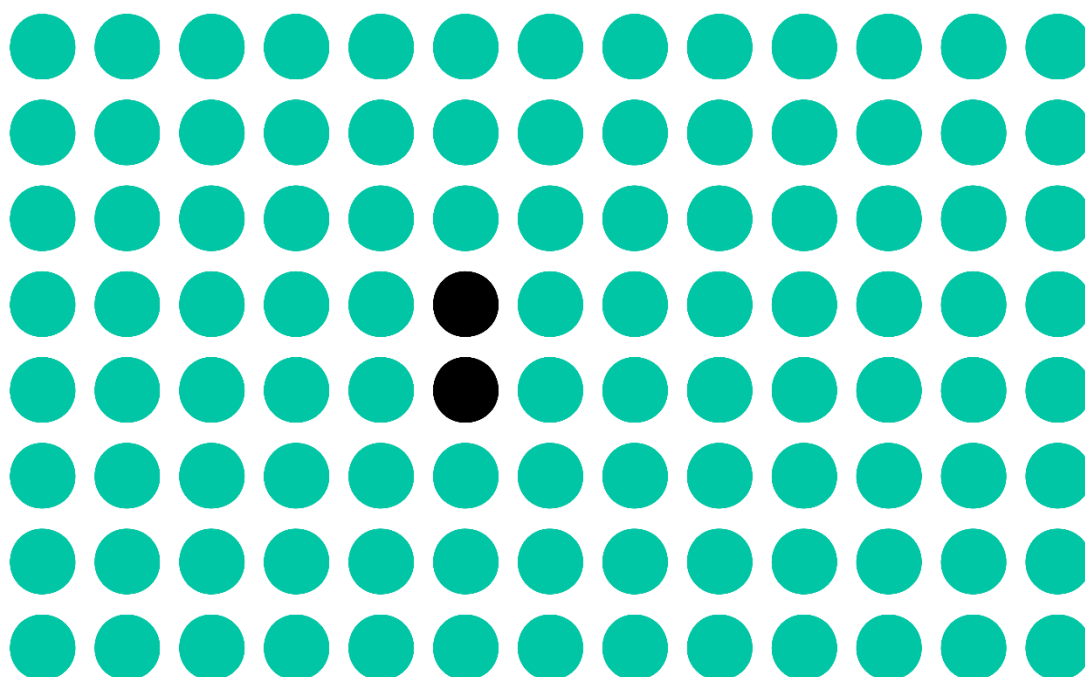




Instituto
de Medicina
Molecular

João
Lobo
Antunes

Scientific Report 2019



Lisbon, May 2020

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Structure & Organisation

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

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

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 provide assistance to the Technology Transfer Office team in the definition of a strategy and action plan to drive innovation at iMM.

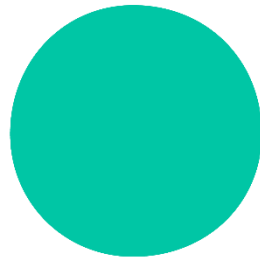
Daniela Couto – Biogeneration Ventures Fund

David Malta – Vesalius Biocapital

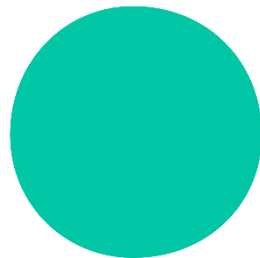
Isabel Ferreira – Versameb

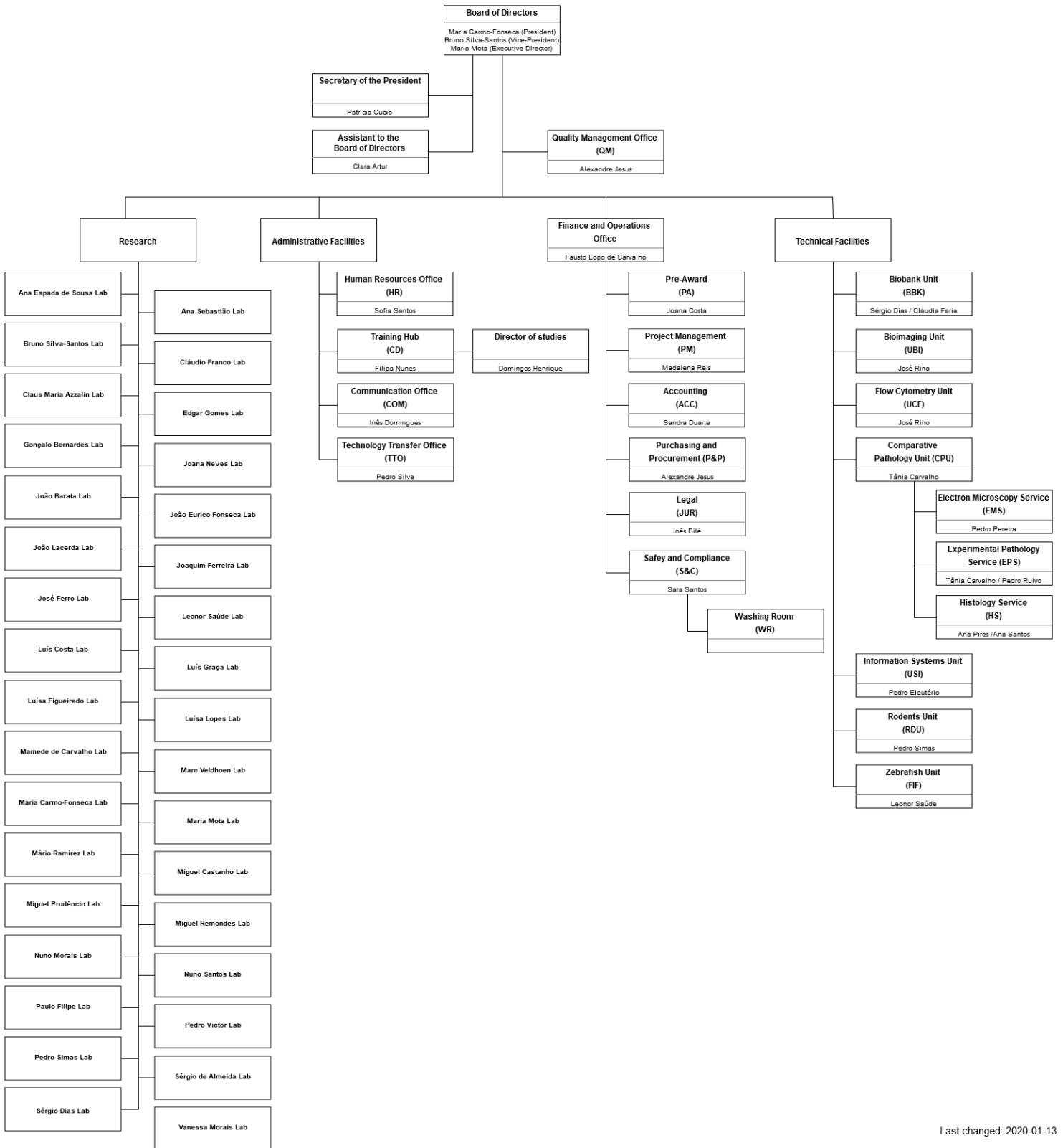
Miguel Forte – Zelluna Immunotherapy

Pascale Redig – Janssen



Organigram





Last changed: 2020-01-13

Evaluation Reports 2019

2013 FCT Evaluation of R&D Units

Period of Evaluation:

2008 – 2012: Scientific and technological activities (performance indicators);

2015 – 2020: Research strategies and planned work consolidated as a strategic programme.

Evaluation Panel:

Panel 3: Health and Life Sciences

Final Classification: Excellent

Panel's overall comments (Stage 2 – Site visit):

The site visit confirmed to a large extent the conclusions of the initial assessment that the unit has an excellent overall standing. It pointed out to some insufficiencies in the scientific output of a significant fraction of the integrated members listed in the initial application, and in the intensity of technology transfer that were openly discussed with both the unit leaders and the active group of students and postdocs. The site visit team recommended (i) a redefinition of the role of the less productive integrated members in research, teaching or management tasks that should lead to a reduction in the number of integrated members and independent groups; (ii) increased efforts in securing substantial financial resources through contracts with industry. It was satisfied with the clarification of the novel management and governance processes that have been established and praised Prof Maria Carmo-Fonseca, the Principal Investigator of the proposal and the Executive Director of iMM since 2002, to have promoted Dr. Maria Mota as the unit Director. Prof Maria Carmo-Fonseca now serves as iMM President in an oversight role with veto power on strategic decisions, and a focus on international development. Dra. Maria Mota is supported on her role as Executive Director by two Vice Directors, Dr. Henrique Veiga-Fernandes and Bruno Silva-Santos, and an experienced Finance Director, Mrs. Margarida Pinto-Gago¹. In order to achieve this in a transition period of reorganization of its staff dedicated to research and a context of potential shortage of public funding, the new iMM Board of Directors will require strong financial and managerial support from the University of Lisbon and the Faculty of Medicine. The Panel considered that the proposed strategic programme provides a solid basis for the future development of the unit in the next period, and that the budget requested was adequate, but recommended that the full executive power should be endowed to the coordinator during her term for its implementation, while the former director and President takes charge of international cooperation.

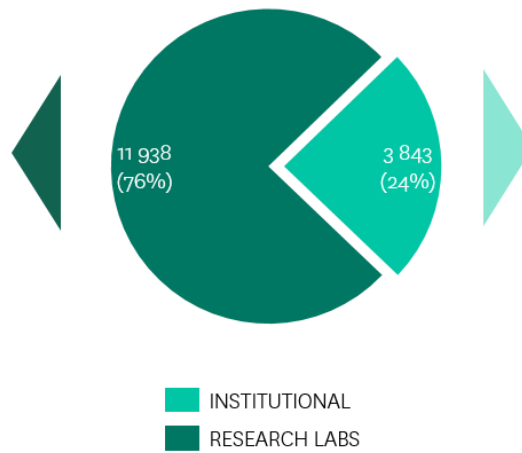
¹ Since 2017, Dra. Maria Mota is supported on her role as Executive Director by one Vice-Director, Dr. Bruno Silva-Santos, and a Finance and Operations Director, Dr. Fausto Lopo de Carvalho.

Research Funding

Expenditure in 2019 by Funding Source

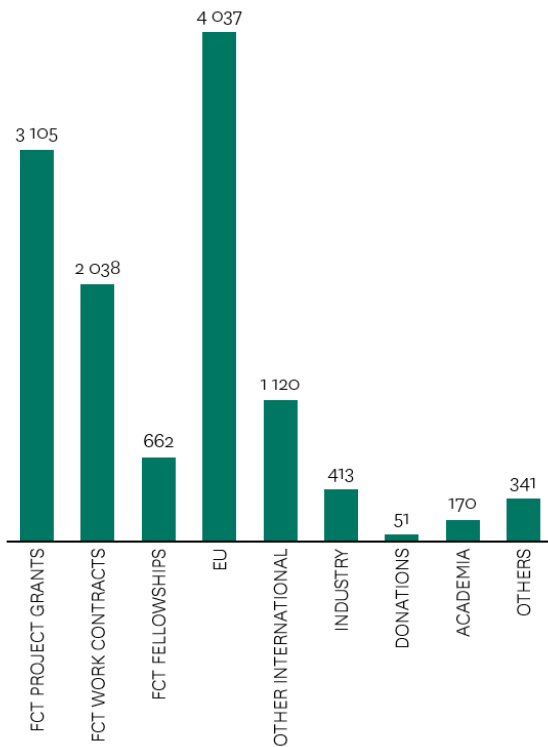
Total Expenditure: € 15 781 665²

Total Expenditures 15,7M



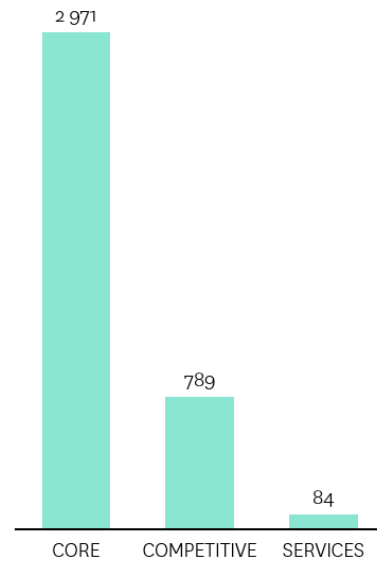
Research Labs

All Values in 000 Euros



Institutional

All Values in 000 Euros



² Figures for this exercise only consider costs registered in the exercise of 2019, 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 2019 onwards.

2019 Expenditure

			(EUROS)
INSTITUTIONAL	CORE	2 970 556	
	COMPETITIVE SERVICES	788 735	
		84 139	3 843 431
RESEARCH LABS	FCT PROJECT GRANTS	3 105 115	
	FCT WORK CONTRACTS	2 037 910	
	FCT FELLOWSHIPS	661 913	
	EU	4 037 485	
	OTHER INTERNATIONAL	1 119 625	
	INDUSTRY	413 380	
	ACADEMIA	51 264	
	DONATIONS	170 380	
	OTHERS	341 161	11 938 234
TOTAL			15 781 665³

³ Figures for this exercise only consider costs registered in the exercise of 2019, 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 2019 onwards.

Number of Ongoing Research Grants in 2019

206 Research Grants:

Public National FCT: 108

Private National: 26

Public National Other: 2

Of which with the industry – 9

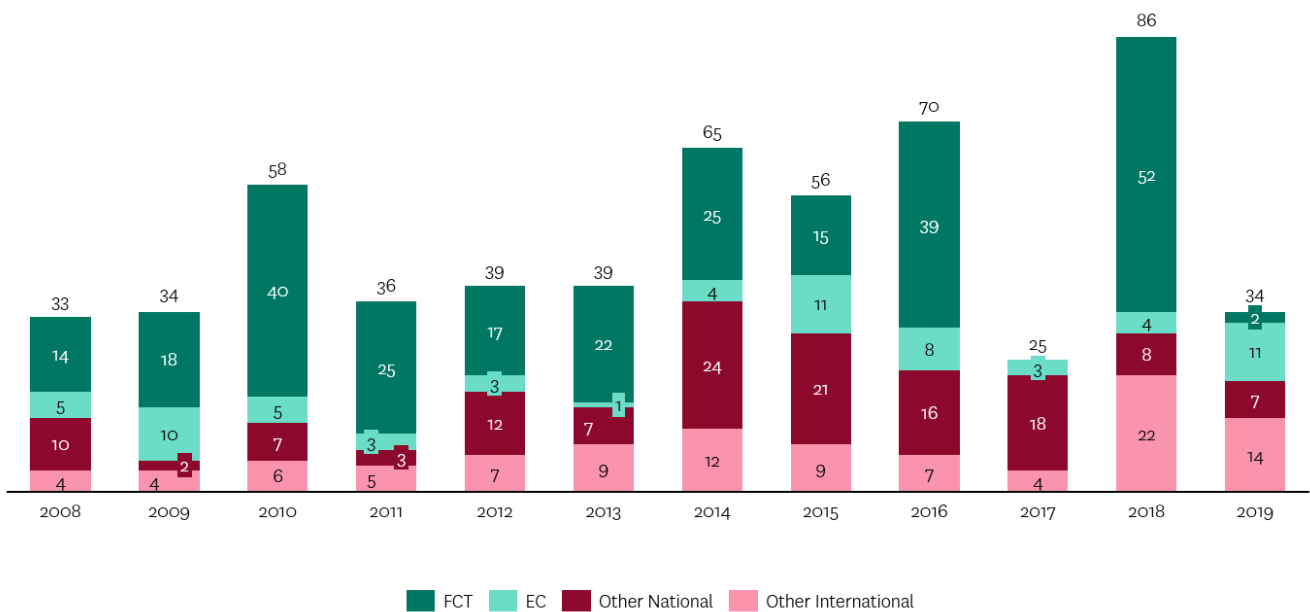
Public European Commission: 31

Private International: 39

Public International Other: 0

Of which with the industry – 19

Number of Research Grants Initiated at IMM from 2008 to 2019



Number of Research Funding Grants Initiated in 2019

Research Grants (34):

National Public: 2

International Public: 11

National Private: 7

International Private: 14

Projects Initiated in 2019 through Competitive Funds

FUNDING AGENCY	RESEARCHER	iMM BUDGET
Fundação para a Ciência e a Tecnologia (FCT)	Miguel Castanho	€ 2 000,00
	Ana Espada de Sousa	€ 800,00
"la Caixa" Foundation	Pedro Sousa-Víctor	€ 297 900,00
	Bruno Silva-Santos	€ 499 999,51
	Leonor Saúde	€ 444 048,00
	Carolina Pacini	€ 115 092,00
	Marc Veldhoen	€ 497 158,00
	Miguel Castanho	€ 2 113 125,00
European Commission	Maria Carmo-Fonseca	€ 424 750,00
	Cláudio Franco	€ 150 000,00
	Marie Ourné	€ 147 815,04
	Edgar Gomes	€ 3 207 935,00
	Joaquim Ferreira	€ 289 500,00
	Luísa Figueiredo	€ 228 720,24
	Luísa Figueiredo	€ 159 815,04
	Bruno Oliveira	€ 353 750,00
	João Eurico Fonseca	€ 290 996,25

Protocols, Donations & Awards⁴

FUNDING AGENCY	RESEARCHER	iMM BUDGET
Astellas Farma, Lda	Luís Costa	€ 10 000,00
Astrazeneca-Produtos Farmacêuticos	Luís Costa	€ 10 000,00
Celgene Sociedade Unip., Lda.	Maria Carmo-Fonseca	€ 2 245,18
Centro Hospitalar Lisboa Norte, E.P.E	João Lacerda	€ 1 290,41
COST Action	Maria Carmo-Fonseca	€ 10 000,00
Fundação Bial	Maria Carmo-Fonseca	€ 5 000,00
	Luísa Lopes	€ 45 000,00
Fundo iMM-Laço	Marc Veldhoen	€ 29 700,00
	Sérgio de Almeida	€ 30 000,00
Human Frontier Science Program	Mariana de Niz	€ 69 120,00
Illumina, Inc.	Luís Costa	€ 12 355,60
Janssen-Cilag Farmacêutica,Lda	Ana Espada de Sousa	€ 1 500,86
	João Lacerda	€ 19 800,00
	Luís Costa	€ 8 000,00
Merck Sharp & Dohme	Luís Costa	€ 7 000,00
Prémio L'Oreal Mulheres na Ciência	Patrícia Costa Reis	€ 15 000,00
Prémios Santa Casa Neurociências - Prémio Mantero Belard	Luísa Lopes	€ 175 000,00
Roche Farmaceutica Quimica	Luís Costa	€ 35 000,00
Roche Farmaceutica Quimica - Neuroses	Luísa Lopes	€ 1 200,00
Sanofi - Produtos Farmacêuticos, Lda	Luís Costa	€ 10 000,00
Sociedade Portuguesa de Medicina Interna	Ana Espada de Sousa	€ 10 000,00

⁴ Considered protocols, donations and awards that fund projects, infrastructures and seminars.

iMM Applications and Secured Competitive Funding

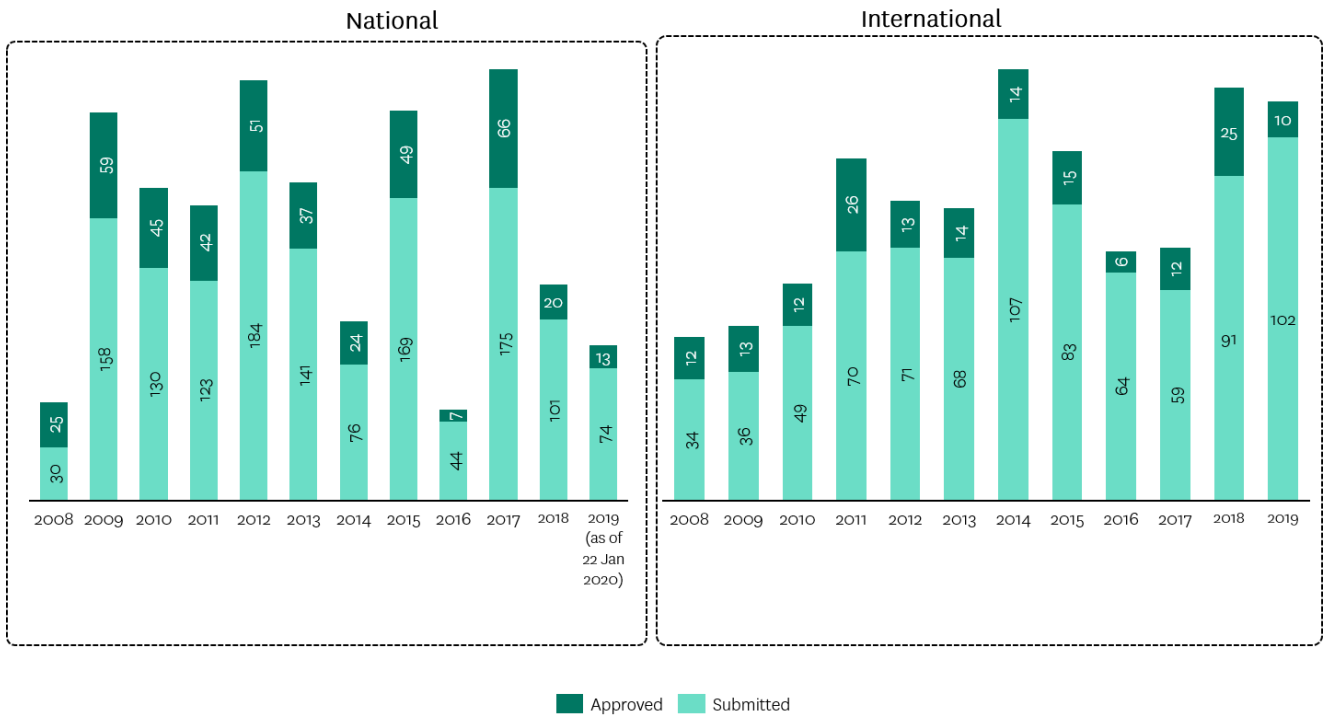


Figure 1: Submitted and approved applications to national and international competitive funding schemes since 2008. The number of submitted applications corresponds to those effectively communicated to the Pre-Award. The number of approved applications for 2019 corresponds to those with known results as of January 2020.

Funds Secured (Values in Million Euros)

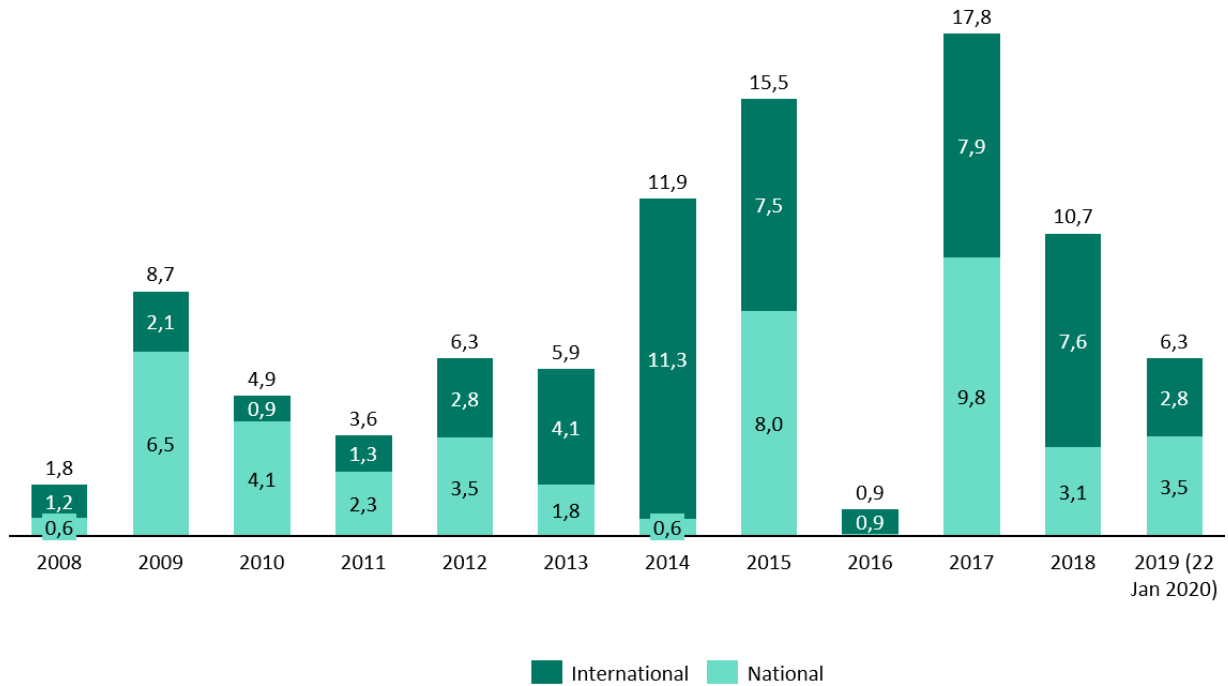


Figure 2: Total funds secured by iMM (in millions of €) in international and national competitive funding schemes since 2008. Secured funds per year correspond to the sum of the iMM budget of the approved applications submitted in the corresponding year (irrespective to the project starting date). Information for 2019 corresponds to known results as of January 2020.

Funding Sources of iMM Applications

In 2019, iMM researchers and staff have submitted grants to the following funding schemes:

INTERNATIONAL					
PRIVATE FUNDS		PUBLIC FUNDS			
Alzheimer's Association	American Association for Cancer Research	European Commission - Horizon 2020	Excellent Science	European Research Council	Consolidator Grant
Angelman Syndrome Foundation	Beug Foundation for Metastasis Research				Advanced Grant
Biocodex Microbiota Foundation	British Society for Antimicrobial Chemotherapy				Synergy Grant
BrightFocus Foundation	Chan Zuckerberg Initiative				Proof of Concept
Celgene - Portugal	CURE			Marie Skłodowska-Curie Actions	Individual Fellowships
Concern Foundation	Ernst Schering Research Foundation				Research and Innovation Staff Exchange
Duchenne UK	FEBS				Innovative Training Networks
EMBO	Long-Term Fellowship			European Innovation Council (EIC) Pilot	EIC Pathfinder Pilot (FET-Proactive) Boosting Emerging Echnologies
	Installation Grant				
European Association for the Study of Diabetes	Foundation for Research in Rheumatology			European Research Infrastructures (including e-Infrastructures)	
International OCD Foundation	Kenneth Rainin Fondation			Industrial Leadership	Nanotechnologies, Advanced Materials, Advanced Manufacturing and Processing, and Biotechnology
Leukemia Research Fondation	Merck/EMD Serono			Societal Challenges	Health, Demographic Change and Well-being
"la Caixa"	Junior Leader Fellowship			Spreading Excellence and Widening Participation	Twinning
	Health Research Projects				ERA Chair
Motor Neurone Disease Association	Muscular Dystrophy Association	European & Developing Countries Clinical Trials Partnership (EDCTP)			
North American Spine Society	National Multiple Sclerosis Society	Innovative Medicines Initiative (IMI) EU Public-Private Partnership			
One Mind	Rally Foundation	COST European Cooperation in Science and Technology			
Rettsyndrome.org	United Mitochondrial Disease Foundation	European Regional Development Fund	Interreg Sudoe Programme		
Worldwide Cancer Research		National Institute for Health (NIH), US			

NATIONAL			
PRIVATE FUNDS		PUBLIC FUNDS	
Bial	Gilead	Fundação para a Ciência e Tecnologia	Scientific Employment Stimulus
MSD Portugal	Foundation L'Oreal		Data Science and Artificial Intelligence in Public Administration
Pfizer Sociedade das Ciências Médicas de Lisboa	Santa Casa da Misericórdia de Lisboa		R&D Projects on the Occasion of the Celebrations of the V Centenary of the Circumnavigation Voyage
LPCC	LPCC-Terry Fox		International Cooperation European Joint Programme on Rare Diseases (EJP RD) EU Joint Programme – Neurodegenerative Disease Research (JPND)
	Bolsa LPCC / Fundação PT	Fundação para a Ciência e Tecnologia Portugal 2020	International Partnerships MIT-Portugal, UTA-Portugal and CMU-Portugal
	Bolsa LPCC / Pfizer	Fundação para a Ciência e Tecnologia Maratona da Saúde	
Fundação Amélia de Mello		Ciência Viva	

Funding Sources - Evolution of the diversity

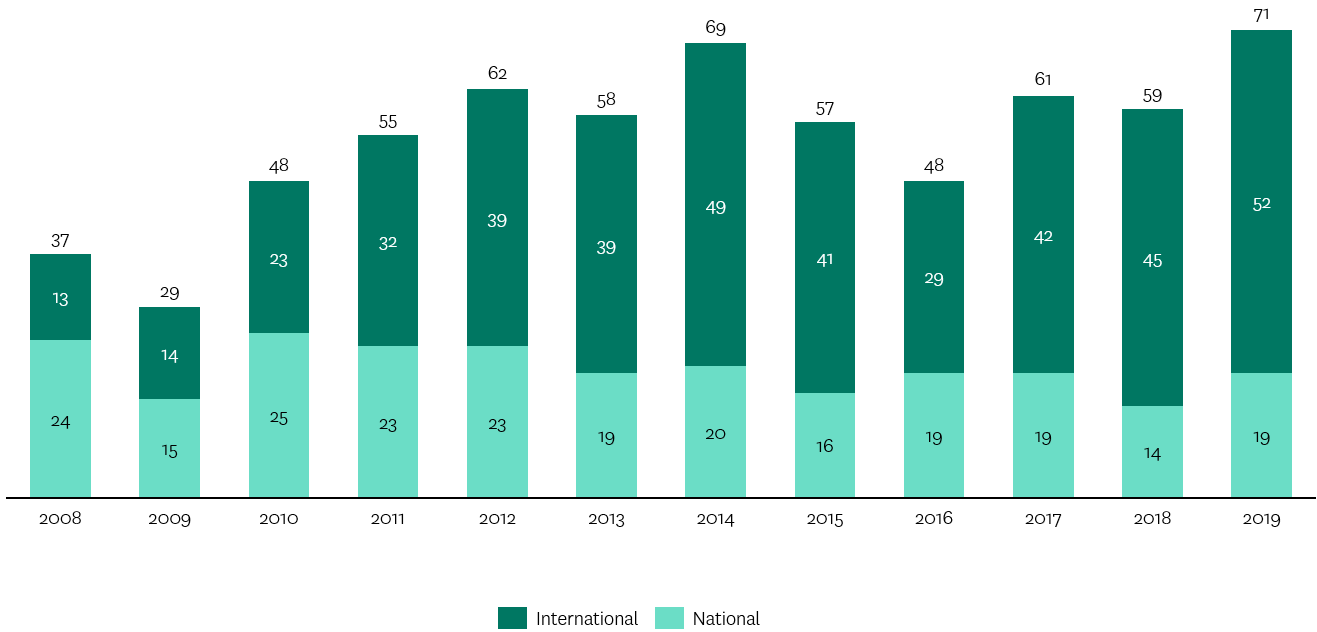


Figure 3: Evolution of the diversity of international and national funding schemes for which iMM researchers submitted applications from 2008 to 2019.

2019 iMM Activities Highlights

Human Resources 2019

		2018	2019
Researchers	PhD	206	231
	PhD Students	138	139
	MSc Students	94	64
	Master	88	52
	Graduate	37	21
	Other	3	6
		566	513
Technical Staff	PhD	8	8
	Master	26	61
	Graduate	20	19
	Other	25	11
		79	99
Administrative Staff	PhD	6	11
	Master	7	15
	Graduate	16	17
	Other	6	9
		35	52
TOTAL		680	664

Selection of Prizes and Awards

SPBf Young Biophysicist 2019

Tiago Figueira (Miguel Castanho Lab)

Marie Skłodowska-Curie Actions Individual Fellowship

Maria Ouarné (Cláudio Franco Lab, Rosina Savisaar (Carmo-Fonseca Lab) and Sara Pereira (Luísa Figueiredo Lab)

L'Oréal-UNESCO for Women in Science Award

Patrícia Reis (João Eurico da Fonseca Lab)

Fundo iMM-Laço: A Caminho da Cura (2018 Edition – Announced in 2019)

Marc Veldhoen (Group Leader)

Sérgio de Almeida (Group Leader)

Universidade de Lisboa/Caixa Geral Depósitos Scientific Award

Luís Graça (Group Leader)

Miguel Castanho (Group Leader)

Human Frontier Science Program Fellowship

Mariana De Niz (Luísa Figueiredo Lab)

FAZ Ciência Award

Bruno Silva-Santos (Group Leader) and Noella Lopes (Bruno Silva-Santos Lab)

H2020 ERC Proof of Concept

João Barata (Group Leader)

Banco Carregosa/SRNOM Award

Luís Graça (Group Leader)

Aboim Sande Lemos Award (Identidade Portuguesa da Sociedade Histórica da Independência de Portugal)

M. Carmo-Fonseca (Group Leader)

25 Most Influential Women of Portugal Award (2018 Edition - Announced in 2019)

M. Carmo-Fonseca (Group Leader)

EMBO Member

Bruno Silva-Santos (Group Leader)

la Caixa – Individual Project

Bruno Silva-Santos (Group Leader)

Leonor Saúde (Group Leader)

Marc Veldhoen (Group Leader)

H2020 Twinning: RiboMed

M. Carmo-Fonseca (Group Leader)

H2020 Twinning: SIMICA

Gonçalo Bernardes (Group Leader)

Gilead Génese Program

Amelia Trombetta (Ana Espada de Sousa Lab)

João Lacerda (Group Leader)

M. Carmo-Fonseca (Group Leader)

iMM Best Master Thesis Award

Pedro Ruivo (Comparative Pathology Unit)

Arthur Schneider (Nuno Morais Lab)

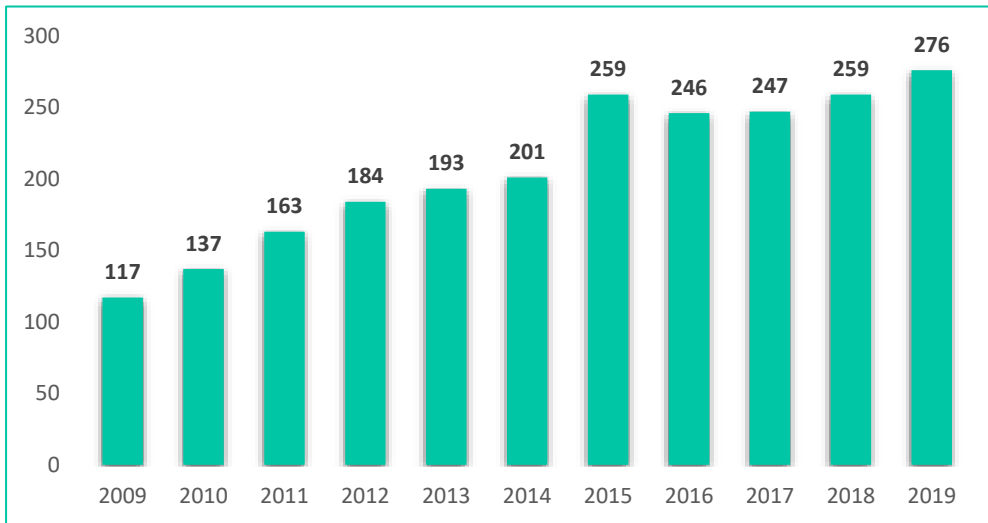
Catarina Pelicano (Bruno Silva-Santos Lab)

Productivity at a Glance

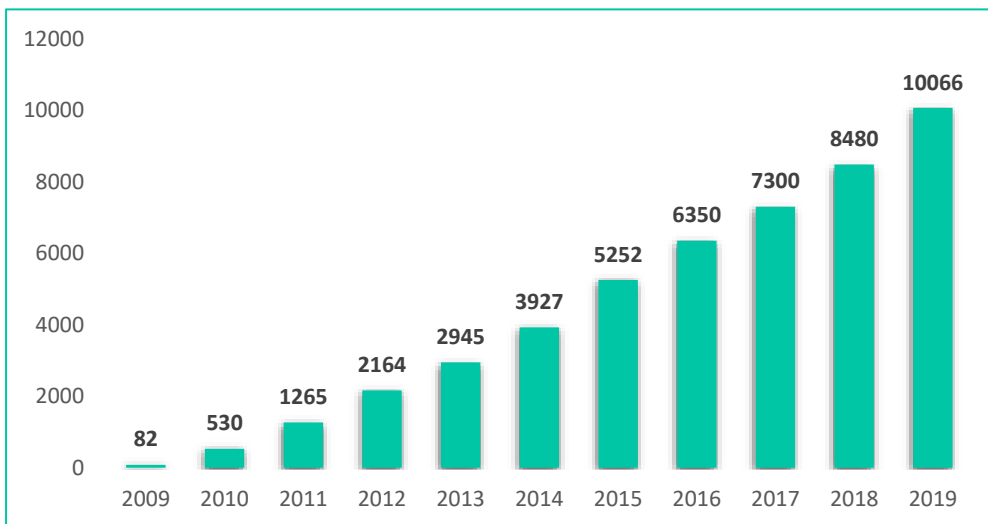
	2018	2019
Total Publications International Journals	254	276
Publications in Journals with Impact Factor > 10	53	43
Communications in International Conferences	561	411
Communications in National Conferences	316	374
Seminars and Invited Lectures	372	414
Organisation of Conferences	104	102
PhD Thesis Completed	23	23
MSc Thesis Completed	65	84
Prizes, Honours and Awards	96	107

iMM Publications in International Journals

(Source: Web of Science™)



Published Items in Each Year: 2009-2019



Citations in Each Year: 2009-2019

Papers in 2019: 276

Papers since 2009: 2.282

Sum of the times cited: 51.805

Average citations per item: 22.7

h-index: 91

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: 2009-2019. 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 2002-2019

(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. (IF: 17.728, Citations: 873. Source: Web of Science).

Healy DG, Falchi M, O'Sullivan SeanS et al (2008). Phenotype, genotype, and worldwide genetic penetrance of LRRK2-associated Parkinson's disease: a case-control study. **Lancet Neurology**. 7(7):583-590. (IF: 28.755, Citations: 759. Source: Web of Science).

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. (IF: 3.675, Citations: 698. Source: Web of Science).

Henry DH, Costa L, Goldwasser F et al (2011). 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**. 29(9):1125-1132. (IF: 28.349, Citations: 608. Source: Web of Science).

Ratziu V, Bellentani S, Cortez-Pinto H et al (2010). A position statement on NAFLD/NASH based on the EASL 2009 special conference. **Journal of Hepatology**. 53(2):372-384. (IF: 18.946, Citations: 572. Source: Web of Science).

Klose CSN, Flach M, Moehle L et al (2014). Differentiation of Type 1 ILCs from a Common Progenitor to All Helper-like Innate Lymphoid Cell Lineages. **Cell**. 157(2):340-356. (IF: 36.216, Citations: 507. Source: Web of Science).

Hansen C, Angot E, Bergstrom AL et al (2011). alpha-Synuclein propagates from mouse brain to grafted dopaminergic neurons and seeds aggregation in cultured human cells. **Journal of Clinical Investigation**. 121(2):715-725. (IF: 12.282, Citations: 465. Source: Web of Science).

Barbosa-Morais NL, Irimia M, Pan Q et al (2012). The Evolutionary Landscape of Alternative Splicing in Vertebrate Species. **Science**. 338(6114):1587-1593. (IF: 41.063, Citations: 438. Source: Web of Science).

Zerr I, Kallenberg K, Summers DM et al (2009). Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. **Brain**. 132:2659- 2668. (IF: 11.814, Citations: 418. Source: Web of Science).

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. (IF: 4.517, Citations: 413. Source: Web of Science).

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

(IF Source: Web of Science™)

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. (IF: 4.428, Citations: 3. Source: Scopus).

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. (IF: 5.547, Citations: 0. Source: Web of Science).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC (2019). Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. **Science Immunology** 4(40):eaay5199. (IF: 10.551).

Jesus TF, Ribeiro-Gonçalves B, Silva DN, Bortolaia V, Ramirez M, Carriço JA (2019). Plasmid ATLAS: plasmid visual analytics and identification in high-throughput sequencing data. **Nucleic Acids Research** 47:D188–D194. (IF: 11.147).

Saraiva-Agostinho N, Barbosa-Morais NL (2019). psichomics: graphical application for alternative splicing quantification and analysis. **Nucleic Acids Research** 47(2):e7. (IF: 11.147).

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Seminars, Workshops & Events

Computational Biology and Bioinformatics Seminars

9th January

“Docker Compose: Deploying reproducible development environments”

Bruno Gonçalves – Mário Ramirez Lab

23rd January

“FlowCraft: a modular, extensible and flexible tool to build, monitor and report genomics nextflow pipelines”

C I Mendes – Mário Ramirez Lab

6th February

“The potential of exosome proteome in lung cancer diagnostics”

Rune Matthiesen - CEDOC

20th February

“Genome-wide analysis of the nascent RNA pol II transcriptome during Drosophila development”

Kenny Rebelo – Carmo-Fonseca Lab

6th March

“Why studying molecular alterations in Alzheimer’s and Parkinson’s brains requires single-cell RNA-seq”

Marie Bordone – Nuno Morais Lab

17th April

“Lobo Cluster Birthday Party: best practices, technical limits, and future optimizations”

André Fragoso – Information Systems Unit

29th May

“T follicular helper (Tfh) cells under different immune responses”

Samuya Kumar – Luís Graça Lab

10th July

“DEN-IM: Dengue Virus genotyping from shotgun and targeted metagenomics”

Inês Mendes – Mário Ramirez Lab

25th September

“Computational Biology: bridging statistical learning and bioengineering for modeling high-dimensional data”

Susana Vinga – Instituto Superior Técnico and INESC-ID

9th October

“Sequence evolution and the dynamics of splicing”

Rosina Savisaar – Carmo-Fonseca Lab

6th November

“Computational analysis of isoform level regulation in T helper cells”

António Gonçalves – Luís Graça Lab

20th November

“Data frame handling in R with dplyr (and some pandas for the Pythonistas)”
Filipe Cadete – Claus Azzalin Lab

4th December

“Genomic and transcriptomic characterization of a leukemia mouse model”
João Neto – João Barata Lab

18th December

“The Gulbenkian Training Programme in Bioinformatics, a method for sustainable provision of skills to scientists 1999-2019”
Pedro Fernandes – Instituto Gulbenkian de Ciência

EXCELLtoINNOV Seminars

1st July

“Lactate, from waste metabolite to homeostatic signal in gastrointestinal tract?”
Martin Rumbo – National University of La Plata, Argentina

4th July

“Metabolic programs controlling immune cell function”
Tim Spanwasser – University of Mainz

19th September

“Regulation of mucosal immune responses by integrins and TGF-beta”
Mark Andrew Travis - University of Manchester

14th November

“Crosstalk between EGFR and TGFbeta as a regulator of local inflammation”
Dietmar Martin Werner Zaiss – University of Edinburgh

Immunology Club

23rd January

“Functional genomics of human T cell differentiation”
Alexandre Raposo – Ana Espada de Sousa Lab

20th March

“Immune response to Hepatitis B and Influenza vaccines in rheumatic patients under biological therapies”
Pedro Ribeiro – João Eurico da Fonseca Lab

3rd April

“Control of IFN-gamma expression in CD8 T cells by microRNAs”
Tiago Amado – Bruno Silva-Santos Lab

29th May

“The interplay of B and T follicular cell subsets in early arthritis patients”
Catarina Tomé – João Eurico da Fonseca Lab

12th June

“Exploring new facets of interleukin-7 receptor-mediated signaling in T-cell leukemia”
Ana Sofia Ramalho – João Barata Lab

26th June

“Activation of Intra-epithelial lymphocytes (IELs)”
Patrícia Figueiredo-Campos – Marc Veldhoen Lab

9th October

“Multifunctional nanovaccine synergizes with immune checkpoint therapy against triple negative breast cancer”
Carina Peres – Luís Graça Lab

23rd October

“Follicular helper T cells are major HIV-2 reservoirs and support productive infection”
Ana Catarina Santos – Ana Espada de Sousa Lab

20th November

“The role of JAK-STAT signalling pathway as key to chronic arthritis onset”
Rui Teixeira – João Eurico da Fonseca Lab

Internal Seminars

9th January

“Lost in translation? - fundamental research with clinical significance”
Luísa Lopes – Group Leader

6th February

“Tackling cancer chemoresistance with epigenetics and immunotherapy”
Bruno Silva-Santos – Group Leader

10th April

“Generating tissue resident memory T cells”
Marc Veldhoen – Group Leader

29th May

“An RNA modification on the polyA tail promotes mRNA stability”
Luísa Figueiredo – Group Leader

12th June

“Spinal cord regeneration: what can we learn from zebrafish?”
Leonor Saúde – Group Leader

26th June

“Developing Treg therapies”
João Lacerda – Group Leader

10th July

“Liquid Biopsy in Advanced Breast Cancer: ready to explore new opportunities?”
Luís Costa – Group Leader

24th July

“The timing of splicing”

M. Carmo-Fonseca – Group Leader

18th September

“Intuitive analyses of transcriptomes in (mostly) human disease contexts”

Nuno Morais – Group Leader

2nd October

“Killing straight, killing fast, killing deep: chasing bacteria in biofilms”

Miguel Castanho – Group Leader

16th October

“Chemical Physiology of Antibody Conjugates and Natural Products”

Gonçalo Bernardes – Group Leader

13th November

“The importance of being naïve”

Ana Espada de Sousa – Group Leader

27th November

“Follicular T cell subsets”

Luís Graça – Group Leader

11th November

“*Plasmodium* liver infection & antimalarial strategies - Overview of work from 2019”

Miguel Prudêncio – Group Leader

Metabolism Club

10th January

“Biomarkers and therapeutic targets in metabolic liver disease”

Cecília Rodrigues – Faculty of Pharmacy of the University of Lisbon

7th March

“Unravelling the functional fingerprint of synaptic mitochondria”

Andreia Pereira – Vanessa Morais Lab

4th April

“Measuring cell metabolism and ATP production with the Agilent Seahorse XF Analyzer”

Alfredo Maldonado

9th May

“To divide or differentiate – the fate of *Drosophila* neural stem cells”

Catarina Homem - CEDOC

6th June

“Metabolic Regulation of Delta One T cells”

Carolina Jardim – Bruno Silva-Santos Lab

11th October

“Carotid body: A major contributor for sympatho- activation in metabolic diseases”

Sílvia Conde – CEDOC

Host: Luísa Figueiredo

7th November

“IL-7 regulates autophagy in opposite manners to consistently promote T-cell acute lymphoblastic leukemia cell viability”

Daniel Ribeiro – João Barata Lab

Monday Lecture

7th January

“Transcriptional and epigenetic states of oligodendroglia in development and disease: insight from single cell omics”

Gonçalo Castelo-Branco – Karolinska Institutet

Host: Sérgio de Almeida

14th January

“Exploring the role of non-coding mutations in pancreatic diseases through the analysis of the zebrafish pancreas regulome”

José Bessa – i3S

Host: Domingos Henrique

21st January

Best Master Thesis: “Programmed DNA damage as a new tool to regulate gene activation”

Cristiana Morgado – Sérgio de Almeida Lab

21st January

Best Master Thesis: “Dissecting functional and molecular signatures of anti-tumour myeloid cells *in vivo*”

Raquel Lopes – Bruno Silva-Santos Lab

21st January

Best Master Thesis: “New insights into interferon-mediated immune responses elicited by *Plasmodium* liver stage infection”

Diana Moita – Miguel Prudêncio Lab

28th January

“Bacterial Cell Division: may the force be with you”

Mariana Gomes Pinto – ITQB

Host: Mário Ramirez

4th February

“Getting in and out of cell division with the right number of chromosomes”

Claudio Sunkel – i3S

Host: Domingos Henrique

18th February

“Self-organization and patterning dynamics in *Drosophila*”

Francois Schweisguth – Institut Pasteur

Host: Domingos Henrique

25th February

“Our first choices: decoding signals during developmental transitions (lessons from quantitative biology)”

Sílvia Santos – The Francis Crick Institute

Host: Domingos Henrique

11th March

“Spatial control of time during chromosome segregation”

Hélder Maiato – i3S

Host: Domingos Henrique

18th March

“Sensing the matrix: transducing mechanical signals from integrins to the nucleus”

Pere Roca-Cusachs – Institute for Bioengineering of Catalonia

Host: Francisca Vasconcelos (Cláudio Franco Lab)

25th March

“Molecular studies of biological rhythms”

Charalambos P. Kyriacou – University of Leicester

Host: Luísa Lopes

1st April

“The role of lipolysis in metabolic tissue crosstalk”

Rudolph Zechner – University of Graz

Host: Luísa Figueiredo

8th April

“Genome organization of pluripotency states”

Raffaella Santoro – University of Zurich

Host: Claus Azzalin

29th April

“Disease tolerance as an inherent component of immunity”

Miguel Soares – Instituto Gulbenkian de Ciência

Host: Domingos Henrique

6th May

“IL-17 regulates CNS autoimmunity via modulation of gut microbiota”

Ari Waisman – Institute for Molecular Medicine Mainz

Host: Marc Veldhoen

13th May

“Harnessing the placebo: Using the brain to control immunity”

Asya Rolls – Technion - Israel Institute of Technology

Host: Julie Ribot (Bruno Silva-Santos Lab)

20th May

“Regnase-1: an endoribonuclease important for inflammatory and immune responses”

Shizuo Akira – Osaka University

Host: Marc Veldhoen

3rd June

“Molecular control of T cell tolerance and function”

Chen Dong – Tsinghua University, Beijing

Host: Luís Graça

17th June

“Relief of transcriptional repression by phosphorylation”

Zeev Paroush – Faculty of Medicine, Hebrew University of Jerusalem

Host: Domingos Henrique

24th June

“*In vitro* studies investigating the mechanobiology of epithelial tissues”

Benoit Ladoux – Université Paris Diderot and CNRS

Host: Cláudio Franco

1st July

“Novel approaches to face an old problem: how to manipulate immune response after transplantation”

José Pérez Simón – Instituto de Biomedicina de Sevilla/Hospital Universitario Virgen del Rocío

Host: João Lacerda

8th July

“Epileptogenesis and inflammation: what we have learned from neuropathology”

Eleonora Aronica – University of Amsterdam

Host: Ana Sebastião

2nd September

“Regulation of alternative splicing by transcription elongation and the therapy of a hereditary disease”

Alberto Kornblihtt – Buenos Aires University

Host: M. Carmo-Fonseca

9th September

“The many faces of Xist RNA in 3D”

Jeannie T. Lee – Massachusetts General Hospital, Harvard Medical School

Host: Claus Azzalin

16th September

“New Monocytes/macrophages abnormalities in Rheumatoid Arthritis”

Xavier Marriette – Hôpitaux Universitaires Paris-Sud

Host: João Eurico da Fonseca

23rd September

“Multifunctional nanovaccines as effective immunotherapies against solid tumors”

Helena Florindo – Faculty of Pharmacy of the University of Lisbon

Host: Sérgio de Almeida

30th September

“Epigenetic modulation of repeat elements - implications for non-genetic inheritance”

Anne Ferguson-Smith – University of Cambridge

Host: Simão Rocha (Carmo-Fonseca Lab)

7th October

“Positioning of secretory organelles in dendrites: focus on F-actin”

Marina Mikhaylova – Center for Molecular Neurobiology, Hamburg

Host: Vanessa Morais

14th October

“Innate Immunity of baboons and men and GMO cattle-how ion channels kill parasites”

Jayne Raper – Hunter College - New York University School of Medicine

Host: Luísa Figueiredo

21st October

“What can we learn from experimental fitness landscapes?”

Claudia Bank – Instituto Gulbenkian de Ciência

Host: Nuno Morais

28th October

“A multiplicity of mechanisms for proactive behavioral control in the basal ganglia”

Joe Paton – Champalimaud Foundation

Host: Miguel Remondes

4th November

“Insights into the secretion machine of virulence factors in apicomplexan parasites”

Maryse Lebrun – University of Montpellier

Host: Luísa Figueiredo

11th November

“Drug Discovery in the Academic Setting – the Tri-Institutional Therapeutics Discovery Institute in New York”

Ivo Lorenz – Therapeutics Discovery Institute and Weill Cornell Medicine

Host: Gonçalo Bernardes

18th November

“Telomeres and the control of cell proliferation”

Teresa Teixeira – Institut de Biologie Physico-Chimique

Host: Claus Azzalin

25th November

“Serotonin, artificial intelligence and depression”

Zach Mainen – Champalimaud Foundation

Host: Miguel Remondes

2nd December

“Targeted Protein Aggregation”

Joost Schymkowitz – VIB-KU Leuven Center for Brain & Disease Research

Host: Nuno Santos

9th December

“Metabotropic glutamate receptors in autism spectrum disorder and intellectual disability”

João Peça – Center for Neuroscience and Cell Biology, Coimbra

Host: Luísa Lopes

16th December

Best Master Thesis: “Dissecting the role of miRNAs on the balance between effector and regulatory CD4+ T cell subsets differentiation *in vitro*”

Catarina Pelicano – Bruno Silva-Santos Lab

16th December

Best Master Thesis: “Modelling of ageing-associated gene expression alterations”

Arthur Schneider – Nuno Morais Lab

16th December

Best Master Thesis: “Aging pathology in Sprague dawley rats: background lesions and comparative study between wild type and transgenic rats with neuronal overexpression of human adenosine A2A receptors”

Pedro Ruivo – Comparative Pathology Unit

Neurosciences Seminars

7th January

“Crosstalk between CB1 receptor and adenosine A2A receptor in astrocytes”

Joana Ribeiro – Ana Sebastião Lab

14th January

“Aging Pathology in Sprague Dawley: Background lesions and Comparative study between wild type and transgenic rats with Neuronal Overexpression of Human Adenosine A2A receptors”

Pedro Ruivo – Comparative Pathology Unit

21st January

“Role of SNARE-dependent gliotransmitters release by astrocytes upon A β -mediated excitotoxicity”

Joana Gomes – Ana Sebastião Lab

28th January

“Exploring brain diseases from the perspective of brain development”

Ricardo Rodrigues – Center for Neuroscience and Cell Biology, Coimbra

11th February

“Astrocytic GABA Transporter Dysfunction in Childhood Absence Epilepsy”

Carolina Pina – Ana Sebastião Lab

18th February

“Feeling control: affective and neurophysiological mechanisms of familiarity and conflict”

Gonçalo Aires de Oliveira – Miguel Remondes Lab

25th February

“Exploring the activation of NLRP3 inflammasome by reactive oxygen species in a model of epileptogenesis in organotypic slices”

Margarida Godinho – Ana Sebastião Lab

11th March

“Brain-derived neurotrophic factor & Cannabinoids: potent modulators of neural stem cells”

Rui Rodrigues – Ana Sebastião Lab

18th March

“How Our Brain Solves Dilemmas”

Bárbara Pinto Correia – Miguel Remondes Lab

25th March

“Meningeal IL-17+gd Tcells: Role in Alzheimer’s disease?”

Helena Brigas – Luísa Lopes Lab and Bruno Silva-Santos Lab

1st April

“Unravelling the expression of the NLRP3 inflammasome in astrocytes”

Antónia Ribeiro – Ana Sebastião Lab

8th April

“PINK1 and its impact in different neural cells”

Elvira Leites – Vanessa Morais Lab

29th April

“Playing with adenosine on a Rett Syndrome mouse model”

Catarina Lourenço – Ana Sebastião Lab

6th May

“Role of adenosine on the resistance to temozolomide anti-tumor agent in glioblastoma”

Vanda Nogueira – Universidade da Beira Interior and Ana Sebastião Lab

13th May

“Caffeine modulates NMDA receptor activity in the hippocampus of adolescent mice”

Robertta Martins – Instituto Biomédico, Universidade Federal Fluminense and Ana Sebastião Lab

20th May

“The endocannabinoid system, phytocannabinoids and their association with therapeutics”

Luzia Sampaio – Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro

3rd June

“Engineering of human forebrain organoids from human induced pluripotent stem cells for modeling of Rett Syndrome”

Ana Rita Gomes – Instituto Superior Técnico and Ana Sebastião Lab

24th June

“How much of Alzheimer have Alzheimer's disease mouse models?”

Sara Mendes – Nuno Morais Lab

1st July

“The neurobiology of anxiety disorders: the role played by serotonin”
Milena Viana – Universidade Federal de São Paulo

8th July

“Assessment of NLRp3 expression in A1 astrocytes”
Andrea Babić – Molecular Biology from University of Zagreb

15th July

“Targeting oligodendrogenesis in Multiple Sclerosis”
Joana Mateus – Ana Sebastião Lab

22nd July

“Síndrome de dependência de álcool: visão geral com foco nos aspetos neurobiológicos”
Isabel Cristina Céspedes – Universidade Federal de São Paulo

9th September

“Microreactors to support rat primary cortical neurons against excitotoxicity”
Adam Armada-Moreia – Ana Sebastião Lab

16th September

“Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory”
Miguel Ribeiro – Luísa Lopes Lab and Bruno Silva-Santos Lab

23rd September

“Synaptic mitochondria: In search of its functional fingerprint”
Andreia Pereira – Vanessa Morais Lab

30th September

“Interaction between BDNF/TrkB signaling and neurogenesis in epilepsy”
Leonor Rodrigues – Ana Sebastião Lab

7th October

“Modulating postnatal neurogenesis”
Filipa Ribeiro – Ana Sebastião Lab

14th October

Pitch Presentation by Master Students: “Searching for a new biomarker for Alzheimer's Disease based on BDNF receptor cleavage”
Carolina Borlido – Ana Sebastião Lab

14th October

Pitch Presentation by Master Students: “Characterization of BDNF signalling in the prefrontal cortex in the neonatal phencyclidine mouse model of schizophrenia”
Celine Freitas – Ana Sebastião Lab

14th October

Pitch Presentation by Master Students: “NLRP3 inflammasome inhibition in a model of epileptogenesis in organotypic slices – impact in neurodegeneration and epileptiform activity”
Francisco Meda – Ana Sebastião Lab

21st October

“GABAergic Dysfunction in Childhood Absence Epilepsy: From Astrocytes to Circuits”
Carolina Pina – Ana Sebastião Lab

28th October

Pitch Presentation by Master Students: “Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β -induced toxicity”
Mariana Van Zeller – Ana Sebastião Lab

28th October

Pitch Presentation by Master Students: “Impact of NLRP3 inflammasome inhibition in a model of A β -induced toxicity”
Diogo Dias – Ana Sebastião Lab

4th November

“Hippocampal tim”
Marcelo Dias – Miguel Remondes Lab

25th November

Pitch Presentation by Master Students: “Parkinson's disease: identification of novel substrates for the mitochondrial kinase PINK1”
Ana Ramos – Vanessa Morais Lab

25th November

Pitch Presentation by Master Students: “The impact of BDNF receptor cleavage in Alzheimer's disease-associated Neuroinflammation”
Mafalda Manso – Ana Sebastião Lab and iMED

25th November

Pitch Presentation by Master Students: “Cannabinoid actions on Rett Syndrome's associated deficits and its effect on post-natal neurogenesis in a female MECP2-mutant mouse model”
Svitlana Savalko – Ana Sebastião Lab

2nd December

“PINK1: A link between Mitochondria and Parkinson's Disease”
Filipa Gonçalves – Vanessa Morais Lab

16th December

“Autologous transmission”
Sodikdzhon Kodirov – Ana Sebastião Lab

Oncobiology Club

16th January

“CASZ1 in T-cell Acute Lymphoblastic Leukemia (T-ALL): adding an oncogene to the bunch!”
Bruno Cardoso – João Barata Lab

30th January

“cTRAP: inferring causality from cancer transcriptomic changes”
Nuno Agostinho – Nuno Morais Lab

27th February

“CANCER: inviting BIOMATERIALS to waltz with the devil - The GBM case study”
João Conde – Gonçalo Bernardes Lab

10th April

“Metabolic Profiling of Human Lung Tumor Metastasis”
Teresa Serafim – Sérgio Dias Lab

24th April

“PLCy1: A new Biomarker of Cetuximab Resistance in Metastatic Colorectal Cancer”
Marta Martins – Luís Costa Lab

5th June

“Methionine intake improves breast cancer immunotherapy efficacy”
Sofia Mensurado – Bruno Silva-Santos Lab

2nd October

“Reshaping myeloid cells to fight cancer”
Mariana Reis Sobreiro – Bruno Silva-Santos Lab

16th October

“Genomic and transcriptomic characterization of a leukemia mouse model”
João Neto – João Barata Lab

23rd October

“Modelling of ageing-associated gene expression alterations”
Arthur Schneider – Nuno Morais Lab

30th October

“Extracellular vesicles: from cell-cell communication to biomarkers discovery”
Bruno Costa-Silva – Champalimaud Foundation

13th November

“Single-cell transcriptomics in unravelling the cellular diversity and molecular signature that govern anti-tumour functions of myeloid cells *in vivo*”
Marta Bica – Nuno Morais Lab

11th November

“Biological effect of Clinically Relevant collagen I Fragments in the Tumour Microenvironment”
Ana Cavaco – Luís Costa Lab

Other Events

14th January

Leica Microsystems Seminar: “The Latest Microscopy Technology: decoding the 3D biology”
Francisco Porto – Leica Microsystems

31st January

CAML Session: “O que há de novo no CAML: Bruno Silva-Santos Lab | EIT Health (UL)”

1st February

“Exploring the contribution of human retroelements in species-specific mechanisms of X chromosome inactivation”

Miguel Casanova – Epigenetics and Cell Fate Unit Paris

5th February

“Molecular portraits of breast cancer and the influence of the proteomic landscape”

Anne-Lise Børresen-Dale – Oslo University Hospital

Host: M. Carmo-Fonseca

12th February

CAML Rheumatology Series: “Systemic sclerosis: improving outcomes and emerging therapies”

Christopher Denton – Institute of Immunity and Transplantation. Centre for Rheumatology and Connective Tissue Diseases, Royal Free Hospital

13th February

Back to Basics 1:0:1 Workshops: “Let’s Get Organized! With 5S Methodology”

Ana Medeiros – Pbp, Lda

20th February

Horizontes IMM: Uma Pergunta a Três | “Porque é que o cancro nos escapa?”

Fernando Rosas, Luís Costa and Bruno Silva-Santos

25th February

iMM Postdoc Day

28th February

CAML Session: “O que há de novo no CAML: Ana Sebastião Lab | Vanessa Morais Lab”

7th March

Fundo iMM-Laço | Projects Presentation

12th March

NeuroSeS Seminar: “Novos modelos pré-clínicos no estudo da doença de Alzheimer”

Luísa Lopes – Group Leader

20th March

Horizontes IMM: Uma Pergunta a Três | “Porque é que os músculos deixam de obedecer?”

Pedro Souto, Mamede de Carvalho and Edgar Gomes

26th March

CAML Rheumatology Series: “Obstetric anti-phospholipid syndrome”

Laura Andreoli – University of Brescia

15-16th April

iMM Scientific Retreat | Évora

17th April

BIG | Projects Presentation: “Selective cancer cell death using a microRNA-detector system in T-ALL”

João Barata – Group Leader

17th April

BIG | Projects Presentation: “Sensing telomeric fusions in cells”
Claus Azzalin – Group Leader

17th April

BIG | Projects Presentation: “Using the regenerative potential of zebrafish extracellular matrix to promote spinal cord repair in mammals”
Leonor Saúde – Group Leader

17th April

BIG | Projects Presentation: “A fundamental question... an amazing and straightforward hypothesis...a not easy answer!”
Maria Mota – Group Leader

14th May

NeuroSeS Seminar: “Does physical exercise improves cognition? Methodological challenges in clinical studies”
Ana Verdelho – Hospital Santa Maria, Faculty of Medicine of the University of Lisbon

15-17th May

XIII CAML PhD Students' Meeting

30th May

CAML Session: “O que há de novo no CAML: Maintaining and generating tissue resident T-cells”
Marc Veldhoen – Group Leader

19th June

Horizontes iMM: Uma Pergunta a Três | "Porque é que o cérebro deixa de comunicar com o corpo"
Paulo Teixeira Pinto, Joaquim Ferreira and Luísa Lopes

9th July

NeuroSeS Seminar: “Spinal cord injury. What can we learn from animal models?”
Leonor Saúde – Group Leader

10th September

NeuroSeS Seminar: “Preclinical models of brain metastases: how they recapitulate human disease and inform patients’ treatment”
Cláudia Faria – Hospital Santa Maria, iMM and Faculty of Medicine of the University of Lisbon

11th September

“The growing family of CD1d-restricted NKT cells”
Catarina Almeida – Peter Doherty Institute for Infection and Immunity and the University of Melbourne

27th September

European Researchers’ Night

16th October

Horizontes iMM: Uma Pergunta a Três | “Porque é que a medula espinhal não regenera?”
Salvador Mendes de Almeida, António Francisco and Leonor Saúde

24th October

Akoya Biosciences Seminar: “Integrated Approach for High-Throughput and High-Dimensional Multiplexing with Single-Cell Resolution”

29th October

“Creation and collective processes in Science and Art”

Catarina Pombo Nabais – Dept. History and Philosophy of Science, University of Lisbon

Host: Luís Graça

29th October

“Some artworks developed during residencies at research institutes”

Katrin Von Lehmann – Academy of Fine Arts, Munich

Host: Luís Graça

12th November

NeuroSeS Seminar: “Bases neuronais do processo decisional baseado na memória”

Miguel Remondes – Group Leader

18th November

Sustainable Science and Green Lab Workshop

Martin Farley – UCL, King’s College London, Green Lab Associates

18th November

JAX Seminars: “Immune System Humanized Mice for Preclinical Research”

Ralph Gareus – JAX Director Business Development – Europe

Host: Iolanda Moreira (Rodents Unit)

18th November

JAX Seminars: “Sophisticated Humanized Mouse Models to Investigate the Mechanisms of Cancer Immunotherapy”

James Keck – Senior Director of Innovation and Product Development

Host: Iolanda Moreira (Rodents Unit)

21st November

“Optogenetics: Light-controlled activation of the T cell receptor reveals kinetic proofreading”

Wolfgang Schamel – University of Freiburg, Germany

Host: Gina Fiala (Bruno Silva-Santos Lab)

22nd November

“RNA binding proteins in cancer: essential, yet undruggable?”

Jean Bertoldo – University of Halle-Wittenberg

Host: Gonçalo Bernardes

28th November

CAML Session: “Studying the neuropeptide kyotorphin: from pain to Alzheimer's, from mouse to man”

Miguel Castanho – Group Leader

12th November

“Super-Resolution made easy!”

Pedro Matos Pereira – ITQB-UNL

Parasitology Club

15th January

Sandra Trindade – Luísa Figueiredo Lab

22nd January

Back to the Future Seminar: “Prudêncio Lab: from the beginning and back to the future”

Miguel Prudêncio – Group Leader

29th January

“Back to Basics. The ‘bizarre’ *Plasmodium* Replication”

Inês Bento – Maria Mota Lab

5th February

“Microbiota’ - A new player in Host-*Plasmodium* affair”

Debanjan Mukherjee – Maria Mota Lab

12th February

“A novel role for EXP2 in invasion of *Plasmodium* sporozoites”

João Vieira – Maria Mota Lab

19th February

“Role of adipose lipolysis during *Trypanosoma brucei* infection”

Henrique Machado – Luísa Figueiredo Lab

26th February

“Pb-MDR3, a possible new player on the *Plasmodium*-Host Front-line”

Viriato M’Bana – Maria Mota Lab

12th March

Idálio Viegas – Luísa Figueiredo Lab

26th March

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

Diana Fontinha – Miguel Prudêncio Lab

2nd April

“HIV treatment has malaria transmission blocking activity”

Raquel Azevedo – Miguel Prudêncio Lab

9th April

“Metabolic Oligosaccharide Engineering - A Tool for Malaria?”

Annabel Kitowski – Gonçalo Bernardes Lab

30th April

“APPL (Apple) and EEF (Eve): Plucking a fruit of host signalling endosomes”

Aparajita Lahree – Maria Mota Lab

14th May

“Glycerol: a tissue-specific stumpy inducing factor in trypanosomes?”

Fabien Guegan – Luísa Figueiredo Lab

21st May

“*Trypanosoma brucei* infection protects against malaria”

Ana Margarida Vaz – Miguel Prudêncio Lab and Luísa Figueiredo Lab

28th May

“PbVac: an open label randomized safety and efficacy trial”

António Mendes and Helena Cabaço – Miguel Prudêncio Lab

4th June

“Optimization of a protocol to produce gametocyte cultures of *Plasmodium falciparum*”

Denise Francisco – Miguel Prudêncio Lab

11th June

“Establishing a blood-stage infection: The role of SAM in *plasmodium* development”

Maria Inês Marreiros – Maria Mota Lab

18th June

“Pre-erythrocytic malaria and the hepatic methionine metabolism”

Vanessa Zuzarte-Luís – Maria Mota Lab

25th June

“Severe Malaria: what's liver got to do with it?”

