro DM, Duarte-Samartinho M, Aroeira RI, Ferreira E, Valero J, Solá S, Mira H, Sebastião AM, Xapelli S (2021) [Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: Interaction with brain-derived neurotrophic factor](#). **Stem Cells** 39(10):1362-1381.

Ribeiro FF, Xapelli S (2021) [An Overview of Adult Neurogenesis](#). **Adv Exp Med Biol.** 1331:77-94. Review (book chapter).

Ribeiro FF, Xapelli S (2021) [Intervention of Brain-Derived Neurotrophic Factor and Other Neurotrophins in Adult Neurogenesis](#). **Adv Exp Med Biol.** 1331:95-115. Review (book chapter).

Rodrigues NC., Silva-Cruz, A., Caulino-Rocha, A., Bento-Oliveira, A., Alexandre Ribeiro, J., Cunha-Reis, D. (2021). [Hippocampal CA1 theta burst-induced LTP from weaning to adulthood: Cellular and molecular mechanisms in young male rats revisited](#). **The European Journal of Neuroscience**, 54(4), 5272–5292.

Rodrigues RS (2021) [Seizing balance and success during your PhD experience](#). **European Journal of Neuroscience** 54(6), 5907- 5914. Opinion article.

Silva TP, Sousa-Luís R, Fernandes TG, Bekman E, Rodrigues CAV, Vaz SH, Moreira L, Hashimura Y, Jung S, Lee B, Carmo-Fonseca M, Cabral JMS. (2021) [Transcriptome profiling of human pluripotent stem cell-derived cerebellar organoids reveals faster commitment under dynamic conditions](#). **Biotechnology and Bioengineering.** 2781-2803.

Soares R, Ribeiro FF, Lourenço DM, Rodrigues R S, Moreira J B, Sebastião A M, Morais V A, Xapelli S (2021) [The neurosphere assay: an effective in vitro technique to study neural stem cells](#). **Neural Regeneration Research** 16(11):2229-2231. Perspective.

Tanqueiro SR, Mouro FM, Ferreira CB, Freitas CF, Fonseca-Gomes J, Simões do Couto F, Sebastião AM, Dawson N, Diógenes MJ (Epub 2021). Sustained NMDA receptor hypofunction impairs brain-derived neurotropic factor signalling in the PFC, but not in the hippocampus, and disturbs PFC-dependent cognition in mice. **J Psychopharmacol.** 35(6):730-743.

Valente CA, Meda F, Carvalho M, Sebastião AM (2021). [A model of epileptogenesis in rhinal cortex-hippocampus organotypic slice cultures](#). **J. Vis. Exp.** (169), e61330.

Van Zeller M, Diogo Dias, Ana M. Sebastião, Cláudia A. Valente (2021). [NLRP3 Inflammasome: A Starring Role in Amyloid- \$\beta\$ - and Tau-Driven Pathological Events in Alzheimer's Disease](#). **J. Alzheimer's Dis.** 83: 939-961. Review.

Vaz SH, Pinto S, Sebastião AM, Brites D. [Astrocytes in ALS. In: Araki T, editor. Amyotrophic Lateral Sclerosis \[Internet\]. Brisbane \(AU\): Exon Publications; 2021 Jul 25. Chapter 3. Review \(refereed chapter in book\).](#)

Viana MB, Martins RS, Silva MSCF, Xapelli S, Vaz SH, Sebastião AM. (2021) [Deep Brain Stimulation of the dorsal raphe abolishes serotonin 1A facilitation of AMPA receptor-mediated synaptic currents in the ventral hippocampus.](#) *Behavioural Brain Research*. 403:113134.

Pre-Print Publications

Farinha Ferreira M, Rei N, Fonseca-Gomes J, Miranda-Lourenço C, Serrão P, Vaz SH, Gomes JI, Martins V, Pereira BA, Sebastião AM. [Unexpected short- and long-term effects of chronic adolescent HU-210 exposure on emotional behaviour.](#) bioRxiv.

Gomes JI, Jesus J, Macau R, Gonçalves-Ribeiro J, Pinto S, Pina CC, Armada-Moreira A, Sebastião AM, Vaz SH. (2021) [Astrocytes are implicated in BDNF-mediated enhancement of hippocampal long-term potentiation.](#) bioRxiv.

Invited Lectures and Seminars

Diógenes MJ. No roteiro na descoberta de novos fármacos no âmbito académico. Conferência Juntos por uma Vida Melhor/Virtual meeting, Lisbon, Portugal, November 16 2021.

Farinha-Ferreira, M., Sebastião, A.M. Good Times, Bad Times: exploring the contextual dependency of drug effects. Pharmacology Series, FMUL, Lisboa, Portugal.

Lourenço DM. Unravelling the role of the non-psychotomimetic cannabinoid Cannabidivarin in the modulation of neurogenesis – Relevance for Rett Syndrome. Pharmacology Series, FMUL, Lisbon, Portugal, February 8, 2021.

Ribeiro FF. Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: interaction with brain-derived neurotrophic factor. Young Investigator Symposium, PURINES 2021: X Meeting of the Brazilian Purine Club (Online Event), Brasil, June 19, 2021.

Sebastião AM. Purinergic nucleosides and its neurotrophic actions. PURINES 2021: X Meeting of the Brazilian Purine Club (Online Event), Brasil, June 20, 2021.

Sebastião AM. Esclerose Lateral Amiotrófica: mais do que uma doença motora? Palestra de abertura do IX Simpósio de Neurociências da Universidade Federal Fluminense (online event), Niterói, Rio de Janeiro, Brasil, June 24, 2021.

Sebastião AM, Silva-Cruz A, Mouro FM, Ribeiro JA. Modulation of synaptic signalling by adenosine and cannabinoids. Invited oral presentation at the Neurobiochemistry Symposium of the 24th FEBS Congress, Ljubljana, Eslovénia (online event), July 5, 2021.

Sebastião AM. Medical Cannabis: Hit or Flop? XIII Minho Medical Meeting (online event) Universidade do Minho, March 26, 2021.

Sebastião AM. Canabinoides e cognição: implicações para o uso em control de dor. Invited lecture on the occasion of the Grunenthal awards. Fundação Calouste Gulbenkian, October 19, 2021.

Vaz SH. Understanding the role of astrocytes in absence seizures and their comorbidities. Trends and challenges in epilepsy research, of the Twining Action EpiEpiNet, Costa de Caparica, Portugal, 27 September, 2021.

Xapelli S. Animal models of epilepsy. Trends and challenges in epilepsy research, of the Twining Action EpiEpiNet, Costa de Caparica, Portugal, 27 September, 2021.

Communications

Abreu DS, Gomes JI, Sottomayor MN, Ribeiro FF, Vicente Miranda H, Marques MC, Summavielle T, Socodato R, Relvas JB, Sebastião AM, Déglon N, Vaz SH. Astrocyte's dysregulation: a central hub in Alzheimer's disease pathophysiology? XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021, POSTER COMMUNICATION; NATIONAL CONFERENCE.

Abreu DS, Gomes JI, Sottomayor MN, Ribeiro FF, Vicente Miranda H, Marques MC, Summavielle T, Socodato R, Relvas JB, Sebastião AM, Déglon N, Vaz SH. Astrocyte-driven changes in synaptic plasticity and memory function in Alzheimer' disease. V Symposium Portuguese Glial Network, Coimbra, Portugal, November 30, 2021, ORAL COMMUNICATION; NATIONAL CONFERENCE.

Abreu DS, Gomes JI, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Astrocytes in Alzheimer's disease: friends, foes and potential therapeutic targets. iMed Conference, Lisbon, Portugal, October 7, 2021, ORAL COMMUNICATION; NATIONAL CONFERENCE.

Abreu DS, Gomes JI, Sottomayor M, Solano F, Ribeiro F, Sebastião AM, Vaz SH. Astrocytes: a model to study synaptic plasticity, learning and memory, and disease research. EpiEpiNet Summer School - Epileptogenesis & Epilepsy Network, Costa de Caparica, Portugal, September 27- October 1, 2021, POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Abreu DS, Gomes JI, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Astrocytes as potential targets to reduce neurotoxicity in Alzheimer's disease. 16th YES (Young European Scientist) Meeting, Porto, Portugal, September 16-19, 2021, ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Abreu DS, Gomes JI, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Impact of astrocytes in neurotoxicity mediated by amyloid- β : potential role of D-serine. AIMS Meeting – Annual International (bio)Medical Students Meeting / Lisboa, Portugal, March 18-21, 2021, POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Abreu DS, Pinto S, Gomes JI, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH (2021) “Gliotransmission role upon amyloid- β mediated excitotoxicity” LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Alemán-Serrano N, Cardoso-Amaral R, de Almeida-Borlido C, Costa-Coelho T, Miranda-Lourenço C, Ribeiro-Rodrigues L, Sebastião AM, Diógenes MJ. Method optimization to evaluate TrkB-ICD in Cerebrospinal Fluid and Blood of mice. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Alemán-Serrano N, Cardoso-Amaral R, de Almeida-Borlido C, Costa-Coelho T, Miranda-Lourenço C, Ribeiro-Rodrigues L, Sebastião AM, Diógenes MJ. Therapeutic monitorization of TAT-TrkB effect in preventing BDNF (TrkB-FL) receptor cleavage in CSF and blood of animal model. Dia da Investigação 10ª edição, Lisbon, Portugal, December, 15, 2021. POSTER AND SELECTED FOR ORAL COMMUNICATION; NATIONAL CONFERENCE.

Alves Dias PG, Rodrigues RS, Sebastião AM, Xapelli S. Decoding adult gliogenesis in the context of depression: exercise and cannabinoid type 2 receptor actions. Dia da Investigação “Science is Alive” 10th edition. Faculdade de Medicina da Universidade de Lisboa. December 15, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Belo RF, Martins MLF, Shvachiy L, Costa-Coelho T, Almeida-Borlido C, Fonseca-Gomes J, Neves V, Vicente-Miranda H, Outeiro TF, Coelho JE, Xapelli S, Valente CA, Heras M, Bardaji ER, Castanho MARB, MJ, Sebastião AM. Unveiling the molecular mechanism of amidated-kyotorphin: a neuroprotection action against A β -induced Alzheimer’s Disease pathophysiology. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Catarino M, Mendes F, Sebastião AM, Pinto S, Vaz SH. Functional Role of Endocannabinoid Receptors in Amyotrophic Lateral Sclerosis (ALS). Dia da investigação 10ª edição, Lisbon, Portugal, December, 15, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Correia DS, Ribeiro-Rodrigues L, Xapelli S. The role of restored BDNF/TrkB signalling on neurogenesis in a rat model of epilepsy. Dia da investigação 10ª edição, Lisbon, Portugal, December, 15, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Umemori J, Castrén E, Sebastião AM, Brites D, Diógenes MJ. SH-SY5Y-derived extracellular vesicles drive the release of a BDNF receptor fragment: relevance for Alzheimer’s disease. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Savchak OK, Pinto S, Vaz SH, Sebastião AM, Brites D, Diógenes MJ. Secretion of a BDNF receptor cleavage fragment in

Alzheimer's disease. 35^a Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demência (GEECD), Lisbon, Portugal, July 2-3, 2021, ORAL COMMUNICATION; NATIONAL CONFERENCE.

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Savchak OK, Pinto S, Sebastião AM, Brites D, Diógenes MJ. Vesicle dissemination of neuronal TrkB-ICD in secretome: relevance for Alzheimer's disease pathophysiology. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), virtual conference, February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Costa-Pinto S, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH. Astrocytic dysfunction is a key player in synaptic plasticity and transmission deficits in SOD1G93A mice. V Symposium Portuguese Glial Network 2021, Reitoria da Universidade de Coimbra, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

de Almeida-Borlido C, Fonseca-Gomes J, Ferreira CB, Sebastião AM, de Mendonça A, Diógenes MJ. Searching for a potential novel biomarker for Alzheimer's disease based on BDNF receptor cleavage. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Diógenes MJ. Inhibition of BDNF receptor (TrkB-FL) cleavage as a therapeutic strategy for Alzheimer's disease. (2021). 8th european (virtual) congress of pharmacology - EPHAR 2021, Prague, Czech Republic, December 6-8, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Diógenes MJ, Miranda-Lourenço C, Duarte ST, Palminha C, Gaspar C, Rodrigues TM, Magalhães-Cardoso T, Colino Oliveira M, Gomes R, Ferreira S, Rosa J, Xapelli S, Armstrong J, García-Cazorla À, Correia-de-Sá P, Sebastião AM. Modulation of adenosinergic system: new strategy to boost BDNF actions in Rett syndrome. (2021). 8th European (virtual).

Congress of pharmacology - EPHAR 2021, Prague, Czech Republic, December 6-8, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Farinha-Ferreira M., Miranda-Lourenço, C., Simões, H., Danylyuk, M.I., Santos, R., Lenkei, Z., Sebastião, A.M. Titrating the Trip: a dose-response antagonist-controlled study of persistent psilocybin effects on affective behavior. Presented at the 17th meeting of the Portuguese Society for Neurosciences, Coimbra, Portugal.

Farinha-Ferreira M., Rei, N., Miranda-Lourenço, C., Gomes, J.I., Serrão, P., Sebastião A.M. Do not judge a rat by its (forced) swimming: exploring the contradictory affective behavioral effects of chronic adolescent HU-210 exposure. Presented at the 34th meeting of the European College of Neuropsychopharmacology (ENCP), Lisbon, Portugal.

Ferreira-Manso M. TAT-TrkB, a novel peptide able to restore TrkB-FL levels and the learning curve of 5xFAD mice. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Ghosh A, Ribeiro-Rodrigues L, Rei N, Tosh DK, Morais TP, Vaz SH, Valente CA, Crunelli V, Jacobson KA, Ribeiro JA, Sebastião AM (2021). On the search of the mechanism of action of MRS5474, a putative antiepileptic drug with affinity for adenosine A1 receptors. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ghosh A, Ribeiro-Rodrigues L, Rei N, Tosh DK, Morais TP, Vaz SH, Valente CA, Crunelli V, Jacobson KA, Ribeiro JA, Sebastião AM (2021). On the Search of the Mechanism of Action of MRS5474, a putative antiepileptic drug with affinity for Adenosine A1 Receptors” 51st Meeting of the Portuguese Society for Pharmacology (SPF) 2021, Faculty of Pharmacy (FFUL), University of Lisbon, Lisbon, Portugal from February 17th – 19th 2021. Oral Communication, National Meeting.

Ghosh A, Ribeiro-Rodrigues, L, Rei N, Tosh DK, Morais TP, Vaz SH, Valente CA, Jacobson KA, Ribeiro JA, Sebastião AM. A putative antiepileptic compound that affects excitatory hippocampal synaptic transmission in adult rats following kainate-induced status epilepticus (SE) but not in non-SE animals”. EpiEpiNet 1st Annual Summer School "Trends and Challenges in Epilepsy Research Summer School" Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon, Lisbon, Portugal at Costa da Caparica, Lisbon, Portugal from September 27th – October 1st, 2021 (Poster Communication. International Conference).

Gonçalves-Ribeiro J, Sottomayor MN, Pinto S, Magalhães D, Sebastião AM, Vaz SH. Duality CB1R Effect is dependent on astrocytic calcium signalling in rodent mPFC. V Symposium Portuguese Glial Network 2021/Reitoria da Universidade de Coimbra, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Gonçalves-Ribeiro J, Savchak O, Morais TP, Lopes RF, Meneses C, Santisteban R, Lillo A, Crunelli, Navarro-Brugal G, Franco R, Sebastião AM, Vaz SH. Dual effect of A1R and A2AR upon CB1R signalling in cortical astrocytes: Ca²⁺ dependent modulation of glutamate transporters. XV European Meeting on Glial Cells in Health and Disease, Marseille (hybrid congress), France. July 7th-10th, 2021. POSTER COMMUNICATION. INTERNATIONAL CONFERENCE.

Gonçalves-Ribeiro J, Savchak O, Morais TP, Lopes RF, Meneses C, Santisteban R, Lillo A, Crunelli V, Navarro-Brugal G, Franco R, Sebastião AM, Vaz SH. Dual effect of A1R and A2AR upon CB1R signalling in cortical astrocytes. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ. Screening of small, non-peptide compounds to prevent TrkB-FL cleavage in Alzheimer’s disease. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Kodirov SA, Tosh DK, Jacobson KA, Sebastião AM. Disinhibition of interneurons by a new antiepileptic drug. 51st Meeting of the Portuguese Society for Pharmacology (SPF) 2021, Faculty

of Pharmacy (FFUL), University of Lisbon, Lisbon, Portugal from February 17th – 19th 2021. Oral Communication, National Meeting.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. Exploring the neurogenic potential of Cannabidivarin as a novel target for Rett Syndrome. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal. December 1-3, 2021. SELECTED ORAL COMMUNICATION. NATIONAL CONFERENCE.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. Exploring the neurogenic potential of Cannabidivarin as a novel target for Rett Syndrome. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. Exploring the neurogenic potential of Cannabidivarin as a novel target for Rett Syndrome. EpiEpiNet Summer School 2021 “Trends and Challenges in Epilepsy Research” at Tryp Lisboa Caparica Mar Hotel, Costa da Caparica, Almada, Portugal; September 27 – October 1, 2021. POSTER PRESENTATION; NATIONAL CONFERENCE.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. Exploring the neurogenic potential of Cannabidivarin as a novel target for Rett Syndrome. EpiEpiNet Summer School 2021 “Trends and Challenges in Epilepsy Research” at Tryp Lisboa Caparica Mar Hotel, Costa da Caparica, Almada, Portugal; September 27 – October 1, 2021. POSTER PRESENTATION; NATIONAL CONFERENCE.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. Unravelling the role of the non-psychotomimetic cannabinoid Cannabidivarin in the modulation of neurogenesis – Relevance for Rett Syndrome. ENCODS 2021, virtual meeting, 4-6 June 4-6 202. ORAL PRESENTATION, INTERNATIONAL CONFERENCE.

Lourenço DM, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Sebastião AM, Mouro FM, Diógenes MJ, Xapelli S. The Neurogenic potential of Cannabidivarin and its relevance for Rett Syndrome. Annual CAML PhD Students’ Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL COMMUNICATION. NATIONAL CONFERENCE.

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Regulation of in vitro postnatal neurogenesis by the vanilloid receptor TRPV1. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Mateus JM; Lourenço DM; Sebastião AM and Xapelli S. Modulators of in vitro postnatal oligodendrogenesis. XVII Meeting of the Portuguese Society for Neuroscience (SPN2021), Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Mateus JM; Lourenço DM; Sebastião AM and Xapelli S. BDNF potentiates oligodendrogenesis from subventricular zone neural stem cell cultures. V Symposium Portuguese Glial Network –

Glial cells at the crossroad of health and disease, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Mateus JM, Lourenço DL, Sebastião AM and Xapelli S. Searching for modulators of adult oligodendrogenesis. *Glia* – Wiley online library. Conference Abstract: XV European Meeting on Glial cells in health and disease. *GLIA* 69, S1:E118–E611 (2021). XV European Meeting on Glial Cells in Health and Disease, virtual meeting, July 5-9, 2021. POSTER PRESENTATION, INTERNATIONAL CONFERENCE

Mateus JM; Lourenço DM; Sebastião AM and Xapelli S. Calling on potential modulators of postnatal oligodendrogenesis. ENCODS 2021, virtual meeting, 4-6 June 4-6 202. POSTER PRESENTATION, INTERNATIONAL CONFERENCE.

Mateus JM, Lourenço DL, Sebastião AM, Dawson N and Xapelli S. Modulation of postnatal oligodendrogenesis: role of BDNF, A2AR and cannabinoid receptors. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, virtual meeting, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Meda FJ, Carvalho M, Ribeiro-Rodrigues L, Sebastião AM, Valente CA. NLRP3 Inflammasome-driven neuro degeneration and epileptiform activity in a model of epileptogenesis in organotypic slices. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Miranda-Lourenço C, Palminha C, Duarte ST, Rodrigues TM, Magalhães-Cardoso T, Colino-Oliveira M, Rei N, Rosa J, Xapelli S, Ferreira F, Correia-de-Sá P, Sebastião AM, Diógenes MJ. Adenosinergic impairment in Rett Syndrome: exploring a new possible therapeutic target. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), virtual conference, February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Miranda-Lourenço C, Palminha C, Duarte ST, Rodrigues TM, Magalhães-Cardoso T, Rei N, Rosa Jessica, Colino-Oliveira M, Rei N, Rosa J, Xapelli S, Ferreira F, Correia-de-Sá P, Sebastião AM, Diógenes MJ. Adenosinergic system as a new therapeutic target in Rett Syndrome. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Miranda-Lourenço C. Adenosine as a new therapeutic target in Rett Syndrome. 1st Epiepinet Data Club, virtual meeting, March 26, 2021.

Morais TP, Pina CC, Sottomayor MN, Sebastião, AM, de Giovanni G, Vaz SH, Crunelli V. GAT1 uptake dysfunction in absence seizures. Society for Neuroscience 50th annual meeting. Chicago, Illinois, USA. November 8-11, 2021 POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Moreira JB, Vink MA, Sebastião AM, Lévi S, Lopes LV, Xapelli S. Characterizing the effects of caffeine on an in vitro model of postnatal neurogenesis. XVII Meeting of the Portuguese Society

for Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Moreira JB, Vink MA, Sebastião AM, Lévi S, Lopes LV, Xapelli S. Unveiling the effects of caffeine in adult neurogenesis and synaptogenesis. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Murtinheira F., Migueis M., Letra-Vilela R., Martin V., Rodriguez C., Valente C. A., Duarte-Olivenza C., Herrera F. Sacsin deletion promotes intermediate filaments aggregation in glial cells: potential implications for ARSACS. V Symposium of the Portuguese Glial Network, November 30, 2021, Coimbra, Portugal. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Nunes JC, Paulo SL, Sebastião AM, Xapelli S. Searching for new neurogenic niches in the central nervous system of adult mice. Dia da investigação 10ª edição, Lisbon, Portugal, December, 15, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Paulo SL, Ribeiro-Rodrigues L, Rodrigues RS, Mateus JM, Fonseca-Gomes J, Soares R, Diógenes MJ, Solá S, Sebastião AM, Ribeiro FF, Xapelli S. Mind the bias: lessons on the reproducibility of an amyloid- β -induced Alzheimer's disease model. XVII Meeting of the Portuguese Society for Neuroscience (SPN2021), Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Paulo SL, Sebastião AM, Valero J, Xapelli S. Unconventional neurogenic niches and where to find them: from postnatal to aging. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, virtual meeting, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Pinto S, Gomes JI, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH. Unveiling the mechanisms of astrocytic dysfunction in ALS. XIV CAML · IV NeurULisboa PhD Students Virtual Meeting/Online, May 5, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Pinto S, Gomes JI, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH. Use of artificial astrocytes as a novel therapeutic to Amyotrophic Lateral Sclerosis. International Astrocyte School 2021/Online, April 14, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Pinto S, Gomes JI, Sebastião AM, Vaz SH. Role of astrocytes in hippocampal synaptic dysfunction in ALS. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Porfirio MF, Mateus JM, Sebastião AM, Xapelli S. The potential of Neural Stem Cells in Multiple Sclerosis: The effect of Adenosine A2A receptors in postnatal oligodendrogenesis after demyelination. Dia da investigação 10ª edição, Lisbon, Portugal, December, 15, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Pedro DM, Duarte-Samartinho M, Aroeira RI, Ferreira E, Valero J, Solá S, Mira H, Sebastião AM, Xapelli S. Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: interaction with brain-derived neurotrophic factor. Young Investigator Symposium, PURINES 2021: X Meeting of the Brazilian Purine Club (Online Event), Brazil, June 19, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Pedro DM, Duarte-Samartinho M, Aroeira RI, Ferreira E, Valero J, Solá S, Mira H, Sebastião AM, Xapelli S. Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: Interaction with brain-derived neurotrophic factor. iMM PostDoc Day, iMM, Lisbon, Portugal, May 27, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Ribeiro-Rodrigues L. Impact of kainate-induced *status epilepticus* in BDNF/TrkB signaling. Epileptogenesis and Epilepsy Network: From genes, synapses and circuits to pave the way for novel drugs and strategies, virtual conference, January 20, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Ribeiro-Rodrigues L, Fonseca-Gomes J, Paulo SL, Zavalko S, Paiva VH, Sebastião AM, Xapelli S, Diógenes, MJ. Cleavage of BDNF receptor in a model of epilepsy. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), virtual conference, February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ribeiro-Rodrigues L, Fonseca-Gomes J, Paulo SL, Zavalko S, Paiva VH, Sebastião AM, Xapelli S, Diógenes MJ. Cleavage of BDNF receptor in a model of *status epilepticus*. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal, May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Ribeiro-Rodrigues L, Fonseca-Gomes J, Paulo SL, Zavalko S, Paiva VH, Sebastião AM, Xapelli S, Diógenes MJ. TrkB-FL cleavage and anxiety-like behaviour depends on kainate-induced seizure severity. Trends and challenges in epilepsy research, Summer School, Epiepinet, Costa da Caparica, Portugal, September 27 - October 1, 2021. POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Ribeiro-Rodrigues L, Fonseca-Gomes J, Paulo SL, Zavalko S, Paiva VH, Sebastião AM, Diógenes, MJ, Xapelli S. TrkB-FL cleavage and anxiety-like behaviour is dependent on kainate-induced seizure severity. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Rodrigues RS, Moreira JB, Loureiro-Campos E, Bielefeld P, Pinto L, Sebastião AM, Fitzsimons CP, Xapelli S. Recharging adult hippocampal neurogenesis with physical exercise together with cannabinoid type 2 receptors to counter chronic stress. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER COMMUNICATION. NATIONAL CONFERENCE

Rodrigues RS, Moreira JB, Loureiro-Campos E, Bielefeld P, Pinto L, Sebastião AM, Fitzsimons CP, Xapelli S. Shaping the depressed brain: exercising adult hippocampal neural stem cells with cannabinoid type 2 receptors. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE

Rodrigues RS, Moreira JB, Sebastião AM, Fitzsimons CP, Xapelli S. Exercising on cannabinoids: shaping depression through adult hippocampal neurogenesis. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Santos SS, Moreira JB, Costa M, Rodrigues RS, Xapelli S, Solá S (2021) The mitochondrial antioxidant Sirtuin3 cooperates with lipid metabolism to safeguard neurogenesis in ageing and depression. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Savchak OK, Armada. Moreira A., Ramos-Docampo MA., Ribeiro FF., Sebastião AM., Städler B., Vaz SH. Flowers and Blades. Manganese oxide nanoparticles in cell like reactors targeting oxidative stress. AIMS Meeting – Annual International (bio)Medical Students Meeting / Lisboa, Portugal, March 18-21, 2021, POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Savchak OK, Armada. Moreira A., Ramos-Docampo MA., Ribeiro FF., Sebastião AM., Städler B., Vaz SH. Manganese oxide nanoflowers containing microreactors to support neuroblastoma cells against oxidative stress. MANA International Symposium 2021, International Center for Materials Nanoarchitectonics, National Institute for Materials Science, Japan. March 2-3, 2021, POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Savchak OK, Armada-Moreira A, Ramos-Docampo M, Spanjers JM, Ribeiro FF, Sebastião AM, Städler B, Vaz SH. Wolf in sheep's clothing: capsosome encapsulated manganese oxide nanoflowers. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: modulator of adult neural stem cell fate. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal. December 1-3, 2021. POSTER PRESENTATION. NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Investigating Mitochondrial Dynamics as regulator of adult neural stem cell differentiation. V Symposium Portuguese Glial Network – Glial cells at the crossroad of health and disease, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Soares R, Lourenço DM, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics as modulator of adult neural stem cell fate, XIV Annual CAML PhD Students' Scientific

Meeting • IV NeurULisboa Meeting, Lisbon, Portugal. May 5-7, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Sottomayor MN, Pina C, Ferreira MF, Solano F, Abreu D, Mouro F, Morais TP, Sebastião AM, Crunelli V, Vaz SH. The puzzle: absence seizures, atypical astrocytes and memory impairments. XVII Meeting of the Portuguese Society for Neuroscience, Coimbra, Portugal, December 1-3, 2021, POSTER COMMUNICATION; NATIONAL CONFERENCE.

Sottomayor MN, Pina C, Ferreira MF, Solano F, Abreu D, Mouro F, Morais TP, Sebastião AM, Crunelli V, Vaz SH. Astrocyte Morphological Changes In Absence Seizures. V Symposium Portuguese Glial Network 2021, Reitoria da Universidade de Coimbra, Coimbra, Portugal, November 30, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Sottomayor MN, Pina C, Ferreira MF, Solano F, Mouro F, Morais TP, Sebastião AM, Crunelli V, Vaz SH. Comorbidities of Childhood Absence Epilepsy: from circuits to behavior. EpiEpiNet Summer School - Epileptogenesis & Epilepsy Network, Costa de Caparica, Portugal, September 27- October 1, 2021, POSTER COMMUNICATION; INTERNATIONAL CONFERENCE.

Sottomayor MN, Pina C, Ferreira JM, Mouro F, Morais TP, Sebastião AM, Crunelli V, **Vaz SH**. Role of ethosuximide on childhood absence Epilepsy comorbidities. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Valentim R, Miranda-Lourenço C., Diogenes MJ, Epigenetic changes in a mouse model of Rett Syndrome: optimizing a technique to evaluate DNA methylation. Dia da investigação 10^a edição, Lisbon, Portugal, December, 15, 2021. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Van Zeller M, Sebastião AM, Valente CA (2021). Unravel the contribution of astrocytes for the neuroinflammatory milieu in Alzheimer’s disease – an insight into the NLRP3 inflammasome cascade. XVII Meeting of the Portuguese Society for Neuroscience, Dezembro 1-3, 2011, Coimbra, Portugal. POSTER COMMUNICATION; NATIONAL CONFERENCE.

Van Zeller M, Sebastião AM, Valente CA. Relevance of NLRP3 Inflammasome – Impact of A β -induced toxicity. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Zavalko S, Mouro FM, Lourenço DM, Miranda-Lourenço C, Fonseca-Gomes J, Mateus JM, Rodrigues RS, Tanqueiro SR, Sebastião AM, Diógenes MJ, Xapelli S. Cannabidivarin effects on Rett syndrome’s impairments and on post-natal neurogenesis in a female MECP2-mutant mouse model. EpiEpiNet Summer School 2021 “Trends and Challenges in Epilepsy Research” at Tryp Lisboa Caparica Mar Hotel, Costa da Caparica, Almada, Portugal; September 27 – October 1, 2021. POSTER PRESENTATION; NATIONAL CONFERENCE.

Zavalko S, Mouro FM, Lourenço DM, Miranda-Lourenço C, Fonseca-Gomes J, Mateus JM, Rodrigues RS, Tanqueiro SR, Sebastião AM, Diógenes MJ, Xapelli S. Cannabinoid actions on Rett

Syndrome's associated deficits and its effect on post-natal neurogenesis in a female MECP2-mutant mouse model. LI Virtual Meeting of the Portuguese Society for Pharmacology (SPF), Lisbon, Portugal. February 17-19, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Organization of Conferences

Lourenço DM, Mateus JM, Paulo SL, Ribeiro-Rodrigues L. Co-organizers. XIV Annual CAML PhD Students' Scientific Meeting • IV NeurULisboa Meeting, virtual meeting, May 5-7, 2021.

Ribeiro FF. Co-organizer. iMM PostDoc Day 2021, virtual meeting, May 27, 2021.

Diógenes MJ. Co-organizer. 8th Edition Beyond Med, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 17-20, 2021

Viais R (organizer), Diógenes MJ, Sebastião AM, Valente CA, Vaz SH, Xapelli S (Co-organizers). "Trends and Challenges in Epilepsy Research" Summer School – EpiEpiNet: Epileptogenesis & Epilepsy Network, Costa de Caparica, Portugal, September 27- October 1, 2021

Vaz SH. Organizer. Neuroscience Seminars at iMM, Lisboa, Portugal, Weekly meetings from January - December, 2021

Xapelli S. Co-organizer. PhD Advanced Course: Stem Cell Technologies, Faculty of Pharmacy, University of Lisbon, and Champalimaud Foundation, Lisboa, Portugal, November 08-12 (Course Coordinator: Susana Solá and Christa Rhiner).

Networks & Research Infrastructures

Participation in European Research Networks:

Vaz SH. Working group member (WG1) of Cost Action CA20135 "Improving biomedical research by automated behaviour monitoring in the animal home-cage".

Vaz SH. Working group member (WG2) of Cost Action CA20135 "Improving biomedical research by automated behaviour monitoring in the animal home-cage".

Xapelli S. Working group member (WG1) of Cost Action CA20135 "Improving biomedical research by automated behaviour monitoring in the animal home-cage".

Xapelli S. Management Committee member of Cost Action CA18116, "Aniridia: networking to address an unmet medical, scientific, and societal challenge"

Xapelli S. Inclusiveness Target Country (ITC) Conference Grant Coordinator of COST Action CA18116

Participation in international reviewing committees:

Sebastiao AM: Expert evaluator of Noora Puhakka merits for a Tenure Track position as Assistant Professor. Academy of Finland.

Sebastião AM: Expert evaluator of the call for Support of Young Investigators, Clube Brasileiro de Purinas.

Sebastião AM: Handling Editor of Journal of Neurochemistry

Sebastião AM: Associate Editor of European Journal of Pharmacology

Valente CA. Associate editor of Journal of Alzheimer's Disease,

Xapelli S: Expert of the Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI) of the “Experimental Demonstrative Project Call – PED 2021
 Xapelli S: Expert evaluator of Marie Skłodowska-Curie (Call: H2020-MSCA-IF-2020 - LIF panel)
 Xapelli S: Evaluator of the National Research Foundation (NRF) South Africa
 Xapelli S: Evaluator of the EPFL Science Seed Fund
 Xapelli S: Evaluator of the French National Research Agency (ANR) 2021 generic call
 Xapelli S: Evaluator of the International Evaluation Committee de EuroTechPostdoc (Co-funded by Marie Curie Postdoc Fellowships)
 Xapelli S: Review Editor of Frontiers in Neuroscience section Neurogenesis.
 Xapelli S: Topic Editor of International Journal of Molecular Sciences.

Prizes & Honors in 2021

Diógenes MJ. Mantero Belard 2021 Award. “TAT-TrkB, a novel neuroprotective compound to fight Alzheimer’s disease”.

Abreu D. Won Best Oral Communication Award of the V Symposium Portuguese Glial Network, November 30, 2021, Coimbra, Portugal.

Abreu D. Won the Second-Best Oral Communication Award of the 16th YES (Young European Scientist) Meeting, Porto, Portugal, September 16-19, 2021.

Armada-Moreira A: Won the Merit PhD Thesis Award 2021 from Instituto de Medicina Molecular João Lobo Antunes.

Costa-Coelho T. Best Oral Communication in Fundamental Science at the 35ª Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demência (GEECD), Lisbon, Portugal, July 2-3, 2021.

Farinha-Ferreira M. Best pitch presentation, XIV Annual CAML PhD Students’ Scientific Meeting • IV NeurULisboa Meeting, virtual meeting, May 5-7, 2021.

Ferreira-Manso M. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Inteiro-Oliveira S. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Lourenço DM. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Lourenço DM. Winner of ENCODS 2021 Best Early Career Researcher [ECR] Talks. June 2021.

Moreira J. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Paulo SL. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Rodrigues L. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Rodrigues R. Scholarship from Portuguese Society for Neuroscience (SPN) to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Rodrigues R. Winner of Science Communication Workshop at FENS Regional Meeting 2021 (grant amount: 1000 EUR) with “Fala-me Neuro” communication project. September 2021.

Rodrigues R. Full Stipend from FENS and IBRO-PERC to attend the FENS-Hertie Winter School 2022 on "Multiscale approaches to probe psychiatric disorders", Obergurgl, Austria. September 2021 (cancelled due to COVID19 pandemic).

Soares R. Mobility grant from Horizon 2020 SIMICA project to attend the XVII Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal. December 2021.

Vaz SH. Elected for the board of Rede Glial Portuguesa.

Vaz SH. Referee on the Cerebral Cortex, European Journal of neuroscience and Frontiers in Cellular Neuroscience.

Vaz SH. Won an ACORN Scholarship to participate in XV European Meeting on Glial Cells in Health and Disease 2021 (Marseille, France)

Vaz SH. Won the International Society for Neurochemistry Career Development Grant (USD 10,000)

Advanced Teaching

Directive Roles:

Sebastião AM. Member of the Executive Council of the Mind-Brain College ‘Mind and Brain’, Universidade de Lisboa, which integrates 7 Schools (Faculdade de Ciências (FCUL), Faculdade de Farmácia (FFUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL), Instituto Superior Técnico (IST) e Instituto de Ciências Sociais (ICS), and their corresponding research centres, to promote the interaction between scientific, technical and formative valences to further understand brain and cognition as well as to communicate with and for the main achievements to the society.

Sebastião AM. Director of the Integrated Neurosciences PhD Programme (Supported by FCT) which involves 6 Schools (Faculdade de Ciências (FCUL), Faculdade de Farmácia (FFUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL), Instituto Superior Técnico (IST).

Sebastião AM. Member of the Scientific Board of the MScs/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa.

Sebastião AM. Member of the Scientific Board MSc/PhD Programme in Cognitive Sciences, Universidade de Lisboa, which involves 4 Schools (Faculdade de Ciências (FCUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL).

Sebastião AM. Member of the Coordination Board of the Master in Biomedical Engineering, IST/FMUL.

Ribeiro JA. Coordinator of the Module on Neuroethics, Ms/PhD in Neurosciences.

Sebastião AM. Coordinator of the following modules of the MSc/PhD in Neurosciences: 'Cellular and Molecular Neurosciences', 'Neuronal Networks', 'Neuronal Degeneration and Regeneration'.

Sebastião AM. Coordinator of the Curricular Unit 'Neuropharmacology' offered as optional to the post-graduate students at FMUL and ULisboa (under the ULisboa mobility programme)

Organization and Teaching at Practical Workshops:

Vaz S. Organizer. Recordings of synaptic potentials from hippocampal slices. October 15, 2021.

Valente C. Organizer. Methodological approaches for neuroinflammation research. October 18-19, 2021.

Xapelli S. Organizer. Neural stem cells and its potential for neuroregeneration. October 28-29, 2021.

Farinha-Ferreira M. Organizer. Behaviour assessment in laboratory animals. November 15, 2021.

Invited Lectures from Abroad:

Detlev Boison (Rutgers University, New Jersey, USA). Translational research in neurosciences: the adenosine case. February 1, 2021.

Sabine Levi (PhD, École des Neurosciences de Paris, Île de France, France). Lecture on the Neuroscience Seminar. Adenosine signaling detects and stabilizes newly formed GABAergic synapses during development. iMM, FMUL, Lisbon, Portugal, October 11, 2021.

Adriana Marcassa Tucci (PhD, Departamento de Saúde, Educação e Sociedade, Universidade Federal de São Paulo, Brasil). Drugs: Socio-historical and Cultural Context. iMM, FMUL, Lisbon, Portugal, December 13, 2021.

Neuroscience Seminars (Organizer: Sandra H Vaz)

These seminars run once per week on Mondays, constituting a forum for discussion of scientific achievements, projects to start or running, as well as to invite members from other institutions to share their ideas on different topics. These seminars are open to the iMM community, but are particularly designed for training of Master and PhD students at the Unit. The seminars are also open to Medical students as well as to members of the Mind-Brain College of the University

of Lisbon. Seminars given by members of other iMM Units are not listed to avoid repetition with other Unit reports.

Invited speakers from outside iMM/FMUL:

Teresa Summavielle (I3S, Universidade do Porto). Neuroinflammation and substance abuse: partners in crime. iMM, FMUL, Lisbon, Portugal, January 18, 2021.

Rosalina Fonseca (PhD, CEDOC, Universidade Nova de Lisboa) Modulation of synaptic cooperation and competition by the endocannabinoids. iMM, FMUL, Lisbon, Portugal, February 1, 2021.

Hugo Vicente Miranda (PhD, CEDOC, Universidade Nova de Lisboa) Zooming in on the effects of Diabetes in Parkinson's disease neuropathology. iMM, FMUL, Lisbon, Portugal, February 8, 2021.

Federico Herrera (PhD, BioISI Research Unit, Faculty of Sciences, University of Lisbon) The role of asymmetric post-translational modifications on the behavior of protein homodimers and oligomer. iMM, FMUL, Lisbon, Portugal, May 3, 2021.

Cláudio Gomes (PhD, Protein Misfolding and Amyloids in Biomedicine Laboratory BioISI / FCUL) Lecture on the Neuroscience Seminar. Extracellular regulation of protein aggregation in Alzheimer's Disease. iMM, FMUL, Lisbon, Portugal, June 7, 2021.

João Oliveira (PhD, ICVS, University of Minho) Lecture on the Neuroscience Seminar. The involvement of astrocytes in cortico-limbic function and cognition. iMM, FMUL, Lisbon, Portugal, June 21, 2021.

Cláudia Almeida (PhD, CEDOC, Universidade Nova de Lisboa) Mechanisms of Neuronal Aging relevant for Alzheimer's disease. iMM, FMUL, Lisbon, Portugal, July 5, 2021.

By Unit Members:

Mariana Sottomayor (Master student). Role of Brain-Derived Neurotrophic Factor on Childhood Absence Epilepsy: from circuits to behavior. iMM, FMUL, Lisbon, Portugal, January 04, 2021.

Sara Oliveira (Master student). Search for novel compounds to prevent TrkB-FL cleavage. iMM, FMUL, Lisbon, Portugal, January 04, 2021.

Hugo Simões (Master student). Characterization of neuroinflammatory and synaptic plasticity dysfunction in Wistar-Kyoto model of depression. iMM, FMUL, Lisbon, Portugal, January 11, 2021.

João Moreira (PhD Student). Unveiling the effects of caffeine in adult neurogenesis and synaptogenesis. iMM, FMUL, Lisbon, Portugal, January 25, 2021.

Catarina Lourenço (PhD student, Ana Sebastião Lab) Rett Syndrome, Adenosine and BDNF: a tale of the last four years. iMM, FMUL, Lisbon, Portugal, February 22, 2021.

Diogo Dias (Master Student) Impact of NLRP3 Inflammasome Inhibition on a Model of A β -Induced Toxicity. iMM, FMUL, Lisbon, Portugal, March 1, 2021.

Mariana Van Zeller (Master Student) Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β induced toxicity. iMM, FMUL, Lisbon, Portugal, March 15, 2021.

Francisco Meda (Master Student) NLRP3 inflammasome-driven neurodegeneration and epileptiform activity in a model of epileptogenesis in organotypic slices. iMM, FMUL, Lisbon, Portugal, April 5, 2021.

Daniela Magalhães (PhD student) Unveiling the NLRP3 Inflammasome Cascade in Ageing and Social Isolation. iMM, FMUL, Lisbon, Portugal, April 19, 2021.

Jacinta Manta (Master Student) Unravelling the contribution of astrocytes for the neuroinflammatory milieu of epileptic-like organotypic slice. iMM, FMUL, Lisbon, Portugal, April 26, 2021.

Rita Belo (PhD student). KTP vs KTP-NH₂: Should KTP arrive to the party alone or with a plus one? iMM, FMUL, Lisbon, Portugal, May 17, 2021.

Tiago Coelho (Master student) Neuronal TrkB-ICD fragment in Alzheimer's disease: an unexpected journey. iMM, FMUL, Lisbon, Portugal, May 24, 2021.

Leonor Rodrigues (PhD student) Is seizure severity related to increased TrkB-FL cleavage? iMM, FMUL, Lisbon, Portugal, May 31, 2021.

Mariana Vendeirinho (Master student) The role of brain-derived neurotrophic factor (BDNF) in amyotrophic lateral sclerosis (ALS). iMM, FMUL, Lisbon, Portugal, June 28, 2021.

Joana Gonçalves Ribeiro (PhD Student) Adenosine receptors impact on astroglial CB1R: relevance for synaptic function. iMM, FMUL, Lisbon, Portugal, July 12, 2021.

Diogo Lourenço (PhD Student). Unravelling the role of the non-psychotomimetic cannabinoid Cannabidivarin in the modulation of neurogenesis – Relevance for Rett Syndrome. iMM, FMUL, Lisbon, Portugal, July 19, 2021.

Anwasha Ghosh (PhD student) An adenosine A1R agonist with anticonvulsant properties but devoid of effect on excitatory hippocampal synaptic transmission. iMM, FMUL, Lisbon, Portugal, September 6, 2021.

Carolina Borlido (Master Student). BDNF receptor cleavage: a novel biomarker for Alzheimer's disease. iMM, FMUL, Lisbon, Portugal, September 20, 2021.

Sara Paulo (PhD student). From unconventional niches to adult hypothalamic neurogenesis in Alzheimer's Disease. iMM, FMUL, Lisbon, Portugal, November 22, 2021.

Isa Mota (Master student). Characterization of the metabolic profile of differentiated cells derived from Subventricular Zone Neural Stem Cells. iMM, FMUL, Lisbon, Portugal, November 29, 2021.

Gonçalo Costa (Master student) Developing a strategy to improve neuronal regeneration after glial scar formation. iMM, FMUL, Lisbon, Portugal, November 29, 2021.

Tiago Ferreira (Master student) Pyroptotic Deadly Curse of Neurons in Alzheimer's Disease – Unravelling the NLRP3 Inflammasome pathway. iMM, FMUL, Lisbon, Portugal, December 6, 2021.

iMM Pizza Seminars (by Unit Members):

Lourenço DM. Unravelling the role of the non-psychotomimetic cannabinoid Cannabidiol in the modulation of neurogenesis – Relevance for Rett Syndrome. iMM, FMUL, Lisbon, Portugal, January 21, 2021.

Rodrigues RS. Exercising on cannabinoids: targeting adult neural stem cells to treat Major Depression. iMM, FMUL, Lisbon, Portugal, April 6, 2021.

Costa-Coelho T. BDNF receptor cleavage promotes shedding of TrkB-ICD-containing extracellular vesicles in Alzheimer's disease. iMM, FMUL, Lisbon, Portugal, October 26, 2021.

iMM Seminar:

Sebastião AM. Amyotrophic Lateral Sclerosis: more than just a motor neuron disease? iMM, FMUL, Lisbon, Portugal, June 6, 2021.

Seminars/Lectures at the PhD and at the Master Courses in Neuroscience:

(The list below refers to the seminars presented by Unit members or, whenever indicated, by those invited from outside iMM. Seminars given by members of other iMM Units are not listed to avoid repetition with other Unit reports):

Invited speakers from outside iMM:

29/9 – Molecular Anatomy of the Blood Brain Barrier (Alexandra Brito, FFUL)

29/9 - Protein aggregation in Alzheimer's disease (Cláudio Gomes, FCUL)

30/9 – Plasticity of glutamatergic synaptic transmission (Raquel Dias, IPO) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)

13/10 – Modulation of AMPA receptor recycling: molecular aspects (Dominique Fernandes, FCTUC, CNC)

20/10 – Genetic approaches to fight neurodegenerative diseases (Luis Pereira de Almeida, FFUC)

20/10 – Molecular dysfunctions in multiple sclerosis (Adelaide Fernandes, FFUL).

27/10 – Purinergic signaling and brain development – (Ricardo Rodrigues, FMUC, CNC)

27/10 – Driving Cell Death Machinery towards Neural Differentiation (Susana Solá, FFUL)

28/10 – Apoptosis and neuronal death (Cecília Rodrigues, FFUL).

2/11 – Neuronal regeneration (Mónica Sousa, UP).

- 3/11** – The ubiquitin/proteasome system and control of neuronal death (Carlos Duarte, FCTUC, CNC)
- 4/11** – Neuroinflammation and Microglia: functions and dysfunction in neurodegenerative diseases (Dora Brites, FFUL).
- 10/11** – Neuroimaging: an overview (Eduardo Ducla-Soares, FCUL)
- 10/11** – The involvement of astrocytes in cortico-limbic function and behavior (João Oliveira, ICVS, U Minho)
- 11/11** – Optogenetic manipulation of neuronal circuits (João Peça, CNC) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 18/11** – Neurobiological basis of reward (Ana João Rodrigues, ICVS, Univ Minho) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 30/11** – Nociceptive pathways and Mechanisms involved in the genesis of pain (Fani Neto, FMUP) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 2/12** – Neuronal correlates of psychiatric diseases (Frederico Couto, Universidade Católica Portuguesa) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 15/12** – Artificial Intelligence: a view on Morality, or artificial agents with qualities (Helder Coelho, FCUL)
- 9/12** – Role of an Ethics Committee in a University Hospital (Luisa Figueira, FMUL/HSM) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 14/12** – Conscious States (Luis Madeira, FMUL/HSM) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 16/12** – Advanced Directives (Abel García Abejas, FMUL/HSM) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 15/12** – Ethics and legislation in animal research – Carla Fonseca (FMUL)
- 15/12** – The ethics in neurological research (Alexandre de Mendonça)
- 15/12** – Reciprocal inputs between Neuroscience and Robotics (José Santos Victor, IST)

By Unit Members:

- 14/9** – Basics of neuronal excitability: electrochemical gradients and equilibrium potential; membrane potential, action potential (Ana M Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 15/9** – Imaging molecules by immunofluorescence and Western Blot – Applications to neuroscience (Claudia Valente)
- 16/9** – Basics of neuronal communication: synaptic potential, inhibitory vs excitatory transmission, synaptic integration. Ionotropic receptors vs metabotropic receptors (Ana M Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 21/9** – Metabotropic receptors, G proteins and transducing pathways (Sandra Vaz) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 21/9** – Ion channels and ion transporters; comparison with ionotropic receptors (Ana M Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)

- 22/9** – Evaluation of synaptic activity through electrophysiological recording techniques (Diogo Rombo)
- 23/9** – Glutamatergic and GABAergic transmission – receptors and inactivation mechanisms (Ana M Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 28/9** – Modulation of GABAergic transmission (Diogo Rombo) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 6/10** - Drug-receptor interactions and its relevance for neuroscience research (Ana M Sebastião)
- 7/10** – Cholinergic, noradrenergic and dopaminergic transmission; receptors and inactivation mechanisms. Concept of neuromodulation and main neuromodulators; concept of co-transmission (Ana M Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 14/10** – Glial Cells and their ability to control synaptic activity (Sandra Vaz) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 19/10** – Neurotrophic factors: key molecules for neuronal survival and plasticity (Maria José Diógenes).
- 21/10** – The role of glial cells in neuroinflammation (Cláudia Valente)
- 26/10** – Neural Stem cells and its neuroregenerative potential (Sara Xapelli)
- 27/10** – Synaptic dysfunction in Rett Syndrome (Catarina Lourenço)
- 27/10** – Modulation of neuronal maturation and differentiation by adenosine (Ana Filipa Ribeiro)
- 27/10** – Modulation of postnatal neurogenesis by cannabinoids (Rui Rodrigues)
- 27/10** – Microtubule nucleation during brain development: from mitosis to neuronal morphology augmin takes the lead» (Ricardo Viais)
- 9/11** – Major neurotransmitter pathways and their role in brain function (Ana Sebastião) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 10/11** – Animal models of epilepsy (Sara Xapelli)
- 16/11** – Animal Behavioral Testing in Theory and Practice: How to Assess Memory, Anxiety and Depression (Miguel Ferreira) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 17/11** – Circuitry dysfunction in absence epilepsy (Tatiana Morais)
- 23/11** – Mechanisms of drug dependence (Alexandre Ribeiro) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)
- 7/12** – Ethics of Neurosciences and Neurosciences of Ethics (J. Alexandre Ribeiro) (Lecture also for the Master and PhD Courses for Cognitive Sciences of the ULisboa)

Lectures/Seminars for the Master of Biomedical Research:

21/11 – Basics in Excitability and Neuronal Communication (Ana M Sebastião).

Seminars and Lectures at Non CAML Post-graduation Courses/Events:

Diógenes MJ. Webinar Aspirina de 100 a 1000: Papel do Farmacêutico na Recomendação de Aspirina" organized by LisbonPH. Portugal, December, 9, 2021.

Diógenes MJ. Lesson in module Neuronal degeneration and regeneration of Msc/PhD Neuroscience Program. Neurotrophic factors: key molecules for neuronal survival and

plasticity». Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, October 19, 2021.

Diógenes MJ. Theoretical Lesson in module preclinical research of Master in Clinical Investigation. “O Objeto da farmacologia e Princípios básicos de farmacocinética”, October, 15, 2021.

Diógenes MJ. Theoretical and practical lesson in module preclinical research of Master in Clinical Investigation. “O Objeto da farmacologia e Princípios básicos de farmacocinética”, October, 22, 2021.

Lourenço DM. Technical assistant in the practical workshop “Cell culture and neural stem cell microscopy” for the Master/PhD course in Neuroscience, Faculty of Medicine, University of Lisbon, Portugal. October 28-29, 2021.

Miranda-Lourenço C. Seminar in Module 2: Neuronal degeneration and regeneration of Msc/PhD Neuroscience Program. Synaptic Dysfunction in Rett Syndrome. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, October 27, 2021.

Morais TP. Seminar in Module 2: Neuronal Circuits of Msc/PhD Neuroscience Program. Circuitry dysfunction in absence epilepsy. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, November 17, 2021.

Ribeiro FF. Lecture at Master/PhD course in Neuroscience, Faculty of Medicine, University of Lisbon, Portugal. Title: “Imaging modulation of neuronal outgrowth in cultured neurons”. October 27, 2021.

Rodrigues R. Technical assistant in the practical workshop “Cell culture and neural stem cell microscopy” for the Master/PhD course in Neuroscience, Faculty of Medicine, University of Lisbon, Portugal. October 28-29, 2021.

Rodrigues R. Lecture at Master/PhD course in Neuroscience, Faculty of Medicine, University of Lisbon, Portugal. Title: “Modulation of postnatal neurogenesis by cannabinoids”. October 27, 2021.

Rodrigues R. Lecture at Master course in Applied Neuropsychology, School of Psychology and Life Sciences, Lusófona University, Lisbon, Portugal. Title: “The regenerative capacity of the adult brain”. December 7, 2021.

Sebastião AM. Amyotrophic Lateral Sclerosis: more than just a motor neuron disease? IMM Seminar, July, 2021.

Soares R. Technical assistant in the practical course integrated in the Medicine degree, Faculty of Medicine, University of Lisbon, Portugal. September 13-23, 2021.

Valente C. Neuroscience Master/PhD, FMUL, Practical Workshop Organizer. Methodological approaches for neuroinflammation research. Lisbon, Portugal, October 18-19, 2021.

Vaz SH. Lesson in module Cellular and Molecular Neurobiology of Msc/PhD Neuroscience Program. Metabotropic receptors, G proteins and transducing pathways. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, September 21, 2021.

Vaz SH. Lesson in module Cellular and Molecular Neurobiology of Msc/PhD Neuroscience Program. Glial Cells and their ability to control synaptic activity. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, October 10, 2021.

Vaz SH. Practical Workshop 1 Organizer of the Neuroscience Master/PhD, FMUL. Recordings of synaptic potentials from hippocampal slices. Lisbon, Portugal, October 18-19, 2021.

Vaz SH. Lecture on the Master in Biomedical Research of the iMM, FMUL. How neurons and glia in neuronal circuits interact with each other? iMM, FMUL, Lisbon, Portugal, November 29, 2021.

Viais R. Seminar in Module 2: Neuronal degeneration and regeneration of Msc/PhD Neuroscience Program. Microtubule nucleation during brain development: from mitosis to neuronal differentiation augmin takes the lead. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, October 27, 2021.

Xapelli S. Neural Stem cells and its neuroregenerative potential. Master in Biomedical Engineering Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Portugal. April 20 2021.

Xapelli S. Cannabinoid Actions on Neural Stem Cells: Implications for Pathophysiology. PhD Advanced Course: Stem Cell Technologies, Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, November 8, 2021.

MSc Theses

Ana Margarida Garção Godinho, 30/04/2021. Exploring the activation of NLRP3 inflammasome by Reactive Oxygen Species in a model of epileptogenesis. Master in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Valente CA.

Daniela Abreu, 22/12/2021, Role of SNARE-dependent Gliotransmitters Release in Alzheimer's Disease: from astrocytes to circuits. Master in Biomedical Research – specialization on Neuroscience, Centro de Estudos de Doenças Crónicas (CEDOC), Universidade NOVA de Lisboa, NOVA Medical School | Faculdade de Ciências Médicas (NMS|FCM), Lisboa, Portugal. Supervisor: Vaz SH. Co-supervisor: Diógenes MJ and Vicente-Miranda H.

Diogo André Mendonça Dias, 22/02/2021. Impact of NLRP3 inflammasome inhibition in a model of A β -induced toxicity. Master in Neurosciences, Faculdade de Medicina, Universidade de Lisboa. Supervisor: Valente CA.

Francisco José Gonçalves Meda, 18/03/2021. NLRP3 inflammasome inhibition in a model of epileptogenesis in organotypic slices – impact in epileptiform activity and neurodegeneration. Master in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Valente CA.

João Carvalho, 15/07/2021, Efeito da administração de memantina ao longo do envelhecimento nos níveis dos recetores de BDNF, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Diógenes MJ.

Mafalda Cagica Pinto de Carvalho, 22/03/2021. Unravelling the contribution of glial cells for the neuroinflammatory milieu of epileptic-like organotypic slices. Master in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Valente CA.

Mafalda Ferreira-Manso, 18/3/2021, The impact of BDNF receptor cleavage in Alzheimer's disease-associated Neuroinflammation. Faculdade de Ciências da Universidade de Lisboa. Supervisor's Name: Fernandes Borralho A; Co-Supervisor: Supervisor: Diógenes MJ.

Mariana Fernandes Van Zeller da Silva Campos, 16/03/2021. Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β -induced toxicity. Master in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Valente CA.

Oksana Savchak, 07/05/2021, Nanoparticle and liposome-based microreactors as reactive oxygen species scavengers in neuroinflammation 3D models. Master in Biochemistry for Health, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa. Supervisor: Vaz SH. Co-supervisor: Vicente-Miranda H.

Tiago Costa-Coelho, 13/7/2021, Unveiling paracrine dissemination and toxicity of neuronal TrkB-ICD via secretome signalling in Alzheimer's disease, Faculdade de Ciências Médicas | NOVA Medical School da Universidade NOVA de Lisboa. Supervisor's Name: Supervisor: Diógenes MJ ; Co-Supervisor: Brites D.

Valentim Rodrigues, 30/7/2021, Epigenetic changes in a mouse model of Rett Syndrome: optimizing a technique to evaluate DNA methylation, Faculdade de Medicina da Universidade de Lisboa. Supervisor's Name: Supervisor: Diógenes MJ.

PhD Theses

Sara R. Tanqueiro, 22 July 2021, Unveiling the link between BDNF alterations and cognitive deficits in Schizophrenia, Faculdade de Medicina da Universidade de Lisboa. Supervisor's Name: Maria José de Oliveira Diógenes Nogueira; Co-Supervisors: Neil Dawson and Frederico Simões do Couto.

Valorization of Knowledge / Social and Economic Impact

Intellectual Property Rights in 2021

Applicants: Instituto de Medicina Molecular João Lobo Antunes [PT]; Universidade de Coimbra [PT]; Faculdade de Medicina da Universidade de Lisboa [PT]. Inventors: Maria José de Oliveira Diógenes Nogueira [PT]; João Filipe Fonseca Gomes [PT]; André Jerónimo Santos [PT]; Ana Maria

de Sousa Sebastião [PT]; Carlos Bandeira Duarte [PT]. Title of the invention: Therapeutic agents, pharmaceutical composition, and associated biomarkers based on TRK-B. Priority reference (if applicable): GB202004832A. Application reference (if applicable): PT2021050011W.