Ângelo Chora – Maria Mota Lab

2nd July

“Unraveling the role of *Trypanosoma brucei* proteins in the impairment of *Plasmodium* infection”

Adriana Temporão – Miguel Prudêncio Lab

9th July

“Towards a better understanding of *Trypanosoma brucei* metabolism in the adipose tissue”

Juan Macedo – Luísa Figueiredo Lab

23rd July

“Beyond humans: vascular sequestration of livestock trypanosomes”

Sara Pereira – Luísa Figueiredo Lab

10th September

“Breaking and entering: following the *Trypanosoma brucei* voyage into host adipose tissues”

Mariana De Niz – Luísa Figueiredo Lab

17th September

“A novel host-*Plasmodium* interaction: hope for a new antimalarial drug target”

Sonali Setua – Maria Mota Lab

24th September

Meeting Report: “Highlights of the Molecular Parasitology Meeting 2019”

Luísa Figueiredo, Sara Silva Pereira, Aparajita Lahree and Viriato M'Bana – Group Leader, Luísa Figueiredo Lab and Maria Mota Lab

1st October

“*Plasmodium* exploitation of host methionine metabolism”

Catarina Pedro – Maria Mota Lab

1st October

“Schizogony in *Plasmodium*: one cytoplasm, many nuclei”

Camila Mariano – Maria Mota Lab

8th October

“Energetic adaptation of extravascular African trypanosomes”

Inês Vicente – Luísa Figueiredo Lab

8th October

“Improved Acid-fast Stain and Histology Method for the Detection of Mycobacteria in Tissue Samples”

Pedro Marinho – Mário Ramirez Lab/Thomas Hanscheid

15th October

“Comparative immunological analyses of whole-sporozoite malaria vaccines”

Teresa Maia – Miguel Prudêncio Lab

15th October

Andreia Barreto – Miguel Prudêncio Lab

22nd October

“Studying pathogens using cryo electron tomography”

Josie Ferreira

29th October

Susan Keen Pierce and Louis Miller - National Institutes of Health

Host: Maria Mota

5th November

“*Plasmodium* cross-stage interplay modulates parasite virulence”

Sónia Pereira – Maria Mota Lab

12th November

“Homeostasis of red blood cells: A key to understand malarial anemia?”

Cristina Arias – Maria Mota Lab

19th November

“The role of EXP2 in the invasion by *Plasmodium* sporozoites”

João Vieira – Maria Mota Lab

3rd December

Henrique Machado – Luísa Figueiredo Lab

10th September

“Clock parasites: where circadian rhythm finds malaria”

Inês Bento – Maria Mota Lab

17th December

“Acting on the host actin, a novel way of *Plasmodium* to prevent its death”

Viriato M’Bana – Maria Mota Lab

Pizza Seminar

8th January

“The role of UBE2C in brain metastases”

Eunice Paisana – João Barata Lab

22nd January

“A novel role for EXP2 in *Plasmodium* sporozoite invasion”

João Vieira – Maria Mota Lab

22nd January

“Elucidating the role of synucleins in retinal neurodegeneration in Parkinson's disease, Diabetes and Ageing”

Luís Sousa – CEDOC

5th February

“Innovative therapies for Spinal Cord Injury”

Diana Pires – Technophage and Leonor Saúde Lab

19th February

“Profiling the alternative splicing landscape of senescent cells”

Mariana Ferreira – Nuno Morais Lab

19th February

“Programmed DNA damage as a new tool to regulate gene activation”

Cristiana Morgado – Sérgio de Almeida Lab

19th March

“Interplay between BDNF signaling and cognitive alterations in the subchronic phencyclidine mouse model of schizophrenia”

Sara Tanqueiro – Ana Sebastião Lab

19th March

“Immune based therapies against cancer”

Carlos Labão-Almeida – Gonçalo Bernardes Lab

2nd April

“Dissecting mechanisms of innate immune evasion in a zebrafish xenograft model”

Vanda Póvoa – Champalimaud Foundation

2nd April

“The IL-7 signaling: can we unveil novelty through proteomics?”

Luís Monteiro – João Barata Lab

30th April

“Combining in-silico and experimental approaches to study antimicrobial peptides effective against gram-negative bacteria”

Marcin Makowski – Nuno Santos Lab

30th April

“People exert more effort to avoid losses than to win”

Ana Catarina Farinha – Mamede de Carvalho Lab

14th May

“Network medicine: from the mind to the cell”

Bernardo Moura – Clínica Universitária de Psiquiatria e Psicologia Médica, Faculty of Medicine of the University of Lisbon

14th May

“Localizing skeletal muscle mRNA: does size matter?”

Helena Pinheiro – Edgar Gomes Lab

28th May

“Unraveling the impact of epigenetics on R-loop-mediated genomic instability”

João Sabino – Sérgio de Almeida Lab

28th May

"The role of PINK1 in neural cells"

Elvira Leites – Vanessa Morais Lab

11th June

“Functionalized Ionic Liquids and Deep Eutectic Solvents: Enhancing the Bioavailability of Ibuprofen”

Joana C. Bastos – LAQV-REQUIMTE, FCT-UNL

25th June

“A new player in the orchestra of nuclear positioning”

Cátia Janota – Edgar Gomes Lab

25th June

"Coupling Cell-Penetrating Peptides to exosomes: a promising strategy to target metastatic breast cancer"

Filipa Oliveira – Miguel Castanho Lab

24th September

“Functional dissection of the Xist lncRNA conserved sequences in X-chromosome inactivation”

Cláudia Gil – Carmo-Fonseca Lab

24th September

“Establishing a Blood-Stage Infection: The Role of SAM in *Plasmodium* Development”

Maria Inês Marreiros – Maria Mota Lab

8th October

“Dengue virus: from sequencing to awareness with DEN-IM”

Catarina Mendes – Mário Ramirez Lab

8th October

“Deciphering the role of DNA secondary structures in HIF1-mediated transcription”
Madalena Almeida – Sérgio de Almeida Lab

22nd October

“Unravelling the role of Ctdnep1-Eps8L2 interaction during nuclear positioning in migrating fibroblasts”
Sofia Marques – Edgar Gomes Lab

22nd October

“Diaries of a Structural Biologist: The R2TP complex”
Paulo Santo – IBET/ITQB-NOVA

5th November

“Cooperation between IL-7R signaling and HOXA9 in leukemogenesis”
Beatriz Raposo – João Barata Lab

5th November

“Revolving around circular RNAs: exploring their biogenesis and functions”
Nuno Agostinho – Nuno Morais Lab

19th November

“Mechanisms of hypoxia-independent angiogenesis”
Marta Fidalgo – Cláudio Franco Lab

19th November

“Dissecting the role of sphingosine kinases in IL-7R-mediated leukemogenesis”
Marta Fernandes – João Barata Lab

3rd December

“Identifying new regulators of flow-dependent endothelial cells polarization”
Catarina Fonseca – Cláudio Franco Lab

3rd December

“Unveiling the DNA damage response in multinucleated cells”
Inês Faleiro – Sérgio de Almeida Lab

17th December

“Generating tissue-resident memory T cells”
Leandro Fernandes – Marc Veldhoen Lab

RiboMed Seminar Series

4th September

“Coupling of transcription and alternative splicing in a whole organism: the plant response to light”
Alberto Kornblihtt – Buenos Aires University
Host: M. Carmo-Fonseca

12th November

“Dysregulation of alternative splicing in cancer and its modulation for therapy”

Rotem Karni – Hebrew University-Hadassah Medical School, Israel

Host: M. Carmo-Fonseca

Special Seminar

21st March

“New insights from genetic mouse models relevant to schizophrenia and autism: will they translate to the development of new therapeutics?”

Neil Dawson – Faculty of Health and Medicine, Lancaster University

26th March

“Searching for Common Pathogenic Mechanisms and Therapeutic Targets in Niemann-Pick Diseases”

Silvana Zanlungo – Pontifical Catholic University of Chile

Host: M. Carmo-Fonseca

28th March

“What it takes to publish in a high-impact journal? A conversation with Orla Smith, Editor at the journal Science Translational Medicine”

Orla Smith – Editor of Science Translational Medicine

Host: Marcia Triunfol (Carmo-Fonseca Lab)

28th March

“Microbiota-Host Interactions in Health and Disease”

Gabriel Nunez – University of Michigan

Host: Marc Veldhoen

29th March

“Disease Signature in Parkinson: Altered Regulons, disease mechanism and new therapeutic venues”

Fabio Klamt – Universidade Federal do Rio Grande do Sul, Brazil

Host: Marcia Triunfol (Carmo-Fonseca Lab)

10th May

“Lipid driven membrane nanodomains are fluid and interleaflet coupled”

Martin Hof – J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, Prague

Host: Nuno Santos

18th July

“Peculiar aspects of DNA and messenger RNA methylation in malaria parasites”

Artur Scherf – Institut Pasteur

Host: Luísa Figueiredo

10th September

“Fueling the firestarters”

Lydia Lynch – Harvard University & Trinity College Dublin

Host: Bruno Silva-Santos

16th September

“HIV/AIDS: Research Achievements and Future Challenges”

Jay A. Levy – University of California

Host: Ana Espada de Sousa

10th October

“Novogene, Leading Edge Genomic Services & Solutions. An introduction”

Óskar Martínez de Ilárduya – Novogene Europe

Host: Karine Serre (Bruno Silva-Santos Lab) and Pedro Prudêncio (Carmo-Fonseca Lab)

14th October

“Science to Medicine at Regeneron: Human Genetics, and Curing Ebola using New Technologies”

Neil Stahl – Regeneron Pharmaceuticals

Host: Luísa Figueiredo Lab

iMM Training Hub

The iMM is strongly committed to provide 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

Executive Manager: Filipa Nunes, PhD

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

Director of Studies and LisbonBioMed PhD Program Director: Domingos Henrique, PhD

Advanced Training in Numbers

	2019
Postdoctoral Fellows	154
Started in 2019	25
PhD Students	141
Started in 2019	20
MSc Students	58
Started in 2019	33

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-centered training, our MSc/PhD students and Postdoctoral researchers benefit from a varied curricular offer organized into several thematic Advanced Courses - scientific and thematic courses, complementary skills courses and workshops - distributed along each academic year.

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).

In 2013, iMM was awarded FCT funding to create the Lisbon Biomedical and Clinical Research PhD Programme – **LisbonBioMed**. Furthermore, iMM is a partner in five other multi-institutional FCT PhD Programmes: the PhD Programme in Bioengineering - Cell Therapies and Regenerative Medicine (**CTRM**), the PhD Programme in Molecular Biosciences - Biology at the Host Microbe Interface (**B@HMI, or INTERFACE**), the Lisbon University Doctoral Programme in Integrative Neuroscience (**NeurULisboa**), the Medicinal Chemistry PhD Programme (**MedChemTrain**), and the Medical Biochemistry and Biophysics (**M2B-PhD**) Doctoral Programme.

In 2019, iMM hosted students enrolled in 9 different FCT PhD Programmes:

- LisbonBioMed: 44
- MedChemTrain: 2
- INTERFACE: 5
- GABBA: 1
- M2B-PhD: 13
- PGCD: 4
- NeurULisboa: 14
- MIT-Portugal: 4
- CTRM: 4

In 2019, iMM has been chosen by one PhD student awarded with the “**la Caixa**” **Foundation INPhINIT – Incoming** doctoral fellowship.

Three **Innovative Training Networks (ITN)** from the European Commission programme Marie Skłodowska-Curie Actions (MSCA) anchored 4 PhD students at iMM.

Besides CAML PhD students, iMM hosted **13 PhD students from other Institutions/Universities**: Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil (1), Universidade do Porto (1), Universidade de Coimbra (2), Universidade do Algarve (1), Instituto Superior Técnico (8), Universidade de Lisboa.

In the **2019 FCT Call for PhD Scholarships**, 19 doctoral fellowships were granted to iMM as host institution.

In 2019, **23 iMM students concluded their PhD theses**, 20 of which were attributed by Faculdade de Medicina da Universidade de Lisboa (FMUL).

Advanced Courses

A total of 11 Advanced Courses were organized

6 Courses organised under the CAML PhD Programme in 2019

Basics of programming (First Steps in R for Data Science)

Organizer: Workshop group of the PhD Students Committee.

Date: 18th, 20th, 25th, 27th March, and 2nd and 3rd April (17-19h; six 2-hour sessions).

Speaker: Filipe Cadete, Postdoctoral bioinformatician at Claus Azzalin Lab.

Hands-on assistant #1: Mariana Ferreira, PhD Student at Nuno Morais Lab.

Hands-on assistant #2: Nuno Agostinho, PhD Student at Nuno Morais Lab.

In this workshop, PhD students learn the basics of programming in R, a language focused on statistical analysis widely used in bioinformatics. Students are able to grasp the concepts behind data analysis, including how to manipulate and visualize data in a reproducible and automated manner.

Graphical design: Creating Figures for Publications (Workshop)

Organizer: Workshop group of the PhD Students Committee.

Date: 30th April.

Speaker: Samuel Hertig, Science Visualization Specialist / Founder of Hertig Visualizations

The workshop approaches the most important aspects to take into account when preparing a figure for a scientific publication or poster. These include the general considerations relevant to scientific visualizations and how these are influenced by the target audience, focusing also on the differences between scientific publications and scientific posters. The basics of Adobe Illustrator and Adobe Photoshop essential for the conception of scientific figures are introduced and a hands-on session comprise a discussion of previous works and the analysis of good and bad examples of scientific images.

Scientific Communication: Turn Yourself into a Successful Speaker (Workshop)

Organizer: Workshop group of the PhD Students Committee.

Date: 23rd May.

Speaker: Michael Daniels, Postdoctoral research fellow at UK Dementia Research Institute

“Turn Yourself into a Successful Speaker” is a dynamic and interactive workshop which tackles some aspects that PhD Students find challenging when delivering a presentation, such as presenting the work as if telling a story (how to start/end and transition between slides), tackling different types of presentations, creating a dynamic speech, overcoming fear of public speaking, having a confident attitude, capturing the attention and adapting to the audience. In a second part, students do a 3-min presentation about their PhD projects, considering what they have learned in the previous session. In this way, they are able to receive direct feedback about their presentation skills and how to improve them.

Laboratory Animal Science Course for Function A (former FELASA Category B) CONGENTO-harmonized program

Organizer: Iolanda Moreira and Lara Carvalho.

Date: 17th June to 31st July (6 ECTS).

The course was organized under the CONGENTO-harmonized programme and was targeted to Function A (former FELASA Category B). 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 obtain accreditation as competent person for the practice of animal experimentation.

Network yourself into the scientific world Networking (Workshop)

Organizer: Workshop group of the PhD Students Committee.

Date: 2nd July.

Speaker: Nuno Afonso.

The workshop is targeted to biomedical research PhD students who are seeking an improvement in their capabilities on networking as a resource to advance their careers and foster their capability to develop relationships into their communities as well as out of the framework of academic research, i.e., into industry communities. The lecturer highlights the relevance of networking, pointing out as many of the myths behind it and describes ways to address networking in a manner that builds confidence while growing relationships both in academia and in industry to achieve professional objectives.

Science Careers Workshop

Organizer: Workshop group of the PhD Students Committee.

Date: 19th November.

Speaker: Filipa Robalo, Project Coordinator of Real World Evidence and Late Phase of Europe and Latin America at Eurotrials; and Inês Lopes, In-House Clinical Research Associate at PRA Health Sciences.

“Science Careers” is a series of talks to get to know jobs in science beyond research. In this session participants had the opportunity to talk with two workers of Clinical Research Organizations (CRO). During the session participants had the opportunity to know more about the daily work of the speakers, how they got there, the pros and cons of working in a CRO and to ask questions about their path and work.

Other iMM Courses

Scientific Writing Course: Structuring and writing a hypothesis-driven research paper

Organizer: Filipa Nunes.

Date: 26th September to 12th December, every Thursday (09.30-12.30h; twelve 3-hour classes plus final exam).

Speaker: Marcia Triunfol, and invited professor, Edson Rondinelli.

The goal of the course is for participants to be able to write a full hypothesis-driven research paper based on data that are provided to them (which should be considered as real and genuine data). The participants build and write each section of the research paper (Introduction, Materials and Methods, Results and Discussion) and learn how to navigate through the steps involved in producing and publishing a research paper. Additionally, participants learn how to better use the language (English) in order to produce an article that effectively conveys its message, increasing the chances of being accepted for publication in a high-impact scientific journal.

Laboratory Animal Science Course for Function A (former FELASA Category B) CONGENTO-harmonized program

Organizer: Iolanda Moreira and Lara Carvalho.

Date: 21st October to 22nd November.

The course was organized under the CONGENTO-harmonized programme and was targeted to Function A (former FELASA Category B). 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.

Data Visualization Workshop - Reveal, Don't Conceal: How to Avoid Common Data-Visualization Errors and Create More Informative Figures

Organizer: Workshop group of the PhD Students Committee.

Date: 23rd October.

Speaker: Tracey Weissgerber.

This workshop focuses on creating informative visualizations for scientific publications. Participants learn to identify common problems with visualizations in small sample size studies in the basic biomedical, translational, and biological sciences. Participants learn what types of graphs to use and how to determine which option is best for their dataset. Participants learn why it's important to use study design diagrams and flow charts and how to design these types of figures. Participants also discuss free online tools that allow users with no programming expertise to create interactive visualizations. Participants learn strategies for creating informative figures based on images, including photographs, microscopy or electron microscopy images, or images obtained using clinical techniques such as ultrasound or MRI. Finally, participants discuss how to use figures and infographics to emphasize the message of their paper and simplify the writing process.

Sustainable Science and Green Lab Workshop

Organizer: Postdoctoral Association (PDA).

Date: 18th November.

Speaker: Martin Farley (UCL, King's College London, Green Lab Associates).

Through this workshop participants learn about the relevance of sustainability within the sciences, and in particular within the laboratory. Participants are familiarized with the contributions of labs towards plastic waste, about what equipment uses the most energy, and more. In groups, participants are challenged to overcome real-world scenarios in laboratory sustainability.

Finally, future directions of sustainability in science are shared, as well as practical means to organize action within the institute through a step-wise process to support the new sustainable lab actions learned in this workshop.

Portuguese Course (Foreign Language)

Organizer: Training Hub and Postdoctoral Association (PDA).

Dates: Level A2.1, May to July (20h, 1 class/week); Levels A1 and A2/B1: December to June 2020 (45h, 1 class/level/week).

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

Other Events

Open Afternoon at iMM (targeted to 1st year Master students)

Organizer: Filipa Nunes.

Date: 28th March.

The goal of this event is to introduce iMM to Master students (1st year of the 2nd cycle of studies) and to disseminate iMM's Master projects/vacancies. The event includes presentations by the group leaders, round table discussions, visit to the labs/facilities, and social gathering with the iMM community.

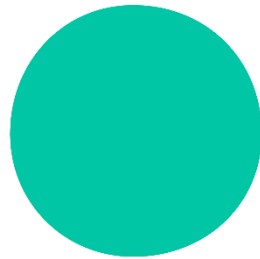
Lisbon Area PostDoctoral Meeting

Organizer: Postdoctoral Association (PDA).

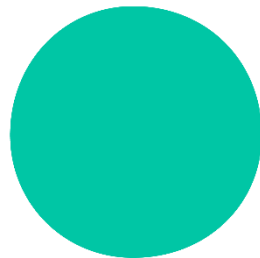
Date: 14-15th November.

Venue: Aldeia dos Capuchos Golf & SPA Hotel.

The Lisbon Area PostDoctoral (LAPD) Meeting was co-organized by the Postdoc Associations of iMM, Champalimaud Foundation, ITQB, CEDOC, iMed.Ulisboa, and UCIBIO/Requimte (FCT-NOVA). During this two-day meeting postdoctoral researchers had the opportunity to present/discuss their science, to network, to find partners, to build collaborations, and also to discuss other issues that relate to a scientific career.



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:

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

Ana Espada de Sousa Lab

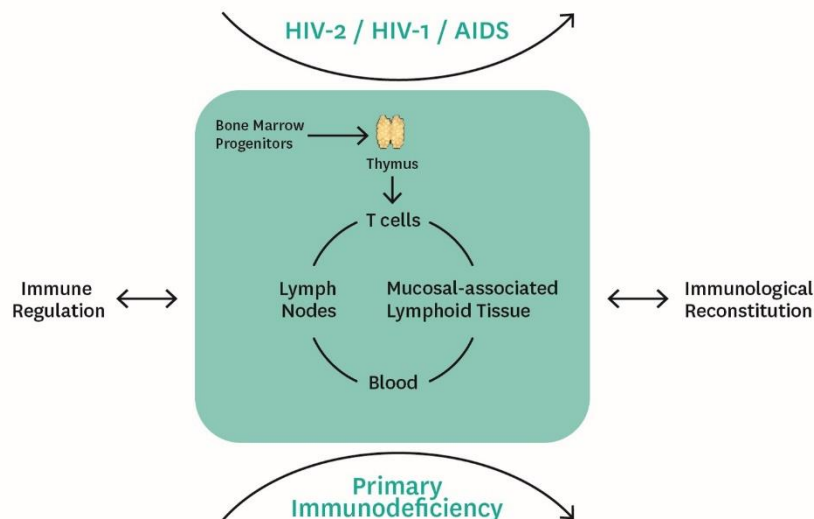
Major Interests/Objectives

- The Human Immunodeficiency & Immune Reconstitution Lab research focuses on human T-cell homeostasis and immune regulation with the ultimate goal of identifying new strategies for immunological reconstitution and targets for immune-based therapies.
- An important part of the Human Immunodeficiency & Immune Reconstitution Lab research effort is centred on HIV/AIDS immunopathogenesis, mainly through the study of HIV-2 infection, a naturally attenuated form of HIV disease.
- Human Immunodeficiency & Immune Reconstitution Lab prioritises the “bedside to the bench” approach and, given the transversal nature of Clinical Immunology, brings together physician/clinical researchers, from different medical areas, and basic researchers.

Head of Laboratory

Ana Cristina Gomes Espada de Sousa, MD, PhD

Graphical Abstract



Team

Adriana Motta Raymundo	MD/University Degree	MSc Student (Started August)
Afonso Rocha Martins de Almeida	PhD	Senior Postdoctoral Researcher (Started November)
Alexandre Augusto da Silva Figueiredo e Raposo	PhD	Senior Postdoctoral Researcher
Amelia Chiara Trombetta	MD/PhD	Clinical Researcher
Ana Berta da Fonseca Vieira Álvares e Sousa Ferrand de Almeida	MD/PhD	Clinical Researcher
Ana Catarina Taborda Godinho dos Santos	PhD	Postdoctoral Researcher
Ana Cláudia Viseu Varandas	MD/Master Degree	Trainee
Ana Cristina Costa Santos Ferreira de Oliveira Dias	MD/University Degree	Clinical Researcher
Ana Filipa Potes Semião	Master Degree	Lab Technician
Ana Isabel Gouveia Costa da Fonseca Lopes	MD, PhD With Habilitation	Clinical Researcher
Carlos José Cordeiro Lopes	MD/University Degree	Clinical Researcher (Left October)
Diana Isabel Feliciano dos Santos	University Degree	Lab Manager
Diogo Karim Hassam Carmali	University Degree	MSc Student (Started October)
Diogo Miguel Rosa Tomaz	Master Degree	Lab Technician (Left August)
Emília de Jesus da Encarnação Valadas	MD/PhD	Clinical Researcher
Inês Filipa dos Santos Martins	Master Degree	Consultant (Left October)
Inês Moranguinho Bastardo Moura	Master Degree	PhD Student
Isabel Cristina e Castro de Menezes Esteves	MD/University Degree	Clinical Researcher
Joana Merciano Labisa	University Degree	MSc Student (Started March)
João Manuel Henriques Felício Moniz	University Degree	MSc Student (Left June)
José Gonçalo Duque Pereira Monteiro Marques	MD/University Degree	Clinical Researcher
Júlio Joel Laia Henriques	Master Degree	Lab Technician (Started October)
Maria Adão Serrano de Sousa Uva	MD/University Degree	Clinical Researcher (Started October)
Maria Catarina Mota da Silva	MD/PhD	Clinical Researcher
Maria da Conceição Galvão Barata Pinto Pereira dos Santos	MD/PhD	Clinical Staff Scientist
Pedro Mota Prego Rosmaninho	PhD	Postdoctoral Researcher
Robert Alfred Badura	MD/Master Degree	Clinical Researcher
Rui Manuel Martins Victorino	MD/PhD With Habilitation	Clinical Staff Scientist
Sara Branco Pereira da Silva Fialho	MD/University Degree	Clinical Researcher
Susana Clara Barão Lopes da Silva dos Anjos	MD/PhD	Clinical Staff Scientist
Susana Maria Santos do Paço	Master Degree	Trainee (Started September)
Susana Mendes Fernandes	MD/PhD	Clinical Staff Scientist
Vitória Rafaela Costa Curto	Master Degree	PhD Student

Laboratory Keywords / Research Areas

Human T-cell Homeostasis, T-cell development in the human thymus, Immune Regulation, HIV/AIDS Immunopathogenesis, HIV-2 Infection, Primary Immunodeficiencies, Immunological Reconstitution.

Major Scientific Achievements

We showed for the first time that HIV-2 infects follicular helper CD4 T-cells and that this subset, which plays a critical role in the mounting of antibody responses, supports productive HIV-2 replication and is a major viral reservoir in HIV-2-infected individuals. These data on a model of attenuated HIV disease provides novel perspectives on the generation of protective germinal centre responses that may inform vaccine development.

Taking advantage of a natural model of intermittent exposure to bee-venom in non-allergic beekeepers, we generated *in vivo* evidence that bee-venom promotes the expansion of FOXP3-expressing CD4 T-cells in line with our previous work, supporting a possible therapeutic use of bee-venom in clinical settings that benefit from transient regulatory T-cell boost.

We pursued our goal of contributing to the design and validation of human immunology tests, and reported, in collaboration with an international consortium, a set of validated and standardized flow-cytometry based protocols to evaluate human primary immunodeficiency.

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 FOXP3 deficiency (nude/SCID): a report of 2 cases. **Blood** 117(2):688-696. (IF: 16.601, Citations: 41. Source: Web of Science).

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. (IF: 16.601, Citations: 52. Source: Web of Science).

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. (IF: 4.471, Citations: 59. Source: Web of Science).

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. (IF: 4.718, Citations: 368. Source: Web of Science).

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. (IF: 30.641, Citations: 357. Source: Web of Science).

Ongoing Research Projects

2019/2021: Contributo dos monócitos/macrófagos para a patogénese distinta da infeç o por HIV-2 em comparaç o com HIV-1: correla es cl nicas e perspetivas terap uticas. Coordinator: Amelia Chiara Trombetta. Funding Agency: Gilead Sciences. Amount: € 23 215,00. Total Amount: € 23 215,00.

2019/2020: Revealing lung repair after ARDS through the IL-22 path. Coordinator: Susana Mendes Fernandes. Funding Agency: Sociedade Portuguesa de Medicina Interna and Funda o AstraZeneca. Amount: € 10 000,00. Total Amount: 10 000,00.

2018/2021: HIV2CURE: C lulas T foliculares no cerne da infeç o HIV. Coordinator: Ana Espada de Sousa. Funding Agency: Funda o para a Ci ncia e a Tecnologia. Reference: HIV2CURE - LISBOA-01-0145-FEDER-030474. Amount: € 239 999,01. Total Amount: € 239 999,01.

2014/2019: Mye-EUNITER: European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells. Coordinator: Ana Espada de Sousa. Funding Agency: European Commission. Reference: COST BM1404. Amount: Not Applicable. Total Amount: € 645 550,00.

Transmiss o VIH-1 na infeç o aguda: evoluç o dos reservat rios em casais com terap utica precoce. Coordinator: Robert Badura. Funding Agency: Gilead Sciences. Reference: Programa Gilead G NESE. Amount: € 32 000,00. Total Amount: € 32 000,00.

Preservation of human thymic T cell production mediated by host restriction factors during HIV infection. Coordinator: Helena Cabaço. Funding Agency: Gilead Sciences. Reference: PGG/009/2015. Amount: € 30 000,00. Total Amount: € 30 000,00.

HIV-2 Infection: Clinical and Biological Repository. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences. Reference: PGG/054/2014. Amount: € 20 000,00. Total Amount: € 20 000,00.

HIV-2 impact on Lymph Nodes. Coordinator: Susana Fernandes. Funding Agency: Gilead Sciences. Reference: PGG/059/2014. Amount: € 20 000,00. Total Amount: € 20 000,00.

Other Projects

2018/2021: Estudos quantitativos de latência no VIH. Coordinator: Ruy Ribeiro. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MAT-APL/31602/2017. Amount: € 52 500,00. Total Amount: € 239 766,06.

2018/2021: Explorando o papel de microRNAs na função de células T e defesa anti-HIV. Coordinator: Margarida Gama-Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/29257/2017. Amount: € 41 187,50. Total Amount: € 239 911,12.

2017/2020: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Ramirez. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

2016/2020: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

2015/2019: ENLIGHT-TEN: European Network linking informatics and genomics of helper T cells. Coordinator: Luís Graça. Funding Agency: European Commission. Reference: MSCA ITN 675395. Amount: € 433 512,72. Total Amount: € 3 354 685,20.

Specific Donations

2019/2019: FACC - HIV Dynamics and Evolution. Coordinator: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FACC - HIV Dynamics and Evolution. Amount: € 800,00. Total Amount: € 800,00.

2019/2019: 26th HIV Dynamics and Evolution Workshop. Coordinator: Ana Espada de Sousa. Funding Agency: Janssen-Cilag Farmacêutica,Lda. Reference: 26th HIV Dynamics and Evolution Workshop. Amount: € 1 500,00. Total Amount: € 1 500,00.

2018/2019: Identification of Common Variable Immunodeficiency genetics. Coordinator: Susana Silva. Funding Agency: Octapharma, Lda; Kedrion Portugal; CSL Behring. Reference: Identification of Common Variable Immunodeficiency genetics. Amount: € 15 000,00. Total Amount: € 15 000,00.

Publications in Peer Review Journals

Godinho-Santos A, Foxall RB, Antão AV, Tavares B, Ferreira T, Serra-Caetano A, Matoso P, Sousa AE (2019). Follicular Helper T Cells Are Major Human Immunodeficiency Virus-2 Reservoirs and Support Productive Infection. **The Journal of Infectious Diseases** 221(1):122-126. (IF: 5.045, Citations: 0. Source: Web of Science).

Silva SL, Fonseca M, Pereira MLM, Silva SP, Barbosa RR, Serra-Caetano A, Blanco E, Rosmaninho P, Pérez-Andrés M, Sousa AB, Raposo AASF, Gama-Carvalho M, Victorino RMM, Hammarstrom L, Sousa AE (2019). Monozygotic Twins Concordant for Common Variable Immunodeficiency: Strikingly Similar Clinical and Immune Profile Associated With a Polygenic Burden. **Frontiers in Immunology** 10:2503. (IF: 4.716, Citations: 0. Source: Web of Science).

Blanco E, Pérez-Andrés M, Arriba-Méndez S, Serrano C, Criado I, Del Pino-Molina L, Silva S, Madruga I, Bakardjieva M, Martins C, Serra-Caetano A, Romero A, Contreras-Sanfeliciano T, Bonroy C, Sala F, Martín A, Bastida JM, Lorente F, Prieto C, Dávila I, Marcos M, Kalina T, Vlkova M, Chovancova Z, Cordeiro AI, Philippé J, Haerynck F, López-Granados E, Sousa AE, van der Burg M, van Dongen JJM, Orfao A; EuroFlow PID group (2019). Defects in memory B-cell and plasma cell subsets expressing different immunoglobulin-subclasses in patients with CVID and immunoglobulin subclass deficiencies. **The Journal of Allergy and Clinical Immunology** 144(3):809-824.(IF: 14.110, Citations: 12. Source: Web of Science).

van Dongen JJM, van der Burg M, Kalina T, Perez-Andres M, Mejstrikova E, Vlkova M, Lopez-Granados E, Wentink M, Kienzler AK, Philippé J, Sousa AE, van Zelm MC, Blanco E, Orfao A (2019). EuroFlow-Based Flowcytometric Diagnostic Screening and Classification of Primary Immunodeficiencies of the Lymphoid System. **Frontiers in Immunology** 10:1271. (IF: 4.716, Citations: 4. Source: Web of Science).

Santos MCP, Serra-Caetano A, Pedro E, Melo A, Caramalho I, Barbosa MP, Victorino RMM, Sousa AE (2019). Expansion of FOXP3+ regulatory CD4 T-cells upon exposure to hymenoptera venom during the beekeeping season. **Allergy** 74(6):1182-1184. (IF: 6.771, Citations: 0. Source: Web of Science).

Dorhoi A, Glaría E, Garcia-Tellez T, Nieuwenhuizen NE, Zelinskyy G, Favier B, Singh A, Ehrchen J, Gujer C, Münz C, Saraiva M, Sohrabi Y, Sousa AE, Delputte P, Müller-Trutwin M, Villedor AF (2019). MDSCs in infectious diseases: regulation, roles, and readjustment. **Cancer Immunology Immunotherapy** 68(4):673-685. (IF: 4.900, Citations: 2. Source: Web of Science).

van der Burg M, Kalina T, Perez-Andres M, Vlkova M, Lopez-Granados E, Blanco E, Bonroy C, Sousa AE, Kienzler AK, Wentink M, Mejstříková E, Šinkorova V, Stuchly J, van Zelm MC, Orfao A, van Dongen JJM (2019). The EuroFlow PID Orientation Tube for Flow Cytometric Diagnostic Screening of Primary Immunodeficiencies of the Lymphoid System. **Frontiers in Immunology** 10:246. (IF: 4.716, Citations: 15. Source: Web of Science).

McDermott DH, Pastrana DV, Calvo KR, Pittaluga S, Velez D, Cho E, Liu Q, Trout HH 3rd, Neves JF, Gardner PJ, Bianchi DA, Blair EA, Landon EM, Silva SL, Buck CB, Murphy PM (2019). Plerixafor for the Treatment of WHIM Syndrome. **New England Journal of Medicine** 380(2):163-170. (IF: 70.67, Citations: 7. Source: Web of Science).

Duarte RF, Ornelas C, Silva S, Morgado R, Pereira D, Escalera D, Moreira S, Valença J, Pedro E, Branco Ferreira M, Pereira Santos MC, Pereira Barbosa M (2019). Contribution of *in vivo* and *in vitro* testing for the diagnosis of local allergic rhinitis. **Journal of Investigational Allergology and Clinical Immunology** 29(1):46-48. (IF: 3.802, Citations: 1. Source: Web of Science).

Cosme J, Spinola Santos A, Pereira Santos MC, Pereira Barbosa M (2019). Salmon roe as an emergent allergen in western countries. **Journal of Investigational Allergology and Clinical Immunology** 29(2):139-141. (IF: 3.802, Citations: 0. Source: Web of Science).

Cosme J, Spínola Santos A, Pereira Santos MC, Pereira Barbosa M (2019). Venom Immunotherapy: a 20-year experience with an ultra-rush protocol (210-min). **European Annals of Allergy and Clinical Immunology** 51(3):122-128. (IF: 1.050, Citations: 0. Source: Scopus).

Fernandes M, Lourenço T, Lopes A, Spínola Santos A, Pereira Santos MC, Pereira Barbosa M (2019). Chlorhexidine: a hidden life-threatening allergen. **Asia Pacific Allergy** 9(4):e29. (IF: 2.000, Citations: 0. Source: Web of Science/Scopus).

Pereira Santos MC, Lourenço T, Pedro E, Pereira Barbosa M, Branco Ferreira M (2019). Evolution of Api m10 specific IgE and IgG4 after one year of bee venom immunotherapy. **European Annals of Allergy and Clinical Immunology**. (IF: 1.050, Citations: 0. Source: Scopus).

Carvalho S, Marcelino J, Duarte F, Costa C, Pereira Barbosa M, Pereira Santos MC (2019). Characterization of population of patients with fish allergy and contribution of recombinant Parvalbumin Gad c 1 in diagnosis and prognosis. **Journal of Investigational Allergology and Clinical Immunology**. (IF: 3.802, Citations: 0. Source: Web of Science).

Smets F, Dobbelaere D, McKiernan P, Dionisi-Vici C, Broué P, Jacquemin E, Lopes AI, Gonçalves I, Mandel H, Pawlowska J, Kamińska D, Shteyer E, Torre G, Shapiro R, Eyskens F, Clapuyt P, Gissen P, Pariente D, Grunewald S, Yudkoff M, Binda MM, Najimi M, Belmonte N, Vos B, Thonnard J, Sokal E (2019). Phase I/II Trial of Liver Derived Mesenchymal Stem Cells in Pediatric Liver Based Metabolic Disorders: A Prospective, Open Label, Multicenter, Partially Randomized, Safety Study of One Cycle of Heterologous Human Adult Liver-Derived Progenitor Cells (HepaStem®) in Urea Cycle Disorders and Crigler-Najjar Syndrome patients. **Transplantation** 103(9):1903-1915. (IF: 4.743, Citations: 4. Source: Web of Science).

Miranda M, Martins AT, Carvalho S, Serra-Caetano A, Esteves I, Marques JG (2019). Vacinas Vivas em Crianças com Síndrome de DiGeorge/ Deleção 22q11.2. **Acta Médica Portuguesa** 32(7–8):514–19. (IF: 0.581, Citations: 0. Source: Web of Science).

Other National Publications

Pestana L, Campos Melo A, Pedro E, Pereira Barbosa M, Pereira Santos MC (2019). Biomarcadores de sensibilização primária e reatividade cruzada em doentes alérgicos a veneno de himenópteros. **Revista Portuguesa de Imunoalergologia** 27(2):105-114.

Tatiana Lourenço, Mara Fernandes, Anabela Lopes, Elisa Pedro, Manuel Pereira Barbosa, M. Conceição Pereira Santos (2019): Contribution of molecular diagnosis of bee venom allergic patients with systemic reactions during build-up phase of bee venom immunotherapy. **Arquivos de Asma Alergia e Imunologia-ASBAI**. Aceite para publicação.

Invited Lectures and Seminars

Sousa AE. Overview of the IMM participation in the Euroflow. 21st Euroflow-PID, Ghent, Belgium, March 19, 2019.

Silva SL. Polygenic burden in CVID: insights from concordant monozygotic twins. 21st Euroflow-PID, Ghent, Belgium, March 20, 2019.

Sousa AE. The Immune perturbations with ageing & HIV. Workshop “Immunology and Ageing with HIV”, Forum Janssen Infectious Diseases 2019, Lisbon, Portugal, March 23, 2019.

Sousa AE. Expansion of FOXP3⁺ regulatory CD4 T-cells upon exposure to hymenoptera venom during the beekeeping season. VI Congresso Nacional de Autoimunidade/XXV Reunião Anual do NEDAI, Luso, Portugal, April 14, 2019.

Sousa AE. Phenotypic heterogeneity of CD4 T cells: relationship with functional roles. XVI Congress of the Iberian Society of Cytometry, Salamanca, Spain, May 10, 2019.

Sousa AE. Lymphoid Tissues in HIV-2 Infection. HIV Pathogenesis: Lessons from HIV-2. ANRS AC41 International Workshop, Paris, France, June 12, 2019.

Silva SL. Infections and Inflammation - Guided Poster Walk – Conductor. International Primary Immunodeficiencies Congress 2019, Madrid, Spain, November 8, 2019.

Sousa AE. The Importance of Being Naïve. Instituto de Medicina Molecular João Lobo Antunes Seminar, Lisbon, Portugal, November 13, 2019.

Communications in International Conferences

Jesus GN, Bessa F, Amorim J, Santos J, Candeias C, Fernandes SM. Clinical outcome prediction after admission in intermediate level critical care unit: role of severity scores. 39th ISICEM, Brussels, Belgium, March, 2019. (*Selected Abstract for E-Poster Session Presentation*).

Semedo P, Fernandes SM. Mean platelet volume as a prognosis factor in cancer patients admitted to intensive care. 39th ISICEM, Brussels, Belgium, March, 2019. (*Selected Abstract for E-Poster Session Presentation*).

Raposo ASF, Tomaz D, Ângelo-Dias M, Godinho-Santos A, Tokunaga Y, Serra-Caetano A, Nunes-Cabaço H, Sousa AE. Monitoring human T-cell homeostasis: identification of different mechanisms of maintenance of regulatory and conventional naïve compartments. First meeting of the national consortium “GenomePT”, CIBIO-InBIO, Vairão, Portugal, May 10, 2019. (*Oral Presentation*).

Rosmaninho P, Raposo ASF, Abolhassani H, Hammarström L, Sousa AE, Silva SL. Mining the multigenic landscape underlying Common Variable Immunodeficiency Disorders. First meeting of the national consortium “GenomePT”, CIBIO-InBIO, Vairão, Portugal, May 10, 2019. (*Poster Presentation*).

Bajanca-Lavado P, Bettencourt C, Cunha F, Marques JG. Haemophilus influenzae serotype b vaccine failure in Portugal: a new threat. 5th Congress of the European Meningococcal and Haemophilus Disease Society, Lisbon, Portugal, May 27-30, 2019. (*Oral Presentation*).

Godinho-Santos A, Nunes-Cabaço H, Antão AV, Matoso P, Foxall RB, Rocha C, Pires AR, Fernandes SM, Sousa AE. HIV-2 is more constrained by cellular/tissue context than HIV-1: comparison of thymus and tonsil in vitro infections. HIV Pathogenesis: Lessons from HIV-2 / ANRS AC41 Workshop, Paris, France, June 11-12, 2019.

Trombetta AC, Labisa JM, Foxall RB, Tendeiro R, Godinho-Santos A, Badura R, Valadas E, Sousa AE. Similar Tfh and Tfr population proportions in aviremic HIV-2 compared to viremic HIV-1 patients: preliminary data from a single centre cross-sectional study in ART naïve patients. HIV Pathogenesis: Lessons from HIV-2 / ANRS AC41 Workshop, Paris, France, June 11-12, 2019.

Cunha M, Valadas E, Sutre AF, Domingos J, França L, Badura R. Superinfection of HIV-1 on an HIV-2 infected Portuguese Caucasian Patient. International Workshop- HIV Pathogenesis: Lesson From HIV-2 – ANRS AC41. Institute Cochin, Paris, France, June 11-12, 2019. (*Oral Presentation*).

Pedro DM, Valadas E, Sutre AF, Domingos J, França L, Badura R. SHIV-2 Infection in a large University Hospital. International Workshop- HIV Pathogenesis: Lesson From HIV-2 – ANRS AC41. Institute Cochin, Paris, France, June 11-12, 2019. (*Oral Presentation*).

Varandas C, Silva SP, Barbosa RR, Serra-Caetano A, Barbosa MP, Sousa AE, Silva SL. Autoimmunity and lymphoproliferation: different or converging phenotypes in common variable immunodeficiencies? XXXVIII Congress of the European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June 2019. *(Oral Presentation)*.

Coutinho C, Pedro E, Pereira Barbosa M, Pereira Santos MC. Characterization of the sensitization profile of honeybee sting allergic patients. XXXVIII Congress of the European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June, 2019. *(Poster Presentation)*.

Carvalho S, Cabral Duarte F, Costa C, Pereira Barbosa M, Pereira Santos MC. Contribution of molecular diagnosis in the prognosis of egg tolerance acquisition. XXXVIII Congress of the European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June, 2019. *(Oral Presentation)*.

Fernandes M, Lourenço T, Spínola Santos A, Pereira Barbosa M, Pereira Santos MC. Molecular sensitization profile to animal epithelia in an atopical population. XXXVIII Congress of the European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June, 2019. *(Poster Presentation)*.

Le Thi TG, Werkstetter K, Cabral J, Kotilea K, Urruzuno P, Kori M, Lima R, Tavares M, Homan M, Kalach N, Chiaro A, Pascual MLC, Misak Z, Miele E, Matusiewicz K, Papadopoulou A, Ugras MK, Sykora J, Rea F, Urbonas V, Krahl A, Roma E, Rogalidou M, Klemenak M, Lopes AI, Casswall T, Bontems P, Koletzko S. Current treatment of Helicobacter pylori infected children and adolescents in Europe: Interim Results of the new EuroPedHp Registry. Selected Oral Presentation (Main Session). Espghan Annual Meeting, Glasgow, Scotland, June, 2019. *(Oral Presentation)*.

Kalach N, Zrinjka M, Delebarre M, Verdum S, Bontems P, Kori M – Israel, Homan M – Slovenia, Alaron T, Cabral J, Cadranel S, Casswall T, Chong S, Cilleruelo ML, Faraci S, Koletzko S, Lopes AI, Martinez Gomez MJ, Megraud F, Miele E, Oleastro M, Papadopoulou A, Pehlivanoglu E, Raymond J, Rea F, Rogalidou M, Roma E, Rowland M, Tavares M, Ugras M, Urbonas V, Urruzuno P, Yahav J. Systematic review and meta-analysis of histological gastritis according to the updated Sydney classification in Helicobacter pylori positive and negative children (on Behalf the ESPGHAN Helicobacterpylori working group). Espghan Annual Meeting, Glasgow, Scotland, June, 2019. *(Oral Presentation)*.

Rebello SD, Duarte Ferreira R, Silva SL, Fernandes I, Tornada A. Good' Syndrome In Young Women – an Unusual Presentation. XVIII European Congress of Internal Medicine, Lisbon, Portugal, August 29-31, 2019. *(Poster Presentation)*.

Raposo ASF, Tomaz D, Ângelo-Dias M, Godinho-Santos A, Tokunaga Y, Serra-Caetano A, Nunes-Cabaço H, Sousa AE. Homeostasis of human naïve CD4 T-cells: changes in transcriptomes of regulatory and conventional cells reveal distinct mechanisms of maintenance independent of thymic output. 2019 Focused Meeting of the European Society for Immunodeficiency ESID 2019, Brussels, Belgium, September 18-21, 2019. *(Selected Abstract for E-Poster Session Presentation)*.

Rosmaninho P, Ferreira RD, Silva S, Cavadas B, Pereira L, Camara R, Faria E, Regateiro F, Hammarstrom L, Raposo ASF, Sousa AE, Silva SL. Genome-wide study of patients with primary antibody deficiency and gastric carcinoma. 2nd European Society for Immunodeficiencies Focused Meeting - ESID 2019, Brussels, Belgium, September 18-21, 2019. *(Selected Abstract for E-Poster Session Presentation)*.

Duarte Ferreira R, Rosmaninho P, Silva SP, Raposo A, Ferreira C, Sousa AE, Silva SL. Synchronous gastric and hepatocellular carcinomas in a patient with primary antibody deficiency. Focused Meeting of the European Society for Immunodeficiency ESID 2019, Brussels, Belgium, September 18-21, 2019. *(Selected Abstract for E-Poster Session Presentation)*.

Barreiros C, Abecassis M, Martins J, Fernandes SM. Prognostic implication and adverse events associated with very high-dose norepinephrine in septic shock patients. 32nd Annual Congress of European Society of Intensive Care, Berlin, Germany, October 2019. *(Selected Abstract for E-Poster Session Presentation)*.

Monteiro J S, Mendo T, Reis G, Carlos M, Seves G, Marques, JG. Periodic Fever – diagnostic challenge. 11th Excellence in Pediatrics Conference, Copenhagen, Denmark, December 5-7, 2019. *(Poster Presentation)*.

Communications in National Conferences

Claro AR, Teixeira A, Esteves I, Marques JG. Profilaxia Pós Contacto com Varicela em Imunodeficientes: Imunoglobulina e Aciclovir? XXV Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 13-15, 2019. *(Poster Presentation)*.

Moreira B, Gonçalves C, Jorge J, Castaninha S, Esteves I, Prata F, Marques JG. Sífilis Congénita – ainda uma realidade. XXV Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 13-15, 2019. (*Poster Presentation*).

Claro AR, Varandas AC, Fraga S, Sousa AB, Alcobendas R, Esteves I, Maruques JG. Canakinumab na Síndrome de hiperimmunoglobulinémia. IX Reunião do Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Poster Presentation*).

Viegas IF, Curado AD, Pereira-Santos MC, Albuquerque AS, Salgado C, Palaré MJ, Esteves I, Marques JG, Ferrão A. Citopenias Imunes – a Complexidade Diagnóstica e Terapêutica. IX Reunião do Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Poster Presentation*).

Fernandes M, Silva SP, Potes AF, Santos DF, Pais M, Ferrão A, Sousa AE, Silva SL. Citopenias, Doença linfocítica-granulomatosa pulmonar e infeção – Um caso representativo da complexidade na IDCV. A interface imuno-hematológica – IX Reunião do Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Poster Presentation*).

Curado AD, Viegas IF, Santos DF, Potes AF, Palaré MJ, Salgado C, Esteves I, Ferrão A. Quando a Síndrome de Evans finalmente se revela. A interface imuno-hematológica – IX Reunião do Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Poster Presentation*).

Gonçalves CA, Soares M, Omoyinmi E, Sousa AE, Sousa AB, Pinto SR, Marques JG. Variante A91v em estado homozigótico no gene da perforina como causa de síndrome Hemofagocítica. IX Reunião do Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Oral Presentation*).

Duarte Ferreira R, Silva SP, Marques T, Serra-Caetano A, Sousa AB, Sousa AE, Silva SL. Severe autoimmunity and granulomatous disease in a complex CVID patient - a diagnostic challenge- A interface imuno-hematológica. IX Reunião Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Oral Presentation*).

Carvalho S, Cosme J, Silva SP, Serra-Caetano A, Sousa AE, SilvaSL. Síndrome de Hiper-IgM: Caso Clínico. A interface imuno-hematológica. IX Reunião Grupo Português de Imunodeficiências Primárias, Lisbon, Portugal, March 8, 2019. (*Poster Presentation*).

Fernandes A, Gonçalves C, Azevedo S, Lopes AI. Estão os Adolescentes com Doença Inflamatória preparados para a transição? Estudo Piloto. XXXII Reunião Anual da Sociedade Portuguesa de Gastrenterologia, Hepatologia e Nutrição Pediátrica, Curia, Portugal, March 21-22, 2019. (*Oral Presentation*).

Azevedo S, Fernandes A, Gonçalves C, Lopes AI. Utilização de Vedolizumab na Colite Ulcerosa Pediátrica. Serie de Casos. XXXII Reunião Anual da Sociedade Portuguesa de Gastrenterologia, Hepatologia e Nutrição Pediátrica, Curia, Portugal, March 21-22, 2019. (*Oral Presentation*).

Fernandes A, Carvalho A, Lopes AI. Utilização de Vedolizumab na Colite Ulcerosa Pediátrica. Serie de Casos. XXXII Reunião Anual da Sociedade Portuguesa de Gastrenterologia, Hepatologia e Nutrição Pediátrica, Curia, Portugal, March 21-22, 2019. (*Oral Presentation*).

Silva PM, Amorim AC, Claro AR, Varandas AC, Mouzinho A, Prata F, Marques JG. Criptosporidiose grave em adolescente com SIDA: Eficácia da associação de paromomicina, azitromicina, morfina e TARc. 3º prémio de comunicações livres. XVI Jornadas Nacionais de Infeciologia Pediátrica da SIP-SPP, Braga, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Claro AR, Amorim A, Silva P, Varandas AC, Esteves I, Mouzinho A, Santos T, Marques JG. Meningite tuberculosa. XVI Jornadas Nacionais de Infeciologia Pediátrica da SIP-SPP, Braga, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Rebelo SD, Duarte Ferreira R, Silva SL, Fernandes I, Tornada A. Síndrome de Good em mulher jovem – uma apresentação pouco comum. 25º Congresso Nacional de Medicina Interna, Vilamoura, Portugal, May 23-26, 2019. (*Poster Presentation*).

Varandas CV, Gouveia V, Claro A, Silva P, Amorim A, Pinto S, Mouzinho A, Prata F, Marques JG. Fusobacterium necrophorum – uma bactéria emergente na etiologia da otomastoidite. XVI Jornadas Nacionais de Infeciologia Pediátrica da SIP-SPP, Braga, Portugal, May 30- June 1, 2019. (*Poster Presentation*).

Lourenço T, Lopes A, Spinola Santos A, Pereira Santos MC, Pereira Barbosa M. Hipersensibilidade à cefazolina no perioperatório: casuística de um centro de referência. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. (*Oral Presentation*).

Silva MI, Paulina M, Costa C, Duarte FC, Pereira Barbosa M, Pereira Santos MC. Síndrome LTP: caracterização do perfil de sensibilização-Método Alex Macroarray. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Oral Presentation)*.

Carvalho S, Lopes A, Spínola Santos A, Pereira Santos MC, Pereira Barbosa M. Reações alérgicas perioperatórias em idade pediátrica. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Oral Presentation)*.

Limão R, Spínola Santos A, Araújo L, Cosme J, Inácio F, Tomaz E, Ferrão A, Santos N, Sokolova A, Môteite A, Falcão H, Cunha L, Ferreira A, Braz A, Ribeiro F, Lozoya C, Leiria Pinto, Pptrates S, Plácido J, Coimbra A, Taborda-Barata L, Pereira Santos MC, Pereira Barbosa M, Pineda F. Perfil de sensibilização molecular do ácaro Dermatophagoides Pteronyssinus em Portugal. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Oral Presentation)*.

Fernandes M, Lourenço T, Duarte Ferreira R, Spínola Santos A, Pereira Barbosa M, Pereira Santos MC. Perfil de sensibilização molecular a epitélios de animais numa população atópica. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Oral Presentation)*.

Paulino M, Duarte Ferreira R, Castillo M, Costa C, Pedro E, Pereira Barbosa M, Pereira Santos MC. Alergia ao abelhão: dupla sensibilização ou reatividade cruzada? XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Oral Presentation)*.

Coutinho C, Pineda F, Castilho M, Pedro E, Pereira Barbosa M, Pereira Santos MC. Caracterização do perfil de sensibilização de doentes alérgicos a veneno de abelha. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Paulino M, Costa C, Pereira Barbosa M, Pereira Santos MC. Perfil de sensibilização molecular de doentes com síndrome de proteínas de transferência lipídica e associação com características clínicas. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Carvalho S, Lopes A, Pereira Santos MC, Pereira Barbosa M. Ondansetron: amigo ou inimigo? XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Limão R, Lopes A, Pereira Santos MC, Pereira Barbosa M. Reacção de hipersensibilidade ao paracetamol mediada por IgE - Caso clínico. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Fernandes M, Lourenço T, Brás R, SP Silva, Silva SL, Barbosa MP. Agamaglobulinémia ligada ao X: a experiência de um centro de referência. Comunicação Oral XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Lourenço T, Fernandes M, Silva S, Silva, Barbosa MP. Síndrome de Good: uma entidade a reconhecer. Casuística de um centro de referência. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Varandas AC, Caldeira L, Silva SL, Costa C, Lopes A, Caiado J, Pedro E, Cosme J, Alonso E, Marcelino J, Fátima Duarte, FD, Fernandes NP, Neto M, Ferreira MB, Santos AS, Pereira Barbosa M. Angioedema hereditário: 24 anos de experiência de um centro de referência. XL Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019. *(Poster Presentation)*.

Rebelo D, Vassal H, Prata F, Fernandes S, Marques JG. Esporotricose – Caso Clínico. 20º Congresso Nacional de Pediatria, Estoril, Portugal, November 12-15, 2019. *(Poster Presentation)*.

Claro AR, Silva P, Varandas AC, Amorim AC, Esteves I, Pinto S, Prata F, Mouzinho A, Marques JG. Sarcoma de Kaposi em adolescente com SIDA- remissão sob terapêutica antirretroviral. 20º Congresso Nacional de Pediatria, Estoril, Portugal, November 12-15, 2019. *(Poster Presentation)*.

Amorim AC, Claro AR, Varandas C, Silva P, Esteves I, Marques JG. Dacrioadenite relacionada com doença IgG4. 20º Congresso Nacional de Pediatria, Estoril, Portugal, November 12-15, 2019. *(Poster Presentation)*.

Organization of Conferences

Lopes AI. President of Organizing Committee. Reunião Anual da Seção de Endoscopia Digestiva Pediátrica da SPED. Avanços e perspetivas atuais em Endoscopia Digestiva Pediátrica e Mini-Curso com Simulador, Lisbon, Portugal, January 11-12, 2019.

Lopes AI. President of Scientific and Organizing Committee. Jornadas Anuais do Departamento de Pediatria, Hospital Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February, 2019.

Lopes AI. Co-President of Scientific and Organizing Committee. I Simpósio Ibérico Diagnóstico Precoce da Doença Celíaca, Lisbon, Portugal, March 16, 2019.

Sousa AE. Co-Organizer. 26th International HIV Dynamics & Evolution, Cascais, Portugal, March 24-27, 2019.

Sousa AE. Co-Organizer. HIV Pathogenesis: Lessons from HIV-2. ANRS AC41 International Workshop, Paris, France, June 11-12, 2019.

Silva SL. Co-Organizer. International Primary Immunodeficiencies Congress 2019, Madrid, Spain, November 8, 2019.

Internationalization

Sousa AE, Silva Susana SL. Part of the EuroFlow International Consortium on Primary Immunodeficiency. <http://euroflow.org/>

Sousa AE. National Coordinator and Member of the Management Committee of the COST Action BM1404 “European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells (Mye-EUNITER)”. 2014/2019. Agency: European Commission. Reference: COST BM1404. <http://www.mye-euniter.eu/>

Sousa AE. Member of ENLIGHT-TEN - European Network Linking Informatics and Genomics of Helper T cells comprising TEN beneficiaries. 2015/2019 – ETN funded by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No.: 675395. <http://www.enlight-ten.eu/>

Sousa AE. Member of the EFIS-Immunology Letters (IL) Study Group titled “T_CELL_CONNECT_EUROPE”, European Federation of Immunology Societies (EFIS). <https://www.efis.org/efis-support/efis-il-study-groups/index.html>

Sousa AE. Expert panel member for the Norway Research Council for grant reviews in the area of Immunology and Infection.

Prizes, Honours and Awards

Prémio NEDAI de Autoimunidade 2019, NEDAI, Sociedade Portuguesa de Medicina Interna, Portugal, April 14, 2019.

Prémio SPAIC_ROXALL – Pereira Santos MC, Lourenço T, Pedro E, Pereira-Barbosa M, Branco Ferreira M. Evolution of Api m10 specific IgE and IgG4 after one year of bee venom immunotherapy. Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019.

Prémio melhor Poster SPAIC 2019 – Coutinho C, Pineda F, Castillo M, Pedro E, Pereira Barbosa M, Pereira-Santos MC. Caracterização do Perfil de Sensibilização de Doentes Alérgicos à Picada de Abelha. Reunião anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica a SPAIC, Albufeira, Portugal, October, 2019.

Industry Contract Research

Badura R. Advisory board of VIIV.

Government / Organization Contract Research

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 Board of the FCT PhD program LisbonBioMed, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa.

Sousa AE. Member of the Comissão Científica de Biociências da Santa Casa da Misericórdia de Lisboa.

Victorino RMM, Sousa AE, Lopes AI. Members of the Scientific Council. Faculdade de Medicina da Universidade de Lisboa.

Victorino RMM, Sousa AE. Members of the Scientific Board of the PhD Program of the Lisbon Academic Medical Centre.

Victorino RMM. Member of the Scientific Council of the Fundação Pulido Valente.

Victorino RMM. Member of the Clinical Research Committee from University Hospital Santa Maria.

Silva SL, Marques JG. Members of the Comissão Técnica de Vacinação da Direção-Geral de Saúde.

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 *Haemophilus influenzae* Invasive Disease Study Group in the Child.

Lopes AI. Member of the Working Group for Clinical Curriculum Review. Faculdade de Medicina da Universidade de Lisboa.

Lopes AI. Member of the Commission for Assessment of Teaching Performance, Faculdade de Medicina da Universidade de Lisboa.

Lopes AI. Pedagogical Year Coordinator (5th Year), Faculdade de Medicina da Universidade de Lisboa.

Lopes AI. Member of the Board of the Pediatric Gastroenterology College - Portuguese Medical Association (Ordem dos Médicos).

Lopes AI. Member of the Ethical Committee of Hospital Santa Maria and Lisbon Academic Medical Centre.

Lopes AI. Member of the Lisbon University College “Food, Farming and Forestry” (F3).

Lopes AI. Head of Pediatric Department, University Hospital Santa Maria, Centro Hospitalar Lisboa Norte.

Lopes AI. Member of the Working Group for Leadership Training in Health Management, University Hospital Santa Maria, Centro Hospitalar Lisboa Norte.

Lopes AI. President of Endoscopy Pediatric Section of Portuguese Endoscopy Society (SPED).

Lopes AI. Coordination of the *Anemia and Pediatric IBD* Study Group of Pediatric Society of Gastroenterology

Fernandes SM. Member of the GAPIC - Department for promotion of scientific research for medical students and MDs. Faculdade de Medicina da Universidade de Lisboa.

Advanced Teaching

Sousa AE, Pereira-Santos MC, Victorino RMM, Silva SL, Fernandes SM. 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, Victorino RMM, Silva SL, 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.

Sousa AE, Silva SL, Fernandes SM, Mota C, Godinho-Santos A, Valadas E, and Badura R. Collaboration and Lectures in Master-course Clinical Microbiology and Emerging Infectious Diseases. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Pereira Santos MC. Specialty in Immunoallergology: Supervision of the Clinical Immunology Laboratory training period for the final degree (Ordem dos Médicos/Ministry of Health).

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. Chair of Pediatrics University Clinic (3 Disciplines of Pediatrics (Introduction to Childhood Medicine, Module VI I, Module VI II), core curriculum, 2nd, 4th and 5th year of the Degree in Medicine. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Lopes AI. Scientific Coordination of I Post-Graduated Course in Childhood Neurodevelopment, 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.

Marques JG. Terapêutica com Oseltamivir. Sessão clínica do Serviço de Pediatria do Hospital Garcia de Orta, Almada, Portugal, January 7, 2019.

Marques JG. Vacinas e Doenças Raras, o que é importante saber. VI Simpósio Doenças Raras, Sintomas Comuns, Porto, Portugal, January 23, 2019.

Silva SL. Infecções de repetição na criança sem imunodeficiência – que critérios, como avaliar e que propostas terapêuticas. XV Jornadas de Alergologia de Lisboa, Lisbon, Portugal, January 25, 2019.

Marques JG. O Programa Nacional de Vacinação em Imunodeprimidos. CIMAGO – Curso Vacinação no Doente com Imunodepressão. Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, January 25, 2019.

Marques JG. Doença Invasiva por Haemophilus influenzae em Portugal. 14º Curso de Infeciologia Pediátrica, Coimbra, Portugal, February 1, 2019.

Marques JG. Terapêutica antiviral com oseltamivir e aciclovir: a quem, quando e como. 14º Curso de Infeciologia Pediátrica, Coimbra, Portugal, February 1, 2019.

Lopes AI. Para Além da Alergia na Doença Gastrointestinal: Doença Celiaca. Simposio. IX Congresso Nacional de Patologia Clínica, Organização Sociedade Portuguesa de Patologia Clínica, February 22-23, 2019.

Marques JG. Exantemas. Curso Pediatria na Urgência. Centro de Formação do Centro Hospitalar Lisboa Norte, Lisbon, Portugal, March 1, 2019.

Lopes AI. Anemia e Doença Inflamatória em Idade Pediátrica – Perspetiva Atual. XXXII Reunião Anual da Sociedade Portuguesa de Gastreenterologia, Hepatologia e Nutrição Pediátrica, Curia, Portugal, March 21-22, 2019.

Lopes AI. Anemia e Doença Inflamatória. Consenso do Grupo de Trabalho da SPGP. XXXII Reunião Anual da Sociedade Portuguesa de Gastreenterologia, Hepatologia e Nutrição Pediátrica, Curia, Portugal, March 21-22, 2019.

Silva SL. Síndrome de Evans à luz dos novos conhecimentos. A interface imuno-hematológica. IX Reunião Grupo Português de Imunodeficiências Primárias, Lisboa, Portugal, March 8, 2019

Silva SL. Bases Imunológicas da Vacinação. Vaccines Academy, Lisbon, Portugal, March 29, 2019.

Marques JG. O Programa Nacional de Vacinação. Vaccines Academy, Lisbon, Portugal, March 29, 2019.

Sousa AE. Primary Immune Deficiency in the Adult: an under-recognized common condition. Congresso NEDAI 25 anos 2019, Curso Pré-Congresso, Imunologia básica a partir da clínica. Academia de Imunologia. Luso, Portugal, April 6, 2019.

Sousa AE. “HIV Cure”. Congresso NEDAI 25 anos 2019, Curso Pré-Congresso, Imunologia básica a partir da clínica. Academia de Imunologia. Luso, Portugal, April 6, 2019.

Sousa AE. HIV-2 infection: functional cure? Congresso NEDAI 25 anos 2019, Curso Pré-Congresso, Imunologia básica a partir da clínica. Academia de Imunologia. Luso, Portugal, April 6, 2019.

Silva SL. Vigilância de neoplasias em IDP. Curso Pre-Congresso “Imunodeficiências Primárias”, satélite ao VI Congresso Nacional de Autoimunidade, Luso, Portugal, April 10 2019.

Marques JG. Vacinas extra-PNV: Hepatite A, HPV nos rapazes, Meningococos B e ACWY, Varicela e Gripe. 2º Curso de Pós-Graduação em Infeciologia Pediátrica, Lisbon, Portugal, April 12, 2019.

Badura R. Big Data e Doenças Infecciosas. IV Conferência Infeção e Doenças Infecciosas, Campo Maior, Portugal, May 25, 2019.

Marques JG. Otimização da prescrição de antibióticos em Pediatria. XVI Jornadas Nacionais de Infeciologia Pediátrica da SIP-SPP, Braga, Portugal, May 30-June 1, 2019.

Marques JG. Doença invasiva por Haemophilus influenzae em Portugal. XVI Jornadas Nacionais de Infeciologia Pediátrica da SIP-SPP, Braga, Portugal, May 30-June 1, 2019.

Sousa AE. HIV Pathogenesis: from Acute through Chronic Infection HCPA Advanced Course in HIV Therapeutic Management - 4th Ed. HPCA – Hospital and Clinical Academy, Lisbon, Portugal, June 6, 2019.

Silva SL. Etiologias a não esquecer – Imunodeficiências Primárias. Reunião da Comissão de Trabalho de Bronquiectasias da SPP, Lisbon, Portugal, June 29, 2019.

Marques JG. Vacinas – Mitos e controvérsias. 9ªs Jornadas de Pediatria Aveiro-Viseu. Viseu, Portugal, October 3-4, 2019.

Silva SP. Workshop I – Hipogamaglobulinemia primária ou secundária. 40ª Reunião Anual da SPAIC, Albufeira, Portugal, October 11-13, 2019.

Silva SL. Infecções recorrentes na Infância. Escolas SPAIC de Alergia e Asma em Medicina Geral e Familiar 2019, Carcavelos, Portugal, October 18, 2019.

Fernandes SM. The art of clinical Reasoning Workshop. 6th Beyond Med. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. October 23, 2019.

Marques JG. Exantemas infecciosos. 14^o Curso de Pós-Graduação em Doenças Infecciosas, Lisboa, Portugal, October 28, 2019.

Marques JG. Anti-vacinação e o Perigo para a Saúde Pública. Congresso Nacional de Estudantes de Medicina 2019, Lisbon, Portugal, November 17, 2019.

Marques JG. Antibioterapia em pediatria. 10^o Curso de Antibioterapia do Hospital da Luz, Lisbon, Portugal, November 20, 2019.

Silva SL. Sistema Imunitário – Imunoreposição e imunomodulação. Workshop “O medicamento hemoderivado”, satélite ao VII Congresso Nacional da APFH, Estoril, Portugal, November 23, 2019.

Lopes AI. Infecção por *H. pylori* em Idade Pediátrica. Perspetiva atual. Congresso Nacional de Pediatria, Lisbon, Portugal, November, 2019.

Lopes AI. Estágio Profissionalizante do 6^o Ano Clínico da FMUL. Sessões de Formação para Docentes, Departamento de Educação Médica, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December, 2019.

Science and Society

Silva SL. Medical Advisor for Associação Portuguesa de Doentes com Imunodeficiências Primárias.

Sousa AE. Member of the Conselho Consultivo do GAT - Grupo de Ativistas em Tratamentos (www.gatportugal.org), a NGO with main participation of people living with HIV.

Lopes AI. Dia Mundial do Sono. FMUL. Apresentação do Livro “ O Relógio Avariado”. Dr. Miguel Meira Cruz, Lisbon, Portugal, March 14, 2019.

Lopes AI. Feminização nas Profissões em Saúde. Trends Atuais. Revista Administração Hospitalar APDH. ANO V, Nº24 27-31// Edição Especial Conferência APDH 2019.

MSc Theses

Internships:

Clinical Immunology Laboratory training period for the final degree (Ordem dos Médicos/Ministry of Health):

Catarina Coutinho, MD, January to March 2019. Project: Characterization of the sensitization profile of honeybee sting allergic patients. Serviço de Imunoalergologia, Centro Hospitalar Universitário Lisboa Norte, Hospital Santa Maria.

Marisa Paulino, MD, May to July 2019. Project: Perfil de sensibilização molecular de doentes com síndrome de proteínas de transferência lipídica e associação com características clínicas. Serviço de Imunoalergologia, Centro Hospitalar Universitário Lisboa Norte, Hospital Santa Maria.