Science and Society in 2021

Diógenes MJ. WEBINAR: “Epilepsia no Síndrome de RETT” organized by *Associação Nacional de Pais e Amigos de Rett* (ANPAR) “Epilepsia Medicação e investigação”. October 17, 2021.

Diógenes MJ. Inspiring talk to high school students “Posso ser cientista em Portugal? Como?”. Escola Secundária do Bocage, Setúbal. March 26, 2021.

Ribeiro J A. Neuroética e Inteligência Artificial, Published in *Jornal Publico*, February, 2021.

Rodrigues R. Virtual lecture at Escola de Portalegre entitled “Being a neuroscientist in Portugal” in the context of Brain Awareness Week, March 15-21. Audience: 60 high-school students. April 9, 2021.

Sebastião AM. Como adquirimos e como perdemos memórias. Public debate organized by o Panteão Nacional entitled ‘O futuro da memória’, April 18, 2021.

Sebastião AM. Participation in a debate ‘Antes e Depois de Editar. Estudos Filológicos’ organized by Grupo de Filologia do Centro de Linguística da Universidade de Lisboa, January 14, 2021.

Sebastião AM. Participation in a public debate entitled “Brain Gain - À descoberta das Neurociências”, focusing on historical aspects and technological challenges. University of Coimbra, March 10, 2021.

Vaz SH. Participation on the Pint of Science 2021 Portugal – “Os neurónios têm assistentes?”, May 18, 2021.

Xapelli S. Online Seminar entitled “Terá o cérebro algum potencial para se regenerar?” organized by Sociedade Portuguesa de Células Estaminais e Terapia Celular (SPCE-TC) and Ciência Viva in the context to the International Day of the Stem Cell. Audience: 30 high-school students from Agrupamento de Escolas D. Lourenço Vicente. October 14, 2021.

Participation at the Lisbon’s Noite Europeia dos Investigadores 2021: Ciência do Clima | European Researchers’ Night 2021 SciCli (September 24th), a public event in which the main role is the dissemination and transparency of scientific content to the general audience. Interaction with public of all ages about neurosciences and neurological disorders. Participants: Tiago Costa-Coelho, Mafalda Ferreira-Manso, Sara Inteiro-Oliveira, Sara Costa-Pinto, Joana Gonçalves-Ribeiro, Hugo Simões.

Participation in the Brain Awareness week with scientific talks for high school students. Participants: Ricardo Viais, João Moreira, Sandra Vaz.

Bruno Silva- Santos Lab

Head of Laboratory: Bruno Silva-Santos, PhD, Group Leader and Associate Professor, Faculdade de Medicina Universidade de Lisboa

Team

Afonso Maria Douwens da Costa Teixeira da Mota	University Degree	MSc Student (Left July)
Ana Carolina Graís Condeço	Master Degree	Lab Technician (Started June)
Ana Maria de Amarante Pamplona Dias Santos	PhD	Senior Postdoctoral Researcher
André Luis Bombeiro	PhD	Senior Postdoctoral Researcher (Started January)
André Miguel Vaz Pinto Santos	University Degree	MSc Student (Started September)
Anita Raquel Quintal Gomes	PhD	Senior Postdoctoral Researcher
Carolina Emanuel Carreira Gomes Jardim	Master Degree	PhD Student
Daniel Pereira Inácio	Master Degree	PhD Student
Gisela da Silva Gordino	Master Degree	PhD Student
Joana Carolina Marinho Cunha	PhD	Postdoctoral Researcher
Julie Cécile Caroline Ribot	PhD	Staff Scientist
Julie Darrigues	PhD	Postdoctoral Researcher
Karine Marie Serre	PhD	Staff Scientist
Mariana Reis Sobreiro	PhD	Senior Postdoctoral Researcher (Left July)
Marta Gaspar Rodrigues da Silva	University Degree	MSc Student (Left September)
Marta Maria Curado Avelar	Master Degree	MSc Student (Left May)
Natacha Maria Gonçalves Silva Sousa	Master Degree	Lab Manager
Noella Lopes Pappalardo	PhD	Postdoctoral Researcher (Left January)
Rui Miguel Lopes Coelho	Master Degree	Lab Technician (Started April. Left July)
Sara Coelho Dias O'Connor Shirley	University Degree	MSc Student (Left April)
Sofia Mensurado Santos	PhD	Postdoctoral Researcher
Tiago Filipe Serrano Constantino	Master Degree	MSc Student
Tomás Miguel Custódio dos Santos	University Degree	MSc Student
Vicente Jorge Galego de Almeida	University Degree	MSc Student (Started September)
Vladimir Ghilas	University Degree	MSc Student (Started September)

Lab Interests

We are interested in the pleiotropic roles of immune cells in tissue (patho)physiology. Within our major research line of Immuno-Oncology, we study T lymphocytes, using in vitro and in vivo models, for the identification of molecular mechanisms involved in their differentiation, activation and functions in cancer, with the ultimate goal of designing novel immunotherapy strategies.

In a more recent area in our lab – Neuroimmunology – we explore the crosstalk between the immune system, particularly T cells that populate the meninges, and the brain – either in health (cognition) or in disease (neurodegeneration).

We have a particular focus on the less studied gamma-delta T cell lineage, with a marked interest in their differentiation, starting with the earliest steps of development in the thymus.

On the other hand, we investigate their activities in inflamed tissues, including tumors or infected organs, but also sterile inflammation in murine models of tissue degeneration.

Research Field

- Immunity, Infection and Immunotherapy

Major Scientific Achievements in 2021

In 2021 we graduated 4 new Master students in the areas of Developmental Immunology, Immuno-Oncology and Neuroimmunology.

We published 13 scientific articles, including an original paper in Nature Immunology (Lopes et al.) and a review paper in Nature Microbiology (Papotto et al.). Our new findings included:

- in Immuno-Oncology, the dissection of the metabolic pathways that promote gamma-delta T cell responses to tumors (Lopes et al. Nat Immunol 2021);
- in Neuroimmunology, the discovery that a dysregulated IL-17 response by meningeal gamma-delta T cells promotes the onset of neuropathology in a pre-clinical model of Alzheimer's Disease (Brigas et al. Cell Rep 2021).

Finally, with regard to technology transfer and clinical application, the cellular therapy developed in our laboratory, Delta One T (DOT) cells, licensed and transferred (as GDX012) to GammaDelta Therapeutics, entered a phase 1 clinical trial in leukemia patients in the USA in September 2021.

Ongoing Projects in 2021

2021/2024: Regulation of gamma-delta T cells in the tumor microenvironment and their manipulation towards immunotherapy of solid cancers. Coordinator: Bruno Silva-Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/6829/2020. Amount: 250 000,00€. Total Amount: 250 000,00€.

2021/2024: Regulating meningeal $\gamma\delta$ 17 T cell homeostasis: Molecular mechanisms and pathophysiological implications. Coordinator: Julie Ribot. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/1988/2020. Amount: 250 000,01€. Total Amount: 250 000,01€.

2020/2021: GDT - Research Agreement. Coordinator: Bruno Silva-Santos. Funding Agency: Lymphocyte Activation Technologies SA. Reference: GDT - Research Agreement. Amount: 163 986,00€. Total Amount: 163 986,00€.

2020/2021: Cellular and molecular regulators of multifaceted $\gamma\delta$ T-cells in the tumor microenvironment. Coordinator: Bruno Silva-Santos. Funding Agency: Fundação AstraZeneca. Reference: FAZ_PremioCiencia_2020. Amount: 35 000,00€. Total Amount: 35 000,00€.

2019/2022: Next-generation CAR-DOT cells for allogeneic adoptive cancer immunotherapy. Coordinator: Bruno Silva-Santos. Funding Agency: “la Caixa” Foundation. Reference: HEALTH RESEARCH 2018 - HR18-00069 - ALLO_CAR_DOT. Amount: 499 999,51€. Total Amount: 999 997,00€.

2018/2021: Impacto das células T gd17 residentes nas meninges em funções cognitivas num contexto fisiológico e neuropatológico. Coordinator: Julie Ribot. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: iMMunoCOGNITION - LISBOA-01-0145-FEDER-028241. Amount: 239 679,45€. Total Amount: 239 679,45€.

2018/2021: PROMISE: Programação de células mielóides anti-tumorais para aplicação em imunoterapia do cancro. Coordinator: Karine Serre. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PROMISE - LISBOA-01-0145-FEDER-030948. Amount: 239 896,60€. Total Amount: 239 896,60€.

2015/2021: DevoTed_miR: MicroRNA determinants of the balance between effector and regulatory T cells in vivo. Coordinator: Bruno Silva-Santos. Funding Agency: European Commission. Reference: ERC CoG 646701. Amount: 2 000 000,00. Total Amount: 2 000 000,00.

Scientific Impact

Academic Collaborations

Pablo Menéndez, Josep Carreras Leukaemia Research Institute
 Anne Schaefer, Icahn School of Medicine at Mount Sinai
 Renaud Lesourne, Toulouse Institute for Infectious and Inflammatory Diseases
 Alexandre Carmo, Instituto de Investigação e Inovação em Saúde, Universidade do Porto
 Luisa Lopes, Instituto de Medicina Molecular João Lobo Antunes
 Elva Bonifácio Andrade, Instituto de Investigação e Inovação em Saúde, Universidade do Porto
 Leonor Saude, Instituto de Medicina Molecular João Lobo Antunes
 Henrique Veiga-Fernandes, Champalimaud Foundation
 Daniel Pennington, Queen Mary University of London
 Lydia Lynch, Harvard Med Sch, Brigham & Womens Hosp, Boston, USA and Trinity Coll Dublin, Trinity Biomed Sci Inst, Dublin, Ireland

Selected Publications

Ribeiro M*, Brigas HC*, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Cláudia Valente C, Omenetti S, Stockinger B, Waissman A, Manadas B, Lopes LV, Silva-Santos B** and Ribot JC** (2019). [Meningeal \$\gamma\delta\$ T cell-derived IL-17 controls synaptic plasticity and short-term memory](#). *Science Immunol*, 4 (40). (**Co-corresponding)

Relevance of the publication: We identified a meningeal population of $\gamma\delta$ T cells that control brain cognitive functions through the production of IL-17. We showed that this cytokine stimulated the production of brain derived neurotrophic factor (BDNF) by glial cells, which promoted neuronal synaptic plasticity required for short-term memory and learning. These findings provided a key missing piece to the puzzle of immune populations infiltrating the meninges and the regulation of neurophysiology, thus becoming a seminal paper in Neuroimmunology. The study was particularly well received, largely covered

by the media (Público, Alzforum, Cosmosmag, Technology Network); highlighted in Nature Immunology and Nature Review Immunology; and awarded a Pfizer Award for Basic Research.

Silva-Santos B*, Mensurado S, Coffelt SB* (2019). [γδ T cells: pleiotropic immune effectors with therapeutic potential in cancer](#). **Nature Rev Cancer** 19(7):392-404. (*Co-corresponding)

Relevance of the publication: Key review on the multifaceted roles of γδ T cells in cancer, from pre-clinical models to patient-centered research and clinical application. This paper in Nature Reviews Cancer updated our take on the state-of-the-art previously reviewed for Nature Reviews Immunology (Silva-Santos et al. 2015), which had been cited 280 times. Both these reviews have been major contributions of our laboratory to the Immuno-Oncology community.

Muñoz-Ruiz M, Ribot JC, Grosso AR, Gonçalves-Sousa N, Pamplona A, Pennington DJ, Regueiro JR, Fernandez-Malavé E, Silva-Santos B (2016). [TCR signal strength controls thymic differentiation of discrete proinflammatory γδ T cell subsets](#). **Nature Immunol** 17(6):721-7.

Relevance of the publication: In this study, we – in collaboration with Regueiro/ Malavé lab in Madrid – generated a new mouse model to modulate TCR signal strength selectively in γδ T cells, and demonstrated how it differentially impacts the thymic development of their main functional subsets producing either interferon-γ (IFN-γ) or interleukin-17 (IL-17). This novel model also allowed us to unravel the key contribution of IFNγ-producing γδ T cells to the pathogenesis of cerebral malaria, which we then followed up in Ribot et al. PNAS 2019.

Almeida AA, Correia DV, da Silva CL, da Silva MG, Anjos DR, Silva-Santos B (2016). [Delta One T cells for immunotherapy of chronic lymphocytic leukemia: clinical-grade expansion/ differentiation and preclinical proof-of-concept](#). **Clinical Cancer Research** 22(23):5795-5804.

Relevance of the publication: Here we characterized a new method for clinical-grade expansion of human CD27^{hi}T cells for adoptive immunotherapy. We showed that the Vδ1-enriched product, named “Delta One T” (DOT) cells, upregulated the expression of multiple natural killer receptors, which enhanced their cytotoxic function against tumors. Furthermore, we demonstrated the therapeutic potential of DOT cells in vivo, using a pre-clinical model of chronic lymphocytic leukemia. These data, together with our patented expansion/ differentiation protocol, was critical for the acquisition of our iMM’s spin-off company, Lymphact, by the British biotech company, GammaDelta Therapeutics, in 2018.

Ribot JC, deBarros A, Pang DJ, Neves JF, Peperzak V, Girardi M, Borst J, Hayday AC, Pennington DJ and Silva-Santos B (2009). [CD27 is a thymic determinant of the balance between IFN-γ- and IL-17-producing γδ T cell subsets](#). **Nature Immunol** 10(4): 427-36.

Relevance of the publication: Seminal paper describing two main functional γδ T cell subsets, producing either interferon-γ (IFN-γ) or interleukin-17 (IL-17), that we distinguished on the basis of CD27 expression levels. We showed that the two subsets diverge early in ontogeny during thymic development, with CD27 signals promoting the IFN-γ pathway over the IL-17-producing fate. These findings inspired many subsequent studies, including ours: Schmolka et al. Nat Immunol 2013, Rei et al. PNAS 2014, Muñoz-Ruiz et al. Nat Immunol 2016, Mensurado et al. PLoS Biol 2018 and Lopes et al. Nat Immunol 2021.

2021 Publications in Peer-Reviewed Journals

Brigas H.C, Ribeiro MR, Coelho JR, Gomes R, Gomez V, Carvalho K, Faivre E, Pereira S, Darrigues J, Almeida AA, Buée L, Dunot J, Marie H, Pousinha PA, Blum D, Silva-Santos B, Lopes LV* and

Ribot JC*. (2021) [IL-17 triggers the onset of cognitive and synaptic deficits in early stages of Alzheimer's disease](#). **Cell Reports**, 36, 109574.

Canto E Castro L, Gomes A, Serrano M, Pereira AHG, Ribeiro R, Napoleão P, Domingues I, Silva C, Fanczal J, Afonso Â, Lopes A, Toader I, de Sousa MJR, de Sousa JGR, de Sousa G, Mota MM, Silva-Santos B, Veldhoen M, Ribeiro RM (2021). [Longitudinal SARS-CoV-2 seroprevalence in Portugal and antibody maintenance 12 months after infection](#). **European journal of Immunology** 2022 Jan;52(1):149-160. Epub 2021 Nov 10.

Darrigues, J., Ribot, J.C. (2021). [\$\gamma\delta\$ T cells, Tregs and epithelial cells interact with IL-33 in the lung](#). **Cell Mol Immunol** 18, 790–791.

Gordino G, Costa-Pereira S, Corredeira P, Alves P, Costa L, Gomes AQ, Silva-Santos B and Ribot JC (2022). [MicroRNA-181a Restricts Human \$\gamma\delta\$ T Cell Functional Differentiation by Targeting Map3k2 and Notch2](#). **EMBO Rep**. Jan 5;23(1):e52234, Epub 2021 Nov9]

Lopes N, McIntyre C, Martin S, Raverdeau M, Sumaria N, Kohlgruber AC, Fiala GJ, Agudelo LZ, Dyck L, Kane H, Douglas A, Cunningham S, Prendeville H, Loftus R, Carmody C, Pierre P, Kellis M, Brenner M, Argüello RJ, Silva-Santos B, Pennington DJ, Lynch L (2021) [Distinct metabolic programs established in the thymus control effector functions of \$\gamma\delta\$ T cell subsets in tumor microenvironments](#). **Nat Immunol**. 2021 Feb;22(2):179-192.

Lopes N, Silva-Santos B (2021). [Functional and metabolic dichotomy of murine \$\gamma\delta\$ T cell subsets in cancer immunity](#). **Eur J Immunol**. 2021 Jan;51(1):17-26.

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Pena A.C., Pamplona A. (2022). [Heme Oxygenase-1, Carbon Monoxide, and Malaria – The Interplay of Chemistry and Biology](#). **Coordination Chemistry Reviews**. Epub 2021 Nov 27.

Reis-Sobreiro M, Teixeira da Mota A, Jardim C, Serre K. (2021). [Bringing Macrophages to the Frontline against Cancer: Current Immunotherapies Targeting Macrophages](#). **Cells**. 9;10(9):2364.

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Wilharm A, Brigas HC, Sandrock I, Ribeiro M, Amado T, Reinhardt A, Demera A, Hoenicke L, Strowig T, Carvalho T, Prinz I, Ribot JC (2021). [Microbiota-dependent expansion of testicular IL-17-producing V \$\gamma\$ 6+ \$\gamma\delta\$ T cells upon puberty promotes local tissue immune surveillance](#). *Mucosal Immunol.* 2021 Jan;14(1):242-252.

Invited Lectures and Seminars

Bruno Silva-Santos. Functional and metabolic dichotomy of effector $\gamma\delta$ T cell subsets. Erlangen University (Online), Erlangen, Germany, January 26th, 2021.

Ribot JC. Emerging Roles of T Cells in CNS Health and Disease. Society of Biological Psychiatry (Online), San Diego, USA, May 30th, 2021.

Ribot JC. $\gamma\delta$ T Cells in tissue pathophysiology. Immunoconcept seminar, Bordeaux, France, October 20th, 2021.

Bruno Silva-Santos. Developing a $\gamma\delta$ T cell-based adoptive therapy for cancer. Leuven f-TALES, Leuven, Belgium, October 25th, 2021

Sofia Mensurado. Delta One T cells: a new player in adoptive immunotherapy of cancer? LatinFlow 2021, Online, November 11th, 2021.

Ribot JC. Meningeal gamma-delta T cells: Impact on cognition in health and disease. Symposium "Molecular Organization of Immune Cell Communication", Magdeburg, Germany, November 25th, 2021.

Bruno Silva-Santos. Molecular programming of innate $\gamma\delta$ T cells: focus on metabolism and microRNAs. Innate T cell Meeting. Institut Curie, Paris, France, December 6th, 2021.

Bruno Silva-Santos. Delta One T cells: developing a "universal" adoptive immunotherapy for cancer. Rede Saúde da Universidade de Lisboa (Online), Lisboa, Portugal, December 10th, 2021

Communications

M. Reis Sobreiro. TLR3 and CD40 induce iNOS, expression and metabolic fitness in macrophages leading to tumor regression and anti-tumor immunity. 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Gordino G, Costa-Pereira S, Corredeira P, Alves P, Costa L, Gomes AQ, Silva-Santos B and Ribot JC. MicroRNA-181a Restricts Human $\gamma\delta$ T Cell Functional Differentiation by Targeting Map3k2 and Notch2. 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Pedro H. Papotto, Gonçalo Pimenta, Bahtiyar Yilmaz, Sofia Mensurado, Carolina Cunha, Natacha Gonçalves-Sousa, Gina Fiala, Daniel Gomes da Costa, Brian H. K. Chan, Birte Blankenhaus, Tânia Carvalho, Andrew J. Macpherson, Judith E. Allen, Bruno Silva-Santos. Maternal $\gamma\delta$ T cells shape

offspring pulmonary type-2 immunity in a microbiota-dependent manner. 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Cunha C., Romero P.V., Pelicano C., Pais T.R., Inácio D., Papotto P., Amado T., Gomes A.Q., Silva-Santos B. Dissecting the role of microRNAs in effector versus regulatory CD4⁺ T cell differentiation during (auto)immune responses *in vivo*. XLVI Annual Meeting of the Portuguese Society for Immunology, Online conference, Portugal, May 20-21, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Inácio D., Amado T., Sobral D., Enguita F., Cunha C., Enguita F., Silva-Santos B. and Gomes A.Q. Role of microRNAs on T cell differentiation during immune responses *in vivo*. III H&TRC BootCam, Hotel Aldeia dos Capuchos, Costa da Caparica, Portugal, September 15th 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Gina J Fiala, Marta M Curado Avelar, Birte Blankenhaus, Tobias Suske, Julie Darrigues, Daniel Inácio, Heidi A Neubauer, Richard Moriggl, Bruno Silva-Santos. CD8 co-receptor expression identifies a novel subset of IFN- γ $\gamma\delta$ T cells abundant in early life. 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Pedro H. Papotto, Gonçalo Pimenta, Bahtiyar Yilmaz, Sofia Mensurado, Carolina Cunha, Natacha Gonçalves-Sousa, Gina Fiala, Daniel Gomes da Costa, Brian H. K. Chan, Birte Blankenhaus, Tânia Carvalho, Andrew J. Macpherson, Judith E. Allen, Bruno Silva-Santos. Maternal $\gamma\delta$ T cells shape offspring pulmonary type-2 immunity in a microbiota-dependent manner. The 9th International $\gamma\delta$ T cell Conference (Online). Zhuhai, China. November 05th-08th, 2021. ORAL COMMUNICATION. INTERNATIONAL CONFERENCE

Inácio D., Amado T., Silva M., Sobral D., Cunha C., Pamplona A., Enguita F., Gomes A.Q. and Silva-Santos, B. A key role for microRNAs in the development and functional differentiation of $\gamma\delta$ T cell subsets. The 9th International $\gamma\delta$ T cell Conference, Online conference, Zhuhai, China, November 5-8, 2021. ORAL COMMUNICATION; INTERNATIONAL CONFERENCE

Gordino G, Costa-Pereira S, Corredeira P, Alves P, Costa L, Gomes AQ, Silva-Santos B and Ribot JC. MicroRNA-181a Restricts Human $\gamma\delta$ T Cell Functional Differentiation by Targeting Map3k2 and Notch2. The 9th International $\gamma\delta$ T cell Conference (Online). Zhuhai, China. November 05th-08th, 2021. ORAL COMMUNICATION. INTERNATIONAL CONFERENCE

Julie Darrigues, Sara Costa-Pereira, Vicente Almeida, André L. Bombeiro, Tiago Amado, Bruno Silva-Santos and Julie C. Ribot, Stress-derived signals control $\gamma\delta$ 17 T cell homeostasis. The 9th International $\gamma\delta$ T cell Conference (Online). Zhuhai, China. November 05th-08th, 2021. POSTER COMMUNICATION. INTERNATIONAL CONFERENCE

Bruno Silva-Santos. Maternal $\gamma\delta$ T cells shape offspring pulmonary type-2 immunity in a microbiota-dependent manner. Annual Meeting of the French Society for Immunology, Paris, France, December 8th, 2021 ORAL COMMUNICATION; INTERNATIONAL CONFERENCE.

Organization of Conferences

Bruno Silva-Santos Co-organizer. 5th Annual Meeting of Rede Saúde da Universidade de Lisboa, Lisboa, Portugal, November 30th, 2021.

Prizes & Honors in 2021

Pedro Papotto received the João Lobo Antunes Merit PhD Thesis Award.

Carolina Cunha - Best Oral communication at the 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021.

Pedro H. Papotto - Best Oral communication at the 46th Annual Meeting of the Portuguese Society for Immunology, Online Conference, Portugal, May 20th-21st, 2021.

Anita Q. Gomes - Merit Certificate, Technology and Engineering Scientific prizes from IPL-CGD, June 2021.

Prémio GAPIC David Ferreira, awarded to Afonso Antunes de Almeida, on December, 15th 2021, for his Master thesis "Impact of IL-17 on Alzheimer's Disease progression".

1^o Prémio AEFML Dia da Investigação awarded to Tomás Santos on December 15th 2021 for his project "Overcoming roadblocks to DOT-cell immunotherapy of colon cancer".

Advanced Teaching

Sofia Mensurado. Lecture. Adoptive cell (immuno)therapy of cancer. Oncolmmunology for Master course in Oncobiology, FMUL, Lisbon, Portugal, February 3rd, 2021.

Sofia Mensurado. Lecture. Journal Club. Oncolmmunology for Master course in Oncobiology, FMUL, Lisbon, Portugal, February 5th, 2021.

Sofia Mensurado. Lecture. Evading and Hijacking the Immune System. Cellular and Molecular Biology of Cancer for Master courses Biochemistry and Biology, FCUL, Lisbon, Portugal, March 15th, 2021.

Bruno Silva-Santos. Lecture. Cancer Immunotherapy: Upgrading your Defenses. AIMS Meeting (Online), Lisbon, Portugal, March 21st, 2021.

Bruno Silva-Santos. Lecture. Delta One T cells: developing a novel adoptive cell therapy for cancer. Faculdade de Farmácia da Universidade de Lisboa (Online), Lisbon, September 20th, 2021.

Bruno Silva-Santos. Lecture. Delta One T cells: developing a novel adoptive cell therapy for cancer. Basel PostDoc Retreat (Online), Basel, Switzerland, October 15th, 2021.

Sofia Mensurado. Lecture. Journal Club. Immunity and Infection for Master course in Biomedical Research, iMM, Lisbon, Portugal, November 4th, 2021.

Bruno Silva-Santos. Lecture. Immuno-Oncology: targets and selection. Immuno-Oncology Iberic Course (Online). Madrid, Spain, November 11st, 2021.

Karine Serre. Lecture. Dietary restriction and immune responses, Licenciatura Ciências da Nutrição, FMUL, Lisbon, Portugal, November 18th, 2021.

Karine Serre. Lecture. Tumour Immunology, Licenciatura Ciências da Nutrição, FMUL, Lisbon, Portugal, December 9th, 2021.

Karine Serre. Lecture. Cancer Immunotherapy, Licenciatura Ciências da Nutrição, FMUL, Lisbon, Portugal, December 14th, 2021.

Anita Q. Gomes. Lecture. Postgraduated course of Advances in Oncobiology applied to Diagnostics and Therapeutics”, module of Immunology “ $\gamma\delta$ T cells: Example of anti-tumour lymphocytes”, ESTeSL, IPL, Lisbon, Portugal, May 11th, 2021.

Anita Q. Gomes. Lecture. Master Course in Biomedical Research: “Molecular basis of $\gamma\delta$ T cell differentiation”, IMM, Lisbon, Portugal, November 3rd, 2021.

MSc Theses

Marta Avelar, 12/01/2021, Molecular Determinants of Thymic Development of CD8-expressing $\gamma\delta$ T cells, Instituto Superior Técnico – Universidade de Lisboa. Supervisor: Gina Fiala. Co-Supervisor: Bruno Silva-Santos.

Teresa Pais, 17/03/2021, MicroRNA determinants of the balance between effector and regulatory CD4⁺ T cells, Master in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Bruno Silva Santos, Co-supervisor: Carolina Cunha.

Afonso da Mota Teixeira, 14/05/2021, Programming anti-tumour myeloid cells for effective immunotherapy, Supervisor’s Name: Karine Serre

Marta Gaspar Rodrigues da Silva, 29/09/2021, The role of microRNA-181a in the development and differentiation of pro-inflammatory $\gamma\delta$ T cell subsets, Master in Biomedical Engineering, Instituto Superior Técnico, Universidade de Lisboa. Supervisor: Anita Q. Gomes Co-Supervisor: Bruno Silva-Santos.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Identification of the molecular mechanisms of AML recognition by DOT cells; Study of the therapeutic potential of DOT cells in colon cancer, GammaDelta Therapeutics, Sponsored Research.

Science and Society in 2021

Silva-Santos, B. (2021, December 26). Lineage decisions in the thymus: T cell lineage commitment [Video file]. In *The Biomedical & Life Sciences Collection*, Henry Stewart Talks: <https://hstalks.com/bs/4705/>.

Silva-Santos, B. (2021, December 26). Lineage decisions in the thymus: $\alpha\beta$ and $\gamma\delta$ T cell lineages [Video file]. In *The Biomedical & Life Sciences Collection*, Henry Stewart Talks: <https://hstalks.com/bs/4821/>.

The article by Brigas et al (doi: 10.1016/j.celrep.2021.109574) was covered in the media, in the following links:

<https://www.publico.pt/2021/09/22/ciencia/noticia/estudo-liga-celulas-imunitarias-sinais-doenca-alzheimer-1978266>

<https://saudeonline.pt/alzheimer-estudo-do-imm-confirma-influencia-da-proteina-il-17-na-manifestacao-da-doenca/>

Pedro Simas Lab

Head of Laboratory: João Pedro Simas, PhD, Group Leader at Instituto de Medicina Molecular
João Lobo Antunes (Left December)

Team

Ana Cláudia Rodrigues Fonseca	PhD	Postdoctoral Researcher (Left December)
André Miguel Ventura Gomes	University Degree	Trainee (Started January. Left December)
Andreia Filipa Bonecas Mósca	PhD	Postdoctoral Researcher
Catarina Neves Costa	Master Degree	PhD Student
Filipa Prata Silva	University Degree	PhD Student (Started October)
Francisca Bixirão Ferreira Andersen	University Degree	MSc Student (Started October)
Maria Beatriz Dias Salgado Lotra	University Degree	MSc Student (Started October)
Marta Pires de Miranda	PhD	Senior Postdoctoral Researcher
Ricardo João Lopes de Oliveira	University Degree	MSc Student

Lab Interests

We utilize murid herpesvirus 4, which causes persistent infection in B-lymphocytes in laboratory mice, as a model to study human gammaherpesvirus pathogenesis, namely Kaposi's sarcoma associated herpesvirus (KSHV). KSHV is the etiologic agent of KS and primary effusion lymphoma. KSHV infection of tumor cells is primarily latent and KSHV drives cells to proliferate. KSHV persists in latently infected tumor cells as an extrachromosomal, multi-copy episome (plasmid). KSHV latency-associated nuclear antigen (kLANA) mediates KSHV episome persistence, thus tumor cell viability. Our laboratory is focused on LANA molecular functions with the goal to inhibit its function and therefore eradicating virus infection and cure associated cancers.

Ongoing Projects in 2021

2021/2022: CDKI. Coordinator: Pedro Simas. Funding Agency: National Institutes of Health (NIH). Reference: NIH 2020 - KSHV LATENT INFECTION REPLICATION. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2022: LEO FARMACÊUTICOS. Coordinator: Pedro Simas. Funding Agency: Dompé. Reference: PRECLINICAL RESEARCH AGREEMENT – DOMPÉ. Amount: 25 759,50€. Total Amount: 25 759,50€.

2020/2021: Apoio Pedro Simas Lab. Coordinator: Pedro Simas. Funding Agency: Vários. Reference: Apoio Pedro Simas Lab. Amount: 9 700,00€. Total Amount: 9 700,00€.

2020/2021: Consultoria PSimas Lab. Coordinator: Pedro Simas. Funding Agency: Vários. Reference: Consultoria PSimas Lab. Amount: 211 218,06€. Total Amount: 211 218,06€.

2020/2021: PLANTCOVID - Aplicações de extratos de plantas com ação dirigida ao SARS-CoV-2. Coordinator: Pedro Simas. Funding Agency: CCDRs. Reference: LISBOA-01-02B7-FEDER-054870. Amount: 100 000,00€. Total Amount: 497 877,13€.



2018/2021: Investigação de um gene tumoral viral num modelo de infecção em murganho através de um vírus quimera. Coordinator: Pedro Simas. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 027947/2017. Amount: 239 156,12€. Total Amount: 239 156,12€.

Ana Espada de Sousa Lab

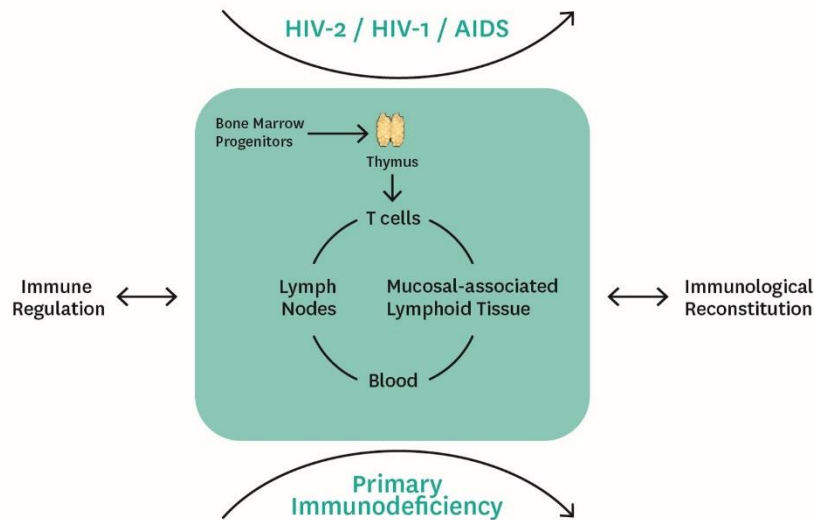
Head of Laboratory: Ana Espada de Sousa, MD, PhD Group Leader, Investigator Coordinator and Full Professor, Faculdade de Medicina da Universidade de Lisboa

Team

Adriana Motta Raymundo	University Degree	PhD Student (Started March)
Afonso Rocha Martins de Almeida	PhD	Senior Postdoctoral Researcher
Alexandre Augusto da Silva Figueiredo e Raposo	PhD	Senior Postdoctoral Researcher
Amelia Chiara Trombetta	PhD	Postdoctoral Researcher (Left May)
Ana Berta da Fonseca Vieira Álvares e Sousa Ferrand de Almeida	PhD	Clinical Researcher
Ana Catarina Taborda Godinho dos Santos	PhD	Postdoctoral Researcher (Left August)
Ana Cláudia Viseu Varandas	MD/Master Degree	Trainee
Ana Cristina Costa Santos Ferreira de Oliveira Dias	MD	Clinical Researcher
Ana Isabel Gouveia Costa da Fonseca Lopes	MD/PhD with Habilitation	Clinical Researcher
André Lopes Reis Gomes Pires	University Degree	Trainee
André Miguel Carapinha Gomes	Master Degree	PhD Student
Carolina Marques Martins	University Degree	Trainee (Left July)
Carolina Martins da Conceição	Master Degree	Lab Technician (Left August)
Diana Isabel Feliciano dos Santos	University Degree	Lab Manager
Diogo Karim Hassam Carmali	University Degree	Trainee (Left February)
Emília de Jesus da Encarnação Valadas	MD/PhD	Clinical Researcher
Guilherme Borlido de Carvalho Farias	Master Degree	Lab Technician
Henrique José Atalaia Barbacena	MD/Master Degree	Trainee
Inês Moranguinho Bastardo Moura	Master Degree	PhD Student
Isabel Cristina e Castro de Menezes Esteves	MD	Clinical Researcher
José Gonçalo Duque Pereira Monteiro Marques	MD	Clinical Researcher
Madalena Pimentel Marques	Master Degree	Lab Technician (Started October)
Manuel António Freire Dias da Silva	University Degree	MSc Student
Maria Adão Serrano de Sousa Uva	MD	Clinical Researcher
Maria Catarina Mota da Silva	MD/PhD	Clinical Researcher
Maria da Conceição Galvão Barata Pinto Pereira dos Santos	PhD	Clinical Staff Scientist (Left October)
Maria de Medeiros Mota	University Degree	MSc Student (Started April. Left December)
Maria Inês Tostão Neiva	University Degree	MSc Student (Left July)
Patrícia Nicole Guilherme Silva	University Degree	MSc Student (Started September)
Pedro Mota Prego Rosmaninho	PhD	Postdoctoral Researcher
Ramona Karina Adameck	University Degree	MSc Student (Started April)
Rita Da Cunha Taborda Junqueiro Marques	University Degree	Trainee (Started September)
Rita Diniz de Moura	University Degree	MSc Student
Robert Alfred Badura	MD/Master Degree	Clinical Researcher
Sara Branco Pereira da Silva Fialho	MD	Clinical Researcher
Susana Clara Barão Lopes da Silva dos Anjos	MD/PhD	Clinical Staff Scientist (Started September)

Susana Maria Santos do Paço	Master Degree	MSc Student
Susana Mendes Fernandes	MD/PhD	Clinical Staff Scientist
Zoe-Isabella Junginger	Master Degree	Lab Technician

Graphical Abstract



Lab Interests

- We investigate immune regulation and human T-cell homeostasis with the ultimate goal of identifying new strategies for immunological reconstitution and targets for immune-based therapies.
- An important part of our Lab research effort is centred on HIV/AIDS immunopathogenesis, mainly through the study of HIV-2 infection, a naturally attenuated form of HIV disease, and on Inborn Errors of Immunity leading to Human Immunodeficiency.
- We prioritise the “bedside to the bench” approach and, given the transversal nature of Clinical Immunology, our Lab brings together physician/clinical researchers, from different medical areas, and basic researchers.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

Major Scientific Achievements in 2021

Our main research focus is immune regulation in health and human disease. During 2021 we identified key gene regulatory networks defining the signature of human thymic FOXP3+ CD4 T-cells. This population commits to the regulatory lineage during T-cell development in the thymus and is critical for autoimmunity control. We are now applying the generated knowledge to decipher genotype-phenotype relationships in complex inborn errors of immunity and explore their role in disease development.

Additionally, we pursued our work on mechanisms of immune deregulation in persistent infections through the comparison of HIV-2 and HIV-1 infections of follicular helper T-cells in-vitro and ex-vivo. This investigation was mainly oriented to the role of SAMHD1, a cell-intrinsic host restriction factor with relevant function in follicular cells that is uniquely targeted to ubiquitination by HIV-2.

Finally, our work also helped clarify how the immune system modulates the course of COVID-19.

Ongoing Projects in 2021

2021/2025: MYE-INFOBANK - Converting molecular profiles of myeloid cells into biomarkers for inflammation and cancer. COST Action CA20117. MC Member from Portugal: Ana Espada de Sousa.

2021/2024: Imunodeficiências humanas: papel reparador das células T CD4 naïve - Targeting naïve CD4 T cells to avoid human immunodeficiency. Coordinator: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/0938/2020. Amount: 249 998,75€. Total Amount: 249 998,75€.

2021/2022: RNAscope dos tecidos linfóides de indivíduos infectados pelo HIV-2 ou pelo HIV-1. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences, Lda. Reference: APOIO BOLSA DE INVESTIGAÇÃO. Amount: 25 100,00€. Total Amount: 25 100,00€.

2021/2021: CSL BEHRING-IMM. Coordinator: Susana Lopes da Silva. Funding Agency: CSL Behring. Reference: CSL BEHRING-IMM. Amount: 5 100,00€. Total Amount: 5 100,00€.

2020/2022: CT de Apoio a Bolsas de Investigação Científica. Coordinator: Ana Espada de Sousa. Funding Agency: Janssen-Cilag Farmacêutica. Reference: CT de Apoio a Bolsas de Investigação Científica. Amount: 28 703,36€. Total Amount: 28 703,36€.

2020/2021: Contributo dos monócitos/macrófagos para a patogénese distinta da infeção por VIH-2 em comparação com VIH-1: correlações clínicas e perspetivas terapêuticas. Coordinator: Amelia Trombetta. Funding Agency: Gilead Science. Reference: Programa Gilead GÉNESE 2019. Amount: 23 215,00€. Total Amount: 23 215,00€.

2019/2021: Revealing lung repair after ARDS through the IL-22 path. Funded by Sociedade Portuguesa de Medicina Interna and Fundação AstraZeneca. Coordinator: Susana Mendes Fernandes. Amount: 9 000,00€. Total Amount: 9 000,00€.

2018/2022: Estudos quantitativos de latência no VIH. Coordinator: Ruy Ribeiro. Co-PI: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MAT-APL/31602/2017. Amount: 52 500,00€. Total Amount: 239 766,06€.

2018/2022: Explorando o papel de microRNAs na função de células T e defesa anti-HIV. Coordinator: Margarida Gama-Carvalho. Co-PI: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/29257/2017. Amount: 41 187,50€. Total Amount: 239 911,12€.

2018/2021: HIV2CURE: Células T foliculares no cerne da infecção HIV. Coordinator: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: HIV2CURE - LISBOA-01-0145-FEDER-030474. Amount: 239 999,01€. Total Amount: 239 999,01€.

Scientific Impact

Academic Collaborations

Zvi Grossman, National Institutes of Health (NIH), USA

Ruy Ribeiro, Los Alamos National Laboratory, USA

Margarida Gama-Carvalho, Faculdade de Ciências da Universidade de Lisboa (FCUL)

Ana Abecasis, Instituto de Higiene e Medicina Tropical, da Universidade Nova de Lisboa (IHMT-NOVA)

Salomé Pinho, Instituto de Investigação e Inovação em Saúde, da Universidade do Porto (i3S)

Charlotte Cunningham Runddles, Mount Sinai, USA

Fátima Carneiro and Carla Oliveira, Instituto de Investigação e Inovação em Saúde, da Universidade do Porto (i3S) / Instituto de Patologia e Imunologia Molecular da Universidade do Porto (Ipatimup)

Jacques Van Dongen, MD, PhD and Alberto Orfão, MD, PhD and other members of the Euroflow Consortium, Euroflow Consortium

Selected Publications

Markert ML, Marques JG, Neven B, Devlin BH, McCarthy EA, Chinn IK, Albuquerque AS, Silva SL, Pignata C, de Saint Basile G, Victorino RM, Picard C, Debre M, Mahlaoui N, Fischer A, Sousa AE (2011). [First use of thymus transplantation therapy for FOXN1 deficiency \(nude/SCID\): a report of 2 cases](#). **Blood** 117(2):688-696. Original article.

Relevance of the publication: First report of thymus transplantation in FOXN1 deficiency.

Azevedo RI, Soares MV, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE (2009). [IL-7 sustains CD31 expression in human naive CD4+ T cells and preferentially expands the CD31+ subset in a PI3K-dependent manner](#). **Blood** 113(13):2999-3007. Original article.

Relevance of the publication: Identification of a role for IL-7 in the maintenance of the CD31 compartment of naïve CD4 T cells considered critical for the preservation of immune competence with ageing.

Pereira-Santos MC, Baptista AP, Melo A, Alves RR, Soares RS, Pedro E, Pereira-Barbosa M, Victorino RMM, Sousa AE (2008). [Expansion of circulating FoxP3+CD25bright CD4+ T cells during specific venom immunotherapy](#). **Clinical & Experimental Allergy** 38(2):291-297. Original article.
Relevance of the publication: First report of induction of regulatory CD4 T cells by hymenoptera venom.

Sousa AE, Carneiro J, Meier-Schellersheim M, Grossman Z, Victorino RM (2002). [CD4 T cell depletion is linked directly to immune activation in the pathogenesis of HIV-1 and HIV-2 but only indirectly to the viral load](#). **Journal of Immunology** 169(6):3400-3406. Original article.
Relevance of the publication: Reference paper on the role of persistent immune activation in HIV/AIDS immunopathogenesis.

Grossman Z, Meier-Schellersheim M, Sousa AE, Victorino RM, Paul WE (2002). [CD4+ T-cell depletion in HIV infection: are we closer to understanding the cause?](#) **Nature Medicine** 8(4):319-323. Editorial Material.
Relevance of the publication: Reference perspective paper on HIV/AIDS immunopathogenesis.

2021 Publications in Peer-Reviewed Journals

Gomes AMC, Farias GB, Dias-Silva M, Laia J, Trombetta AC, Godinho-Santos A, Rosmaninho P, Santos DF, Conceição CM, Costa-Reis R, Adão-Serrano M, Mota C, Almeida ARM, Sousa AE, Fernandes SM (2021). [SARS-CoV2 pneumonia recovery is linked to expansion of innate lymphoid cells type 2 expressing CCR10](#). **Eur J Immunol**. Dec;51(12):3194-3201. Original article.

Almeida ARM, Neto JL, Cachucho A, Euzébio, Meng X, Kim R, Fernandes MB, Raposo B, Oliveira ML, Ribeiro D, Fragoso R, Zenatti PP, Soares T, Matos MR, Corrêa JR, Duque M, Roberts KG, Gu Z, Qu C, Pereira C, Pyne S, Pyne NJ, Barreto VM, Bernard-Pierrot I, Clappier E, Mullighan CG, Grosso AR, Yunes JA, Barata JT (2021). [Interleukin-7 receptor \$\alpha\$ mutational activation can initiate precursor B-cell acute lymphoblastic leukemia](#). **Nature communications** Dec 14. 12 (1), 1-16. Original article.

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Invited Lectures and Seminars

Ana E Sousa. HIV - do 1º caso à actualidade. XII BelnMed - Beira Interior Medical Meeting, February 6, 2021.

Susana L. Silva. *Unmet needs* na terapêutica com imunoglobulinas. Webinar IDPs e Terapêutica com imunoglobulinas. Sociedade Portuguesa de Alergologia e Imunologia Clínica. Lisbon, Portugal, March 30, 2021.

Susana L Silva. Papel da genética na orientação clínica dos defeitos de produção de anticorpos. Novos paradigmas em Imunodeficiências Primárias. 20ª Reunião da Primavera da SPAIC. Online. April 17, 2021.

Ana E Sousa. Recovery from COVID-19, International Immunology Day: Advances on the Immune Responses during COVID-19, Online, April 29, 2021.

Ana E Sousa. Regulatory T cell development in the human thymus, T-Cell Connect Europe Online Immunology Lecture Series, June 1, 2021.

José Gonçalo Marques. Testes para SARS-CoV-2 nos serviços de saúde e nas escolas: quais e quando. 17as Jornadas de Infecçiology Pediátrica. Online. June 5, 2021.

MC Pereira Santos, Moderador Workshop “Diagnóstico Molecular e Medicina de Precisão (GIAIT), XLII Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC, virtual meeting, October 7-9, 2021.

Communications

Silva MI, Coutinho C, Lourenço T, Pineda F, Pedro E, Pereira-Santos MC. Molecular sensitization profile in patients allergic to bee venom and possible association with reaction during Ultra-Rush induction immunotherapy protocol. 19th Immunology Winter School on basic Immunology research in Allergy and Clinical Immunology. Digital event, January 22-24, 2021. POSTER; INTERNACIONAL E-CONFERENCE.

Trombetta AC, Farias GB, Gomes AMC, Godinho-Santos A, Rosmaninho P, Conceição CM, Henriques JLL, Santos DF, et al. Timely acquisition of myeloid cell immune-regulatory phenotype and COVID-19 outcome. CROI (Conference on Retroviruses and Opportunistic Infections), Online, March 6-10, 2021. ORAL COMMUNICATION; INTERNATIONAL E-CONFERENCE.

Almeida ARM. IL7R Gain-of-Function Mutation Is Sufficient to Initiate B-Cell Acute Lymphoblastic Leukemia in Vivo with Features of PAX5 P80R and Ph-like ALL. ESH 2nd Translational Research Conference on Acute Lymphoblastic Leukaemia. Online, May 7-9, 2021. ORAL PRESENTATION; INTERNACIONAL E-CONFERENCE.

Trombetta AC, Farias GBC, Godinho-Santos A, Gomes AMC, Rosmaninho P, Conceição CM, Henriques JLL, Santos DF, Neiva MIT, Almeida A, Sousa AE, Fernandes SM. SARS-CoV-2 plasma viral load polarizes the systemic myeloid cell compartment towards an immunosuppressive/regulatory phenotype in severe COVID-19 patients. Virtual IMMUNOLOGY 2021, The American Association of Immunologists (AAI), Online, May 10-15, 2021. ORAL COMMUNICATION; INTERNATIONAL E-CONFERENCE.

Rosmaninho P, Raposo A. The signature of human regulatory CD4 thymocytes and its modulation by the chromatin landscape. XLVI Annual Meeting of the Portuguese Society for Immunology, Online, Portugal, May 20-21, 2021. Abstract selected for ORAL COMMUNICATION, delivered by Pedro Rosmaninho. NATIONAL E-CONFERENCE.

Motta A, Rosmaninho P, Santos DF, Ferreira RD, Silva SP, Ferreira C, Sousa AE, Silva SL. Contribution of Helicobacter pylori infection to the clinical and immunological profile of Common Variable Immunodeficiency (CVID) and relationship with the underlying genetic

landscape. XLVI Annual Meeting of the Portuguese Society for Immunology, Online, Portugal, May 20-21, 2021. POSTER PRESENTATION; NATIONAL E-CONFERENCE.

Trombetta AC, Farias GB, Gomes AM, Godinho-Santos A, Rosmaninho P, Conceição CM, Laia J, Santos DF, Neiva I, Almeida A, Mota C, Veldhoen M, Sousa AE, Fernandes SM. Severe COVID-19 recovery is associated with timely acquisition of a myeloid cell immune-regulatory phenotype. XLVI Annual Meeting of the Portuguese Society for Immunology, Online, Portugal, May 20-21, 2021. POSTER; NATIONAL E-CONFERENCE.

Gomes AMC, Farias GB, Dias-Silva M, Laia J, Trombetta AC, Godinho-Santos, Rosmaninho P, Santos DF, Conceição CM, Reis R, Uva MS, Mota C, Almeida ARM, Sousa AE, Fernandes SM. SARS-CoV-2 pneumonia recovery is linked to an expansion of type 2 innate lymphoid cells expressing CCR10. XLVI Annual Meeting of the Portuguese Society for Immunology, Online, Portugal, May 20-21, 2021. POSTER; NATIONAL E-CONFERENCE.

Farias GB, Gomes AM, Godinho-Santos A, Rosmaninho P, Santos DF, Conceição CM, Laia J, Almeida A, Mota C, Sousa AE, Fernandes SM, Badura R, Trombetta AC. Distinct profile of the systemic myeloid cell response in HIV-1 and SARS-CoV-2 acute infections. XLVI Annual Meeting of the Portuguese Society for Immunology, Online, Portugal, May 20-21, 2021. POSTER; NATIONAL E-CONFERENCE.

Thi TGL, Werkstetter K, Cabral J, Kotilea K, Bontems P, Barrio J, Pascual MLC, Homan M, Kori M, Urruzuno P, Kalach N, Misak Z, Lima R, Tavares M, Miele E, Urbonas V, Chiaro A, Papadopoulou A, Sykora J, Krahl A, Matusiewics K, Ugras MK, Rea F, Roma E, Casswall T, Klemenak M, Cseh A, Laffolie J, Rogalidou M, Lopes AI, Banoub H, Koletzko S on behalf of the Helicobacter pylori Working Group of ESPGHAN. Treatments after failed therapy in H. Pylori infected children in Europe: results of the europedhp registry. Annual Espghan Meeting. Online. June 4, 2021. POSTER; INTERNATIONAL E-CONFERENCE.

Bettencourt C, Cunha F, Gonçalo-Marques J, Bajanca-Lavado MP. Epidemiology and molecular characterisation of invasive disease in children twenty years after the implementation of Haemophilus influenzae serotype b vaccine in Portuguese immunisation programme. 31st ECCMID, Online, July 9-12, 2021. ORAL COMMUNICATION; INTERNATIONAL E-CONFERENCE.

Romana A, Brito I, Rodrigues AB, Araújo D, Andrade A, Figueiredo C, Grilo RD, Virtuoso MJ, Pedro M, Braz M, Lopes C, Gaspar M, Banganho D, Mesquita A, Condessa L, Costa A, Shchomak Z, Vieira C, Oliveira S, Almeida M, Franco J, Marques JG. Group A Streptococci Invasive Disease in Portuguese Children: A nationwide retrospective study between 2010-2019. 31st ECCMID, Online, July 9-12, 2021. ORAL COMMUNICATION; INTERNATIONAL E-CONFERENCE.

Varandas C, Lopes A, Neto M, Duarte F, Fernandes N, Paulino M, Coutinho C, Mendes A, Cosme J, Caiado J, Costa C, Spínola A, Branco Ferreira M., Lopes Da Silva S, Pereira Santos MC. IL-22 and IL-22 Binding Protein in Atopic Dermatitis. Congress of the European Academy of Allergy and Clinical Immunology. EACCI Hybrid Congress, Madrid, Spain. July 10-12, 2021. POSTER; INTERNACIONAL CONFERENCE.

Silva MI, Brás R, Paulino M, Costa C, Cabral Duarte F, Pedro E, Pereira-Santos MC. Characterization of peach allergy patients and their molecular sensitization profile with ALEX Macroarray method. Congress of the European Academy of Allergy and Clinical Immunology. Hybrid Congress, Madrid, Spain. July, 2021. POSTER; INTERNACIONAL CONFERENCE.

Motta A, Rosmaninho P, Santos DF, Silva SP, Sousa AE, Silva SL. Genetic Evaluation of Complex Primary Immunodeficiency. GenomePT Symposium. eMeeting. July 7, 2021. POSTER PRESENTATION; NATIONAL E-CONFERENCE.

Bernardo M, Graça IS, Silva SL, Costa-Reis P. Juvenile systemic lupus erythematosus presenting with recurrent angioedema controlled with rituximab. 27th European Paediatric Rheumatology e-Congress. September 19-21, 2021. POSTER PRESENTATION; INTERNATIONAL E-CONFERENCE.

Vilardouro AS, Loreto H, Mourato P, Azevedo S, Fernandes A, Costa S, Lopes AI. Emergency endoscopy in children during SARS-CoV-2 pandemic in a tertiary center – a changing pattern? UEG Week Virtual 2021, Online, October 3-5, 2021. POSTER PRESENTATION; INTERNATIONAL E-CONFERENCE.

Cosme J, Spínola-Santos A, Pedro E, Pereira-Santos MC, Lopes A, Caiado J, Paulino M, Tomás E, Farinha S, Matos E, Pinela A, Jacinto H, São-Braz MA, Ribeiro F, Paes MJ, Santos N, Rodrigues-Carvalho S, Duarte-Ferreira R, Todo-Bom A, Regateiro F, Botelho-Alves P, Môte A, Falcão H, Cunha L, Falcão I, Neves E, Plácido JL, Silva D, Vasconcelos MJ, Silva R, Abreu C, Ferreira-Horta A, Martins S, Lozoya-Ibáñez C, Paulos-Viegas L, Morais-Silva P, Nogueira C, Costa-Viana J, Borrego LM, Cruz C, Piedade S, Forstenlechner P, Aumayr M, Pineda F. Perfil de sensibilização molecular para os pólenes de gramíneas e de oliveira em Portugal. XLII Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC. Online. October 7-9, 2021. ORAL COMMUNICATION; NACIONAL E-CONFERENCE.

Varandas C, Lopes A, Neto M, Duarte F, Fernandes N, Paulino M, Coutinho C, Mendes A, Cosme J, Caiado J, Costa C, Spínola A, Branco Ferreira M, Lopes Da Silva S, Pereira Santos MC. IL-22 Binding Protein como marcador sérico de atividade de Dermatite Atópica e de resposta ao Dupilumab. XLII Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC. Online. October 7-9, 2021. ORAL COMMUNICATION; NACIONAL E-CONFERENCE.

Varandas C, Caldas C, Santos AR, Silva SP, Santos DF, Fernandes L, Ferreira C, Marques T, Sousa AE, Silva SL. Da clínica ao gene – do gene à terapêutica. XLII Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC. Online. October 7-9, 2021. POSTER PRESENTATION; NACIONAL E-CONFERENCE.

Bernardo M, Graça IS, Silva SL, Reis PC. Angioedema adquirido como manifestação inaugural de uma doença sistémica. 1.ª Reunião de Casos Clínicos de Pediatria. Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, October 9, 2021. ORAL COMMUNICATION; NATIONAL CONFERENCE.

Carvalho D, Sabino R, Veríssimo C, Simões H, Silva SL, Marques T, Janeiro J, Marques-Lito L, Melo-Cristino J. Subcutaneous phaeohyphomycosis due to *Phaeoacremonium parasiticum* in a

patient with Chronic Granulomatous Disease. 10th Trends in Medical Mycology. Aberdeen, Scotland, UK. October 8-11, 2021. POSTER PRESENTATION; INTERNATIONAL CONFERENCE.

Brás R, Silva MI, Paulino M., Costa C., Duarte FC, Pedro E, Pereira-Santos MC. Síndrome de LTP: Caracterización del perfil de sensibilización molecular utilizando dos métodos de diagnóstico in vitro. 33º Congreso Sociedad Española de Alergología e Inmunología Clínica - SEAIC, Zaragoza, October 20-23, 2021. ORAL COMMUNICATION; INTERNACIONAL E-CONFERENCE.

Motta-Raymundo A, Silva SL, Rosmaninho P, Santos DF, Silva SP; Esteves I, Bandeira M, Sousa AB, Costa-Reis P, Sousa AE. A20 haploinsufficiency and immunodeficiency - diverse phenotype across 3 generations. 25th Annual Meeting of the Portuguese Society of Human Genetics. eMeeting. Portugal, November 18-19, 2021. POSTER PRESENTATION. NATIONAL E-CONFERENCE.

Costa ELM, Loreto H, Lopes AI. Laceração, dissecação e perfuração do esófago no contexto de EoE: Mini-série de casos. XXXIII Reunião Anual da Sociedade Portuguesa de Gastreenterologia Pediátrica, Amarante, Portugal, November 25-26, 2021. POSTER; NATIONAL CONFERENCE.

Costa R, Azevedo S, Lopes AI. *Clostridium Difficile* e DII- Mini série de casos. XXXIII Reunião Anual da Sociedade Portuguesa de Gastreenterologia Pediátrica, Amarante, Portugal, November 25-26, 2021. POSTER; NATIONAL CONFERENCE.

Abrantes F, Virtuoso MJ, Esteves I, Marques JG. Vacinação Covid-19 e Infecção EBV associada a Síndrome Hemofagocítica: Causa ou Coincidência? 1ª Reunião Sociedade Pediátrica de Imunodeficiências Primárias- SPP. Webinar. December 3, 2021. ORAL COMMUNICATION; NATIONAL E-CONFERENCE.

Networks & Research Infrastructures

Ana E Sousa, Afonso Almeida, Susana L Silva, Adriana Raymundo, Diana F. Santos. EUROFLOW – European Consortium for the development and standardization of flow cytometric tests for diagnosis and monitoring of hematological and immunological diseases. AES is member of the Board. <http://euroflow.org/>

Susana L. Silva, Adriana Raymundo, Diana F. Santos, Alexandre Raposo, Ana E Sousa, José G Marques. ERN RITA - An European Reference Network that aims at improving the care of patients with Rare Immunological Disorders. <https://ern-rita.org/>

Susana L Silva. Local vice-representative of ERN-RITA Reference Center – Hospital de Santa Maria – Centro Hospitalar Universitário Lisboa Norte. <https://ern-rita.org/>

Ana E Sousa, Alexandre Raposo. MYE-INFOBANK - Converting molecular profiles of myeloid cells into biomarkers for inflammation and cancer. COST Action CA20117. AES is MC Member from Portugal. <https://www.cost.eu/actions/CA20117/>

Ana E Sousa. Member of the EFIS-Immunology Letters (IL) Study Group titled "T_CELL_CONNECT_EUROPE", European Federation of Immunology Societies (EFIS). <http://www.t-cells.eu/>

Ana E Sousa, Alexandre Raposo, Afonso Almeida. COLAB BIOSCALE - Laboratório CoLABorativo para promoção da translação e descoberta de medicamentos.