Ana Sebastião Lab

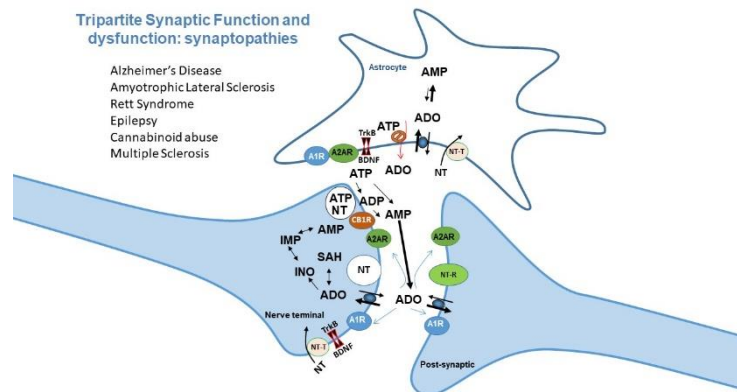
Major Interests/Objectives

Correction of abnormal synaptic function is a main challenge to Neurosciences. It impacts in the possibility to fight 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, under normal and pathological conditions, 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.

Head of Laboratory

Ana Maria Sebastião, Habilitation in Neurosciences, Full Professor, Faculdade de Medicina, Universidade de Lisboa, Vice-Dean of the Faculdade de Medicina da Universidade de Lisboa, Member of the Scientific Council of the Faculdade de Medicina da Universidade de Lisboa, Member of the Executive Council of the Mind-Brain College of the Universidade de Lisboa, Member of the Scientific Board of the Master and PhD Programmes in Neuroscience, Faculdade de Medicina da Universidade de Lisboa, Director of the PhD Programme 'Integrative Neuroscience', involving several Faculties of NeurULisboa, Member of the Scientific Board of the Master and PhD Programmes in Cognitive Sciences, Universidade de Lisboa, Member of the Coordinating Board of the Biomedical Engineering Integrated Master Course, Universidade de Lisboa.

Graphical Abstract



Team

Adam Ioshua D'Armada Moreira	Master Degree	PhD Student
Ana Filipa Ferreira da Cunha Ribeiro	PhD	Postdoctoral Researcher
Ana Margarida Garção Godinho	University Degree	MSc Student (Left September)
Ana Marta Alonso Gomes	Master Degree	Trainee (Left September)
Ana Rita Carreira Baptista Gomes	Master Degree	PhD Student
Antónia Sofia Fortunato Ribeiro	University Degree	MSc Student (Left September)
Anwasha Ghosh	Master Degree	PhD Student
Armando Dulcídio da Silva Cruz	Master Degree	PhD Student
Carolina de Almeida Borlido	University Degree	MSc Student (Started October)
Carolina de Campos Pina	University Degree	MSc Student
Catarina Beatriz Silva Ferreira	Master Degree	PhD Student
Catarina Miranda Lourenço	Master Degree	PhD Student
Céline Felicidade Freitas	University Degree	MSc Student (Started September)
Cláudia Alexandra dos Santos Valente de Castro	PhD	Senior Postdoctoral Researcher
Cristina Maria de Oliveira Varandas	Other	Administrative Technician
Daniela Cristina Melo Magalhães	Master Degree	PhD Student
Diogo André Mendonça Dias	University Degree	MSc Student (Started September)
Diogo Miguel da Palma Lourenço	Master Degree	PhD Student
Diogo Miguel Santos Rombo	PhD	Postdoctoral Researcher (Started January)
Francisco José Gonçalves Meda	University Degree	MSc Student (Started September)
Francisco Melo Albuquerque Saraiva Mouro	PhD	Postdoctoral Researcher
Giulia Viganì	Master Degree	PhD Student (Left February)
Jéssica Lúcia Albuquerque Rosa	University Degree	MSc Student (Left October)
Joana Filipa Gonçalves Ribeiro	Master Degree	PhD Student (Started September)
Joana Isabel Ferreira da Graça Gomes	University Degree	MSc Student
Joana Moura Mateus	Master Degree	PhD Student
João Baptista Moreira	University Degree	Trainee
João Filipe Fonseca Gomes	Master Degree	PhD Student
João Jorge Pedro Baião	High School Diploma	Senior Technician (Left August)
Joaquim Alexandre Ribeiro	PhD	Staff Scientist

Jorge Miguel Farinha Ferreira	Master Degree	Trainee
Leonor Pedro Oliveira Ribeiro Rodrigues	Master Degree	PhD Student
Mafalda Cagica Pinto de Carvalho	University Degree	MSc Student (Started September)
Mafalda Ferreira Manso	University Degree	MSc Student (Started October)
Maria Alexandra Pereira Botelho	High School Diploma	Administrative Technician
Maria José de Oliveira Diógenes Nogueira	PhD	Staff Scientist
Mariana Fernandes Van Zeller da Silva Campos	University Degree	MSc Student (Started September)
Milena de Barros Viana	PhD	Senior Postdoctoral Researcher (Started February. Left December)
Miranda Mele	PhD	Postdoctoral Researcher
Nádia Raquel Henriques Rei	Master Degree	PhD Student
Oksana Savchak	High School Diploma	MSc Student (Started July)
Pedro Guilherme Alves Dias	High School Diploma	MSc Student (Started December)
Rita Abrunhosa Soares	Master Degree	PhD Student
Rita Alexandra Figueira Belo	Master Degree	PhD Student
Rita Isabel Pedro Aroeira	PhD	Project Manager (Left February)
Robertta Silva Martins	Master Degree	PhD Student (Left October)
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 (Started October)
Sara Luísa Ramalho Tanqueiro	Master Degree	PhD Student
Sara Raquel Landeira Nabais do Paulo	Master Degree	PhD Student
Sodikdzhon Kodirov	PhD	Postdoctoral Researcher (Started November)
Svitlana Zavalko	University Degree	MSc Student (Started September)
Tatiana Pinto Morais	Master Degree	PhD Student
Tiago Rodrigo da Costa Coelho	University Degree	MSc Student (Started October)
Vanda Cristina Simões Nogueira	University Degree	MSc Student (Left September)

Laboratory Keywords / Research Areas

Research Areas:

Tripartite Synapse Modulation, Neuronal Excitation/Inhibition Balance, Synaptopathies.

Keywords:

Neuroinflammation, Adult Neurogenesis, Neurotrophins, Synaptic Plasticity, Psychoactive Agents.

Major Scientific Achievements

In the search of the mechanism of neurodegeneration caused by neurotrophic signaling dysregulation we found out that the fragment formed from cleavage of the receptor for the major neurotrophin in the brain, the TrkB-ICB fragment, is translocated to the cell nucleus and phosphorylates nuclear and axonal proteins (Fonseca-Gomes *et al.*, 2019, *Front Molec Neurosci*).

We discovered a novel action for adenosine that may have a major impact in the control of astroglia proliferation (Marcelino *et al.*, 2019, *J Neurochem*).

We found that blockade of adenosine receptors is still able to prevent memory deficits caused by cannabinoid consumptions even when cannabinoid intake is chronic (Mouro *et al.*, 2019, *Neuropharmacology*).

We identified molecular dysfunctions in an animal model of Rett Syndrome that recapitulates dysfunctions in post-Mortem tissue samples. Doing so, we validated the animal model for studying the pathophysiology of the disease (Ruffolo *et al.*, 2019, *Neuroscience*).

Selected Publications

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. (IF: 5.700, Citations: 5. Source: Web of Science).

Mouro FM, Batalha VL, Ferreira DG, Coelho JE, Baqi Y, Müller CE, Lopes LV, Ribeiro JA, Sebastião AM (2017). Chronic and acute adenosine A2A receptor blockade prevents long-term episodic memory disruption caused by acute cannabinoid CB1 receptor activation. **Neuropharmacology** 117:316-327. (IF: 4.367, Citations: 13. Source: Web of Science).

Ribeiro FF, Xapelli S, Miranda-Lourenço C, Tanqueiro SR, Fonseca-Gomes J, Diógenes MJ, Ribeiro JA, Sebastião AM (2016). Purine nucleosides in neuroregeneration and neuroprotection, **Neuropharmacology** 104:226-242. (IF: 4.367; Citations: 27; Source: Web of Science).

Rocha, MC, Pousinha PA, Correia AM, Sebastião AM, Ribeiro JA (2013). Early changes of neuromuscular transmission in the SOD1 (G93A) mice model of ALS start long before motor symptoms onset. **PLOS ONE** 8:e73846. (IF: 2.776, Citations: 69. Source: Web of Science).

Dias RB, Rombo DM, Ribeiro JA, Henley JM, Sebastião AM (2013). Adenosine: setting the stage for plasticity. **Trends in Neuroscience** 36:428-257. (IF: 12.314, Citations: 72. Source: Web of Science).

Cristóvão-Ferreira S, Navarro G, Brugarolas M, Pérez-Capote K, Vaz SH, Fattorini G, Conti F, Lluís C, Ribeiro JA, McCormick PJ, Casadó V, Franco R, Sebastião AM (2013) A1R-A2AR heteromers coupled to Gs and Gi/o proteins modulate GABA transport into astrocytes. **Purinergic Signalling** 9:433-449. (IF: 3.038; Citations: 63; Source: Web of Science).

Diogenes MJ, Costenla AR, Lopes LV, Jerónimo-Santos A, Sousa VC, Fontinha BM, Ribeiro JA, Sebastião AM (2011). Enhancement of LTP in aged rats is dependent on endogenous BDNF. **Neuropsychopharmacology** 36:1823-1836. (IF: 7.160, Citations: 72. Source: Web of Science).

Ongoing Research Projects

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.

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: € 239 677,82. Total Amount: € 239 677,82.

2018/2021: Na procura do mecanismo de ação de um novo e seletivo fármaco antiepiléptico. Coordinator: Ana M 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: Regulação da homeostase e polarização pró-inflamatória da microglia Rac1. Coordinator: Ana M. 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: 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: Controlo mecanístico e optogenético da astrogliã para reparaçãõ neuronal. Coordinator: Ana M. Sebastião. Funding Agency: Fundaçãõ para a Ciênciã e a Tecnologia. Reference: PTDC/MED-NEU/31417/2017. Amount: € 21 250,00. Total Amount: € 239 884,80.

2018/2020: Novel therapeutic strategy and new biomarker for Alzheimer's Disease based on BDNF receptor cleavage. Coordinator: Maria José Diógenes. Funding Agency: Santa Casa da Misericórdia de Lisboa. Reference: Prémio Santa Casa M^a José Diógenes. Amount: € 152 388,90. Total Amount: € 198 951,40.

2017/2019: New therapeutics strategy for Rett Syndrome. Coordinator: Maria José de Oliveira Diógenes Nogueira. Funding Agency: L'Association Française du Syndrome de Rett. Reference: Rett MJDígenes. Amount: € 30 000,00. Total Amount: € 30 000,00.

2016/2019: Synaptic, mechanisms involved in the brain cannabinoid actions and their modulation by adenosine receptors: implications for memory and mood control. Coordinator: Ana Sebastião. Funding Agency: Fundaçãõ para a Ciênciã e a Tecnologia. Reference: PTDC/DTP-FTO/3346/2014. Amount: € 189 900,00. Total Amount: € 199 900,00.

2016/2019: Optogenetic dissection of neural circuits controlling adiposity. Coordinator: Ana M. Sebastião. Funding Agency: Fundaçãõ para a Ciênciã e a Tecnologia. Reference: PTDC/BIM-MET/3750/2014. Amount: € 19 800,00. Total Amount: € 199 999,00.

2016/2019: Relationship between adenosine and chromosomal instability: a new perspective to understand the oncogenic mechanism in glioblastoma. Coordinator: Ana M. Sebastião. Funding Agency: Fundaçãõ para a Ciênciã e a Tecnologia. Reference: PTDC/BIMONC/7121/2014. Amount: € 25 000,00. Total Amount: € 155 000,00.

Publications in Peer Reviewed Journals

Branco MA, Cotovio J, Rodrigues CAV, Vaz SH, Fernandes TG, Moreira LM, Cabral JMS, Diogo MM (2019). Transcriptomic analysis of 3D Cardiac Differentiation of Human Induced Pluripotent Stem Cells Reveals Faster Maturation Compared to 2D Culture. **Scientific Reports** 9:9229. Original paper. (IF: 4.011, Citations: 2. Source: Web of Science).

Chern Y, Rei N, Ribeiro JA, Sebastião AM (2019). Adenosine and its receptors as potential drug targets in amyotrophic lateral sclerosis (ALS). **Journal of Caffeine and Adenosine Research** 9:157-166. Review. (IF:--, Citations:--).

Fonseca-Gomes J, Jerónimo-Santos A, Lesnikova A, Casarotto P, Castrén E, Sebastião AM, Diógenes MJ (2019). TrkB-ICD Fragment, Originating From BDNF Receptor Cleavage, Is Translocated to Cell Nucleus and Phosphorylates Nuclear and Axonal Proteins. **Frontiers Molecular Neurosciences** 1:12:4. Original paper. (IF: 3.720, Citations: 0. Source: Web of Science).

Gomes C, Cunha C, Nascimento F, Ribeiro JA, Vaz AR, Brites D (2019). Cortical Neurotoxic Astrocytes with Early ALS Pathology and miR-146a Deficit Replicate Gliosis Markers of Symptomatic SOD1G93A Mouse Model. **Molecular Neurobiology** 56:2137-2158. (IF: 4.586, Citations: 0. Source: Web of Science).

Gonçalves-Ribeiro J, Pina CC, Sebastião AM, Vaz SH (2019). Glutamate transporters in hippocampal LTD/LTP: not just prevention of excitotoxicity. **Frontiers in Cellular Neuroscience** 13:357. Review. (IF: 3.900, Citations: 0. Source: Web of Science).

Marcelino H, Nogueira VC, Santos CRA, Quelhas P, Carvalho TMA, Fonseca-Gomes J, Tomás J, Diógenes MJ, Sebastião AM, Cascalheira JF (2019). Adenosine inhibits human astrocyte proliferation independently of adenosine receptor activation. **Journal of Neurochemistry** 7:e14937. Original paper. (IF: 4.870, Citations: 0. Source: Web of Science).

Marques M, Albuquerque I, Vaz SH, Bernardes G (2019). Overexpression of osmosensitive Ca²⁺ activated channel TMEM63B promotes migration in HEK293T cell. **Biochemistry** 58:2861-2866. Original paper. (IF: 2.952, Citations: 2. Source: Web of Science).

Mateus JM, Ribeiro FF, Gomes MA, Rodrigues RS, Marques JM, Sebastião AM, Rodrigues RJ, Xapelli S (2019). Neurogenesis and gliogenesis: relevance of adenosine for neuroregeneration in brain disorders. **Journal of Caffeine and Adenosine Research** 9:129-144. Review. (IF:--, Citations:--).

Mouro FM, Köfalvi A, André LA, Baqi Y, Christa E Müller CE, Ribeiro JA, Sebastião AM (2019). Memory deficits induced by chronic cannabinoid exposure are prevented by adenosine A2AR receptor antagonism. **Neuropharmacology** 155:10-21. (IF: 4.367, Citations: 0. Source: Web of Science).

Mouro FM, Miranda-Lourenço C, Sebastião AM, Diógenes MJ (2019). From Cannabinoids and Neurosteroids to Statins and the Ketogenic Diet: New Therapeutic Avenues in Rett Syndrome? **Frontiers in Neurosciences** 2:1. (IF: 3.648, Citations: 2. Source: Web of Science).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC (2019). Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. **Science Immunology** 4(40):eaay5199. (IF: 10.551, Citations: 2. Source: Web of Science).

Rodrigues RS, Lourenço DM, Paulo SL, Mateus JM, Ferreira MF, Mouro FM, Moreira JB, Ribeiro FF, Sebastião AM, Xapelli S (2019). Cannabinoid Actions on Neural Stem Cells: Implications for Pathophysiology. **Molecules** 24(7). Review. (IF: 3.060, Citations: 1. Source: Web of Science).

Ruffolo G, Cifelli P, Miranda-Lourenço C, De Felice E, Limatola C, Sebastião AM, Diógenes MJ, Aronica E, Palma E (2019). Rare Diseases of Neurodevelopment: Maintain the Mystery or Use a Dazzling Tool for Investigation? The Case of Rett Syndrome. **Neuroscience** pii:S0306-4522(19)30421-X. Original paper. (IF: 3.244, Citations: 0. Source: Web of Science).

Other International Publications

Abstracts Published in indexed Journal

Armada-Moreira A, Taipaleenmaki E, Baekgaard-Laursen M, Schattling PS, Thingholm B, Andreassen K, Sebastião AM, Stadler B and Vaz SH (2019). Organic and inorganic-based microreactors as a therapeutic approach against excitotoxicity. *Front. Cell. Neurosci. Conference Abstract: XVI Meeting of the Portuguese Society for Neuroscience (SPN2019)* doi: 10.3389/conf.fncel.2019.01.00031.

Ferreira MF, Fonseca-Gomes J, Rei N, Mouro FM and Sebastião AM (2019). “Over the moon” or “down in the dumps”? Contradictory effects of chronic adolescent exposure to HU-210 on depressive-like behaviour. *Front. Cell. Neurosci. Conference Abstract: XVI Meeting of the Portuguese Society for Neuroscience (SPN2019)* doi: 10.3389/conf.fncel.2019.01.00027.

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Lourenço D, Rodrigues R, Soares R, Sebastião AM, Xapelli S (2019). Cannabidiol, capsaicin and the multiple fates of neural stem cells. *J Neurochem.* 150 (Suppl. 1), 73-161. Conference Abstract. doi.org/10.1111/jnc.14776.

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Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM, Xapelli S (2019). One neural stem cell at the time: enhancing adult oligodendrogenesis as a putative target for MS therapy. *Glia* Vol 67 (Issue S1). Conference Abstract. doi:10.1002/glia.23675.

Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM, Xapelli S (2019). From neural stem cells to oligodendrocytes: postnatal oligodendrogenesis as a target for MS therapy. *Front Cell Neurosci.* Conference Abstract. doi: 10.3389/conf.fncel.2019.01.00047.

Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM, Xapelli S (2019). Potentiation of adult oligodendrogenesis as a candidate target for MS therapy. *J Neurochem.* 150 (Suppl. 1), 73-161. Conference Abstract. doi.org/10.1111/jnc.14776.

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Moreira JB, Rodrigues RS, Lourenço DL, Sebastião AM, Xapelli S (2019). Modulation of subventricular zone neurogenesis by cannabinoid type 2 receptor and “exercise-regulated” neurotrophic factors. *Front Cell Neurosci* Conference Abstract. doi: 10.3389/conf.fncel.2019.01.00036.

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Mouro FM, Fonseca-Gomes J, Miranda-Lourenço C, Sebastião AM and Diógenes M (2019). Molecular evaluation of the endocannabinoid system in RTT mice-model: implications for cannabinoid-based treatments. *Front. Cell. Neurosci. Conference Abstract: XVI Meeting of the Portuguese Society for Neuroscience (SPN2019)*. doi: 10.3389/conf.fncel.2019.01.00003.

Paulo SL, Miranda-Lourenço C, Belo RF, Rodrigues RS, Tanqueiro SR, Fonseca-Gomes J, Sebastião AM, Xapelli S, Diógenes MJ (2019). The only free cheese is in the rat trap: long-term consequences of a high-caloric diet upon memory and plasticity. *Front Cell Dev Biol. Conference Abstract*. doi: 10.3389/978-2-88945-675-8.

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Paulo SL, Miranda-Lourenço C, Belo RF, Rodrigues RS, Tanqueiro SR, Fonseca-Gomes J, Sebastião AM, Xapelli S, Diógenes MJ (2019). High caloric intake and aging: consequences for synaptic plasticity and rat behaviour performance. *Front Cell Neurosci. Conference Abstract*. doi: 10.3389/conf.fncel.2019.01.00037.

Rodrigues RS, Armada-Moreira A, Ribeiro FF, Mouro FM, Sebastião AM, Xapelli S (2019). Game of modulators: cannabinoid and adenosine A2A receptors interplay regulating postnatal neurogenesis. *Front Cell Dev Biol. Conference Abstract*. doi: 10.3389/978-2-88945-675-8.

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Simões-Nogueira V, Sebastião AM, Cascalheira JF and Valente CA (2019). Role of adenosine on the resistance to an anti-tumor agent in glioblastoma cell lines. *Front. Cell. Neurosci. Conference Abstract: XVI Meeting of the Portuguese Society for Neuroscience (SPN2019)* doi: 10.3389/conf.fncel.2019.01.00009.

Socodato R, Portugal CC, Canedo T Vaz SH, Baptista FI, Summavielle T, Brakebusch C, Sebastião AM, Ambrosio AF, Relvas JB (2019). RhoGTPase regulation of redox homeostasis in microglia. *Free Radical Biology and Medicine*, 139 (Sup 1) S6 (Conference Abstract).

Tanqueiro SR, Mouro FM, Sebastião AM, Do Couto FS, Dawson N and Diógenes MJ (2019). Does BDNF loss of function in the prefrontal cortex underlie cognitive deficits in the subchronic phencyclidine model of schizophrenia? *Front. Cell. Neurosci. Conference Abstract: XVI Meeting of the Portuguese Society for Neuroscience (SPN2019)*. doi: 10.3389/conf.fncel.2019.01.00017.

Invited Lectures and Seminars

Diógenes MJ. Deregulation of BDNF signaling in Alzheimer's Disease: new opportunities for treatment. *IBILI Seminars, Centro de Neurociências de Coimbra, Coimbra, Portugal, February 15, 2019.*

Rodrigues RS. Deciphering the Role of Cannabinoid Type 2 receptors on Adult Hippocampal Neurogenesis as therapeutic targets for Depression. *Swammerdam Institute for Life Sciences (SILS) Neuroscience Seminar, University of Amsterdam, Amsterdam, Netherlands, February 18, 2019.*

Pina C. Astrocytic GABA Transporter Dysfunction in Childhood Absence Epilepsy. *Students' Talks, Library of the Department of Biomedicine, Faculdade de Medicina da Universidade do Porto, Porto, Portugal, February 19, 2019.*

Sebastião AM. Regulation of neuronal connectivity and synaptic plasticity by endo- and fitocannabinoids. *Centro de Neurociências de Coimbra, Coimbra, Portugal, March 2019.*

Ribeiro JA. Neurociências, neuroética e inteligência artificial. *III Encontro de Bioética da Universidade de Lisboa: A ética do aprimoramento humano. Reitoria da Universidade de Lisboa, March 15th 2019.*

Armada-Moreira A. Chemical Russian Roulette. Noite do Fósforo (celebration of the international year of the periodic table), Pavilhão do Conhecimento, Lisbon, Portugal, April 30, 2019.

Valente CA. The role of NLRP3-expressing astrocytes in the brain. IV Symposium of Portuguese Glial Network, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 29, 2019.

Xapelli S. BDNF and Adenosine A2A receptors: an intimate interaction regulating postnatal neurogenesis The second international Rita Levi-Montalcini's scientific meeting: the multiple life of nerve growth factor and on its potential clinical applications. Bologna, Italy, June 14, 2019.

Sebastião AM. Synaptic and behavioural actions of cannabinoids: control by adenosine and caffeine related drugs. XIV Annual CICS-UBI Symposium 2019, Covilhã, Portugal, July 4-5, 2019.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Mira H, Sebastiao AM, Xapelli S. Adenosine A2A receptors and BDNF: an intimate Interaction regulating postnatal hippocampal Neurogenesis 1st European Purine Meeting, Santiago de Compostela, Spain, September 4-6, 2019.

Vaz SH. Role of astrocytic adenosine on the modulation of synaptic plasticity by BDNF. 1st European Purine Meeting, Santiago de Compostela, Spain, September 4-6, 2019.

Sebastião AM, Silva-Cruz A, Ribeiro JG, Vaz SH, Mouro FM, Ribeiro JA. Modulation of synaptic activity and astrocytic calcium signalling by cannabinoids. 8th ECS Workshop on Calcium Signalling in Aging and Neurodegenerative Diseases, Coimbra, Portugal, September 18-20, 2019.

Gonçalves-Ribeiro J. Crosstalk between CB1R and adenosine receptors in astrocytes. Neuroscience Lectures, University of Barcelona, Barcelona, Spain, October 24, 2019.

Gonçalves-Ribeiro J. Crosstalk between CB1R and adenosine receptors in astrocytes in astrocytes and HEK cells. Neuroscience Lectures, University of Barcelona, Barcelona, Spain, December 16, 2019.

Communications in International Conferences

Silva TP, Fernandes TG, Bekman E, Vaz SH, Rodrigues CAV, Hashimura Y, Jung S, Lee B, Carmo-Fonseca M, Cabral JMS, Scalable generation of cerebellar neurons from pluripotent stem cells, Advancing Manufacture of Cell and Gene Therapies VI, California, USA, January 27-31, 2019. (*Poster Presentation*).

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião AM, Neves V, Castanho M, Diógenes MJ. Amidated-Kyotorphin neuroprotective effect on Alzheimer's Disease. 14th International Conference on Alzheimer's & Parkinson's diseases, Centro de Congressos de Lisboa, Lisbon, Portugal, March 26-31, 2019. (*Poster Presentation*).

Ferreira CB, Paldanius KA, Makinen P, Sebastião AM, de Mendonça A, Diógenes MJ, Hiltunen M. Unveiling the role of SEPT5 in APP processing and on A β peptide production *in vitro*. 14th International Conference on Alzheimer's & Parkinson's diseases, Centro de Congressos de Lisboa, Lisbon, Portugal, March 26-31, 2019. (*Poster Presentation*).

Fonseca-Gomes J, Vaz SH, Rodrigues TM, Jerónimo-Santos A, Belo RF, Makinen P, Takalo M, Lesnikova A, Casarotto P, Umemori J, Miranda HV, Outeiro TF, Haapasalo A, Hiltunen M, Castrén E, Duarte CB, Sebastião AM, Diógenes MJ. Development of a novel therapeutic strategy to prevent the loss of BDNF signalling in Alzheimer's disease. 14th International Conference on Alzheimer's & Parkinson's diseases, Centro de Congressos de Lisboa, Lisbon, Portugal, March 26-31, 2019. (*Oral Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Role of Mitochondrial Dynamics in directing neural stem cell differentiation: relevance for neurological disorders. AD/PD 2019 Meeting, Lisbon, Portugal, March 27-31, 2019. (*Oral Presentation*).

Fonseca-Gomes J, Vaz SH, Rodrigues TM, Jerónimo-Santos A, Belo RF, Makinen P, Takalo M, Lesnikova A, Casarotto P, Umemori J, Miranda HV, Outeiro TF, Haapasalo A, Hiltunen M, Castrén E, Duarte CB, Sebastião AM, Diógenes MJ. Prevention of BDNF receptor cleavage as a therapeutic strategy for Alzheimer's disease pathophysiology. Gordon Research Conference on Neurotrophic Mechanisms in Health and Disease, Newport, Rhode Island, USA, June 2-6, 2019. (*Poster Presentation*).

Tanqueiro SR, Almeida-Silva G, Mouro FM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. BDNF loss of function in the prefrontal cortex may underlie cognitive deficits in the subchronic phencyclidine model of schizophrenia. Gordon Research Conference on Neurotrophic Mechanisms in Health and Disease, Newport, Rhode Island, USA, June 2-6, 2019. *(Poster Presentation)*.

Soares R, Sebastião AM, Xapelli S, Morais VA. Characterizing the role of mitochondrial dynamics in adult neural stem cells differentiation. Eurogenesis Meeting 2019, Bordeaux, France, June 11-13, 2019. *(Poster Presentation)*.

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Cannabidiol and Capsaicin promote neuronal differentiation of neural stem cells. 2019 Eurogenesis Meeting, Bordeaux, France, June 11-13, 2019. *(Poster Presentation)*.

Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM, Xapelli S. Adenosine A2AR as modulators of adult oligodendrogenesis: a potential target for MS therapy. 4th Eurogenesis Meeting, Bordeaux, France, June 11-13, 2019. *(Poster Presentation)*.

Rodrigues RS, Armada-Moreira A, Ribeiro FF, Sebastião AM, Xapelli S. Cannabinoids and Adenosine A2A receptors: impact on postnatal neurogenesis. Eurogenesis Meeting 2019, Bordeaux, France, June 11-13, 2019. *(Poster Presentation)*.

Armada-Moreira A, Taipaleenmaki E, Baekgaard-Laursen M, Schattling PS, Thingholm B, Andreassen K, Sebastião AM, Stadler B, Vaz SH. Organic and inorganic-based microreactors as a therapeutic approach against excitotoxicity. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 10-13, 2019. *(Poster Presentation)*.

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. On the role of astrocytes upon A β -mediated neurotoxicity. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 10-13, 2019. *(Poster Presentation)*.

Gonçalves-Ribeiro J, Morais TP, Savchak O, Meneses C, Sebastião AM, Vaz SH. Modulation of GLAST transporters by CB1R in cortical astrocyte. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 10-13, 2019. *(Poster Presentation)*.

Socodato R, Portugal CC, T. Canedo T, Henriques JF, Vaz SH, Magalhães J, Silva CM, Baptista FI, Alves RL, Coelho-Santos V, Silva AP, Paes-de-Carvalho R, Magalhães A, Summavielle T, Brakebusch C, Sebastião AM, Ambrósio AF, Relvas JB. RhoA signaling in microglia and the impact for neurodegeneration. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 10-13, 2019. *(Oral Presentation)*.

Valente CA, Ribeiro AF, Almeida CC, Sebastião AM. Activation of NLRP3 inflammasome in A1 astrocytes. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 10-13, 2019. *(Poster Presentation)*.

Pina C, Morais TP, Sebastião AM, Crunelli V, Vaz SH. Astrocytic GABA Transporter Dysfunction in Childhood Absence Epilepsy. XIV European Meeting on Glial Cells in Health and Disease, Porto, Portugal, July 12, 2019. *(Poster Presentation)*.

Ferreira MF, Fonseca-Gomes J, Rei N, Mouro FM, Sebastião AM. Not all is as it seems: contradictory outcomes in different tests of depressive-like behavior after chronic adolescent HU-210 exposure. Biannual Meeting of the European Behavioural Pharmacology Society, Braga, Portugal, August 2019. *(Poster Presentation)*.

Rei N, Rombo DM, Ferreira MF, Ribeiro JA, Sebastião AM, Vaz SH. Synaptic dysfunctions at the hippocampus of an Amyotrophic Lateral Sclerosis mouse model (SOD1G93A): reversal by adenosine A2AR blockade. 1st European Purine Meeting 2019, Santiago de Compostela, Spain, September 4-6, 2019. *(Poster Presentation)*.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Vaz SH, Solá S, Mira H, Sebastião AM, Xapelli S. Postnatal subventricular zone neurogenesis: adenosine A2A receptors as regulators of brain-derived neurotrophic factor. 1st European Purine Meeting, Santiago de Compostela, Spain, September 4-6, 2019. *(Poster Presentation)*.

Soares R, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target that modulates adult neural stem cell fate. EMBO|FEBS Lecture course – Mitochondria in life, death and disease, Herceg Novi, Montenegro, September 24-28, 2019. *(Poster Presentation)*.

Ferreira MF, Fonseca-Gomes J, Rei N, Mouro FM, Sebastião AM. “Feeling blue” or “Tickled pink”? Opposing effects of adolescent HU-210 exposure on depressive-like behaviors. Cajal Whole-Brain Imaging Course, University of Bordeaux, Bordeaux, France, September 2019. *(Poster Presentation)*.

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Vaz SH, Solá S, Mira H, Sebastião AM, Xapelli S. Postnatal subventricular zone neurogenesis: adenosine A2A receptor endogenous activation is necessary for brain-derived neurotrophic factor-mediated cell proliferation and neuronal differentiation. 11th International Meeting of Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10-12, 2019. *(Poster Presentation)*.

Soares R, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target that regulates adult neural stem cell fate. 11th Annual International Meeting of the Portuguese Society for Stem Cells and Cellular Therapies (SPCE-TC), Lisbon, Portugal, October 10-12, 2019. *(Poster Presentation)*.

Ferreira MF, Fonseca-Gomes J, Rei N, Mouro FM, Sebastião AM. "On cloud nine" or "in a funk"? Contradictory effects of chronic adolescent HU-210 exposure on tests of depressive-like behavior. 28th Meeting of the Hellenic Society for Neuroscience, Heraklion, Greece, October 2019. *(Poster Presentation)*.

Gomes AR, Fernandes TG, Vaz SH, Xapelli S, Sebastião AM, Cabral JMS, Diogo MM. Engineering of Forebrain Organoids from Human Induced Pluripotent Stem Cells for Modeling of Rett Syndrome (RTT). 7th International Conference on Stem Cell Engineering 2019: From Organoids to Synthetic Embryo, Barcelona, Spain, December 11-13, 2019. *(Oral Presentation)*.

Rei N, Rombo DM, Ferreira MF, Baqi Y, Müller CE, Ribeiro JA, Sebastião AM, Vaz SH. Hippocampal synaptic dysfunction in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis: reversal by adenosine A2AR blockade. FENS Hertie-Winter School 2019, Universitätszentrum Obergurgl, Obergurgl, Austria, December 2019. *(Poster Presentation)*.

Communications in National Conferences

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S (2019). The effect of the non-psychoactive cannabinoid Cannabidiol and trpv1 agonist capsaicin on Neural stem cell proliferation and differentiation. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. *(Oral Presentation)*.

Pina C, Morais TP, Sebastião A, Crunelli V, Vaz SH. The Role of Astrocytic GABA Transporter 1 in Childhood Absence Epilepsy Models. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. (*Oral Presentation*).

Gomes MA, Mateus JM, Sebastião AM, Xapelli S (2019) Role of adenosine A2A receptors in adult Oligodendrogenesis using a mouse model of Multiple sclerosis. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. (*Oral Presentation*).

Moreira JB, Rodrigues RS, Lourenço DM, Sebastião AM, Xapelli S. Role of cannabinoid type 2 receptor and physical exercise in subventricular zone neurogenesis. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. (*Oral Presentation*).

Gonçalves-Ribeiro J, Morais T, Savchak O, Meneses C, Sebastião AM, Vaz SH (2019) Astrocytic CB1R increases GLAST activity. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. (*Oral Presentation*).

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Gliotransmission role upon amyloid- β mediated excitotoxicity. XLIX Annual Meeting of Portuguese Pharmacological Society (SPF), XXXVII Annual Meeting of Clinical Pharmacology, XVIII Meeting of Toxicology, Porto, Portugal, February 6-8, 2019. (*Oral Presentation*).

Gomes AR, Fernandes T, Vaz SH, Xapelli S, Sebastião AM, Cabral JMS, Diogo MM. Development and characterization of brain region-specific organoids from human induced pluripotent stem cells for modelling of Rett Syndrome. Stem Cells & Organoids in Development and Disease, Amsterdam, Netherlands, February 20-22, 2019. (*Poster Presentation*).

Ferreira MF, Fonseca-Gomes J, Rei N, Vaz SH, Martins V, Pereira B, Mouro FM, Sebastião AM. The short- and long-term effects of chronic adolescent exposure to HU-210 on depressive-like phenotypes. 49th annual meeting of the Portuguese Society for Pharmacology, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal, February, 2019. (*Oral Presentation*).

Moreira JB, Rodrigues RS, Sebastião AM, Xapelli S. Role of cannabinoid type 2 receptor and physical exercise in subventricular zone neurogenesis. 10th AIMS Meeting, Portugal, March 14-17, 2019. (*Poster Presentation*).

Tanqueiro SR, Mouro FM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. Interplay between BDNF signaling and cognitive alterations in the subchronic phencyclidine mouse model of schizophrenia. IMM Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 19, 2019. (*Oral Presentation*).

Armada-Moreira A. Organic and inorganic-based microreactors as a therapeutic approach against excitotoxicity. NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21-22, 2019. (*Oral Presentation*).

Tanqueiro SR, Mouro FM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. Interplay between BDNF signalling and cognitive alterations in the subchronic phencyclidine model of schizophrenia. NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21-22, 2019. (*Oral Presentation*).

Ferreira CB, Coelho JE, Temido-Ferreira M, Miranda-Lourenço C, Fonseca-Gomes J, Belo RF, Tanqueiro SR, Marttinen M, de Mendonça A, Sebastião AM, Diógenes MJ, Lopes LV, Hiltunen M. Unveiling the effect of SEPT5 on synaptic function. NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21-22, 2019. (*Oral Presentation*).

Fonseca-Gomes J, Vaz SH, Rodrigues TM, Jerónimo-Santos A, Miranda-Lourenço C, Tanqueiro SR, Belo RF, Ferreira CB, Mouro FM, Ribeiro FF, Xapelli S, Miranda HV, Outeiro TF, Duarte CB, Sebastião AM, Diógenes MJ. TrkB-ICD: what is its role *in vivo* and could the prevention of its formation be considered a therapeutic strategy for Alzheimer's disease? NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21-22, 2019. (*Oral Presentation*).

Miranda-Lourenço C, Palminha C, Duarte ST, Gaspar C, Colino-Oliveira M, Rosa J, Gomes R, Xapelli S, Vaz HS, Fonseca-Gomes J, Ferreira S, Rodrigues TM, Lopes LV, Sebastião AM, Diógenes MJ. Playing with adenosine on rett syndrome mouse model. Neurosciences Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 30, 2019. (*Oral Presentation*).

Armada-Moreira A, Taipaleenmaki E, Baekgaard-Laursen M, Schattling PS, Thingholm B, Andreassen K, Sebastião AM, Stadler B, Vaz SH. Organic and inorganic-based microreactors as a therapeutic approach against excitotoxicity. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Miranda-Lourenço C, Rosa J, Palminha C, Duarte ST, Colino-Oliveira M, R. Gomes, Rodrigues TM, Xapelli S, Lopes LV, Sebastião AM, Diógenes MJ. Adenosine augmentation therapy as a possible strategy for Rett Syndrome. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Rodrigues RS, Moreira JB, Sebastião AM, Fitzsimons CP, Xapelli S. Cannabinoids and exercise: a united force modulating postnatal neurogenesis? XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Unveiling the role of mitochondrial dynamics in the regulation of postnatal neural stem cell fate. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião A, Neves V, Castanho M, Diógenes MJ. The neuroprotective effect of Amidated-Kyotorphin on Alzheimer's Disease. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Ferreira CB, Coelho JE, Temido-Ferreira M, Miranda-Lourenço M, Fonseca-Gomes J, Belo RF, Tanqueiro SR, Marttinen M, de Mendonça A, Sebastião AM, Diógenes MJ, Lopes LV, Hiltunen M. Unveiling the effect of SEPT5 on synaptic function. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Rei N, Rombo DM, Ribeiro JA, Sebastião AM, Vaz SH. Characterization of synaptic plasticity in non-motor synapses of the SOD1G93A ALS mouse model. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Fonseca-Gomes J, Vaz SH, Rodrigues TM, Jerónimo-Santos A, Belo RF, Makinen P, Takalo M, Lesnikova A, Casarotto P, Umemori J, Miranda HV, Outeiro TF, Haapasalo A, Hiltunen M, Castrén E, Duarte CB, Sebastião AM, Diógenes MJ. Relevance of BDNF receptor cleavage on Alzheimer's disease pathophysiology. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. *(Oral Presentation)*.

Tanqueiro SR, Almeida-Silva G, Mouro FM, Duarte TA, Deveza MM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. Interplay between BDNF signalling and cognitive alterations in the subchronic phencyclidine model of schizophrenia. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019. *(Poster Presentation)*.

Pina C, Morais TP, Sebastião AM, Crunelli V, Vaz SH. Dysfunctional Astrocytic GABA Transporter in Childhood Absence Epilepsy. IV Symposium of the Portuguese Glial Network: Glia Diversity in Neuromodulation and Neurodegeneration, Lisbon, Portugal, May 19, 2019. *(Poster Presentation)*.

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. The role of astrocytic signaling on AD-like conditions. IV Symposium of the Portuguese Glial Network: Glia Diversity in Neuromodulation and Neurodegeneration, Lisbon, Portugal, May 29, 2019. *(Poster Presentation)*.

Soares R, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target for regulation of adult neural stem cell fate. IV Symposium of the Portuguese Glial Network, Lisbon, Portugal, May 29, 2019. *(Poster Presentation)*.

Gonçalves-Ribeiro J, Morais TP, Savchak O, Meneses C, Sebastião AM, Vaz SH. CB1R enhancement on GLAST activity is adenosine A2A receptor dependent in cultured cortical astrocytes. IV Symposium of the Portuguese Glial Network: Glia Diversity in Neuromodulation and Neurodegeneration, Lisboa, Portugal, May 29, 2019. *(Poster Presentation)*.

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Regulation of neural stem cell fate by Cannabidiol and Capsaicin. IV Portuguese Glial Network Symposium, May 29, 2019. *(Poster Presentation)*.

Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM and Xapelli S. Postnatal oligodendrogenesis modulated by adenosine A2AR: a putative candidate for MS therapy. IV Symposium of the Glial Network on Glia Diversity in Neuromodulation and Neurodegeneration, Lisbon, Portugal, May 29, 2019. (*Poster Presentation*).

Fonseca-Gomes J, Rodrigues TM, Vaz SH, Rita M, Ramalho, Miranda HV, Diogo M, Rombo, Rita F, Belo, Tanqueiro SR, Miranda-Lourenço C, Martins IC, Jerónimo-Santos A, Manso N, Caetano A, Makinen P, Marttinen M, Takalo M, Duarte CB, Haapasalo A, Santos NC, Outeiro TF, Hiltunen M, Sebastião AM, Diógenes MJ. Prevention of BDNF receptor cleavage as a therapeutic strategy for Alzheimer's disease pathophysiology. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Mouro FM, Fonseca-Gomes J, Miranda-Lourenço C, Sebastião AM, Diógenes MJ. Molecular evaluation of the endocannabinoid system in RTT mice-model: implications for cannabinoid-based treatments. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Nogueira VC, Valente CA, Sebastião AM, Cascalheira JF. Role of adenosine on the resistance to an anti-tumor agent in glioblastoma cell lines. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Pina C, Morais TP, Sebastião AM, Crunelli V, Vaz SH. Dysfunctional Astrocytic GABA Transporter in Childhood Absence Epilepsy. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Rei N, Rombo DM, Ribeiro JA, Sebastião AM, Vaz SH. Characterization of synaptic plasticity in non-motor synapses of the SOD1G93A ALS mouse model. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ribeiro AF, Almeida CC, Sebastião AM, Valente CA. NLRP3 Inflammasome assembly in microglia-induced reactive astrocytes. XVI Meeting of the Portuguese Society for Neurosciences, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Solá S, Mira H, Sebastião AM, Xapelli S. Postnatal hippocampal neurogenesis: adenosine A2A receptors as regulators of new neurons formation in the dentate gyrus. XVI Meeting of the Portuguese Society for Neurosciences, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ribeiro M, Brigas HC, Temido-Ferreira M, Santa C, Valente CA, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and cognitive behaviour. XVI Meeting of the Portuguese Society for Neurosciences, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target for neural stem cell fate regulation, XVI Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Tanqueiro SR, Almeida-Silva G, Mouro FM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. Does BDNF loss of function in the prefrontal cortex underlie cognitive deficits in the subchronic phencyclidine model of schizophrenia? XVI Meeting of the Portuguese Society for Neurosciences, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Mateus JM, Soares R, Alonso Gomes M, Paulo SL, Chora AF, Sebastião AM, Xapelli S. Characterization of animal behaviour and adult oligodendrogenesis in a mouse model of multiple sclerosis. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Neurons or Oligodendrocytes: The effect of Cannabidiol and Capsaicin on the fate of neural stem/progenitor cells. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Gonçalves-Ribeiro J, Morais TP, Savchak O, Meneses C, Sebastião AM, Vaz SH. Astrocytic CB1R enhances GLAST activity in a Ca²⁺ dependent manner. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Armada-Moreira A, Taipaleenmaki E, Baekgaard-Laursen M, Schattling PS, Thingholm B, Andreassen K, Sebastião AM, Stadler B, Vaz SH. Organic and inorganic-based microreactors as a therapeutic approach against excitotoxicity. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Barata T, Miranda C, Vaz SH, Carla Ferreira C, Quintas A, Bekman EP. Cannabinoids Affect Differentiation of Human iPSC-derived neurons. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Astrocytic signaling upon A β -mediated excitotoxicity. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Godinho MG, Sebastião AM, Valente CA. ROS-mediated NLRP3 activation in a model of epileptogenesis in organotypic slices. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião A, Neves V, Castanho M, Diógenes MJ. The neuroprotective effect Amidated-Kyotorphin on Alzheimer's Disease. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Enguita FJ, Fonseca-Gomes J, Roque M, Sebastião AM, Maria J. Diógenes. Analysis of the transcriptomic response induced by the intracellular domain (TrkB-ICD) of TrkB receptor in rat cortical neurons. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ferreira MF, Fonseca-Gomes J, Rei N, Gomes J, Mouro FM, Sebastião AM. "Over the moon" or "down in the dumps"? Contradictory effects of chronic adolescent exposure to HU-210 on depressive-like behavior. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Martins RS, Teixeira CHC, Sathler MF, Rombo DM, Gonçalves-Ribeiro J, Vaz SH, Sebastião AM Kubrusly RCC. Caffeine exposure regulated excitatory amino acids transmission in adolescent mice hippocampus. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Pitch and Poster Presentation*).

Miranda-Lourenço C, Palminha C, Duarte ST, Gaspar C, Colino-Oliveira M, Rosa J, Gomes R, Xapelli S, Ferreira S, Rodrigues TM, Lopes LV, Sebastião AM, Diógenes MJ. Reestablishment of adenosine levels: a possible strategy for Rett Syndrome. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Ferreira CB, Coelho JE, Temido-Ferreira M, Miranda-Lourenço C, Fonseca-Gomes J, Belo RF, Tanqueiro SR, Marttinen M, Sebastião A, de Mendonça A, Lopes LV, Diógenes MJ, Hiltunen M. SEPT5 phosphorylation status: importance for synaptic function and mice behavior performance. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Maranga C, Silva TP, Vaz SH, da Rocha ST, Fernandes TG, Bekman E, Cabral JMS. Disease modeling of Angelman Syndrome using hiPSC-derived cerebellar organoids. XVI Meeting of the Portuguese Neuroscience Society (SPN), Lisbon, Portugal, May 30-June 1, 2019. (*Pitch and Poster Presentation*).

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. Role of astrocytic signalling upon synaptic plasticity on AD-like conditions. Fourteenth - Young European Scientist Meeting, Porto, Portugal, September 12-15, 2019. (*Oral Presentation*).

Ribeiro-Rodrigues, L, Fonseca-Gomes, J, Sebastião AM, Xapelli, S, Diógenes, MJ. PhD project: Interaction between BDNF/TrkB signaling and neurogenesis in epilepsy. Neurosciences Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 30, 2019. (*Oral Presentation*).

Gomes AR, Fernandes TG, Vaz SH, Xapelli S, Sebastião AM, Cabral JMS, Diogo MM. Engineering region-specific brain organoids from human induced pluripotent stem cells for disease modeling of Rett syndrome. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10-12, 2019. (*Oral Presentation*).

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Cannabidivarin and Capsaicin as modulators of neural stem cells. 2019. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10-12, 2019. (*Poster Presentation*).

Maranga C, Silva TP, Vaz SH, da Rocha ST, Fernandes TG, Bekman E, Cabral JMS. Cerebellar organoids derived from human pluripotent stem cells to model Angelman Syndrome. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10-12, 2019. (*Poster Presentation*).

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. The role of astrocytic signaling upon A β -induced synaptic deficits. AstraZeneca Foundation Innovate Competition, iMed Conference 11.0, Lisbon, Portugal, October 16-20, 2019. (*Poster Presentation*).

Moreira JB, Rodrigues RS, Lourenço DM, Sebastião AM, Xapelli S (2019) Subventricular zone neurogenesis regulation by exercise factors and cannabinoid type 2 receptor. iMed Conference 11.0, Lisbon, Portugal, October 16-20, 2019. (*Poster Presentation*).

Carvalho M, Meda FJ, Sebastião AM, Valente CA. Phenotypic assessment of astrocytes in a model of epileptogenesis in organotypic slices. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Costa-Coelho T, Fonseca-Gomes J, Ferreira CB, Sebastião AM, Brites D, Diógenes MJ. Unveiling paracrine dissemination and toxicity of neuronal TrkB-ICD via secretome/exosome signalling in Alzheimer's disease. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ferreira CB, Coelho JE, Temido-Ferreira M, Miranda-Lourenço C, Fonseca-Gomes J, Belo RF, Tanqueiro SR, Marttinen M, Sebastião A, de Mendonça A, Lopes LV, Diógenes MJ, Hiltunen M. Role of SEPT5 overexpression on synaptic function and its dependency on S327 phosphorylation. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ferreira MF, Fonseca-Gomes J, Rei N, Gomes J, Mouro FM, Sebastião AM. Do not judge a rat by its (forced) swimming: exploring the contradictory affective behavioral effects of chronic adolescent HU-210 exposure. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ferreira-Manso M, Fonseca-Gomes J, Miranda-Lourenço C, Filipa F. Ribeiro, Xapelli S, Sebastião AM, Adelaide Fernandes, Diógenes MJ. The impact of BDNF receptor cleavage in Alzheimer's disease-associated Neuroinflammation. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Fonseca-Gomes J, Mouro FM, Tanqueiro SR, Miranda-Lourenço C, Belo RF, Ferreira CB, Ribeiro FF, Roque M, Sebastião AM, Xapelli S, Enguita FJ, Diógenes MJ. TrkB-ICD fragment impact upon normal physiology. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Dias DM, Van Zeller M, Sebastião AM, Valente CA. Impact of NLRP3 inflammasome inhibition in a model of A β -induced toxicity. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Freitas CF, Tanqueiro SR, Sebastião AM, Dawson N, Diógenes MJ. Characterization of BDNF signalling in the prefrontal cortex in the neonatal phencyclidine mouse model of schizophrenia. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Gomes J, Fonseca-Gomes J, Vicente Miranda H, Sebastião AM, Diógenes MJ, Vaz SH. The role of tripartite synapse upon A β -mediated synaptic deficits. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Lourenço DM, Soares R, Rodrigues RS, Sebastião AM, Xapelli S. Modulation of neural stem cells by Cannabidiol and Capsaicin. 2019. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Mateus JM, Gomes MA, Soares R, Paulo SL, Chora AF, Sebastião AM and Xapelli S. Fostering adult neural stem cells: adenosine A2AR activation on postnatal oligodendrogenesis in MS. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Meda FJ, Carvalho M, Sebastião AM, Valente CA. NLRP3 inflammasome inhibition in a model of epileptogenesis in organotypic slices – impact in neurodegeneration and epileptiform activity. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Miranda-Lourenço C, Rosa J, Palminha C, Duarte ST, Rei N Colino-Oliveira M, R. Gomes, Rodrigues TM, Xapelli S, Lopes LV, Sebastião AM, Diógenes MJ. Adenosinergic system and BDNF signalling in a severe and a mild mouse model of Rett Syndrome. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Oral Presentation*).

Moreira JB, Rodrigues RS, Sebastião AM, Xapelli S. Modulation of subventricular zone postnatal neurogenesis: actions of exercise-regulated neurotrophic factors and cannabinoid type 2 receptor. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Paulo SL, Ribeiro-Rodrigues L, Rodrigues RS, Mateus JM, Soares R, Fonseca-Gomes J, Diógenes MJ, Solá S, Sebastião AM, Ribeiro FF, Xapelli S. Look before you leap: a perspective on the reproducibility of a sporadic Alzheimer's disease model and its impact on neurogenesis. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Pina C, Morais TP, Sebastião AM, Crunelli V, Vaz SH. GABAergic Dysfunction and Cognitive Impairments in Childhood Absence Epilepsy. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Rei N, Valente CA, Vaz SH, Ferreira MF, Ribeiro JA, Sebastião AM. Progressive changes in the adenosinergic and Vascular Endothelial Growth Factor systems in the SOD1G93A mouse model of ALS and the effect of chronic caffeine treatment. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ribeiro FF, Armada-Moreira A, Sebastião AM, Xapelli S, Vaz SH. Platinum nanoparticle-based microreactors in mixed neural cultures and subventricular-derived cultures. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ribeiro FF, Armada-Moreira A, Sebastião AM, Xapelli S, Vaz SH. Platinum nanoparticle-based microreactors in mixed neural cultures and subventricular-derived cultures. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Ribeiro-Rodrigues L, Fonseca-Gomes J, Sebastião AM, Xapelli S, Diógenes MJ. Interaction between BDNF/TrkB signaling and neurogenesis in epilepsy - The basis for the project. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Savchak O, Armada-Moreira A, Ribeiro FF, Sebastião AM, Vaz SH. Nanoparticle and liposome based microreactors as reactive oxygen species scavengers in a 3D model of neuroinflammation. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Rodrigues RS, Armada-Moreira A, Ribeiro FF, Mouro FM, Sebastião AM, Xapelli S. Interplay between cannabinoid and adenosine A2A receptors: actions on postnatal neurogenesis. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Pitch and Poster Presentation*).

Tanqueiro SR, Mouro FM, Sebastião AM, Simões do Couto F, Dawson N, Diógenes MJ. Is there any relation between BDNF loss of function and cognitive deficits in phencyclidine-induced mouse model of schizophrenia. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Oral Presentation*).

Van Zeller M, Dias DM, Sebastião AM, Valente CA. Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β -induced toxicity. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Zavalko S, Mouro F, Lourenço D, Miranda-Lourenço C, 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. 5th Meeting of Mind-Brain College of the Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Martins RS, Rombo DM, Gonçalves-Ribeiro J, Meneses C, Borges-Martins VPP, Vaz SH, Regina Kubrusly CC, Sebastião AM. The effect of caffeine on NMDAR activity in the hippocampus of adolescent swiss mice. VIII Simpósio de Neurociências da Universidade Federal Fluminense/III Simpósio de Neurociências UFF-Fiocruz, Rio de Janeiro, Brazil, December 3-5, 2019. (*Poster Presentation*).

Organization of Conferences

Ribeiro JA. Honorary Board. XLIX Meeting of the Portuguese Society for Pharmacology, Coimbra, Portugal, February 2019.

Armada-Moreira A, Belo RF, Ferreira CB, Fonseca-Gomes J, Gomes MA, Gonçalves-Ribeiro J, Mateus JM, Miranda-Lourenço C, Moreira J, Lourenço DM, Mouro FM, Paulo SL, Ribeiro FF, Ribeiro-Rodrigues L, Rodrigues RS, Soares R, Sebastião AM, Tanqueiro SR, Valente CA, Vaz SH. Organizing Committee. XVI Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal, May 2019.

Diógenes MJ, Xapelli S. Chairs of Organizing Committee. XVI Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal, May 2019.

Ribeiro JA. Advisory Board. XVI Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal, May 2019.

Sebastião AM. Scientific Committee. 1st European Purine Meeting, Santiago de Compostela, Spain, September 2019.

Diógenes MJ. Organizing Committee. 6th edition, Beyond Med, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 2019.

Ribeiro FF, Xapelli S. Members of the Organizing Committee. 11th Annual International Meeting of the Portuguese Society for Stem Cells and Cellular Therapies, Lisbon, Portugal, October, 2019.

Xapelli S. Scientific Committee. 11th Annual International Meeting of the Portuguese Society for Stem Cells and Cellular Therapies, Lisbon, Portugal, October, 2019.

Armada-Moreira A, Belo RF, Fonseca-Gomes J, Lourenço D, Miranda-Lourenço C, Mouro FM, Rodrigues R, Tanqueiro SR. Organizing Committee. 5th Annual Meeting of the Mind-Brain College of the University of Lisbon and 17th Meeting of Biomedical Engineering IST/FMUL, a tribute to Fernando Lopes da Silva, Lisbon, November 2019.

Sebastião AM. Scientific Committee. 5th Annual Meeting of the Mind-Brain College of the University of Lisbon and 17th Meeting of Biomedical Engineering IST/FMUL, a tribute to Fernando Lopes da Silva, Lisbon, November, 2019.

Ferreira CB, Fonseca-Gomes J, Tanqueiro SR. Organizing Committee. Annual Meeting of the NeurULisboa Doctoral Programme, Lisbon, Portugal, 2019.

Internationalization

- Participation in European Research Networks:

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

- Collaborations in scientific projects:

1) On the action of psychoactive drugs (cannabinoids, psilocybin and other serotonergic agents, caffeine and other adenosinergic agents) on synaptic excitability and cognition (Ana Sebastião projects): Cristha E Muller (Bonn, Germany), Karl Jacobson (NIH, Bethesda, USA), Neil Dawson (Lancaster, England), Luzia Sampaio (Rio de Janeiro, Brasil), Regina Kubrusly (Niterói, Brasil, involving an internship for one year of a PhD student -Robertta Silva Martins at Ana Sebastião Lab); Milena Viana (S. Paulo, Brasil); Tomáš Páleníček (Klečany, Czech Republic); Serge Ferré (Baltimore, USA); Robin Carhart-Harris (London, UK, involving co-supervision of a PhD Student).

2) On pathophysiological mechanisms in Alzheimers’ disease, Rett Syndrome and schizophrenia (Maria José Diógenes projects): Annakaisa Haapasalo (Kuopio, Finland), Christopher Parsons (Frankfurt, Germany), David Blum (Université Lille-Nord de France), Detlev Boison (Portland, USA), Eero Castren (Helsinki, Finland), Mikko Hiltunen (Kuopio, Finland, co-supervision of a PhD Student), Neil Dawson (Lancaster, England, co-supervision of a PhD Student), Tiago Outeiro (Göttingen, Germany).

3) On the role of neurogenesis and oligodendrogenesis in neurologic and psychiatric dysfunctions (Sara Xapelli projects): Carlos Fitzsimons (University of Amsterdam, co-supervision of a PhD Student), Helena Mira (IBV-CSIC, Valencia, Spain), Jorge Valero (Ikerbasque - Basque Foundation for Science, co-supervision of a PhD Student), Neil Dawson (Lancaster, England, co-supervision of a PhD Student).

4) On neuroinflammation and brain dysfunction (Claudia Valente projects): Graham Sheridan, (University of Brighton, England, co-supervision of a PhD Student).

5) On the influence of astrocytes in neuronal function (Sandra Vaz projects): Brigitte Städler - (Aarhus, Denmark, co-supervision of a PhD Student), Vincent Crunelli (Cardiff, UK, co-supervision of a PhD Student), Alfonso Araque (University of Minnesota), Gareth Miles (St. Andrews University), Rafael Franco (University of Barcelona).

- Participation in international reviewing committees:

Xapelli S, Diógenes MJ, Crunelli V, Fitzsimons CP, Vaz SH, Editors of the research topic “Glial and Neural Stem Cells as New Therapeutic Targets for Neurodegenerative Disorders”, *Frontiers in Cellular Neurosciences*.

Diógenes MJ, Xapelli S, Almeida C, Editors of the research topic “Meeting of the Portuguese Society for Neurosciences SPN2019”, *Frontiers*

Sebastião AM: Member of the Peer-Review panel ‘Neuroscience’ of the Academy of Finland Research Council for Health.

Sebastião AM: Reviewer of research projects for the Czech Science Foundation.

Sebastião AM: Member of the external expert committee of Doctoral thesis of the ‘Programa de Doctoradode Bioquímica, Biología Molecular y Biomedicina, Universidad Complutense de Madrid’.

Sebastião AM: Handling Editor of *Journal of Neurochemistry*.

Vaz SH: Expert evaluator of the National Science Centre Poland.

Xapelli S: Expert evaluator of Marie Skłodowska-Curie (Call: H2020-MSCA-IF-2019 - LIF panel).

Xapelli S: Expert evaluator of ALS Association Starter Grant Program.

Xapelli S: International Evaluation Committee of 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*.

- Participation in European committee evaluation of Marketing authorization application of drugs:

Diógenes MJ. Evaluator of Marketing authorisation applications of drugs as expert on Pharmacokinetics (bioavailability and bioequivalence).

Prizes, Honors and Awards

- Meeting Awards:

Rodrigues RS. EMBO Short-term Fellowship. European Molecular Biology Organization (EMBO), Germany, January 2019.

Rodrigues RS. Travel grant of 900 € from the International Brain Research Organization to attend the Eurogenesis Meeting, Bordeaux, France, June 2019.

Soares R. Travel grant of 900 € from the International Brain Research Organization to attend the Eurogenesis Meeting, Bordeaux, France, June 2019.

Ferreira MF. FENS and IBRO-PERC stipend to attend “Drugs and the Brain: from laboratory to clinic” workshop (Heraklion, Greece, October 2019). July 2019.

Lourenço DM. SPCE-TC scholarship (value of registration fee) to attend the 11th International Meeting of SPCE-TC, July 2019.

Lourenço DM. International Society for Neurochemistry Travel Award (1100 USD) to attend ISN-ASN Meeting in Montréal, Canada, August 4-8, 2019.

Rodrigues RS. Travel Award of 1100 USD from the International Society for Neurochemistry, to attend the ISN-ASN Meeting 2019, Montréal, Canada, August 4-8, 2019.

Mateus JM. Travel Award of 1100 USD from the International Society for Neurochemistry, to attend the ISN-ASN Meeting 2019, Montréal, Canada, August 4-8, 2019.

Paulo SL. Travel Award of 1100 USD from the International Society for Neurochemistry, to attend the ISN-ASN Meeting 2019, Montréal, Canada, August 4-8, 2019.

Rei N. FENS stipend to attend “FENS-Hertie Winter School 2019: Genetic and epigenetic mechanisms underlying brain disorders” (Oberurgl, Austria, December 2019). August 2019.

Ferreira MF. Boehringer Ingelheim Fonds travel grant to attend the Cajal Whole Brain Imaging course (Bordeaux, France, September 2019). August 2019.

Gomes J. First prize (oral communication) at the Young European Scientist (YES) Meeting, Porto, Portugal, September 12-15, 2019.

Gonçalves-Ribeiro J. NENS Exchange Grants, Federation of European neuroscience societies, Belgium, October 1, 2019.

Rodrigues RS. Scholarship (value of registration fee) to attend 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Portuguese Society for Pharmacology, Portugal, October 2019.

Martins RS. Honorable mention. VIII Simpósio de Neurociências da Universidade Federal Fluminense/III Simpósio de Neurociências UFF-Fiocruz, Rio de Janeiro, Brazil, December 3-5, 2019.

Armada-Moreira A. Top 10 finalist, Building Tomorrow Together 2019, Imatch and Roche, Portugal, December 11, 2019.

- Positions in Committees or Scientific Societies (National only to avoid repetition with internationalization):

Diógenes MJ. Vice-President of the Portuguese Society for Pharmacology.

Diógenes MJ. Member of the Committee for Evaluation of Medicines at the National Authority of Medicines and Health Products, I.P. (INFARMED).

Ribeiro JA. Expert panel evaluator of A3Es to evaluate post-graduation courses.

Ribeiro JA. Member of Internal Evaluating Committee (CAI) at Faculdade de Medicina da Universidade de Lisboa.

Xapelli S. Secretary General of the Portuguese Society for Neurosciences.

Xapelli S. Voter of the Fiscal Council of the Portuguese Society for Stem Cell and Cell Therapies.

Advanced Teaching

- Directive Roles:

Sebastião AM. Director of the Doctoral Mind-Brain College ‘Mind and Brain’, University of Lisbon, 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, University of Lisbon, 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’.

- Supervision of International Internships:

Giulia Vigani - Erasmus plus internship. Università di Firenze, Italy (Supervisor: Cláudia Valente) January.

Andrea Babić - Erasmus plus internship. University of Zagreb, Croatia (Supervisor: Cláudia Valente), March-July.

Elpida Vasiliadi - Research Exchange Program for Medical Students (Supervisors: Sara Xapelli and Sandra Vaz). University of Moscow, Russia, July 1-31.

Elodie Rainville - Research Exchange Program for Medical Students (Supervisors: Sara Xapelli and Sandra Vaz). University of Montreal, Quebec, Canada, July 1-31.

Stéphanie Mongrain - Research Exchange Program for Medical Students (Supervisors: Sara Xapelli and Sandra Vaz). University of Montreal, Quebec, Canada, July 1-31.

Victor Mormoe - Research Exchange Program for Medical Students (supervisors: Sara Xapelli and Sandra Vaz). University of Medicine and Pharmacy of Craiova, Romania, July 1-31.

- Invited Lectures From Abroad:

7/11 - Robin Carhart-Harris, Imperial College London - An introduction to psychedelic science.

- 'Neuroscience 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. Sandra Vaz, a postdoc of the Unit, is in charge of the seminar scheduling and organisation. Seminars given by members of other iMM Units are not listed to avoid repetition with other Unit reports.

07/01 – Joana Gonçalves Ribeiro (Master, Ana Sebastião Lab), “Crosstalk between CB1 receptor and adenosine A2A receptor in astrocytes”.

21/01 – Joana Gomes (Master Student, Ana Sebastião Lab) “Role of SNARE-dependent gliotransmitters release by astrocytes upon A β -mediated excitotoxicity”.

28/01 – Ricardo Rodrigues (invited, CNC) “Exploring brain diseases from the perspective of brain development”.

11/02 – Carolina Pina (Master Student, Ana Sebastião Lab) “Astrocytic GABA Transporter Dysfunction in Childhood Absence Epilepsy”.

25/02 – Margarida Godinho (Master Student, Ana Sebastião Lab) “Exploring the activation of NLRP3 inflammasome by reactive oxygen species in a model of epileptogenesis in organotypic slices”.

11/03 – Rui Rodrigues (PhD Student, Ana Sebastião Lab) “Brain-derived neurotrophic factor & Cannabinoids: potent modulators of neural stem cells”.

01/04 – Antónia Ribeiro (Master Student, Ana Sebastião Lab) “Unravelling the expression of NLRP3 in astrocytes”.

29/04 – Catarina Lourenço (PhD Student, Ana Sebastião Lab) "Playing with adenosine on a Rett Syndrome mouse model”.

06/05 – Vanda Nogueira (Master Student, Univesidade da Beira Interior and Ana Sebastião Lab) "Role of adenosine on the resistance to temozolomide anti-tumor agent in glioblastoma”.

13/05 – Robertta Silva Martins (PhD Student, FAPERJ, Laboratório de Neurofarmacologia, Instituto Biomédico, Universidade Federal Fluminense, and Ana Sebastião Lab) “Caffeine modulates NMDA receptor activity in the hippocampus of adolescent mice”.

20/05 – Luzia Sampaio (invited, Instituto de Biofísica Carlos Chagas Filho, Centro de Ciências da Saúde, Universidade Federal do Rio de Janeiro) “The endocannabinoid system, phytocannabinoids and their associayion with therapeutics”.

03/06 – Ana Rita Gomes (PhD Student, IST and Ana Sebastião Lab) “Altered functional proprieties in neural network of MeCP2:R255X-derived dorsal organoids”.

1/07 – Milena Viana (UNIFESP - Universidade Federal de São Paulo and Ana Sebastião Lab), “The neurobiology of anxiety disorders: the role played by serotonin”.

8/07 – Andrea Babić (Master Student of Molecular Biology from University of Zagreb, Croatia and Ana Sebastião Lab) “Assessment of NLRp3 expression in A1 astrocytes”.

15/07 - Joana Mateus (Master, Ana Sebastião Lab) “Targeting oligodendrogenesis in Multiple Sclerosis”.

22/07 - Isabel Cristina Céspedes (invited, Departamento de Morfologia e Genética, Universidade Federal de São Paulo – UNIFESP) "Síndrome de dependência de álcool: visão geral com foco nos aspectos neurobiológicos”.

09/09 – Ana Moreira (PhD Student, Ana Sebastião Lab) "Microreactors to support rat primary cortical neurons against excitotoxicity”.

30/09 – Leonor Rodrigues (PhD Student, Ana Sebastião Lab) “Interaction between BDNF/TrkB signaling and neurogenesis in epilepsy”.

07/10 - Filipa Ribeiro (PhD, Ana Sebastião Lab) “Modulating postnatal neurogenesis”.

14/10 – Pitch presentation by new master students at Ana Sebastião Lab: Carolina Borlido “Searching for a new biomarker for Alzheimer's Disease based on BDNF receptor cleavage”; Celine Freitas; “Characterization of BDNF signalling in the prefrontal cortex in the neonatal phencyclidine mouse model of schizophrenia”; Francisco Meda "NLRP3 inflammasome inhibition in a model of epileptogenesis in organotypic slices – impact in neurodegeneration and epileptiform activity”.

21/10 – Carolina Pina (Master Student, Ana Sebastião Lab) “GABAergic Dysfunction in Childhood Absence Epilepsy: From Astrocytes to Circuits”.

28/10 - Pitch presentations by new master students at Ana Sebastião Lab: Mariana Van Zeller “Relevance of NLRP3 inflammasome in A1 astrocytes – impact of A β -induced toxicity”; Diogo Dias “Impact of NLRP3 inflammasome inhibition in a model of A β -induced toxicity”.

11/11 - Pitch presentations by new master students at Ana Sebastião Lab: Mafalda Carvalho "Phenotypic assessment of astrocytes in a model of epileptogenesis in organotypic slices."; Oksana Savchak; "Nanoparticle and liposome-based microreactors as reactive oxygen species scavengers in a 3D model of neuroinflammation."; Tiago Coelho (collab with iMED) "Unveiling paracrine dissemination and toxicity of neuronal TrkB-ICD via secretome/exosome signalling in Alzheimer's Disease”.

18/11 – Ana Rita Vaz (invited, Neuron Glia Biology in Health & Disease, iMed.Ulisboa, FFUL) “Targeting microRNAs in glia & motor neurons to restore neuro-immune function in ALS”.

25/11 - Pitch presentations by new master students at Ana Sebastião Lab: Svitlana Zavalko “Cannabinoid actions on Rett Syndrome’s associated deficits and its effect on post-natal neurogenesis in a female MECP2-mutant mouse model; "Mafalda Manso (collab with iMED); "The impact of BDNF receptor cleavage in Alzheimer's disease-associated Neuroinflammation”.

- Seminars at the PhD and 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:

12/9 – Major neurotransmitter pathways and their role in brain function (Ana Sebastião).

17/09 - Basics of neuronal excitability and neuronal communication: electrochemical gradients and equilibrium potential; membrane potential, action potential, synaptic potential (Ana M Sebastião).

19/09 – Synaptic integration. Ion channels and ion transporters. Ionotropic receptors vs metabotropic receptors (Ana M Sebastião).

24/9 –G proteins and transducing pathways (Sandra Vaz).

26/9 - Inhibitory and excitatory synaptic transmission. Different neurotransmitters, their release and inactivation. (Ana M Sebastião).

1/10 – Concept of neuromodulation and main neuromodulators. Concept of co-transmission (Ana M Sebastião).

3/10 – Plasticity of glutamatergic synaptic transmission (Raquel Dias).

- 8/10 – Modulation of GABAergic transmission (Diogo Rombo).
- 10/10 – Glial Cells and their ability to control synaptic activity (Sandra Vaz).
- 25/09 - Constructing artificial astrocytes against excitotoxicity (Ana Moreira).
- 2/10 - Evaluation of synaptic activity through electrophysiological recording Techniques (Diogo Rombo).
- 2/10 – Receptor quantification assays: relevance for the study of neurodegenerative diseases (Nádia Rei/Rita Belo).
- 15/10 – Neurotrophic factors: key molecules for neuronal survival and plasticity (Maria José Diógenes).
- 17/10 – The role of glial cells in neuroinflammation (Cláudia Valente).
- 22/10 – Neural Stem cells and its neuroregenerative potential (Sara Xapelli).
- 16/10 – Synaptic dysfunction in Rett Syndrome (Catarina Lourenço).
- 23/10 – Modulation of neuronal maturation and differentiation by adenosine (Ana Filipa Ribeiro).
- 23/10 – Modulation of postnatal neurogenesis by cannabinoids (Rui Rodrigues).
- 23/10 – BDNF receptor cleavage: relevance for Alzheimer’s Disease pathophysiology (João Gomes).
- 14/11 - Mechanisms of drug dependence (Alexandre Ribeiro).
- 19/11 – Behavioural testing in laboratory animals - Cannabinoid receptors influence upon memory (Francisco Mouro).

- Seminars and lectures at other post-graduation courses/events given by Unit members:

Sebastião AM. Técnicas microelectrofisiológicas. Faculdade de Farmácia da Universidade de Lisbon, Portugal, 2019.

Sebastião AM. Acção de derivados de canábis no cérebro. Sessões ‘Que há de novo no CAML’, Lisbon, Portugal, March 2019.

Valente CA. Neurobiology of inflammation: concepts and relevance in neurological disorders. Lecture in “Frontiers in Biology”, Mestrado em Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, April 26, 2019.

Xapelli S. Adult neurogenesis and oligodendrogenesis. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, April 2019.

Xapelli S. Modelos experimentais de epilepsias. 2º Curso Tratamento Farmacológico Das Epilepsias, Costa da Caparica, Portugal, October 25-27, 2019.

Xapelli S. Adult neurogenesis and oligodendrogenesis. Universidade do Algarve, Algarve, Portugal, November 2019.

Sebastião AM. Synaptic and behavioural actions of cannabinoids: control by adenosine and caffeine related drugs. Clínica Universitária de Neurologia, Lisbon, Portugal, July 2019.

Diógenes MJ. Mechanisms of cellular death and neuroprotection. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, October, 2, 2019.

Diógenes MJ. Princípios básicos de farmacocinética. 2º Curso Tratamento Farmacológico Das Epilepsias, Costa da Caparica, Portugal, October 25-27, 2019.

Diógenes MJ. Neurotrophic factors: key molecules for neuronal survival and plasticity -new drug and new biomarker. Master, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, October 31, 2019.

Mouro FM. (Alguns) métodos de estudo do cérebro: análise de comportamento animal em laboratório. Universidade Católica Portuguesa, Lisbon, Portugal, October 2019.

Sebastião AM. (Alguns) métodos de estudo do cérebro: abordagem *ex vivo*. Universidade Católica Portuguesa, Lisbon, Portugal, October 2019.

Sebastião AM. Neuronal Communication and Plasticity. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, October 2019.

- Practical Workshops:

Diógenes MJ, Vaz S. Organizers. Recordings of synaptic potentials from hippocampal slices. October 11, 2019.

Valente C. Organizer. Methodological approaches for neuroinflammation research. October 21-22, 2019.

Xapelli S. Organizer. Neural stem cells and its potential for neuroregeneration. October 24-25, 2019.

Mouro F. Organizer. Behaviour assessment in laboratory animals. November 22, 2019.

Science and Society

Unit members participated in activities of the Brain Awareness Week (March 11-17, but other periods also), with 'lectures' and debates in Basic and Secondary Schools, with the objective of increasing awareness on brain function and dysfunctions, as well as on the scientific activity itself. Unit members also participated in 'Noite Europeia dos Investigadores, Lisbon, Portugal, 27/09, 2019.

Also to increase public awareness of brain research was the participation in: 'Caminhada de sensibilização do Síndrome de Rett (Diógenes MJ, Miranda-Lourenço, Seixal, Portugal), October 20, 2019, and the TV programme "Casos Singulares" on Rett Syndrome (Diógenes MJ, RTP1, 1/11, 2019).

We also highlight the participation in: Next Einstein Forum 2019 – Cabo Verde (Sandra Vaz, October 16, 2019), Science Club in Clínica Universitária de Pediatria, HSM (Sandra Vaz, December 10, 2019) round table "research in neurosciences" for the "Grupo IFE" (Diogenes MJ and Sebastião AM, Novotel, Lisboa, 12/04, 2019).

MSc Theses

Miguel Ferreira, 26/02/2019, Characterization of the affective behavioural effects of chronic adolescent exposure to the cannabinoid receptor agonist HU-210 in female rats. Master in Neuroscience, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana M Sebastião.

Beatriz Joana Marques Cardoso, 24/07/2019, The role of posttranslational modifications on STAT3 behavior, Faculdade de Medicina da Universidade de Lisboa e Instituto de Tecnologia Química e Biológica (ITQB). Supervisor: Federico Herrera. Co-Supervisor: Sandra Vaz.

João Batista Moreira, 17/09/2019, Role of cannabinoid type 2 receptor and physical exercise in subventricular zone neurogenesis, Faculdade de Ciências e Tecnologia da Universidade de Coimbra. Supervisor: Sara Xapeli.

Antónia Sofia Fortunato Ribeiro, 17/09/2019, Exploring NLRP3 inflammasome expression in A1 astrocytes. Master in Biomedical Research, Faculdade de Medicina da Universidade de Coimbra. Supervisor: Cláudia A Valente.

Jéssica Rosa, 7/10/2019, Caracterização do sistema adenosinérgico e da sinalização mediada pelo BDNF em fêmeas heterozigóticas do modelo animal da síndrome de Rett, Mestrado em Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria José Diógenes. Co-Supervisor: Catarina Miranda-Lourenço.

Carolina de Campos Pina, 29/10/2019, GABAergic Dysfunction in Absence Epilepsy: From Astrocytes to Circuits, Faculdade de Medicina da Universidade do Porto. Supervisor: Sandra Vaz. Co-Supervisor: Fani Neto (Universidade do Porto).

Bruno Silva-Santos Lab

Major Interests/Objectives

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 and macrophages, 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.

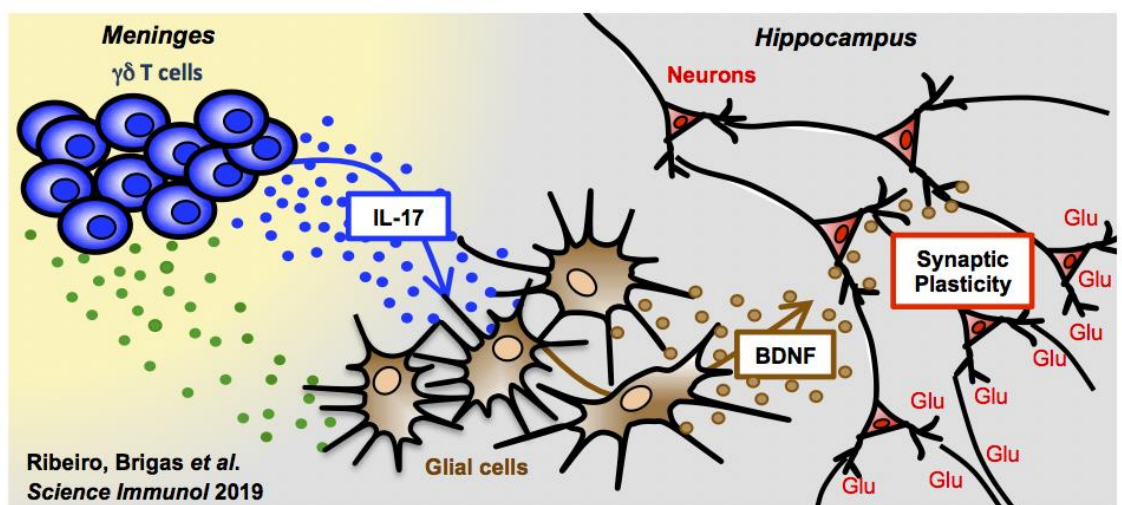
In a more recent area in our lab – Neuroimmunology – we explore the crosstalk between the immune system, particularly T cells that populate the meninges, and the brain – either in health (cognition) or in disease (neurodegeneration).

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.

Head of Laboratory

Bruno Silva-Santos, Associate Professor at Faculdade de Medicina da Universidade de Lisboa, Vice-Director at Instituto de Medicina Molecular João Lobo Antunes

Graphical Abstract



Team

Afonso Figueiredo Antunes Lameiras de Almeida	University Degree	GAPIC Student (Left September)
Afonso Maria Douwens da Costa Teixeira da Mota	University Degree	MSc Student (Started September)
Ana Maria de Amarante Pamplona Dias Santos	PhD	Senior Postdoctoral Researcher
Ana Raquel Vicente Lopes	University Degree	MSc Student (Left April)
Ana Teresa da Silva Pais	University Degree	MSc Student (Started July)
André Gonçalo do Espírito Santo Simões	PhD	Postdoctoral Researcher (Left February)
Anita Raquel Quintal Gomes	PhD	Senior Postdoctoral Researcher
Arno Bindlechner	High School Diploma	Erasmus Student (Started July. Left November)
Carolina Emanuel Carreira Gomes Jardim	Master Degree	PhD Student
Catarina Pelicano da Cunha Branco da Costa	University Degree	MSc Student (Left September)
Daniel Pereira Inácio	Master Degree	PhD Student
Daniel Vargas Correia	PhD	Senior Postdoctoral Researcher (Started January)
Gina Jasmin Fiala	PhD	Postdoctoral Researcher
Gisela da Silva Gordino	Master Degree	PhD Student
Gonçalo Pimenta Pedro Palmeirim	University Degree	MSc Student (Left December)
Heleen Van Acker	PhD	Postdoctoral Researcher (Started January, Left May)
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
Madalena Frota de Carvalho	High School Diploma	Trainee (Started September, Left September)
Maria Helena Cristiano Brigas	Master Degree	PhD Student
Mariana Reis Sobreiro	PhD	Senior Postdoctoral Researcher
Miguel Alves Rovisco Ribeiro	Master Degree	Researcher
Natacha Maria Gonçalves Silva Sousa	Master Degree	Lab Manager
Noella Lopes Pappalardo	PhD	Postdoctoral Researcher (Started January)
Pedro Henrique Papotto Rosa	Master Degree	PhD Student (Left September)
Sara Alexandra da Costa Pereira	BSc Student	MSc Student
Sara Félix Dâmaso	Master Degree	MSc Student (Started October)
Sofia Mensurado Santos	Master Degree	PhD Student
Tiago Maria de Carvalho da Costa Amado	Master Degree	PhD Student (Left December)
Tommaso Scolaro	Master Degree	Erasmus Student (Started February, Left June)

Laboratory Keywords / Research Areas

Keywords:

Thymocyte Development, Gamma-delta T cells, Leukocyte Differentiation, Tumor Microenvironment, Meningeal Immune System.

Areas: Immuno-Oncology, Neuroimmunology, Lymphocyte Differentiation.

Major Scientific Achievements

In 2019, we graduated 3 PhD and 3 MSc students; and published 11 papers in international peer-reviewed journals. Some of our major findings were the identification of meningeal gamma-delta T-cells producing interleukin 17 (IL-17) in the healthy mouse brain, where they control neuronal synaptic plasticity in the hippocampus and short-term memory formation (Ribeiro *et al.*, *Science Immunol* 2019); the characterization of a pathogenic role of interferon-gamma producing hepatic gamma-delta T cells in experimental cerebral malaria, through modulation of parasite virulence (Ribot *et al.*, *PNAS* 2019); and the demonstration that epigenetic modifiers, namely hypomethylating drugs, can suppress the outgrowth of chemoresistant clones with stemness properties in acute myeloid leukemia (AML) (Caiado *et al.*, *Nature Communications* 2019). We also published review articles in the top journals, *Nature Rev Cancer* and *Nature Rev Drug Dev*, on gamma-delta T cells in cancer and their therapeutic application.

Selected Publications

Schmolka N, Papotto PH, Romero PV, Amado T, Enguita FJ, Amorim A, Rodrigues AF, Gordon KE, Coroadinha AS, Boldin M, Serre K, Buck AH, Gomes AQ*, Silva-Santos B* (2018). MicroRNA-146a controls functional plasticity in $\gamma\delta$ T cells by targeting NOD1. **Science Immunology** 3(23):pii: eaao1392. *Co-corresponding and co-last authors. Cover paper**. (IF: 10.551, Citations: 4. Source: Thomson Reuters).

Mensurado S, Rei M, Lança T, Ioannou M, Gonçalves-Sousa N, Kubo H, Malissen M, Papayannopoulos V, Serre K, Silva-Santos B (2018). Tumor-associated neutrophils suppress pro-tumoral IL-17+ $\gamma\delta$ T cells through induction of oxidative stress. **PLoS Biology** 16(5):e2004990. (IF: 9.163, Citations: 15. Sources: Thomson Reuters).

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 $\gamma\delta$ T cell subsets. **Nature Immunology** 17(6):721-7. (IF: 21.506, Citations: 38. Source: Thomson Reuters).

Schmolka N*, Serre K*, Grosso AR, Rei M, Pennington DJ, Gomes AQ**, Silva-Santos B** (2013). Epigenetic and transcriptional signatures of stable versus plastic differentiation of pro-inflammatory $\gamma\delta$ T cell subsets. **Nature Immunology** 14(10):1093-100. (IF: 24.973; Citations: 53. Source: Thomson Reuters).

Correia DV, Fogli M, Hudspeth K, da Silva MG, Mavilio D, Silva-Santos B (2011). Differentiation of human peripheral blood Vdelta1+ T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells. **Blood** 118(4):992-1001. (IF: 9.898, Citations: 83. Source: Thomson Reuters).

Ongoing Research Projects

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: 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.

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: Magiciam: um sistema imunodelador de macrófagos para prevenir a invasão e metastização das células tumorais. Coordinator: Karine Serre. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: MAGICIAM - POCI-01-0145-FEDER-031859. Amount: € 12 500,00. Total Amount: € 238 554,80.

2018/2021: Combinando métodos computacionais e experimentais para obter uma caracterização genérica dos péptidos de fusão de vírus. Coordinator: Karine Serre. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-OUT/31118/2017. Amount: € 48 750,00. Total Amount: € 239 925,00.

2018/2020: Tracking $\gamma\delta$ T cell development and TCR $\gamma\delta$ proximal signalling — DevoSignGammaDelta. Coordinator: Bruno Silva-Santos. Funding Agency: European Commission. Reference: DevoSignGammaDelta – 752932. Amount: € 160 635,60. Total Amount: € 160 635,60.

2018/2019: GDT - Research Agreement. Coordinator: Bruno Silva-Santos. Funding Agency: Lymphocyte Activation Technologies SA. Reference: GDT - Research Agreement. Amount: € 184 176,00. Total Amount: € 184 176,00.

2018/2019: Sulphur-containing amino acid dietary modulation of breast cancer immunity. Coordinator: Karine Serre. Funding Agency: Fundo IMM-Laço. Reference: Fundo Laço. Amount: € 28 125,00. Total Amount: € 28 125,00.

2018/2019: Tumour-associated neutrophils suppress pro-tumoral IL-17+ $\gamma\delta$ T cells through induction of oxidative stress. Coordinator: Bruno Silva-Santos. Funding Agency: Janssen. Reference: Prémio Janssen 2018. Amount: € 30 000,00. Total Amount: € 30 000,00.

2016/2019: Dissection of microRNA mediated post-transcriptional regulation of gd T cell differentiation. Coordinator: Anita Gomes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BCM/3592/2014. Amount: € 172 334,00. Total Amount: € 172 334,00.

2015/2020: 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.

2015/2020: Lineage-specific molecular networks that control pro-inflammatory cytokine production. Coordinator: Karine Serre. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/0004/2014/CP1236/CT0006. Amount: € 50 000,00. Total Amount: € 50 000,00.

2015/2020: Deciphering the outside-in mechanisms of human gd T Cell differentiation. Coordinator: Julie Ribot. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00013/2014/CP1236/CT0004. Amount: € 50 000,00. Total Amount: € 50 000,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria do Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Di Lorenzo B, Simões AE, Caiado F, Tieppo P, Correia DV, Carvalho T, da Silva MG, Déchanet-Merville J, Schumacher TN, Prinz I, Norell H, Ravens S, Vermijlen D, Silva-Santos B (2019). Broad Cytotoxic Targeting of Acute Myeloid Leukemia by Polyclonal Delta One T Cells. **Cancer Immunology Research** 7(4):552-558. (IF: 8.619, Citations: 3. Source: Thomson Reuters).

Staats R, Rodrigues R, Barros A, Bacelar-Nicolau L, Aguiar M, Fernandes D, Moreira S, Simões A, Silva-Santos B, Rodrigues JV, Barbara C, de Almeida AB, Ferreira Moita LF (2019). Role of CD3+ $\gamma\delta$ -T cells in the association of obstructive sleep-disordered breathing and cancer. **Sleep and Breathing** April. (IF: 2.326, Citations: 2. Source: Thomson Reuters).

Ribot JC, Neres R, Zuzarte-Luís V, Gomes AQ, Mancio-Silva L, Mensurado S, Pinto-Neves D, Santos MM, Carvalho T, Landry JJM, Rolo EA, Malik A, Silva DV, Mota MM, Silva-Santos B, Pamplona A (2019). $\gamma\delta$ -T cells promote IFN- γ -dependent Plasmodium pathogenesis upon liver-stage infection. **Proceedings of the National Academy of Sciences** 116(20):9979-9988. (IF: 9.580, Citations: 1. Source: Thomson Reuters).

Silva-Santos B, Mensurado S, Coffelt SB (2019). $\gamma\delta$ T cells: pleiotropic immune effectors with therapeutic potential in cancer. **Nature Reviews Cancer** 19(7):392-404. Review. (IF: 51.848, Citations: 5. Source: Thomson Reuters).

Tan L, Sandrock I, Odak I, Aizenbud Y, Wilharm A, Barros-Martins J, Tabib Y, Borchers A, Amado T, Gangoda L, Herold MJ, Schmidt-Supprian M, Kisielow J, Silva-Santos B, Koenecke C, Hovav AH, Krebs C, Prinz I, Ravens S (2019). Single-Cell Transcriptomics Identifies the Adaptation of Scart1+ V γ 6+ T Cells to Skin Residency as Activated Effector Cells. **Cell Reports** 27(12):3657-3671. (IF: 7.815, Citations: 0. Source: Thomson Reuters).

Di Lorenzo B, Ravens S, Silva-Santos B (2019). High-throughput analysis of the human thymic V δ 1+ T cell receptor repertoire. **Scientific Data** 6(1):115. (IF: 5.929, Citations: 1. Source: Thomson Reuters).

Sebestyén Z, Prinz I, Déchanet-Merville J, Silva-Santos B, Kuball J (2019). Translating gammadelta ($\gamma\delta$) T cells and their receptors into cancer cell therapies. **Nature Reviews Drug Discovery** 19(3):169-184. Review. (IF: 57.618, Citations: 1. Source: Thomson Reuters).

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Invited Lectures and Seminars

Silva-Santos B. Gamma-delta T cell differentiation and roles in immunity. First Symposium of Jinan University-Instituto de Medicina Molecular João Lobo Antunes, Guangzhou, China, January 12, 2019.

Serre K. Why so much hope about immunotherapy? Jornadas de Genética e Biotecnologia/I Jornadas Ibéricas de Genética e Biotecnologia, Vila Real, Portugal, March 15, 2019.

Silva-Santos B. Gamma-delta T cells: pleiotropic roles and therapeutic potential. Cancer Immunotherapy Workshop, Champalimaud Centre for the Unknown, Lisbon, Portugal, March 27-29, 2019.

Silva-Santos B. Gamma-delta T cells: new roles for old cells. Stony Brook Symposium, Stony Brook, New York, USA, April 29, 2019.

Silva-Santos B. Unexpected roles for tissue-resident gamma-delta T cells. Rockefeller Institute, New York, USA, May 1, 2019.

Silva-Santos B. Unanticipated links between gamma-delta T cells and the brain: cerebral malaria and working memory. Harvard Medical School, Boston, USA, May 2, 2019.

Mensurado S. Immunotherapy and its mechanisms of cardiotoxicity. IV Congresso Internacional de Imagem Médica e Radioterapia, Castelo Branco, Portugal, May 10, 2019

Silva-Santos B. Unanticipated roles for tissue-resident gamma-delta T cells in infection and beyond. Lydia Becker Institute, University of Manchester, Manchester, UK, May 23, 2019.

Silva-Santos B. (Patho)physiological roles of gamma-delta T cells in tissues. Annual Meeting of the Spanish Society for Immunology, Seville, Spain, May 30, 2019.

Ribot JC. T cell development, with a little help from CD27. Symposium Paola Romagnoli, Toulouse, France, June 14, 2019.

Serre K. S02 - Finding the strengths that make cancer cells weak - Immunotherapy in cancer. ESHG conference, Gothenburg, Sweden, June 16, 2019.

Gomes AQ. Role of microRNAs in pro-inflammatory cytokine production by T cells. Science with Art, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, July 8, 2019.

Gomes AQ. microRNAs e Imunidade. Opening session of Master in Molecular Technologies in Health, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, September 18, 2019.

Silva-Santos B. Delta One T cells: development of a novel cellular immunotherapy for cancer. First Joint Meeting of the Spanish and Portuguese Societies for Oncology Research, Salamanca, Spain, September 12-13, 2019.

Silva-Santos B. Delta One T cells: development of a novel cellular immunotherapy for cancer. Annual Meeting of the Portuguese Society for Stem Cells and Cellular Therapies, Lisbon, Portugal, October 11, 2019.

Silva-Santos B. Delta One T cells: developing a novel cell therapy for cancer. Immunogenomics conference, Lisbon, Portugal, October 28-31, 2019.

Silva-Santos B. Delta One T cells: developing a novel cell therapy for cancer. Lisbon Investor Conference, Lisbon, Portugal, November 9, 2019.

Silva-Santos B. Physiological or pathological: the double life of gamma-delta T cells. Centro de Doenças Crónicas, Lisbon, Portugal, November 13, 2019.

Ribot JC. Unconventional functions for unconventional T cells. SFI, Nantes, France, November 14, 2019.

Silva-Santos B. Differentiation of gamma-delta T cell subsets and key roles in severe malaria. University of Edinburgh, Edinburgh, UK, November 28, 2019.

Communications in International Conferences

Fiala GJ, Schaffer AM, Merches K, Morath A, Swann J, Herr L, Hils M, Esser C, Minguet S, Schamel WWA. Proximal Lck promoter-driven Cre expression is inefficient in gamma delta T cells and varies between neonatal and adult gamma delta T cell development. Harald von Boehmer Midwinter Conference on Advances in Immunology, Seefeld, Austria, January 19-23, 2019. *(Poster Presentation)*.

Silva-Santos B. Midwinter Conference, Seefeld, Austria, January 20-23, 2019. *(Oral Presentation)*.

Brigas HC*, Ribeiro M*, Coelho J E, Temido M, Marques Morgado I, Valente C, Omenetti S, Stockinger B, Manadas B, Silva-Santos, Lopes LV and Ribot JC. Elucidating the impact of IL-17 on memory: From physiology to Alzheimer's Disease. 14th International Conference on Alzheimer's and Parkinson's Diseases, Lisbon, Portugal, March 26-31, 2019. *(Poster Presentation)*.

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Methionine intake improves breast cancer immunotherapy efficacy. 5th Workshop on Dendritic Cell Biology, Lisbon, Portugal, March 27-29, 2019. *(Poster Presentation)*.

Lopes R, Pinto M, Mensurado S, Kubo H, Boekhoff H, Scolaro T, Reis-Sobreiro M, Silva-Santos B, Serre K. Characterization of macrophages with anti-tumour functions in vitro and in vivo. 5th Workshop on Dendritic Cell Biology: Anti-tumoral immunotherapy, from biology to the clinic, Champalimaud Foundation, Lisbon, Portugal, March 27-29, 2019. *(Poster Presentation)*.

Silva-Santos B. ECM talk, 13th World Immune Regulation Meeting, Davos, Switzerland, April 7, 2019. (*Oral Presentation*).

Silva-Santos B. Meningeal gd17 talk. 13th World Immune Regulation Meeting, Davos, Switzerland, April 9, 2019. (*Oral Presentation*).

Lopes R, Pinto M, Mensurado S, Kubo H, Silva-Santos B, Serre K. Different signalling pathways govern the emergence of macrophages and neutrophils with anti-tumour functions. Cost-action Mye-EUNITER - 5th Management Committee & Working Group Meeting, 5th Early Career Investigators' Workshop, Heraklion, Crete, Greece, April 16-17, 2018. (*Poster Presentation*).

Cunha C, Romero PV, Pelicano C, Papotto P, Amado T, Inácio D, Gomes AQ, Silva-Santos B. MicroRNA determinants of the balance between effector and regulatory CD4⁺ T cells *in vivo*. 14th Microsymposium on small RNAs, Vienna BioCenter, Vienna, Austria, May 15-17, 2019. (*Poster Presentation*).

Lopes R, Pinto M, Mensurado S, Kubo H, Boekhoff H, Scolaro T, Reis-Sobreiro M, Silva-Santos B, Serre K. Characterization of macrophages with anti-tumour functions *in vitro* and *in vivo*. 5th International Conference of Translational Medicine on Pathogenesis and Therapy of Immunomediated Diseases Travel Award (Italian Society of Clinical Immunology and Allergology), Milan, Italy, May 16-18, 2019. (*Poster Presentation*).

Fiala GJ, Schaffer AM, Merches K, Morath A, Swann J, Herr L, Hils M, Esser C, Minguet S, Silva-Santos B, Schamel WWA. Proximal Lck promoter-driven Cre expression in gamma delta T cells: Constricted during neonatal and ineffective in adult gamma delta T cell development. EMBO Workshop "ThymE: T cell and thymus biology" at the Weizmann Institute of Science in Rehovot, Israel, May 19-24, 2019. (*Oral Presentation*).

Inácio D, Amado T, Sobral D, Enguita F, Gomes AQ and Silva-Santos B. Uncovering the role of microRNAs in the control of effector $\gamma\delta$ T cell differentiation. Workshop $\gamma\delta$ FOR 2799 "Receiving and Translating Signals via the $\gamma\delta$ TCR", Erlangen, Germany, June 12-14, 2019. (*Poster Presentation*).

Papotto PH, Pimenta G, Yilmaz B, Fiala G, Gomes da Costa D, Chan BHK, Mensurado S, Blankenhaus B, Carvalho T, Macpherson AJ, Allen JE, Silva-Santos B. Maternal $\gamma\delta$ T cells shape pulmonary type-2 immunity of the offspring in a microbiota-dependent manner. Workshop FOR2799 "Receiving and Translating Signals via the $\gamma\delta$ TCR workshop", Erlangen, Germany, June 12-14, 2019. (*Poster Presentation*).

Fiala GJ, Schaffer AM, Merches K, Morath A, Swann J, Herr L, Hils M, Esser C, Minguet S, Schamel WWA. Proximal Lck promoter-driven Cre function is limited in neonatal and ineffective in adult gamma delta T cell development. Workshop FOR 2799 "Receiving and Translating Signals via the gamma delta TCR", Erlangen, Germany, June 12-14, 2019. (*Poster Presentation*).

Inácio D, Amado T, Sobral D, Enguita F, Gomes AQ and Silva-Santos B. A key role for microRNAs in regulating IL-17 versus IFN- γ production by $\gamma\delta$ T cells. 3rd International Symposium on Frontiers in Molecular Science — RNA Regulatory Networks, Lisbon, Portugal, June 26-28, 2019. (*Poster Presentation*).

Cunha C, Romero PV, Pelicano C, Papotto P, Schmolka N, Amado T, Inácio D, Gomes AQ, Silva-Santos B. MicroRNA determinants of the balance between effector and regulatory CD4⁺ T cells *in vivo*. 3rd International Symposium on Frontiers in Molecular Science – RNA Regulatory Network, Pavilhão do Conhecimento, Lisbon, Portugal, June 26-28, 2019. (*Oral Presentation*).

Corredeira P, Alves P, Gordino G, Pereira S, Ribot J, Andrade P, Bruçó L, Pinheiro C, Casimiro S, Martins M, Mansinho A, Ribeiro L, Fernandes I, Vendrell I, Pinto C, Dionísio MR, Sousa R, Silva-Santos B, Costa L. T cell profiling in metastatic breast cancer reveals a subtype independent immunosuppressive state. 1st ASEICA-ASPIC International Meeting, Salamanca, Spain, September 12-13, 2019. (*Poster Presentation*).

Mensurado S, Pestana T, Lopes R, Serre K, Silva-Santos B. Methionine increases the efficacy of suboptimal anti-PD-1 treatment by boosting an anti-tumor gamma-delta/ CD8⁺ T cell crosstalk. Cancer Immunotherapy Conference, Paris, France, September 25-28, 2019. (*Poster Presentation*).

Inácio D, Amado T, Sobral D, Enguita F, Silva-Santos B* and Gomes AQ*. Uncovering the role of microRNAs in the control of effector gd T cell differentiation. EMBL Symposium: The Non-Coding Genome, EMBL, Heidelberg, Germany, October 16-19, 2019. (*Poster Presentation*).

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Methionine increases the efficacy of suboptimal anti-PD-1 treatment by boosting an anti-tumour $\gamma\delta$ / CD8⁺ T cell crosstalk. Immunogenomics 2019 Conference, Lisbon, Portugal, October 28-30, 2019. (*Poster Presentation*).

Lopes R, Pinto M, Mensurado S, Kubo H, Boekhoff H, Scolaro T, Reis-Sobreiro M, Silva-Santos B, Serre K. Characterization of macrophages with anti-tumour functions *in vitro* and *in vivo*. Immunogenomics, Champalimaud Foundation, Lisbon, Portugal, October 28-30, 2019. (*Poster Presentation*).

Lopes N, Martins S, Arguello R, Sumaria N, Silva-Santos B and Pennington DJ, Metabolic regulation of pleiotropic $\gamma\delta$ T cell subsets in the tumor microenvironment. Immunogenomics 2019 Conference, Champalimaud Foundation, Lisbon, Portugal, October 28-30, 2019. (*Poster Presentation*).

Communications in National Conferences

Inácio D, Amado T, Sobral D, Enguita F, Gomes AQ, Silva-Santos B. Uncovering the role of microRNAs in the control of effector $\gamma\delta$ T cell differentiation. XLV Annual Meeting of the Portuguese Society for Immunology – Leaping Forward Translational Immunology, Coimbra, Portugal, May 15-17, 2019. (*Oral Presentation*).

Gordino G, Costa-Pereira SA, Corredeira P, Costa L, Gomes AQ, Silva-Santos B, Ribot JC. miR-181a negatively regulates human $\gamma\delta$ T cell differentiation into anti-tumor effectors. XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Brigas HC*, Ribeiro M*, Coelho JE, Temido M, Marques Morgado I, Valente C, Omenetti S, Stockinger B, Manadas B, Silva-Santos, Lopes LV, Ribot JC. Elucidating the impact of IL-17 on memory: From physiology to Alzheimer's Disease. XLV Annual Meeting of Sociedade Portuguesa de Imunologia, Coimbra, Portugal, May 15-17, 2019. (*Oral Presentation*).

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Methionine intake improves breast cancer immunotherapy efficacy. XLV Annual Meeting of Sociedade Portuguesa de Imunologia, Coimbra, Portugal, May 15-17, 2019. (*Poster Presentation*).

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Methionine intake improves breast cancer immunotherapy efficacy. XLV Annual Meeting of Sociedade Portuguesa de Imunologia, Coimbra, Portugal, May 15-17, 2019. (*Oral Presentation*).

Mensurado S. Regulation of T cell fitness in the tumour microenvironment: From myeloid cells to dietary factors. XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Brigas HC*, Ribeiro M, Coelho JE, Silva-Santos, Lopes LV and Ribot JC. Elucidating the impact of IL-17 on Alzheimer's Disease. XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Brigas HC, Ribeiro M, Coelho JE, Silva-Santos, Lopes LV and Ribot JC. Elucidating the impact of IL-17 on Alzheimer's Disease. SPN2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. SPN2019, Lisbon, Portugal, May 30-June 1, 2019. (*Oral Presentation*).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. SPN2019, Lisbon, Portugal, May 30- June 1, 2019. (*Poster Presentation*).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. Champalimaud Research Symposium 2019, Lisbon, Portugal, October 8-10, 2019. (*Poster Presentation*).

Gordino G, Costa-Pereira SA, Gomes AQ, Silva-Santos B, Ribot JC. miR-181a negatively regulates human $\gamma\delta$ T cell differentiation into anti-tumor effectors. Champalimaud Research Symposium 2019, Lisbon, Portugal, October 8-10, 2019. (*Poster Presentation*).

Lopes N, Martins S, Arguello R, Sumaria N, Silva-Santos B, Pennington DJ. Metabolic regulation of pleiotropic $\gamma\delta$ T cell subsets in the tumor microenvironment. 3rd IGC symposium 'Crosstalks of Immunity and Metabolism', Instituto Gulbenkian de Ciência, Oeiras, Portugal, November 11-14, 2019. (*Poster Presentation*).

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Methionine increases the efficacy of suboptimal anti-PD-1 treatment by boosting an anti-tumour $\gamma\delta$ / CD8⁺ T cell crosstalk. 3rd IGC symposium 'Crosstalks of Immunity and Metabolism', Instituto Gulbenkian de Ciência, Oeiras, Portugal, November 11-14, 2019. (*Oral Presentation*).

Organization of Conferences

Gonçalves-Sousa N. Co-Organizer. XLV Annual Meeting of the Portuguese Society for Immunology, Coimbra, Portugal, May 15-17, 2019.

Prizes, Honors and Awards

Lopes N. EMBO long-term fellowship, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 15, 2019.

Silva-Santos B, Lopes N. Faz Ciência Award, AstraZeneca & Portuguese Society for Oncology, Portugal, April 23, 2019.

Reis-Sobreiro M. Travel Award to support presentation at International conference, 5th International Conference of Translational Medicine on Pathogenesis and Therapy of Immunomediated Diseases, Italian Society of Clinical Immunology and Allergology, Italy, May 16-18, 2019

Mensurado S, Pestana T, Lopes R, Silva-Santos B*, Serre K*. Best Poster Award at XLV Annual Meeting of Sociedade Portuguesa de Imunologia, Sociedade Portuguesa de Imunologia, Portugal, May, 17, 2019

Mensurado S, Rei M, Lança T, Ioannou M, Gonçalves-Sousa N, Kubo H, Malissen M, Papayannopoulos V, Serre K, Silva-Santos B. Best Paper Award at XLV Annual Meeting of Sociedade Portuguesa de Imunologia, Sociedade Portuguesa de Imunologia, Portugal, May, 17, 2019

Fiala GJ was awarded a Travel Grant from the EMBO Workshop “ThymE: T cell and thymus biology” at the Weizmann Institute of Science in Rehovot, Israel, from May 19-24, 2019.

Papotto P. Best Poster Award – Receiving and Translating Signals via the $\gamma\delta$ TCR workshop – FOR2799 Consortium, Germany, June 13, 2019.

Papotto P. EMBO Long Term Fellowship – EMBO, Germany, June 6, 2019.

Pelicano C. IMM Best Master Thesis Award 2018/2019 (2nd Prize), Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, December 3, 2019.

Advanced Teaching

Silva-Santos B. Imunoterapia no cancro digestivo. Workshop sobre Cancro Digestivo, Lisbon, Portugal, January 26, 2019.

Serre K. Lecture. Leukocyte subsets in the tumor microenvironment - Tumor immunity. Module of Onco-Immunology of the Oncobiology Master, Universidade de Lisboa, Lisbon, Portugal, February 5, 2019.

Serre K. Lecture. The Cancer & the host (½ lecture shared with Professor Luis Costa). 3rd year Med students, Module of Oncobiology, Universidade de Lisboa, Lisbon, Portugal, March 8, 2019.

Silva-Santos B. CAR-T cells in cancer immunotherapy. Gilead, Lisbon, Portugal, March 26, 2019.

Silva-Santos B. Gamma-delta T cells in cancer. Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisbon, Portugal, April 4, 2019.

Serre K. Lecture. “Why so much hope about immunotherapy? Harnessing the power of the immune system: Immunotherapy”. 4th year of Mestrado Integrado em Ciências Farmacêuticas module Oncobiologia e Terapias de Precisão, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, April 30, 2019.

Silva-Santos B. Immunology and cancer. Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisbon, Portugal, May 8, 2019.

Silva-Santos B. Mechanisms of resistance to PD-1/ PD-L1 inhibitors. Shaping Tomorrow – Redefining Cancer Immunotherapy, Roche, Oeiras, Portugal, May 11, 2019.

Silva-Santos B. (Patho)physiological roles of gamma-delta T cells in tissues. Symposium of the DFG Doctoral Training Program GRK 16060, Bad Endorf, Germany, June 5, 2019.

Fiala GJ. Lecture. Immune cell signaling. Signaling and Gene Expression Regulation course of the Molecular Technologies in Health MSc Program, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, September 26, 2019.

Gomes AQ. miRNAs as regulators of gd T cell differentiation. Signaling and Gene Expression Module, Master in Molecular Technologies in Health, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, October 10, 2019.

Serre K. Lecture. Caloric restriction and immune response. Licenciatura Ciências da Nutrição (LNC), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 31, 2019.

Serre K. Lecture. Harnessing the immune system for immunotherapy. Mestrado integrado em ciências farmacêuticas - Alvos Terapêuticos e Biomarcadores- Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, November 26, 2019.

Serre K. Lecture. Tumor Immunology. Licenciatura Ciências da Nutrição (LNC), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 28, 2019.

Serre K. Lecture. Diversification of T helper cell functions. MCDIE mestrado em infecção: immunology classes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 09, 2019.

Serre K. Lecture. Cancer Immunotherapy. Licenciatura Ciências da Nutrição (LNC), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 03, 2019.

Gomes AQ. $\gamma\delta$ T cells as an example of anti-tumour lymphocytes. Post-graduation in Oncobiology, Immunotherapy Module, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, December 13, 2019.

Science and Society

Silva-Santos B. Debate. Porque é que o cancro nos escapa? Horizontes IMM: Uma pergunta a três, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 20, 2019.

Silva-Santos B. Radio show. Porque é que o cancro nos escapa? Antena 3, Lisbon, Portugal, February 27, 2019.

Mensurado S. Participation on "Cancro da Mama: Saúde e Ciência", Escola Secundária Braamcamp, Pontinha, Portugal, April 4, 2019.

Mensurado S. Organization and participation on "Dia da Imunologia", Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 29, 2019.

Cunha C, Sobreiro M, Papotto P, Fiala GJ. Participation on "Dia da Imunologia", Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 29, 2019.

Silva-Santos B. TV show. Projeto/ Prémio Faz Ciência. Saúde+, Sintra, Portugal, May 10, 2019.

Silva-Santos B. Radio show. A minha ciência/Election to the EMBO Membership. Antena 1, Lisbon, Portugal, June 18, 2019.

Silva-Santos B. Debate. Delta One T cells: uma nova imunoterapia para o cancro? Instituto Miguel Galvão Teles, Lisbon, Portugal, July 2, 2019.

Mensurado S. Participation on "Projeto Passo a Passo", São Pedro da Afurada, Vila Nova de Gaia, Portugal, September 18, 2019.

Pais T. Participation on "Noite Europeia dos Investigadores", Museu Nacional de História Natural e da Ciência, Lisbon, September 27, 2019.

Mensurado S. Participation on "GHD Event", Lisbon, Portugal, October 3, 2019.

MSc Theses

Arno Bindlechner, 15/07/2019, Metabolic regulation of pleiotropic gamma delta T Cell subsets in the Tumor Microenvironment, IMC University of Applied Sciences, Krems, Austria. Supervisor: Noella Lopes.

Catarina Pelicano, 20/09/2019, Dissecting the role of specific microRNAs on effector and regulatory CD4⁺ T cell subsets differentiation in vitro. Faculdade de Medicina da Universidade de Coimbra. Supervisor: Bruno Silva-Santos. Co-Supervisor: Carolina Cunha.

Gonçalo Palmeirim, 13/12/2019, The parental effect in the immune system, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Bruno Silva-Santos. Co-Supervisor: Maria Margarida Telhada.

PhD Theses

Biagio Di Lorenzo, 09/07/2019, Characterization of the Vdelta1+ T Cell Receptor repertoire during early and adult human life: implication of clonal diversity for cancer immunotherapy, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Bruno Silva-Santos.

Pedro Papotto, 10/09/2019, Homeostasis and response of IL-17-producing $\gamma\delta$ T cells in peripheral tissue, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Silva-Santos.

Tiago Amado, 16/12/2019, MicroRNAs in the functional differentiation of T cells, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Silva-Santos. Co-Supervisor: Anita Q. Gomes.

Cláudio Franco Lab

Major Interests/Objectives

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 aims to understand the molecular mechanisms regulating coordinated endothelial cell behavior. Our work targets:

- Regulators of endothelial cell migration and cell polarity;
- Mechanobiology in endothelial cells in response to hemodynamic forces;
- Novel model organism to understand physiology of blood vessels in health and disease;
- Novel anti-angiogenic therapies.

Head of Laboratory

Cláudio Areias Franco, PhD

Team

Ana Isabel Cosme Nunes Rolo	PhD	Senior Postdoctoral Researcher (Started January, Left January)
Ana Isabel Prim Padilha	PhD	Postdoctoral Researcher (Started November)
Ana Raquel Martins Figueiredo Fonseca	PhD	Postdoctoral Researcher
Andreia Alexandra Santos de Areosa Pena	Master Degree	PhD Student
Catarina Gonçalves Fonseca	Master Degree	PhD Student
Daniela Maria Grou Ramalho	Master Degree	Lab Technician (Started April)
Francisca Ferreira de Vasconcelos	PhD	Postdoctoral Researcher
Isabela Corina Santos Fortunato	Master Degree	Lab Technician (Left October)
Joana Cristina Reino Carvalho	Master Degree	Lab Technician (Left January)
João Manuel Coelho Carreira	Master Degree	PhD Student (Started January)
Maria Angeles Domínguez-Cejudo	PhD	Postdoctoral Researcher (Left July)
Marie Ouarné	PhD	Postdoctoral Researcher
Marta Filipa Alves Fidalgo	Master Degree	Lab Technician
Pedro Miguel Branco Barbacena	PhD	Postdoctoral Researcher
Pedro Miguel Tomaz da Silva	University Degree	MSc Student (Started May, Left September)
Rita Joana Rodrigues da Silva Rua Ferreira	PhD	Post-Doctoral Researcher (Started January)

Silvia Vaccaro	Master Degree	PhD Student (Started March, Left September)
Yulia Carvalho	Master Degree	Lab Technician

Laboratory Keywords/Research Areas

Angiogenesis, Cell Migration and Polarity, Vascular Patterning, Tumor Angiogenesis, Vascular Malformations.

Major Scientific Achievements

In 2019, we uncovered that a novel mechanotransduction pathway regulating the collective migration of endothelial cells during sprouting angiogenesis. We demonstrated that a secreted molecule, Wnt5a, strengthens cell-to-cell contacts (adherens junctions) which in turn promotes efficient transmission of forces (pulling and shear) between endothelial cells. This transmission of forces is essential for coordination of movements between cells, and thus, the efficiency of angiogenic growth (Carvalho *et al.*, eLIFE 2019). In addition, we published and patented a novel mouse strain that enables live-imaging of cell polarity with unprecedented resolution (Barbacena *et al.*, Genesis 2019). Finally, we successfully graduated 2 PhD students and 1 master student.

Selected Publications

Franco CA, Jones M, Geudens I, Bernabeu MO, Ragab A, Collins RT, Phng LK, Coveney PV, Gerhardt H (2015). Dynamic endothelial cell rearrangements drive developmental vessel regression. **PLoS Biology** 13(5):e1002163. (IF: 9.797, Citations: 119/75. Sources: Google Scholar/Scopus).

Bentley K, Franco CA, Philippides A, Blanco R, Dierkes M, Gebala V, Stanchi F, Jones J, Cagna G, Kutschera S, Claesson-Welsh L, Vestweber D, Gerhardt H (2014). The role of differential VE-cadherin dynamics in cell rearrangement during angiogenesis. **Nature Cell Biology** 16(4):309-21. (IF: 20.06, Citations: 228/155. Sources: Google Scholar/Scopus).

Guarani V, Deflorian G*, Franco CA*, Krüger M, Phng LK, Bentley K, Toussaint L, Dequiedt F, Mostoslavsky R, Schmidt MH, Zimmermann B, Brandes RP, Mione M, Westphal CH, Braun T, Zeiher AM, Gerhardt H, Dimmeler S, Potente M, *co-second (2011). Acetylation-dependent regulation of endothelial Notch signalling by the SIRT1 deacetylase. **Nature** 473(7346):234-8. (IF: 40.137, Citations: 298/232. Sources: Google Scholar/Scopus).

Stenzel D*, Franco CA*, Estrach S, Mettouchi A, Sauvaget D, Rosewell I, Schertel A, Armer H, Domogatskaya A, Rodin S, Tryggvason K, Collinson L, Sorokin L, Gerhardt H, * co-first (2011). Endothelial basement membrane limits tip cell formation by inducing Dll4/Notch signalling in vivo. **EMBO Reports** 12(11):1135-43. (IF: 8.568, Citations: 105/77. Sources: Google Scholar/Scopus).

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. **Nature Cell Biology** 12(10):943-53. (IF: 20.06, Citations: 733/488. Sources: Google Scholar/Scopus).

Ongoing Research Projects

2019/2021: ADAPT2FLOW: Adaptive and maladaptive endothelial cell dynamics. Coordinator: Marie Ourné. Funding Agency: European Commission. Reference: MSCA-IF 842498. Amount: € 147 815,04. Total Amount: € 147 815,04.

2019/2020: VeCare: Selective retention of VEGF for cancer and retinopathies therapeutics. Coordinator: Cláudio Franco. Funding Agency: European Commission. Reference: ERC PoC 825508. Amount: € 150 000,00. Total Amount: € 150 000,00.

2018/2022: ATTRACT: Arterial flow as attractor for endothelial cell migration. Coordinator: Cláudio Franco. Funding Agency: Leducq Foundation. Reference: ATTRACT. Amount: € 425 424,99. Total Amount: \$ 5 000 000,00.

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.

2018/2021: Invasiveness: Identify the mechanisms of endothelial tip cell 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-CEL/32180/2017. Amount: € 238 865,33. Total Amount: € 238 865,33.

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.

Other Projects

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.

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Camo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Review Journals

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** 8:e45853 (IF: 7.616, Citations: 3/1. Sources: Google Scholar/Scopus).

Barbacena P, Ouarné M, Haigh JJ, Vasconcelos FF, Pezzarossa A, Franco CA (2019). GNrep mouse: A reporter mouse for front-rear cell polarity. **Genesis** 57(6):e23299. (IF: 2.667, Citations:1/1. Sources: Google Scholar/Scopus).

Hendrikx S, Coso S, Prat-Luri B, Wetterwald L, Sabine A, Franco CA, Nassiri S, Zangger N, Gerhardt H, Delorenzi M, Petrova TV (2019). Endothelial Calcineurin Signaling Restrains Metastatic Outgrowth by Regulating Bmp2. **Cell Reports** 26(5):1227-1241.e6. (IF: 8.032, Citations: 4/3. Sources: Google Scholar/Scopus).

Invited Lectures and Seminars

Franco CA. Endothelial Cell Orienteering. Institut Jacques Monod, Paris, France, May 2019. Invited by: Benoit Ladoux.

Franco CA. Endothelial Cell Orienteering. NIH - National Heart, Lung, and Blood Institute (NHLBI), Bethesda, USA, October 2019. Invited by: Robert Adelstein.

Communications in International Conferences

Fonseca C, Franco CA. Identifying new regulators of flow-dependent ECs polarization using high-throughput microfluidic systems. Leducq ATTRACT Meeting, Palmela, Portugal, April 2-4, 2019. (*Oral Presentation*).

Franco CA. Wnt5a regulates junctional mechanocoupling during angiogenic collective cell migration. ESM-EVBO – Maastricht, Netherlands, April 2019.

Franco CA. Endothelial Cell Orienteering. EMBO Workshop - Cell Polarity & Membrane Dynamics, St. Feliu, Spain, May 2019.

Communications in National Conferences

Vasconcelos F. Introduction to digital bioimage analysis Workshop, i3S, Porto, Portugal, September 24-27, 2019.

Vasconcelos F. Lisbon Area Postdoc Meeting 2019, Caparica, Portugal, November 14-15, 2019.

Fonseca A. Lisbon Area Postdoc Meeting 2019, Caparica, Portugal, November 14-15, 2019.

Ouarne M. Lisbon Area Postdoc Meeting 2019, Caparica, Portugal, November 14-15, 2019.

Ouarne M. Sustainable and Green Lab Workshop, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 18, 2019.

Vasconcelos F. 1st DevBioMed Symposium – From Developmental Biology to Medicine and Back, Champalimaud Center for the Unknown, Lisbon, Portugal, December 13, 2019.

Marta Fidalgo. 1st DevBioMed Symposium – From Developmental Biology to Medicine and Back, Champalimaud Center for the Unknown, Lisbon, Portugal, December 13, 2019.

Padilha A. 1st DevBioMed Symposium – From Developmental Biology to Medicine and Back, Champalimaud Center for the Unknown, Lisbon, Portugal, December 13, 2019.

Patents/Prototypes

Claudio Franco and Pedro Barbacena. GNREP MOUSE: A TRANSGENIC REPORTER MOUSE LINE FOR FRONT-REAR CELL POLARITY. Provisional Patent application (Portugal) id: 2019100006333. January, 2019.

Advanced Teaching

Franco CA. Jury of the PhD thesis of Sofia Moreira, “Phosphoregulation of the *Drosophila* tumor suppressor *lgl* during the cell – cycle”. Faculty of Medicine, Health and Dentistry, University of Melbourne, Melbourne, Australia.

Franco CA. Jury of the PhD thesis of Zoe Grant, “Mechanisms of angiogenesis in development and disease”. Faculdade de Ciências da Universidade do Porto / Instituto de Ciências Biomédicas Abel Salazar, Porto, Portugal.

Franco CA. Theoretical classes. Mestrado Integrado em Engenharia Biomédica, Instituto Superior Técnico, Lisbon, Portugal. Supervisor: Professor Cláudia Lobato and Margarida Diogo.

MSc Thesis Completed

Marta Fidalgo, 22/11/2019, Mechanisms of hypoxia-independent angiogenesis, Faculdade de Medicina da Universidade do Porto. Supervisor: Cláudio Franco. Co-Supervisor: Francisca Vasconcelos.

PhD Thesis Completed

Joana Carvalho, 7/11/2019, Force transmission and endothelial cell rearrangements during vascular remodeling, Programa Doutoral Lisbon Biomedical and Clinical Research (LisbonBioMed), Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Cláudio Franco.

Pedro Barbacena, 4/11/2019, Molecular mechanisms regulating endothelial cell axial polarity during vascular morphogenesis, Programa Doutoral Lisbon Biomedical and Clinical Research (LisbonBioMed), Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Cláudio Franco.

Claus M. Azzalin Lab

Major Interests/Objectives

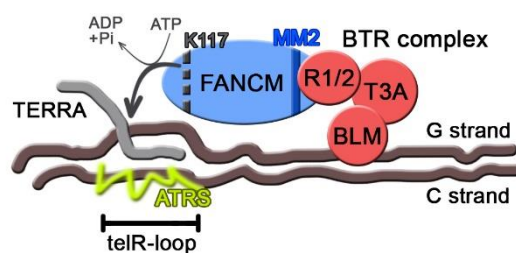
Telomeres are heterochromatic nucleoprotein structures 'capping' the ends of linear eukaryotic chromosomes. Dysfunctional telomeres cause severe chromosome instability, which unleashes cascades of cellular reactions that are common hallmarks of human diseases including cancer and premature aging. We 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 participates in maintaining proper telomere structure and functions in both normal and diseased human cells. During last year, our research mostly focused on the regulation of TERRA association with chromatin and TERRA-mediated telomere stability in telomerase positive cancer cells, as well as in cancer cells maintaining their telomeres through the so-called Alternative Lengthening of Telomeres (ALT) pathway.

Head of Laboratory

Claus Maria Azzalin, PhD

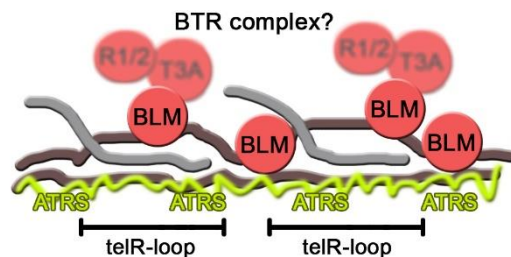
Graphical Abstract

FANCM-proficient ALT cell



- TelR-loop resolution
- Controlled BTR recruitment
- Controlled BLM activity
- Restricted ATRs
- Regulated ALT (telomere elongation)
- Cell proliferation

FANCM-deficient ALT cell



- Unresolved telR-loops
- Uncontrolled BLM (BTR?) recruitment
- Uncontrolled BLM activity
- Excessive ATRs
- Excessive ALT (telomere dysfunction)
- Cell death

Team

Ana Beatriz Domingues Silva	Master Degree	Lab Technician
Ana Margarida da Silva Figueira	Master Degree	Administrative Technician
Beatriz Pedrosa Moleirinho	University Degree	MSc Student (Started September)
Bruno Adriano de Sousa Silva	PhD	Postdoctoral Researcher
Filipe Bernardes da Silva Tavares Cadete	PhD	Postdoctoral Researcher (Left December)
Joana Cristina Pedro Rodrigues	PhD	Postdoctoral Researcher
João Pedro Abreu Pessoa	PhD	Postdoctoral Researcher
Leonardo Amaro Gaio	University Degree	MSc Student
Marcelino Tapada Saramago	Master Degree	Lab Technician (Started February, Left July)
Patrícia Alexandra Lona Abreu	Master Degree	PhD Student

Laboratory Keywords / Research Areas

TERRA, Telomeres, ALT, Cancer, Aging, Genome Stability.

Major Scientific Achievements

We discovered that the FANCM ATPase maintains telomere stability in human ALT cells. When FANCM is depleted, telomeres become dysfunctional and cells die. FANCM depletion increases ALT-associated features indicating that FANCM restricts ALT activity. Finally, FANCM unwinds telomeric RNA:DNA hybrids (telR-loops) in vitro and suppresses their accumulation in ALT cells. Thus, TERRA promotes ALT, likely through formation of telR-loops, while FANCM allows controlled ALT activity and cell proliferation by limiting the toxicity telR-loops.

We also discovered that the telomeric protein TRF2 promotes invasion of TERRA into telomeric DNA, inducing formation of telomeric telR-loops independently of ongoing transcription. Conversely, the telomeric factor TRF1 suppresses TRF2-induced TERRA invasion. Depletion of TRF1 in cells causes deregulated TRF2-mediated formation of telR-loops and telomere loss. This was the first example of a human factor stimulating R-loop formation in trans.

Selected Publications

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. (IF: 12.109, Citations: 8. Source: Web of Science).

Moravec M, Wischnewski H, Bah A, Hu Y, Liu N, Lafranchi L, King MC and Azzalin CM (2016). TERRA promotes telomerase-mediated telomere elongation in *Schizosaccharomyces pombe*. **EMBO Reports** 17(7):999-1012. (IF: 8.383, Citations: 28. Source: Web of Science).

Lorenzi LE, Bah A, Wischnewski H, Shchepachev V, Sonesson C, Santagostino M, Azzalin CM (2015). Fission yeast Cactin restricts telomere transcription and elongation by controlling Rap1 levels. **EMBO Journal** 34(1):115-129. (IF: 9.792, Citations: 6. Source: Web of Science).

Arora R, Lee YW, Wischnewski H, Brun CM, Schwarz T and Azzalin CM (2014). RNaseH1 regulates TERRA-telomeric DNA hybrids and telomere maintenance in ALT tumour cells. **Nature Communications** 5:e5220. (IF: 11.878, Citations: 111. Source: Web of Science).

Shchepachev V, Wischnewski H, Missiaglia E, Sonesson C and Azzalin CM (2012). Mpn1, Mutated in Poikiloderma with Neutropenia Protein 1, Is a Conserved 3'-to-5' RNA Exonuclease Processing U6 Small Nuclear RNA. **Cell Reports** 2(4):855-865. (IF: 7.815, Citations: 37. Source: Web of Science).

Chawla R, Redon S, Raftopoulou C, Wischnewski H, Gagos S and Azzalin CM (2011). Human UPF1 interacts with TPP1 and telomerase and sustains telomere leading-strand replication. **EMBO Journal** 30(19):4047-4058. (IF: 11.227, Citations: 57. Source: Web of Science).

Azzalin CM, Reichenback P, Khoriantuli L, Giulotto E and Lingner J (2007). Telomeric Repeat Containing RNA and RNA surveillance factors at mammalian chromosome ends. **Science** 318(5851):798-801. (IF: 41.063, Citations: 701. Source: Web of Science).

Ongoing Research Projects

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 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.

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 M. Azzalin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 029352/2017. Amount: € 239 789,17. Total Amount: € 239 789,17.

2017/2020: TERRA and telomere transcription: towards therapies for healthy aging. Coordinator: Claus M. Azzalin. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG 3576. Amount: € 150 000,00. Total Amount: € 150 000,00.

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

Publications in Peer Reviewed Journals

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. (IF: 11.878, Citations: 5. Source: *Web of Science*).

Domingues-Silva B, Silva B, Azzalin CM (2019). ALternative functions for human FANCM at telomeres. **Frontiers in Molecular Biosciences** 6:UNSP84. Review. (IF: 3.565, Citations: 0. Source: *Web of Science*).

Hu Y, Bennett HW, Liu N, Moravec M, Williams JF, Azzalin CM, King MC (2019). RNA-DNA hybrids support recombination-based telomere maintenance in fission yeast. **Genetics** 213(2):431-447. (IF: 3.564, Citations: 0. Source: *Web of Science*).

Invited Lectures and Seminars

Azzalin CM. Conflicts between RNA and DNA at human telomeres. VIII National RNA Meeting: ptRNA 2019, i3S, Porto, Portugal, January 24-25, 2019.

Azzalin CM. Telomeric replication stress in ALT cells—Causes and management. CSHL Meeting ‘Telomeres & Telomerase’, CSH, New York, USA, April 30-May 4, 2019.

Azzalin CM. Causes and Management of Telomeric Replication Stress in Human ALT Cancer Cells. 'RiboClub 20th Anniversary & Canada Gairdner International Symposium', Orford, Canada, September 22-27, 2019.

Communications in International Conferences

Abreu PL, Azzalin CM. Plasmid Invasion Assay: an *in vitro* technique to study protein-assisted formation of telomeric R-loops. EMBO YIP PhD course, EMBL, Heidelberg, Germany, January 14-19, 2019. (*Poster Presentation*).

Abreu PL, Azzalin CM. Understanding how telomere integrity is maintained. EMBO YIP PhD course, EMBL, Heidelberg, Germany, January 14-19, 2019. (*Oral Presentation*).

Silva B, Pentz R, Figueira AM, Arora R, Lee YW, Hodson C, Wischnewski H, Deans AJ, Azzalin CM. FANCM restricts R-loop-induced telomeric replication stress in ALT cells. CSHL Meeting 'Telomeres & Telomerase', CSH, New York, USA, April 30-May 4, 2019. (*Poster Presentation*).

Communications in National Conferences

Abreu PL, Lee YW, Azzalin CM. *In vitro* analysis of TRF1-mediated inhibition of TRF2-induced telR-loop formation. XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Organization of Conferences

Azzalin CM. Co-Organizer. EMBO workshop 'Telomere function and evolution in health and disease', Tróia, Portugal, May 04-09, 2020.

Internationalization

Our group is collaborating with several laboratories in Europe, USA and Australia. Additionally, members of our laboratory regularly attend and present at international conferences on genomic stability and telomere biology and participate in international schools and courses.

Patents/Prototypes

Azzalin CM. Treatment of ALT cancer, GB1907518.3. May, 2019.

Advanced Teaching

Tavares-Cadete F. Course. Basics of programming (First Steps in R for Data Science). Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 18,20,25,27, 2019.

Azzalin CM. Lecture. Telomeric Replication Stress in ALT Cancer Cells: Causes and Management. 3rd NCCR RNA & Disease Summer School, Saas-Fee, Switzerland, August 26-30, 2019.

Edgar Gomes Lab

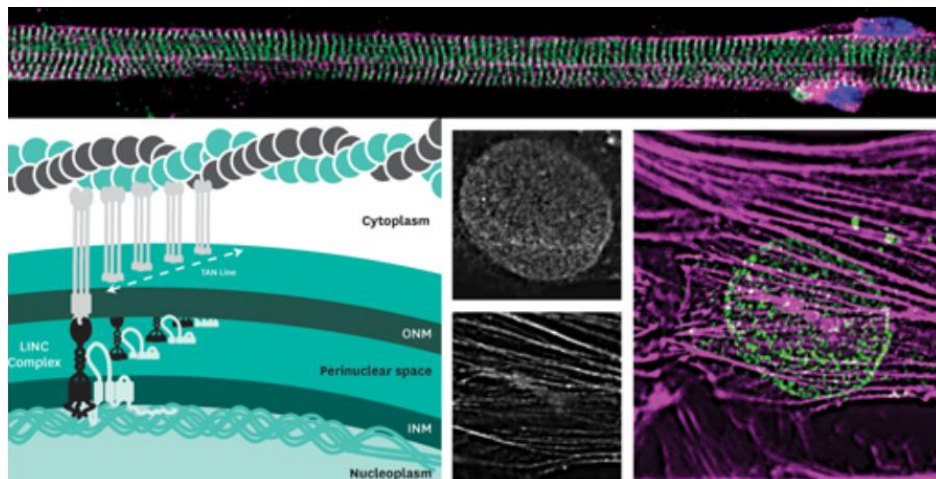
Major Interests/Objectives

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.

Head of Laboratory

Edgar Rodrigues Almeida Gomes, PhD

Graphical Abstract



Team

Ana Sofia Carvalho Marques	Master Degree	Lab Technician
Cátia Alexandra da Silva Janota	Master Degree	PhD Student
David Miguel Baião Barata	PhD	Postdoctoral Researcher (Started February)
Francisco Javier Calero Cuenca	PhD	Postdoctoral Researcher
Graciano da Silva Leal	PhD	Postdoctoral Researcher
Helena Alexandra Ribeiro de Carvalho Pinheiro	Master Degree	PhD Student
Hélia Cristina de Oliveira Neves	PhD	Senior Postdoctoral Researcher (Started December)
Inês Isabel Baltazar Belo Martins	Master Degree	Lab Technician (Started February)
Isabel da Conceição Alves Alcobia Príncipe Henriques	PhD	Senior Postdoctoral Researcher (Started December)
João Pedro Nunes Paulo da Silva Martins	Master Degree	PhD Student
Katharina Hennig	PhD	Postdoctoral Researcher (Started February)
Lilian Mathilde Sluimer	University Degree	MSc Student (Started May. Left November)
Lou Martha Wackerbarth	University Degree	MSc Student (Left March)
Luís Manuel Farinha Bernardino de Oliveira	Master Degree	Lab Technician (Started January)
Mafalda Ramos de Melo Pimentel	Master Degree	Postdoctoral Researcher (Left June)
Maria Judite Sousa da Costa	PhD	Lab Manager
Sara Sofia Gasalho Ferreira	University Degree	Lab Technician
William Roman	PhD	Postdoctoral Researcher

Laboratory Keywords / Research Areas

Skeletal Muscle, Nucleus, Cell Migration, Cell Biology, Cytoskeleton.

Major Scientific Achievements

We successfully differentiated human iPS cells into motor neurons to be used in an *in vitro* 3D muscle chip irrigated with blood vessels and controlled by motor neurons. These human iPS cells were differentiated in a microfluidic multicompartiment device and they contact myofibers in a different compartment (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. (Oral communication at FASEB RNA localization and local translation meeting, Colorado, USA)

We found a mechanism to generate asymmetric nuclear-cytoskeleton interactions for nuclear movement (Oral Communication at ASCB annual meeting, Washington, USA) and a complex between a nuclear envelope phosphatase (CTDNEP1) and a actin binding protein (Eps8L2) are involved in nuclear movement (under revision).

Selected Publications

Roman W, Martins J, Gomes ER (2018). Local arrangement of fibronectin by myofibroblasts governs peripheral nuclear positioning in muscle cells. **Developmental Cell** 46(1):102-111.e6. (IF: 9.6, Citations: 1. Source: Web of Science).

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 α -Dependent Microtubule Nucleation from the Nuclear Envelope via Akap450 Is Necessary for Nuclear Positioning in Muscle Cells. **Current Biology** 27(19):2999-3009.e9. (IF: 8.9, Citations: 39. Source: Web of Science).

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** 28:1189–1201. (IF: 20.1, Citations: 22. Source: Web of Science).

Janota CS, Calero-Cuenca FJ, Costa J, Gomes ER (2017). SnapShot: Nucleo-cytoskeletal Interactions. **Cell** 169(5):970-970.e1. (IF: 31.4, Citations: 7. Source: Web of Science).

Vilmont V, Cadot B, Ouanounou G, Gomes ER (2016). A system to study mechanisms of neuromuscular junction development and maintenance. **Development** 143:2464-2477. (IF: 5.8, Citations: 9. Source: Web of Science).

Falcone S, Roman W, Hnia K, Gache V, Didier N, Lainé J, Aurade F, Marty I, Nishino I, Charlet-Berguerand N, Romero N, Marazzi G, Sassoon D, Laporte J, Gomes ER (2014). N-WASP is required for Amphiphysin-2/BIN1 dependent nuclear positioning and triad organization in skeletal muscle and is involved in the pathophysiology of centronuclear myopathy. **EMBO Molecular Medicine** 6:1455–1475. (IF: 10.3, Citations: 38. Source: Web of Science).

Metzger T, Gache V, Xu M, Cadot B, Folker E, Richardson B, Gomes ER*, Baylies MK* (2012). MAP and Kinesin dependent nuclear positioning is required for skeletal muscle function. **Nature** 484:120–124. *co-last and corresponding author. (IF: 41.6, Citations: 125. Source: Web of Science).

Cadot B, Gache V, Vazyutina E, Falcone S, Birchmeier C, Gomes ER (2012). Nuclear movement during myotube formation is microtubule and dynein dependent and is regulated by Cdc42, Par6 and Par3. **EMBO Reports** 13(8):741-9. (IF: 8.6, Citations: 62. Source: Web of Science).

Luxton GW*, Gomes ER*, Folker ES, Vintinner E, Gundersen GG (2010). Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement. **Science** 329(5994): 956-9. *co-first author. (*IF: 37.2, Citations: 259. Source: Web of Science*).