Ana E Sousa, Alexandre Raposo, Pedro Rosmaninho, Susana L Silva. GenomePT – National Laboratory for Genome Sequencing and Analysis. POCI-01-0145-FEDER-022184. <https://www.genomept.pt>

Alexandre Raposo, Pedro Rosmaninho, Susana Paço. 1Million Genomes workgroup 6, "Health economics and outcome research".

Ana Isabel Lopes. Member of the *Helicobacter Pylori* ESPGHAN Study Group. <https://www.espghan.org>

Prizes & Honors in 2021

2021 Pfizer Prize on Basic Research. Afonso RM Almeida (1st author): Overexpression of wild type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. (Blood 2021).

Prémio Melhor Comunicação Oral SEAIC 2021. Brás R, Silva MI, Paulino M, Costa C, Duarte FC, Pedro E, Pereira-Santos MC. Síndrome de LTP: Caracterización del perfil de sensibilización molecular utilizando dos métodos de diagnóstico in vitro. Sociedad Espanola de Alergología e Inmunología Clínica – SEAIC, Zaragoza, Spain. October, 2021.

Best Research work on Atopic Dermatitis – Grant. Varandas C, Lopes A, Neto M, Duarte F, Fernandes N, Paulino M, Coutinho C, Mendes A, Cosme J, Caiado J, Costa C, Spínola A, Branco Ferreira M, Lopes Da Silva S, Pereira Santos MC. IL-22 Binding Protein como marcador sérico de atividade de Dermatite Atópica e de resposta ao Dupilumab. XLII Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC. Online. October 7-9, 2021. ORAL COMMUNICATION; NACIONAL E-CONFERENCE.

Best Clinical Case in the Meeting. Varandas C, Caldas C, Santos AR, Silva SP, Santos DF, Fernandes L, Ferreira C, Marques T, Sousa AE, Silva SL. Da clínica ao gene – do gene à terapêutica. XLII Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica – SPAIC. Online. October 7-9, 2021. POSTER PRESENTATION; NACIONAL E-CONFERENCE.

Advanced Teaching

Sousa AE, Pereira-Santos MC, Silva SL, Fernandes SM, Almeida A. Clinical Immunology teaching in the core curriculum for Medical Students, Area: Medicine 2, 5th year. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Sousa AE, Pereira-Santos MC, Silva SL, Almeida A, Fernandes SM, Mota C, Godinho-Santos A. Teaching of the optional discipline of Clinical Immunology of the 4th and 5th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Almeida A, Sousa AE. Organization and Teaching of the area of Infection and Immunity in the Master-course of Biomedical Research. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Sousa AB, Sousa AE. Collaboration in the teaching of Immunology in the core curriculum for Medical Students, 2nd year. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Fernandes SM. Regency and teaching of the Discipline of Intensive Care Medicine of the 4th and 5th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Lopes AI. Coordinator of Pediatrics Disciplines; Regency of Pediatrics – Module VI-II, 5th Year; Regency of Elective Discipline – Pediatrics Procedures. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Marques JG. Teaching of the Discipline of Pediatrics (Module VI II), core curriculum, 5th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Marques JG. Coordination of the Seminar on Vaccination of the Discipline of Pediatrics (Module VI II), core curriculum, 4th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Esteves I. Teaching of the Discipline of Pediatrics (Module VI I), core curriculum, 4th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Badura R. Clinical teaching and Lectures of Infectious Diseases in the core curriculum for Medical Students, Area: Medicine 2, 5th year and 2nd year. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Badura R. Lectures of the optional disciplines Tropical Medicine, and Neglected Diseases 4th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Badura R. Collaboration and Lectures in Post-graduate course in Update of Infectious Diseases Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Fernandes SM. Teaching on the course on Antibiotics of Grupo de Infecção e Sepsis, Porto, Portugal.

Silva SL. ePhyalis – Advanced Course for Allergology and Clinical Immunology Residents. Alterações Laboratoriais em Imunoalergologia. Genética – estudo de IDPs, angioedema, fibrose quística e défice de alfa1 anti-tripsina. Cascais, Portugal, November 20, 2021.

Silva SL. Coordination of Course: 4h Course on Drug Allergy to non-Allergy MDs (Cooperation with Santa Casa da Misericórdia de Lisboa) – Reconhecer e Orientar – Alergia Medicamentosa, digital course. November 1-25, 2021.

Silva SL. Coordination of Course: 4h Course on Primary Immunodeficiencies to non-Allergy MDs (Cooperation with Santa Casa da Misericórdia de Lisboa) – Reconhecer e Orientar – Imunodeficiências Primárias. Lecture: IDP no adulto – para além dos defeitos de anticorpos Digital course. November 25 – December 7, 2021.

José Gonçalo Marques. Infecções por vírus varicela-zoster. 2ª Reunião Infecção VIH em Pediatria. Online. March 25, 2021.

Susana. L Silva. Meet the professor - Inovação e Novos Paradigmas em Imunodeficiências Primárias – Introdução. SPAIC, Virtual Meeting. October 8, 2021.

Susana M. Fernandes. Can we monitor immune function in non-neutropenic patients, 26th Infection and Sepsis Symposium. Porto, Portugal, October 27, 2021.

José Gonçalo Marques. Painel Vacinas da 5ª Conferência Anual da redeSAÚDE - Uma Agenda de Investigação em Saúde para 2030, Novos Desafios em Saúde na Ulisboa. Lisbon, November 30, 2021.

José Gonçalo Marques. Hesitação em Vacinar. 5º Curso Básico de Vacinas. Hospital Pediátrico de Coimbra. Online, December 15, 2021.

José Gonçalo Marques. Perguntas frequentes sobre vacinas. 5º Curso Básico de Vacinas. Hospital Pediátrico de Coimbra. Online, December 15, 2021.

Susana M. Fernandes. Follow-up and evaluation of hospital acquired pneumonia. Tertúlias do Grupo de Infecção e sepsis, Porto, Portugal, May 27, 2021.

MSc Theses

Carolina Marques Martins (16/07/2021), Regulatory T Cells Expressing FOXP3 and Low CD25 in Common Variable Immunodeficiency: Unsupervised Analysis of a Flow Cytometry Study. Tese de mestrado do Mestrado Integrado em Medicina. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Afonso R.M. Almeida.

Zoe Junginger (06/2021). RANK-RANKL in human thymic Regulatory T cells. Master thesis from Goethe Universitat- Frankfurt AM Main-Germany. Supervisor: Afonso R.M. Almeida.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Marques JG. PI no CHULN do ensaio clínico TMC278HTX2002 A Phase 2, Open-label, Single-arm, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability, and Efficacy of Switching to RPV Plus Other ARVs in HIV-1-infected Children (Aged 2 to <12 years) who are Virologically Suppressed.

Lopes AI. PI in the *International Clinical Trial*: Budesonide in Pediatric Eosinophilic Esophagitis. CHULN Investigators: Helena Loreto, Ima Figueiredo and Ana Isabel Lopes (PI).

Policy

Sousa AE. Member of the National Ethics Committee for Clinical Research (CEIC).

Sousa AE. Member of the Executive Committee of the National Ethics Committee for Clinical Research (CEIC).

Sousa AE. Member of the “Comissão de Avaliação de Tecnologias de Saúde (CATS)”. Autoridade Nacional do Medicamento e Produtos de Saúde, I. P. (INFARMED, I.P.).

Sousa AE. Coordinator of the GAPIC - Department for the promotion of scientific research for medical students and MDs. Faculdade de Medicina da Universidade de Lisboa.

Sousa AE. Member of the “Comissão Científica de Biociências da Santa Casa da Misericórdia de Lisboa”.

Sousa AE, Lopes AI. Members of the Scientific Council. Faculdade de Medicina da Universidade de Lisboa.

Lopes AI. Member of the Ethical Commission of Centro Académico de Medicina de Lisboa (CAML).

Lopes AI. Member of EVA – Entidade de Verificação de Admissibilidade de colheita para transplante.

Lopes AI. Member of the Direction of GEDII 2021-2023 – Grupo de Estudo da Doença Inflamatória Intestinal.

Lopes AI. Member of the Conselho Consultivo da ANSIC – Associação Nacional de Síndrome de Intestino Curto.

Fernandes SM. Head of the Clínica Universitária de Medicina Intensiva. Faculdade de Medicina da Universidade de Lisboa.

Fernandes SM. Member of the GAPIC - Department for promotion of scientific research for medical students and MDs. Faculdade de Medicina da Universidade de Lisboa.

Fernandes SM. Member of the direction of Grupo de Infecção e Sepsis. Porto.

Silva SL. Member of Grupo de Trabalho de Reações de Hipersensibilidade Vacinas COVID-19 da Direção-Geral de Saúde.

Silva SL, Marques JG. Members of the Comissão Técnica de Vacinação da Direção-Geral de Saúde.

Marques JG. Colaborator for the elaboration of Norma, 001/21 de 14 de janeiro, Campanha de Vacinação contra a COVID-19, COVID-19 Vaccine MODERNA®

Marques JG. Colaborator for the elaboration of Norma nº 021/2020 de 23/12/2020 atualizada a 14/01/2021 Campanha de Vacinação contra a COVID-19, Vacina COMIRNATY®

Marques JG. Colaborator for the elaboration of Norma 019/2020 de 26/10/2020 atualizada em 11/02/2021: COVID-19 Estratégia Nacional de Testes para SARS-CoV-2

Marques JG. Adjunt-Coordinator of Comissão Técnica de Vacinação contra COVID-19. Despacho da DGS 012/2020 de 04-11, until May, 2021.

Marques JG. Member of the Comissão Nacional de Verificação da Eliminação do Sarampo e da Rubéola.

Marques JG. Member of the Centro Hospital Lisboa Norte Local Coordination Group of the Program for the Prevention and Control of Infections and Resistance to Antimicrobials.

Marques JG. Coordination of the Portuguese Pediatric Haemophilus influenzae Invasive Disease Study Group.

Marques JG. Membro do Grupo Operativo - COVID-19 do Centro Hospitalar Universitário Lisboa Norte.

Science and Society in 2021

Silva SL. Medical Advisor for APDIP – Associação Portuguesa de Doentes com Imunodeficiências Primárias.

Silva SL. Recomendações COVID a doentes com IDP – SPAIC & CHULN.

Mota C, Fernandes SM, Sousa AE. Participation in the Instituto de Medicina Molecular João Lobo Antunes task force for the establishment in the iMM Biobank of a collection of biological samples from COVID-19 patients.

Pereira-Santos MC. Participation in the Instituto de Medicina Molecular João Lobo Antunes task force for the development of serological tests for COVID-19.

Sousa AE. Participation in several public activities related to the SARS-CoV-2 pandemic in the press, secondary schools and in online platforms.

Fernandes SM. Invited guest at RTP1's program "É ou Não É? O Grande Debate – A obesidade em tempo de vírus". June 29, 2021.

<https://www.rtp.pt/play/p8071/e554795/e-ou-nao-e-o-grande-debate>

Raposo A. Interview on national radio Antena 1, to "Os Dias do Futuro", a weekly show about innovation and researchers and their projects. Here he had the opportunity to describe the work on Precision Medicine at the IMM, including the projects he's involved in AESousa Lab, on their relevance in the context of Primary Immunodeficiencies, and the translational synergies developed with the FMUL and clinicians in the Hospital Santa Maria.

<https://www.rtp.pt/play/p383/e548566/os-dias-do-futuro>

Marc Veldhoen Lab

Head of Laboratory: Marc Veldhoen, PhD, Group Leader and Assistant Professor, Faculdade de Medicina Universidade de Lisboa

Team

Cristina da Conceição Varandas Ferreira	PhD	Senior Postdoctoral Researcher
Gonçalo André Barata Malpica	Master Degree	PhD Student (Started May)
Himadri Mukhopadhyay	PhD	Postdoctoral Researcher (Started October)
Íris da Mota Lima Correia Ramos	University Degree	MSc Student (Started September)
Jean-Christophe Lone	Master Degree	PhD Student (Started September)
Joana Alexandra Lima Gonçalves	University Degree	MSc Student (Left February)
Júlia Fanczal	PhD	Lab Technician (Left December)
Leandro Joel Barros Fernandes	Master Degree	PhD Student
Patrícia Isabel Figueiredo Campos	Master Degree	PhD Student
Silvia Ariotti	PhD	Senior Postdoctoral Researcher
Sofia Carreira Pereira Ribeiro	Master Degree	Lab Manager

Lab Interests

We are interested in how T cells are activated and differentiate, and how tissue resident T-cells are generated, maintained and activated at the epithelial barrier, especially in the small intestine. We aim to understand the cellular and molecular cues, which result in epithelial T-cell generation and activation. Furthermore, we assess how the biology of these cells effect tissue homeostasis, immune protection and pathology.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Immunity, Infection and Immunotherapy

Major Scientific Achievements in 2021

2021 saw the completion of a 4-year project on the metabolism of intraepithelial T cells. These cells are much differently wired with respect to their metabolic pathways. We found that this is a way to control their activity. Manuscript will be submitted in February 2022. Our La Caixa work has progressed very well, with a next manuscript to be completed in the first half of 2022.

The year was dominated with completion and work on the COVID-19 effort; with over 10 manuscripts delivered, including the results from two national surveys; a collective effort with many IMM scientists.

Ongoing Projects in 2021

2021/2024: Um novo interveniente na ativação de células T - Role of a Novel Player in T cell Activation. Coordinator: Marc Veldhoen. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/2295/2020. Amount: 249 995,00€. Total Amount: 249 995,00€.

2019/2022: Enhancing Tissue Resident Immunity. Coordinator: Marc Veldhoen. Funding Agency: “la Caixa” Foundation. Reference: HR18-00104, “ETERNITY” - “ENHANCING TISSUE RESIDENT. Amount: 497 158,00€. Total Amount: 497 158,00€.

2018/2021: Regulação da rede de resposta imunológica epitelial. Coordinator: Marc Veldhoen. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 028003/2017. Amount: 164 988,93€. Total Amount: 164 988,93€.

2015/2021: EXEuropean Commission LLe to INNOV: Leverage research EXEuropean Commission LLe to INNOV and INNOVation potential of Instituto de Medicina Molecular (iMM) through translational biomedical research in Immunity and Infection. Coordinator: Marc Veldhoen. Funding Agency: European Commission. Reference: ERA Chair 667824. Amount: 2 499 465,00€. Total Amount: 2 499 465,00€.

Scientific Impact

Academic Collaborations

Yogesh Kulathu, Dundee University

Patrick Varga-Weisz, Essex University and São Paulo University

Selected Publications

Ferreira C, Barros L, Baptista M, Blankenhaus B, Barros A, Figueiredo-Campos P, Konjar S, Laine A, Kamenjarin N, Stojanovic A, Cerwenka A, Probst HC, Marie JC, Veldhoen M (2020). [Type 1 Treg cells promote the generation of CD8\(+\) tissue-resident memory T cells](#). **Nature Immunology** 21:766-776.

Relevance of the publication: A senior author publication from the lab at iMM. This publication is setting the foundations of more projects and investigated the establishment of tissue resident memory T cells. The preliminary data formed the foundation for the successful La Caixa application. The paper describes how the establishment of Tissue Resident Memory T cells (T_{RM}) is enhanced by regulatory T cells (T_{REG}); a surprising finding since the later are associated with blunting responses. The system setup gave additional insights in the molecular mechanism and may become important to better understand how T_{RM} cells may be generated for vaccination strategies or tumourtherapies.

Konjar S, Frising UC, Ferreira C, Hinterleitner R, Mayassi T, Zhang Q, Blankenhaus B, Haberman N, Loo Y, Guedes J, Baptista M, Innocentin S, Stange J, Strathdee D, Jabri B, Veldhoen M (2018). [Mitochondria maintain controlled activation state of epithelial-resident T lymphocytes](#). **Science Immunology** 3:eaan2543.

Relevance of the publication: A senior author publication from the lab at iMM. The origin of the publication is our interest in the arylhydrocarbon receptor (AhR), the activation of which is required to maintain intestinal T cells. However, we discovered that multiple metabolic pathways are altered in tissue T cells, including the lipid membranes of their mitochondria. These alterations are in part responsible to maintain the semi-activated status of the intestinal T cells. This spurred on more detailed investigations of tissue resident T cells.

Li Y, Innocentin S, Withers DR, Roberts NA, Gallagher AR, Grigorieva EF, Wilhelm C, Veldhoen M (2011). [Exogenous stimuli maintain intraepithelial lymphocytes via aryl hydrocarbon receptor activation](#). *Cell* 147:629-640.

Relevance of the publication: One of the first senior author publications at the start of the setup of my own lab. The paper describes how the arylhydrocarbon receptor (AhR), is highly expressed in tissue resident T cells such as found in the skin and intestine. There it plays a fundamental role to maintain this particular cell population. Of note, we showed that ligands able to stimulate the AhR pathway can be derived from food; the brassica family of vegetables. The paper publication coincided with the ERC consolidator grant application and EMBO YIP election.

Veldhoen M, Hirota K, Westendorf AM, Buer J, Dumoutier L, Renaud JC, Stockinger B (2008). [The aryl hydrocarbon receptor links TH17-cell-mediated autoimmunity to environmental toxins](#). *Nature* 453:106-109.

Relevance of the publication: First author publication showing how a to that point not appreciated factor, the arylhydrocarbon receptor (AhR), links T cell immune response, via Th17 cells, to external and metabolic influences. AhR has an impact on how well Th17 cells differentiate, which in turn effects severity of autoimmunity. This paper stood at the basis of much subsequent work and the labs interest in T cells residing in tissues and their metabolism, which remain very relevant.

Veldhoen M, Hocking RJ, Atkins CJ, Locksley RM, Stockinger B (2006). [TGFbeta in the context of an inflammatory cytokine milieu supports de novo differentiation of IL-17-producing T cells](#). *Immunity* 24:179-189.

Relevance of the publication: First author publication showing the differentiation of a novel helper T cell subset; Th17. This paper stood at the basis of a paradigm shift in immunology, moving away from a fixed dichotomy of helper subsets providing protection to intracellular pathogens and helminths to include a third effector subset against extracellular pathogens, which shows high flexibility and ability to convert into other subsets. In addition, the resulting Th17 subset has been shown to be highly relevant in autoimmune diseases, with subsequent successful clinical applications deriving from the work, especially successful against psoriasis.

2021 Publications in Peer-Reviewed Journals

Abidi, S.H., Imtiaz, K., Kanji, A., Qaiser, S., Khan, E., Iqbal, K., Veldhoen, M., Ghias, K., Simas, J.P., and Hasan, Z. (2021). [A rapid real-time polymerase chain reaction-based live virus microneutralization assay for detection of neutralizing antibodies against SARS-CoV-2 in blood/serum](#). *PLoS One* 16, e0259551.

Barros, L., Ferreira, C., and Veldhoen, M. (2021). [The fellowship of regulatory and tissue-resident memory cells](#). *Mucosal Immunol.*

Canto, E.C.L., Gomes, A., Serrano, M., Pereira, A.H.G., Ribeiro, R., Napoleao, P., Domingues, I., Silva, C., Fanczal, J., Afonso, A., et al. (2021). [Longitudinal SARS-CoV-2 seroprevalence in Portugal and antibody maintenance 12 months after infection](#). *Eur J Immunol.*

Canto, E.C.L., Pereira, A.H.G., Ribeiro, R., Alves, C., Veloso, L., Vicente, V., Alves, D., Domingues, I., Silva, C., Gomes, A., et al. (2021). [Prevalence of SARS-CoV-2 Antibodies after First 6 Months of COVID-19 Pandemic, Portugal](#). *Emerg Infect Dis* 27, 2878-2881.

Clement, C.C., D'Alessandro, A., Thangaswamy, S., Chalmers, S., Furtado, R., Spada, S., Mondanelli, G., Ianni, F., Gehrke, S., Gargaro, M., et al. (2021). [3-hydroxy-L-kynurenamine is an immunomodulatory biogenic amine](#). **Nat Commun** 12, 4447.

Esperança-Martins, M., Lisa Gonçalves, Soares-Pinho, I., Gomes, A., Serrano, M., Blankenhaus, B., Figueiredo-Campos, P., Catarina-Marques, A., Castro-Barbosa, A., Cardoso, A., et al. (2021). [Humoral immune response of SARS-CoV-2 infected cancer patients: influencing factors and its mechanisms](#). **The Oncologist**.

Konjar, S., Pavsic, M., and Veldhoen, M. (2021). [Regulation of Oxygen Homeostasis at the Intestinal Epithelial Barrier Site](#). **Int J Mol Sci** 22.

Stober, C.B., Ellis, L., Goodall, J.C., Veldhoen, M., and Gaston, J.S.H. (2021). [Th17 Expansion Is Partially Inhibited by IL-23, Where Polyfunctional Th17-Derived Cells Are Amplified by Cellular Stress in Psoriatic Arthritis](#). **Clin Exp Rheumatol** 39, 1159-1159.

Trombetta, A.C., Farias, G.B., Gomes, A.M.C., Godinho-Santos, A., Rosmaninho, P., Conceicao, C.M., Laia, J., Santos, D.F., Almeida, A.R.M., Mota, C., et al. (2021). [Severe COVID-19 recovery is associated with timely acquisition of a myeloid cell immune-regulatory phenotype](#). **Frontiers in Immunology** 12.

Veldhoen, M., and Simas, J.P. (2021). [Endemic SARS-CoV-2 will maintain post-pandemic immunity](#). **Nat Rev Immunol** 21, 131-132.

Veldhoen, M., and Zuzarte-Luis, V. (2021). [Academic labs supporting COVID-19 diagnostics](#). **Eur J Immunol** 51, 13-16.

Viana, J., van Dorp, C.H., Nunes, A., Gomes, M.C., van Boven, M., Kretzschmar, M.E., Veldhoen, M., and Rozhnova, G. (2021). [Controlling the pandemic during the SARS-CoV-2 vaccination rollout](#). **Nat Commun** 12, 3674.

Pre-Print Publications

Ana Rita Cruz-Machado, S.C.B., Marc Veldhoen, Matilde Bandeira, Catarina Duarte, Maria Rato, Bruno Fernandes, Salomé Garcia, Filipe Pinheiro, Miguel Bernardes, Nathalie Madeira, Cláudia Miguel, Rita Torres, Ana Bento Silva, Carolina Mazedo, Filipe Cunha Santos, Marlene Sousa, Hugo Parente, Maria José Santos, João Eurico Fonseca, Vasco C Romão, On behalf of the COVID-Reuma.pt study group. (2021). [Risk factors for infection, predictors of severe disease and antibody response to COVID-19 in patients with rheumatic diseases in Portugal—a multicentre, nationwide study](#). **MedRxiv**.

Hasan, M., Moiz, B., Qiaser, S., Ghous, Z., Hussain, A., Masood, K.I., Ali, N., Simas, J.P., Veldhoen, M., Alves, P., et al. (2021). [Increasing IgG antibodies to SARS-CoV-2 in asymptomatic blood donors through the second COVID-19 wave in Karachi associated with exposure and immunity in the population](#). **Research Square**.

Invited Lectures and Seminars

Advances on the immune response during COVID-19 International Immunology day, ZOOM, April 29th.

ECI 2021; Belgrade via ZOOM September 1-4.

Edinburgh University, Edinburgh, UK, December 2.

Communications

American College of Rheumatology (ACR) Convergence November 3-10 2021, Poster.

<https://acrabstracts.org/abstract/antibody-response-after-sars-cov-2-infection-in-patients-with-rheumatic-diseases-a-multicenter-nationwide-study/>

Organization of Conferences

TCCE OIL meetings; Online Immunology seminar series.

Advanced Teaching

Veldhoen M. Imunidade Celular II, Tronco Comum Ila, Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 11, 2021.

Veldhoen M. Imunidade das Mucosas, Tronco Comum Ila Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 15, 2021.

Veldhoen M. T helper cell types and cytokines. Licenciatura Ciências da Nutrição, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 28, 2021.

Veldhoen M. T helper cell types and cytokines. iMM Mestrado em Investigação Biomédica, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 27, 2021.

Veldhoen M. Mucosal immunology (T cells and ILCs). Licenciatura Ciências da Nutrição, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 2, 2021.

Veldhoen M. Microbiota and immunity, Licenciatura Ciências da Nutrição, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 9, 2021.

Veldhoen M. Metabolism and Immunity, Licenciatura Ciências da Nutrição, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 16, 2021.

Veldhoen M. The complexity of Thelper subsets. Master Immunology Course, Pasteur Institute and Paris Universities, Paris, France, December 10, 2021.

PhD Theses

Luis Almeida, 12/11/2021, The Role of Mitochondrial Translation in T cell Function and Autoimmunity, Hannover, Tim Sparwasser, Jochen Hühn and Lothar Jänsch.



Felicity Macdonald, 02/12/2021, Dissecting the role of HB-EGF in the shaping of CD4+ T cell immune responses, Edinburg, Dietmar Zaiss.

Pedro Sousa-Victor Lab

Head of Laboratory: Pedro Sousa-Victor, PhD, Group Leader

Team

Inês Curado Batista Antunes	Master Degree	Lab Manager
Maria Margarida Ferreira Brás	University Degree	MSc Student (Started August)
Neuza Sofia Simões de Sousa	University Degree	MSc Student

Graphical Abstract

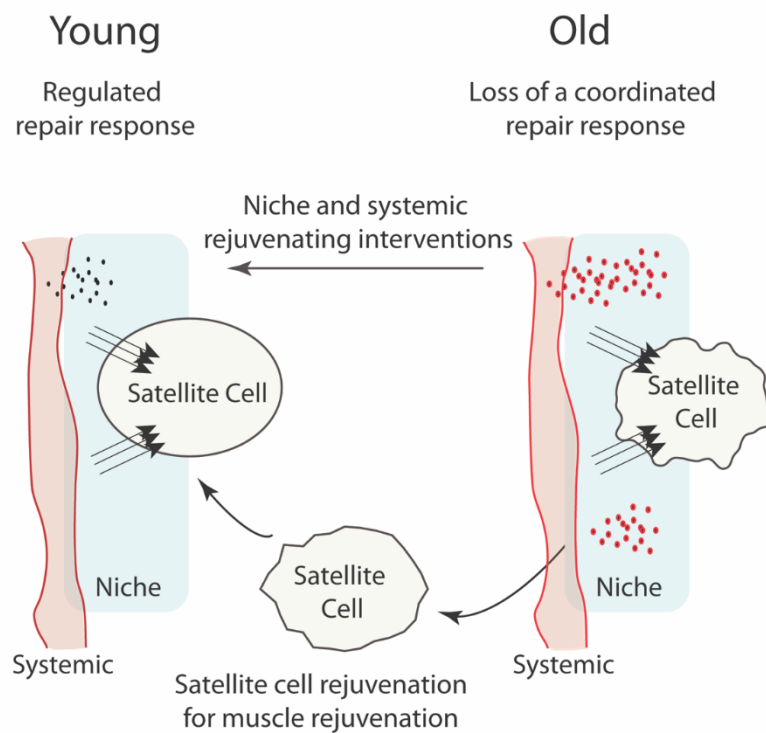


Image caption: Muscle stem cell rejuvenation requires combined interventions, involving rejuvenation of intrinsic properties of the muscle stem cell along with interventions that modulate the systemic and local environment to optimize the tissue repair response. These combinatorial interventions can be envisioned as a path for rejuvenation of skeletal muscle tissue function and regenerative capacity.

Lab Interests

We are interested in regenerative medicine as a solution to the general decline in physiological integrity and vulnerability to disease that accompanies the aging process. Our goal is to understand the mechanisms of stem cell aging and develop stem cell-based interventions to rejuvenate aged organs. Currently, we are using muscle aging as a model system to explore and modulate the repair response of old organisms.

Our approach involves the integration of the knowledge of mechanisms that drive stem cell loss of function with a better understanding of the immune-derived signals during regeneration, with the ultimate goal of devising combinatorial approaches for improving the success stem-cell based therapies applied to sarcopenia. The Sousa-Victor lab is part of the Aging & Tissue Repair joint lab, running two independent, complementary and cooperative research programs focused on the biology of stem cell aging and the age-associated changes in the immune environment.

Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging

Major Scientific Achievements in 2021

In 2021, we completed our project exploring the link between age-related changes in immune signaling and regenerative failure in aging. Through the comparative analysis of aged mice and genetic mouse models of immune dysfunction, we showed how altered macrophage functions and a blunted myeloid recruitment to the site of injury in the old skeletal muscle are associated with defects in stem cell expansion and reduced regenerative capacity. Importantly, we showed that the delivery of an immune modulator (MANF) through intramuscular injections is sufficient to improve regenerative capacity in aged animals. This work also uncovered an unexpected link between immune signaling dysfunction and loss of stem cell lineage fidelity during regeneration. We are now exploring the mechanistic links between these two phenomena with the goal of better understanding how changes in niche environment drive intrinsic defects in aged stem cells.

Ongoing Projects in 2021

2020/2022: EMBO Young Investigator Network. Coordinator: Pedro Sousa-Victor. Funding Agency: European Molecular Biology Organization. Reference: EMBO Young Investigator Network. Amount: 150 000,00€. Total Amount: 150 000,00€.

2020/2021: MANF role in bone marrow hematopoiesis. Coordinator: Pedro Sousa-Victor and Joana Neves. Funding Agency: Genentech, Inc. Reference: MANF ROLE IN BONE MARROW HEMATOPOIESIS. Amount: 42 200,00€. Total Amount: 42 200,00€.

2021/2023: Estratégias de Rejuvenescimento para Terapias com Células Estaminais no Músculo Esquelético Envelhecido - Rejuvenating Strategies for Stem Cell-Based Therapies in the Aged Skeletal Muscle. Coordinator: Pedro Sousa-Victor. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-OUT/8010/2020. Amount: 249 967,50€. Total Amount: 249 967,50€.

2019/2022: New mechanisms driving stem cell aging. Coordinator: Pedro Sousa-Victor. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - JUNIOR LEADER FELLOWSHIPS PROGRAMME. Amount: 297 900,00€. Total Amount: 297 900,00€.