Gomes ER, Jani S, Gundersen GG (2005). Nuclear movement regulated by Cdc42, MRCK, myosin, and actin flow establishes MTOC polarization in migrating cells. **Cell** 121:451-63. (*IF: 31.4, Citations: 397. Source: Web of Science*).

Ongoing Research Projects

2018/2022: MyoChip: Building a 3D innervated and irrigated muscle on a chip. Coordinator: Edgar Gomes. Funding Agency: European Commission. Reference: MyoChip 801423. Total Amount: € 1,266,861.25. Amount: € 3,153,553.74.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Total Amount: € 1,199,140.10. Amount: € 2,499,827.92 €

Invited Lectures and Seminars

Gomes ER. Role for nuclear positioning in muscle contraction. Life Sciences Switzerland (LS2) Annual Meeting, Zurich, Switzerland, February 14-15, 2019.

Gomes ER. Nuclear positioning in migrating cells. Center for Neurosciences, Cantanhede, Portugal, February 18, 2019.

Gomes ER. Nuclear movement in migrating cells. Catholic University, Santiago, Chile, March 12, 2019.

Gomes ER. Mechanisms of nuclear positioning during muscle formation. San Raffaele Institute, Milan, Italy, March 3, 2019.

Gomes ER. Nuclear movement in migrating cells. JCS Cell Dynamics: Organelle-Cytoskeleton Interface, Lisbon, Portugal, May 2019.

Gomes ER. Invited Lecture. Nuclear Positioning during muscle differentiation. *Frontiers in Myogenesis - Skeletal Muscle: Development, Regeneration and Disease*, San Jose, Costa Rica, September 2019.

Communications in International Conferences

Leal G. Regulation of excitation-contraction coupling in skeletal muscle by nuclei positioning. GRS "Muscle: Excitation-Contraction Coupling", Lucca, Italy, May 2019. (*Oral and Poster Presentation*).

Leal G. Regulation of excitation-contraction coupling in skeletal muscle by nuclei positioning. GRC "Muscle: Excitation-Contraction Coupling", Lucca, Italy, May 2019. (*Poster Presentation*).

Janota CS. Climp-63 regulates nuclear movement during polarization of migrating cells. JCS Cell Dynamics: Organelle-Cytoskeleton Interface, Lisbon, Portugal, May 2019. (*Poster Presentation*).

Calero-Cuenca FJ. Dullard-Eps8L2 interaction regulates nuclear positioning in migrating fibroblasts by perinuclear actin organization. JCS Cell Dynamics: Organelle-Cytoskeleton Interface, Lisbon, Portugal, May 2019. (*Poster Presentation*).

Hennig K. Building an innervated and irrigated muscle-on-chip. Nanomed Europe 2019, Braga, Portugal, June 2019. (*Poster Presentation*).

Pinheiro H. mRNA transport and stability interplay to localize mRNA in skeletal muscle. FASEB RNA localization and local translation, Snowmass Village, Colorado, USA, July 2019. (*Oral and Poster Presentation*).

Pimentel MR. mRNA transport and stability interplay to localize mRNA in skeletal muscle. *Frontiers in Myogenesis - Skeletal Muscle: Development, Regeneration and Disease*, San Jose, Costa Rica, September 2019. (*Poster Presentation*).

Janota CS. Climp-63 regulates nuclear movement during polarization of migrating cells. ASCB, Washington, USA, December 2019. (*Oral and Poster Presentation*).

Communications in National Conferences

Gomes ER. Positioning the nucleus in migrating cells. X Jornadas de Bioquímica Universidade do Minho, Braga, Portugal, March 20, 2019. (*Oral Presentation*).

Gomes ER. Mechanisms for nuclear positioning during myofiber differentiation. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 2019 (*Oral Presentation*).

Barata D, Hennig K, Martins I, Costa J, Franco C, Gomes ER, Roman W. MyoChip a stem cell powered organ on chip for muscle modelling. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 2019. (*Poster Presentation*).

Organization of Conferences

Gomes ER. Co-Organizer. Cell dynamics: organelle-cytoskeleton Interface Meeting, Company of Biologists, Lisbon, Portugal, 2019.

Internationalization

Gomes ER. Coordinates a European FET OPEN project “Generating a 3D in vitro innervated and vascularized muscle”.

ERC Synergy grant “Defining the role of Arp2/3 complex diversity at multiple scales of biology”, together with Michael Way (Crick, London) and Carlyn Moores (Birkbeck, London).

Several members of the EGomes Lab spent the months of June and July at the Marine Biological Laboratory (MBL), University of Chicago interacting with multiple groups from US and Europe.

Prizes, Honors and Awards

Whitman Center Fellowship, Marine Biological Laboratory, University of Chicago, Chicago, USA.

Advanced Teaching

Gomes ER. Lecture. Stem Cell Biology course of the Bioengineering – Cell Therapies and Regenerative Medicine PhD Program, Lisbon, Portugal, May 4 2019.

Gomes ER. Lecture. Introdução à Engenharia Biomédica. Mestrado Integrado em Medicina. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, September 21, 2019.

Gomes ER. Lecture. Engenharia de Células e Tecidos. Mestrado Integrado Engenharia Biomédica, Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, October 9, 2019.

Gomes ER. Lecture. Tissues, Cells and Molecules, Mestrado Integrado em Medicina, Nova Medical School, Lisbon, Portugal, October 15, 2019.

Science and Society

EGomes Lab is actively working to reach not only the science community but also the general public. We have printed flyers explaining some of our work, both in English and Portuguese. We have also printed bookmarks with beautiful illustrations of our work with brief explanations. All these have been used at several events such as Horizontes at iMM and European Researchers Nights. We initiated a partnership with Science4you, whom donated 6 microscopes to be used in different projects that aim to bring science to the general population, particularly to young students.

Our main outreach project was 3D printing of a real size model of muscles in a human arm and a myofiber. The muscles in the arm are easily recognized and associated with muscle. The bicep area is removable and itself is a Russian-doll inspired set of muscle/fascicle/myofiber. The myofiber in a amplified version allows us to better explain the importance of the interaction with the blood vessels and neurons, as well as the molecular details inside the muscle cell.



MSc Theses

Ana Sofia Marques, 23/10/2019, Unravelling the role of Ctdnep1-Eps8L2 interaction during nuclear positioning in migrating fibroblasts, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Edgar Gomes and Maria Helena Trindade.

PhD Theses

Mafalda Pimentel, 08/3/2019, The role of nuclear positioning in muscle function, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Edgar Gomes.

Gonçalo Bernardes Lab

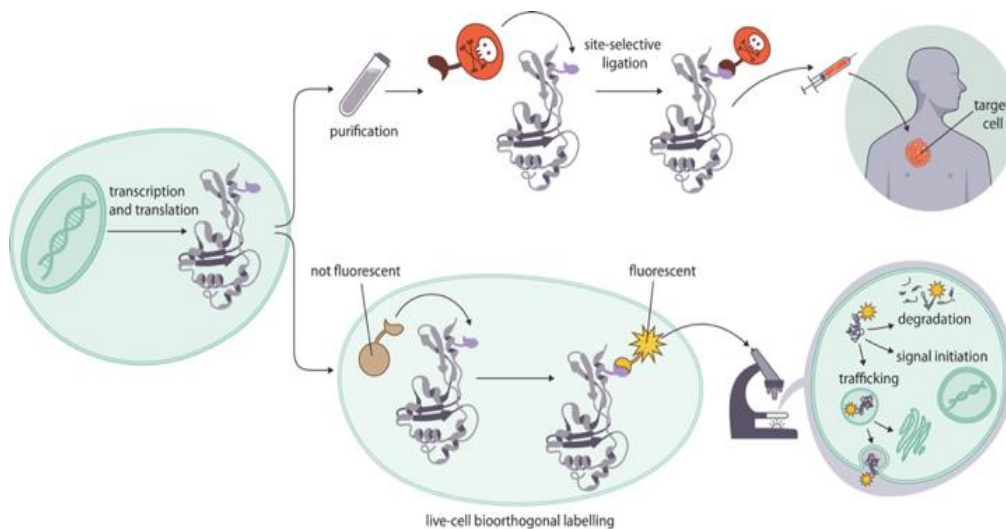
Major Interests/Objectives

At the core of our research program is the development of novel chemoselective methods that are compatible with biological systems, and their use to redesign the structure & function of proteins of biological & therapeutic interest, with the aim of understanding & influencing human disease. We are mostly interested in the specific delivery of natural products with specific mechanism of action to cancer cells and in the construction of homogenous glycoproteins as vaccines candidates. We are also investigating the use of CO-releasing molecules to safely deliver therapeutic amounts of CO to diseased tissues, by controlling CO release *in vivo* in a spatial and temporal manner. And finally, we are using principles of data science and statistical learning to swiftly deconvolute phenotypic screen hits, and prioritize target-based biochemical assays. To that end, we have assembled a platform leveraging proprietary machine learning models for drug target identification.

Head of Laboratory

Gonçalo José Lopes Bernardes, D. Phil, Associate Professor

Graphical Abstract



Team

Alexandra Isabel Freitas Rosa	PhD	Project Manager
Ana Maria dos Santos Guerreiro	Master Degree	PhD Student
Annabel Katharina Kitowski	Master Degree	PhD Student (Left July)
Bárbara Beatriz da Costa Botelho Sousa	Master Degree	PhD Student
Bruno Luís Jesus Pinto de Oliveira	PhD	Senior Postdoctoral Researcher
Carlos Diogo Labão Alpiarça Sousa de Almeida	Master Degree	PhD Student
Cátia Diana Parente Caldeira Carvalho	PhD	Postdoctoral Researcher (Left March)
Cláudia Filipa Martins Afonso	Master Degree	PhD Student
João Daniel da Silva Seixas	PhD	Staff Scientist
João Diogo Osório de Castro Conde	PhD	Postdoctoral Researcher
Maria Inês Sousa de Albuquerque	Master Degree	PhD Student
Marta Franco Coimbra Marques	PhD	Postdoctoral Researcher
Padma Akkapeddi	Master Degree	PhD Student (Left February)
Pedro Miguel Saraiva Duarte Cal	PhD	Postdoctoral Researcher
Pedro Ricardo Morgado Henriques	Master Degree	PhD Student (Left August)
Ravikumar Govindan	PhD	Postdoctoral Researcher (Started June)
Roberto Russo	Master Degree	PhD Student (Left April)
Tiago Correia de Oliveira Rodrigues	PhD	Staff Scientist
Unnikrishnan Vickraman Nair Bindu	Master Degree	PhD Student (Started August)
Vera Filipa Cerqueira Ferreira	Master Degree	PhD Student (Started June)

Laboratory Keywords / Research Areas

Bioconjugation, Cancer, Vaccines, Site-selective Protein modification, Biorthogonal Chemistry, Machine Learning.

Major Scientific Achievements

Our research group has made significant advances in the areas of reaction engineering for protein modification, machine-learning models for drug target identification and antibody therapeutics. Key highlights include: development of an efficient method for irreversible antibody-cysteine bioconjugation using carbonyl acrylic reagents; development of new reactions for protein labelling and cysteine protein modification; *de novo* design of potent and selective mimics of IL-2/IL-15; one-pot stapling of interchain disulfides of antibodies; development of new computational methods to avoid colloidal aggregation in drug discovery; development of a fully human anti-IL-7R α antibody that promotes anti-tumor activity against T-ALL; development of a potential MUC1-based vaccine; development of new reactions for tetrazine-triggered release of molecules; development of natural product-drug conjugates for modulation of TRPV1 and TRPV2 expressing tumors.

Selected Publications

Lindstedt PR, Aprile FA, Matos MJ, Perni M, Bertoldo JB, Bernardim B, Peter Q, Jiménez-Osés G, Knowles TPJ, Dobson CM, Corzana F, Vendruscolo M, Bernardes GJL* (2019). Enhancement of the anti-aggregation activity of a molecular chaperone using a rationally designed post-translational modification. **ACS Central Science** 5(8):1417-1424 (*IF: 12.837, Citations: 0. Source: ACS Publications*).

Matos MJ, Navo CD, Hakala T, Ferhati X, Guerreiro A, Hartmann D, Bernardim B, Saar KL, Compañón I, Corzana F, Knowles TPJ, Jiménez-Osés G, Bernardes GJL* (2019). Quaternization of vinyl/alkynyl pyridine enables ultrafast cysteine-selective protein modification and charge modulation. **Angewandte Chemie-International Edition** 58(20):6640–6644. (*IF: 12.257. Citations: 2. Source: Wiley*).

Compañón I, Guerreiro A, Mangini V, Castro-López J, Escudero-Casao M, Avenzoza A, Busto JH, Castellón S, Jiménez-Barbero J, Asensio JL, Jiménez-Osés G, Boutureira O, Peregrina JM, Hurtado-Guerrero R, Fiammengo R, Bernardes GJL*, Corzana F* (*co-senior authors) (2019). Structure-based design of potent tumor-associated antigens: Modulation of peptide presentation by single-atom O/S or O/Se substitutions at the glycosidic linkage. **Journal of the American Chemical Society** 141(9):4063–4072. (*IF: 14.695, Citations: 5. Source: ACS Publications*).

Akkapeddi P, Fragoso R, Hixon JÁ, Ramalho AS, Oliveira ML, Carvalho T, Gloger A, Matasci M, Corzana F, Durum SK, Neri D, Bernardes GJL*, Barata JT* (*co-senior authors) (2019). A fully human anti-IL-7R α antibody promotes anti-tumor activity against T-cell acute lymphoblastic leukemia. **Leukemia** 33(9):2155–2168. (*IF: 9.944, Citations: 6. Source: Leukemia*).

Silva D-A, Yu S, Ulge U, Spangler JB, Jude KM, Labão-Almeida C, Ali LR, Quijano-Rubio A, Ruterbusch M, Leung I, Biary T, Crowley S, Marcos E, Walkey CD, Weitzner BD, Pardo-Avila F, Carter L, Stewart L, Riddell S, Pepper M, Bernardes GJL, Dougan M, Garcia C, Baker D (2019). De novo design of potent and selective mimics of IL-2/IL-15. **Nature** 565(7738):186–191. (*IF: 43.070. Citations: 40. Source: Nature*).

See also, “Designer protein delivers signal of choice” E. Yvonne Jones, *Nature* 2019, 565, 165–166

“Researchers redesign a cancer-busting protein—without the side effects” Service RF, *Science* 2019, Jan. 9, doi:10.1126/science.aaw6158.

Bernardim B, Matos MJ, Ferhati X, Compañón I, Guerreiro A, Akkapeddi P, Burtoloso ACB, Jiménez-Osés G, Corzana F, Bernardes GJL* (2019). Efficient and irreversible antibody-cysteine bioconjugation using carbonylacrylic reagents. **Nature Protocols** 14(1):86–99. (IF: 11.334. Citations: 3. Source: *Nature Protocols*).

Ongoing Research Projects

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: Libertação controlada de agentes bioactivos por reacção química selectiva. Coordinator: Tiago Rodrigues. 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: 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: Nanoparticle-Based Therapeutic Applications and Detection of Carbon Monoxide Releasing. Coordinator: Tiago Rodrigues. Funding Agency: European Commission. Reference: Twinning-ACORN. Amount: € 353 750,00. Total Amount: € 1 000 000,00.

2017/2019: TRPLigDrugConj: TRPV1-targeted ligand-drug conjugates to treat prostate cancer. Coordinator: Tiago Rodrigues. Funding Agency: European Commission. Reference: MSCA IF 743640. Amount: € 160 635,60. Total Amount: € 160 635,60.

2016/2019: Unravelling Bronic Acids Bioconjugation and Targeted Delivery. Coordinator: Gonçalo Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-QOR/1434/2014. Amount: € 20 000,00. Total Amount: € 195 060,00.

2016/2019: Técnicas de Imagem Molecular da Fibrose Hepática. Coordinator: Gonçalo Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: HMSP-ICT/0012/2013. Amount: € 142 300,00. Total Amount: € 142 300,00.

2015/2019: GLYCOVAX: A training network for the rational design of the next generation of well-defined glycoconjugate vaccines. Coordinator: Gonçalo Bernardes. Funding Agency: European Commission. Reference: MSCA ITN 675671. Amount: € 238 356,36. Total Amount: € 3 554 499,69.

2015/2019: ProteinConjugates: A training network for the chemical site-selective modification of proteins: Preparation of the next-generation of therapeutic chemically-defined protein conjugates. Coordinator: Gonçalo Bernardes. Funding Agency: European Commission. Reference: MSCA ITN 675007. Amount: € 741 939,48. Total Amount: € 2 542 771,03.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Traquete R, Henderson E, Picaud S, Cal PMSD, Sieglitz F, Rodrigues T, Oliveira R, Filippakopoulos P, Bernardes GJL* (2019). Evaluation of linker length effects on a BET bromodomain probe. **Chemical Communications** 55(68):10128–10131. (IF: 6.164, Citations: 0. Source: *Chemical Communications*).

Adusumalli SR, Bernardes GJL* (2019). Ethynylbenziodoxolone reactivity in cysteine bioconjugation. **Chem** 5(8):1924–1937. (IF: 18.205, Citations: 1. Source: *CellPress*).

Marques MC, Albuquerque IS, Vaz SH, Bernardes GJL* (2019). Overexpression of osmosensitive Ca²⁺-permeable channel TMEM63B promotes migration in HEK293T cells. **Biochemistry** 58(26):2861–2866. (IF: 2.952. Citations: 0. Source: *ACS Publications*).

Davies S, Oliveira B, Bernardes GJL* (2019). Development of a self-immolative linker for tetrazine-triggered release of alcohols in cells. **Organic & Biomolecular Chemistry** 17(23):5725–5730. (IF: 3.564. Citations: 1. Source: *RSC*).

Motloch P, Guerreiro A, Azeredo CQ, Bernardes GJL*, Hunter CA, Kocsis I (2019). Triaminopyrimidine derivatives as transmembrane HCl transporter. **Organic & Biomolecular Chemistry** 17(22):5633–5638. (IF: 3.564. Citations: 1. Source: *RSC*).

Gil de Montes E, Jiménez-Moreno E, Oliveira BL, Navo CD, Cal PMSD, Jiménez-Osés G, Robina I, Moreno-Vargas AJ, Bernardes GJL* (2019). Azabicyclic vinyl sulfones for residue-specific dual protein labelling. **Chemical Science** 10(16):4515–4522. (IF: 9.556. Citations: 1. Source: RSC).

Rodrigues T, de Almeida BP, Barbosa-Morais NL, Bernardes GJL* (2019). Dissecting celastrol with machine learning to unveil dark pharmacology. **Chemical Communications** 55(45):6369–6372. (IF: 6.164, Citations: 2. Source: RSC).

Baker C, Rodrigues T, de Almeida BP, Barbosa-Morais NL, Bernardes GJL* (2019). Natural product-drug conjugates for modulation of TRPV1-expressing tumors. **Bioorganic & Medical Chemistry** 27(12):2531–2536. (IF: 2.793. Citations: 1. Source: Elsevier).

Davies S, Qiao J, Oliveira BL, Navoc CD, Jiménez-Osés G, Bernardes GJL* (2019). Tetrazine-triggered release of carboxylic-acid containing molecules for activation of an anti-inflammatory drug. **ChemBioChem** 20(12):1541–1546. (IF: 2.641. Citations: 1. Source: Wiley).

Alcock LJ, Oliveira BL, Deery MJ, Pukala TL, Perkins MV, Bernardes GJL*, Chalker JM* (*co-senior authors) (2019). Norbornene probes for the detection of cysteine sulfenic acid in cells. **ACS Chemical Biology** 14(4):594–598. (IF: 4.374, Citations: 5. Source: ACS Publications).

Amorim AL, Peterle MM, Guerreiro A, Coimbra DF, Heying RS, Caramori GF, Braga AL, Bortoluzzi AJ, Neves A, Bernardes GJL, Peralta RA (2019). Synthesis, characterization and biological evaluation of new manganese metal carbonyl compounds that contain sulfur and selenium ligands as a promising new class of CORMs. **Dalton Transactions** 48(17):5574–5584. (IF: 4.052, Citations: 1. Source: RSC).

Hoyt EA, Cal PMSD, Oliveira BL, Bernardes GJL* (2019). Contemporary approaches to site-selective protein modification. **Nature Reviews Chemistry** 3(3):147–171. (IF: 30.628, Citations: 20. Source: Nature).

Reker D, Bernardes GJL, Rodrigues T (2019). Computational advances in combating colloidal aggregation in drug discovery. **Nature Chemistry** 11(5):402–418. (IF: 23.193, Citations: 9. Source: Nature Chemistry).

Zwicker VE, Oliveira BL, Yeo JH, Fraser ST, Bernardes GJL, New EJ, Jolliffe KA (2019). A fluorogenic probe for cell surface phosphatidylserine using an intramolecular indicator displacement sensing mechanism. **Angewandte Chemie-International Edition** 58(10):3087–3091. (IF: 12.257. Citations: 7. Source: Wiley).

Sun S, Akkapeddi P, Marques MC, Martínez-Sáez N, Torres VM, Cordeiro C, Boutureira O, Bernardes GJL* (2019). One-pot stapling of interchain disulfides of antibodies using an isobutylene motif. **Organic & Biomolecular Chemistry** 17(7):2005–2012. (IF: 3.564, Citations: 3. Source: RSC).

Matos MJ, Jiménez-Osés G, Bernardes GJL* (2019). Lysine bioconjugation on native albumin with a sulfonyl acrylate reagent. **Methods in Molecular Biology** 2033:25–37. (IF: 0.38, Citations: --. Source: Springer).

António J, Russo R, Carvalho C, Cal P, Góis P (2019). Boronic acids as building blocks for the construction of therapeutically useful bioconjugates. **Chemical Society Reviews** 48(13):3513-36. (IF: 40.443. Citations: 6. Source: RSC).

Invited Lectures and Seminars

Keynote and Prize Lectures:

Bernardes GJL. 2nd PSL Chemical Biology Symposium, France, January 2019.

Bernardes GJL. 2nd Chem East Organic Symposium, Norwich, UK, May 2019.

Bernardes GJL. EFMC-ACSMEDI MedChem Frontiers 2019, MedChemComm Emerging Investigator Lecture, Poland, June 2019.

Bernardes GJL. RICT2019: Interfacing Chemical Biology and Drug Discovery, France, July 2019.

Bernardes GJL. 19^o Congreso de la Sociedad Española de Química Terapéutica, Spain, July 2019.

Bernardes GJL. BrazMedChem, Pirenópolis – Goiás, Brazil, September 2019.

Bernardes GJL. 4th IberoAmerican Symposium on Organic Chemistry (SIBEAQO-IV), Cayo Santa María, Cuba, December 2019.

Invited Seminars:

Bernardes GJL. Host: Prof. Thomas Carell, Ludwig-Maximilians-Universität München, Germany, January 2019.

Bernardes GJL. Host: Prof. Jesús Jiménez-Barbero, CICbioGUNE, Spain, February 2019.

Bernardes GJL. Host: Dr Ramón Hurtado Guerrero, The Institute for Biocomputation and Physics of Complex Systems of the University of Zaragoza, Spain, March 2019.

Bernardes GJL. Host: Prof. Silvia Ortega Gutiérrez, Complutense University Madrid, Spain, April 2019.

Bernardes GJL. Host: Prof. Mariola Tortosa, Universidad Autónoma of Madrid, Spain, April 2019.

Bernardes GJL. 8th Chemical Protein Synthesis Meeting, Germany, June 2019.

Bernardes GJL. Host: Prof. Chas Bountra, Structural Genomics Centre, Oxford, UK, October 2019.

Bernardes GJL. Host: Prof. Christian Olsen, Center for Biopharmaceuticals and Department of Drug Design and Pharmacology, University of Copenhagen, Denmark, October 2019.

Bernardes GJL. Host: Prof. Ashraf Brik, Technion-Israel Institute of Technology, Haifa, Israel, November 2019.

Bernardes GJL. Host: Prof. David Margulies, Weizmann Institute of Science, Rehovot, Israel, November 2019.

Communications in International Conferences

Cal P. Exploring different Routes to generate homogenous ADCs. World ADC London organized by HansonWade, London, UK, March 2019.

Guerreiro A. Novel MUC1-based glycoconjugate vaccines against breast cancer. 13th International Meeting of the Portuguese Carbohydrate Group – GLUPOR 13, I3S, Porto, Portugal, September 3-5, 2019.

Marques M. Overexpression of Osmosensitive Ca²⁺-Permeable Channel TMEM63B Promotes Migration in HEK293T Cells. I NOVA Biophysica International Conference, Lisbon, Portugal, September 4-6, 2019. (*Oral Presentation*).

Sousa B. Biochemical and biophysical characterization of the human recombinant BMX, a target for prostate cancer. I NOVA Biophysica International Conference, Lisbon, Portugal, September 4-6, 2019. (*Oral Presentation*).

Communications in National Conferences

Cal P. 4 Years After... Protein Modification, Medicinal Chemistry and Machine Learning. Chemistry & Biology Crosstalks by FFULisboa, Lisbon, Portugal, January 2019.

Albuquerque I. Unnatural glycopeptides and glycoproteins, and their use in antigen detection and immunization. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Almeida C. CO-conjugated proteins in cancer immunotherapy. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Afonso C. Histone site-selective "click-to-acetylate". XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Internationalization

The internationalization of the laboratory research was achieved through the visit of some members of the group to other laboratories, namely:

- Albuquerque I. Cambridge University, UK, November 2019.
- Kitowski A. GSK, Sienna, Italy, March 2019.

These short stays allowed these members of the group to learn new techniques and to outreach the work from the lab.

Additionally, all the lectures given by Gonçalo Bernardes and the participation of other investigators in international conferences allowed to outreach the results from the projects being developed and to increase the collaborations network of the lab.

Furthermore, our laboratory also received the visit of an external expert, Dr. Jean Bertoldo (Nov-Dec 2019), from the University of Halle, Germany.

Prizes, Honors and Awards

Bernardes GJL. Commissions of Trust. ERC Advanced Grant Expert Reviewer (PE5), 2019-to date.

Bernardes GJL. Prémio Prestígio, Associação Física de Torres Vedras, Portugal. 2019.

Conde J. ERC Starting Grant. European Research Council, 2019.

Seixas J. ACORN Scholarship & Best Poster Award for his poster communication. EFMC-ACSMEDI MedChem Frontiers 2019, Krakow, Poland, 2019.

Seixas J. Assistant Position with a 10.0 score (the national maximum) from the Scientific Employment Stimulus Call, Portugal, 2019.

Bernardes GJL, Seixas J, Cal P, Rodrigues T. Investment from Portugal Ventures in a SpinOut of Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, 2019.

Guerreiro A. Best oral communication. 13th International Meeting of the Portuguese Carbohydrate Group – GLUPOR 13, Porto, Portugal, September 2019.

Industry Contract Research

Research Project in collaboration with Albumedix Ltd, which explores the use of albumin proteins to deliver cytotoxic drugs in the context of cancer. Two-year collaboration.

TargTex, a spin-off from iMM focused on the development of a novel treatment for Glioblastoma Multiforme was launched by some members of the group, in 2019, as a follow up of a project developed in the group (SME Instruments Phase 1 2019).

Patents/Prototypes

Patent Application: Compounds; United Kingdom Patent Application number 1908171.0.

Patent Application: Domingos A, Bernardes GJL. Treatment of obesity-related conditions. Patent reference WO2019/076675 A1.

Patent Application: Rodrigues T, Baker C, Conde J, Bernardes GJL. TRPV2 Antagonists. Patent reference WO 2019/054891 A2.

Patent Application: Rodrigues T, Bernardes GJL. 5-Lipoxygenase Antagonists. Patent Reference WO 2019/050422 A1.

Advanced Teaching

Bernardes GJL. Director of Studies in chemistry. Trinity Hall, Cambridge, UK, 2019–to date.

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

Bernardes GJL. Supervisor of organic and biological chemistry courses. Trinity Hall, Cambridge, UK, 2017–to date.

Bernardes GJL. Part III Course Internal Examiner. University of Cambridge, Cambridge, UK, 2014–to date.

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

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

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

Rodrigues T. Lecturer. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal.

Science and Society

Kitowski A, Seixas J, Guerreiro A, Oliveira B. Hosts of High School Students in lab visits.

Kitowski A, Guerreiro A. Hosts of Primary School Students in lab visits.

Albuquerque I, Almeida C. Participated in the Immunology Day at Instituto de Medicina Molecular João Lobo Antunes, April 29, 2019.

All the group members participated in the iMM Scientific Retreat 2019, Évora, Portugal.

PhD Theses

Charlotte Baker, 16/12/2019, Selective cancer therapies: Targeting TRP channels in glioblastoma and prostate cancer. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Gonalo Bernardes. Co-Supervisor: Tiago Rodrigues.

Annabel Kitowski, 10/09/2019, Bio-orthogonal labelling of carbohydrates and proteins. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Gonalo Bernardes.

Padma Akkapeddi, 02/2019, Antibody based therapy for T-cell acute lymphoblastic leukemia: Targeting IL-7 receptor. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Gonalo Bernardes. Co-Supervisor: Joo Barata.

Joana Neves Lab

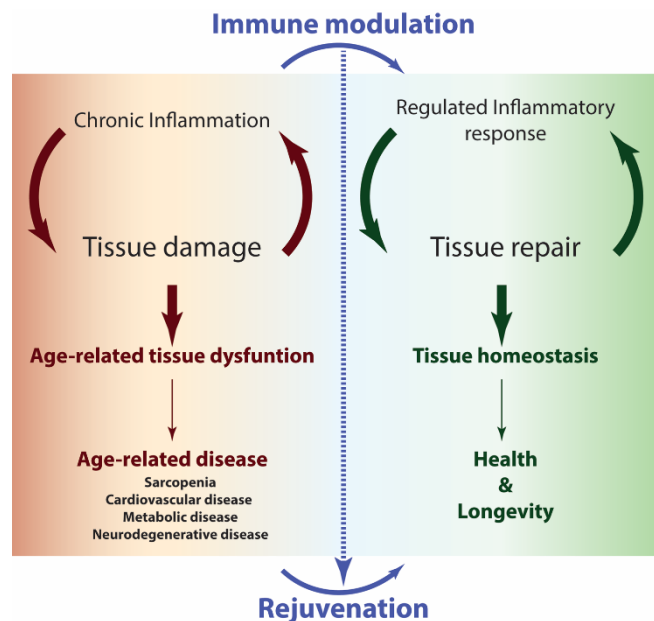
Major Interests/Objectives

Our central interest is the exploration of the tissue repair processes that have evolved to heal damaged organs to improve regenerative success in older individuals. 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 aging 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 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.

Head of Laboratory

Joana Mendes Neves, PhD (Started April)

Graphical Abstract



Laboratory Keywords / Research Areas

Immune Modulation, Inflammation, Regeneration, Aging, Muscle.

Major Scientific Achievements

We established our lab at IMM in the summer of 2019 and initiated the main research lines that will define the first years of research in the lab. We are now ready to start answering our most important questions. We have also published two reviews describing the current knowledge and challenges in the field of immune modulation applied to rejuvenation biology.

Selected Publications

Munoz-Canoves P**, Neves J, Sousa-Victor P** (2019). Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells. **FEBS Journal** 287(3):406416. Review (IF: 4.739, Citations: 0. Source: Google Scholar).

Neves J**, Sousa-Victor P** (2019). Regulation of inflammation as an anti-aging intervention. **FEBS Journal** 287(2020):43–52. Perspective. (IF: 4.739, Citations: 1. Source: Google Scholar).

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. (IF:--, Citations: 4. Source: Google Scholar).

Neves J*, Sousa-Victor P*, Jasper H (2017). Rejuvenating Strategies for Stem Cell-Based Therapies in Aging. **Cell Stem Cell** 20(2):161-175. Review. (IF: 21.464, Citations: 54. Source: Google Scholar).

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. (IF: 41.063, Citations: 86. Source: Google Scholar).

Neves J*, Demaria M*, Campisi J, Jasper H (2015). Of Flies, Mice, and Men: Evolutionarily Conserved Tissue Damage Responses and Aging. **Developmental Cell** 32(1):9-18. Review. (IF: 9.616, Citations: 52. Source: Google Scholar).

*equal contribution

**Corresponding author

Publications in Peer Reviewed Journals

Munoz-Canoves P**, Neves J, Sousa-Victor P** (2019). Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells. **FEBS Journal** 287(3):406-416. Review. (IF: 4.739, Citations: 0. Source: Google Scholar).

Neves J**, Sousa-Victor P** (2019). Regulation of inflammation as an anti-aging intervention. **FEBS Journal** 287(2020):43–52. Perspective. (IF: 4.739, Citations: 1. Source: Google Scholar).

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. (IF: --, Citations: 4. Source: Google Scholar).

*equal contribution. **Corresponding author

Invited Lectures and Seminars

Neves J. Immune modulatory interventions in ageing and tissue repair. Simpósio sobre intercâmbio em Medicina, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 13, 2019.

Neves J. Immune modulatory interventions in ageing and tissue repair. Center for Innovative Biomedicine and Biotechnology (CIBB) Meeting, Coimbra, Portugal, December 19, 2019.

Advanced Teaching

Neves J. 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, September 25, 2019.

Science and Society

Presentation at MDS Conference "Saúde & Longevidade" with the title "Rejuvenescimento e extensão de vida saudável: um desafio biomédico". This was an event organized by insurance companies and opened to the general public where we discussed the state of the art in biomedical research on aging biology and emerging rejuvenating interventions, with a focus on regenerative medicine.

João Barata Lab

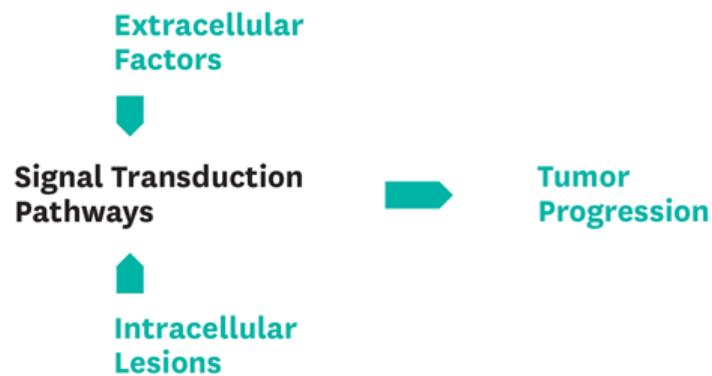
Major Interests/Objectives

We aim to understand the role of cell-autonomous alterations and microenvironmental cues in the development of cancer, focusing mainly on the dissection of signaling pathways essential for tumor maintenance. To do so, we make use of patient material, as a key source of insights into the disease, and integrate different biochemical, cellular and molecular biology techniques with appropriate *in vitro* and *in vivo* models - enabling an overall appreciation of the molecular, cellular and systemic nuances associated with cancer. The basic and pre-clinical research we perform is translation-oriented and enriched by active collaborations with clinicians. Ultimately, we aim to identify and characterize molecular targets for the development of novel, more selective therapies against cancer.

Head of Laboratory

João Pedro Taborda Barata, PhD, Associate Professor

Graphical Abstract



Team

Afonso Rocha Martins de Almeida	PhD	Senior Postdoctoral Researcher (Left November)
Alice Sofia dos Santos Melão	Master Degree	PhD Student
Ana Patrícia Cebola Cachucho	Master Degree	Lab Technician
Ana Rita Cascão Rodrigues	PhD	Senior Postdoctoral Researcher
Ana Rita Freitas Martins de Matos Fragoso	PhD	Staff Scientist
Ana Sofia Navarro Ramalho	Master Degree	MSc Student (Left October)
Beatriz Carrinho Raposo	Master Degree	MSc Student
Bruno António Caetano Cardoso	PhD	Senior Postdoctoral Researcher

Carlos Manuel Tavares da Custódia	Master Degree	PhD Student
Clara Lúcia Gonçalves Dias	PhD	Postdoctoral Researcher (Started June)
Cláudia Maria Coelho de Faria	MD/PhD	Clinical Researcher
Cláudia Vanessa Soares Prego	Master Degree	Lab Manager (Started January, Left May)
Daniel Filipe Silva Ribeiro	PhD	Postdoctoral Researcher
Daniil Anatolievich Shatalov	University Degree	Trainee (Started January, Left July)
Diana Filipa Pereira Vaz	Master Degree	Lab Manager (Started May)
Eunice Ribeiro João Silva Paisana	Master Degree	PhD Student
Francisco Miguel da Cruz Vaz Borges Alexandrino	High School Diploma	MSc Student
Hannah Taylor	High School Diploma	BSc Student (Started January, Left May)
João Luís Aguiar Martins Neto	PhD	Postdoctoral Researcher (Started February)
Luís Pedro Dias Bernardo Maricoto Monteiro	Master Degree	PhD Student
Mafalda Alexandra Ramos de Matos	PhD	Lab Technician (Left February)
Mafalda dos Santos Dias Duque	Master Degree	Lab Technician
Mariana Lobato de Oliveira	Master Degree	PhD Student
Marta Sofia Barbosa Fernandes	Master Degree	PhD Student
Mayara Ferreira Euzébio	Master Degree	Lab Technician

Laboratory Keywords / Research Areas

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

Major Scientific Achievements

The lab studies mainly hematological tumors (especially lymphoid leukemias) and brain tumors. In 2019, we demonstrated that NRARP, a known inhibitor of Notch, can unexpectedly have pro-tumoral effects in T-cell acute lymphoblastic leukemia (T-ALL). We showed that NRARP can in fact display either pro- or anti-tumoral roles in T-ALL depending on Notch and Wnt signaling (Pinto *et al.*, *Oncogene* 2019). We also demonstrated that a fully human anti-IL-7R α antibody we generated, in collaboration with Gonçalo Bernardes and Dario Neri, promotes antitumor activity against T-ALL (Akkapeddi *et al.*, *Leukemia* 2019). These findings may have substantial clinical impact in the future and we will pursue that goal within a European Research Council Proof-of-Concept project awarded to the lab in 2019.

In addition, we contributed to different collaborative research efforts, leading to the finding that T-ALL cells can produce IL-7 in an autocrine fashion (Buffière *et al.*, *Oncogene* 2019), characterizing the tumor-promoting ability of alterations in ALK/ROS1/NTRK/MET in infantile hemispheric gliomas (Guerreiro Stucklin *et al.*, *Nat Comm* 2019), or identifying the critical role of noncoding U1 snRNA mutations in cryptic splicing in SHH medulloblastoma (Suzuki *et al.*, *Nature* 2019). Finally, our contributions to the knowledge on IL-7 and IL-7R signaling in health and disease led to the publication of a commissioned review in *Nature Immunology* (Barata *et al.*, *Nat Immunol* 2019).

Selected Publications

Martins LR, Lúcio P, Melão A, Antunes I, Cardoso BA, Stansfield R, Bertilaccio MT, Ghia P, Drygin D, Silva MG, Barata JT (2014). Activity of the clinical-stage CK2-specific inhibitor CX-4945 against chronic lymphocytic leukemia. **Leukemia** 28:179–182. (IF: 9.944, Citations: 46. Source: *Web of Science*).

Mendes RD, Sarmiento LM, Canté-Barrett K, Zuurbier L, Buijs-Gladdines J, Pova V, Smits WK, Abecassis M, Yunes JA, Sonneveld E, Horstmann MA, Pieters R, Barata JT, Meijerink JPP (2014). PTEN micro-deletions in T-cell acute lymphoblastic leukemia are caused by illegitimate RAG-mediated recombination events. **Blood** 124:567-578. (IF: 16.601, Citations: 42. Source: *Web of Science*).

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. (IF: 25.455, Citations: 203. Source: *Web of Science*).

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 α in T cells. **Blood** 115:2724-2731. (IF: 16.601, Citations: 72. Source: *Web of Science*).

Silva A, Yunes JA, Cardoso BA, Martins LR, Jotta PY, Abecassis 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. (IF: 12.282, Citations: 277. Source: *Web of Science*).

Ongoing Research Projects

2018/2021: 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.

2017/2019: Identificação de novas terapias no tratamento do astrocitoma pilocítico em idade pediátrica. Coordinator: Cláudia Faria. Funding Agency: José de Mello Saúde. Reference: Manuel de Mello CFaria. Amount: € 12 500,00. Total Amount: € 12 500,00.

2016/2019: Aberrant IL7R signaling in leukemogenesis: from the basics to potential therapeutics. Coordinator: João Barata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FAPESP/20015/2014. Amount: € 199 778,00€. Total Amount: € 400 000,00.

2016/2019: Brain Tumours. Coordinator: Cláudia Faria. Funding Agency: Fundação Millennium BCP. Reference: Millenium BTT. Amount: € 90 000,00. Total Amount: € 90 000,00.

2015/2020: IL7SigNeTure: IL-7/IL-7R signaling networks in health and malignancy. Coordinator: João Barata. Funding Agency: European Commission. Reference: ERC CoG 648455. Amount: € 1 988 125,00. Total Amount: € 1 988 125,00.

2011/2020: Research into brain tumours. Coordinator: Cláudia Faria. Funding Agency: Clientes Diversos. Reference: BTT. Amount: € 213 993,00. Total € 213 993,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Review Journals

Barata JT, Durum SK, Seddon B (2019). Flip the coin: IL-7 and IL-7R in health and disease. **Nature Immunology** 20(12):1584-1593. *Corresponding author (Commissioned review). (IF: 23.53, Citations: 1. Source: Web of Science).

Pinto I, Duque M, Gonçalves J, Akkapeddi P, Oliveira ML, Cabrita R, Yunes JA, Durum SK, Barata JT, Fragoso R (2019). NRARP displays either pro- or anti-tumoral roles in T-cell acute lymphoblastic leukemia depending on Notch and Wnt signaling. **Oncogene** 39(5):975-986. (IF: 6.634, Citations: 0. Source: Web of Science).

Buffière A, Uzan B, Aucagne R, Hermetet F, Mas M, Nassurdine S, Aznague A, Carmignac V, Tournier B, Bouchot O, Ballerini P, Barata JT, Bastie JN, Delva L, Pflumio F, Quéré R (2019). T-cell acute lymphoblastic leukemia displays autocrine production of Interleukin-7. **Oncogene** 39(5):975-986. (IF: 6.634. Citations: 0. Source: Web of Science).

Barata JT (2019). Introduction to the special issue on T-cell acute lymphoblastic leukemia genetics, biology and therapeutics. **Advances in Biological Regulation** 74:100671. Editorial. (IF: -, Citations: 1).

Correia NC*, Barata JT* (2019). MicroRNAs and their involvement in T-ALL: A brief overview. **Advances in Biological Regulation** 74:100650. (IF: --. Citations: 1). * co-corresponding authors

Hixon JA, Andrews C, Kashi L, Kohnhorst CL, Senkevitch E, Czarra K, Barata JT, Li W, Schneider JP, Walsh STR, Durum SK (2019). New anti-IL-7R α monoclonal antibodies show efficacy against T cell acute lymphoblastic leukemia in pre-clinical models. **Leukemia** 34(1):35-49. (IF: 9.944, Citations: 1. Source: Web of Science).

P. Akkapeddi, R. Fragoso, J.A. Hixon, A.S. Ramalho, M.L. Oliveira, T. Carvalho, A. Gloger, M. Matasci, F. Corzana, S.K. Durum, D. Neri, G.J.L. Bernardes*, J.T. Barata* (2019). A fully human anti-IL-7R α antibody promotes antitumor activity against T-cell acute lymphoblastic leukemia. **Leukemia** 33(9):2155-2168. * co-corresponding authors. (IF: 9.944, Citations: 1. Source: Web of Science).

Oliveira ML, Akkapeddi P, Ribeiro D, Melão A, Barata JT (2019). IL-7R-mediated signaling in T-cell acute lymphoblastic leukemia: An update. **Advances in Biological Regulation** 71:88-96. (IF: --, Citations: 1).

Guerreiro Stucklin AS, Ryall S, Fukuoka K, Zapotocky M, Lassaletta A, Li C, Bridge T, Kim B, Arnoldo A, Kowalski PE, Zhong Y, Johnson M, Li C, Ramani AK, Siddaway R, Nobre LF, de Antonellis P, Dunham C, Cheng S, Boué DR, Finlay JL, Coven SL, de Prada I, Perez-Somarriba M, Faria CC, Grotzer MA, Rushing E, Sumerauer D, Zamecnik J, Krskova L, Garcia Ariza M, Cruz O, Morales La Madrid A, Solano P, Terashima K, Nakano Y, Ichimura K, Nagane M, Sakamoto H, Gilda-Costa MJ, Silva R, Johnston DL, Michaud J, Wilson B, van Landeghem FKH, Oviedo A, McNeely PD, Crooks B, Fried I, Zhukova N, Hansford JR, Nageswararao A, Garzia L, Shago M, Brudno M, Irwin MS, Bartels U, Ramaswamy V, Bouffet E, Taylor MD, Tabori U, Hawkins C (2019). Alterations in ALK/ROS1/NTRK/MET drive a group of infantile hemispheric gliomas. **Nature Communications** 10(1):4343. (IF: 11.878. Citations: 1. Source: Web of Science).

Suzuki H, Kumar SA, Shuai S, Diaz-Navarro A, Gutierrez-Fernandez A, De Antonellis P, Cavalli FMG, Juraschka K, Farooq H, Shibahara I, Vladoiu MC, Zhang J, Abeysundara N, Przelicki D, Skowron P, Gauer N, Luu B, Daniels C, Wu X, Forget A, Momin A, Wang J, Dong W, Kim SK, Grajkowska WA, Jouvét A, Fèvre-Montange M, Garrè ML, Nageswara Rao AA, Giannini C, Kros JM, French PJ, Jabado N, Ng HK, Poon WS, Eberhart CG, Pollack IF, Olson JM, Weiss WA, Kumabe T, López-Aguilar E, Lach B, Massimino M, Van Meir EG, Rubin JB, Vibhakar R, Chambless LB, Kijima N, Klekner A, Bognár L, Chan JA, Faria CC, Ragoussis J, Pfister SM, Goldenberg A, Wechsler-Reya RJ, Bailey SD, Garzia L, Morrissy AS, Marra MA, Huang X, Malkin D, Ayrault O, Ramaswamy V, Puente XS, Calarco JA, Stein L, Taylor MD (2019). Recurrent noncoding U1 snRNA mutations drive cryptic splicing in SHH medulloblastoma. **Nature** 574(7780):707-711. (IF: 43.07. Citations: 6. Source: Web of Science).

de Medeiros CB, Moxon-Emre I, Scantlebury N, Malkin D, Ramaswamy V, Decker A, Law N, Kumabe T, Leonard J, Rubin J, Jung S, Kim SK, Gupta N, Weiss W, Faria CC, Vibhakar R, Lafay-Cousin L, Chan J, Kros JM, Janzen L, Taylor MD, Bouffet E, Mabbott DJ (2019). Medulloblastoma has a global impact on health related quality of life: Findings from an international cohort. **Cancer Medicine** 9(2):447-459. (IF: 3.357, Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Barata JT. Cell-autonomous and extracellular signaling cues in leukemia development: new targets for therapeutic intervention. 1st Joint iMM-Jinan University Joint Symposium, Jinan University, Guangzhou, Guangdong, China, January 12, 2019.

Faria C, Cascão R. Identification of molecular determinants essential for the metastasis of different types of tumors to the brain. AEICBAS Biomedical Congress, Porto, Portugal, March 17, 2019.

Faria C. The basics of research and options in translational research. 1st European Combined Neuro-Oncology Course of the European Society for Pediatric Oncology - Brain Tumour Group (SIOPE BTG), Budapest, Hungary, April 2-4, 2019.

Faria C. Biobank. 1st Joint Meeting of Life Science Institutes in the Lisbon Area, Lisbon, Portugal, April 24, 2019.

Barata JT. IL-7R and PTEN in T-ALL. European School of Haematology International Conference on Acute Lymphoblastic Leukaemia, Berlin, Germany, May 17-19, 2019.

Barata JT. Plenary Talk "IL-7 and IL-7R: signals impacting on leukemia development". Xth SINAL meeting on Signal Transduction, Olhão, Portugal, October 18-19, 2019.

Barata JT. Acute lymphoblastic leukemia: can basic science contribute to novel therapeutic solutions? ASPIC CONFERENCE - Research on Pediatric Cancer: Where are we? Where are we going?, Calouste Gulbenkian Foundation, Lisbon, Portugal, November 8, 2019.

Faria C. Identificação de novas terapias no tratamento do meduloblastoma em idade pediátrica. In2ME, Universidade da Beira Interior, Coimilhã, Portugal, November 10, 2019.

Barata JT. Development of IL-7R blocking antibodies to treat T-ALL. Session on Research, Joint iBFM Resistant Disease Committee and IntReALL 2010-2020 study group Interim Meeting, Nice, France, November 15-16, 2019.

Faria C. Investigação e Medicina. Congresso Nacional de Estudantes de Medicina, Lisbon, Portugal, November 16, 2019.

Communications in International Conferences

Fernandes MB, Melão A, Matos J, Cadilha H, Pyne S, Pyne NJ, Barata JT. Sphingosine Kinases are key effectors of IL-7R-mediated signaling, viability, growth and proliferation in T-cell Acute Lymphoblastic Leukemia. FEBS 2019 Advanced Course - Sphingolipid Biology: Sphingolipids in Physiology and Pathology, Cascais, Portugal, May 6-10, 2019. (*Oral Presentation*).

Fragoso R, Matos M, Grosso AR, Barata JT. Preliminary characterization of IL-7/IL-7R phospho-signaling landscape. 1st ESH International Conference on Acute Lymphoblastic Leukaemia, Berlin, Germany, May 17-19, 2019. (*Poster Presentation*).

Cardoso BA, Gírio A, Fragoso R, Martins LR, Moreira AS, Correia NC, Bortolini A, Grosso AR, de Almeida SF, Yunes A, Pflumino F, Barata JT. CASZ1 is overexpressed in T-cell acute lymphoblastic leukemia and promotes cell transformation via PI3K-Akt-mTOR signaling. 1st ESH International Conference on Acute Lymphoblastic Leukaemia, Berlin, Germany, May 17-19, 2019. (*Poster Presentation*).

Duque M, Pinto I, Gonçalves J, Akkapeddi P, Oliveira M, Cabrita R, Yunes A, Durum S, Barata JT, Fragoso R. Nrarp Displays Either Pro- or Anti-Tumoral Roles in T-Cell Acute Lymphoblastic Leukemia Depending on Notch and Wnt Signaling. 1st ESH International Conference on Acute Lymphoblastic Leukaemia, Berlin, Germany, May 17-19, 2019. (*Poster Presentation*).

Paisana E, Cascão R, Custódia C, Qin N, Picard D, Carvalho T, Pereira P, Roque R, Pimentel J, Remke M, Miguéns J, Barata JT, Faria C. The role of ubiquitin conjugating enzymes in brain metastases. EACR Cancer Genomics 2019, Cambridge, UK, June 23-26, 2019. (*Poster Presentation*).

Silva A, Almeida A, Matos M, Semeyer S, Cachucho A, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT. Overexpression of wild type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. 2nd European Society for Immunodeficiencies Focused Meeting - "Malignancy and PID", Brussels, Belgium, September 17-21, 2019. (*Poster Presentation*).

Ribeiro D, Lopes I, Abreu M, Custódia C, Barata JT. IL-7 either promotes or inhibits autophagy, depending on the stress context, to promote the viability of T-cell acute lymphoblastic leukemia cells. 6th meeting of the International Society of Cancer Metabolism (ISCaM), Braga, Portugal, October 17-19, 2019. (*Poster Presentation*).

Communications in National Conferences

Paisana E, Cascão R, Custódia C, Qin N, Picard D, Carvalho T, Pereira P, Roque R, Pimentel J, Remke M, Miguéns J, Barata JT, Faria C. The role of ubiquitin conjugating enzymes in brain metastases. XI Congresso Nacional da Associação Portuguesa de Neuro-Oncologia, Lisbon, Portugal, January 18-19, 2019. (*Poster Presentation*).

Ramalho AS, da Silva JF, Perez F, Barata JT. Exploring new facets of interleukin-7 receptor-mediated signaling in T-cell leukemia. 10th AIMS Meeting, Lisbon, Portugal, March 14-17, 2019. (*Poster Presentation*).

Silva A, Almeida A, Matos M, Demeyer S, Cachucho A, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT. Overexpression of wild type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. XLV Reunião Anual da Sociedade Portuguesa de Imunologia - SPI 45, Coimbra, Portugal, May 15-19, 2019. (*Oral Presentation*).

Oliveira ML, Garcia EG, Langenau DM, Barata JT. Mutant IL-7 receptor cooperates with Myc and activated Notch to accelerate T-cell leukemogenesis in zebrafish. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Custódia C, Cascão R, Paisana E, Carvalho T, Roque R, Pimentel J, Miguéns J, Barata JT, Faria C. Targeting CCL2/CCR2 axis in metastatic medulloblastoma. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Paisana E, Cascão R, Custódia C, Qin N, Picard D, Carvalho T, Pereira P, Roque R, Pimentel J, Remke M, Miguéns J, Barata JT, Faria C. The role of ubiquitin conjugating enzymes in brain metastases. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Monteiro LP, Alcobia I, Serafim T, Barata JT. Exploring the IL-7 Signaling based on Proteomics - The Quest for new Drugable Targets in Leukemia. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Fernandes MB, Melão A, Matos J, Cadilha H, Pyne S, Pyne NJ, Barata JT. Sphingosine Kinases are key effectors of IL-7R-mediated signaling, viability, growth and proliferation in T-cell Acute Lymphoblastic Leukemia. SINAL 2019 - 10th meeting of Signal Transduction, Olhão, Portugal, October 18-19, 2019. (*Poster Presentation*).

Silva A, Almeida A, Matos M, Demeyer S, Cachucho A, Hogan T, Li Y, Meijerink J, Cools J, Grosso AR, Seddon B, Barata JT. Overexpression of wild type IL-7R α promotes T-cell acute lymphoblastic leukemia/lymphoma. SINAL 2019 - 10th meeting of Signal Transduction, Olhão, Portugal, October 18-19, 2019. (*Oral and Poster Presentation*).

Alexandrino F, Cardoso BA, Barata JT. Unraveling the role of CASZ1 in T-ALL. Dia da Investigação - 22^o Programa "Educação para a Ciência" - GAPIC, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019. (*Poster Presentation*).

Organization of Conferences

Faria C is the President of the Portuguese Neuro-Oncology Association and organized the XI Annual Meeting, Lisbon, Portugal, January 18-19, 2019.

Faria C is Chair of the Young Investigators and Innovators Group of the European Society for Pediatric Oncology - Brain Tumour Group (SIOPE BTG), and organized the 1st European Combined Neuro-Oncology Course of the European Society for Pediatric Oncology - Brain Tumour Group (SIOPE BTG), Budapest, Hungary, April 2-4, 2019.

Faria C. Co-Organizer with Luisa Lopes. The Neuroscience Seminar Series (NeuroSe) at CAML, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 12, May 14 and September 10, 2019.

Fragoso R was a member of the Evaluation panel of the Poster Session II of the XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15, 2019.

Almeida A was a member of the evaluation committee for the posters in the 45th annual meeting of the Portuguese Society of Immunology (SPI), Coimbra, Portugal, May 15-17, 2019.

Faria C was a member of the organizing committee of the Annual Meeting of the Portuguese Society of Neurosurgery, Cascais, Portugal, May 23-25, 2019.

Barata JT was a member of the Scientific Committee, SINAL 2019 - Xth Meeting on Signal Transduction, Olhão, Portugal, October 18-19, 2019.

Faria C. Organizer. The Annual Training Course for Neurosurgery Residents through the Portuguese Society of Neurosurgery (SPNC), Hotel Palace da Curia, Portugal, October 24-26, 2019.

Cardoso B, Faria C were members of the Organizing Committee of the ASPIC Conference “Research on Pediatric Cancer”, Lisbon, November 8, 2019.

Almeida A was a member of the evaluation committee for the poster session at the GAPIC meeting “Educação pela Ciência” at the Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 9, 2019.

Fragoso R was a member of the Evaluation panel of the Poster Session V of the 8th edition of “Dia da Investigação”, GAPIC, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019.

Faria C. Organizer. 8th edition of “Dia da Investigação”, GAPIC, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019.

Internationalisation

Our projects regularly involve collaborations with international research groups in Europe, USA and Brazil. Current international collaborators in the leukemia projects include: Ben Seddon (UCL, England), David Langenau (MGH, Harvard University, USA), Doreen Cantrell (University of Dundee, Scotland), Nigel Pyne (University of Strathclyde, England), Scott Durum (NCI, USA), Charles Mullighan (St. Jude Children’s Hospital, USA), Pieter van Vlierberghe (Ghent, Belgium), Jan Cools (VIB, Belgium), and J. Andres Yunes (Centro Infantil Boldrini, Brazil).

Current international collaborators in the brain tumor projects include: Michael D. Taylor (University of Toronto, Canada), James T. Rutka (University of Toronto, Canada) and Marc Remke (University of Dusseldorf, Germany).

Faria C. participates in international consortia for the study of the most common pediatric brain tumors: MAGIC – Medulloblastoma Advanced Genomics International Consortium; GENE – Global Ependymoma Network of Excellence.

Faria C. is the Chair of the Young Investigators and Innovators Group of the International Society of Pediatric Oncology – Europe (SIOP-E) Brain Tumor Group (BTG) since September 2017.

Faria C. is the Portuguese representative in the Board of National Directors of the European translational network EATRIS-ERIC and responsible for the creation of the Portuguese National Hub (since 2018).

Prizes, Honors and Awards

Fernandes MB was awarded the best poster presentation, for the work entitled “Sphingosine Kinases are key effectors of IL-7R-mediated signaling, viability, growth and proliferation in T-cell Acute Lymphoblastic Leukemia”, SINAL 2019 - 10th meeting of Signal Transduction, Olhão, Portugal.

Fernandes MB was awarded with a travel grant for a short talk presentation, for the work entitled “Sphingosine Kinases are key effectors of IL-7R-mediated signaling, viability, growth and proliferation in T-cell Acute Lymphoblastic Leukemia”, FEBS 2019 Advanced Course - Sphingolipid Biology: Sphingolipids in Physiology and Pathology, Cascais, Portugal.

Paisana E was awarded the best poster presentation, for the work entitled “The role of ubiquitin conjugating enzymes in brain metastases”, XI Congresso Nacional da Associação Portuguesa de Neuro-Oncologia, Lisbon, Portugal.

Oliveira ML was awarded the second best oral presentation, for the work entitled “Mutant IL-7 receptor cooperates with Myc and activated Notch to accelerate T-cell leukemogenesis in zebrafish”, XIII Annual CAML PhD Students’ Meeting, Lisbon, Portugal.

Francisco A was awarded second best poster presentation, for the work entitled “Unraveling the role of CASZ1 in T-ALL”, Dia da Investigação - 22º Programa "Educação para a Ciência" - GAPIC, Faculdade de Medicina da Universidade de Lisboa. Lisbon, Portugal

Advanced Teaching

Barata JT taught on “Signal Transduction in Cancer”, Molecular and Cellular Biology of Cancer course, Masters in Molecular Biology and Genetics/ Masters in the Biology of Evolution and Development, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, March 11, 2019.

Fragoso R taught the topic “Wnt signaling pathway” at the “Signal Transduction in Cancer” Course of the Masters in Oncobiology, Centro Académico de Medicina de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 30-31 January, 2019.

Science and Society

Barata JT participated in the round table “PhD? Check!; Post-Doc? Check! What's next? - Canonical and Non-canonical Research”, iMM Postdoc Day - Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 25, 2019.

The lab joined the Brain Tumour Team (BTT) on April 28, 2019, to participate in a run/walk event to create awareness for cancer research and, particularly, for brain tumor research. The BTT gathered health care professionals, scientists, patients and their families aiming to support cancer research and to create hope for the future of patients affected with brain cancer.

Barata JT. “Sinalização em cancro: travões, reviravoltas, música e um pouco de literatura na procura de novos tratamentos [Signaling in cancer: breaks, turns, music and a little bit of literature while seeking for new treatments]”, Pint of Science Festival, Lisbon, Portugal, May 20, 2019.

Fragoso R taught the topic “Teaching to Teach Science” at the Africa Science Week Cabo Verde 2019 edition, Cidade da Praia, Cabo Verde, October 4-6 2019.

Barata JT participated in the round table on *Cuidados de Saúde – Perspetivando o Futuro [Health Care – Picturing the Future]*, discussing the talks of Faustino Ferreira, Adalberto Campos Fernandes, Carlos Alberto Ferreira, Manuel Sobrinho Simões, José Santos-Victor, Henrique Bicha Castelo, Catarina Oliveira and Alexandre Castro Caldas, 25th Anniversary of Hospital SAMS, Lisbon, Portugal, November 9, 2019.

Fragoso R participated in iMM Science Club at the Santa Maria Pediatric Department, Hospital de Santa Maria, Lisbon, Portugal, December 10, 2019.

MSc Thesis Completed

Sofia Ramalho, 07/05/2019, Unveiling new facets of interleukin-7 receptor-mediated signaling in acute lymphoblastic leukemia, Faculdade de Medicina da Universidade de Lisboa. Supervisor: João Barata.



Beatriz Carrinho, 20/11/2019, Cooperation between IL-7R signaling and HOXA9 in leukemogenesis, Instituto de Ciências Biomédicas Abel Salazar. Supervisor: João Barata. Co-Supervisor: Afonso Almeida.

Mayara Euzébio, 10/11/2019, Potencial leucemogenico do *IL-7R* mutante *in vivo*, Instituto de Biologia, Universidade de Campinas, Campinas. Supervisor: José Andrés Yunes.

João Eurico Fonseca Lab

Major Interests/Objectives

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 specific research objectives are 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.

Head of Laboratory

João Eurico Cortez Cabral da Fonseca, MD/PhD

Team

Alexandre Figueiredo Brito	Master Degree	MSc Student
Ana Filipa Brojo Lopes de Oliveira Ramos Cordeiro	MD/University Degree	Clinical Researcher
Ana Isabel Zenha Leite Tavares	High school Diploma	Administrative Technician (Started February)
Ana Patrícia Costa Reis	MD/PhD	Postdoctoral Researcher (Started June)
Ana Rita da Cruz Machado	MD/Master Degree	Clinical Researcher
Ana Rita Durão da Graça Godinho Sofio	Master Degree	MSc Student
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
Diana de Almeida Carmona Fernandes	PhD	PhD Student (Left July)
Elsa Cristina Vieira de Sousa	MD/PhD	Clinical Researcher
Fernando Manuel Diamantino Saraiva	MD/University Degree	Clinical Researcher (Started September)
Inês Filipa Pereira Abrunhosa Amaral	University Degree	MSc Student (Left July)
Joana da Silva Marques Coelho Dinis	MD/Master Degree	Clinical Researcher
João Carço Fernandes Pedro	High School Diploma	MSc Student (Started January. Left July)
João Pedro Ribeiro da Silva Garcês Marques	University Degree	MSc Student (Started January. Left July)
Joaquim Miguel Polido Pereira	MD/University Degree	PhD Student
José Guilherme Gonçalves Nobre	University Degree	MSc Student (Started January. Left July)

Manuel Quaresma Jorge Silvério António	MD/Master Degree	Clinical Researcher
Maria Beatriz Almeida Santos	University Degree	MSc Student (Started January, Left July)
Maria Catarina Nobre Semedo Tenazinha	MD/Master Degree	Clinical Researcher (Started April)
Maria Helena Regalo da Fonseca	University Degree	Senior Postdoctoral Researcher
Maria José Parreira dos Santos	MD/PhD	Clinical Staff Scientist
Mónica da Silva	University Degree	MSc Student (Started September)
Neide Fernanda Meireles da Silva	University Degree	MSc Student (Started September)
Nikita Khmelinskii	MD/Master Degree	Clinical Researcher (Started April)
Patrícia Godinho Bexiga Martins	MD/Master Degree	Clinical Researcher
Pedro Manuel Ávila Ribeiro	Master Degree	PhD Student
Raquel Patrícia Campanilho Marques Ruivo	MD/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
Sónia Filipa da Silva Figueiredo	Master Degree	Technician (Started April)
Susana Paula Leonardo Dias Abreu Capela	MD/University Degree	Clinical Researcher
Vasco Madeira Crispim Romão	MD/PhD	Clinical Researcher
Vítor André Silvestre Teixeira	MD/Master Degree	Clinical Researcher

Laboratory Keywords / Research Areas

Diagnostic, Prognostic and Response to Treatment Markers in Rheumatic Diseases, Inflammation and Bone, Cohorts, Registries and Databases, Recommendations and Guidelines, Collaboration in Clinical Trials.

Major Scientific Achievements

- Characterization of the effect of TNF antagonists on psoriatic arthritis manifestations.
- Characterization of the adult phenotype of childhood arthritis.
- Early diagnosis of giant cell arteritis.
- Implementation of synovial tissue biopsy for patient stratification.
- Pre-clinical characterization of Celastrol as an effective treatment for arthritis.
- Impact of early arthritis on bone nanostructure.
- Impact of Jak inhibitors in early arthritis.

Selected Publications

Carmona-Fernandes D, Santos MJ, Canhão H, Fonseca JE (2013). Anti-ribosomal P protein IgG autoantibodies in patients with systemic lupus erythematosus: diagnostic performance and clinical profile. **BMC Medicine** 11: R196. (IF: 8.285, Citations: 21. Source: Web of Science).

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 favours B cell activation and survival. **Rheumatology** 50(2):278-82. (IF: 5.245, Citations: 36. Source: Web of Science).

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE (2010). Neutrophils in rheumatoid arthritis: More than simple final effectors. **Autoimmunity Reviews** 9:531-535. (IF: 7.716, Citations: 121. Source: Web of Science).

Cascão R, Moura RA, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE (2010). Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early rheumatoid arthritis. **Arthritis Research and Therapy** 12(5):R196. (IF: 4.1148, Citations: 61. Source: Web of Science).

Caetano-Lopes J, Nery AM, Canhão H, Duarte J, Cascão R, Rodrigues A, Perpétuo I, Abdulghani S, Amaral PM, Sakaguchi S, Konttinen YT, Graça L, Vaz MF, Fonseca JE (2010). Chronic arthritis leads to disturbances in the bone collagen network. **Arthritis Research and Therapy** 12(1):R9. (IF: 4.148, Citations: 24. Source: Web of Science).

Ongoing Research Projects

2019/2029: Biovas - Biobanco de vasculitis. Coordinator: João Eurico da Fonseca. Amount: Private Funding.

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.

2019/2023: 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. Coordinator: João Eurico da Fonseca. Funding Agency: Merck Sharp & Dohme. Amount: € 59 175,00. Total Amount: € 59 175,00.

2019/2022: Estudo da permeabilidade intestinal e do microbioma em doentes com lúpus eritematoso sistémico. Coordinator: João Eurico da Fonseca. Funding Agency: L'Óreal/FCT. Amount: € 15 000,00. Total Amount: € 15 000,00.

2019/2022: Study of the immune-modulatory effect of Tofacitinib on B cell function in rheumatoid arthritis patients. Coordinator: João Eurico da Fonseca. Amount: Private Funding.

2019/2022: The role of JAK-STAT signalling pathway as key to chronic arthritis onset. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Amount: € 9 000,00. Total Amount: € 9 000,00.

2018/2022: Immune response to Hepatitis B and Influenza vaccines in rheumatic patients under biological therapies. Coordinator: João Eurico da Fonseca. Funding Agency: Novartis. Amount: € 10 000,00. Total Amount: € 10 000,00.

2018/2022: Loss of follow up dos doentes sob biológicos. Coordinator: João Eurico da Fonseca. Funding Agency: Novartis. Reference: Loss Follow Up. Amount: € 6 650,00. Total Amount: € 6 650,00.

2019/2021: MILES STUDY – Mesotherapy in Lateral Epicondylitis, a prospective randomized controlled Study. Coordinator: João Eurico da Fonseca. Funding Agency: Fundação Grünenthal. Amount: € 10 000,00. Total Amount: € 10 000,00.

2018/2021: Long term effect of tofacitinib on bone: friend or foe? Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Amount: € 15 000,00. Total Amount: € 15 000,00.

2017/2027: PROTEA - Prognosis of temporal arteritis. Coordinator: João Eurico da Fonseca. Amount: Private Funding.

2017/2022: The effect of Tofacitinib on B cells in Rheumatoid Arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Amount: € 15 000,00. Total Amount: € 15 000,00.

2017/2022: B Cells in Juvenile Idiopathic Arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: B cell in AIJ. Amount: € 18 000,00. Total Amount: € 18 000,00.

2017/2021: Preclinical evaluation of celastrol for the treatment of RA: long-term efficacy and safety in the chronic DBA/1 mice model. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Amount: € 10 000,00. Total Amount: € 10 000,00.

2017/2020: Predictors of response to ultrasound-guided sacroiliac joint corticosteroid-injection in patients with active sacroiliitis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: US IN SACROILITIS. Amount: € 5 884,00. Total Amount: € 5 884,00.

2017/2020: Linking Biomechanics, Inflammation and Bone Formation in Psoriatic Arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: UCB Pharma. Reference: UCB ES. Amount: € 51 350,00. Total Amount: € 51 350,00.