Scientific Impact

Academic Collaborations

Heinrich Jasper, Genentech

Pura Munoz-Canoves, Universitat Pompeu Fabra

Selected Publications

Sousa-Victor P*, Neves J*, Cedron-Craft W, Ventura PB, Liao CY, Riley RR, Soife I, van Bruggen N, Kolumam GA, Villeda SA, Lamba DA, Jasper H (2019). [MANF regulates metabolic and immune homeostasis in ageing and protects against liver damage](#). **Nature Metabolism** 1(2):276–290.

Relevance of the publication: This work provides the first demonstration that MANF (Mesencephalic Astrocyte-derived Neurotrophic Factor) is a systemic regulator of organismal homeostasis that declines during ageing and a proof of principle for the use of MANF as a treatment for age related diseases. We found that MANF levels are systemically down-regulated during ageing in flies, mice and humans and we used genetic manipulations in flies and mice to demonstrate that MANF is necessary to limit inflammation and maintain tissue homeostasis in young organisms. Moreover, using genetic and pharmacologic interventions, we showed that MANF is an effective therapy to reverse several hallmarks of tissue ageing in older organisms and extend lifespan in flies. This work described the potential of immune modulators to prevent or delay age-related tissue dysfunction and described an important model of chronic inflammation that can be used in subsequent studies to isolate the inflammatory component of the ageing process.

Sousa-Victor P, Gutarra S, Garcia-Prat L, Rodriguez-Ubreva J, Ortet L, Ruiz-Bonilla V, Jordi M, Ballestar E, Gonzalez S, Serrano AL, Perdiguero E, Munoz-Canoves P (2014). [Geriatric muscle stem cells switch reversible quiescence into senescence](#). **Nature** 506(7488): 316-321.

Relevance of the publication: This work uncovered a mechanism of intrinsic ageing of muscle stem cells which underlies the irreversible loss of regenerative capacity in geriatric muscles and a rejuvenation strategy based on the genetic silencing of p16INK4 locus. We showed that after a certain age, muscle stem cells can no longer be rejuvenated by exposure to youthful extrinsic signals. Instead, these geriatric stem cells lose reversible quiescence by switching to an irreversible pre-senescence state, caused by the epigenetic derepression of the INK4a locus and the expression of p16INK4a. Once the geriatric muscle suffers an injury, muscle stem cells expressing p16INK4a fail to activate and undergo a full conversion to a senescent state. This publication had a significant impact in the field of stem cell ageing, establishing the existence of intrinsic age-related muscle stem cell alterations, which cannot be reversed by environmental interventions, and need to be considered in stem cell rejuvenation interventions.

Sousa-Victor P, Ayyaz A, Hayashi R, Qi Y, Madden DT, Lunyak VV, Jasper H (2017). [Piwi Is Required to Limit Exhaustion of Aging Somatic Stem Cells](#). **Cell Reports** 20(11):2527-2537.

Relevance of the publication: This work identified a protective mechanism involved in heterochromatin stability maintenance in stem cells under regenerative pressure, demonstrating the importance of retrotransposon control in somatic adult stem cell function. We showed that, in the *Drosophila* intestine, stem cells exposed to inflammatory acute proliferative signals induce the Argonaute family Piwi as a protective mechanism to ensure heterochromatin maintenance, suppress retrotransposon activation, and prevent DNA damage. Re-establishing this protective response in aged stem cells improved epithelial homeostasis, highlighting the importance of the identification of nodal points where extrinsic and intrinsic age-related changes converge to drive the loss of stem cell function.

Neves J*, Sousa-Victor P*, Jasper H (2017). [Rejuvenating Strategies for Stem Cell-Based Therapies in Aging](#). *Cell Stem Cell* 20(2):161-175.

Relevance of the publication: In this review we discuss the major roadblocks imposed by aging to regenerative medicine. We highlight studies that have identified a growing number of promising rejuvenating interventions and propose a strategy to improve stem cell-based therapies through the simultaneous targeting of stem cell intrinsic limitations and niche dysregulations.

Sousa-Victor P*, García-Prat L*, Muñoz-Cánoves P* (2021). [Control of satellite cell function in muscle regeneration and its disruption in ageing](#). *Nature Reviews Molecular Cell Biology*, 1-23.

Relevance of the publication: In this review, we discuss mechanisms underlying muscle stem cell function and its disruption with aging. We specifically highlight the cell-intrinsic control of quiescence versus activation, the importance of muscle stem cell–niche communication, and the dysregulation of these mechanisms during ageing, together with potential rejuvenation therapies.

2021 Publications in Peer-Reviewed Journal

Sousa-Victor P*, García-Prat L*, Muñoz-Cánoves P* (2021). [Control of satellite cell function in muscle regeneration and its disruption in ageing](#). *Nature Reviews Molecular Cell Biology*, 1-23.

Advanced Teaching

Pedro Sousa-Victor (Lecture). Rejuvenating Strategies for stem cell-based therapies in aging. Stem Cell Technologies PhD Advanced Course, virtual, November 8, 2021.

Pedro Sousa-Victor (Lecture). Ageing and Tissue Repair. Lisbon BioMed PhD Program seminar series “Towards a Creative and Critical Mind”, University of Lisbon, Lisbon, Portugal, April 29, 2021.

Valorization of Knowledge / Social and Economic Impact

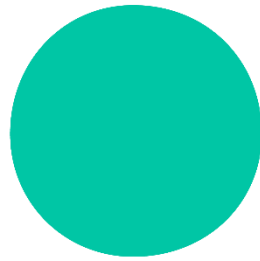
Partnerships with Industry in 2021

Characterize the role of MANF in bone-marrow hematopoiesis, Genentech, Sponsored Research/Collaborative Research.

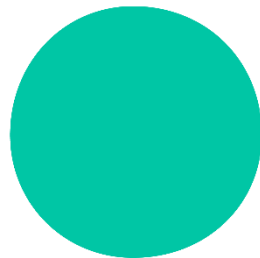
Science and Society in 2021

Pedro Sousa-Victor was interviewed for Radio Observador on the program “Mentes Brilliantes” about the ongoing project supported by the LaCaixa Junior Leader Fellowship. April 13th 2021. Target Audience: General Public.

Pedro Sousa-Victor was interviewed for the Portuguese Newspaper “Publico” about career path and direction of aging research. January 18th 2021. Target Audience: General Public.



Technical Facilities



Analytical and Structural Biochemistry Unit

Director: Francisco J. Enguita, PhD, Assistant Professor – Senior Scientist

Team

André Filipe Gonçalves Gabriel	Master Degree	PhD Student
Marina Célia Nunes Ferreira da Costa Henriques da Silva	PhD	Senior Postdoctoral Researcher

Graphical Abstract

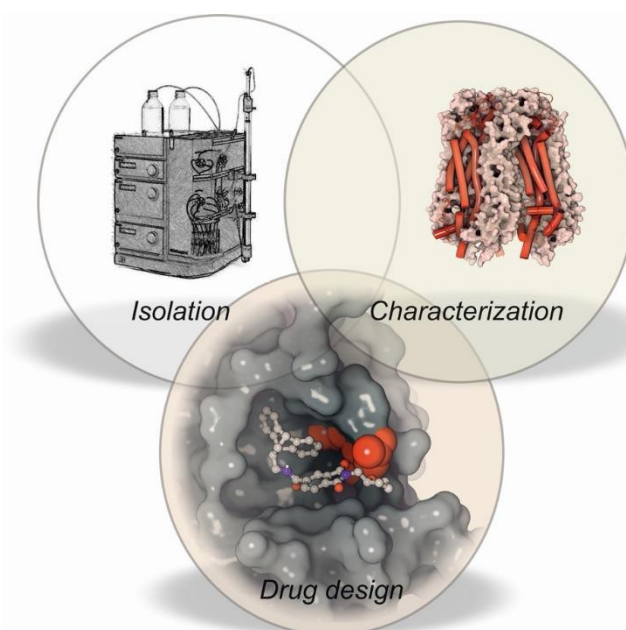


Image caption: Portfolio of techniques available at the ASB facility for the isolation and functional characterization of biomolecules.

Description of the Facility

The Analytical and Structural Biochemistry (ASB) unit is devoted to the production, analysis and functional characterization of biological macromolecules including recombinant proteins, antibodies and nucleic acids. We also offer our expertise in bioinformatics and structural biology to the iMM community for the study of structure-function relationships in biological macromolecules and in-silico drug design by computer-aided methods.

Major Achievements in 2021

The Analytical and Structural Biochemistry (ASB) unit has continued its implementation in the scientific community of the iMM and Lisbon Medical School, expanding its portfolio of chromatographic techniques and the network of internal collaborations.

Scientific Impact

Academic Collaborations

Ana Lúcia Leitão, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa.

Claus Azzalin, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa.

Nuno Santos, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa.

Nuno Santos, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa.

Maria José Diógenes, Instituto de Neurociências, Faculdade de Medicina, Universidade de Lisboa.

Maria Manuel Mota, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa.

2021 Publications in Peer-Reviewed Journals

Costa M.C., Calderon-Dominguez M., Mangas A., Campuzano O., Sarquella-Brugada G., Ramos M., Quezada-Feijoo M., Pinilla J.M.G., Robles-Mezcua A., Del Aguila Pacheco-Cruz G., Belmonte T., Enguita F.J., Toro R. [Circulating circRNA as biomarkers for dilated cardiomyopathy etiology](#). **J Mol Med (Berl)**, 2021, 99(12):1711-1725.

Leitão A.L., Enguita F.J. [Systematic structure-based search for ochratoxin-degrading enzymes in proteomes of filamentous fungi](#). **Biomolecules**, 2021, 11(7): 1040.

Leitão A.L., Enguita F.J. [Structural insights into carboxylic polyester-degrading enzymes and their functional depolymerizing neighbors](#). **Int J Mol Sci.**, 2021, 22, 2332.

McDonald J.T., Enguita F.J., Taylor D., Griffin R.J., Priebe W., Emmett M.R., Sajadi M.M., Harris A.D., Clement J., Dybas J.M., Aykin-Burns N., Guarnieri J.W., Singh L.N., Grabham P., Baylin S.B., Yousey A., Pearson A.N., Corry P.M., Saravia-Butler A., Aunins T.R., Sharma S., Nagpal P., Meydan C., Foux J., Mozsary C., Cerqueira B., Zaksas V., Singh U., Wurtele E.S., Costes S.V., Davanzo G.G., Galeano D., Paccanaro A., Meinig S.L., Hagan R.S., Bowman N.M.; UNC COVID-19 Pathobiology Consortium, Wolfgang M.C., Altinok S., Sapoval N., Treangen T.J., Moraes-Vieira P.M., Vanderburg C., Wallace D.C., Schisler J.C., Mason C.E., Chatterjee A., Meller R., Beheshti A. [Role of miR-2392 in driving SARS-CoV-2 infection](#). **Cell Rep.**, 2021, 37(3):109839.

Miller W.B. Jr., Enguita F.J., Leitão A.L. [Non-random genome editing and natural cellular engineering in cognition-based evolution](#). **Cells**, 2021, 10(5): 1125.

Invited Lectures and Seminars

Francisco J. Enguita. A primer into molecular art. Institute of Chemistry, Polish National Academy of Sciences, Poznan, Poland, December 13th, 2021.

Francisco J. Enguita. Host genome dynamics during SARS-CoV-2 infection: the role of long non-coding RNAs. Congresso Ibérico de Biofísica, Coimbra, Portugal, June 15th, 2021.

Francisco J. Enguita. Studying the role of lncRNAs during SARS-CoV-2 infection. COV-IRT 3rd symposium, Boston, USA, March 31st, 2021.

Biobank Unit

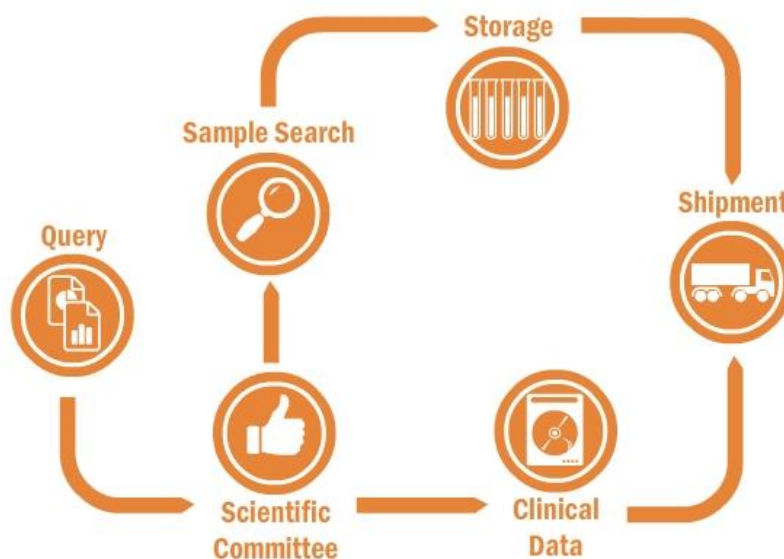
Director: Cláudia Faria, MD, PhD, Neurosurgeon at Hospital Santa Maria, Professor at Faculdade de Medicina da Universidade de Lisboa

Director: Sérgio Dias, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Professor at Faculdade de Medicina da Universidade de Lisboa

Team

Andreia Alexandra Farinha Lopes	Master Degree	Lab Technician
Ângela Maria Cerqueira Coelho Afonso	Master Degree	Biobank Unit Area Manager
Inês Duarte Dias Almeida Lourenço	High School Diploma	MSc Student
Ionela Alexandra Filofteia Toader	Master Degree	Lab Technician

Graphical Abstract



Description of the facility

Biobanks are strategic tools for the development of medicine and translational research. The Biobanco-iMM CAML includes biological samples (from surgery, biopsies, blood samples, ...) which are voluntarily donated with permission for preservation and future use in biomedical research.

The Biobanco-iMM CAML allows the study of the pathogenesis of multiple diseases with enormous impact on human health (such as neurological diseases, rheumatic disorders and cancer), improving the identification of new prognostic and diagnostic tests and new therapeutic targets. Our vision is that the Biobanco-iMM CAML will be a contribution for promoting health and well-being of society, but will also have the potential to act as a catalyst for new opportunities for cooperation between national and international researchers, institutions and pharmaceutical industry.

Major Achievements in 2021

We consider that innovation in biomedical research will allow not only to improve the knowledge of the disease mechanisms but also to develop novel diagnostic and prognostic tests and new treatments. The Biobanco-IMM will have a significant impact on the scientific activity of Centro Académico de Medicina de Lisboa (CAML), which will be reflected in an increased number of patents and partnerships aiming at the development of novel medical concepts. In 2021 we were able to process 23353 new samples which represents an increase of 2290 new donors. We start a new collection in sarcomas each will create a unique opportunity for a deeper characterization and a sharper picture of sarcoma metabolic and microenvironment landscape may pave the way for diagnostic and staging refinement and identification of new potential therapeutic targets, resulting in benefits for patients. In 2021, we also increase the samples turnover in 35%.

Ongoing Research Projects

2021/2023: INITIATIVE NEUROPO – NOVARTIS. Coordinator: Ângela Afonso. Funding Agency: Liga Portuguesa contra o Cancro. Reference: LPCC – CFARIA. Amount: 20 060,00€. Total Coordinator: 20 060,00€.

Scientific Impact

2021 Publications in Peer-Reviewed Journals

Canto, E.C.L., Gomes, A., Serrano, M., Pereira, A.H.G., Ribeiro, R., Napoleao, P., Domingues, I., Silva, C., Fanczal, J., Afonso, A., et al. (2021). [Longitudinal SARS-CoV-2 seroprevalence in Portugal and antibody maintenance 12 months after infection](#). *Eur J Immunol*. 10(10):1002. Original article.

Esperança-Martins, M., Lisa Gonçalves, Soares-Pinho, I., Gomes, A., Serrano, M., Blankenhaus, B., Figueiredo-Campos, P., Catarina-Marques, A., Castro-Barbosa, A., Cardoso, A., et al. (2021). [Humoral immune response of SARS-CoV-2 infected cancer patients: influencing factors and its mechanisms](#). *The Oncologist*. 9(9): e1619–e1632. Original article.

Cortes-Figueiredo F, Carvalho FS, Fonseca AC, Paul F, Ferro JM, Schönherr S, Weissensteiner H, Morais VA (2021) [From forensics to clinical research: expanding the variant calling pipeline for the precision ID mtDNA whole genome panel](#). *International Journal of Molecular Sciences* 22(21): 12031.

Leal I, Romão VC, Mano S, Khmelinskii N, Campanilho-Marques R, Ponte C, Macieira C, Oliveira-Ramos F, Vieira-Sousa E, Rosa CM, Rodrigues W, Abegão Pinto L, Marques-Neves C, Fonseca JE. [A non-infectious uveitis multidisciplinary clinic in a tertiary referral center: clinical impact and added value](#). *J Multidiscip Healthc*. 14: 695-704. Original article.

Kumar R, Smith KS, Deng M, Terhune C, Robinson GW, Orr BA, Liu APY, Lin T, Billups CA, Chintagumpala M, Bowers DC, Hassall TE, Hansford JR, Khuong-Quang DA, Crawford JR, Bendel AE, Gururangan S, Schroeder K, Bouffet E, Bartels U, Fisher MJ, Cohn R, Partap S, Kellie SJ, McCowage G, Paulino AC, Rutkowski S, Fleischhack G, Dhall G, Klesse LJ, Leary S, Nazarian J, Kool M, Wesseling P, Ryzhova M, Zheludkova O, Golanov AV, McLendon RE, Packer RJ, Dunham C, Hukin J, Fouladi M, Faria CC, Pimentel J, Walter AW, Jabado N, Cho YJ, Perreault S, Croul SE,

Zapotocky M, Hawkins C, Tabori U, Taylor MD, Pfister SM, Klimo P, Boop FA, Ellison DW, Merchant TE, Onar-Thomas A, Korshunov A, Jones DTW, Gajjar A, Ramaswamy V, Northcott PA (2021). [Clinical Outcomes and Patient-Matched Molecular Composition of Relapsed Medulloblastoma](#). **Journal of Clinical Oncology** 39(7):807-821.

Baroni LV, Sundaresan L, Heled A, Coltin H, Pajtler KW, Lin T, Merchant TE, McLendon R, Faria C, Buntine M, White CL, Pfister SM, Gilbert MR, Armstrong TS, Bouffet E, Kumar S, Taylor MD, Aldape KD, Ellison DW, Gottardo NG, Kool M, Korshunov A, Hansford JR, Ramaswamy V (2021). [Ultra high-risk PFA ependymoma is characterized by loss of chromosome 6q](#). **Neuro-Oncology** 23(8):1360-1370.

Skowron P, Farooq H, Cavalli FMG, Morrissy AS, Ly M, Hendrikse LD, Wang EY, Djambazian H, Zhu H, Mungall KL, Trinh QM, Zheng TN, Dai SZ, Stucklin ASG, Vladioiu MC, Fong V, Holgado BL, Nor C, Wu XC, Abd-Rabbo D, Berube P, Wang YC, Luu B, Suarez RA, Rastan A, Gillmor AH, Lee JY, Zhang XY, Daniels C, Dirks P, Malkin D, Bouffet E, Tabori U, Loukides J, Doz FP, Bourdeaut F, Delattre OO, Masliah-Planchon J, Ayrault O, Kim SK, Meyronet D, Grajkowska WA, Carlotti CG, de Torres C, Mora J, Eberhart CG, Van Meir EG, Kumabe T, French PJ, Kros JM, Jabado N, Lach B, Pollack IF, Hamilton RL, Rao AAN, Giannini C, Olson JM, Bogner L, Klekner A, Zitterbart K, Phillips JJ, Thompson RC, Cooper MK, Rubin JB, Liau LM, Garami M, Hauser P, Li KKW, Ng HK, Poon WS, Gillespie GY, Chan JA, Jung S, McLendon RE, Thompson EM, Zagzag D, Vibhakar R, Ra YS, Garre ML, Schuller U, Shofuda T, Faria CC, Lopez-Aguilar E, Zadeh G, Hui CC, Ramaswamy V, Bailey SD, Jones SJ, Mungall AJ, Moore RA, Calarco JA, Stein LD, Bader GD, Reimand J, Ragoussis J, Weiss WA, Marra MA, Suzuki H, Taylor MD (2021). [The transcriptional landscape of Shh medulloblastoma](#). **Nature Communications** 12, 1749.

Conde J, Pumroy RA, Baker C, Rodrigues T, Guerreiro A, Sousa BB, Marques MC, de Almeida BP, Lee S, Leites EP, Picard D, Samanta A, Vaz SH, Sieglitz F, Langini M, Remke M, Roque R, Weiss T, Weller M, Liu Y, Han S, Corzana F, Morais VA, Faria CC, Carvalho T, Filippakopoulos P, Snijder B, Marbosa-Morais NL, Moiseenkova-Bell VY, Bernardes GJL. (2021) [Allosteric Antagonist Modulation of TRPV2 by Piperlonguemine Impairs Glioblastoma Progression](#). **ACS Central Science**. 7(5):868-881.

Noronha C, Ribeiro AS, Taipa R, Castro DS, Reis J, Faria C, Paredes J (2021). [Cadherin Expression and EMT: A Focus on Gliomas](#). **Biomedicines** 9(10):1328.

Martins EP, Gonçalves CS, Pojo M, Carvalho R, Ribeiro AS, Miranda-Gonçalves V, Taipa R, Pardal F, Pinto AA, Custódia C, Faria CC, Baltazar F, Sousa N, Paredes J, Costa BM (2021). [Cadherin-3 is a novel oncogenic biomarker with prognostic value in glioblastoma](#). **Molecular Oncology**.

Invited Lectures and Seminars

Cláudia Faria. “Patient-derived xenografts of brain metastases – a tool for translational medicine” Session bridging the gap, Programa Doutoral do CAML (LisbonBioMed PhD Program), Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 27, 2021.

Ângela Afonso. Biobancos. Mestrado em Investigação Clínica/virtual, Aveiro, Portugal, May 20, 2021.

Sérgio Dias. "Biobancos: implicações Éticas e protecção de dados", Seminário/Aula no Âmbito do Programa de Formação Avançada (Programa Doutoral) da Universidade do Algarve, Algarve, Portugal, September 2021.

Cláudia Faria. ANEM Research Week "Investigação Clínica: do internato à prática clínica" Online, September 18, 2021.

Sérgio Dias. Biobanco- Seminário no âmbito do Programa Doutoral da Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, October 2021.

Cláudia Faria. Semana de introdução ao curso de Medicina "GAPIC, pela educação científica dos futuros médicos e nutricionistas" Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 6 2021.

Cláudia Faria. PhD Advanced Course – Advances in Neuropharmaceutics, "Using Genomics for drug discovery in brain tumors – from patient samples to preclinical trials", Faculdade de Farmácia da Universidade de Lisboa, Online, December 14, 2021.

Communications

Cláudia Faria. "Identificação de alvos terapêuticos nos tumores cerebrais". A Universidade de Lisboa à Procura de Respostas para o Cancro. Webinar Rede Saúde da Universidade de Lisboa, June 30, 2021. Oral Communication, International Conference.

Cláudia Faria. "Neurocirurgiões-Investigadores: importância para os serviços hospitalares e para a academia". 36º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia (SPNC), Porto, Portugal, September 9 and 11, 2021. Oral Communication, National Conference.

Cláudia Faria. "Patient-derived models of brain metastases: a tool for translational medicine", European Association of Neurological Societies (EANS) Meeting 2021 Neurosurgery in Translation, Virtual, October 5, 2021. Oral Communication, International Conference.

Organization of Conferences

Cláudia Faria. Organizer. EATRIS Summer School in Personalized Medicine, Online, June 14-18, 2021.

Networks & Research Infrastructures

Cláudia Faria. EATRIS. Chair do Board of National Directors of EATRIS.

Sérgio Dias. Biobanco.pt. Coordinator of the National Biobanks Network.

Science and Society in 2021

Cláudia Faria. Promoted the creation of the iMM Science Club in the Pediatrics Department at Hospital de Santa Maria, Lisbon, Portugal.

Bioimaging Unit

Director: José Rino, PhD

Team

Aida Andreia Pereira Pires Lima dos Santos	Master Degree	Technician
Ana Margarida Santos do Nascimento	Master Degree	Senior Technician
António Francisco Pinção Loução Homem Temudo	Master Degree	Senior Technician

Graphical Abstract



Image caption: The Bioimaging Unit provides support in all steps of research done with Light Microscopy at the iMM, from the first ideas in Project Planning to the final Data Publication, with a strong focus in Microscope Training and Support and Image Analysis and Processing.

Description of the Facility

The Bioimaging Unit acts as a support structure to help and nurture research done with Light Microscopy inside the institute. Besides managing high-end resources that include multi-photon, point-scanning confocal, spinning disk confocal, light-sheet and widefield systems, we sit with researchers to teach, train, and create software tools focusing on people and their questions. We provide iMM scientists and visitors with excellence in scientific know-how and expertise in using light microscopy methods for their research, in a personalized approach. We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. We develop image analysis and processing tools for microscopy data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques.

Major Achievements in 2021

In 2021, the Bioimaging Unit services were used by 203 users from 35 research labs, 6 of which from outside the iMM. During the year, we trained 74 users in at least one microscopy system, with a total of 198 training sessions and 1130 assistances. We also developed image analysis and processing tools (ImageJ macros) for 22 researchers. In 2021 we moved 6 microscopy systems from 3 rooms in different floors to a new room on floor 2 of the iMM building. This allowed for 70% of the systems, corresponding to 85.5% of total usage time, to be strategically located in two adjacent rooms, improving user assistance, and increasing the response time.

The Bioimaging Unit is a Zeiss labs@location Partner, integrating a community of expert leading research facilities that provide in-depth knowledge and scientific support to Zeiss customers. We are also a node of the Portuguese Platform of Bioimaging (PPBI), a nationwide consortium of imaging facilities which is a Node of the Euro-Bioimaging ERIC.

Scientific Impact

Academic Collaborations

Ana Varela Coelho, Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Oeiras, Portugal

2021 Publications in Peer-Reviewed Journals

Andrade, C., Oliveira, B., Guatelli, S., Martinez, P., Simões, B., Bispo, C., Ferrario, C., Bonasoro, F., Rino, J., Sugni, M., Gardner, R., Zilhão, R., Coelho, A. V. (2021) [Characterization of Coelomic Fluid Cell Types in the Starfish *Marthasterias glacialis* Using a Flow Cytometry/Imaging Combined Approach](#). **Front. Immunol.** 12:641664

Calero-Cuenca, F. J., Osorio, D. S., Carvalho-Marques, S., Sridhara, S. C., Oliveira, L. M., Jiao, Y., Diaz, J., Janota, C. S., Cadot, B., Gomes, E. R. (2021) [Ctdnep1 and Eps8L2 regulate dorsal actin cables for nuclear positioning during cell migration](#). **Curr Biol** 31(7): 1521-1530.E8.

de Almeida, M. R., Gameiro, E., de Almeida, S. F., Martin, R. M. (2021) [Live-Cell Imaging of Transcriptional Activity at DNA Double-Strand Breaks](#). **J. Vis. Exp.** (175), e62968.

De Niz, M., Brás, D., Ouarné, M., Pedro, M., Nascimento, A. M., Misikova, L. H., Franco, C. A., Figueiredo, L. M. (2021) [Organotypic endothelial adhesion molecules are key for Trypanosoma brucei tropism and virulence](#). **Cell Reports** 36(12):109741

Dias, M., Marques-Morgado, I., Coelho, J. E., Ruivo, P., Lopes, L. V., Remondes, M. (2021) [Transection of the Superior Sagittal Sinus Enables Bilateral Access to the Rodent Midline Brain Structures](#). **eNeuro** 8 (4) ENEURO.0146-21.2021.

Figueiredo, A. M., Barbacena, P., Russo, A., Vaccaro, S., Ramalho, D., Pena, A., Lima, A. P., Ferreira, R. R., Fidalgo, M. A., El-Marjou, F., Carvalho, Y., Vasconcelos, F. F., Lennon-Duménil, A., Vignjevic, D. M., Franco, C. A. (2021) [Endothelial cell invasion is controlled by dactylopodia](#). **PNAS** 118(18) e2023829118.

Paulo, S. L., Ribeiro-Rodrigues, L., Rodrigues, R. S., Mateus, J. M., Fonseca-Gomes, J., Soares, R., Diógenes, M. J., Solá, S., Sebastião, A. M., Ribeiro, F. F., Xapelli, S. (2021) [Sustained Hippocampal Neural Plasticity Questions the Reproducibility of an Amyloid- \$\beta\$ -Induced Alzheimer's Disease Model](#). **JAD** 1 Jan. 2021 : 1183 – 1202.

Paramos-de-Carvalho, D., Martins, I., Cristóvão, A. M., Dias, A. F., Neves-Silva, D., Pereira, T., Chapela, D., Farinho, A., Jacinto, A., Saúde, L. (2021) [Targeting senescent cells improves functional recovery after spinal cord injury](#). **Cell Reports**, 36(1):109334.

Pinheiro, H., Pimentel, M. R., Sequeira, C., Oliveira, L. M., Pezzarossa, A., Roman, W., Gomes, E. R. (2021) [mRNA distribution in skeletal muscle is associated with mRNA size](#). *J Cell Sci* 134 (14): jcs256388.

Roman, W., Pinheiro, H., Pimentel, M. R., Segalés, J., Oliveira, L. M., García-Domínguez, E., Gómez-Cabrera, M. C., Serrano, A. L., Gomes, E. R., Muñoz-Cánoves, P. (2021) [Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction](#). *Science* 374(6565), 355-359

Silva, B., Arora, R., Bione, S. et al. (2021) [TERRA transcription destabilizes telomere integrity to initiate break-induced replication in human ALT cells](#). *Nat Commun* 12, 3760.