2017/2020: Autoinflammatory Diseases: analysis based on The Rheumatic Diseases Portuguese Register. Coordinator: João Eurico da Fonseca. Funding Agency: Novartis. Reference: REUMA.PT. Amount: € 12 680,00. Amount: € 12 680,00.

2017/2020: Tapering Biologics in PSA. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: PSA. Amount: € 9 500,00. Total Amount: € 9 500,00.

2017/2020: Systemic Sclerosis Clinical Study. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: SSPECT. Amount: € 8 750,00. Total Amount: € 8 750,00.

2017/2020: The role of lncRNAs in Rheumatoid Arthritis-associated bone degradation. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: lncRNA. Amount: € 12 500,00. Total Amount: € 12 500,00.

2017/2020: Ensaio clínico de mesoterapia. Coordinator: João Eurico da Fonseca. Funding Agency: Bial. Reference: Mesoterapia. Amount: € 4 831,25. Total Amount: € 4 831,25.

2016/2022: The interplay of B and T follicular cell subset in early arthritis patients. Coordinator: João Eurico da Fonseca. Amount: Private Funding.

2016/2020: The role of certolizumab in non-infectious uveitis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Oftalmologia. Reference: Uveítes. Amount: € 5 000,00. Total Amount: € 5 000,00.

2016/2020: Blood biomarkers of synovial tissue phenotype as predictors of response to TNF inhibitors and tocilizumab in rheumatoid arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Amount: € 6 500,00. Total Amount: € 6 500,00.

2016/2020: Is ultrasound a good surrogate marker for remission in RA? (Association of ultrasound and histological synovitis in rheumatoid arthritis patients in clinical remission). Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: Ultrasound - SPR JPP. Amount: € 10 000,00. Total Amount: € 10 000,00.

2016/2019: Serum sphingolipids as candidate biomarkers in Rheumatoid Arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: SPHINGOLIPIDS IN RA. Amount: € 25 000,00. Total Amount: € 25 000,00.

2016/2019: Carbon monoxide guided shuttles (COGSs) to fight Rheumatoid Arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/1902/2014. Amount: € 22 000,00. Total Amount: € 199 966,00.

2015/2020: Synovial pathobiology and clinical differences in elderly and younger-onset of rheumatoid arthritis. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: BioTB. Amount: € 3 850,00. Total Amount: € 3 850,00.

2015/2019: Disease course and adult outcomes of childhood-onset rheumatic diseases. Coordinator: João Eurico da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: Bolsa de Inovação Diagnóstica. Amount: € 14 500,00. Total Amount: € 14 500,00.

2014/2019: IL-6 blockade in rheumatoid arthritis patients: impact on Tfh subsets and humoral responses. Coordinator: João Eurico da Fonseca. Funding Agency: Pfizer. Reference: BioTB. Amount: € 2 500,00. Total Amount: € 2 500,00.

2014/2019: Post-transcriptional regulation of response to Etanercept in patients with rheumatoid arthritis. Coordinator: Helena Canhão. Funding Agency: Pfizer. Reference: WI187429. Amount: € 40 000,00. Total Amount: € 40 000,00.

2013/2019: Inhibition of bone and cartilage degradation in rat induced arthritis treated with tofacitinib. Coordinator: João Eurico da Fonseca. Funding Agency: Pfizer. Reference: WI180320. Amount: € 60 000,00. Total Amount: € 60 000,00.

2012/2019: Golimumab as first line DMARD therapy in MTX naive psoritic arthritis - a 24 weeks eddicacy and safety study focussing on dactylitis and enthesitis. Coordinator: Elsa de Sousa. Funding Agency: Merck Sharp & Dohme. Reference: GO-DACT. Amount: € 36 087,50. Total Amount: € 36 087,50.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria do Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Polido-Pereira J*, Serra S*, Teixeira F*, Ponte C, Cerqueira M, Cruz M, Araújo F, Barros R, Costa T, Faria D, Lopes C, Madruga-Dias J, Oliveira M, Teixeira RL, Vilar A, Falcão S, Saraiva F, Figueiredo G *These authors contributed equally to this manuscript (2019). Portuguese recommendations for the use of ultrasound in rheumatology. **Acta Reumatológica Portuguesa** 44(1):7-28. (IF: 0.776, Citations: 0. Source: Web of Science).

Martins P, Marques D, Janeiro J, Romeu JC, Ponte C (2019). Tumoral calcinosis in a rheumatoid arthritis patient - a rare case report. **Acta Reumatológica Portuguesa** 44:158-160. (IF: 0.776, Citations: 0. Source: Web of Science).

Martins P, Teixeira V, Saraiva F, Ponte C (2019). The geyser sign: an unusual presentation of a rotator cuff tear. **Acta Reumatológica Portuguesa** 44(2)155-157. (IF: 0.776, Citations: 0. Source: Web of Science).

Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, Cassie R, Cid MC, Dasgupta B, Dejaco C, Hatemi G, Hollinger N, Mahr A, Mollan SP, Mukhtyar C, Ponte C, Salvarani C, Sivakumar R, Tian X, Tomasson G, Turesson C, Schmidt W, Villiger PM, Watts R, Young C, Luqmani RA (2019). 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. **Annals of the Rheumatic Diseases** 79(1)19-30. (IF: 14.299, Citations: 0. Source: Web of Science).

Gribbons KB, Ponte C, Carette S, Craven A, Cuthbertson D, Hoffman G, Khalidi N, Koenig CL, Langford C, Maksimowicz-McKinnon K, McAlear C, Monach P, Moreland L, Pagnoux C, Quinn K, Robson JC, Seo P, Sreih AG, Suppiah R, Warrington KJ, Ytterberg S, Luqmani RA, Watts RA, Merkel PA, Grayson PC (2019). Patterns of Arterial Disease in Takayasu's Arteritis and Giant Cell Arteritis. **Arthritis Care & Research (Hoboken)**. (IF: 4.53, Citations: 0. Source: Web of Science).

Monti S, Águeda AF, Luqmani RA, Buttgereit F, Cid M, Dejaco C, Mahr A, Ponte C, Salvarani C, Schmidt WA, Hellmich B (2019). Systematic literature review informing the 2018 update of the EULAR recommendation for the management of large vessel vasculitis: focus on giant cell arteritis. **RMD Open** 5(2): e001003. (IF: 3.47, Citations: 0. Source: Web of Science).

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Capela S. Caso clínico “Lesão desportiva osteocondral e osteoartrose inicial – o papel da condroproteção”, brochura Structomax, Pierre Fabre, 2019.

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Melo AT, Campanilho-Marques R. “O que precisa de saber sobre... Dermatomiosite (DM) e Polimiosite (PM)”. *Reuma Flyer - Sociedade Portuguesa de Reumatologia*, 2019.

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Invited Lectures and Seminars

Reis PC. Epigenética da Nefrite Lúpica: do laboratório à prática clínica. Sessão do Serviço de Genética do Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, January 18, 2019.

Macieira C. Consulta Dedicada ao Doente com Lúpus no CHULN/Hospital de Santa Maria. Fórum Art & Treat Lúpus da SPR 2019, Centro de Congressos de Aveiro, Aveiro, Portugal, February 8, 2019.

Reis PC. Prevenir a doença renal crónica no doente crítico. XXV Jornadas Anuais de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 14-15, 2019.

Oliveira Ramos F. Será possível prevenir as doenças reumáticas juvenis? XXV Jornadas Anuais de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 14-15, 2019.

Marques R. Pele - Espelho de Doença Sistémica - Doenças imunomediadas. 6ª Reunião Temática - Alergia de expressão cutânea, Lousã, Portugal, February 23, 2019.

Fonseca JE. Doenças Inflamatórias Articulares. 3ª Edição da Pós-Graduação em Medicina Laboratorial, Universidade Católica Portuguesa, Lisbon, Portugal, March 1, 2019.

Fonseca JE. Doenças Autoinflamatórias. 3ª Edição da Pós-Graduação em Medicina Laboratorial, Universidade Católica Portuguesa, Lisbon, Portugal, March 1, 2019.

Ponte C. Vasculitis - Clinical perspective. European Society of Cardiology Annual Congress 2019, Lisbon, Portugal, March 14, 2019

Romeu JC. Quando ocorre uma fractura durante o tratamento da osteoporose. Reunião - Breaking Barriers on osteoporosis fractures, Lisbon, Portugal, March 16, 2019.

Resende C. Pulmonary hypertension associated with connective tissue disease. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21-22, 2019.

Vieira-Sousa E, Antunes J. What are the benefits of a multidisciplinary approach to psoriasis/psoriatic arthritis patients? CrossTalk from a Rheumatology and Dermatology Perspective, Lisbon, Portugal, March 27, 2019.

Ponte C. Evidências do uso do USD na ACG. Workshop de USD para diagnóstico de arterite de células gigantes. Sociedade Brasileira de Reumatologia, São Paulo, Brazil, March 29, 2019.

Ponte C. Técnica de USD para avaliação de pacientes com suspeita de ACG - artérias temporais e axilares. Workshop de USD para diagnóstico de arterite de células gigantes. Sociedade Brasileira de Reumatologia, São Paulo, Brazil, March 29, 2019

Ponte C. Treinamento prático em indivíduos saudáveis. Workshop de USD para diagnóstico de arterite de células gigantes. Sociedade Brasileira de Reumatologia, São Paulo, Brazil, March 29, 2019

Ponte C. Treinamento prático em pacientes com ACG. Workshop de USD para diagnóstico de arterite de células gigantes. Sociedade Brasileira de Reumatologia, São Paulo, Brazil, March 29, 2019.

Santos MJ. Lúpus Eritematoso Sistémico – a perspetiva do reumatologista. Encontro Renal, Vilamoura, Portugal, March 30, 2019.

Machado RC, Melo R, Pinto V, Mano S, Teixeira F, Vaz-Pereira S, Leal I, Rosário M, Parreira S, Francisco AR, Ponte C, Pedro LM, Pinto L, Capela S, Macieira. Papel da colaboração multidisciplinar para um final feliz. Sessões do Centro Académico de Medicina de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, April 4, 2019.

Fonseca JE. Os novos medicamentos orais para a artrite reumatoide. XIX Jornadas da ANDAR, Lisbon, Portugal, April 6, 2019.

Fonseca JE. Biobancos nacionais: como, quando e onde? Congresso Português de Cardiologia 2019, Vilamoura, Portugal, April 28, 2019.

Fonseca JE. Inflamação, osso e progressão nas espondilartrites. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Eficácia e segurança do Sarilumab na artrite reumatoide. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Tofacitinib e as implicações sistémicas da inflamação. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Existe um perfil típico de um doente candidato a tocilizumab? XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Em que posição devo colocar o tocilizumab na terapêutica da artrite de células gigantes? XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Há doentes ser mais susceptíveis a infeções com o tocilizumab do que com TNFi? XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. O que caracteriza a síndrome de libertação de citocinas e quando devo preferir o tocilizumab a outras alternativas terapêuticas? XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Marques R. Miopatias inflamatórias: Estado da arte da valorização dos auto anticorpos e da terapêutica. Curso de Actualização em Reumatologia, XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Santos MJ. Pedidos de apoio para crianças com suspeita de doença reumática – como gerir e cuidados a ter. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Ponte C. Polymyalgia Rheumatic and Giant Cell Arteritis. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Saraiva F. Como a ecografia pode ajudar o clínico no diagnóstico e monitorização dos reumatismos inflamatórios. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Cordeiro I, Ferreira L. Doenças do Interstício Pulmonar no contexto das Doenças Reumáticas. Curso de Atualização em Reumatologia, XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Oliveira Ramos F. Transição dos cuidados pediátricos para os de adulto. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Dourado E. Queixas musculo-esqueléticas no Serviço de Urgência. II Curso Básico de Urgência, Centro de Formação do Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 15, 2019.

Oliveira Ramos F. Terapêutica das AIJ – Orientações gerais. Fórum de Reumatologia Pediátrica, Porto, Portugal, May 16, 2019.

Dourado E. Reumatologia Geriátrica. Curso Intensivo de Geriatria, Iniciativa Médica 3M's, Espinho, Aveiro, Portugal, May 30, 2019.

Marques R. Should we worry about anything else – also young people have multi-morbidities - Watch out for more. EULAR, Madrid, Spain, June 13, 2019.

Fonseca JE. Biosia sinovial-biomarcadores. XXXVI Congresso Brasileiro de Reumatologia, Fortaleza, Brasil, September 4-7, 2019.

Fonseca JE. Remission in chronic arthritis: lessons from early arthritis studies and animal models. XXXVI Congresso Brasileiro de Reumatologia, Fortaleza, Brasil, September 4-7, 2019.

Fonseca JE. Experiência do Reuma.pt. XXXVI Congresso Brasileiro de Reumatologia, Fortaleza, Brasil, September 4-7, 2019.

Fonseca JE. Remission and treat to target. Lançamento Olumiant, Lisbon, Portugal, September 14, 2019.

Fonseca JE. Exploring the patent expiry of biologics and entry of biosimilars. Inflammation value Masterclass, Lisbon, Portugal, September 19, 2019.

Ponte C. Diagnosis of Giant Cell Arteritis. 3rd EUVAS Vasculitis Course 2019, Cambridge, UK, September 23, 2019.

Romão VC. Treat to target in Rheumatology: psoriatic arthritis. Janssen First - III Curso de Formação para Internos, Porto, Portugal, September 28, 2019.

Dourado E. Queixas musculoesqueléticas no Serviço de Urgência. III Curso Básico de Urgência, Centro de Formação do Centro Hospitalar Lisboa Norte, Lisbon, Portugal, October 2, 2019.

Fonseca JE. New techniques for obtaining high quality synovial tissue: The biopsy in daily practice. 5th International Symposium on Intra-Articular Treatment (ISIAT), Lisbon, Portugal, October 3-5, 2019.

Reis PC. Exame Reumatológico. XXVI Jornadas de Pediatria de Leiria e Caldas da Rainha, Caldas da Rainha, Portugal, October 10, 2019.

Oliveira Ramos F. Como avaliar as alterações da massa óssea em idade pediátrica? Fórum de Doenças Imunomediadas, Porto, Portugal, October 18, 2019.

Saraiva F, Marques R. How can ultrasound help in the diagnosis of musculoskeletal complaints in the paediatric group? Paediatric Musculoskeletal Ultrasound Course, Antalya, Turkey, October 2019.

Ponte C. Vasculites primárias. Atualização no diagnóstico e tratamento. Congresso Português de Neurologia 2019, Coimbra, Portugal, November 14, 2019.

Reis PC. Clínica e Diagnóstico da Lesão Renal Aguda. 20º Congresso Nacional de Pediatria, Estoril, Portugal, November 14, 2019.

Reis PC. Vacinação e Imunossupressão. 20º Congresso Nacional de Pediatria, Estoril, Portugal, November 14, 2019.

Khmelinskii N. Terapêutica biológica - a experiência e a visão da Reumatologia. Reunião Multidisciplinar Reumatologia/Imuno-Alergologia/Pneumologia, Lisbon, Portugal, November 21, 2019.

Barreira SC, Cruz-Machado A, Fernandes AL, Genrinho I, Sequeira G, Monteiro P, Fonseca JE. Prescription Patterns and disease activity in Portuguese Women of Childbearing Age with Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and Juvenile Idiopathic Arthritis. IX Rheumatology in Practice, November 23, 2019.

Fonseca JE. Biosimilars: an introduction and Switching: outstanding questions. Biologics in Inflammation: the role of manufacturing and the biosimilars environment, Dublin, Ireland, November 24, 2019.

Barreira SC. Abordagem às doenças reumáticas. Workshop Practical Essentials da Associação de Estudantes da Faculdade de Medicina de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 28, 2019.

Barreira SC, Godinho I, Nogueira E, Macieira C, Ponte C. Caso clínico de vasculite ANCA. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Ponte C. Vasculites - Abordagem diagnóstica pelo Reumatologista. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Ponte C. Monitorização das Vasculites de pequenos Vasos. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Macieira C. Orientações para o diagnóstico/classificação e tratamento do doente com Lúpus Eritematoso Sistémico. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Cordeiro I. Casos clínicos – Esclerose Sistémica. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Romão VC. Artrite reumatoide e síndrome de Sjögren: Abordagem pelo Reumatologista. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Cordeiro I, Pereira M, Resende C. Systemic Sclerosis. Curso de Nefro-Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Saraiva F. Biópsia ecoguiada da sinovial – estado da arte. Colóquio ANDAR 2019, Lisbon, Portugal, November 29, 2019.

Romão VC. O que a biopsia sinovial já nos trouxe. Colóquio ANDAR 2019, Lisbon, Portugal, November 29, 2019.

Vieira-Sousa E. Biópsia sinovial e miniartroscopia – estado da arte. Biópsia Sinovial na Artrite Reumatoide: será agora que a promessa se concretiza? Colóquio ANDAR 2019, Lisbon, Portugal, November 29, 2019.

Reis PC. Renal Manifestations in Children with Juvenile Systemic Sclerosis. 12th Hamburg Symposium on Juvenile Systemic Sclerosis, Hamburgo, Germany, December 2, 2019.

Romeu JC. Tratamento da Osteoporos e tratamento dentário: Realidade e Controvérsia. XXVII Jornadas Internacionais de Reumatologia, Lisbon, Portugal, December 5-6, 2019.

Communications in International Conferences

Vieira-Sousa E, Eusébio M, Ribeiro P, Khmelinskii N, Cruz-Machado AR, Martins-Rocha T, Bernardes M, Santos-Faria D, Leite Silva J, Santos H, Miguel C, Carvalho PD, Costa T, Teixeira L, Meirinhos T, Nero P, Fonseca JE, Santos MJ. Gender differences in Psoriatic Arthritis Impact on tumor necrosis factor inhibitors persistence and response. 5^o Fórum Imunologia Janssen, Tróia, Portugal, April 6, 2019. (*Oral Presentation*).

Papo M, Sinico A, Teixeira V, Urban M, Mahrhold J, Cassone G, Schiavon F, Groh M, Marvisi C, Samson M, Barba T, Jayne D, Hellmich B, Salvarani C, Kahn J, Bonnotte B, Durel C, Cohen P, Puéchal X, Mouthon L, Guillevin L, Emmi G, Vaglio A, Terrier B, on behalf of the French Vasculitis Study Group and the EGPA European Collaborative Initiative. Prediction of Long-Term Evolutionary Profiles in Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss) Based on Baseline and Follow-Up Characteristics. 19th International Vasculitis and ANCA Workshop, Pennsylvania, USA, April 7-10, 2019. (*Poster Presentation*).

Papo M, Sinico A, Teixeira V, Urban M, Mahrhold J, Cassone G, Schiavon F, Groh M, Marvisi C, Samson M, Barba T, Jayne D, Hellmich B, Salvarani C, Kahn J, Bonnotte B, Durel C, Cohen P, Puéchal X, Mouthon L, Guillevin L, Emmi G, Vaglio A, Terrier B, on behalf of the French Vasculitis Study Group and the EGPA European Collaborative Initiative. Efficacy of Eosinophilic Granulomatosis with Polyangiitis Treatments According to the Type of Manifestations Based on Analysis of 636 Patients. 19th International Vasculitis and ANCA Workshop, Pennsylvania, USA, April 7-10, 2019. (*Poster Presentation*).

Ponte C*, Grayson P*, Suppiah R, Robson J, Gribbons KB, Craven A, Khalid S, Judge A, Hutchings A, Merkel PA, Watts RA, Luqmani RA (*these authors contributed equally to the work). Classification Criteria for Large-Vessel Vasculitis. 19th International Vasculitis and ANCA Workshop, Pennsylvania, USA, April 7-10, 2019. (*Oral Presentation*).

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Almeida S, Rodrigues AC, Farias F, Rios J, Reis PC, Oom P. When fever is not an infection. ESPID 2019, Ljubljana, Slovenia, May 6-11, 2019. (*Poster Presentation*).

Barreira SC*, Martins P*, Melo AT, Campanilho-Marques R, Fonseca JE, Oliveira-Ramos F. Transition in a Paediatric Rheumatology Unit – experience from a tertiary center. EULAR Annual Meeting 2019/PreS, Madrid, Spain, June 11-12, 2019. (*Poster Presentation*).

Papo M, Sinico A, Teixeira V, Urban M, Mahrhold J, Cassone G, Schiavon F, Groh M, Marvisi C, Samson M, Barba T, Jayne D, Hellmich B, Salvarani C, Kahn J, Bonnotte B, Durel C, Cohen P, Puéchal X, Mouthon L, Guillevin L, Emmi G, Vaglio A, Terrier B, on behalf of the French Vasculitis Study Group and the EGPA European Collaborative Initiative. Prediction of Long-Term Evolutionary Profiles in Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss) Based on Baseline and Follow-Up Characteristics. EULAR Annual Meeting 2019, Madrid, Spain, June 23-25, 2019. (*Poster Presentation*).

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Saraiva F. Princípios Físicos da ecografia. Funcionamento do Ecógrafo. Artefactos e limitações. 5º Curso Básico de Ecografia Musculoesquelética da ESPER, Lisbon, Portugal, March 2019. (*Oral Presentation*).

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Martins P, Barreira SC, Fonseca JE, Romeu JC. Features of patients with rheumatic diseases admitted in a rheumatic inpatient unit: 8 year experience. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Barreira SC, Martins P, Macieira C, Fonseca JE, Romeu JC. Rheumatology role in hospitalized patients' management in a tertiary hospital. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Cruz-Machado AR, Khmelinskii N, Paulo S, Resende C, Romeu JC. Systemic Inflammatory syndrome in a patient with systemic sclerosis - case report of underlying chronic Q fever. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Neto A, Martins P, Capela S, Araújo C., Centeno M, Costa M, Pinto L. Pregnancy outcomes in antiphospholipid syndrome: 8 year-experience from a multidisciplinary unit. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Barreira SC, Cruz-Machado AR, Centeno M, Araújo C, Costa M, Capela S, Pinto L. Anti-Ro/SSA and anti-La/SSB positive pregnant women - Experience from a tertiary centre. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Martins P, Barreira SC, Melo AR, Campanilho-Marques R, Reis PC, Fonseca JE, Ramos FO. Outcome of transition of care in young adults with juvenile onset chronic rheumatic diseases. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Martins P, Tenazinha C, Cordeiro I, Fonseca JE, Resende C. The value of tocilizumab in articular and cutaneous manifestations of Systemic Sclerosis: a case report. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Tenazinha C, Martins P, Barros R. Reactive Arthritis following treatment with Bacillus Calmette-Guèrin for bladder adenocarcinoma. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

António M. et al. Assessment of digits' circumference in the Portuguese population to calculate the Leeds Dactylitis Index. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Barreira SC, Cruz-Machado AR, Fonseca JE, Capela S. Effectiveness and safety of febuxostat: experience from a tertiary portuguese center. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Ávila-Ribeiro P, Fonseca JE, Vieira-Sousa E. Remission persistence in rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis under biologic treatment. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Oral Presentation)*.

Vieria-Sousa E, Eusébio M, Ávila-Ribeiro P, Khmelinskii N, Machado R, Rocha TM, Bernardes M, Santos-Faria D, Leite Silva J, Santos H, Miguel C, Carvalho P, Costa T, Teixeira L, Meirinhos T, Nero P, Fonseca JE, Santos MJ. Gender Differences in Psoriatic Arthritis – Impact on Tumor Necrosis Factor Inhibitors Persistence and Response. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Oral Presentation)*.

Vieira-Sousa E, Alves P, Rodrigues AM, Teixeira F, Tavares-Costa J, Bernardo A, Pimenta S, Pimentel-Santos FM, Gomes JL, Aguiar R, Videira T, Pinto P, Catita C, Santos H, Borges J, Sequeira G, Ribeiro C, Teixeira L, Ávila-Ribeiro P, Martins FM, Canhão H, Ribeiro RM, Fonseca JE. Go-Dact: A phase 3b Randomized Double-Blind Placebo-Controlled Proof-Of-Concept Trial, Of Golimumab Plus Methotrexate (MTX) Versus MTX Monotherapy, In Improving Dactylitis, In MTX-Naïve Psoriatic Arthritis Patients. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Amaral IA, Calado A, da Glória VA, Teixeira RL, Barreira S, Fonseca JE. Probing the expression of lncRNAs in monocytes and osteoclasts of rheumatoid arthritis patients. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Cruz-Machado AR, Miltenberger-Miltenyi G, Conceição VA, Calado A, Lopes I, Fuller M, Fonseca JE. Serum sphingolipids as candidate biomarkers in rheumatoid arthritis. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Cruz-Machado AR, Khmelinskii N. Arthritis mutilans as a radiographic feature of systemic sclerosis. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Cruz-Machado AE, Guerra M, Polido-Pereira J. Bicipitoradialis bursitis – a curious point of view. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Guerra M, Martins P, Cruz-Machado AR, Barreira S, Khmelinskii N, Vieira-Sousa E, Romeu JC. Natural evolution of untreated tuberculous arthritis of the ankle: the relevance of ultrasound guided biopsy for the diagnosis". XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019. *(Poster Presentation)*.

Tomé C, Barreira S, Martins P, Ramos FO, Valido A, Barros R, Polido-Pereira J, Graça L, Fonseca JE, Moura RA. Established rheumatoid arthritis patients have increased frequencies of follicular regulatory T cells in peripheral blood. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. *(Poster Presentation)*.

Miguel P, Farias F, Rios J, Campanilho-Marques R, Ramos FO, Reis PC. Caso clínico: doença mista do tecido conjuntivo e síndrome de ativação macrofágica. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Oral Presentation*).

Martins P, Barreira SC, Melo AT, Campanilho-Marques R, Fonseca JE, Ramos FO. Outcome of transition of care in young adults with juvenile onset chronic rheumatic diseases. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Oral Presentation*).

Viegas I, Rodrigues A, Campanilho-Marques, Ramos FO, Reis PC. Granulomatose eosinofílica com poliangeíte. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Viegas I, Rodrigues A, Campanilho-Marques, Ramos FO, Reis PC. Lúpus induzido pela lamotrigina. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Melo AT, Sousa S, Cordeiro A, Cordeiro I, Reis PC, Ramos FO, Fonseca JE, Campanilho-Marques R. Distinct clinical features between adult and juvenile dermatomyositis patients. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Oral Presentation*).

Miguel P, Mata M, Rebelo M, Sousa HS, Reis PC. Disfunção do Nódulo Sinusal em Adolescente com Lúpus Eritematoso Sistémico. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Viegas I, Rodrigues AB, Oliveira-Ramos F, Reis PC. Eosinophilic granulomatosis with polyangiitis – a clinical case. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Viegas I, Rodrigues AB, Oliveira-Ramos F, Reis PC. Lamotrigine-induced systemic lupus erythematosus. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Melo A, Dourado E, Campanilho-Marques R, Ramos FO, Reis PC. O papel dos anti-TNF no tratamento da calcinose em doentes com dermatomiosite juvenil – a propósito de dois casos clínicos. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Dinis JS, Valido A, Reis PC, Campanilho-Marques R, Ramos FO. Caso clínico - calcinose cutis como apresentação inicial de uma doença difusa do tecido conjuntivo. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Oral Presentation*).

Melo AT, Dourado E, Campanilho-Marques R, Reis PC, Ramos FO. O papel dos anti-TNF no tratamento da calcinose em doentes com dermatomiosite juvenil – a propósito de dois casos clínicos. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Dinis JS, Martis P, Valido A, Reis PC, Campanilho-Marques R, Ramos FO. Caso clínico – Utilização de Denosumab na Osteogenesis Imperfecta. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Melo AT, Sousa S, Cordeiro A, Cordeiro I, Reis PC, Ramos FO, Fonseca JE, Campanilho-Marques R. Distinct clinical features between adult and juvenile dermatomyositis patients. Fórum de Reumatologia, Porto, Portugal, May 2019. (*Poster Presentation*).

Pinto AS, Santos FC, Melo AT, Dourado E, Carneiro T, Campanilho-Marques R, Ferreira JF, Vaz CC. Impact of rheumatic diseases: an eight-item questionnaire. IX Rheumatology in Practice, Caldas da Rainha, Portugal, November 23, 2019. (*Oral Presentation*).

Barreira SC, Cruz-Machado A, Fernandes AL, Genrinho I, Sequeira G, Monteiro P, Fonseca JE. Prescription Patterns and disease activity in Portuguese Women of Childbearing Age with Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and Juvenile Idiopathic Arthritis. IX Rheumatology in Practice, Caldas da Rainha, Portugal, November 23, 2019. (*Oral Presentation*).

Saraiva F. Procedimentos ecoguiados. 3º Curso Intermédio de Ecografia Musculoesquelética da ESPER, Viana do Castelo, Portugal, November 2019. (*Oral Presentation*).

Melo AT, Dourado E, Campanilho-Marques R, Reis PC, Ramos FO. O papel dos anti-TNF no tratamento da calcinose em doentes com dermatomiosite juvenil – a propósito de dois casos clínicos. Jornadas Internacionais do IPR, Lisbon, Portugal, December 2019. (*Poster Presentation*).

Melo AT, Campanilho-Marques R. Um caso de policondrite. Jornadas Internacionais do IPR, Lisbon, Portugal, December 2019. (*Image Presentation*).

Dourado E, Melo AT, Vieira-Sousa E. Avaliação axial, de articulações periféricas, enteses e dactilite nas espondiloartrites (incluindo artrite psoriática). Curso de Metrologia nas Espondilartrites, Jornadas de Outono da Sociedade Portuguesa de Reumatologia 2019. (*Oral Presentation*).

Organization of Conferences

Cordeiro I. Organization and coordination as Adjunct Secretary-General of Sociedade Portuguesa de Reumatologia. Fórum Art&Treat: Lúpus, Aveiro, Portugal, February 7-9, 2019.

Fonseca JE. Presidente da sessão 2: 12 topics in Rheumatology, CEDOC, Lisbon, Portugal, March 1-2, 2019.

Ponte C. Jurada. Research Competition (Poster Sessions), 9th Annual International (bio)Medical Students Meeting (AIMS), Lisbon, Portugal, March 16, 2019.

Saraiva F. Organização e coordenação em nome da ESPER e tutor nas sessões práticas de “hands-on”. 5º Curso Básico de Ecografia Musculoesquelética da ESPER, Lisbon, Portugal, March 2019.

Fonseca JE. Presidente da sessão síndrome metabólica. Fórum Jansen, Tróia, Portugal, April 5-6, 2019.

Santos MJ. Member of the scientific committee of the XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Macieira C. Chair of the Poster Jury. Casos Clínicos, XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Cordeiro I. Organization and coordination as Adjunct Secretary General of Sociedade Portuguesa de Reumatologia. XXII Congresso Português de Reumatologia. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Organizador e Presidente do Curso de Atualização em Reumatologia. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Presidente da mesa redonda sobre Reumatologia Pediátrica. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Fonseca JE. Presidente da sessão SPR-Lilly sobre o uso do baricitinib. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Khmelinskii N. Júri de Posters. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Romão VC. Member of Júri de Poster de Trabalhos Originais. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Polido-Pereira J. Jury President. Uma Imagem, Um Diagnóstico. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Marques R. Organization and coordination as member of the EMERGE group from the Paediatric Rheumatology European Society. Young Investigator Meeting of the Paediatric Rheumatology European Society. Madrid, Spain, May 2019.

Marques R. Organization and coordination as responsible for the Education and Training pillar of the Juvenile Dermatomyositis Working Party from the Paediatric Rheumatology European Society. Juvenile Dermatomyositis Working Party Annual Meeting, Madrid, Spain, May 2019.

Fonseca JE. Presidente da sessão de abstracts Difficult to manage Sjogren's Syndrome and Myositis. European League Against Rheumatism Congress, Madrid, Spain, June 12-15, 2019.

Fonseca JE. Co-Organizador do segundo curso EULAR - Synovial biopsies, Madrid, Spain, September 12-13, 2019.

Fonseca JE. President. Inflammation Value Masterclass, Lisbon, Portugal, September 19, 2019.

Fonseca JE. Presidente da sessão. Evolving from clinical trials to daily practice, Together as 1, Lisbon, Portugal, September 27, 2019.

Cordeiro I. Organization and coordination as Adjunct Secretary General of Sociedade Portuguesa de Reumatologia. Jornadas de Outono da Sociedade de Portuguesa de Reumatologia, Luso, Portugal, October 11-12, 2019.

Capela SC. Moderadora de mesa. Os fármacos: Manusear antidepressivos, escolher o ideal; qual ajuda a dormir, qual ajuda mais a dor. Opióides. Canabinóides", II Curso de Dor, Sociedade Portuguesa de Reumatologia, Caldas da Rainha, Portugal, November 22, 2019.

Macieira C. Organization and Coordination on behalf of Rheumatology Department. Curso de Nefro Reumatologia Expressão Renal de Doenças Reumáticas Sistémica, Centro Hospital Lisboa Norte, Lisbon, Portugal, November 29, 2019.

Cordeiro I. Curso de Nefrologia e Reumatologia, on behalf of Consulta Multidisciplinar de Nefrologia e Reumatologia do CHULN, Lisbon, Portugal, November 29, 2019.

Khmelinskii N. Organization and presentation of “Indicadores de Monitorização do Lúpus Eritematoso Sistémico”. Curso de Nefro-Reumatologia – Expressão Renal de Doenças Reumáticas Sistémicas, Lisbon, Portugal, November 29, 2019.

Fonseca JE. Organizador e Presidente da sessão. Abertura do Colóquio ANDAR, Lisbon, Portugal, November 29, 2019.

Saraiva F. Saraiva F. Organização e coordenação em nome da ESPER e tutor nas sessões práticas de “hands-on”. 3º Curso Intermédio de Ecografia Musculoesquelética da ESPER, Viana do Castelo, Portugal, November 2019.

Polido-Pereira J. Table moderator - Pitzalis C. EULAR Synovitis Study Group, EULAR Course on Synovial Biopsy and future perspectives, Colóquio ANDAR 2019.

Internationalization

Marques R. Young Investigator Meeting of the Paediatric Rheumatology European Society. Organization and coordination as member of the EMERGE group from the Paediatric Rheumatology European Society, Madrid, Spain, May 2019.

Marques R. Jury of the abstracts from the Young Investigator Meeting of the Paediatric, Rheumatology European Society, Madrid, Spain, May 2019.

Santos MJ. Member of the EULAR task force “points to consider when analysing and reporting comparative effectiveness research with observational data in rheumatology”, EULAR Annual Congress of Rheumatology, Madrid, Spain, June 2019.

Reis PC. Júri da Agência Nacional de Investigação Francesa (Agence nationale de la recherche - ANR) 2019.

Fonseca JE. Abstract reviewer for the EULAR congress of Rheumatology and the ACR Annual Meeting 2019.

Prizes, Honors and Awards

Reis PC. Gut Permeability and Microbiome in Systemic Lupus Erythematosus. L’Oreal FCT UNESCO Women in Science Award, February 2019.

Dinis JS, Valido A, Reis PC, Campanilho-Marques R, Ramos FO. Award of best poster presentation. Caso Clínico: Calcinose Cutis Como Apresentação Inicial De Uma Doença Do Tecido Conjuntivo Em Idade Pediátrica. Fórum de Reumatologia Pediátrica, Porto, Portugal, April 2019.

Vieira-Sousa E, Alves P, Rodrigues AM, Teixeira F, Tavares-Costa J, Bernardo A, Pimenta S, Pimentel-Santos FM, Gomes JL, Aguiar R, Videira T, Pinto P, Catita C, Santos H, Borges J, Sequeira G, Ribeiro C, Teixeira L, Ávila-Ribeiro P, Martins FM, Canhão H, Ribeiro RM, Fonseca JE. Go-Dact: A phase 3b Randomized Double-Blind Placebo-Controlled Proof-Of-Concept Trial, Of Golimumab Plus Methotrexate (MTX) Versus MTX Monotherapy, In Improving Dactylitis, In MTX-Naïve Psoriatic Arthritis Patients”. Best poster. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019

Cruz-Machado AR, Khmelinskii N. Arthritis mutilans as a radiographic feature of systemic sclerosis. 1º prémio concurso melhor imagem. XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Romão VC. Desmistificando a Análise Estatística. XIII Seminário do Trabalho Final de Mestrado, Lisbon, Portugal, May 3, 2019.

Teixeira RL. Bolsa JAKIE Dr. Roberto Martins. The role of JAK-STAT signaling in early arthritis. Sociedade Portuguesa de Reumatologia e Pfizer Immunology, May 2019.

Machado R, Melo R, Pinto V, Manos, Teixeira F, Vaz-Pereira S, Leal I, Rosário M, Francisco A, Ponto C, Pedro L, Pinto L, Capela S, Macieira C. Prémio “ Best clinical report “Papel da colaboração multidisciplinar para um final feliz”. CAML Sessions, Centro Hospitalar Lisboa Norte, Lisbon Portugal, June 24, 2019.

Teixeira V, Andrade P, Narciso ML, Sousa E, Saraiva F, Fonseca JE. Prémio Dor da Fundação Grunenthal. Miles study- mesotherapy in lateral epicondylitis, a prospective randomized controlled study, Lisbon, Portugal, October 2019.

Marques R, Moura R, Rosser E, Callis J, Fonseca JE. EMERGE/EMEUNET Cooperation grant. B cells in Juvenile Idiopathic Arthritis: Effect of immunosuppressive treatment. EULAR and PRES, October 2019.

Martins P, Neto A, Capela S, Araújo C., Centeno M, Costa M, Pinto L. Pregnancy outcomes in antiphospholipid syndrome: 9 year-experience from a multidisciplinary unit. Received a bursary from Graham Hughes International Charity. ACR American Congress of Rheumatology, Atlanta, USA, November 2019.

Ávila-Ribeiro P, Fonseca JE, Vieira-Sousa E. Bolsa Educacional SPR Lilly Dr. João Figueirinhas 2019. Remission persistence in rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis under biologic treatment.

Viera-Sousa E, Eusébio M, Ávila-Ribeiro P, Khmelinskii N, Machado R, Rocha TM, Bernardes M, Santos-Faria D, Leite Silva J, Santos H, Miguel C, Carvalho P, Costa T, Teixeira L, Meirinhos T, Nero P, Fonseca JE, Santos MJ. Gender Differences in Psoriatic Arthritis – Impact on Tumor Necrosis Factor Inhibitors Persistence and Response. 1st prize - Real Word Evidence Award-Janssen Immunology 2019.

Machado RC, Melo R, Pinto V, Mano S, Teixeira F, Vaz-Pereira S, Leal I, Rosário M, Parreira S, Francisco AR, Ponte C, Pedro LM, Pinto L, Capela S, Macieira C. Papel da colaboração multidisciplinar para um final feliz”. Melhor apresentação de caso clínico. Centro Académico de Medicina de Lisboa, Lisbon, Portugal, 2019.

Cruz-Machado AR. EULAR scientific training bursary for young fellows. EULAR, 2019.

Advanced Teaching

Calado A. Respostas metabólicas à hiperglicemia e à hipoglicémia. Mestrado em Doenças Metabólicas e Comportamento Alimentar. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 2019.

Calado A. Metabolismo Glicídico. Mestrado em Doenças Metabólicas e Comportamento Alimentar. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 2019.

Capela SC. Palestra de Reumatologia no mestrado “Reabilitação em enfermagem”, Instituto Politécnico de Portalegre, Portalegre, Portugal, March 1, 2019.

Fonseca JE. Doenças Inflamatórias Articulares. 3ª Edição da Pós-Graduação em Medicina Laboratorial, Universidade Católica Portuguesa, Lisbon, Portugal, March, 2019.

Fonseca JE. Doenças Inflamatórias. 3ª Edição da Pós-Graduação em Medicina Laboratorial, Universidade Católica Portuguesa, Lisbon, Portugal, March, 2019.

Fonseca JE. Organização. Lisbon Precision medicine update – A Perceptorship on precision medicine, CAML, Lisbon, Portugal, April 29-30, 2019.

Fonseca JE. Medicina de precisão na era dos biológicos. Lisbon Precision medicine update – A Perceptorship on precision medicine, CAML, Lisbon, Portugal, April 29-30, 2019.

Fonseca JE. Pesquisa Clínica e Real World data”; Lisbon Precision medicine update – A Perceptorship on precision medicine, CAML, Lisbon, Portugal, April 29-30, 2019.

Fonseca JE. Organização e palestra. Investigação de translação. Programa de Formação em Investigação Clínica, Centro Hospital Lisboa Norte, Lisbon, Portugal, May 23, 2019.

Fonseca JE. Biobancos. Seminário SEAT&SEED, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, June 28, 2019.

Fonseca JE. Synovitis in RA and SpA: same or different? Rheuma Summerschool, Santiago de Compostela, Spain, July 4, 2019.

Fonseca JE. Atlas of Synovial Histopathology. 2nd EULAR Course - Synovial biopsies, Madrid, Spain, September 12-13, 2019.

Fonseca JE. Investigação científica e experimentação humana, realização de ensaios clínicos e relação com a indústria. 1º Curso de Ética/Deontologia e Comunicação Médica do CHBV, Aveiro, Portugal, September 19, 2019.

Marques R, Saraiva F. How Can Ultrasound Help in the Diagnosis of Musculoskeletal Complaints. Paediatric Musculoskeletal Ultrassound Course, Antalya, Turkey, October 2019.

Capela SC. Orientadora de tese de mestrado no âmbito de Patient reported Outcomes nas doenças reumáticas na gravidez, 2019.

Science and Society

Cordeiro I. Entrevista de divulgação sobre Lúpus Eritematoso Sistémico ao Canal Saúde +, em representação da Sociedade Portuguesa de Reumatologia, February 12, 2019.

Reis PC. Interview. Women in Science Award, February 27, 2019.

Reis PC. Interview. Women in Science Award, Público, February 27, 2019.

Reis PC. Interview. Women in Science Award, Diário de Notícias, February 27, 2019.

Reis PC. Interview. Women in Science Award, Jornal de Notícias, February 27, 2019.

Reis PC. Interview. Antena 1, February 27, 2019.

Reis PC. Participation. TV Show “Os Dias do Futuro”, about Systemic lupus erythematosus, Antena 1, March 9, 2019.

Reis PC. Interview. Visão magazine, March 11, 2019.

Barreira SC, Macieira C. Elaboração do Folheto “Contraceção e Doenças Reumáticas” para divulgação pela Sociedade Portuguesa de Reumatologia. Lançamento dos folhetos, XXI Congresso Português de Reumatologia, Vilamoura, Portugal, May 1-4, 2019.

Capela S. Entrevista de divulgação da Osteoartrose ao canal CMTV, na qualidade de coordenadora da consulta de Osteoartrose e Artrites Microcristalinas do Hospital de Santa Maria, CHULN, com posterior publicação nos jornais Coreio da Manhã e Sábado, July 1, 2019.

Reis PC. Interview. Notícias Magazine, October 26, 2019.

Fonseca JE. Interview. Arthritis Rheumatoid. TVI, November 2019.

Saraiva F. Entrevista de divulgação da ecografia musculoesquelética e das atividades da ESPER, Boletim Informativo SPR, nº 1, V série, 2019.

MSc Theses

Inês Filipa Pereira Abrunhosa Amaral, Analysis of lncRNAs expression in monocytes and osteoclasts of rheumatoid arthritis patients, Mestrado em Biomedicina Molecular, Departamento de Ciências Médicas, Universidade de Aveiro.

Ana Rita Sofio, The effect of exercise and tumor necrosis factor inhibitor on peripheral and axial inflammation in an animal model of spondyloarthritis, Mestrado em Ciências Biofarmacêuticas, Faculdade de Farmácia da Universidade de Lisboa.

PhD Theses

Diana Carmona- Fernandes, Coupling of atherosclerosis progression and bone disturbances in inflammatory rheumatic diseases, Doutoramento em Ciências Biomédicas (Ciências Biopatológicas), Faculdade de Medicina da Universidade de Lisboa. Supervisors: João Eurico Fonseca and Helena Canhão.

Elsa Sousa, New perspectives on tumor necrosis factor inhibition for the treatment of psoriatic arthritis, Doutoramento em Medicina, Faculdade de Medicina da Universidade de Lisboa. Supervisors: João Eurico Fonseca and Helena Canhão.

João F. Lacerda Lab

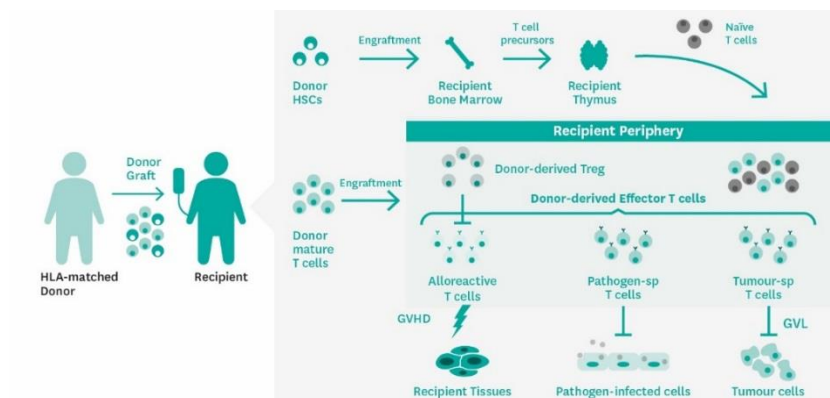
Major Interests/Objectives

We study immunity after Hematopoietic Stem Cell Transplantation (HSCT), aiming to identify immunological risk factors for complications occurring post-HSCT, such as Graft-versus-Host Disease (GVHD), viral and fungal infections, as well as the mechanisms by which these complications emerge. Our lab is currently investigating the clinical benefits of donor-derived regulatory T cell (Treg) infusion in patients with steroid-resistant GVHD, while simultaneously monitoring tissue regeneration markers and immunological parameters. We are also interested in further improving the field of cellular therapies using Treg by developing new therapies with 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.

Head of Laboratory

João Mascarenhas Forjaz de Lacerda, MD/PhD, Professor of Medicine of the Universidade de Lisboa and Senior Hematologist at Hospital Santa Maria.

Graphical Abstract



Team

Ana Cláudia Batista Jordão Ribeiro	Master Degree	Lab Technician (Left December)
Ana Cristina Frazão Lopes Alho	MD	PhD Student
Carolina Paulino Pacini	Master Degree	PhD Student (Started October)
Eduardo Lima da Silva Espada	MD/Master Degree	PhD Student
Joana Bianchi Marques Bettencourt Gesta	PhD	Postdoctoral Researcher
Joana Brioso Infante	MD/Master Degree	PhD Student (Started September)
Maria Godinho Alves Vieira Duarte Soares	PhD	Senior Postdoctoral Researcher
Mariana Torres Goulart Peixoto Maurício	BSc - Bachelor Degree	MD Student (Started October)
Paulo Nelson Gomes Pereira	PhD	Lab Technician
Rita Isabel Silva de Azevedo	PhD	Senior Postdoctoral Researcher

Laboratory Keywords / Research Areas

Immune Reconstitution After Hematopoietic Stem Cell Transplantation (HSCT), Graft versus Host Disease (GvHD), Regulatory T Cell Homeostasis in HSCT Recipients, Adoptive Immunotherapy after HSCT, Pathogen-specific Immunity after HSCT, Genetic Susceptibility for Fungal and Viral Infections.

Major Scientific Achievements

In 2019, we published the manuscript *“Naive and Stem Cell Memory T Cell Subset Recovery Reveals Opposing Reconstitution Patterns in CD4 and CD8 T Cells in Chronic GVHD”* in the journal *Frontiers in Immunology*, and the manuscript entitled *“In vitro recruitment of human regulatory T cells (Treg) in mesenchymal stem cell (MSC) co-cultures”* is currently under review. These studies have contributed to the characterization of T cell subpopulations involved in cGVHD, immune tolerance and T cell reconstitution post-transplant, as well as the mechanisms of MSC-mediated regulatory T cell recruitment. We are currently finalizing a third manuscript on the generation and expansion of antigen-specific Treg, which may disclose novel and more specific regulatory T cell populations for clinical usage.

Our team has continued to coordinate the TREGeneration consortium, a multinational project encompassing parallel clinical trials using purified donor Tregs for the treatment of steroid-refractory cGVHD. This project involves meticulous prospective immune monitoring and T cell tracking of the infused donor regulatory T cells by Next Generation Sequencing.

In the Portuguese trial, we concluded the Phase I trial and continue to actively recruit patients for the Phase II trial.

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: 540. (IF: 4.716, Citations: 0. Source: Web of Science).

Stappers MHT, Clark AE, Amanianda V, Bidula S, Reid DM, Asamaphan P, Hardison SE, Dambuza IM, Valsecchi I, Kerschler B, Plato A, Wallace CA, Yuecel R, Hebecker B, da Glória Teixeira Sousa M, Cunha C, Liu Y, Feizi T, Brakhage AA, Kwon-Chung KJ, Gow NAR, 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(7696):382-386. (IF: 43.07, Citations: 41. Source: Web of Science).

Gresnigt MS, Cunha C, Jaeger M, Gonçalves SM, Malireddi RK, Ammerdorffer A, Lubbers R, Oosting M, Rasid O, Jouvion G, Fitting C, Jong DJ, Lacerda JF, Campos A Jr, Melchers WJG, Lagrou K, Maertens J, Kanneganti TD, Carvalho A, Ibrahim-Granet O, van de Veerdonk FL (2018). Genetic deficiency of NOD2 confers resistance to invasive aspergillosis. **Nature Communications** 9:2636. (IF: 11.878, Citations: 9. Source: Web of Science).

Hirakawa M, Matos T, Liu H, Koreth J, Kim HT, Paul NE, Murase K, Whangbo J, Alho AC, Nikiforow S, Cutler C, Ho VT, Armand P, Alyea EP, Antin JH, Blazar BR, Lacerda JF, Soiffer RJ, Ritz J (2016). Low-dose IL-2 selectively activates subsets of CD4+ Tregs and NK cells. **JCI Insight** 1(18):e89278. (IF: 6.014, Citations: 43. Source: Web of Science).

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. (IF: 16.601, Citations: 63. Source: Web of Science)

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 deficiency of PTX3 and invasive aspergillosis in stem cell transplantation. **The New England Journal of Medicine** 370(5): 421-432. (IF: 70.67, Citations: 152. Source: Web of Science).

Azevedo RI, Soares MV, Albuquerque AS, Tendeiro R, Soares RS, Martins M, Ligeiro D, Victorino RM, Lacerda JF, Sousa AE (2013). Long-Term Immune Reconstitution of Naive and Memory T Cell Pools after Haploidentical Hematopoietic Stem Cell Transplantation. **Biology of Blood and Marrow Transplantation** 19:703. (IF: 4.48, Citations: 13. Source: Web of Science).

Ongoing Research Projects

2019/2020: Apoio Educacional. Coordinator: João Lacerda. Funding Agency: Janssen. Reference: Apoio Educacional. Amount: € 19 800,00. Total Amount: € 19 800,00.

2019/2020: Apoio Doutoral Inphinit Incoming. Coordinator: Carolina Pacini. Funding Agency: “la Caixa” Foundation. Reference: "la Caixa" Foundation Doctoral Fellowships INPHINIT em Centros de Investigação de Excelência de Espanha e Portugal. Amount: € 115 092,00. Total Amount: € 115 092,00.

2015/2019: 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: € 1 792 894,46. Total Amount: € 5 899 250,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Review Journals

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. (IF: 4.716, Citations: 1. Source: Web of Science)

Campos CF, Leite L, Pereira P, Vaz CP; Branca R, Campilho F, Freitas F, Ligeiro D, Marques A, Torrado E, Silvestre R, Lacerda JF, Campos A, Cunha C, Carvalho A (2019). PTX3 Polymorphisms Influence Cytomegalovirus Reactivation After Stem-Cell Transplantation. **Frontiers in Immunology** 31(10):88. (IF: 4.716, Citations: 1. Source: Web of Science).

Other Publications International

Bianchi J, Azevedo RI, Vieira AIS, Ligeiro D, da Silva CL and Lacerda JF (2019). Phenotypic and functional characterization of expanded antigen-specific regulatory T cells (Ag-sp Treg), towards clinical translation. **Journal of Immunology** 202(1):57.2. (IF: 4.718, Citations:--. Source: Web of Science).

Invited Lectures and Seminars

Lacerda JF. Utilização terapêutica de células. Comemorações dos 195 anos da Sociedade das Ciências Médicas de Lisboa - As fronteiras das Ciências Médicas - Faculdade de Ciências Médicas NOVA Medical School, Lisboa, Lisbon, Portugal, January 24, 2019.

Lacerda JF. Chair of Plenary Session: Hematopoietic Stem Cell Transplantation. 33rd European Immunogenetics and Histocompatibility Conference, Lisbon, Portugal, May 8-11, 2019.

Soares M. Immunological Conditioning in GVHD. Hematopoietic Stem Cell Graft Function and Immune Reconstitution Session, 33rd European Immunogenetics and Histocompatibility Conference, Lisbon, Portugal, May 8-11, 2019.

Azevedo R. Terapia Celular Papel dos linfócitos T reguladores (Treg) na imunidade celular após transplante alogénico. XI Congresso da APIH Albufeira, Albufeira, Portugal, October 11-12, 2019.

Communications in International Conferences

Espada E, Ligeiro D, Trindade H, Lacerda JF. Update on the HLA frequency distribution of Portuguese Bone Marrow Donor Registry. 45th Annual Meeting of the European Society for Blood and Marrow Transplantation, Frankfurt, Germany, March 26, 2019. (*Poster Presentation*).

Bianchi J, Azevedo RI, Vieira AIS, Ligeiro D, da Silva CL, Lacerda JF. Phenotypic and functional characterization of expanded antigen-specific regulatory T cells (Ag-sp Treg), towards clinical translation. 103rd Annual Meeting of the American association of Immunologists San Diego 9-13, San Diego, USA, May 2019. (*Oral Presentation*).

Organization of Conferences

JLacerda Lab Organized the TREGeneration General Assembly on the 14th and 15th of February 2019, Seville, Spain.

Internationalization

Our Unit actively collaborated in 2019 with the following international investigators under the TREGeneration Consortium of the Horizon 2020 Program:

Jerome Ritz and John Koreth, 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 Arpinati, Department of Hematology “Seragnoli”, University Hospital S. Orsola-Malpighi, Bologna.

Marie-Laure Yaspo and Hans-Jörg Warnatz, 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 at the University of Seville, Spain.

Prizes, Honors and Awards

National Prize for Hematology 2019 (Prémio Nacional de Hematologia) from the Portuguese Society for Hematology attributed to the publication: 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*, Mar 6;10:334.

Science and Society

João Lacerda participated in the program 90 Segundos de Ciência, December 9, 2019, Antena 1. <https://www.rtp.pt/play/p2936/e442819/90-segundos-ciencia>

PhD Theses

Joana Bianchi, 01/07/2019, Expansion and in-depth characterization of antigen-specific regulatory T cells in vitro for subsequent clinical translation, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: João Mascarenhas Forjaz de Lacerda. Co-Supervisors: Rita Isabel Silva de Azevedo and Cláudia Alexandra Martins Lobato da Silva.

Joaquim Ferreira Lab

Major Interests/Objectives

The main mission of the Joaquim Ferreira Lab is to contribute to the development of effective and safe therapeutic interventions through the establishment of optimized methodologies for the design, conduction, analysis and report of clinical trials. The main clinical pharmacology domains of interest are clinical trials methodology, outcomes, systematic reviews, safety, pharmaco MRI and drug utilization. The emphasis is mainly on novel, early phase proof-of-principle clinical studies and new methodological and trial designs but the scope extends throughout the clinical development spectrum. We also envision collaborations with the pharmaceutical industry, facilitating the conduction of clinical trials to a shared role in the early stages of drug and planning of clinical development.

Head of Laboratory

Joaquim José Coutinho Ferreira, MD/PhD; Associate Professor of Neurology and Clinical Pharmacology (FMUL); Head of Laboratory of Clinical Pharmacology and Therapeutics (FMUL); Group Leader Clinical Pharmacology Unit - JFerreira Lab (iMM), Medical Director at Campus Neurológico Sénior (CNS), Torres Vedras; President of the Pedagogic Council, Faculty of Medicine, University of Lisbon; Past-chair, European Section at International Parkinson and Movement Disorder Society (MDS); Chair, Movement Disorders Scientific Panel, European Academy of Neurology.

Team

Ana Cristina Brito Almeida Sampaio Cruz	MD/PhD	Clinical Staff Scientist
Ana Marta Teixeira Anes	MD/Master Degree	Clinical Researcher (Left April)
Ana Patrícia Silva Pita Lobo	MD/Master Degree	Clinical Researcher
Ana Raquel Duque Gonçalves Fernandes	MD/Master Degree	Clinical Researcher
Ana Rita Simões Cardoso	MD/Master Degree	Clinical Researcher (Left October)
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 (Started February)
Catarina Afonso Godinho	MD/PhD	Clinical Researcher (Left May)
Catarina Filipa Severiano e Sousa	Master Degree	PhD Student (Left January)
Cláudio Virgílio Antunes David	MD/Master Degree	Clinical Researcher
Daisy Andreina Vieira de Abreu	MD/PhD	Clinical Researcher
Daniel Gomes Caldeira	MD/PhD	Clinical Researcher

Daniela Marina Dias Guerreiro	University Degree	Trainee
Ema Dulce Henriques Roque	University Degree	Senior Technician (Left May)
Helena Isabel Vicente dos Santos	Master Degree	Clinical Researcher (Left May)
Isabel Cristina Ramos Peixoto Guimarães	MD/PhD	Clinical Researcher
Joana Margarida do Nascimento Fagundes Carvalho	MD/University Degree	Clinical Researcher
Joana Micaelo Grilo	MD/Master Degree	Clinical Researcher
João José Simões Santos	MD/Master Degree	PhD Student
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Clinical Researcher
Kelli Destri	Master Degree	Lab Technician (Left May)
Luís António Garcez Duarte da Costa Ferreira	MD/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 Atougua	MD/University Degree	Clinical Researcher
Maria João Bettencourt Pereira Forjaz	MD/PhD	Clinical Researcher
Maria Leonor Brito de Arriaga Correia Guedes Möller Miranda	MD/PhD	Clinical Researcher
Mariana da Cruz Alves	Master Degree	PhD Student
Mário Miguel Coelho da Silva Rosa	MD/PhD	Clinical Researcher
Miguel Vilhena Soares Coelho	MD/PhD	Clinical Researcher
Nilza Karina Cabral Gonçalves	MD/Master Degree	Clinical Researcher (Left December)
Olga Sofia de Oliveira Caetano	University Degree	Administrative Technician (Left May)
Rafaela Alexandra Policarpo da Rosa	Master Degree	Language Area Coordinator (Left December)
Raquel de Queirós Bouça Ribeirinho Machado	Master Degree	PhD Student
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
Solange Carolino Alves de Gouveia Carvalho	Master Degree	Trainee
Tânia Sofia Santos Silva	Master Degree	Lab Technician
Tiago Alexandre Mestre	MD/Master Degree	Clinical Researcher
Tiago Heleno Mendes	MD/Master Degree	Clinical Researcher
Tiago Rodrigues Teodoro	MD/Master Degree	Clinical Researcher
Vanda Viseu Filipa Cândido de Freitas	MD/Master Degree	Clinical Researcher
Verónica Candeias Caniça	University Degree	Clinical Researcher

Laboratory Keywords / Research Areas

Keywords:

Methodology, Clinical Trials, Parkinson, Huntington, Outcomes.

Research Areas:

Movement Disorders, Neuropharmacology, Systematic Reviews.

Major Scientific Achievements

The main achievement of our group this year was the generation of a set of data generating a construct for additional functional outcomes in Parkinson's disease. In line with this objective was the definition of the concept of functional mobility applied to Parkinson's disease. Also in line with this objective was the publication of the first studies evaluating the ability to swim as a functional outcome in Parkinson's disease.

Selected Publications

Faustino PR, Duarte GS, Chendo I, Castro Caldas A, Reimão S, Fernandes RM, Vale J, Tinazzi M, Bhatia K, Ferreira JJ (2019). Risk of Developing Parkinson Disease in Bipolar Disorder: A Systematic Review and Meta-analysis. **JAMA Neurology** 77(2):192-198. (IF: 12.321, Citations 0. Source: Web of Science).

Fabrizi M, Coelho M, Abreu D, Guedes LC, Rosa MM, Godinho C, Cardoso R, Guimarães I, Antonini A, Zibetti M, Lopiano L, Ferreira, JJ (2019). Dysphagia predicts poor outcome in late-stage Parkinson's disease. **Parkinsonism & Related Disorders** 64:73-81. (IF: 4.360, Citations: 0. Source: Web of Science).

Ferreira JJ, Mestre TA, Lyons K, Benito-Leon J, Tan EK, Abbruzzese G, Hallett M, Haubenberger D, Elble R, Deuschl G, Autor(es) grupo: MDS Task Force Tremor; MDS Evidence Based Med Comm. (2019). MDS evidence-based review of treatments for essential tremor. **Movement Disorders** 34(7):950-958. (IF: 8.222, Citations: 2. Source: Web of Science).

Neves MA, Bouça-Machado R, Guerreiro D, Caniça V, Pona-Ferreira F, Ferreira JJ (2019). Swimming Is Compromised in Parkinson's Disease Patients. **Movement Disorders** 35(2):365-369. (IF: 8.222, Citations: 1. Source: Web of Science).

Caldeira D, Marques A, Almeida J, Rodrigues T, Alves M, David C, Pinto FJ (2019). Recommendations and levels of evidence in the guidelines of the European Society of Cardiology: current scenario and time trends. **European Heart Journal-Cardiovascular Pharmacotherapy** 6(2):122-124. (IF: 6.723, Citations: 0. Source: Web of Science).

Ongoing Research Projects

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: € 289 500,00. Total Amount: € 20 997 522,50.

2015/2020: 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.

Publications in Peer Reviewed Journals

Pollock M, Fernandes RM, Pieper D, Tricco AC, Gates M, Gates A, Hartling L (2019). Preferred Reporting Items for Overviews of Reviews (PRIOR): a protocol for development of a reporting guideline for overviews of reviews of healthcare interventions. **Systematic Reviews** 8(1):335. (IF:--, Citations: 0. Source: Web of Science).

Bouça-Machado R, Duarte GS, Patriarca M, Castro Caldas A, Alarcão J, Fernandes RM, Mestre TA, Matias R, Ferreira JJ (2019). Measurement Instruments to Assess Functional Mobility in Parkinson's Disease: A Systematic Review. **Movement Disorders Clinical Practice** 7(2):129-139. (IF:--, Citations: 0. Source: Web of Science).

Cláudia MS, Travessa A, Bouça-Machado R, Caldeira D, Ferreira JJ (2019). Reporting and methodological quality of clinical trials on exercise therapy for Parkinson's disease, **Parkinsonism & Related Disorders** 69:150-156. (IF: 4.360, Citations: 0. Source: Web of Science).

Jácome C, Pereira AM, Almeida R, Ferreira-Magalhaes M, Couto M, Araujo L, Pereira M, Correia MA, Loureiro CC, Catarata MJ, Maia Santos L, Pereira J, Ramos B, Lopes C, Mendes A, Cidrais Rodrigues JC, Oliveira G, Aguiar AP, Afonso I, Carvalho J, Arrobas, A, Coutinho Costa J, Dias J, Todo Bom A, Azevedo J, Ribeiro C, Alves M, Leiria Pinto P, Neuparth N, Palhinha A, Gaspar Marques J, Pinto N, Martins P, Todo Bom F, Alvarenga Santos M, Gomes Costa A, Silva Neto A, Santalha M, Lozoya C, Santos N, Silva D, Vasconcelos MJ, Taborda-Barata L, Carvalhal C, Teixeira MF, Alves RR, Moreira AS, Sofia Pinto C, Morais Silva P, Alves C, Câmara R, Coelho D, Bordalo D, Fernandes RM, Ferreira, R., Menezes F, Gomes R, Calix MJ, Marques A, Cardoso J, Emiliano M, Gerardo R, Nunes C, Ferreira JA, Carvalho A, Freitas P, Correia R, Fonseca JA, group I. (2019). Patient-physician discordance in assessment of adherence to inhaled controller medication: a cross-sectional analysis of two cohorts. **BMJ Open** 9(11):e031732. (IF: 2.376, Citations: 0. Source: *Web of Science*).

Faustino PR, Duarte GS, Chendo I, Castro Caldas A, Reimão S, Fernandes RM, Vale J, Tinazzi M, Bhatia K, Ferreira JJ (2019). Risk of Developing Parkinson Disease in Bipolar Disorder: A Systematic Review and Meta-analysis. **JAMA Neurology** 77(2):192-198. (IF: 12.321, Citations 0. Source: *Web of Science*).

Jácome C, Almeida R, Pereira AM, Araújo L, Correia M, Pereira M, Couto M, Lopes C, Chaves Loureiro C, Catarata MJ, Santos LM, Ramos B, Mendes A, Pedro E, Cidrais Rodrigues JC, Oliveira G, Aguiar AP, Arrobas AM, Costa J, Dias J, Todo Bom A, Azevedo J, Ribeiro C, Alves M, Leiria Pinto P, Neuparth N, Palhinha A, Gaspar Marques J, Martins P, Trincão D, Neves A, Todo Bom F, Alvarenga Santos M, Branco J, Lozoya C, Costa A, Silva Neto A, Silva D, Vasconcelos MJ, Teixeira MF, Ferreira-Magalhães M, Taborda Barata L, Carvalhal C, Santos N, Pinto CS, Rodrigues Alves R, Moreira AS, Morais Silva P, Fernandes R, Ferreira R, Alves C, Câmara R, Ferraz de Oliveira J, Bordalo D, Calix MJ, Marques A, Nunes C, Menezes F, Gomes R, Almeida Fonseca J, group, I. (2019). Asthma apps use and interest among patients with asthma: a multicentre study. **Journal of Investigational Allergology and Clinical Immunology**. (IF 3.802, Citations 0. Source: *Web of Science*).

Horton MC, Nopoulos P, Nance M, Landwehrmyer GB, Barker RA, Squitieri F, Burgunder JM, Quarrell O, Bachoud-Levi AC, Bentivoglio AR, REGISTRY Investigators European. (2019). Assessment of the Performance of a Modified Motor Scale as Applied to Juvenile Onset Huntington's Disease, **Journal of Huntingtons Disease** 8(2):181-193. (IF:--, Citations: 0. Source: *Web of Science*).

Boaventura I, Costa J, Fernandes RM, Ferreira JJ (2019). Perception and attitudes about rational prescription during medical training: results of focus groups including medical students and residents. **Acta Médica Portuguesa** 32(9):593-599. (IF: 0.581, Citations: 0. Source: Web of Science).

Alves M, Caldeira D, Ferro JM, Ferreira JJ (2019). Does Parkinson's disease increase the risk of cardiovascular events? A systematic review and meta-analysis. **European Journal of Neurology** 27(2):288-296. Review. (IF: 4.387. Citations, 1. Source: Google Scholar).

Miranda D, Breda J, Cardoso R, Gonçalves N, Caldas AC, Ferreira JJ (2019). Should the energy contribution of commercial thickeners be considered in the nutrition plan of patients with dysphagia? **Nutrition in Clinical Practice**. (IF: 2.587, Citations: 0. Source: Web of Science).

Gorayeb RP, Forjaz MJ, Ferreira AG, Duarte GNS, Machado T, Ferreira JJ (2019). Electronic search strategies fail to identify randomized controlled trials (RCTs) in neurosurgery. **Clinical Neurology and Neurosurgery** 184:105446. (IF: 1.672, Citations: 0. Source: Web of Science).

Caldeira D, Nunes-Ferreira A, Rodrigues R, Vicente E, Pinto FJ, Ferreira JJ (2019). Non-vitamin K antagonist oral anticoagulants in elderly patients with atrial fibrillation: A systematic review with meta-analysis and trial sequential analysis. **Archives of Gerontology and Geriatrics** 83:338-338. (IF: 2.611, Citations: 0. Source: Web of Science).

Mestre TA, Eberly S, Tanner C, Grimes D, Lang AE, Oakes D, Marras C (2019). Reply to "Studying reproducibility of data-driven Parkinson's disease subtypes, **Parkinsonism & Related Disorders** 66:245-246. (IF: 4.360, Citations: 0. Source: Web of Science).

Constant C, Cosme J, Fernandes RM, Fonte P, Fonseca JA, Alves C, Bandeira T (2019). Practice of spirometry among physicians caring for children with asthma in Portugal - The EspiroPed survey. **Pulmonology** 26(1):54-56. (IF:--, Citations 0. Source: Web of Science).

Jamal A, Finkelstein Y, Kuppermann N, Freedman SB, Florin TA, Babl FE, Dalziel SR, Zemek R, Plint AC, Steele DW, Schnadower D, Johnson DW, Stephens D, Kharbanda A, Roland D, Lyttle MD, Macias CG, Fernandes RM, Benito J, Schuh S, Autor(es) grupo: Pediat Emergency Res Networks. (2019). Pharmacotherapy in bronchiolitis at discharge from emergency departments within the Pediatric, emergency Research Networks: a retrospective analysis. **Lancet Child & Adolescent Health** 3(8):539-547. (IF:--, Citations: 1, Source: Web of Science).