Temporão A, Sanches-Vaz M, Luís R, Nunes-Cabaço H, Smith TK, Prudêncio M, et al. (2021) [Excreted Trypanosoma brucei proteins inhibit Plasmodium hepatic infection](#). *PLoS Negl Trop Dis* 15(10): e0009912.

Tjalsma, S. J. D., Hori, M., Sato, Y., Bousard, A., Ohi, A., Raposo, A. C., Roensch, J., Le Saux, A., Nogami, J., Maehara, K., Kujirai, T., Handa, T., Bagés-Arnal, S., Ohkawa, Y., Kurumizaka, H., da Rocha, S. T. Zylicz, J. J., Kimura, H., Heard, E. (2021) [H4K20me1 and H3K27me3 are concurrently loaded onto the inactive X chromosome but dispensable for inducing gene silencing](#). *EMBO Rep* 22: e51989.

Valente, C. A., Meda, F. J., Carvalho, M., Sebastião, A. M. (2021) [A Model of Epileptogenesis in Rhinal Cortex-Hippocampus Organotypic Slice Cultures](#). *J. Vis. Exp.* (169), e61330.

Other Publications with the Facility

Cavaco, M., Fraga, P., Valle, J., Andreu, D., Castanho, M.A.R.B., Neves, V. (2021) [Development of Breast Cancer Spheroids to Evaluate Cytotoxic Response to an Anticancer Peptide](#). *Pharmaceutics* 13, 1863.

Oliveira, F. D., Cavaco, M., Figueira, T. N., Valle, J., Neves, V., Andreu, D., Gaspar, D., Castanho, M. A. R. B. (2021) [The antimetastatic breast cancer activity of the viral protein-derived peptide vCPP2319 as revealed by cellular biomechanics](#). *FEBS J* 16247.

Silva, T. P., Sousa-Luís, R., Fernandes, T. G., Bekman, E. P., Rodrigues, C. A. V., Vaz, S. H., Moreira, L. M., Hashimura, Y., Jung, S., Lee, B., Carmo-Fonseca, M., & Cabral, J. M. S. (2021). [Transcriptome profiling of human pluripotent stem cell-derived cerebellar organoids reveals faster commitment under dynamic conditions](#). *Biotechnology Bioengineering*. 118, 2781– 2803

Invited Lectures and Seminars

José Rino. Bioimaging @COLife. COLife Community Webinar, Lisbon and Oeiras, Portugal, March 4, 2021.

Clara Barreto. “Scientists hate her: discover this simple trick for consistent results with image analysis”. Computational Biology and Bioinformatics Seminar (virtual), Lisbon, Portugal, May 12, 2021.

Organization of Conferences

José Rino. Co-Organizer (Scientific Committee). SPAOM 2021 – Spanish and Portuguese Advanced Optical Microscopy. Virtual conference hosted by IGC, Oeiras, November 23-25, 2021.

Networks & Research Infrastructures

José Rino. PPBI – Portuguese Platform of Bioimaging. Node Manager. POCI-01-0145-FEDER-022122

Advanced Teaching

José Rino. Lecture and Course organization. Confocal Microscopy and Optical Sectioning. Optical microscopy at COLife and Friends: learning the basics. Virtual Workshop organized by COLife microscopy facilities, Lisbon and Oeiras, Portugal, February 2-4, 2021.

José Rino. Lecture. Invisible samples: a challenge for Microscopy. Tissue Clearing Online Workshop, Virtual Workshop organized by CNC, Coimbra, Portugal, May 18, 2021.

Clara Barreto. Trainer and Course organization. Automation and action recording in FIJI. Introduction to image analysis – COLife and FCUL course. Virtual Course organized by COLife and FCUL microscopy facilities, Lisbon and Oeiras, Portugal, September 21-23, 2021.

José Rino. Trainer. Automation and action recording in FIJI. Introduction to image analysis – COLife and FCUL course. Virtual Course organized by COLife microscopy facilities, Lisbon and Oeiras, Portugal, September 21-23, 2021.

José Rino. Coordination of Curricular Unit and Lecturer. Advanced Techniques in Biomedical Research I, Mestrado em Investigação Biomédica, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal, February 9-26, 2021.

Valorization of Knowledge / Social and Economic Impact

Partnerships with Industry in 2021

Zeiss Labs@location. Microscope system presentations, institute excursions within the scope of sales tours or out-side of sales tours, performance of customer courses and customer training, production of de-fined samples and cooperation in the production of application notes (so called "White Papers"). Carl Zeiss Microscopy GmbH. Collaborative Research.

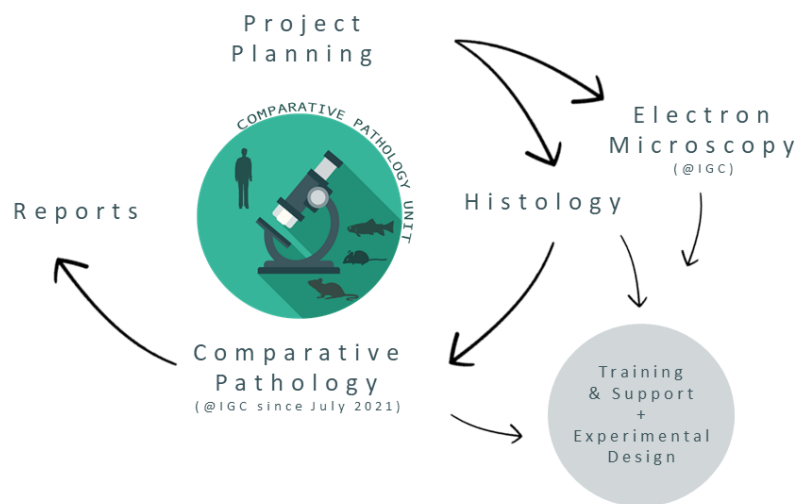
Comparative Pathology Unit

Team

Luísa Figueiredo, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes –
Commissary

Ana Margarida Biscaia Fernandes dos Santos	Master Degree	Senior Technician
Ana Margarida Pereira Cristóvão Pinto	University Degree	Senior Technician
Ana Rita Correia Pires	Master Degree	Senior Technician
Pedro Reis Ruivo	Master Degree	Veterinarian (Left July)

Graphical Abstract



Description of the Facility

With almost 40 years of combined experience, we are experts in transforming fresh and fixed biological samples (from human, mouse, rat, fish, mosquitoes et al.) into thin sections to be viewed under a microscope.

In our unit, we have available all standard techniques, such as paraffin embedding, microtome sectioning, cryoembedding and cryosectioning. We can provide consultation and optimization of more specialized techniques, like Immunohistochemistry, Immunofluorescence, RNAscope and Special Stainings, as help you achieve the best Electron Microscopy results at the IGC.

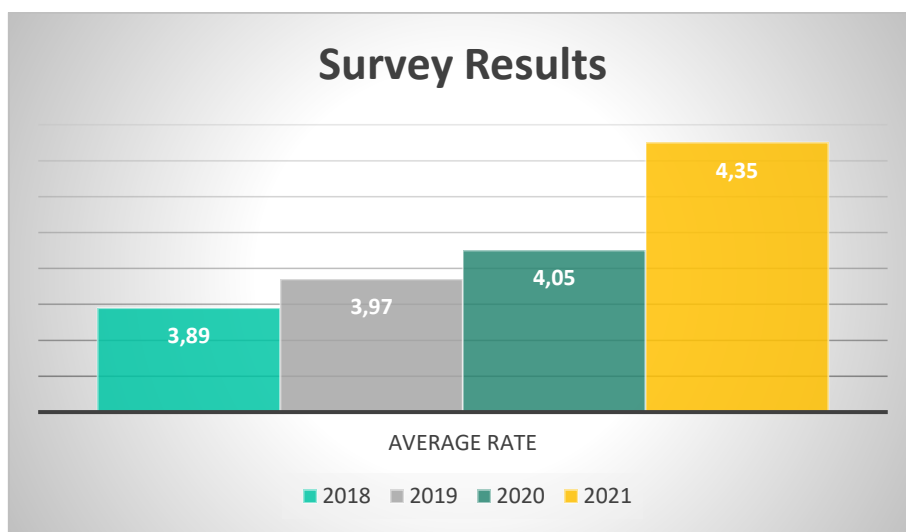
Our mission is to achieve the highest level of quality in supporting researchers and to create meaningful data from gross pathology observations and histopathology. We focus our work on a continuous improvement policy to provide efficient, high quality flexible services with responsive turn-around time to researchers.

In summary: Originality, integrity, sympathy and productivity while maintaining the highest level of technical proficiency and ethical principles is our motto.

Major Achievements in 2021

Quality and performance of our Unit improved during 2021 and all main goals were completed successfully, including the implementation of a cutting-edge technology – RNAscope - as a new provided service in order to keep pace with innovation.

Our methodology and increased automation during this year allowed us to build-up on several important key performance indicators (KPI), like turnaround time and our average rate on annual “Facilities Satisfaction Survey”: 3.89 in 2018, 3.97 in 2019, 4.05 in 2020 and 4.35 on 2021! Our Best Result Ever!



Scientific Impact

Academic Collaborations

Diana Cruz, Escola Superior de Tecnologia da Saúde de Lisboa, Internship, A 4-week work experience that is integrated into the academic program of “Licenciatura de Ciências Biomédicas Laboratoriais”.

2021 Publications in Peer-Reviewed Journals

Almeida, A. R., Neto, J. L., Cachucho, A., Euzébio, M., Meng, X., Kim, R., ... & Barata, J. T. (2021). [Interleukin-7 receptor \$\alpha\$ mutational activation can initiate precursor B-cell acute lymphoblastic leukemia](#). *Nature communications*, 12(1): 1-16.

Cavaco, M., Fraga, P., Valle, J., Andreu, D., Castanho, M. A., & Neves, V. (2021). [Development of Breast Cancer Spheroids to Evaluate Cytotoxic Response to an Anticancer Peptide](#). *Pharmaceutics*, 13(11): 1863.

Conde, J., Pumroy, R. A., Baker, C., Rodrigues, T., Guerreiro, A., Sousa, B. B., ... & Bernardes, G. J. (2021). [Allosteric Antagonist Modulation of TRPV2 by Piperlongumine Impairs Glioblastoma Progression](#). *ACS central science*, 7(5): 868-881.

Cruz, T. B., Carvalho, F. A., Matafome, P. N., Soares, R. A., Santos, N. C., Travasso, R. D., & Oliveira, M. J. (2021). [Mice with Type 2 Diabetes Present Significant Alterations in Their Tissue Biomechanical Properties and Histological Features](#). *Biomedicines*, 10(1): 57.

Dias, M., Marques-Morgado, I., Coelho, J. E., Ruivo, P., Lopes, L. V., & Remondes, M. (2021). [Transection of the superior sagittal sinus enables bilateral access to the rodent midline brain structures](#). *Eneuro*, 8(4).

Dos Santos Rocha, A., Südy, R., Bizzotto, D., Kassai, M., Carvalho, T., Dellacà, R. L., ... & Habre, W. (2021). [Benefit of Physiologically Variable Over Pressure-Controlled Ventilation in a Model of Chronic Obstructive Pulmonary Disease: A Randomized Study](#). *Frontiers in physiology*, 11: 1774.

Konjar, Š.; Pavšič, M.; Veldhoen, M. (2021). [Regulation of Oxygen Homeostasis at the Intestinal Epithelial Barrier Site](#). *International Journal of Molecular Sciences*, 22(17): 9170.

Paramos-de-Carvalho, D., Martins, I., Cristóvão, A. M., Dias, A. F., Neves-Silva, D., Pereira, T., ... & Saúde, L. (2021). [Targeting senescent cells improves functional recovery after spinal cord injury](#). *Cell Reports*, 36(1): 109334.

Machado, H., Bizarra-Rebelo, T., Costa-Sequeira, M., Trindade, S., Carvalho, T., Rijo-Ferreira, F., ... & Figueiredo, L. M. (2021). [Trypanosoma brucei triggers a broad immune response in the adipose tissue](#). *PLoS pathogens*, 17(9): e1009933.

Melo, B. F., Prieto-Lloret, J., Cabral, M. D., Martins, F. O., Martins, I. B., Sacramento, J. F., Ruivo, P., Carvalho, T., ... & Conde, S. V. (2021). [Type 2 diabetes progression differently affects endothelial function and vascular contractility in the aorta and the pulmonary artery](#). *Scientific reports*, 11(1): 1-14.

Silva, T. P., Pereira, C. A., Oliveira, A. R., Raposo, A. C., Arez, M., Cabral, J. M., ... & da Rocha, S. T. (2021). [Generation and characterization of induced pluripotent stem cells from a family carrying the BRCA1 mutation c. 3612delA](#). *Stem Cell Research*, 52: 102242.

Silva, A., Almeida, A., Cachucho, A., Neto, J. L., Demeyer, S., Matos, M., ... & Barata, J. T. (2021). [Overexpression of wild type IL-7R \$\alpha\$ promotes T-cell acute lymphoblastic leukemia/lymphoma](#). *Blood*, 138(12): 1040-1052.

Silva, T. P., Pereira, C. A., Raposo, A. C., Oliveira, A. R., Arez, M., Cabral, J. M., ... & da Rocha, S. T. (2021). [Generation and characterization of induced pluripotent stem cells heterozygous for the Portuguese BRCA2 founder mutation](#). *Stem Cell Research*, 53: 102364.

Temporão, A., Sanches-Vaz, M., Luís, R., Nunes-Cabaço, H., Smith, T. K., Prudêncio, M., & Figueiredo, L. M. (2021). [Excreted Trypanosoma brucei proteins inhibit Plasmodium hepatic infection](#). *PLoS neglected tropical diseases*, 15(10): e0009912.

Wilharm, A., Brigas, H. C., Sandrock, I., Ribeiro, M., Amado, T., Reinhardt, A., Carvalho, T. ... & Ribot, J. C. (2021). [Microbiota-dependent expansion of testicular IL-17-producing V \$\gamma\$ 6+ \$\gamma\delta\$ T cells upon puberty promotes local tissue immune surveillance](#). *Mucosal immunology*, 14(1): 242-252.

Communications

Ana M Biscaia Santos. RNAScope™ @COLife. 1st Seminar of the Histology and Pathology Series, online, June 2nd, 2021/ ORAL COMMUNICATION.

Organization of Conferences

CPU's 1st Users Meeting. Ana M Biscaia Santos. IMM JLA, Lisbon, Portugal, October 29th, 2021.

Networks & Research Infrastructures

CPU Team. COLife's Histology and Pathology Platforms. Members of the network.

Ana M Biscaia Santos. GreenLab Portugal. Member of the Network.

Ana Cristóvão Pinto. IMM Get2gether. Member of the Network.

Flow Cytometry Unit

Director: Mariana Fernandes, MSc

Team

Andreia Sofia Ramalho dos Santos	Master Degree	Technician
Margarida Nóbrega Campos de Freitas Araújo	Master Degree	Trainee (Started October)
Rute Regina Ferreira Gonçalves	Master Degree	Technician

Graphical Abstract



Image caption: Services provided by the Flow Cytometry Unit

Description of the Facility

The Flow Cytometry Unit provides a state-of-the-art flow cytometry service to iMM researchers as well as external groups from other research institutes. We aim at training researchers in the adequate use of the instruments and also on flow cytometry principles, experiment planning, as well as data analysis and interpretation. The facility is equipped with four cell analyzers (one BD LSRFortessa X-20, two BD LSRFortessa - one of which equipped with a High Throughput Sampler - and one BD Accuri C6 Plus), two High Speed Cell Sorters (BD FACSAria III and BD FACSAria Fusion) and one imaging flow cytometer (Amnis ImageStreamX). In addition to providing a cell sorting service, we also ensure quality control and maintenance procedures on all instruments and the implementation of a Quality Management System, according to ISO 9001.

Major Achievements in 2021

In 2021, a total of 188 users from 37 research labs, 10 of which are external groups, used the Flow Cytometry Unit. During the year, we trained 64 new users in at least one flow cytometry analyzer. The Flow Cytometry Unit is one of the founders of FLxFlow – a regional network for Flow Cytometry created in 2016, which aims at bringing together the know-how of four core flow cytometry facilities in the Lisbon area, enabling advanced training and access to cutting-edge applications to the scientific community. In 2021, some equipment upgrades and a new BD FACSAria Fusion have been installed at the facility, some of the special features of this new equipment include: a fully integrated biosafety cabinet for BSL-2 samples (including human samples), 4 lasers, multicolor analysis up to 16 parameters and up to 4-way sorting.

Scientific Impact

2021 Publications in Peer-Reviewed Journals

Andrade C, Oliveira B, Guatelli S, Martinez P, Simões B, Bispo C, Ferrario C, Bonasoro F, Rino J, Sugni M, Gardner R, Zilhão R, Coelho AV (2021). [Characterization of Coelomic Fluid Cell Types in the Starfish *Marthasterias glacialis* Using a Flow Cytometry/Imaging Combined Approach](#). **Frontiers in Immunology** 18 (12):641664.

Brigas HC, Ribeiro M, Coelho JE, Gomes R, Gomez-Murcia V, Carvalho K, Faivre E, Costa-Pereira S, Darrigues J, de Almeida AA, Buée L, Dunot J, Marie H, Pousinha PA, Blum D, Silva-Santos B, Lopes LV, Ribot JC (2021). [IL-17 triggers the onset of cognitive and synaptic deficits in early stages of Alzheimer's disease](#). **Cell Reports** 31;36(9):109574

Farias GB, Badura R, Conceição CM, Gomes AMC, Godinho-Santos A, Laia J, Rosmaninho P, Santos DF, Mota C, Almeida ARM, Fernandes SM, Trombetta AC, Sousa AE (2021). [Acute HIV-1 and SARS-CoV-2 Infections Share Slat+ Monocyte Depletion-Evidence from an Hyperacute HIV-1 Case Report](#). **Viruses** 10;13(9):1805.

Felício MR, Silveira GGOS, Oshiro KGN, Meneguetti BT, Franco OL, Santos NC, Gonçalves S (2021). [Polyalanine peptide variations may have different mechanisms of action against multidrug-resistant bacterial pathogens](#). **Journal of Antimicrobial Chemotherapy** 13;76(5):1174-1186.

Gomes AMC, Farias GB, Dias-Silva M, Laia J, Trombetta AC, Godinho-Santos A, Rosmaninho P, Santos DF, Conceição CM, Costa-Reis R, Adão-Serrano M, Mota C, Almeida ARM, Sousa AE, Fernandes SM (2021). [SARS-CoV2 pneumonia recovery is linked to expansion of innate lymphoid cells type 2 expressing CCR10](#). **European Journal of Immunology** 51(12):3194-3201.

Lopes N, McIntyre C, Martin S, Raverdeau M, Sumaria N, Kohlgruber AC, Fiala GJ, Agudelo LZ, Dyck L, Kane H, Douglas A, Cunningham S, Prendeville H, Loftus R, Carmody C, Pierre P, Kellis M, Brenner M, Argüello RJ, Silva-Santos B, Pennington DJ, Lynch L (2021). [Distinct metabolic programs established in the thymus control effector functions of \$\gamma\delta\$ T cell subsets in tumor microenvironments](#). **Nature Immunology** 22(2):179-192.

Silva B, Arora R, Bione S, Azzalin CM (2021). [TERRA transcription destabilizes telomere integrity to initiate break-induced replication in human ALT cells](#). **Nature Communications** 18;12(1):3760.

Temporão A, Sanches-Vaz M, Luís R, Nunes-Cabaço H, Smith TK, Prudêncio M, Figueiredo LM (2021). [Excreted *Trypanosoma brucei* proteins inhibit Plasmodium hepatic infection](#). **PLoS Neglected Tropical Diseases** 15(10):e0009912.

2021 Pre-Print Publications

Papotto P, Yilmaz B, Pimenta G, Mensurado S, Cunha S, Fiala G, Costa DG, Gonçalves-Sousa N, Chan BHK, Blankenhaus B, Carvalho T, Macpherson AJ, Allen JE, Silva-Santos B (2021). Maternal $\gamma\delta$ T cells shape offspring pulmonary type-2 immunity in a microbiota-dependent manner. bioRxiv. 10.1101/2021.08.13.456265.

Networks & Research Infrastructures

FLxFlow, Mariana Rafael-Fernandes, Lisbon Flow Cytometry Network. Member

Advanced Teaching

Rafael-Fernandes M. Lecturer. Principles of Flow Cytometry; Fluorochromes Spill-over and Compensation; Panel Design and Experimental Planning; Data analysis and Reporting; and Cell Sorting - Basic Notions. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 17-19, 2021.

Rafael-Fernandes M. Workshop Coordinator. Flow Cytometry. Annual International (Bio)Medical Students Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, March 18, 2021.

Gonçalves R. Workshop Instructor. Flow Cytometry. Annual International (Bio)Medical Students Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, March 18, 2021.

Santos A. Workshop Instructor. Flow Cytometry. Annual International (Bio)Medical Students Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, March 18, 2021.

Rafael-Fernandes M. Seminar Organization. FCS Express - Turning Cytometry data into results. Online, April 27, 2021.

Rafael-Fernandes M. Lecturer. Introduction to Flow Cytometry. LisbonBiomed – iMM International PhD Programme, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, April 28, 2021.

Rafael-Fernandes M. Workshop Coordinator. Getting started with FCS Express 7. Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, April 29, 2021.

Rafael-Fernandes M. Course Co-Organizer. FLxFlow Course: Principles and Applications of Flow Cytometry. Online, May 10-17, 2021.

Rafael-Fernandes M. Workshop Coordinator. Panel Design. FLxFlow Course: Principles and Applications of Flow Cytometry, online, May 10, 2021.

Gonçalves R. Workshop Instructor. Panel Design. FLxFlow Course: Principles and Applications of Flow Cytometry, online, May 10, 2021.

Santos A. Workshop Instructor. Panel Design. FLxFlow Course: Principles and Applications of Flow Cytometry, online, May 10, 2021.

Rafael-Fernandes M. Lecturer. Tips and Tricks for Sample Preparation. FLxFlow Course: Principles and Applications of Flow Cytometry, online, May 12, 2021.

Rafael-Fernandes M. Seminar Organization. Cytex Aurora - Pushing the limits of fluorescence in a fluorescent limited world. Online, June 17, 2021.

Rafael-Fernandes M. Workshop organization. Cytex Aurora - Pushing the limits of fluorescence in a fluorescent limited world. Instituto de Medicina Molecular João Lobo Antunes, Lisboa, Portugal, June 21-23, 2021.

Rafael-Fernandes M. Workshop Organization. FLxFlow Workshop: Best Practices in Training and Teaching Facility Staff, Users and Community. Online, July 8, 2021.

Rafael-Fernandes M. Lecturer. Experimental methodologies that use Flow Cytometry: practical sessions. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 1-15, 2021.

Information Systems Unit

Director: Stéphane Martins, High School Diploma

Team

André Filipe Cardoso Gonzalez Fragoso	High School Diploma	Information Systems Senior Technician (Left December)
Pedro André Lozano Luiz de Castro	High School Diploma	Information Systems Senior Technician
Ricardo da Silva Martinho	University Degree	Information Systems Technician

Description of the Facility

The System Information Unit is the facility responsible for the informatics at IMM.

At the SIU we provide data storage and backup, windows server management and AI development, as well as apps development and assistance to the researchers with anything related to computers.

The main goal is to assure that all labs and facilities have the right tools to help them on their work.

We can summarize the USI in those words: Knowledge, Responsibility, Team Work and, of course, Geeks!

Major Achievements in 2021

- The beginning of External Cloud backups;
- New platform for online COVID-19 test booking and check-in;
- Automatic system to send COVID-19 Results and Reports;
- The installation of dedicated fiber channel for backups;
- Updating some of our hardware and software;
- Lobo training is back.

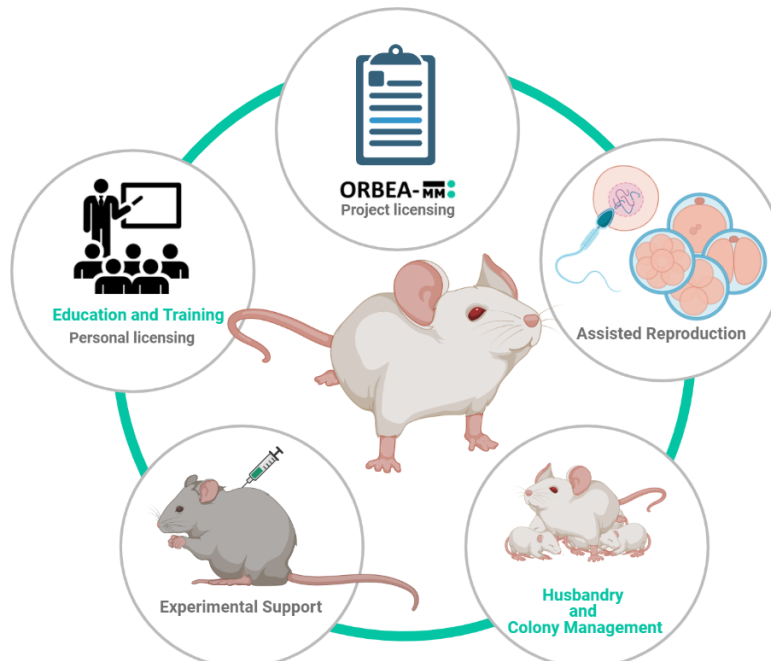
Rodents Unit

Director: João Pedro Louro Machado Simas, DVM, PhD (Left December)

Team

Ana Filipa Peixoto da Cunha	University Degree	Caretaker
Ana Patrícia da Silva Almeida	Master Degree	Caretaker (Started January)
Cecília Gonçalves Simão	University Degree	Caretaker
Daniel Corte Real Gomes da Costa	Master Degree	Veterinarian
Emílio Jurandir do Carmo	High School Diploma	Caretaker
Felícia Maria Augusto Ramos	University Degree	Caretaker
Iolanda Safira Sousa Moreira	University Degree	Rodents Unit Area Manager
Márcia Pereira da Silva	University Degree	Animal Welfare Officer
Mariana Coelho Quintanilha Mantas	University Degree	Caretaker
Mihaela Elena Morari	High School Diploma	Caretaker
Olena Pavlovska Borges Pinho	High School Diploma	Caretaker
Pedro Manuel Nogueira Santos	High School Diploma	Senior Technician
Pedro Manuel Ribeiro de Araújo	Other	Caretaker
Sara Ghirelli	High School Diploma	Caretaker (Started February)

Graphical Abstract



Description of the Facility

With a total capacity for 3392 mouse cages (16960 animals) and 104 rat cages (416 animals), the Rodent Facility supports scientific projects associated with animal experimentation, working towards a state-of-the-art animal-based research while maintaining the highest standards of animal welfare.

The Rodent Facility strictly follows Portuguese and international laws and recommendations governing good practices and animal welfare. The facility is highly committed to provide training and education in Laboratory Animal Science for functions A (carrying out procedures on animals), C (taking care of animals) and D (killing animals).

In addition to normal husbandry routines, the Rodent Unit also provides specialized services such as colony management and assisted reproduction techniques as well as surgical and experimental support.

Major Achievements in 2021

Creation and implementation of a competence assessment system within the scope of the use of animals for scientific purposes, in order to comply with legal requirements and guarantee that researchers performing procedures in animals are proficient for the techniques.

Adaptation of laboratory animal science courses to respond to the COVID-19 pandemic restrictions, replacing most classroom lessons by audiovisual tools without proximity contact and decreasing the student/monitor ratio in hands-on lessons.

Increase of 20% housing space for rats (experimental area) and 8% housing space for mice (production area).

Scientific Impact

2021 Publications in Peer-Reviewed Journals

Afonso R. M. Almeida, João L. Neto, Ana Cachucho, Mayara Euzébio, Xiangyu Meng, Rathana Kim, Marta B. Fernandes, Beatriz Raposo, Mariana L. Oliveira, Daniel Ribeiro, Rita Fragoso, Priscila P. Zenatti, Tiago Soares, Mafalda R. de Matos, Juliana Ronchi Corrêa, Mafalda Duque, Kathryn G. Roberts, Zhaohui Gu, Chunxu Qu, Clara Pereira, Susan Pyne, Nigel J. Pyne, Vasco M. Barreto, Isabelle Bernard-Pierrot, Emannelle Clappier, Charles G. Mullighan, Ana R. Grosso, J. Andrés Yunes & João T. Barata (2021). [Interleukin-7 receptor \$\alpha\$ mutational activation can initiate precursor B-cell acute lymphoblastic leukemia](#). **Nat Communications**, Dec 14;12(1):7268.

Brigas HC, Ribeiro M, Coelho JE, Gomes R, Gomez-Murcia V, Carvalho K, Faivre E, Costa-Pereira S, Darrigues J, de Almeida AA, Buée L, Dunot J, Marie H, Pousinha PA, Blum D, Silva-Santos B, Lopes LV, Ribot JC. [IL-17 triggers the onset of cognitive and synaptic deficits in early stages of Alzheimer's disease](#). **Cell Reports**. 36(9):109574.

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Henao Misikova L, Franco CA, Figueiredo LM (2021). [Organotypic endothelial adhesion molecules are key for Trypanosoma brucei tropism and virulence](#). **Cell Reports** 21;36(12):109741.

Dias M, Ferreira R, Remondes M (2021). [Medial entorhinal cortex excitatory neurons are necessary for accurate timing](#). **Journal of Neuroscience** 41 (48): 9932-9943.

M Dias, I Marques-Morgado, JE Coelho, P Ruivo, LV Lopes, M Remondes (2021). [Transection of the superior sagittal sinus enables bilateral access to the rodent midline brain structures.](#) **eNeuro**.

Machado H, Bizarra-Rebelo T, Costa-Sequeira M, Trindade S, Carvalho T, Rijo-Ferreira F, Rentroia-Pacheco B, Serre K, Figueiredo LM (2021). [Trypanosoma brucei triggers a broad immune response in the adipose tissue.](#) **PLoS Pathogens** 15;17(9):e1009933.

Paulo SL, Miranda-Lourenço C, Belo RF, Rodrigues RS, Fonseca-Gomes J, Tanqueiro SR, Galdes V, Rocha I, Sebastião AM, Xapelli S, Diógenes MJ (2021) [High caloric diet induces memory impairment and disrupted synaptic plasticity in aged rats.](#) **Current Issues in Molecular Biology** 43, 2305–2319.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Pedro DM, Duarte-Samartinho M, Aoreira RI, Ferreira E, Valero J, Solá S, Mira H, Sebastião AM, Xapelli S (2021) [Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: interaction with brain-derived neurotrophic factor.](#) **Stem Cells**

Silva TP, Pereira CA, Raposo AC, Oliveira AR, Arez M, Cabral JMS, Milagre I, Carmo-Fonseca M, Rocha STD (2021). [Generation and characterization of induced pluripotent stem cells heterozygous for the Portuguese BRCA2 founder mutation.](#) **Stem Cell Research** May;53:102364.

Ana Silva, Afonso R. M. Almeida, Ana Cachucho, João L. Neto, Sofie Demeyer, Mafalda de Matos, Thea Hogan, Yunlei Li, Jules Meijerink, Jan Cools, Ana Rita Grosso, Benedict Seddon, João T. Barata (2021). [Overexpression of wild-type IL-7R \$\alpha\$ promotes T-cell acute lymphoblastic leukemia/lymphoma.](#) **Blood** Sep 23;138(12):1040-1052.

Temporão A, Sanches-Vaz M, Luís R, Nunes-Cabaço H, Smith TK, Prudêncio M, Figueiredo LM (2021). [Excreted Trypanosoma brucei proteins inhibit Plasmodium hepatic infection.](#) **PLoS Neglected Tropical Diseases** 15(10): e0009912.

2021 Pre-Print Publications

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Franco CA, Figueiredo LM (2021). Organotypic endothelial adhesion molecules are key for Trypanosoma brucei tropism and virulence. bioRxiv. DOI: 10.1101/2021.02.26.433042

Arez M, Eckersley-Maslin M, Klobučar T, von Gilsa Lopes J, Krueger F, Raposo AC, Gendrel A-V, Bernardes de Jesus B, da Rocha ST. (2020) Sex of donor cell and reprogramming conditions predict the extent and nature of imprinting defects in mouse iPSCs. bioRxiv 2020.11.20.370973; DOI: <https://doi.org/10.1101/2020.11.20.370973>

Silva Pereira S, De Niz M, Serre K, Ouarné M, Franco CA, Figueiredo LM (2021). Immunopathology and parasite sequestration cause severe cerebral trypanosomiasis in animals. Research Square. DOI: 10.21203/rs.3.rs-1050698/v1

Trindade S, De Niz M, Costa-Sequeira Bizarra-Rebello T, Bento F, Dejung M, Ferreira J, Butter F, Bringaud F, Gjini E, Figueiredo LM (2021). Persistence behavior in African trypanosomes during adipose tissue colonization. Research Square. DOI: 0.21203/rs.3.rs-499897/v1

Networks & Research Infrastructures

CONGENTO, Iolanda Moreira Education and Training working group, iMM member for laboratory animal science education and training.

CONGENTO, Iolanda Moreira, Márcia Silva, Daniel Costa, ORBEA working group, iMM's members for Animal Welfare Bodies initiatives.

Advanced Teaching

Iolanda Moreira. Laboratory Animal Science Course for Function A and D (former FELASA Category B) CONGENTO-harmonized program. Course organization. Lisbon, August 9th to September 30th, 2021.

Daniel Costa. Animal Models in Biomedical Research. Course organization. Lisbon, July, 2021.

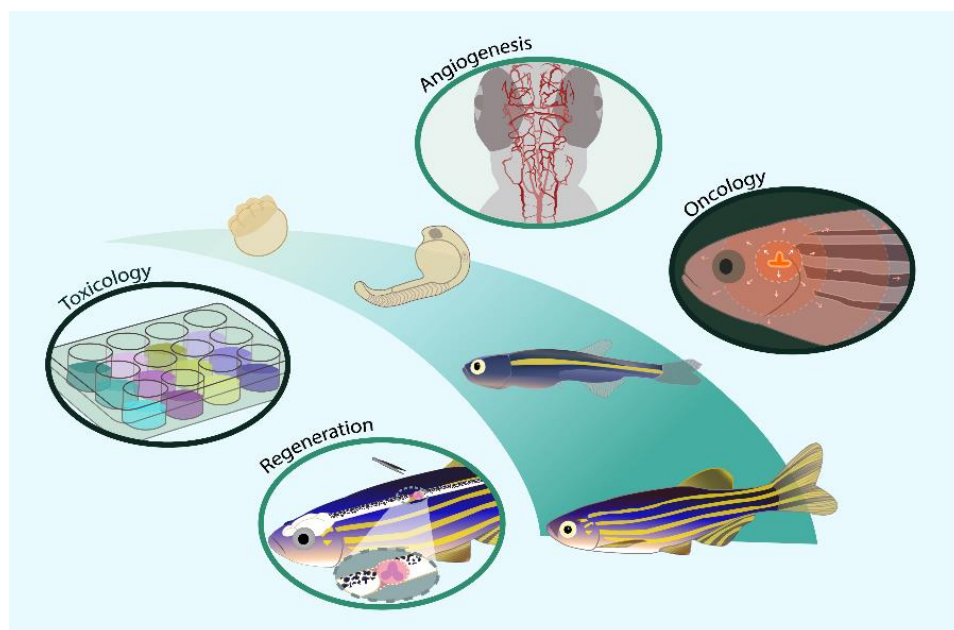
Zebrafish Unit

Director: Leonor Saúde, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Associate Professor at Instituto de Histologia e Biologia do Desenvolvimento, Faculdade de Medicina da Universidade de Lisboa

Team

Aida Gonçalves Lino Barros	High School Diploma	Senior Technician
Lara Margarida Marques Saraiva de Carvalho	Master Degree	Zebrafish Unit Area Manager
Miguel Filipe Portugal do Canto e Costa	University Degree	Technician (Started December)

Graphical Abstract



Description of the Facility

Provide a fully functional facility to be used by the iMM research units.

Provide technical assistance to facilitate the use of zebrafish in a wide range of experimentation sets.

Major Achievements in 2021

The Fish Facility implemented a new live diet of rotifers, that increased the survival and growth rates of zebrafish larvae.

Scientific Impact

2021 Publications in Peer-reviewed Journals

Estronca, L., Francisco, V., Pitrez, P., Honório, I., Carvalho, L., Vazão, H., Bleresch, J., Rai, A., Nissan, X., Simon, U., Grãos, M., Saúde, L., & Ferreira, L. (2021). [Induced pluripotent stem cell-derived vascular networks to screen nano-bio interactions](#). *Nanoscale Horizons*, 6(3), 245–259.

Paramos-de-Carvalho, D., Martins, I., Cristóvão, A. M., Dias, A. F., Neves-Silva, D., Pereira, T., Chapela, D., Farinho, A., Jacinto, A., & Saúde, L. (2021). [Targeting senescent cells improves functional recovery after spinal cord injury](#). *Cell Reports*, 36(1), 109334.

Organization of Conferences

Lara Carvalho. Co-Organizer. Curso do CAML | Curso Laboratory Animal Science Course for Function A, IMM, Lisbon, Portugal, September and November, 2021.

Networks & Research Infrastructures

COLife. Leonor Saúde. Participation in a promotional video.

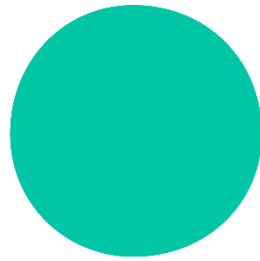
Congento. Lara Carvalho. Collaborator in the Education and Training Group and in the Zebrafish Group.

Advanced Teaching

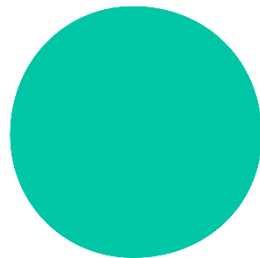
Lara Carvalho, Aida Barros. UC Animal Models in Biomedical Research, Master in Biomedical Research (MIB), IMM, Lisbon, Portugal, July 2021.

Lara Carvalho, Aida Barros. Practical module in zebrafish. CAML Course, Laboratory Animal Science Course for Function A, IMM, Lisbon, Portugal, September and November 2021.

Leonor Saúde, Lara Carvalho. Biomedical Science with Zebrafish, 8th Edition AIMS Masterclasses, IMM/FMUL, Lisbon, Portugal, November 2021.



Administrative Facilities



Communication Office

Director: Inês Domingues, PhD

Team

Ana Cláudia Marques da Silva	University Degree	Communication Officer
Gonçalo Martins Farinha de Figueiredo Ribeiro	Master Degree	Multimedia Officer

Description of the facility

The Communication is iMM's first line of interaction with society providing updated, reliable and relevant information on all of iMM's thematic areas, as well as promoting the very best scientific successes made by its research teams. Its mission is to support the internal and external communication of iMM's activities as well to advice iMM Direction on Public Affairs issues. With the firm belief that science should inform decisions because it impacts everyone's lives, the Communication targets a wide range of audiences (policy makers, public opinion, patients' associations, medical societies, schools, academia, industry, media, arts, amongst others). It serves as spokesman for the institute and it's responsible to manage iMM's image aligned with the institute values and mission. The Communication Office is responsible for the overall image of iMM, our day-to-day activities encompass Media Relations, Science and Society Outreach, Conferences and Events, Institutional Visits, Awareness Campaigns, Social Media, Internal Communication and Public Affairs Training.

Major Achievements in 2021

In 2021, we continued our communication strategy with the media initiated in 2020 as iMM's structured and extended response to the COVID-19 pandemic. The pandemic largely occupied the media space, with iMM researchers making the news in Portugal and internationally, with recorded values of 3659 media clippings (estimated value), of which more than 3130 are clippings related to the pandemic. In 2021, we witnessed a significant increase in television (1377) and radio (250) presences, compared to 2020. There was also an international media interest that sought the direction of iMM as a spokesperson for the positive evolution of the pandemic in Portugal.

We have seen a greater response to the COVID-19 pandemic with the introduction of vaccines at the beginning of 2021. The iMM launched several communication actions such as interactive sessions and informative webinars, with the aim of clearly answering to citizens' questions and concerns. The multimedia materials we produce and the scientists' direct communication with the public add up to more than 25,000 views on YouTube. This work during 2021 of developing and implementing informative tools has contributed to a better scientific literacy in the country. In 2021, we highlight the work developed with some iMM scientists, Maria Carmo-Fonseca and Luis Graça that has granted us a funding from NOVARTIS to establish an educational program for neuropediatricians, called NeuroP.

Ongoing Projects in 2021

2021/2021: INITIATIVE NEUROP – NOVARTIS. Coordinator: Inês Domingues. Funding Agency: Novartis. Reference: INITIATIVE NEUROP – NOVARTIS. Amount: 41 400,00€. Total Amount: 41 400,00€.

Finance and Operations Office

Director: Fausto da Costa Santos Lopo de Carvalho, Master/MBA

Team

Assistant to the Board of Directors:

Ana Clara Pereira Faria Artur	Assistant to the Board of Directors
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Pre-Award:

Joana Cristina Costa	Pre-Award Area Manager
Marija Petkovic Garcia	Grants Officer
Sílvia da Conceição Santos Pereira da Costa	Grants Officer (Left August)

Project Management:

Madalena Gil Martins Reis	Project Management Area Manager
Andreia Sofia Gonçalves Almeida Vaz Veiga	Senior Project Manager
Ana Maria Branco Alves	Project Manager
Maria José Flores Marques Antunes	Senior Project Manager
Mariana Advirta da Silva Matos Pereira	Project Manager
Josué Ruben Nunes Barão	Project Manager (Started July)
Eduarda Maria Seabra Rosmaninho	Project Manager (Left April)

Accounting:

Sandra Paula da Silva Duarte	Accounting Area Manager
Maria Elisabete Santos Liberato	Senior Accounting Administrative Technician
Maria Fernanda Gonçalves da Veiga Vila-Chã	Administrative Technician
Maria José Serra da Silva	Senior Accounting Administrative Technician
Pedro Miguel da Rosa Santos	Senior Accounting Administrative Technician
Vera Cristina Felício da Conceição Rêgo	Senior Accounting Administrative Technician

Purchasing and Procurement:

Alexandre Manuel Raposo de Jesus	Purchasing and Procurement Area Manager
Ana Rita Fonseca Vicente	Senior Purchasing Administrative Technician
Lúcia Cristina Manso Alves	Purchasing Administrative Technician
Manuel Carlos Nunes Abalada	Administrative
Sandra Isabel Francisco Lopes	Senior Purchasing Administrative Technician
Vânia Isabel Estevens Polido Marques Paula	Senior Purchasing Administrative Technician

Legal and Human Resources:

Inês Bilé da Silva Plácido	Legal Counsel and Area Manager
André Daniel dos Santos Brás Pereira	HR Administrative Technician
Cláudia Aurora Mira Soeiro	Senior HR Administrative Technician
Mafalda de Carvalho Lourenço Morais da Silva	Administrative Trainee (Started August)
Pedro Humberto Fernandes Monteiro Leite	HR Administrative Technician
Sara Duarte Pifano da Costa Eiras	Senior HR Administrative Technician

Safety and Compliance:

Sara Diana Pinheiro dos Santos	Safety and Compliance Area Manager
Ana Francisca Barroca Lemos	Technician
Cláudia Sofia Palmeiro Alves da Costa	Senior Technician
Maria Jardim Caramelo Dias Cabral	Technician
Mafalda Peixoto Costa	Trainee (Started May)

Washing Room:

Ana Cristina dos Santos Anunciação	Senior Technician (Started March)
Bashir Shamshudin Habib Alibhai	Senior Technician (Started March)
Daiani Barcelos Barbosa	Technician (Left February)
Edna Neias Ferreira Gomes	Senior Technician
João Paulo Marques Cunha	Technician (Started March. Left May)
Lucas Araújo da Silva	Technician (Started April)
Leonardo Giraldo Carraça	Technician (Left January)
Monique Maira Melo Madureira	Technician (Started April)

Front Office:

Ana Catarina Ramalheira	Administrative (Started January)
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Description of the Facility

The Finance and Operations Office operates under an agile organizational model with six departments - Pre-Award, Project Management, Purchases and Procurement, Accounting, Legal and Safety and Compliance each with a dedicated Area Manager empowered to design and implement the strategy for each department, aligned with iMM overall priorities.

The Finance and Operations Office main purpose is to maintain an extremely agile structure to give the best possible support to the scientific community, viewed as internal clients. The six areas working collaboratively, allow for a unified 360º view of the full science management loop, starting with pre-award counselling and application revision to post-award financial and operational follow-up, coordinated by the project management team in proximity with the purchases team, responsible for maintaining full compliance in procurement alongside with internal legal counseling. The process ends with the accounting booking processes and reporting executed by the accounting team.

Finally, all safety procedures regarding lab management are fully integrated in this process as a vital part of iMM's operations infrastructure. The Finance and Operations Office is also responsible for all audit processes coordination and to assure the liaison with all financing bodies and develops, upon request, specific studies on relevant matters with nationwide impact for the Portuguese scientific landscape.

In 2022 two important organizational changes that started in 2021 will have their first full year in the new structure: 1) The Human Resources facility ceased to exist as a standalone facility and merged with the Legal department under Finance and Operations giving origin to the Legal & HR department and 2) The Pre-Award will regain its status of a standalone facility with direct report to the Board of Directors.

Pre-Award – Proposal design support; Support in consortium formation - identifying missing competences; Liaison with funding agencies; Administrative and financial grant support; Support to grant writing namely impact (dissemination, communication, exploitation) and implementation sections; Budgeting support and validation; Ethics compliance advice; Support on intermediate reporting closer with project management and with lab managers.

Core Services:

- Dissemination of interesting funding opportunities for iMM’s community
- Tailored support to match project idea with open or forthcoming calls
- Support in grant preparation:
 - provide administrative and institutional information
 - provide advice on financial and ethics compliance
 - ensure compliance with both funding agencies and iMM’s regulations
 - perform proposal review and proofreading
 - manage and consolidate consortium information
- Negotiation of contracts and agreements
- Support in Institutional funding-related initiatives

Accounting – iMM statutory accounts and tax returns; Cost accounting; Reporting and compliance with funding bodies accounting practices; Dedicated report building on cash flow and HR costs.

Core Services:

Accounting is divided in three major areas:

- Invoicing – iMM Invoicing, Supplier Invoicing and Invoice Archive Management
- Payments and refunds – Accounts Payable, Refunds and Advance Payments
- Tax/Fiscal – Human Resources (social security and withholding tax) and Suppliers (VAT; withholding tax; income statements)

Project Management – From contractual start to final report submission; Related-support to researchers; Execution control through project life cycle; Coordination of internal and external audits to projects; Risk monitoring to foresee future tendencies in cost evolution.

Core Services:

- Monitoring of project financial execution
- Ensuring projects deadlines are met
- Preparation and submission of financial reports
- Preparation and monitorization of financial audits
- Administrative support in interactions with funding agencies

Purchasing Office – Tendering according to Portuguese and European legislation; Verification of the validity of expenses associated with a research project; Placing the order to the supplier; Tracking delivery times and updating the researcher on lead times.

Core Services:

- **Procurement** - to help make informed, best-value (money, quality and time) purchasing decisions by establishing transversal contracts and agreements with a wide supplier network.
- **Purchasing** - to maintain, interpret, and enforce the purchasing policy (according to funding bodies) while ensuring that all expenses are eligible, by approving purchases with the help of all departments and handling the dispatching of all Purchase Orders to vendors.
- **Logistics** - to manage incoming products from suppliers by handling importation procedures and customs clearance while also checking-in and register in our internal system.

Legal & Human Resources

Legal

Institutional and Researcher's support

Core Services:

Preparation and revision of agreements and other acts and ensure the legal adequacy of processes, providing the optimum balance between the management promptness and efficiency with the legal utmost clarity and safety.

Human Resources

The purpose of the Human Resources Office is to develop, implement and support programs and processes that add value to iMM and its employees. The mission is to provide effective human resource management through the development and implementation of policies, programs and services that contribute to the pursuit of iMM's Vision "to promote individual freedom and ambition, not a culture of individuality", and the common goal of "creating new knowledge that will impact human health". Cornerstone to the success of HR actions is the agile articulation with all iMM internal stakeholders (several areas and departments of iMM) and external stakeholders (partners and funding agencies) that have common touch points in human resources specific processes.

The Finance and Operations Office through its Director also provides support to the Executive Director in all matters regarding financial and management strategy while being responsible for overall budget submission and follow-up execution of the operational budget of all iMM facilities.

The Finance and Operations Office is also requested to give support in matters concerning inter-institutional collaborations. Finally, the Finance and Operations Office is accountable for promoting Quality Management System actions regarding up-to-date procedures, reports and assessments per facility and fulfilment of ISO 9001 requirements.

Major Achievements

The year of 2021 continued to be impacted by the pandemic situation of caused by COVID-19. The Diagnostic and Serology Unit continued its fast-paced response with the capacity reaching a peak of 2000 daily RT-PCR tests in May and June 2021. In November and December 2021, iMM enrolled in a significantly complex operation regarding RT-PCR testing in nursing homes in 81 counties across 5 districts in Portugal in 45 days of operation.

But the year of 2021 wasn't all about COVID-19, in fact 2021 was the year were the teams tried to be back to a new normal and continue to pursue some strategic projects that were somehow put on hold in 2020 due to the outbreak of COVID-19. In this line, iMM successfully implemented the VAT refund policy in scientific activity in the first full year of this initiative and pursued with the strategy of digitalization within the Finance and Operations departments of Procurement and Accounting.

A new purchasing portal was implemented allowing for a fully integrated procurement processes from A to Z and a new digital invoicing add-on to Navision was developed allowing for invoice registration in an almost automatic way. The pre-award continued its activity supporting c.300 applications aligned with more than 70 funding programmes and thanks to this extensive effort iMM was the most successful institute in the Iberia Peninsula in securing competitive funding for “La Caixa” Foundation Research projects.

The liaison with the Project Management team continued to be very efficient testing the ability of iMM Project Managers to maintain the high levels of focus and compliance in their normal daily tasks adding the complexity of the relation with private donors and with the COVID-19 operations. Regarding infrastructures under the safety and compliance branch, 2021 was also a very busy year with new transformations and fit-out works to take place where several rooms were transformed in to the new Bioimaging equipment room, new Bioimaging office, two new Common Equipment rooms among others. Finally, the last quarter of 2021 brought a merger of two departments, Legal and Human Resources, and a promising plan to generate synergies between the two areas while the support of external legal advisors will pursue in 2022 for specific and complex legal matters.

Pre-Award:

Dissemination of 470+ funding opportunities; Support to 278 applications to 60 different International and 13 different National Funding Programmes, namely regarding eligibility, legal, technical and administrative aspects, as well as the ethics and data management requirements; Preparation of specific material of support for applications to the FCT call for SR&TD projects, the FCT call for Individual Scientific Employment and “la Caixa” Foundation Health Call; Writing and proof-reading of institutional proposals, namely the FCT Institutional Scientific Employment Call and the Horizon Europe Teaming for Excellence Call; Preparation of the Institutional Policy on Gender Equality; Increased compliance of iMM researchers with the Pre-Award regulations; Project implementation monitoring and advice on selected on-going projects (e.g. H2020 ERC, FET Open and Widening, “la Caixa” Foundation Health Research).

Accounting:

During 2021 the management reports of the Finance and Operations Office were updated monthly and the accounting specific documents (balance sheet and income statement) started to be updated at a quarterly basis. The Purchasing Portal and Continia System has been successfully implemented allowing for an automatic digitalization of documents in close communication with our main accounting software - Navision. This action potentiates optimization of working times, reducing manual tasks related with physical document management, and generating improvements for both accounting and project management in terms of projects accountability tasks.

The VAT refund scheme is now operational and VAT is being reported to the Portuguese fiscal authority in a quarterly since the beginning of 2021 and the respective records are reflected in Navision. Regarding team alignment and motivation, a checklist of tasks to be performed and deadlines to be met is now seen as a normal (and good) practice with visible efficiency results.

Purchasing and Procurement:

The year of 2021 was the continuation of our strategy: the creation of synergies with suppliers allowing the reduction or, in some case, nullify the disruption of the supply-chain to the researchers, creating alternatives so research would not stop and maintaining a nimble process while still allowing the validation of expenses. Despite the team being teleworking for the whole year, we were able to increase our response time and process 6542 orders with the highest total value in euros in the last 4 years.

In the year of 2021 it was also installed the new Purchasing System directly connected to the accounting software that will go into full use in the first trimester of 2022.

Project Management:

In 2021, the project management team strengthened its core activities of reporting and liaising communication with financing bodies while supporting laboratories in administrative tasks related to the project's execution. The increased range of donors and project types, with the underlying complexity of stakeholders involved, brought additional complexity to the team's daily activities. The focus on standardization, communication and teamwork set the stage for the needed flexibility.

Additionally, following the agility path the department has been going through within the F&O unit, the project management team took part in key internal iMM projects such as the COVID-19 diagnostic task force, fundraising activities and processes digitalization supporting the administrative and operational implementation.

Legal:

The Legal department maintained its support to the successful implementation of all COVID-19 related activities and private donor relations and continue to support the remaining activity of the iMM allowing the institute to operate in an always compliant level.

During the last quarter of 2021, due to a major reorganization in the administrative structure of the Institute, the Human Resources area became part of the Finance and Operations Office and were joined with the Legal department creating the Legal & HR department. This merge aims to improve and optimize the human resources operations while the Legal department continues to maintain its goal of providing the best legal counselling for all main legal questions concerning the service provision of the iMM.

Safety & Compliance:

In the year of 2021, the Safety and Compliance continued to implement the measures for COVID-19 prevention of all iMMers.

In the first semester, Safety and Compliance remodeled several rooms that were transformed in to the new Bioimaging equipment room, new Bioimaging office, two new Common Equipment rooms and the remodeling of the Flow Cytometry/Comparative Pathology Unit office. In the second semester the remodeling of the new videoconference room, the Communication office, the Information Systems Unit Office and the HR Office was concluded.

To improve the pool of common equipment available, two new equipment's were acquired: one purification water system and a western blot imaging system. In the Washing Room, a new washing equipment was acquired and more common glassware, in order to improve the support of iMM Labs and Facilities and continue the transition from disposable to reusable lab material.

The Legal Compliance Audit for the Safety and Environment areas was also completed and the results are going to continue to be followed during 2022 to improve the iMM's performance in these areas. Following iMM's risk assessment, new Biosafety cabinets were acquired and installed in selected labs.

Human Resources Office

Director: Sofia Isabel Lopes dos Santos Vicente dos Santos, University Degree (Left August)

Team

André Daniel dos Santos Brás Pereira	University Degree	HR Administrative Technician
Cláudia Aurora Mira Soeiro	University Degree	Senior HR Administrative Technician
Mafalda de Carvalho Lourenço Morais da Silva	University Degree	Administrative Trainee (Started August)
Pedro Humberto Fernandes Monteiro Leite	Master Degree	HR Administrative Technician
Sara Duarte Pifano da Costa Eiras	University Degree	Senior HR Administrative Technician

Description of the Facility

The purpose of the Human Resources Office is to develop, implement and support programs and processes that add value to iMM and its employees, leading to improvements in employee well-being, empowerment and growth, while committed to iMM's key activity: Research.

The mission is to provide effective human resource management through the development and implementation of policies, programs and services that contribute to the pursuit of iMM's Vision "to promote individual freedom and ambition, not a culture of individuality", and the common goal of "creating new knowledge that will impact human health". In order to increase the response capacity to internal requests and to improve the welcoming of new members, HR Office reinforced the team.

The last quarter of 2021 brought a merger of two departments, Legal and Human Resources, and a promising plan to generate synergies between the two areas while the support of external legal advisors will pursue in 2022 for specific and complex legal matters.

Technology Transfer Office

Director: Pedro Silva, University Degree, President of the Board of Directors at AccelBio CoLAB

Team

Bárbara Sofia Lopes Gomes	PhD	Senior Technology Transfer Officer
Beatriz Paisana Ferreira Bouza da Costa	Master Degree	Administrative (Started July)
Miguel Filipe Duarte	Master Degree	Technology Transfer Officer (Started October)

Description of the Facility

We stimulate the valorization of knowledge produced at iMM through:

- The creation of a favorable internal environment to foster innovation and speed up the translation of promising ideas and results into new medical solutions;
- The protection and licensing of intellectual property;
- The promotion of entrepreneurship and the creation of start-ups;
- A closer interaction with industry (at national and international level) leading to new collaborations;
- the participation in relevant National and European networks and initiatives related with translational research (e.g.: NIBR Global Scholars Program, EATRIS, PTCRIN), open innovation (e.g.: Open Innovation Test Bed – “SAFE-N-MEDTECH”, “INNO4COV-19”, AccelBio CoLAB, Health Cluster Portugal) and business acceleration (e.g.: Start4Health@ULisboa).

Major Achievements in 2021

Our IP portfolio was strengthened with 24 new inventions and 34 patents filed in different territories. 7 license agreements have been set with companies to exploit iMM IP. Efforts to create 6 new start-up companies are undergoing. 3 of our start-ups have raised 20.5 M€ in funding.

192 collaborations with industry were promoted and 54 formalized. Among collaborations with industry, it is worth highlighting the enrolment of iMM in the Novartis NIBR Global Scholars Program. iMM is the first Portuguese research institute to participate in this program along with 50 other world-class research institutions.

The TTO also promoted the creation of the Collaborative Laboratory AccelBio, with an approximate total investment of 5 M€. The AccelBio Colab is led by iMM and aims at developing the early drug discovery capacity in Portugal.

Training Hub

Director: Domingos Henrique, PhD, Investigador Auxiliar at Faculdade de Medicina da Universidade de Lisboa

Team

Ana Filipa Duarte Nunes Almeida	PhD	Training Hub Area Manager
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Description of the Facility

The Training Hub ensures the proper integration of overall training activities at iMM that are tailored for researchers at different stages of their careers, aiming for an internationally competitive career in academia, industry or clinical medicine environments.

We work closely with MSc students, PhD students, and Postdoctoral researchers to maximize their career prospects through specific programs and activities. These include:

- **A MSc Program** that supports students developing their Master thesis at iMM every year, and a **Master Course in Biomedical Research**, which started in 2020 within the framework of the CAML consortium.
- An international PhD Program – **LisbonBioMed** – which offers all PhD students at iMM a flexible and tailored curricular structure at the interplay between laboratory and clinical practice.
- A **Post-Doctoral Training Program**, structured around specific actions that promote scientific discussion and sharing of experiences, in academia and beyond.

Major Achievements in 2021

Specific Achievements:

- Overall managerial and administrative execution of the LisbonBioMed PhD Program, including the production of metrics, and reporting;
- Launch of the new LisbonBioMed website;
- Second edition of the “Merit Award João Lobo Antunes” to award the best Doctoral Theses;
- Operationalization of the Master in Biomedical Research (2nd Edition), in articulation with IFA-FMUL;
- “Master Program @ iMM”: assembly and dissemination of iMM’s Master project proposals/vacancies; “Best Master Thesis” Awards; MSc Day;
- “Training Program for the Next Step”: personalized reviewing of full applications (including cover letters, research projects and CVs) for PhD, postdoctoral, and group leader positions;
- Organization of webinars (Bullying in Science) and traineeships at iMM (IST CoLabs, summer internships).

Transversal managerial support to:

- FCT fellowships: applications, periods abroad, thesis committees and defenses, general queries;
- PhD students/Postdocs-driven initiatives.