Rato ML, Duarte GS, Ferreira AN, Alves M, Mainoli B, Teodoro T, Mestre TA, Costa J, Ferreira JJ (2019). Nocebo response in Parkinson's disease: A systematic review and meta-analysis. **Parkinsonism & Related Disorders** 65:13-19. (IF: 4.360, Citations: 0. Source: Web of Science).

Fernandes RM, Wingert A, Vandermeer B, Featherstone R, Ali S, Plint AC, Stang AS, Rowe BH, Johnson DW, Allain D, Klassen TP, Hartling L (2019). Safety of corticosteroids in young children with acute respiratory conditions: a systematic review and meta-analysis. **BMJ Open** 9(8):e028511. (IF 2.376, Citations: 0. Source: Web of Science).

Gates A, Caldwell P, Curtis S, Dans L, Fernandes RM, Hartling L, Kelly LE, Vandermeer B, Williams K, Woolfall K, Dyson MP (2019). Reporting of data monitoring committees and adverse events in paediatric trials: a descriptive analysis. **BMJ Paediatrics Open** 3(1):e000426. (IF:--, Citations: 0. Source: Web of Science).

Kirolos A, Manti S, Blacow R, Tse G, Wilson T, Lister M, Cunningham S, Campbell A, Nair H, Reeves RM, Fernandes RM, Campbell H, RESCEU Investigators (2019). A Systematic Review of Clinical Practice Guidelines for the Diagnosis and Management of Bronchiolitis. **Journal of Infectious Diseases** jiz240. (IF: 5.045, Citations: 0. Source: Web of Science).

Bachoud-Levi AC, Ferreira JJ, Massart R, Youssouf K, Rosser A, Busse M, Craufurd D, Reilmann R, De Michele G, Rae D, Squitieri F, Seppi K, Perrine C, Scherer-Gagou C, Audrey O, Verny C, Burgunder JM (2019). International Guidelines for the Treatment of Huntington's Disease, **Frontiers in Neurology** 10:710. (IF: 2.635, Citations: 0. Source: Web of Science).

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Other International Publications

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Caldeira D, Pereira H (2019). Adjuvant antithrombotic therapy in ST-elevation myocardial infarction: A narrative review. **Revista portuguesa de Cardiologia**, 38(4):289-297. (IF: 0.785, Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Fernandes R. Introdução à Investigação Clínica. Acolhimento a Médicos Internos, Centro de Formação, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, January 3, 2019.

Fernandes R. Os diferentes fenótipos da criança asmática e as respetivas implicações clínicas. XV Jornadas de Alergologia de Lisboa, Lisbon, Portugal, January 25, 2019.

Guimarães I. The speech sounds and its disorders. Seminar at ISPA (Instituto Superior de Psicologia Aplicada), Lisbon, Portugal, February 11 2019.

Fernandes R. Terapêutica biológica na asma. XXI Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 12-13, 2019.

Ferreira JJ. Como envolver as associações de doente, Consentimento informado, Informar e Ficar informado, Infarmed, Lisbon, Portugal, February 26, 2019.

Ferreira JJ. Como simplificar o consentimento informado, Consentimento informado, Informar e Ficar informado, Infarmed, Lisbon, Portugal, February 26, 2019.

Fernandes R. Dos fenotipos aos endótipos: implicações clínicas na asma grave da criança e adolescente. Reunião Anual da ASIA, Associação de Serviços e Unidades de Imunoalergologia, Setúbal, Portugal, March 2, 2019.

Ferreira JJ. Simpósio Bial, Opicapona: o novo inibidor da COMT no tratamento da Doença de Parkinson, Congresso SPDMov 2019, Curia, Portugal, March 15-16, 2019.

Ferreira JJ. O sono e o envelhecimento saudável. Programa da Reunião da Comissão de trabalho de Patologia respiratória, Curia, Portugal, March 30, 2019.

Ferreira JJ. Moderador: International DBS Masters Roundtable, Boston Scientific, Lisbon, Portugal, April 2, 2019.

Ferreira JJ. Tremor e doença de Parkinson: dicas práticas na avaliação e tratamento. VIII Curso de Atualização em geriatria e gerontologia, Hotel Real Palácio, Lisbon, Portugal, April 5-6, 2019.

Rosa MM. O que é não fazer mal? Tomada de Decisão em Bio(ética) Clínica. Discussão de casos em Doenças Neurodegenerativas, 2º Congresso CNS, Torres-Vedras, Portugal, April 13, 2019.

Ferreira JJ. Complementaridade entre o setor público, privado e social como fator de proximidade e satisfação das pessoas, Torres-Vedras, Portugal, May 18, 2019.

Ferreira JJ. Membro do painel: Ensaio clínicos: questões éticas e jurídicas, Ensaio clínicos – Por uma Melhor Participação do Cidadão, Infarmed, Lisbon, Portugal, May 24, 2019.

Ferreira JJ. O Café pode prevenir ou tratar a Doença de Parkinson? IV Conferência Infecção e Doenças Infeciosas, Centro de Ciência do Café, Campo Maior, Portugal, May 25, 2019.

Fernandes R. Deficit de Vitamina D. Mito ou Realidade: Relações e Implicações com a Doença Alérgica. 8º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica, Braga, Portugal, May 25, 2019.

Ferreira JJ. CCG3 Training & Mentoring, icare-PD inaugural meeting & Technology-enabled Care Workshop 2019, Hospital Universitario HM Puerta del Sur, Madrid, Spain, May 27, 2019.

Ferreira JJ. Wearable sensors, icare-PD inaugural meeting & Technology-enabled Care Workshop 2019, Hospital Universitario HM Puerta del Sur, Madrid, Spain, May 27, 2019.

Ferreira JJ. Porque é que o cérebro deixa de comunicar com o corpo? Conversa sobre Parkinson. Horizontes IMM: Uma pergunta a três, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 19, 2019.

Ferreira JJ. Bottlenecks in therapeutics development in Parkinson Disease. XIV annual CICS-UBI Symposium, Covilhã, Portugal, July 4-5, 2019.

Ferreira JJ, Poewe W: a life and a “Movement disorders” mentor. Symposium 24 Jahre Neurologie Innsbruck, Prof. Dr. Werner Poewe, Innsbruck, Austria, September 13, 2019.

Ferreira JJ. Parkinson’s Disease Management, Hot topic – Parkinson Disease and Epilepsy, 11º Fórum Bial de Neurologia, Fundação Champalimaud, Lisbon, Portugal, October 19, 2019.

Ferreira JJ. Soulful Neurology. 6th Beyond MEd, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 23, 2019.

Ferreira JJ. A dimensão social, económica e clínica das Doenças Neurodegenerativas, simpósio Científico – Doenças Degenerativas, O que nos traz o futuro? Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, October 26, 2019.

David C. UNiworkshop. Diagnóstico integrado, Lisbon, Portugal, November 23, 2019.

Communications in International Conferences

Ferreira N, Rigueira J, Aguiar-Ricardo I, Agostinho J, Santos-Goncalves I, Santos R, Plácido R, David C, Pinto F, Almeida A. Bicuspid aortic valve: which valvular lesions and how to predict the need for surgery? *European Heart Journal Cardiovascular Imaging* 20 (Suppl 1), i451, January 2019. *(Poster Presentation)*.

Rigueira J, Nunes-Ferreira A, Aguiar-Ricardo I, Santos-Goncalves I, Agostinho J, Santos R, Plácido R, David C, Pinto F, Almeida A. Bicuspid aortic valve disease-is there any association with neoplasia? *European Heart Journal Cardiovascular Imaging* 20 (Suppl 1), i1102, January 2019. *(Poster Presentation)*.

Rigueira J, Nunes-Ferreira A, Aguiar-Ricardo I, Agostinho J, Santos-Goncalves I, Santos R, Rodrigues T, Cunha N, Plácido R, David C, Pinto F, Almeida A. Bicuspid aortic valve: insights into natural history of the disease according to phenotype. *European Heart Journal Cardiovascular Imaging* 20 (Suppl 1), i1295, January 2019. *(Poster Presentation)*.

Almeida A, Menezes M, Lima-Silva G, Guimarães T, Francisco A, Plácido R, David C, Pinto F. Myocardial strain changes as assessed by feature tracking CMR in patients with acute myocarditis and preserved ejection fraction. Impact on prognosis. *European Heart Journal Cardiovascular Imaging* (Suppl 1), 1198, January 2019. *(Poster Presentation)*.

Jácome C, Almeida R, Pereira AM, Chaves Loureiro C, Lopes C, Mendes A, Cidrais Rodrigues JC, Carvalho J, Arrobas AM, Todo Bom A, Azevedo J, Ribeiro C, Leiria Pinto P, Neuparth N, Todo Bom F, Costa A, Lozoya C, Santos N, Silva D, Taborda-Barata L, Teixeira F, Rodrigues Alves R, Moreira AS, Pinto CS, Morais Silva P, Alves C, Câmara R, Bordalo D, Fernandes R, Ferreira R, Ferraz De Oliveira J, Menezes F, Gomes R, Cálix MJ, Cardoso J, Nunes C, Câmara R, Ferreira JA, Carvalho A, Ferreira-Magalhães M, Almeida Fonseca J. Clusters of asthma control: Data from the Portuguese inspirers studies. Clusters of asthma control: Data from the Portuguese inspirers studies. EAACI Congress 2019, European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June 1-5, 2019. PD0539. *Allergy*, 2019; 74(S106):294. *(Poster Presentation)*.

Jácome C, Almeida R, Pereira AM, Chaves Loureiro C, Lopes C, Mendes A, Cidrais Rodrigues JC, Carvalho J, Arrobas AM, Todo Bom A, Azevedo J, Ribeiro C, Leiria Pinto P, Neuparth N, Todo Bom F, Costa A, Lozoya C, Santos N, Silva D, Taborda-Barata L, Teixeira F, Rodrigues Alves R, Moreira AS, Pinto CS, Morais Silva P, Alves C, Câmara R, Bordalo D, Fernandes R, Ferreira R, Ferraz De Oliveira J, Menezes F, Gomes R, Calix MJ, Cardoso J, Nunes C, Câmara R, Ferreira JA, Carvalho A, Ferreira-Magalhães M, Almeida Fonseca J. Patient-physician discordance in the assessment of adherence to inhaled medication. EAACI Congress 2019, European Academy of Allergy and Clinical Immunology, Lisbon, Portugal, June 1-5, 2019. TP0809. *Allergy*, 2019; 74(S106):458. (*Poster Presentation*).

Almeida AMG, Rigueira J, Plácido R, Rosário LB, Aguiar Ricardo I, Campos P, David C, Pinto FJ. Myocardial fibrosis is a predictor of atrial fibrillation in dilated cardiomyopathy-role of cardiovascular magnetic resonance. *European Heart Journal-Cardiovascular Imaging* 20 (Suppl 2), 115, June, 2019. (*Meeting Abstract*).

Rigueira J, Plácido R, David C, Rosário Lb, Aguiar-Ricardo I, Campos P, Francisco ARG, Pinto FJ, Almeida AG. Left ventricular systolic dysfunction in Marfan syndrome is related to aortic distensibility *European Heart Journal-Cardiovascular Imaging* 20 (Suppl 2), 116, June, 2019. (*Meeting Abstract*).

Plácido R, Rigueira J, Rosário LB, Carrilho-Ferreira P, David C, Pinto FJ, Almeida AMG. Aortic distensibility as assessed by CMR is independently associated with left ventricle function in patients with aortic valve regurgitation. *European Heart Journal-Cardiovascular Imaging* 20 (Suppl 2), 118, June, 2019. (*Meeting Abstract*).

Guimarães I. Speech sounds data for typically developing European Portuguese children 6-9 years old. 19th International Congress of Phonetic Sciences, Melbourne, Australia, August 5-9, 2019. (*Oral Presentation*).

Nitchingham D, Hawcutt D, Fernandes R, Kapitein B, Andrew L, Grice J, Cibinda H, O'Connor M, Sinha I. Dexamethasone or prednisolone for acute asthma exacerbations in children: a meta-analysis. International Congress Madrid 2019, European Respiratory Society, Madrid, September 28-October 2, 2019. *European Respiratory Journal* 2019 54(63):PA952. (*Poster Presentation*).

Murphy J, King C, Kapitein B, Fernandes R, Lilley A, Messahel S, Hawcutt DB, Sinha I. Oral steroids for preschool children with acute wheeze: a systematic review and meta-analysis. International Congress Madrid 2019, European Respiratory Society, Madrid, September 28-October 2, 2019. *European Respiratory Journal* 2019 54(63): OA4941. *(Poster Presentation)*.

Lewis L, Fernandes R, Kapitein B, Davies J, Holden J, Messahel S, Sinha I. Predicting failure of high flow nasal cannula in bronchiolitis: a systematic review. International Congress Madrid 2019, European Respiratory Society, Madrid, September 28-October 2, 2019. *European Respiratory Journal* 2019 54(63): PA1005. *(Poster Presentation)*.

Pollock M, Fernandes RM, Pieper D, Tricco AC, Gates M, Gates A, Hartling L. Coming soon - reporting guideline for overviews of reviews of healthcare interventions! Preferred Reporting Items for Overviews of Reviews (PRIOR). 26th Cochrane Colloquium, Cochrane, Santiago, Chile, October 22-23, 2019. *(Poster Presentation)*.

Gates M, Gates A, Duarte G, Cary M, Becker M, Prediger B, Vandermeer B, Fernandes RM, Pieper D, Hartling L. The reliability, usability, and applicability of tools to appraise quality and risk of bias in systematic reviews: a prospective evaluation of AMSTAR, AMSTAR 2 and ROBIS. 26th Cochrane Colloquium, Cochrane, Santiago, Chile, October 22-23, 2019. *(Poster Presentation)*.

Cardoso M, Sousa R, Lourenço F, Silva Miguel L, Costa J, Borges M. Estimation of the number of patients with cutaneous squamous cell carcinoma in Portugal. ISPOR Europe 2019, Copenhagen, Denmark, November 2-6, 2019. *(Poster Presentation)*.

Guerreiro R, Alarcão J, Pinheiro B, Borges M, Silva Miguel L, Inês M, Costa J. Ceftazidime-avibactam for the treatment of infections due to aerobic gram-negative organisms in patients with limited treatment options- a systematic review and meta-analysis. ISPOR Europe 2019, Copenhagen, Denmark, November 2-6, 2019. *(Poster Presentation)*.

Alarcão J, Ascensão R, Gouveia M, Costa J, Araújo F, Mello e Silva A, Borges M. Atherosclerosis-burden of disease in Portugal. ISPOR Europe 2019, Copenhagen, Denmark, November 2-6, 2019. *(Poster Presentation)*.

Alarcao J, Ascensão R, Lourenço F, Fiorentino F, Borges M, Costa J, Araújo F, Mello e Silva A, Gouveia M. Atherosclerosis- the cost of illness in Portugal. ISPOR Europe 2019, Copenhagen, Denmark, November 2-6, 2019. *(Poster Presentation)*.

Atherosclerosis- real-world insights from a Portuguese primary care database. Ascensão R, Alarcão J, Fiorentino F, Gouveia M, Costa J, Araújo F, Mello e Silva A, Borges M. ISPOR Europe 2019, Copenhagen, Denmark, November 2-6, 2019. *(Poster Presentation)*.

Guimarães I. Speech Disorders in Parkinson's disease. Third Allied Health Rehabilitation Course for Parkinson's Disease. International Parkinson and Movement Disorders Society Asian & Oceanian Section, Dubai, December 13, 2019. *(Poster Presentation)*.

Guimarães I. Speech & Swallowing assessment in Parkinson's disease Third Allied Health Rehabilitation Course for Parkinson's Disease. International Parkinson and Movement Disorders Society Asian & Oceanian Section. Dubai, December 13, 2019. *(Poster Presentation)*.

Guimarães I. Assessment strategies. Third Allied Health Rehabilitation Course for Parkinson's Disease. International Parkinson and Movement Disorders Society Asian & Oceanian Section. Dubai, December 13, 2019. *(Poster Presentation)*.

Communications in National Conferences

Santos M, Mourão M, Curado AD, Sousa R, Bandeira T, Rosa M, Ferreira J, Fernandes R POPPI STUDY: OFF-LABEL PRESCRIPTION – ARE PORTUGUESE PARENTS AWARE? XXV Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 14-15, 2019. *(Oral Presentation)*.

Oliveira SR, Dionísio PA, Correia Guedes L, Gonçalves N, Coelho M, Rosa MM, Amaral JD, Ferreira JJ, Rodrigues CMP. Identification of deregulated miRNAs in the serum of Parkinson's disease patients. Livro de Resumos: o exame Clínico nas Doenças do Movimento, Curia, Portugal, March 16, 2019. *(Oral Presentation)*.

Silva DP, Coelho M, Soares T, Vale T, Correia Guedes L, Maciel R, Antunes AP, Camargos S, Valadas A, Godinho C, Maia D, Lobo PP, Maia R, Teodoro T, Rieder C, Velon A, Rosas MJ, Calado A, Caniça V, Cardoso F, Ferreira JJ, no âmbito do Grupo de estudo da Validação Portuguesa da MDS-UPDRS. Livro de Resumos: o exame Clínico nas Doenças do Movimento, Curia, Portugal, March 16, 2019. *(Oral Presentation)*.

Kaupilla LA, Silva DP, Castro-Caldas A, Coelho M, Ferreira JJ, Correia Guedes L. Doença de Parkinson GBA-LRRk2: caso clínico. Livro de Resumos: o exame Clínico na nas Doenças do Movimento, Curia, Portugal, March 16, 2019. *(Poster Presentation)*.

Carvalho V, Correia Guedes L. Tremor e Parkinsonismo em doentes com cromossomopatias – uma revisão sistemática da literatura. Livro de Resumos: o exame Clínico na nas Doenças do Movimento, Curia, Portugal, March 16, 2019. (*Poster Presentation*).

Grilo J, Nunes R, Simões R, Correia Guedes L, Castro Caldas A, Ferreira JJ, Reimão S. Pharmac MRI Movement Disorders Database. Livro de Resumos: o exame Clínico na nas Doenças do Movimento, Curia, Portugal, March 16, 2019. (*Poster Presentation*).

Martins R, Ferreira S, Fermeiro J, Fernandes R, Neves AM. Toxidermia: que mecanismo? 8º Congresso da Sociedade Portuguesa de Alergologia Pediátrica, Braga, Portugal, May 24-25, 2019. (*Oral Presentation*).

Organization of Conferences

Ferreira JJ. Diretor do *Curso de Boas práticas clínicas*, Programa de Formação em investigação, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 8, 2019.

Ferreira JJ. Diretor do *Curso de Introdução à Investigação Clínica*, Campus Neurológico Sénior, Torres Vedras, Portugal, October 12-13, 2019.

Internationalization

Guimarães I. [2020-2019] Cross-validation of outcome measures to be applied at the Camp Dream for children who stutter (Portugal, 2010). Partners: ECSF (European Consortium of Speech Fluency) and University of Texas at Austin, USA; and ESSA, Portugal.

Guimarães I. [2020-2016] *BioVisualSpeech* - An interactive platform for Speech Therapy with visual bio-feedback. Sponsored by FCT - CMUP-ERI/TIC/0033/2014. Partners: USA (Language Technologies Institute – Carnegie Mellon University) and Portugal (Faculdade de Ciências e Tecnologia-Universidade Nova de Lisboa, Instituto de Engenharia de Sistemas e Computadores – Investigação e Desenvolvimento (INESC-ID); Voice Interaction and Escola Superior de Saúde do Alcoitão).

Guimarães I. [2019-2016] Establishment of an Interdisciplinary Clinical Master Program in Rehabilitation at JUST (*JUST-CR*) sponsored by ERASMUS+ Programme, Project number: 573758-EPP-1-2016-1-JO-EPPKA2-CBHE-JP. Partners: Jordan (University of Jordan), Turkey (Hacettepe University), United Kingdom (Brookes University) and Portugal (Escola Superior de Saúde do Alcoitão).

Guimarães I. Member of the panel - 'Examining the Relationship between Motor Learning, Cognition, Sleep Quality and Related Biomarkers in Individuals with Parkinson's Disease (PD)', Student: Ismail Alhaj, Interdisciplinary Clinical Master Program in Rehabilitation at JUST, Jordan, May 2019.

Guimarães I. Member of the panel - 'Occupational performance and satisfaction in daily life activities as perceived by individuals with vestibular disorders'; Student: Safaa Kamal Nazzal Interdisciplinary Clinical Master Program in Rehabilitation at JUST, Jordan, July 2019.

Prizes, Honors and Awards

Award from the Portuguese Journal for Speech Therapy (Revista Portuguesa de Terapia da Fala, RPTF). Best article: Monteiro J, Trigo C & Guimarães I. The Preterm Oral Feeding Readiness Assessment Scale: Contribute to its validation, RPTF Casa das histórias, Cascais, Portugal, November 8-10, 2019.

Industry Contract Research

Infarmed, Unidade de Farmacovigilância de Lisboa e Vale do Tejo.

Fundação Merck, Sharp & Dohme, Base Editorial do Cochrane Movement Disorders Group.

Government/Organization Contract Research

CHDI Foundation, Research Design and Data Analysis in Support of Clinical Trial Design and Clinical Research Projects. 2017-2020.

Advanced Teaching

Ferreira, JJ. Beside examination: - Clinician's perspective on Movement Disorders. Neuro Update Chennai 2019, Movement Disorders and Neuro Ophthalmology, Chennai, India, January 4-6, 2019.

Ferreira, JJ. Gait abnormalities in Movement Disorders. Neuro Update Chennai 2019, Movement Disorders and Neuro Ophthalmology, Chennai, India, January 4-6, 2019.

Ferreira, JJ. Critical appraisal of clinical trials in Movement Disorders. Neuro Update Chennai 2019, Movement Disorders and Neuro Ophthalmology, Chennai, India, January 4-6, 2019.

Ferreira, JJ. Practical approach to Parkinsonisms. Neuro Update Chennai 2019, Movement Disorders and Neuro Ophthalmology, Chennai, India, January 4-6, 2019.

Ferreira, JJ. Tardive syndromes – Recognition & Management. Neuro Update Chennai 2019, Movement Disorders and Neuro Ophthalmology, Chennai, India, January 4-6, 2019.

Ferreira JJ. Design of clinical trials and protocol development. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 11, 2019.

Rosa MM, Clinical development. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 11, 2019.

Fernandes R. Assessment tools and outcomes. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 11, 2019.

Caldeira D. Critical appraisal of clinical trials. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 11, 2019.

Guimarães I. Workshop 1 - Communication and Voice Education and Practice - ToT (Training of Tutors) of the Interdisciplinary Clinical Master Program in Rehabilitation. JUST (JUST-CR), Escola Superior de Saúde do Alcoitão, Portugal, January 18, 2019.

Ferreira JJ. Chorea: updates. 1st MDS African School for Young Neurologists: Fundamentals of Movement Disorders, Cairo, Egypt, January 17-19, 2019.

Ferreira, JJ. Management of early Parkinson disease: state of art. 1st MDS African Scholl for Young Neurologists: Fundamentals of Movement Disorders, Cairo, Egypt, January 17-19, 2019.

Ferreira, JJ. Introduction to Movement Disorders. 1st MDS African Scholl for Young Neurologists: Fundamentals of Movement Disorders, Cairo, Egypt, January 17-19, 2019.

Ferreira, JJ. How to examine a patient with MD faculty assignments: Introduction, personal history, compliant. 1st MDS African Scholl for Young Neurologists: Fundamentals of Movement Disorders, Cairo, Egypt, January 17-19, 2019.

Ferreira JJ. Ataxias. 1st MDS African Scholl for Young Neurologists: Fundamentals of Movement Disorders, Cairo, Egypt, January 17-19, 2019.

Ferreira JJ. Chorea and Related Disorders. MDS-ES 98th Winter School for Young Neurologists, London, UK, February 7-9, 2019.

Guimarães I. Member of the panel – "Fado and its voices: Contribution to the prevention of occupational voice disorders". Candidate: Pedro Pestana PhD Programme at Universidade Fernando Pessoa, Porto, Portugal, March 1, 2019.

Costa J. Teacher at the European Academy of Neurology Guideline production group meeting. GRADE Overview, Vienna, Austria, March 2, 2019.

Ferreira JJ. Síndromes parkinsónicas. Curso Pré-Congresso: O exame clínico nas Doenças do Movimento, Congresso SPDMov 2019, Curia, Portugal, March 15-16, 2019.

Ferreira JJ. Tremor e doença de Parkinson: dicas práticas na avaliação e tratamento. VIII Curso de Atualização em Geriatria e Gerontologia, Hotel Real Palácio, Lisbon, Portugal, April 5, 2019.

Ferreira JJ. Componente de um protocolo: da pergunta às conclusões, Workshop: Revisões Sistemáticas e meta-análises. IV Conferência Internacional de Investigação em Saúde, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 10, 2019.

Ferreira JJ. Análise crítica de estudos e resultados. Workshop: Revisões Sistemáticas e meta-análises, IV Conferência Internacional de Investigação em Saúde, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 10, 2019.

Rosa MM. Safety and medicinal products and medical devices. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 23, 2019.

Caldeira D. Systematic reviews, meta-analysis and critical appraisal of data. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 23, 2019.

Ferreira JJ. How to design a clinical trial, Therapeutic in Neurosciences. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 23, 2019.

Fernandes R. Clinical outcomes and biomarkers. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 24, 2019.

Costa J. Introduction to pharmacoeconomics, Therapeutic in Neurosciences. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 24, 2019.

Ferreira JJ. Drug discovery, preclinical and clinical development. Therapeutic in Neurosciences. Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 24, 2019.

Costa J. Teacher at the Assessing Therapeutic Effectiveness in Drug Life Cycle Research. Advanced Training Course for Updating Skills, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 2-3, 2019.

Ferreira JJ. Ensaios clínicos. Programa de Formação em Investigação, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 7, 2019.

Ferreira JJ. Boas práticas clínicas. Programa de Formação em Investigação, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 8, 2019.

Costa, J. Training GRADE methodology. Evidence Based Medicine in Movement Disorders. Meeting of the International Parkinson and Movement Disorders Society, Lisbon, Portugal, May 10-11, 2019.

Costa J. Curso de atualização em Diagnóstico e Terapêutica de Doenças Neurológica. Fórum de Neurologia 2019, Universidade de Trás-os-Montes e Alto Douro, Portugal, May 17-18, 2019.

Costa J. Revisões Sistemáticas da Literatura. Curso Prático de Introdução à Investigação Clínica do Centro Académico Médico de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Libson, Portugal, May 24-25, 2019.

Costa J. Módulo de “Econometria aplicada à avaliação económica em saúde”. Curso de Avaliação Económica das Tecnologias e Intervenções em Saúde, ISEG, Lisbon, Portugal, May 2019.

Ferreira JJ. State of the art of wearable devices in Parkinson’s Disease. 5th World Parkinson’s Congress, Kyoto, Japan, June 5, 2019.

Ferreira JJ. Genetic and acquired chorea. MDS-ES 12th Summer School for Young Neurologists, Padua, Italy, July 19-21, 2019.

Ferreira JJ. Physical Rehabilitation in PD. MDS-ES 12th Summer School for Young Neurologists, Padua, Italy, July 19-21, 2019.

Ferreira JJ. An approach to patients with Movement Disorders. Physiotherapy Summer School, Beelitz-Heilstatten, Germany, September 6-8, 2019.

Ferreira JJ. Long-term complications and their management in Parkinson’s Disease. Physiotherapy Summer School, Beelitz-Heilstatten, Germany, September 6-8, 2019.

Ferreira JJ. Spasticity management, Adult neurological disorders- the unknown driver. Lisbon foot & ankle, Clinical Biomechanics Corse 2019, Lisbon, Portugal, September 28, 2019.

Ferreira JJ. Ten years challenge: advances in diagnosis and treatment in MD. X^o Corso di Aggiornamento Non Solo Parkinson, Dip. Ingegneria – Università degli Studi di Ferrera, Ferrara, Italy, October 4, 2019.

Science and Society

Ferreira JJ. Doentes de Parkinson reclamam menos tempo de espera em consultas de acompanhamento. RTP Notícias, April 9, 2019.

Ferreira JJ. Doentes de Parkinson chegam a esperar um ano por consulta de acompanhamento. April 11, 2019.

Ferreira JJ. Doença de Parkinson. Edição da Manhã, SIC Notícias, April 11, 2019.

Ferreira JJ. Horizontes iMM: Uma pergunta a três, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 19, 2019.

Guimarães I. Closing ceremony of the Interdisciplinary Clinical Master Program in Rehabilitation, JUST (JUST-CR), Aman, Jordan, September 2-7, 2019.

Ferreira JJ. The time course of motor complications in Parkinson's, MDS 2019. Filmed at the International Congress of Parkinson's Disease and Movement Disorders (MDS), Nice, France, September 2019.

Ferreira JJ. A Nossa Tarde, October 25, 2019.

Ferreira JJ. Pode uma palmadinha nas costas tratar doenças? FMUL Talks, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 20, 2019.

MSc Theses

Maria Ana Dias Rato Neves, 08/01/2019, Avaliação da perda da capacidade para nadar na Doença de Parkinson, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

Ana Filipa Lopes Rosário, 15/01/2019, Ensaios clínicos para a avaliação do exercício clínico como intervenção terapêutica na Doença de Parkinson, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

Diana Filipa Santos Miranda, 11/02/2019, Frailty and nutritional status in patients with neurodegenerative disorders, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

Beatriz Machado Serra, 18/12/2019, Quality and reporting of clinical practice guidelines on the management of Parkinson's Disease", Faculdade de Farmácia da Universidade de Lisboa. Supervisor: Joaquim Ferreira.

PhD Theses

Margherita Fabbri, 30/05/2019, Multimodal response to levodopa treatment in advanced and late Parkinson's Disease, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Joaquim Ferreira. Co-Supervisor: Angelo Antonini.

José Ferro Lab

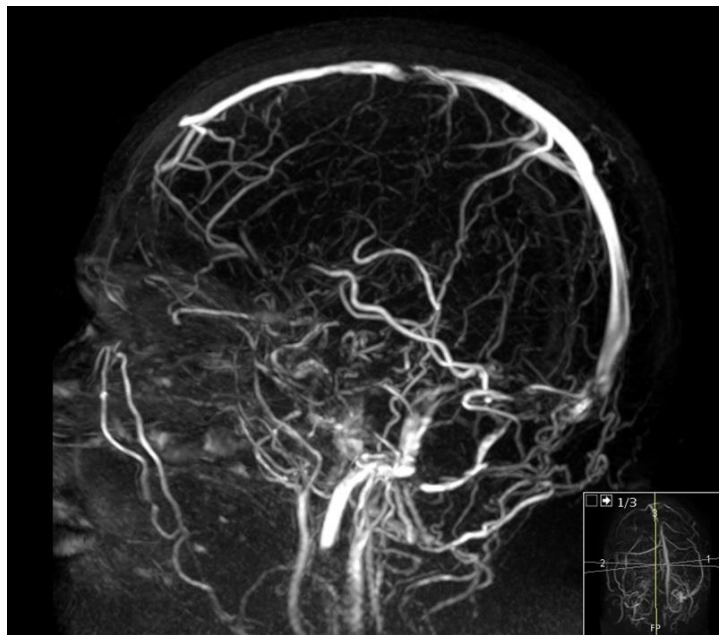
Major Interests/Objectives

We study the prevention and treatment of the cerebrovascular diseases using clinical investigation methodologies, clinical genetics, advanced statistical methods, neuropsychology, artificial intelligence, and neuroimaging. The researchers of the Unit conduct observational and experimental studies to clinical impact of different interventions in multinational efforts to get new targeted and personalized treatments for these widespread and disabling brain disorders.

Head of Laboratory

José Manuel Morão Cabral Ferro, MD/PhD

Graphical Abstract



Team

Alcina Amparo Fraga Luz	High School Diploma	Administrative Technician
Alexandre Valério de Mendonça	MD/PhD with Habilitation	Clinical Staff Scientist
Ana Catarina Gaspar Fonseca	MD/PhD	Clinical Researcher
Ana Isabel Figueira Verdelho	MD/PhD	Clinical Staff Scientist
Bruno André e Silva Miranda	MD/Master Degree	Clinical Researcher
Carla Cristina Paulo Gabriel Bentes	MD/PhD	Clinical Researcher
Carolina Pires Maruta	MD/PhD	Clinical Researcher
Diana de Aguiar Dias de Sousa	Master Degree	PhD Student

Dina Gomes Lúcia da Silva	PhD	Visiting Researcher
Elisa Cristina Leal Martins de Nunes	Master Degree	Lab Technician (Started April)
Frederico Simões Oliveira Fernandes do Couto	MD/PhD	Clinical Researcher
Gislaine Castilho de Oliveira	Master Degree	Lab Technician (Left January)
Jorge Miguel Aldinhas Ramos Ferreira	MD/Master Degree	Clinical Researcher (Started August)
José Manuel Borges Fonseca	PhD	Senior Technician
Lara Isabel Pires Melo Caeiro	MD/PhD	Clinical Researcher
Maria Gabriela Mariano Leal	University Degree	Lab Technician
Maria Isabel Segurado Pavão Martins Catarino Petiz	MD/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
Maria Manuela Gil Guerreiro	MD/PhD	Clinical Staff Scientist
Mariana Durão Borges	Master Degree	Lab Technician
Mário Rui Jesus Santos Rodrigues	Master Degree	Lab Technician
Marisa Marina Fatuda Costa	High School Diploma	Administrative Technician
Neuza Margarida Nascimento Costa	Master Degree	Lab Technician (Started February. Left August)
Patrícia Martins Canhão	MD/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	MD/University Degree	Clinical Researcher

Laboratory Keywords / Research Areas

Cryptogenic Stroke, Aphasia, Small Cognitive Impairment, Cerebral Venous Thrombosis.

Major Scientific Achievements

1. We showed that warfarin and dabigatran have similar efficacy and safety for the prevention of venous thrombotic events after cerebral venous thrombosis.
2. We proved that dabigatran is not better than aspirin for the prevention of recurrent events after an ESUS type of stroke.
3. We demonstrated that thrombolysis can be used in acute stroke patient who had a recent non-ST elevation myocardial infarction, but not in those with a ST elevation.

Selected Publications

Diener HC, Sacco RL, Easton JD, Granger CB, Bernstein RA, Uchiyama S, Kreuzer J, Cronin L, Cotton D, Grauer C, Brueckmann M, Chernyatina M, Donnan G, Ferro JM, Grond M, Kallmünzer B, Krupinski J, Lee BC, Lemmens R, Masjuan J, Odinak M, Saver JL, Schellinger PD, Toni D, Toyoda K, RE-SPECT ESUS Steering Committee and Investigators (2019). Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined Source. **The New England Journal of Medicine** 380(20):1906-1917. (IF: 70.67, Citations: 30. Source: Web of Science).

Marto JP, Kauppila LA, Jorge C, Calado S, Viana-Baptista M, Pinho-E-Melo T, Fonseca AC (2019). Intravenous Thrombolysis for Acute Ischemic Stroke After Recent Myocardial Infarction: Case Series and Systematic Review. **Stroke** 50(10):2813-2818. (IF: 6.05, Citations: 0. Source: Web of Science).

Aguiar de Sousa D, Canhão P, Crassard I, Coutinho J, Arauz A, Conforto A, Béjot Y, Giroud M, Ferro JM, ISCVT-2-PREGNANCY Investigators (2017). Safety of Pregnancy After Cerebral Venous Thrombosis: Results of the ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis)-2 Pregnancy Study. **Stroke** 48(11):3130-3133. (IF: 6.05, Citations: 9. Source: Web of Science).

Ferro JM, Santos AC (2019). Emotions after stroke: A narrative update. **International Journal of Stroke**. (IF: 4.46, Citations: 0. Source: Web of Science).

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 (2019). Safety and Efficacy of Dabigatran Etxilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis: A Randomized Clinical Trial. **JAMA Neurology** 76(12):1457-1465. (IF: 6.058, Citations: 1. Source: Web of Science).

Ongoing Research Projects

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.

2016/2020: 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.

2013/2019: International study on dural sinus and cerebral vein thrombosis 2. Coordinator: José Ferro. Funding Agency: Congrex Schweiz AG. Reference: ISCVT-2. Amount: € 155 000,00 Total Amount: € 155 000,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Abilleira S, Aguiar de Sousa D, Gattringer T, Kobayashi A, Fazekas F, Szikora S, Feigin V, Caso V, Gallofré M, Fischer U, on behalf of the ESO ESMINT EAN SAFE Survey on Stroke Care collaborators (2019). Planning of Stroke Care and Urgent Prehospital Care across Europe. Results of the ESO ESMINT EAN SAFE Survey. **European Stroke Journal** 4(4):329-336. (IF:--. Citations: 0. Source: *Web of Science*).

Aguiar de Sousa D, Lucas Neto L, Jung S, Penas S, Panos L, Heldner MR, Fischer U, Arnold M, Canhão P, El-Koussy M, Ferro JM, Hakim A (2019). Brush Sign Is Associated With Increased Severity in Cerebral Venous Thrombosis. **Stroke** 50(6):1574-1577. (IF: 6.058, Citations: 1. Source: *Web of Science*).

Aguiar de Sousa D, von Martial R, Abilleira S, Gattringer T, Kobayashi A, Gallofré M, Fazekas F, Szikora I, Feigin V, Caso V, Fischer U (2019). Access to and delivery of acute ischaemic stroke treatments: A survey of national scientific societies and stroke experts in 44 European countries. **European Stroke Journal** 4(1):13-28. (IF:--. Citations: 23. Source: *Web of Science*).

Alves PN, Foulon C, Karolis V, Bzdok D, Margulies DS, Volle E, Thiebaut de Schotten M (2019). An improved neuroanatomical model of the default-mode network reconciles previous neuroimaging and neuropathological findings. **Communications Biology** 2(1):370. (IF:--. Citations: 0. Source: *Web of Science*).

Carcel C, Woodward M, Balicki G, Koroneos GL, Sousa DA, Cordonnier C, Lukaszyk C, Thompson K, Wang X, Davies L, Bassi M, Anderson CS, Peters SA, Sandset E (2019). Trends in recruitment of women and reporting of sex differences in large-scale published randomised controlled trials in stroke. **International Journal of Stroke** 14(9):931-938. (IF: 4.466, Citations: 0. Source: Web of Science).

Caso V, Aguiar de Sousa D, Fischer U (2019). Status and perspectives of acute stroke care in Europe. **Neurological Sciences** 40(5):1087-1088. (IF: 2.484, Citations: 1. Source: Web of Science).

Crespo Pimentel B, Willeit J, Töll T, Kiechl S, Pinho E Melo T, Canhão P, Fonseca C, Ferro J (2019). Etiologic Evaluation of Ischemic Stroke in Young Adults: A Comparative Study between Two European Centers. **Journal of Stroke & Cerebrovascular Diseases** 28(5):1261-1266. (IF: 1.646, Citations: 0. Source: Web of Science).

Diener HC, Sacco RL, Easton JD, Granger CB, Bernstein RA, Uchiyama S, Kreuzer J, Cronin L, Cotton D, Grauer C, Brueckmann M, Chernyatina M, Donnan G, Ferro JM, Grond M, Kallmünzer B, Krupinski J, Lee BC, Lemmens R, Masjuan J, Odinak M, Saver JL, Schellinger PD, Toni D, Toyoda K; RE-SPECT ESUS Steering Committee and Investigators (2019). Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined Source. **The New England Journal of Medicine** 380(20):1906-1917. (IF: 70.67, Citations: 30. Source: Web of Science).

Ferro JM, Aguiar de Sousa D (2019). Cerebral Venous Thrombosis: an Update. **Current Neurology and Neuroscience Reports** 19(10):74. (IF: 3.040, Citations: 0. Source: Web of Science).

Fonseca J, Raposo A, Martins IP (2019). Cognitive functioning in chronic post-stroke aphasia. **Applied Neuropsychology-Adult** 26(4):355-364. (IF: 1.54, Citations: 1. Source: Web of Science).

Fragata I, Bustamante A, Penalba A, Ferreira P, Nunes AP, Canhão P, Montaner J (2019). Venous and arterial TNF-R1 predicts outcome and complications in acute subarachnoid hemorrhage. **Neurocritical Care** 31(1):107-115. (IF: 2.892, Citations: 0. Source: Web of Science).

Fragata I, Canhão P (2019). Imaging predictors of outcome in acute spontaneous subarachnoid hemorrhage: a review of the literature. **Acta Radiologica** 60(2):247-259. (IF: 1.586, Citations: 0. Source: Web of Science).

Fragata I, Canto-Moreira N, Canhão P (2019). Ischemic Lesions in Acute and Subacute Perimesencephalic Subarachnoid Hemorrhage. **American Journal of Roentgenology** 212(2):418-424. (IF: 3.161, Citations: 0. Source: Web of Science).

Hedderich DM, Ferro JM, Kunz WG (2019). Diagnostic imaging in the management of patients with possible cerebral venous thrombosis: a cost-effectiveness analysis. **Neuroradiology** 61(10):1155-1163. (IF: 2.504, Citations: 0. Source: Web of Science).

Leal Rato M, Mares I, Aguiar de Sousa D, Senju A, Martins IP (2019). Direct Gaze Partially Overcomes Hemispatial Neglect and Captures Spatial Attention. **Frontiers of Psychology** 9:2702. (IF: 2.129, Citations: 1. Source: Web of Science).

Marto JP, Kauppila LA, Jorge C, Calado S, Viana-Baptista M, Pinho-E-Melo T, Fonseca AC (2019). Intravenous Thrombolysis for Acute Ischemic Stroke After Recent Myocardial Infarction: Case Series and Systematic Review. **Stroke** 50(10):2813-2818. (IF: 6.058, Citations: 0. Source: Web of Science).

Nzwalo H, Guilherme P, Nogueira J, Félix C, André A, Teles J, Mouzinho M, Ferreira F, Marreiros A, Logallo N, Bentes C (2019). Fine particulate air pollution and occurrence of spontaneous intracerebral hemorrhage in an area of low air pollution. **Clinical Neurology and Neurosurgery** 176:67-72. (IF: 1.672, Citations: 1. Source: Web of Science).

Santos AC, Ferro JM (2019). Profile of Anger in Acute Stroke: A Multifactorial Model of Anger Determinants. **Journal of Neuropsychiatry and Clinical Neurosciences** 31(2):159-164. (IF: 1.971, Citations: 0. Source: Web of Science).

Verdelho A, Madureira S, Correia M, Ferro JM, Rodrigues M, Gonçalves-Pereira M, Gonçalves M, Santos AC, Vilela P, Bárrios H, Borges M, Santa-Clara H. (2019). Impact of physical activity in vascular cognitive impairment (AFIVASC): study protocol for a randomized controlled trial. **Trials** 20(1):114. (IF: 1.975, Citations: 0. Source: Web of Science).

Other International Publications

Coelho S, de Mendonça A. A Case of Philosophical Experimentation upon mild cognitive impairment's Time Perception. *philosophy@lisbon* 2019 9 1-17.

Pompili A, Abad A, Trancoso I, Fonseca J, Martins IP (2019). Evaluation and Extensions of an Automatic. Speech Therapy Platform? 14th edition of the International Conference on the Computational Processing of Portuguese (PROPOR 2020) will be held at the Colégio do Espírito Santo in Evora (Portugal), March 2-4, 2020. Lecture Notes in Artificial Intelligence Series.

Fragata I, Alves M, Papoila AL, Nunes AP, Ferreira P, Diogo M, Canto-Moreira N, Canhão P (2019). Computed tomography perfusion as a predictor of delayed cerebral ischemia and functional outcome in spontaneous subarachnoid hemorrhage: A single center experience. **Neuroradiology Journal** 32(3):179-188.

Amorim IL, Kauppila LA, Costa MR, Bentes C, Peralta R (2019). Epileptiform Activity in Patient with RBD-Like Symptomatology. **Journals of Sleep Disorders Managers** 5(1):024.

Webb A, Heldner MR, Aguiar de Sousa D, Sandset EC, Randall G, Bejot Y, van der Worp B, Caso V, Fischer U; ESO-SAFE Secondary Prevention Survey Steering Group (2019). Availability of secondary prevention services after stroke in Europe: An ESO/SAFE survey of national scientific societies and stroke experts. **European Stroke Journal** 4(2):110-118.

Other National Publications

Miranda B (2019). Vestibulopatia bilateral – Causas neurológicas. Revista da XI Reunião de Inverno”, APO, Lisbon.

Martins IP (2019). Terapêutica da enxaqueca. *Jornal do Médico*. Dossier cefaleias, pp 17-18.

Books/Book Chapters

Fonseca F (2019). Reabilitação neuropsicolinguística em pacientes com afasia de compreensão. In: Neuropsicologia da linguagem. Bases para avaliação e reabilitação. Denise Ren da Fontoura, Jaqueline de Carvalho Rodrigues, Rochele Paz Fonseca, Jerusa Fumagalli de Salles (Eds.). Editora Vetor.

Invited Lectures and Seminars

Martins IP. Enxaqueca crónica. Stand Alone Allergan, Lisbon, Portugal, January 18, 2019.

Fonseca AC. Métodos complementares de imagem utilizados atualmente. 13º Congresso Português do AVC, Porto, Portugal, January 31, 2019.

Fonseca AC. A placa carotídea e o risco de AVC. Reunião monotemática de Angiologia e cirurgia vascular do SAMS, Lisbon, Portugal, February 2, 2019.

Miranda B. Vestibulopatia bilateral – Causas Neurológicas. XI Reunião de Inverno da Associação Portuguesa de Otoneurologia, Cascais, Portugal, February 23, 2019.

Ferro JM. Trombosis venosa cerebral. Novedades en el abordaje terapêutico. II Foro. Debate Multidisciplinar en Trombosis, Optimización tratamiento antitrobótico en pacientes com cáncer, Madrid, Spain, March 5, 2019.

Fonseca AC. rtPA vs TNK it's show time – stick to what we know. Lisbon Stroke Summit 2019, Lisbon, Portugal, April 5, 2019.

Miranda F. Terapia da fala na afasia: Que evidência. Congresso Nacional das Tecnologias da Saúde, Bragança, Portugal, April 5-7, 2019.

Martins IP. Cefaleias. Reunião da ZAMBOM, Lisbon, Portugal, April 11-12, 2019.

Fonseca AC. ESUS how ward to look for AF. Europrevent 2019. Lisbon, Portugal, April 12, 2019.

Alves PN, Martins IP. Falsas identificações delirantes após lesões encefálicas direitas. Sessão da Neurologia na Psiquiatria, Serviço de Psiquiatria, Hospital de Santa Maria, Lisbon, Portugal, May 6, 2019.

Miranda B. Da clínica para a investigação básica e de volta à clínica. Programa de Formação em Investigação, Centro de Formação do Hospital Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 22, 2019.

Miranda B. Vestibulopatia bilateral – Causas Neurológicas. Congresso Anual da Associação Portuguesa de Otoneurologia, Évora, Portugal, May 24, 2019.

Fonseca AC. Primary prevention of stroke in women. European Stroke Organization Conference 2019, Milan, Italy, May 24, 2019.

Aguiar de Sousa D. Clinical practice of treatment of hypercholesterolemia after stroke in Europe. European Stroke Organization Conference 2019, Milan, Italy, May 2019.

Aguiar de Sousa D. Course on emergency management of the Centro Hospitalar Lisboa Norte (CHULN), Lisbon, Portugal, May 2019.

Fonseca J. Cognição como variável influenciadora de recuperação das afasias. 1º Simpósio Brasileiro de Afasia, mesa redonda Atualidades em Terapia. Sociedade Brasileira de Fonaudologia, São Paulo, Brasil, June 29, 2019.

Aguiar de Sousa D. How to plan your residency in neurology? Enclose an experience abroad. European Academy of Neurology Congress 2019, Oslo, Norway, June 2019.

Miranda B. Cortical stimulation for behavior and study in animal model. 11th International Organization for Societies for Electrophysiological Technology Congress, Porto, Portugal, September 9-13, 2019.

Alves PN, Martins IP. Cognitive Functions. Masters in Neuroengineering, Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, September 18, 2019.

Bentes C. Crises epiléticas pós-AVC. Epilepsy in Mind Summit, Lisbon, Portugal, September 20, 2019.

Aguiar de Sousa D. Why can a thrombectomy fail? Is it because there is no clot? Another cause: ICAD, dissection, arteritis. 11th ESMINT Congress (European Society of Minimally Invasive Neurological Therapy, Nice, France, September 2019.

Ferro JM. Challenges in clinical research of less common diseases. 27th Annual Conference of Indian Academy of Neurology, Hyderabad, India, October 4, 2019.

Ferro JM. Embolic Stroke of Undetermined Source - "How far to investigate". 27th Annual Conference of Indian Academy of Neurology, Hyderabad, India, October 6, 2019.

Fonseca AC. Reformulação terapêutica com trombólise - novos fármacos e indicações. 10ª Reunião de unidades de AVC, Lisbon, Portugal, October 25, 2019.

Alves PN (2019). Afasia – bases anatómicas. Conferência: Alterações de Linguagem Pós-AVC. Lisbon, Portugal, October 26, 2019.

Bentes C. Fármacos anti-epilépticos no AVC. Curso sobre Tratamento Farmacológico das Epilepsias, Lisbon, Portugal, October 26, 2019.

Fonseca J. Bateria da afasia de Aachen - versão portuguesa. Alterações da Linguagem pós-AVC. Sociedade Portuguesa de Terapia da Fala, Lisbon, Portugal, October 26, 2019.

Ferro JM. Neurologia – o adulto. XII Minho Medical Meeting. Medicina sem idade, Braga, Portugal, November 9, 2019.

Fonseca AC. DTC na hemorragia subaracnoideia. Curso de introdução à neurosonologia, Coimbra, Portugal, November 13, 2019.

Fonseca. Cohort studies. Curso de investigação clínica/Ensaio clínicos da SPN, Coimbra, Portugal, November 13, 2019.

Bentes C. Formação em Medicina do Sono na Neurologia. Congresso de Neurologia, Coimbra, Portugal, November 14, 2019.

Ferro JM. AVC em doenças sistémicas. Congresso de Neurologia 2019, Coimbra, Portugal, November 14, 2019.

Martins IP. From Science to the Clinic. Fremanezumab: what role can it play? Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019.

Martins IP. Quando suspender a terapêutica preventiva na Enxaqueca Quanto mais tarde melhor... - Atualidades e controvérsias na Terapêutica da SPC. Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019.

Maruta C. Linhas de investigação no Laboratório de Estudos de Linguagem. Neurosciences in Centro Académico Médico de Lisboa, Lisbon, Portugal, November 20, 2019.

Martins IP. Fisiopatologia da enxaqueca. Masters of Migraine. Novartis, Lisbon, Portugal, November, 2019.

Alves PN. Cognition and brain amyloid in transthyretin-related familial amyloid polyneuropathy. 13ª Bolsa de Investigação Fundação AstraZeneca/FMUL, Dia da Investigação, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019.

Alves PN. Research Path – Behavioural Neurology. Early career physician scientists. Dia da Investigação, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019.

Caeiro L. Apathy in stroke. 4^a Symposium FHU VASCOG, Lille, France, December 12, 2019.

Ferro JM. Amnestic strokes. 4^a Symposium FHU VASCOG, Lille, France, December 12, 2019.

Communications in International Conferences

Martins IP. Migraine Auras. 13th World Congress on Controversies in Neurology (CONy), Madrid, Spain, April 5-7, 2019. *(Oral Presentation)*.

Rosário M, Fonseca ACG. HIV-associated vasculopathy as a cause of ischemic stroke. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Presentation)*.

Vargas M, Fonseca M, Basílio G, Fonseca ACG. Pseudoathetosis as rare manifestation of vitamin B12 deficit. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Presentation)*.

Aguiar de Sousa D, Lucas Neto L, Arauz A, Sousa AL, Gabriel D, Correia M, Gil-Gouveia R, Penas S, Dias M, Carvalho M, Canhão P, Ferro JM. Early and late recanalization in patients with cerebral thrombosis – results of a prospective cohort study. 5th European Stroke Organization Conference, Milan, Italy, May 22-24, 2019. *(Poster Presentation)*.

Aguiar de Sousa D, Lucas Neto L, Jung S, Penas S, Panos L, Heldner M, Fischer U, Arnold M, Canhão P, El-Koussy M, Ferro JM, Hakim A. Brush sign is associated with increased severity in cerebral venous thrombosis. 5th European Stroke Organization Conference, Milan, Italy, May 22-24, 2019. *(Poster Presentation)*.

Fonseca AC, Marto JP, Pimenta D, Alves PN, Inácio N, Viana-Baptista M, Melo TP, Ferro JM, Almeida AG. Cardiomyopathies as cause of ischemic stroke: a cardiac magnetic resonance imaging study. 5th European Stroke Organization Conference, Milan, Italy, May 22-24, 2019. *(Poster Presentation)*.

Coelho P, Passão D, Soares F, Almeida V, Fonseca ACG, Melo TP. Reversible cerebral vasoconstriction related to cannabis consumption: an uncommon cause of stroke. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. (*Poster Presentation*).

Kauppila LA, Farinha, N, Martins IP. Nummular headache probably secondary to congenital obstructive hydrocephalus. *European Journal of Neurology*; 26 (Suppl. 1): 947. DOI: 10.1111/ene.14020. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. (*Poster Presentation*).

Kauppila LA, Martins IP. Medication-overuse headache: characterization of the abuse pattern in a tertiary headache Centre. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. (*Oral Presentation*).

Kauppila LA, Franco A, Fonseca AGC, Bentes C, Peralta R. Electroencephalographic characterization of patients with bithalamic ischaemic stroke. 5th Congress of the European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. (*Poster Presentation*).

Rebello-Pinto T, Freitas F, Ferreira F, Almeida C, Reis C, Maruta C. Associação Nuvem Vitória: the impact of bedtime stories in pediatric inpatients settings. World Sleep Congress, Vancouver, Canada, September 20-25, 2019. (*Poster Presentation*).

Brady MC et al. RELEASE-ing the potential of a large, international, systematic review-based Individual Participant Data (IPD) aphasia after stroke database for meta- and network meta-analysis. 20th International Science of Aphasia Conference | The temporal lobe revisited: functional and neural updates, Rome, Italy, September 23-26, 2019. (*Poster Presentation*).

Martins IP. Migraine Unmet needs. Sociedade Espanhola de Neurologia (SEN), Sevilha, Spain, November 19-23, 2019. (*Oral Presentation*).

Communications in National Conferences

Fonseca J. Afasia para não especialistas. Congresso Nacional das Tecnologias da Saúde, Escola Superior Agrária do Instituto Politécnico de Bragança, Bragança, Portugal, April 5-7, 2019. (*Oral Presentation*).

Maruta C, Pinto TR, Pinto HR, Paiva T, Freitas F, Ferreira R. Contar histórias ao deitar a crianças e adolescentes hospitalizados: Estudo do impacto das acções de voluntariado da Associação Nuvem Vitória. Encontro de Investigadores do CRC-W, Faculdade de Ciências Humanas, Universidade Católica Portuguesa, Lisbon, Portugal, July 4, 2019. *(Oral Presentation)*.

Maruta C. On the language and cognition conundrum: What can brain damaged patients tell us? - Emotional and cognitive processes in communication in humans and other primates. Protolang 6, Fundação Calouste Gulbenkian, Lisbon, Portugal, September 6-10, 2019. *(Oral Presentation)*.

Maruta C. Sobre a relação linguagem-cognição: O que nos ensinam os doentes com lesão cerebral? Conferência "Alterações de Linguagem pós-AVC" do Departamento de Linguagem no Adulto da Sociedade Portuguesa de Terapia da Fala, Fundação D. Pedro IV, Lisbon, Portugal, October 26, 2019. *(Oral Presentation)*.

Alves P. Síndrome de Fregoli – estudo de caso de incidência numa cohorte de doentes com lesões vasculares hemisféricas direitas. Reunião Anual da Secção de Neurologia do Comportamento da Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 13, 2019. *(Oral Presentation)*.

Maruta C. Vejo-te mas não sei quem és: a propósito de um caso de prosopagnosia. Reunião Anual da Secção de Neurologia do Comportamento da Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 13, 2019. *(Oral Presentation)*.

Miranda F A escrita com teclado é melhor que a manual – estudo caso. Reunião Anual da Secção de Neurologia do Comportamento da Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 13, 2019. *(Oral Presentation)*.

Alves P. Alterações cognitivas. Sessão SPN – Casos Clínicos. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. *(Oral Presentation)*.

Coelho P, Rato ML, Martins IP. Cronorrisko na cefaleia tipo cluster: relato de 2292 episódios. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. *(Poster Presentation)*.

Delgado S, Peres J, Roque R, Santos L, Alves P, Valverde A, Cruz S (2019) Miosite com corpos de inclusão: apresentação com elevação assintomática da creatina cinase. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Fialho MC, Pinho e Melo T, Canhão P, Ferro JM, Fonseca AC. Acuidade do péptido atrial natriurético para diagnóstico de fibrilação auricular em doentes com AVC isquémico. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Kaupila LA, Martins IP. Cefaleia da diálise: 4 casos de um centro terciário de cefaleias. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Oral Presentation*).

Leal Rato M, Nunes Vicente B, Marques T, Aguiar de Sousa D, Canhão P. Vasculopatia a HSV-2 como causa de AVC isquémico no jovem imunodeprimido. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Leal Rato M, Silva J, Sotero F, Pacheco F, Martins IP. Demência rapidamente reversível associada a VIH. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Sotero F, Martins IP. Análise retrospectiva de uma coorte de doentes com cefaleia predominantemente nocturna. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Oral Presentation*).

Vargas M, Fonseca M, Basilio G, Fonseca AC. Pseudoatetose uma manifestação rara do défice de vitamina B12. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Organization of Conferences

Fonseca J, Miranda F. Bateria de Avaliação da Afasia de Lisboa – BAAL. Curso de certificação. Centro de Negócios do Porto, Porto, Portugal, February 1, 2019.

Fonseca J, Miranda F. Bateria de Avaliação da Afasia de Lisboa – BAAL. Curso de certificação. Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 16, 2019.

Fonseca AC. Co-Organizer. Fórum de Neurologia 2019, Vila Real, Portugal, May 17-18, 2019.

Fonseca J, Miranda F. Bateria de Avaliação da Afasia de Lisboa – BAAL. Curso de certificação. Lar D. Pedro V, Praia da Vitória, Ilha Terceira, Açores, Portugal, May 25, 2019.

Martins IP, Gil-Gouveia R, Sousa A. II Curso Pós-Graduado de Atualização Administração de Toxina Botulínica para o Tratamento de Cefaleias. Departamento de Neurociências, Serviço Neurologia, Centro Hospitalar Lisboa Norte and Laboratório de Estudos de Linguagem da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, May 31, 2019.

Martins IP, Gil-Gouveia R. II Curso Pós-Graduado de Atualização em Cefaleias. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 12, 2019.

Martins IP. Co-Organizer. Beyond MED, Conselho Pedagógico e Departamento de Educação Medica da Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 23, 2019.

Fonseca J, Maruta C, Nascimento A. Reunião Anual da Secção de Neurologia do Comportamento da Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 13, 2019.

Fonseca AC. Co-Organizer. Congresso de Neurologia 2019, Sociedade Portuguesa de Neurologia, Coimbra, Portugal, November 14-16, 2019.

Internationalization

Aguiar de Sousa D. Chair of the Young Stroke Physicians Committee, European Stroke Organization.

Aguiar de Sousa D. Member of the Board of Directors, European Stroke Organization.

Aguiar de Sousa D. Member of the Steering Committee, European Stroke Action Plan 2018-2030.

Aguiar de Sousa D. Co-Editor of the YSPR section of the ESO blog.

Aguiar de Sousa D. Member of the Scientific Panel on Stroke of the European Academy of Neurology (EAN) as Resident and Research Fellow Section (RRFS) representative (since 2016).

Aguiar de Sousa D. Member of the Public Relations Committee – Joint Conference of the European Stroke Organization Conference (ESOC) and World Stroke Organization (WSO) 2020.

Aguiar de Sousa D. Member of the Public Relations Committee, European Stroke Organization Conference (ESOC) 2019.

Ferro JM. Principal Investigator and Member of Steering Committee of Boehringer Ingelheim sponsored clinical trial RESPECT CVT.

Ferro JM. Member Editorial Board “Stroke” and “European Journal of Stroke”, and of the Advisory Board of “Cerebrovascular Disease” and “Journal of Neurology”.

Ferro JM. Member Executive Board of the International Stroke Society.

Ferro JM. Member of the Global Advisory Board of Boehringer Ingelheim.

Industry Contract Research

2019 - GLORIA - Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation. PI: Catarina Fonseca.

2019 – “Phase 3 Study to Evaluate the Efficacy and Safety of Intravenous BII093 (Glibenclamide) for Severe Cerebral Edema Following Large Hemispheric Infarction (CHARM)”. PI: Teresa Pinho e Melo. Sub-Investigator: Pedro Nascimento Alves.

2018-2019 - “A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer’s Disease” (Novartis CNP520A2202J; 2018). Maruta C (in collaboration with the Dementia Study Group).

2019-2020- “A 12-month prospective, randomized, interventional, global, multi-center, active-controlled study comparing sustained benefit of two treatment paradigms (erenumab qm vs. oral prophylactics) in adult episodic migraine patients” (AMGEN AMG334, Clinical Trial Protocol CAMG334A2401) PI: Isabel Pavão Martins.

Advanced Teaching

Martins IP. Estratégias de Ensino de Grande e Médio Grupo. Ações de Formação do Departamento de Educação Médica, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, February 22, 2019.

Fonseca AC. Lectures. Curso de Especialização em Introdução à Investigação Clínica. Prognostic Studies, Lisbon, Portugal, April 13-14 2019.

Caeiro L. How to evaluate cognition in the follow-up of stroke patients? European Master in Stroke Medicine, Krems, Viena, Austria, April 2019.

Martins IP. Functional organization of the mind, Methods in Cognitive assessment. Master/Doctoral Programme in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 8, 2019.

Fonseca AC. Lectures. Programa de Formação em Investigação - Estudos de Prognóstico. Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 10, 2019.

Maruta C. Executive functions and the frontal lobes. Master/Doctoral Programme in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15, 2019.

Alves PN. Right hemisphere syndromes. Master/Doctoral Programme in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 17, 2019.

Miranda B. Models of learning and decision-making. Master/Doctoral Programme in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 22, 2019.

Administração de Toxina Botulínica para o Tratamento de Cefaleias. Departamento de Neurociências, Serviço Neurologia, Centro Hospitalar Lisboa Norte e Laboratório de Estudos de Linguagem da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, May 31, 2019.

Martins IP. Experiência no tratamento das cefaleias com a toxina. II Curso Pós-Graduado de Atualização Administração de Toxina Botulínica para o Tratamento de Cefaleias. Departamento de Neurociências, Serviço Neurologia, Centro Hospitalar Lisboa Norte e Laboratório de Estudos de Linguagem da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, May 31, 2019.

Martins IP. Introdução e objectivos e auto-avaliação. II Curso Pós-Graduado de Atualização Administração de Toxina Botulínica para o Tratamento de Cefaleias. Departamento de Neurociências, Serviço Neurologia, Centro Hospitalar Lisboa Norte e Laboratório de Estudos de Linguagem da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, May 31, 2019.

Martins IP. Utilizações potenciais noutras cefaleias (evidencia IV/V) – Cefaleia Numular. II Curso Pós-Graduado de Atualização Administração de Toxina Botulínica para o Tratamento de Cefaleias. Departamento de Neurociências, Serviço Neurologia, Centro Hospitalar Lisboa Norte e Laboratório de Estudos de Linguagem da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, May 31, 2019.

Martins IP. Introdução e definições & medidas de outcome para a prática clínica (como avaliar a eficácia da intervenção). II Curso Pós-Graduado de Atualização em Cefaleias, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 12, 2019.

Martins IP. Mesa redonda: Prevenção não oral da enxaqueca. Toxina botulinica. II Curso Pós-Graduado de Atualização em Cefaleias, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 12, 2019.

Martins IP. Cefaleia por abuso medicamentoso. II Curso Pós-Graduado de Atualização em Cefaleias, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 12, 2019.

Martins IP. Aula Prática na Consulta. Ações de Formação do Departamento de Educação Médica, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 1, 2019.

Canhão P. Clinical case reports. Curso de investigação clínica/ensaios clínicos. Congresso de Neurologia 2019, Coimbra, Portugal, November 13, 2019.

Ferro JM. Case control-studies. Curso de investigação clínica/ensaios clínicos. Congresso de Neurologia 2019, Coimbra, Portugal, November 13, 2019.

Fonseca AC. Cohort studies. Curso de investigação clínica/ensaios clínicos. Congresso de Neurologia 2019, Coimbra, Portugal, November 13, 2019.

Fonseca AC. DTC na hemorragia subaracnoideia. Curso de introdução à neurosonologia. Congresso de Neurologia 2019, Coimbra, Portugal, November 13, 2019.

Alves P. Which clinical study to choose. Curso de investigação clinica/ensaios clínicos. Congresso de Neurologia 2019, Coimbra, Portugal, November 13, 2019.

Alves PN. Brain connectivity and Neurological Diseases. Masters in Biomedical Engineering and Biophysics, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, November 14, Lisboa, Portugal, 2019.

Martins IP. "A aura". "Enxaqueca". Curso Avançado de Cefaleias da Sociedade Portuguesa de Cefaleias, Lisbon, Portugal, December 6-7, 2019.

Caeiro L. Diagnostic traps in post-stroke dementia, depression and apathy. European Master in Stroke Medicine, Krems, Viena, Austria, 2019.

Aguiar de Sousa D. Introduction to Systematic Review. Doctoral program in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, annual participation since May 2017.

Aguiar de Sousa D. Multivariable Analysis. Introduction to Clinical Research: a practical course, CAML Advanced Course, Universidade de Lisboa, annual participation since January 2018.

Caeiro L. Colaboration Curso de Mestrado/Doutoramento em Neurociências, Faculdade de Medicina da Universidade de Lisboa, sendo preletora da aula de "Metodologia de Descrição de casos neuropsicológicos.

Caeiro L. Professora Adjunto Convidada da Unidade Curricular de Psicofisiologia no Instituto Superior de Ciências da educação.

Science and Society

Alves P. Um AVC Altera o GPS Cerebral. Entrevista sobre o Prémio Professor Lobo Antunes, a propósito da abertura das candidaturas para 2019. Santa Casa da Misericórdia de Lisboa Laboratório de Estudos de Linguagem, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, February 28, 2019.

Martins IP. Scientific Committee of the Exhibition “The brain, wider than the sky”. Fundação Calouste Gulbenkian, Lisbon, Portugal, April 17, 2019.

Ferro JM, Cairo L. O cuidador informal. Conferência na Universidade Intergeracional de Benfica. May 30, 2019.

Ana Catarina Bravo. O Futuro do Trabalho Final de Mestrado. Trabalho Final do Mestrado Integrado em Medicina da Faculdade de Medicina da Universidade de Lisboa, 2019.

MSc Theses

Maria Santos, 12/02/2019, Cognição no ciclo da enxaqueca, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão.

Margarida Rosado, 12/02/2019, Prognostic role of platelet parameters in ischemic stroke: systematic review and meta-analysis, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Patrícia Canhão.

Alexandre Calçada, 12/02/2019, Prognostic Role of Mean Platelet Volume in Acute Ischemic Stroke Patients, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Patrícia Canhão.

Catarina Gregório, 26/06/2019, Biomarcadores de Prognóstico do AVC Isquémico: revisão sistemática e estado da arte, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Catarina Fonseca.

Catarina Sousa, 26/06/2019, Dilated cardiomyopathy and the risk of cardioembolic stroke: a systematic review with meta-analysis, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Catarina Fonseca.

Vitor Encarnação, 27/06/2019, Consumo de Drogas Ilícitas e AVC, Faculdade de Medicina da Universidade de Lisboa. Supervisor: José Ferro.

João Martins, 27/06/2019, Creatinina, um biomarcador de prognóstico e preditor da função respiratória, na Esclerose Lateral Amiotrófica, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Teresa Valido, 18/07/2019, Um Projeto-Piloto em Active Learning na Disciplina de Neurologia da Faculdade de Medicina da Universidade de Lisboa. impacto nos resultados de aprendizagem Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão.

Ana Margarida Fernandes, 18/07/2019, Dissecção Arterial Cervical: Arteriopatia ou Doença do Tecido Conjuntivo? – A propósito de um caso clínico atípico, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Catarina Fonseca.

Daniel Terêncio, 18/07/2019, Avaliação de Desorientação Topográfica após AVC: caso clínico e utilização de questionários e provas em ambiente virtual, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luísa Albuquerque. Co-Supervisor: Pedro Nascimento Alves.

Ana Almeida, 20/12/2019, Vasculopatia do VIH – Caso Clínico, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Catarina Fonseca.

PhD Theses

Annamaria Pompili, 16/12/2019, Speech and language technologies applied to diagnosis and therapy of brain diseases. Provas de doutoramento do programa doutoral em Engenharia Informática e de Computadores na Área de Pós-Graduação, Instituto Superior Técnico da Universidade de Lisboa. Co-Supervisor: Isabel Pavão Martins.

Leonor Saúde Lab

Major Interests/Objectives

We want to understand the molecular and cellular mechanisms controlling fundamental regenerative processes activated in the context of a spinal cord injury.

Head of Laboratory

Maria Leonor Tavares Saúde, PhD, Invited Associate Professor

Team

Ana Catarina Esteves Ribeiro	PhD	Senior Postdoctoral Researcher
Ana Margarida Pereira Cristóvão Pinto	University Degree	Lab Manager (Left October)
Ana Paula Lopes Martins	University Degree	MSc Student
Ana Raquel Dias Quitéria	Master Degree	Lab Manager (Started December)
Carmen de Sena Tomás	PhD	Senior Postdoctoral Researcher (Started February)
Dalila Maria Neves Silva	Master Degree	PhD Student (Started January)
Diana Sofia Chapela Duarte Pires	Master Degree	PhD Student
Diogo de Abreu Paramos de Carvalho	Master Degree	PhD Student (Started January)
Isaura Vanessa Antunes Martins	PhD	Postdoctoral Researcher
Nídia de Sousa	PhD	Postdoctoral Researcher (Started August, Left December)
Sara Isabel Guerreiro Mota	High School Diploma	BSc Student (Started January, Left April)

Laboratory Keywords / Research Areas

Regeneration, Spinal Cord, Microenvironment, Zebrafish, Mouse.

Vascular repair and its involvement in spinal cord injury outcome.

Extracellular matrix and its contribution to spinal cord repair.

Senescent cells and their SASP as modulators of the injured spinal cord microenvironment.

Major Scientific Achievements

Our lab in collaboration with the biotech company TechnoPhage, SA designed and validated a zebrafish larvae platform to screen for new therapeutics for spinal cord injury indication. We were awarded a “la Caixa” Foundation/FCT grant to study the role of senescent cells and their SASP in the context of a spinal cord injury.

Selected Publications

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. (IF: 5.547, Citations: 0. Source: Web of Science).

Ribeiro A, Monteiro JF, Certal AC, Cristovão 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. (IF: 5.36, Citations: 3. Source: Web of Science).

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. (IF: 9.616, Citations: 5. Source: Web of Science).

Fior R, Maxwell AA, Ma TP, Vezzano A, Moens CB, Amacher SL, Lewis J, Saúde L (2012). Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by Mesogenin1. **Development** 139(24):4656-65. (IF: 7.09, Citations: 29. Source: Web of Science).

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. (IF: 3.54, Citations: 35. Source: Web of Science).

Ongoing Research Projects

2019/2022: Targeting induced-senescent cells: a novel approach to promote spinal cord regeneration in mammals. Coordinator: Maria Leonor Saúde. Funding Agency: "la Caixa" Foundation. Reference: Initiative i4b (HR18-00187). Amount: € 444 048,00. Total Amount: € 444 048,00.

2018/2021: A função das células senescentes induzidas na regeneração da medula espinal. Coordinator: Maria 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.

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.

2016/2019: Angiocrine factors as modulators of spinal cord regeneration. Coordinator: Maria Leonor Saúde. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MED/3295/2014. Amount: € 186 229,00. Total Amount: € 186 229,00.

Publications in Peer Reviewed Journals

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. (IF: 5.547, Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Saúde L. Spinal cord regeneration: what can we learn from zebrafish. CEDOC, Lisbon, Portugal, February 13, 2019.

Saúde L. The zebrafish in biomedical research. AIMS Meeting, Lisbon, Portugal, March 14-15, 2019.

Saúde L. Spinal cord regeneration: what can we learn from zebrafish. BSCB/BSDB Spring Meeting, University of Warwick, Coventry, UK, April 9, 2019.

Saúde L. Regeneração da medula espinhal: o que podemos aprender com o Peixe Zebra? NuBioq, FCT-UNL, Caparica, Portugal, May 8, 2019.

Saúde L. Regeneração da medula espinhal: o que podemos aprender com o Peixe Zebra? Centro de Medicina de Reabilitação de Alcoitão, Portugal, May 14, 2019.

Saúde L. Spinal cord regeneration: what can we learn from animal models? NeuroSeS Seminar Series, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, July 9, 2019.

Saúde L. Spinal cord regeneration: what can we learn from zebrafish. Institute of Science and Technology, Vienna, Austria, November 26, 2019.

Saúde L. Spinal cord regeneration: a tissue microenvironment perspective. 1st DevBioMed Symposium, Champalimaud Foundation, Lisbon, Portugal, December 13, 2019.

Communications in International Conferences

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. Gordon Research Conference: Spinal Cord Injury and Repair: From Molecules to Function, Waterville Valley, June 16-22, 2019. (*Poster Presentation*).

Martins I, Ferreira M, Silva D, Dias F, Morais NB, Saúde L. The Endothelial Cells Transcriptome after Spinal Cord Injury. A tale of two opposite models: Zebrafish vs Mouse. 21st Spinal Research Network Meeting, London, UK, September 6-7, 2019. (*Poster Presentation*).

Ribeiro A, Costa M, Maçarico T, Saúde L. Vascular repair after spinal cord injury in zebrafish. Champalimaud Research Symposium - Tissue Environment in Health and Disease, Lisbon, Portugal, October 8-10, 2019. (*Short Talk*).

Ribeiro A. Vascular repair after spinal cord injury in zebrafish. European Developmental Biology Congress, Alicante, Spain, October 23-26, 2019. (*Flash Talk and Poster Presentation*).

Patents/Prototypes

Patent. Treatment of spinal cord injury, GB1913338.8. September 2019.

Advanced Teaching

Ribeiro A. Development of the Central Nervous System. Genes and Molecules in Development Course, Master in Evolution and Developmental Biology, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, March 19, 2019.

Saúde L. Lecture. The zebrafish as a biomedical research system. IBB PhD Program, Instituto Gulbenkian de Ciência, Oeiras, Portugal, November 4, 2019.

Ribeiro A. Spinal cord regeneration in zebrafish. Genes and Molecules in Development Course, Master in Evolution and Developmental Biology, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, November 7, 2019.

Science and Society

Saúde L. Dia Internacional da Mulher Exhibition, Pavilhão do Conhecimento, Lisbon, Portugal, March 8, 2019.

Saúde L. Fundraising Call Centre for Maratona da Saúde, March 23, 2019.

Saúde L. Tarde Aberta Professores, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 3, 2019.

Saúde L. 90 Segundos de Ciência, Antena 2 Interview, July 18, 2019.

Silva D. “Noite Europeia dos Investigadores” - Sociedade Portuguesa de Biologia do Desenvolvimento Stand. Museu Nacional de História Natural e da Ciência, Lisbon, Portugal, September 27, 2019.

Saúde L. Horizontes iMM: Uma pergunta a três, Ciclo de conversas, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 16, 2019.

Luís Costa Lab

Major Interests/Objectives

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 involved in 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.

Head of Laboratory

Luís António Marques da Costa, MD, PhD, Director of the Oncology Division of HSM-CHULN, Director of the Clinical Research Center, CAML, Associate Professor, FMUL

Team

Ana Cláudia Martins Cavaco	PhD	Postdoctoral Researcher (Started January)
Ana Leonor Pereira Bruçó	Master Degree	Lab Technician (Started February)
André Miguel Branco Mansinho	MD/Master Degree	Clinical Researcher (Started February)
António Manuel Marujo Palma	Master Degree	MSc Student (Left June)
Arlindo Júlio Rebelo da Silva Ferreira	MD/Master Degree	Clinical Researcher
Catarina Pinheiro Barracha Pinto de Abreu	Master Degree	MSc Student (Left June)
Daniela Maria Grou Ramalho	Master Degree	Trainee (Left March)
Inês Fernandes Gomes	Master Degree	PhD Student
Isabel Cristina Ferreira Fernandes Borges da Costa	MD/PhD	Clinical Researcher
João Brito Colaço Carvalho Belo	University Degree	MSc Student (Started September)
Marta Sofia Alves Martins	PhD	Staff Scientist
Patrícia Borges Alves	Master Degree	MSc Student
Patrícia Isabel Martins Corredeira	Master Degree	Lab Technician
Paulina Flávia da Costa Piairo	PhD	Lab Technician (Left November)
Pedro Nuno Lopes Mendes Calheiros Andrade	University Degree	Lab Technician (Left December)
Raquel Sofia Cruz Duarte	Master Degree	PhD Student
Sandra Cristina Cara de Anjo Casimiro	PhD	Staff Scientist

Soraia Lobo de Lourdes Martins	MD/Master Degree	Clinical Researcher (Started November)
Teresa Raquel Duarte Pacheco	PhD	Senior Postdoctoral Researcher
Tito Miguel Palmela Leitão	MD/University Degree	Clinical Researcher

Laboratory Keywords / Research Areas

Metastasis, Organotropism, Heterotypic Signaling, Oncodynamics, Liquid Biopsy, Metastization, Resistance to Therapy, Tumor-Host Interface.

Major Scientific Achievements

During 2019, we consolidated patient's enrollment in the Oncodynamics Biobanking project (ODB), which is a clinically annotated prospective collection of liquid biopsies from breast, prostate, colorectal and melanoma cancer patients. This project was designed to characterize both the host immune response and tumor clonal evolution during metastatic cancer progression under therapy. ODB cohort has now 156 patients.

We established an international collaboration with Illumina Inc., towards the comprehensive genetic and genomic portrait of our large and clinically annotated biobank of human colorectal cancer (CRC), focusing in the identification of new prognostic and predictive biomarkers. In the scope of this collaboration, WES and RNAseq were performed in 168 samples of CRC, rendering high quality data for bioinformatics analysis. This collaboration is currently being expanded to the analysis of other types of cancer.

Selected Publications

Ferreira AR, Ribeiro J, Miranda A, Mayer A, Passos-Coelho JL, Brito M, Fernandes J, Gouveia J, Costa L, Vaz-Luis I (2019). Effectiveness of Adjuvant Ovarian Function Suppression in Premenopausal Women With Early Breast Cancer: A Multicenter Cohort Study. **Clinical Breast Cancer** 19(5):e654-e667. (IF: 2.762, Citations: 0. Source: Thomson Reuters).

Willumsen N, Ali SM, Leitzel K, Drabick JJ, Yee N, Polimera HV, Nagabhairu V, Krecko L, Ali A, Maddukuri A, Moku P, Ali A, Poulouse J, Menon H, Pancholy N, Costa L, Karsdal MA, Lipton A (2019). [Collagen fragments quantified in serum as measures of desmoplasia associate with survival outcome in patients with advanced pancreatic cancer.](#) **Scientific Reports** 9(1):19761. (IF: 4.122, Citations: 0. Source: Thomson Reuters).

Costa L, Ferreira AR (2017). Adjuvant zoledronic acid to treat breast cancer: not for all. **Lancet Oncology** 18(11):1437-1439. (IF: 35.386, Citations: 2. Source: Web of Science).

Body JJ, Casimiro S, Costa L (2015). Targeting bone metastases in prostate cancer: improving clinical outcome. **Nature Reviews Urology** 12: 340-56. (IF: 9.333, Citations: 47. Source: Web of Science).

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. (IF: 28.349, Citations: 607. Source: Web of Science).

Ongoing Research Projects

2018/2021: 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 para a Tecnologia. Reference: PTDC/MED-ONC/28636/2017. Amount: € 234 615,31. Total Amount: € 234 615,31.

2018/2021: Inervação patológica em metástases ósseas: OSTEOCLASTOS, o que estão a fazer? Coordinator: Sandra Casimiro. Funding Agency: Fundação para a Ciência e para a Tecnologia. Reference: POCI-01-0145-FEDER-030158. Amount: € 6 250,00. Total Amount: € 239 504,80.

2017/2020: ONCODYNAMICS. Coordinator: Luis Costa. Funding Agency: Several. Reference: ONCODYNAMICS. Amount: € 286 461,20. Total Amount: € 286 461,20.

2009/2019: Cancer Genomics Consortium. Coordinator: Luis Costa. Funding Agency: Several. Reference: GCGC. Amount: € Amount: € 437 174,00. Total Amount: € 437 174,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Alvim CM, Mansinho A, Paiva R, Brás R, Semedo PM, Martins SL, Ponte CB, Macedo D, Ribeiro L, Reis JP, Fernandes I, Costa L (2019). Prognostic factors for patients treated with abiraterone.

Future Science 6(2): FSO436. (IF 2.321, Citations: 0).

Dionísio MR, Mansinho A, Abreu C, Cavaco-Silva J, Casimiro S, Costa L (2019). Clinical and translational pharmacology of drugs for the prevention and treatment of bone metastases and cancer-induced bone loss. **British Journal of Clinical Pharmacology** 85(6):1114-1124. (IF: 3.867,

Citations: 3. Source: Thomson Reuters).

Ferreira AR, Ribeiro J, Miranda A, Mayer A, Passos-Coelho JL, Brito M, Fernandes J, Gouveia J, Costa L, Vaz-Luis I (2019). Effectiveness of Adjuvant Ovarian Function Suppression in Premenopausal Women With Early Breast Cancer: A Multicenter Cohort Study. **Clinical Breast Cancer** 19(5):e654-e667. (IF: 2.762, Citations: 0. Source: Thomson Reuters).

Cancer 19(5):e654-e667. (IF: 2.762, Citations: 0. Source: Thomson Reuters).

Gano L, Pinheiro T, Matos AP, Tortosa F, Jorge TF, Gonçalves MS, Martins M, Morais TS, Valente A, Tomaz AI, Garcia MH, Marques F (2019). Antitumour and Toxicity Evaluation of a Ru(II)-Cyclopentadienyl Complex in a Prostate Cancer Model by Imaging Tools. **Anti-Cancer Agents in Medicinal Chemistry** 19(10):1262-1275. (IF: 2.556, Citations: 0. Source: Thomson Reuters).

Medicinal Chemistry 19(10):1262-1275. (IF: 2.556, Citations: 0. Source: Thomson Reuters).

Garrido P, Fernandes I, Soares-Almeida L, Borges-Costa J (2019). Postirradiation pseudosclerodermatous panniculitis mimicking a Kaposi sarcoma recurrence. **International Journal of Dermatology** 58(12):e249-e250. (IF: 1.794, Citations: 1. Source: Thomson Reuters).

Journal of Dermatology 58(12):e249-e250. (IF: 1.794, Citations: 1. Source: Thomson Reuters).

Gil Marques F, Poli E, Malaquias J, Carvalho T, Portêlo A, Ramires A, Aldeia F, Ribeiro RM, Vitorino E, Diegues I, Costa L, Coutinho J, Pina F, Mareel M, Constantino Rosa Santos S (2019). Low doses of ionizing radiation activate endothelial cells and induce angiogenesis in peritumoral tissues.

Radiotherapy and Oncology 141:256-261. (IF: 5.252, Citations: 0. Source: Thomson Reuters).

Lopes MB, Casimiro S, Vinga S (2019). Twiner: correlation-based regularization for identifying common cancer gene signatures. **BMC Bioinformatics** 20:356. (IF: 2.511, Citations: 0. Source: Thomson Reuters).

BMC Bioinformatics 20:356. (IF: 2.511, Citations: 0. Source: Thomson Reuters).

Loureiro H, Carrasquinha E, Alho I, Ferreira AR, Costa L, Carvalho AM, Vinga S (2019). Modelling cancer outcomes of bone metastatic patients: combining survival data with N-Telopeptide of type I collagen (NTX) dynamics through joint models. **BMC Medical Informatics and Decision Making** 19:13. (IF: 2.067, Citations: 1. Source: Thomson Reuters).

Medical Informatics and Decision Making 19:13. (IF: 2.067, Citations: 1. Source: Thomson Reuters).

Macedo D, Garrido PM, Fernandes I, Santana A, Guerra J, Borges-Costa J (2019). Kaposi sarcoma in solid organ transplant recipients: a challenging case. **Journal of the Portuguese Society of Dermatology and Venereology** 77(3):257-260. (IF:--, Citations: 0. Source: Thomson Reuters).

Magno L, Lessard CB, Martins M, Lang V, Cruz P, Asi Y, Katan M, Bilsland J, Lashley T, Chakrabarty P, Golde TE, Whiting PJ (2019). Alzheimer's disease phospholipase C-gamma-2 (PLCG2) protective variant is a functional hypermorph. **Alzheimer's Research & Therapy** 11:16. (IF: 6.142, Citations: 2. Source: Thomson Reuters).

Mansinho A, Ferreira A, Casimiro S, Alho I, Vendrell I, Costa AL, Sousa R, Abreu C, Pulido C, Macedo D, Pacheco T, Correia L, Costa L (2019). Levels of circulating fibroblast growth factor 23 (FGF23) and prognosis in cancer patients with bone metastases. **International Journal of Molecular Sciences** 20(3):695. (IF: 4.183, Citations: 0. Source: Thomson Reuters).

Martins Cavaco AC, Eble JÁ (2019). A 3D Spheroid Model as a More Physiological System for Cancer-Associated Fibroblasts Differentiation and Invasion *In Vitro* Studies. **Journal of Visualized Experiments** 8(150):e60122. (IF: 1.108, Citations: 0. Source: Thomson Reuters).

Matos CP, Addisa Y, Nunes P, Barroso S, Alho I, Martins M, Matos APA, Marques F, Cavaco I, Pessoa JC, Correia I (2019). Exploring the cytotoxic activity of new phenanthroline salicylaldimine Zn(II) complexes. **Journal of Inorganic Biochemistry** 198:110727. (IF: 3.224, Citations: 2. Source: Thomson Reuters).

Patel VM, Flanagan CE, Martins M, Jones CL, Butler RM, Woollard WJ, Bakr FS, Yoxall A, Begum N, Katan M, Whittaker SJ, Mitchell TJ (2019). Frequent and Persistent PLCG1 Mutations in Sézary Cells Directly Enhance PLCγ1 Activity and Stimulate NFκB, AP-1, and NFAT Signaling. **Journal of Investigation in Dermatology** 140(2):380-389. (IF: 6.29, Citations: 0. Source: Thomson Reuters).

Querido S, Fernandes I, Weigert A, Casimiro S, Albuquerque C, Ramos S, Adragão T, Luz I, Paixão P, Chasqueira M, Santos M, Machado D (2019). High-grade urothelial carcinoma in a kidney transplant recipient after JC virus nephropathy: the first evidence of JC virus as a potential oncovirus in bladder cancer. **American Journal of Transplantation**. (IF: 7.163, Citations: 0. Source: Thomson Reuters).

Rivas F, Medeiros A, Comini M, Suescun L, Rodríguez Arce E, Martins M, Pinheiro T, Marques F, Gambino D (2019). Pt-Fe ferrocenyl compounds with hydroxyquinoline ligands show selective cytotoxicity on highly proliferative cells. **Journal of Inorganic Biochemistry** 199:110779. (IF: 3.224, Citations: 0. Source: Thomson Reuters).

Santos AP, Vinagre J, Soares P, Claro I, Sanches A C, Gomes L, Fernandes I, Catarino AL, Preto J, Pereira BD, Marques AP, Rodrigues F, Amaral C, Rocha G, Mellidez JC, Simões H, Lopes JM, Bugalho MJ (2019). Gastroenteropancreatic Neuroendocrine Neoplasia Characterization in Portugal: Results from the NETs Study Group of the Portuguese Society of Endocrinology, Diabetes and Metabolism. **International Journal of Endocrinology** 2019:4518742. (IF: 2.287, Citations: 0. Source: Thomson Reuters).

Sousa SA, Leitão JH, Silva RAL, Belo D, Santos IC, Guerreiro JF, Martins M, Fontinha D, Prudêncio M, Almeida M, Lorcy D, Marques F (2019). On the path to gold: Monoanionic Au bisdithiolate complexes with antimicrobial and antitumor activities. **Journal of Inorganic Biochemistry** 202:110904. (IF: 3.224, Citations: 0. Source: Thomson Reuters).

von Moos R, Costa L, Gonzalez-Suarez E, Terpos E, Niepel D, Body JJ (2019). Management of bone health in solid tumours: From bisphosphonates to a monoclonal antibody. **Cancer Treatment Reviews** 76:57-67. Review. (IF: 8.332, Citations: 7. Source: Thomson Reuters).

Willumsen N, Ali SM, Leitzel K, Drabick JJ, Yee N, Polimera HV, Nagabhairu V, Krecko L, Ali A, Maddukuri A, Moku P, Ali A, Poulouse J, Menon H, Pancholy N, Costa L, Karsdal MA, Lipton A (2019). [Collagen fragments quantified in serum as measures of desmoplasia associate with survival outcome in patients with advanced pancreatic cancer.](#) **Scientific Reports** 9(1):19761. (IF: 4.122, Citations: 0. Source: Thomson Reuters).

Other International Publications

Liu L, Garbutt C, Golkaram M, Kaplan S, Martins M, Casimiro S, Mansinho A, Macedo D, Alvim C, Costa AL, Fernandes A, Ferreira C, Aldeia F, Quintela A, Costa L, So A, Zhang S, Pawlowski T. (2019). Microsatellite instability testing and lynch syndrome screening for colorectal cancer patients through tumour sequencing. **Annals of Oncology** 30 (suppl_5): v574-v584.

Invited Lectures and Seminars

Mansinho A. Biologia do Cancro e seus desafios. MUNHAC-ULisboa, Lisbon, Portugal, February 21, 2019.

Fernandes I. Sarcomas de tecidos moles e GIST. Curso de Oncologia SPO 2019 (3ª edição) - Sociedade Portuguesa de Oncologia, Curia, Portugal, February 25, 2019.

Costa L. Breast cancer and the bone: recent studies. Innovation Breast Cancer, Madrid, Spain, March 1, 2019.

Mansinho A. Programa de Investigação Clínica EMPOWER 3ª Edição. FFUL, Lisbon, Portugal, March 16, 2019

Leitao T. II Jornadas Temáticas Patient Care — Urologia para Medicina Geral e Familiar, Lisbon, Portugal, April 11, 2019.

Costa L. Impact of Innovation in Patients and Society. Science and Innovation Congress Switzerland - Portugal 2019, Lisbon, Portugal, May 2, 2019.

Costa L. European Association for Cancer Education – 32nd Annual Scientific Meeting, Porto, Portugal, May 9, 2019.

Costa L. Immuno-Oncology in Other Solid Tumors. I ASEICA-ASPIC International Meeting, Salamanca, Spain, September 13, 2019.

Mansinho A. Qual o tratamento de escolha em primeira linha: Imunoterapia, TKI's ou combinação? - GPGU: Curso de Imunoterapia no Carcinoma de Células Renais Metastizado, Lisbon, Portugal, October 12, 2019.

Costa L. Tumor Microenvironment: “Back to Medicine”. Dev BioMed Symposium, Lisbon, Portugal, December 13, 2019.

Communications in International Conferences

Lobo Martins S, Semedo P, Martins-Branco D, Monteiro AM, Alvim C, Pais HL, Vendrell I, Mansinho A, Gouveia E, José-Passos M, Costa L. Hematological profile: prognostic tool in melanoma patients treated with immunotherapy. ASCO-SITC Clinical Immuno-Oncology Symposium 2019, San Francisco, EUA, February 28-March 02, 2019. (*Poster Presentation*).

Lobo-Martins S, Semedo PM, Alvim C, Luna Pais H, Paiva R, Pinto C, Ribeiro L, Macedo D, Fernandes I, Vendrell I, Mansinho A, Sousa R, Costa L. Stage II colon cancer: adjuvant chemotherapy in the real world, still a challenge. 9th European Multidisciplinary Colorectal Cancer Congress, Lisbon, Portugal, March 9-11, 2019. *(Poster Presentation)*.

Janeiro J, Ninitas P, Ferreira NCSD, Presa MD, Fernandes I, Soares de Brito J, Portela J, Fonseca-Santos J. Efficacy and diagnostic accuracy of image guided percutaneous musculoskeletal biopsy – evaluation of 8 years' experience at a tertiary-care hospital. ESSR 2019, Lisbon, Portugal, June 26-29, 2019. *(Poster Presentation)*.

Rebelo SD, Ferreira RD, Lopes Silva S, Fernandes I, Tornada A. Case Report - Good'S Syndrome in Young Women - An Unusual Presentation. 8th European Congress of Internal Medicine, Lisbon, Portugal, August 29-31, 2019. *(Poster Presentation)*.

Corredeira P, Alves P, Gordino G, Pereira S, Ribot J, Andrade P, Bruçó L, Pinheiro C, Casimiro S, Martins M, Mansinho A, Ribeiro L, Fernandes I, Vendrell I, Pinto C, Dionísio MR, Sousa R, Silva-Santos B, Costa L. T cell profiling in metastatic breast cancer reveals a subtype independent immunosuppressive state. ASEICA-ASPIC International Meeting, Salamanca, Spain, September 12-13, 2019. *(Poster Presentation)*.

Castelão M, Claro AR, Silva P, Rodrigues AB, Amorim AC, Fernandes I, Macedo D, Esteves I, Mouzinho A, Marques JG. To “B” or not to “B”: Cervical lymphadenopathy in a previously healthy 16-year-old boy. Congress of European Academy of Pediatrics, Porto, Portugal, September 19-22, 2019. *(Poster Presentation)*.

Liu L, Garbutt C, Golkaram M, Kaplan S, Martins M, Casimiro S, Mansinho A, Macedo D, Alvim C, Costa AL, Fernandes A, Ferreira C, Aldeia F, Quintela A, Costa L, So A, Zhang S, Pawlowski T. Microsatellite instability testing and lynch syndrome screening for colorectal cancer patients through tumour sequencing. ESMO 2019, Barcelona, Spain, September 27-October 1, 2019. *(Poster Presentation)*.

Brás R, Garrido P, Quadros C, Fernandes I, Presa D, Soares-Almeida LM, Costa L, João Borges-Costa. Dermatofibrosarcoma protuberans – a unicentric retrospective analysis of a 10-year period at tertiary teaching hospital. 2019 CTOS Annual Meeting, Tokio, Japan, November 8-11, 2019. *(Poster Presentation)*.

Figueiredo A, Florindo A, Diogo Delgado D, Pais H, Brás R, Fernandes I, Mareco M, Abrunhosa-Branquinho A, Mendonça V, Pina MF. Kaposi's sarcoma: experience of a radiotherapy center. 2019 CTOS Annual Meeting, Tokio, Japan, November 8-11, 2019. *(Poster Presentation)*.

Florindo A, João Ulrich J, Figueiredo A, Brás R, Fernandes I, Virgínia Mareco V, Abrunhosa-Branquinho A, Mendonça V, Pina MF. Retroperitoneal sarcoma patients treated with radiotherapy after R1 surgery – a single center retrospective study. 2019 CTOS Annual Meeting, Tokio, Japan, November 8-11, 2019. *(Poster Presentation)*.

Garrido P, Brás R, Fernandes I, Soares-Almeida LM, Borges-Costa J. Primary cutaneous sarcomas - a retrospective analysis of a 10-year period at a tertiary teaching hospital. 2019 CTOS Annual Meeting, Tokio, Japan, November 8-11, 2019. *(Poster Presentation)*.

Communications in National Conferences

Mansinho A. Sessão V – Cancro Urotelial – Actualização em Imunoterapia” – VII Perspetivas em Oncologia, Porto, Portugal, February 7-9, 2019. *(Oral Presentation)*.

Mansinho A. Cancro Urológico II – Rim – Tratamento da doença avançada – Update do tratamento de 1ª linha – Encontros da Primavera, Évora, Portugal, April 11-14, 2019 *(Oral Presentation)*.

Leitão T. Cancro da Próstata - Tratamento do Cancro da Próstata Localizado. III Jornadas Temáticas Patient Care — Urologia para Medicina Geral e Familiar, Lisbon, Portugal, April 11, 2019. *(Oral Presentation)*.

Fernandes I. Caso clínico de neoplasia da próstata – dependência e justiça. 13º Congresso Campus Neurológico Sénior, Torres Vedras, Portugal, April 13, 2019. *(Oral Presentation)*.

Fernandes I. Patologia oncológica e limitações do trabalho por turnos com horário noturno Encontro anual de medicina do trabalho. Trabalho por turnos com horário noturno em profissionais de saúde - Sociedade Portuguesa de Medicina do Trabalho, Carcavelos, Portugal, May 10-11, 2019. *(Oral Presentation)*.

Costa L. Immunotherapy in metastatic renal cell cancer. XXIV Workshop Urologia Oncológica / III Multidisciplinary Genitourinary Oncology Course, Lisbon, Portugal, May 17, 2019. *(Oral Presentation)*.

Fernandes I. The place of Cabozantinib in metastatic renal cell cancer. XXIV Workshop Urologia Oncológica, Lisbon, Portugal, May 17-18, 2019. *(Oral Presentation)*.

Mansinho A. State of the art: combination therapy TKI's and immunotherapies: Novel agents – III Multidisciplinary Genitourinary Course, Lisbon, Portugal, May 17-18, 2019. *(Oral Presentation)*.

Mansinho A. Clinical Case Presentation - III Multidisciplinary Genitourinary Course, Lisbon, Portugal, May 17-18, 2019. *(Oral Presentation)*.

Costa L. Cancer and the Host: how dynamics explains outcome. Prémio PULIDO VALENTE, Lisbon, Portugal, May 23, 2019. *(Oral Presentation)*.

Fernandes I. Sarcomas de tecidos moles – seleção e sequenciação da terapêutica sistémica na doença avançada. 1ª Reunião multidisciplinar de sarcomas de tecidos moles, Algarve, Portugal, May 24, 2019. *(Oral Presentation)*.

Mansinho A. Novos desafios apresentados com a imunoterapia na gestão do doente oncológico - AEOP, Évora, Portugal, June 31, 2019. *(Oral Presentation)*.

Costa L. Investigação Clínica para uma Saúde de Qualidade. Encontro Ciência'19, Lisbon, Portugal, July 10, 2019. *(Oral Presentation)*.

Costa L. Antibody-drug conjugates in oncology: a clinical perspective. Protein Conjugates ITN Meeting, Lisbon, Portugal, July 18, 2019. *(Oral Presentation)*.

Costa L. Investigação em Portugal: Clínica, básica ou de translação. I Encontro Nacional de Jovens Investigadores em Oncologia, Porto, Portugal, September 24, 2019. *(Oral Presentation)*.

Costa L. Evolução do tratamento neoadjuvante no Cancro da Mama. Opening Conference, XVIII Jornadas da Sociedade Portuguesa de Senologia, Lisbon, Portugal, October 11, 2019. *(Oral Presentation)*.

Mansinho A. Liquid biopsies in advanced prostate cancer – New Frontiers in Uro-Oncology, Lisbon, Portugal, October 18, 2019. *(Oral Presentation)*.

Fernandes I. Paradigm changes in Metastatic Hormone Sensitive Prostate Cancer (mHSPC). New frontiers in Uro-Oncology, Lisbon, Portugal, October 18, 2019. *(Oral Presentation)*.

Mansinho A. Sessão III – Abordagem multidisciplinar de toxicidades complexas – 7º Simpósio Nacional de Melanoma, Lagos, Portugal, October 25-27, 2019. (*Oral Presentation*).

Mansinho A. Que imunoterapia no carcinoma de células renais em primeira linha terapêutica. 16º Congresso Nacional de Oncologia, Estoril, Portugal, November 28-30, 2019. (*Oral Presentation*).

Brás R, Lobo-Martins S, Melo-Alvim C, Paiva R, Mansinho A, Fernandes I, Costa L. mCRPC tratado com cabazitaxel – análise retrospectiva de eficácia e segurança. 16º Congresso Nacional de Oncologia, Lisbon, Portugal, November 28-30, 2019. (*Poster Presentation*).

Organization of Conferences

Costa L. Scientific Coordinator. I ASEICA-ASPIC International Meeting, Salamanca, Spain, September 13, 2019.

Costa L. Chairmen. New Frontiers in Uro-Oncology, Lisbon, Portugal, October 18, 2019.

Costa L. Organizer. ASPIC Conference - Investigação em Cancro Pediátrico: Onde estamos? Para onde vamos?, Lisbon, Portugal, November 18, 2019.

Mansinho A. Co-Organizer. 16º Congresso Nacional de Oncologia, Centro de Congressos do Estoril, Estoril, Portugal, November 28-30, 2019.

Prizes, Honors and Awards

Gomes I. 1st year Best Oral Presentation. XIII Annual CAML PhD Students' Meeting, Lisbon, Portugal, May 15-17, 2019.

Duarte R. 1st year Second Best Oral Presentation. XIII Annual CAML PhD Students' Meeting, May 15-17, 2019.

Vilhais G. Best Oral Presentation. GAPIC – Dia da Investigação 2019, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Advanced Teaching

Casimiro S. First Opponent, Raquel Mendes, Clinical implications of circulating tumour Cells in breast cancer patients – based on a case report, Integrated Masters in Medicine, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 29, 2019.

Casimiro S. Lecture. Epidemiologia, carcinogénese e factores de risco/exógenos: baseado num caso clínico de carcinoma da mama. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 8, 2019.

Casimiro S. Lecture. Oncogénese e factores de risco endógenos (hereditariedade): baseado num caso clínico de Síndrome de Lynch. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 13, 2019.

Casimiro S. Lecture. Ciclo celular e cancro, biologia da metástase: baseado num caso clínico de adenocarcinoma do ovário. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 22, 2019.

Casimiro S. Lecture. Biologia da Metástase. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 25, 2019.

Casimiro S. Lecture. Tradução de sinal e factores de crescimento: baseado num caso clínico de LMC. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 29, 2019.

Casimiro S. Lecture. Tumor primário, micrometastases e recidiva: baseado num caso clínico de carcinoma da próstata. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 3, 2019.

Casimiro S. Lecture. Identificação Pré-Clínica de Novos Alvos Terapêuticos. UC Descoberta e Desenvolvimento de Novas Drogas em Oncologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 5, 2019.

Mansinho A. Drug Development. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 6, 2019.

Casimiro S. Lecture. Competição cancro-hospedeiro, resposta imunológica: baseado num caso clínico de melanoma. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 18, 2019.

Casimiro S. Lecture. Identificação de novas Estratégias na Classificação de risco e na Terapêutica: baseado num caso clínico de carcinoma da mama. UC Oncobiologia, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 30, 2019.

Casimiro S. Coordinator. UC Journal Club, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 17-20, 2019.

Casimiro S. First Opponent, Lucia Deodata Marques, Cancer therapy: A focus on gut microbiota, Integrated Masters in Medicine, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 28, 2019.

André Mansinho. First Opponent, António Palma, PLCE1 rs2274223 A>G polymorphism and its functional role in Colorectal Cancer, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, June 6, 2019.

Casimiro S. First Opponent, Fabiana Rodrigues, Avaliação da qualidade das amostras de biópsias líquidas de pacientes com tumores urológicos, colhidas e armazenadas no Biobanco-iMM, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 23, 2019.

Science and Society

Costa L. Porque é que o cancro nos escapa? Horizontes IMM: Uma pergunta a três, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 20, 2019.

Casimiro S. Fundo iMM-Laço Open Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 23, 2019.

Casimiro S. Interview about Fundo iMM-Laço. "Tudo a ver" with Paula Bollinger, Kuriakos TV, Lisbon, Portugal, November 19, 2019.

MSc Theses

José Rocha, 22/01/2019, Prognostic role of secreted YB-1 in patients with breast cancer. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sandra Casimiro.

Lucia Deodata Marques, 28/05/2019, Cancer therapy: A focus on gut microbiota, Integrated Masters in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: André Mansinho.

Patrícia Alves, 28/05/2019, Impact of YB-1 expression in breast cancer outcomes under estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2)-targeted therapies. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sandra Casimiro.

António Palma, 04/06/2019, PLCE1 rs2274223 A>G polymorphism and its functional role in Colorectal Cancer, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Marta Martins.

Ana Rita Bello, 19/06/2019, Source of secreted YB-1 in breast cancer microenvironment, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sandra Casimiro.

Catarina Abreu, 19/06/2019, Brain metastases immune characterization and the impact over prognosis, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria Rita Dionísio. Co-Supervisor: Sandra Casimiro.

Pedro Félix, 23/07/2019, Quimiorresistência induzida por sobreexpressão de RANK em cancro da mama do sub-tipo luminal, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sandra Casimiro.

Major Interests / Objectives

Our Unit studies mechanisms underlying induction and maintenance of immune tolerance. In other words, we research methods to reprogram the immune response in situations where the immune system is causing a disease, such as allergy, autoimmunity and transplant rejection.

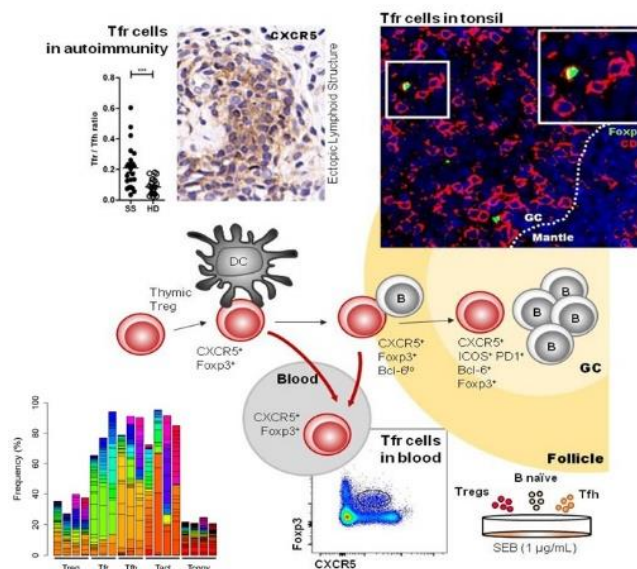
In addition, we are interested in defining the functional properties of lymphocytes that can promote immune tolerance by suppressing pathogenic immune responses. We have been studying how different types of lymphocytes with regulatory function can be induced in the periphery.

We believe that in the foreseeable future antibody therapy, as well as other strategies to modulate the immune system, will have an important repercussion in the quality of life of people suffering from immune mediated diseases.

Head of Laboratory

Luís Ricardo Simões da Silva Graça, MD/PhD, Full Professor

Graphical Abstract



Team

Afonso Silva Pinto Basto	PhD	Senior Postdoctoral Researcher (Left February)
Ana Catarina Jorge Mendes	University Degree	Lab Manager
Ana Isabel Neves de Matos	Master Degree	Trainee
António Maria Forsado Martins Gonçalves	University Degree	MSc Student (Started February, Left December)
Carina Sofia Gonçalves Peres	Master Degree	PhD Student
Filipa Ramos de Moura Ribeiro	Master Degree	PhD Student
Kátia Ribeiro de Jesus	Master Degree	Lab Technician (Left August)
Pedro Manuel Ávila Ribeiro	Master Degree	PhD Student
Raquel Filipa Reis de Freitas	PhD	PhD Student (Left March)
Ricardo Jorge Pires Correia	University Degree	MSc Student (Left July)
Rodrigo Balsinha Pedroso	Master Degree	PhD Student (Started September)
Ruy Miguel Sousa Soeiro de Figueiredo Ribeiro	PhD	Senior Postdoctoral Researcher
Sara Daniela Botelho Rosa	University Degree	MSc Student (Started February)
Saumya Dileep Kumar	Master Degree	PhD Student
Tania Portilla Carmenate	PhD	Consultant (Started May, Left August)
Válter Bruno Ribeiro Fonseca	PhD	Postdoctoral Researcher
Vanessa Alexandra Gonçalves de Oliveira Martins	MD/PhD	Clinical Researcher

Laboratory Keywords / Research Areas

Immune Tolerance, Regulatory T-cell Subsets, T Follicular Helper (Tfh) Cells, T Follicular Regulatory (Tfr) Cells, Germinal Centre, Allergy, Autoimmunity, Transplantation.

Major Scientific Achievements

We found that Tfh and Tfr cells in the same germinal center differ in their TCR usage: Tfh cells are specific to the immunizing antigen, and Tfr cells retain a TCR specificity similar to Tregs. These results suggest Tfh cells select high-affinity BCRs during affinity maturation, while Tfrs prevent autoimmunity.

We established, using human samples, that human circulating Tfr cells are generated in lymphoid tissues following exposure to antigens, and are not fully mature.

We have shown that adoptive transfer of Foxp3+ iNKT cells, due to CXCR6-mediated preferential hepatic homing, leads to liver-specific immune suppression allowing long-term survival of allogeneic islet transplants delivered through intra-portal route in mice.

Finally, we have started a number of clinical studies regarding the impact of Tfh subsets in antibody-mediated human diseases, and how Tfh and Tfr subsets can be used as biomarkers.

Selected Publications

Deng J, Wei Y, Fonseca VR, Graca L*, Yu D* (2019). T follicular helper cells and T follicular regulatory cells in rheumatic diseases. **Nature Reviews Rheumatology** 15:475-490. (IF: 18.545, Citations: 5. Sources: Web of Science and Scopus).

Fonseca VR, Ribeiro F, Graca L (2019). Dissecting the Complexity of T Follicular Regulatory Cells. **Immunological Reviews** 288:112-127. (IF: 11.292, Citations: 4. Sources: Web of Science and Scopus).

Fonseca VR, Romão VC, Agua-Doce A, Santos M, López-Presa D, Ferreiras AC, Fonseca JE, Graca L (2018). The Ratio of Blood T Follicular Regulatory Cells to T Follicular Helper Cells Marks Ectopic Lymphoid Structure Formation While Activated Follicular Helper T Cells Indicate Disease Activity in Primary Sjögren's Syndrome. **Arthritis Rheumatology** 70:774-784. (IF: 9.002, Citations: 23. Sources: Web of Science and Scopus).

Fonseca VR, Agua-Doce A, Maceiras AR, Pierson W, Ribeiro F, Romão VC, Pires AR, Silva SL, Fonseca JE, Sousa AE, Linterman MA, Graca L (2017). Human Blood CXCR5+Foxp3+ T cells Are Indicators of Ongoing Humoral Activity Not Fully Licensed With Suppressive Function. **Science Immunology** 2: eaan1487. (IF: 10.551, Citations: 35. Source: Web of Science and Scopus).

Maceiras R, Almeida SCP, Mariotti-Ferrandiz E, Chaara W, Jebbawi F, Six A, Hori S, Klatzmann D, Faro J, Graca L (2017). T follicular helper and T follicular regulatory cells from the same germinal centers have different TCR-specificity. **Nature Communications** 8:15067. (IF: 12.353, Citations: 34. Sources: Web of Science and Scopus).

Oliveira VG, Água-Doce A, Curotto de Lafaille MA, Lafaille JJ, Graça L (2013). Adjuvant facilitates tolerance induction to factor VIII in hemophilic mice through a Foxp3-independent mechanism that relies on IL-10. **Blood** 121(19):3936-3945. (IF: 16.601, Citations: 13. Sources: Web of Science and Scopus).

Wollenberg I, Água-Doce A, Hernández A, Almeida C, Oliveira VG, Faro J, Graça L (2011). Regulation of the germinal center reaction by Foxp3+ follicular regulatory T cells. *Journal of Immunology* 187(9):4553-4560. (IF: 4.718, Citations: 284. Sources: Web of Science and Scopus).

Ongoing Research Projects

2018/2019: Material Transfer Agreement. Coordinator: Luís Graça. Funding Agency: Alpine Immune Sciences, Inc. Reference: Alpine. Amount: € 26 875,00. Total Amount: € 26 875,00.

2016/2019: Mechanisms used by T follicular helper (Tfh) cells to determine antibody isotype production in Th1 versus Th2 responses. Coordinator: Luis Graca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/IMI-IMU/7038/2014. Amount: € 199 971,00. Total Amount: € 199 971,00.

2016/2019: Immunomodulatory effect of CD6-targeting in neuroinflammation. Coordinator: Vanessa Martins. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-FTO/3080/2014. Amount: € 162 488,00. Total Amount: € 193 092,00.

2015/2019: Multidisciplinary strategy to develop novel multicomponent nanoscale systems for immune modulation. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: UTAP-ICDT/DTP-FTO/0016/2014. Amount: € 27 000,00. Total Amount: € 189 274,00.

2015/2019: ENLIGHT-TEN: European Network linking informatics and genomics of helper T cells. Coordinator: Luís Graça. Funding Agency: European Commission. Reference: MSCA ITN 675395. Amount: € 433 512,72. Total Amount: € 3 354 685,20.

Publications in Peer Review Journals

Alberca Custodio RW, Mirotti L, Gomes E, Nunes FPB, Vieira RS, Graca L, Almeida RR, Câmara NO, Russo M (2019). Dendritic Cells Expressing MyD88 Molecule Are Necessary and Sufficient for CpG-Mediated Inhibition of IgE Production In Vivo. **Cells** 8(10):1165. (IF: 5.656, Citations: 0. Sources: *Web of Science and Scopus*).

Freitas RF, Basto AP, Almeida SCP, Santos RF, Gonçalves CM, Osorio JC, Carmo A, Leon K, Graca L (2019). Modulation of CD4 T cell function via CD6-targeting **EBioMedicine** 47:427-435. (IF: 6.680, Citations: 1. Sources: *Web of Science and Scopus*).

Deng J, Wei Y, Fonseca VR, Graca L, Yu D (2019). T follicular helper cells and T follicular regulatory cells in rheumatic diseases. **Nature Reviews Rheumatology** 15(8):475-490. (IF: 18.545, Citations: 5. Sources: *Web of Science and Scopus*).

Fonseca VR, Ribeiro F, Graca L (2019). Dissecting the Complexity of T Follicular Regulatory Cells. **Immunological Reviews** 288(1):112-127. (IF: 11.292, Citations: 4. Sources: Web of Science and Scopus).

Rojas G, Carmenate T, Santo-Tomas JF, Valiente PA, Becker M, Perez-Riveron A, Tundidor Y, Ortiz Y, de Cossio-Diaz JF, Graca L, Dubel S, Leon K (2019). Directed evolution of super-secreted variants from phage-displayed human Interleukin-2. **Scientific Reports** 9:800. (IF: 4.011, Citations: 0. Sources: Web of Science and Scopus).

Fonseca VR, Graca L (2019). Contribution of Foxp3+ Tfr cells for overall human blood CXCR5+ T lymphocytes. **Clinical and Experimental Immunology** 195(3):302-304. (IF: 3.711, Citations: 1. Sources: Web of Science and Scopus).

Invited Lectures and Seminars

Graça L. Specialized regulatory T cells in human autoimmune rheumatic diseases. University of Jinan, Guangzhou, China, January 12, 2019.

Graça L. Tissue adaptation of different subsets of human T follicular cells. 5th Workshop on Dendritic Cell Biology, Fundação Champalimaud, Lisbon, Portugal, March 27-29, 2019.

Graça L. Tissue adaptation of follicular T cells. 5th Workshop on Dendritic Cell Biology, European Federation of Immunology Societies – T Cell Interest Group, Lisbon, Portugal, May 7-8, 2019.

Graça L. Tissue adaptation of follicular T cells. Departmental Seminar, Institute for Immunology, Ludwig-Maximilians-Universität München, Munich, Germany, May 23, 2019.

Graça L. Tissue adaptation of T cell subsets. 3rd Symposium on Immunomodulation in Cancer and Regeneration, Porto, Portugal, June 25, 2019.

Graça L. Specialized regulatory T cells in human autoimmune diseases. Ciência 2019, Lisbon, Portugal, July 19, 2019.

Graça L. Tissue adaptation of follicular T cell subsets. Single Cell Immunology Symposium, Finnish Society for Immunology, Turku, Finland, August 21, 2019.

Graça L. Tfh and Tfr cell heterogeneity in humoral immunity and autoimmunity. STIMM seminar in translational immunology, University of Zurich, Zurich, Switzerland, October 2, 2019.

Graça L. Specialized regulatory T cells in human autoimmunity. International ITU Molecular Biology and Genetic Congress 2019, Istanbul Technical University, Istanbul, Turkey, October 4-6, 2019.

Graça L. T follicular regulatory cells in humans and mice. IUIS International Congress of Immunology 2019, Beijing, China, October 19-23, 2019.

Graça L. T follicular regulatory cells in humans and mice. International Symposium of Immunity and Health, University of Jinan, Guangzhou, China, October 24, 2019.

Graça L. Immune regulation in protective and pathological immune responses. Departmental Seminar, City University of Hong Kong, Hong Kong, November 8, 2019.

Graça L. Specialized regulatory cells in human tolerance. Departmental Seminar, Chinese University of Hong Kong, Hong Kong, November 8, 2019.

Graça L. Follicular T cell subsets. Internal Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 27, 2019.

Communications in International Conferences

Basto AP, Maceiras A, Almeida SC, Campos P, Ribeiro F, Kumar S, Russo M, Graça L. T follicular helper, T follicular regulatory and germinal center B cells induced by type-1 and type-2 adjuvants. Keystone Symposia on Molecular and Cellular Biology - B Cell-T Cell Interactions/Molecular Approaches to Vaccines and Immune Monitoring, Keystone, Colorado, USA, February 10-14, 2019. (*Poster Presentation*).

Matos AI, Carreira B, Peres C, Moura L, Viana AS, Conde JP, Graça L, Satchi-Fainaro R, Florindo HF. Targeted nanovaccine as a powerful platform to treat colorectal cancer. 11th iMed.Ulisboa Postgraduate Students Meeting & 4th i3DU Meeting, Lisbon, Portugal, July 15, 2019. (*Poster Presentation*).

Peres C, Matos A, Carreira C, Moura L, Coniot C, Scomparin A, Yeini E, Pozzi S, Graça L, Pr at V, Satchi-Fainaro R, Florindo H. Multi-targeting nano-based platform as an effective immunotherapy against solid tumors. Nanotechnology in Cancer: Engineering for Oncology, Cambridge, UK, September 12-14, 2019.

Peres C, Matos AI, Carreira B, Moura L, Conriot J, Scomparin A, Yeini E, Pozzi S, Graça L, Preat V, Satchi-Fainaro R, Florindo HF. Multi-targeting nano-based platform as an effective immunotherapy against solid tumors. *Nanotechnology in Cancer: Engineering for Oncology*, Cambridge, UK, September 12-14, 2019.

Matos AI, Carreira B, Moura L, Peres C, Viana AS, Conde JP, Graça L, Satchi-Fainaro R, Florindo HF. Targeted nanovaccine as a powerful platform to treat colorectal cancer. *Nanotechnology in Cancer: Engineering for Oncology*, Cambridge, UK, September 12-14, 2019. (*Poster Presentation*).

Florindo HF, Peres C, Matos AI, Moura L, Conriot J, Yeini E, Viana AS, Graça L, Pr eat V, Satchi-Fainaro R. Polymeric nano-vaccines improved immune checkpoint anti-tumor efficacy against breast cancer. *NanoBio&Med2018*, Barcelona, Spain, November 20-22, 2019.

Communications in National Conferences

Kumar S, Fonseca R V, Jesus K, Correia R,  gua-Doce A, Monteiro M, Graça L. Tissue adaptation of human T follicular cells. *iMM Scientific Retreat*, Universidade de  vora and Instituto de Medicina Molecular Jo o Lobo Antunes,  vora and Lisbon, Portugal, April 15-16, 2019. (*Oral Presentation*).

Kumar S, Bastos A, Almeida SCP, Campos P, Russo M, Carvalho M, Graça L. T follicular helper (Tfh) cells under different immune responses. *XIII Annual CAML PhD Students' Meeting*, Instituto de Medicina Molecular Jo o Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Organization of Conferences

Graça L. *As Fronteiras das Ci ncias M dicas* (conference series being on advances on medical sciences, being held alternately in the two medical schools in Lisbon, organized by Sociedade das Ci ncias M dicas de Lisboa). One monthly seminar at NOVA Medical School and Faculdade de Medicina da Universidade de Lisboa, 2019.

Graça L. *Symposium on Immunology in cancer and regeneration*, Porto, 25 June 2019. (Member of Scientific Council).

Internationalisation

Filipa Ribeiro has been in Institut Curie, Paris, for 3 weeks (January/February) to work on single-cell genomics experiments. These were performed in collaboration with Eliane Piaggio's group.

Filipa Ribeiro spent 6 weeks at Icahn School of Medicine at Mount Sinai, NY, in Hideki Ueno's group. This collaborative work allowed us to learn an in vitro system to study the differentiation of human follicular T cells.

Prizes, Honours and Awards

Graca L. Prémio Científico Universidade de Lisboa/Caixa Geral de Depósitos in Health Sciences. Universidade de Lisboa, Lisbon, Portugal, January 2019.

Graca L. Prémio Ordem dos Médicos/Banco Carregosa, honorary mention. Ordem dos Médicos, Portugal, March 2019.

Graca L. Recognition for contribution to health sciences. Câmara Municipal de Odemira, Odemira, Portugal, September 2019.

Fonseca V. Prémio Jorge Horta. Ordem dos Médicos, Lisbon, Portugal, June 26, 2019.

EACR-Worldwide Cancer Research Meeting Bursary (travel, accommodation, and free registration awards) from the European Association for Cancer Research - EACR to attend the Nanotechnology in Cancer: Engineering for Oncology, Cambridge, UK, September 12-14, 2019.

Filipa Ribeiro. AAI Travel for Techniques Award for an internship at Icahn School of Medicine at Mount Sinai, New York, USA, May 1-June 15, 2019.

Filipa Ribeiro. Travel Grant. Sociedade Portuguesa de Imunologia, June 2019.

Filipa Ribeiro. Travel Award. Fundação Luso-Americana para o Desenvolvimento, March 2019.

Industry Contract Research

2019/2020: Immune modulatory activity of exosomes. Coordinator: Luís Graça. Funding Agency: Exogenus.

2018/2019: Material Transfer Agreement. Coordinator: Luís Graça. Funding Agency: Alpine Immune Sciences, Inc. Reference: ALPINE. Amount: € 26 875,00. Total Amount: € 26 875,00.

2015/2019: Immune modulatory activity of CD6-targeting monoclonal antibodies. Coordinator: Luís Graça. Funding Agency: Centre of Molecular Immunology. Reference: CUBA - CD6. Amount: € 43 700,00. Total Amount: € 43 700,00.

Advanced Teaching

Graça L. T follicular helper cells. Interface PhD Program, Museu do Oriente, Lisbon, Portugal, March 8, 2019.

Basto AP. Vaccines and Adjuvants – MSc in Clinical Microbiology and Emergent Infectious Diseases, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

Science and Society

Graça Lab collaborated with visual artist Marta de Menezes towards the creation of a new artwork inspired by the lab research. The artworks created in Graça Lab during 2018 were part of exhibitions in: FACT, Mexico City, Mexico; Extravagant Bodies, in Zagreb, Croatia; and Ars Electronica 2019 in Linz, Austria.

Graça L was part of a project to promote art and science at Palácio da Cultura Ilido Lobo, Praia, Cabo Verde, January 19, 2019.

Graça L was invited speaker at a debate to celebrate the International Day of Immunology with the title “How the immune system protects us from infection and cancer”, Palácio do Marquês, Oeiras, Portugal, April 29, 2019.

The Graça Lab participated in activities to promote the awareness of immunology among young audiences as part of the “International Immunology Day”. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 29, 2019.

Graça L was interviewed for the TV program Corpo Clínico, Saude+ TV network, November 2019.

Graça L was part of the organizing committee of FACTT Festival as scientific consultant. FACTT organized visual art exhibitions and seminars, exploring the interface of science and art, in Lisbon (MAAT and Culturgest), New York (School of Visual Arts, Parsons School of Design, and NYU), and Mexico City (Centro de Cultura Digital and UNAM). FACTT is coordinated by the ARTE Institute, New York.

Graça L. Co-Organizer of international conference: ART#18. Faculdade de Belas Artes, Universidade de Lisboa, Lisbon, Portugal, October 2019.

Graca L, de Menezes M led an Artist/scientist walk at Ars Eletronica Festival 2020, Linz, Austria, September 7, 2019.

Invited speaker:

Graça L. Biological Artworks: a View from the Laboratory. II Symposium Art & Science. Universidad de los Andes, Santiago, Chile, September 23-24, 2019.

Graça L. Biological Artworks: a View from the Laboratory. LASER – Leonardo Art Science Evening Rendezvous, organized by the Leonardo Journal. Duddell's Club, Hong Kong, November 6, 2019.

Publications:

Gonzalez Valerio MA, de Menezes M, Vesna V, Sebjanic R, Ballengee B, Gracie A, Bios ex Machina, High K, Ortega L, Bioscenica, Lobato J, Graca L, Abreu Afonso MF, Zaineh JÁ, Tod A, Lopes MM, Bernardino Bastos P (2019). Spaces of Species. In TABOO – TRANSGRESSION – TRANSCENDENCE in Art & Science 2018. Ed. Honorato D, Gonzalez Valerio MA, de Menezes M, Giannakouloupoulos A. Ionian University Press, Corfu, pp: 228-249.

Graca L, De Menezes M (2019). I'am – Immortality'anti-marta. In "Out of the Box – Ars Eletronica Festival". Ed. Leopoldseder H, Schopf C, Stocker G. Hatje Cantz Verlag, Berlin. P: 67.

MSc Thesis Completed

António Gonçalves, 02/12/2019, Computational analysis of isoform level regulation in helper T cells, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Luis Graça and Saumya Kumar.

PhD Theses

Freitas RF, 04/11/2019, The impact of CD6 targeting in T cell function and immunopathology, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luís Graça.

Luísa Figueiredo Lab

Major Interests/Objectives

Parasitism relies on the ability of an organism to exploit its host. African trypanosomes are unicellular parasites responsible for a fatal disease in humans (sleeping sickness), and for a chronic disease in cattle (nagana). We study the cellular and molecular mechanisms employed by Trypanosomes to maintain the host chronically ill. We also study the host response to the infection.

TISSUE TROPISM - The adipose tissue is a major reservoir of parasites, which metabolically adapt to this environment. How do parasites move between tissues? What is the contribution to parasite transmission? What is the relevance of tissue tropism to cachexia?

ANTIGENIC VARIATION allows Trypanosomes to escape the host immune response. A long-standing interest of our group is to understand the underlying molecular mechanisms. We are currently studying the importance of non-coding RNAs and epigenetic modifications in the regulation of Variant Surface Glycoproteins.

Head of Laboratory

Luisa Miranda Figueiredo, PhD

Graphical Abstract



Team

Adriana Beatriz Oliveira Temporão	Master Degree	PhD Student
Alexandra Isabel Vidigal Teixeira	Master Degree	Lab Technician (Left December)
Ana Margarida Roque Sanches Vaz	PhD	PhD Student
Daniela Cristina de Henriques Brás	Master Degree	PhD Student (Started April. Left May)
Fabien Marc Guegan	PhD	Senior Postdoctoral Researcher
Henrique Pedro Pereira da Silva Amaral Machado	Master Degree	PhD Student
Idálio de Jesus Contreiras Viegas	Master Degree	PhD Student
Inês de Haan Vicente	Master Degree	MSc Student (Left November)
Inês Maria Martins Lopes	University Degree	Lab Technician (Started July. Left September)
João Alexandre Guarita da Silva Rodrigues	PhD	Staff Scientist (Left April)
João Francisco Parraga Ribeiro Colaço	University Degree	Lab Technician Started September)
Juan Pereira Macedo	PhD	Postdoctoral Researcher
Leonor Duarte Pinho	Master Degree	Lab Manager
Mariana Isabel de Niz Hidalgo	PhD	Postdoctoral Researcher
Sandra Isabel Gonçalves Trindade	PhD	Senior Postdoctoral Researcher
Sara Silva Pereira	PhD	Postdoctoral Researcher

Laboratory Keywords / Research Areas

Parasite, Adipose Tissue, Metabolism, Antigenic Variation, Gene Expression, Sleeping Sickness, Nagana.

Major Scientific Achievements

- Individual CEEC to three members of the lab: Luísa, Mariana and Juan;
- Award of Post-Doctoral fellowships from Human Frontiers Science Program (to Mariana de Niz) and Marie Curie (to Sara Silva Pereira);
- Award of ITN Cell2Cell, a Marie Curie Action;
- PNAS paper from Francisco Aresta Branco and Ana Margarida Vaz.

Selected Publications

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** 116:20725-20735. (IF: 9.580. Citations: 0. Source: Web of Science).

Sanches-Vaz M, Temporão A, Luis R, Nunes-Cabaço H, Mendes AM, Goellner S, Carvalho T, Figueiredo LM, Prudêncio M (2019). *Trypanosoma brucei* infection protects mice against malaria. **PLoS Pathogens** 15(11):e1008145 (IF: 6.463. Citations: 0. Source: Web of Science)

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(620). (IF: 11.878. Citations: 14. Source: Web of Science).

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. (IF: 14.633. Citations: 18. Source: Web of Science).

Trindade S et al (2016). *Trypanosoma brucei* Parasites Occupy and Functionally Adapt to the Adipose Tissue in Mice. **Cell Host & Microbe** 19(6):837-848. (IF: 15.753. Citations: 87. Source: Web of Science).

Ongoing Research Projects

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: 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.

2019/2021: HFSP fellowship - Human Frontier Science Program. Coordinator: Mariana De Niz. Funding Agency: Human Frontier Science Program. Amount: € 69 120,00. Total Amount: € 69 120,00.

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.

2018/2021: Quando a célula hospedeira já não é tão acolhedora...uma quebra de energia ou um aumento da toxicidade? Coordinator: João Rodrigues. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/28456/2017. Amount: € 50 189,13. Total Amount: € 236.529,90.

2016/2019 Long non-coding RNAs as new diagnostic biomarkers for African sleeping sickness. Coordinator: Fabien Guegan. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-EPI/7099/2014. Amount: € 165 079,00. Total Amount: € 165 079,00.

2016/2019: Metabolic consequences of an infection by African *trypanosomes*. Coordinator: Luísa Figueiredo. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MET/4471/2014. Amount: € 186 946,00. Total Amount: € 186 946,00.

2016/2019: An integrated systems approach to uncover the key players in complex protein N-glycosylation in *Trypanosoma brucei*. Coordinator: João Rodrigues. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BSS/0827/2014. Amount: € 96 106,00. Total Amount: € 149 450,00.

2015/2019: Molecular basis for the efficient biology of *Trypanosome* parasitism. Coordinator: Luísa Figueiredo. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01050/2014/CP1236/CT0008. Amount: € 46 000,00. Total Amount: € 46 000,00.

Other Projects

2017/2019: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Ramirez. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

Publications in Peer Reviewed Journals

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** 116:20725-20735. (IF: 9.580. Citations: 0. Source: Web of Science).

Sanches-Vaz M, Temporão A, Luis R, Nunes-Cabaço H, Mendes AM, Goellner S, Carvalho T, Figueiredo LM, Prudêncio M (2019). *Trypanosoma brucei* infection protects mice against malaria. **PLoS Pathogens** 15(11):e1008145 (IF: 6.463. Citations: 0. Source: Web of Science)

Carvalho T, Santos AM, Figueiredo LM (2019). Detection of Extravascular *Trypanosoma* Parasites by Fine Needle Aspiration. **JoVe** (150):1-11. (IF: 1.108. Citations: 0. Source: Web of Science).

De Niz M, Meehan GR, Brancucci NMB, Marti M, Rotureau B, Figueiredo LM, Frischknecht F (2019). Intravital imaging of host-parasite interactions in skin and adipose tissues. **Cellular Microbiology** 21(5):e13023. (IF: 4.288. Citations: 0. Source: Web of Science).

Silva Pereira S, Trindade S, De Niz M, Figueiredo LM (2019). Tissue tropism in parasitic diseases. **Open Biology** 9(6):190036. (IF: 3.890. Citations: 2. Source: Web of Science).

Invited Lectures and Seminars

Figueiredo LM. New discoveries in Trypanosome biology. The West African Centre for Cell Biology of Infectious Pathogens, University of Ghana, Ghana, January 15, 2019.

Figueiredo LM. African *trypanosomes*: masters of adaption to the environment. University of Helsinki, Helsinki, Finland, March 04, 2019.

Figueiredo LM. RNA epigenetics and antigenic variation in trypanosomes. 3rd Meeting Oneida, ITQB, Oeiras, Portugal, March 14, 2019.

Figueiredo LM. African *Trypanosomes*: masters of adaptation to the environment. CEDOC - Chronic Diseases Research Center, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal, March 27, 2019.

Figueiredo LM. Unexpected phenotypic variability of *Trypanosoma brucei* parasites. 9th Meeting ACETOTRYP/GLYCONOV, Bombannes, France, May 20-23, 2019.

Figueiredo LM. An RNA modification on the polyA tail promotes mRNA stability. CNC – Center for Neuroscience and Cell Biology seminars, Faculdade de Medicina, Universidade de Coimbra, Coimbra, Portugal, July 26, 2019.

Figueiredo LM. Cell-to-cell heterogeneity among parasite tissue populations. ITN meeting, Max Planck Institute, Munich, Germany, November 25-27, 2019.

Communications in International Conferences

Figueiredo LM. Why do parasites love the adipose tissue and can they teach us how to treat obesity? ERC Awardee Summit, International Nanotechnology Laboratory, Braga, Portugal, April 8, 2019. (*Oral Presentation*).

Viegas I, Rodrigues J, Pereira J, Aresta-Branco F, Jaffrey S, Figueiredo LM. m6A methylation of the polyA-tail regulates VSG transcript stability in trypanosomes. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, April 27–May 1, 2019. (*Oral Presentation*).

Guegan F, Teixeira A, Machado H, Calvo Alvarez E, Rotureau B, Figueiredo LM. Glycerol: a tissue-specific stumpy inducing factor in trypanosomes? Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, April 27–May 1, 2019. (*Oral Presentation*).

Trindade S, Sequeira M, Dejung, M, Bento F, Pinto-Neves D, Butter F, Bringaud F, Gjini E, Figueiredo LM. Modeling of *Trypanosoma brucei* population dynamics in mice reveals slow-growing parasites in adipose tissue. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, April 27–May 1, 2019. (*Poster Presentation*).

De Niz M, Viegas I, Guegan F, Figueiredo LM. Investigating *Trypanosoma brucei* dynamics in living mammalian hosts. EMBO Fellows' Meeting, EMBL Operon, Heidelberg, Germany, July 14, 2019. (*Oral Presentation*).

Viegas I, Macedo JP, Rodrigues J, Aresta-Branco F, Jaffrey S, Figueiredo LM. Poly-A tail methylation regulates VSG transcript stability in African trypanosomes. 30th Molecular Parasitology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, September 15-19, 2019. (*Poster Presentation*).

Silva Pereira S, De Niz M, Figueiredo LM. *Trypanosoma congolense* cytoadheres to the brain vasculature. 30th Molecular Parasitology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, September 15-19, 2019. (*Award for Best Poster Presentation*).

Sanches-Vaz M, Luis R, Temporão A, Mendes AM, Goellner S, Carvalho T, Prudêncio M, Figueiredo LM. Interferon-gamma mediates inhibition of Plasmodium hepatic infection by *Trypanosoma brucei*. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, April 27–May 1, 2019. (*Poster Presentation*).

Internationalization

Our research group acts internationally at several levels. First, by being invited to become the next Chair of the Kinetoplastid Molecular and Cellular Biology Meeting (Woods Hole, USA). Second, by participating and presenting our work at international meetings including the Molecular Parasitology Meeting (Woods Hole, USA). Third, by establishing and maintaining collaborations (Samie Jaffrey, Cornell University, USA; Frederic Bringaud, Université de Bordeaux, France; Falk Butter, University of Mainz, Germany; Catarina Gadelha, Nottingham University, UK).

Fourth, by being a member of editorial board of iScience and by acting as a reviewer for Nature Microbiology, Nature Communications, Nucleic Acids Research, Journal of Cell Science and PLoS Pathogens. Fifth, by being a member of the Innovative Training Network Cell2Cell Network (Marie Curie actions) and of the international collaborative award Cobalt by the Wellcome Trust Fund. Finally, by teaching to post-graduate students in University of Accra (Ghana) and by acting as jury member of “Habilitation a diriger des recherches” (HDR) of Dr. Loic Riviere (Université de Bordeaux, France).

Prizes, Honors and Awards

Silva-Pereira S. Individual Fellowship, Marie Skłodowska-Curie Actions, European Commission, February 12, 2019.

de Niz M. Postdoctoral fellowship, Human Frontiers Science Program, Strasbourg, France, March 21, 2019.

Silva-Pereira S. Best poster presentation, 30th Molecular Parasitology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, September 15-19, 2019.

Figueiredo LM, de Macedo J, de Niz M. Individual CEEC, Fundação para a Ciência e a Tecnologia, Lisbon, Portugal, November 27, 2019.

Advanced Teaching

Figueiredo LM. Invited participation at the WACCBIP-ASCB Workshop. The West African Centre for Cell Biology of Infectious Pathogens, University of Ghana, Ghana, January 14-16, 2019.

Figueiredo LM. Evaluation of candidates to participate in Middle Eastern Biology of Parasitism (MeBOP) course. University of Bern, Bern, Switzerland, July 29-August 14, 2019.

Figueiredo LM. Talk. Parasite persistence in the fat. CAML Doctoral Program, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 31, 2019.

Figueiredo LM. Lecture. RNA modifications in trypanosomes. Course of Animal Models in Biomedical Research, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, November 5, 2019.

Science and Society

"Portugal ambiciona ter um novo prémio Nobel?". Opinion article for daily newspaper Público, written jointly with Cláudio Franco and Luísa Lopes.

<https://www.publico.pt/2019/10/19/ciencia/opiniao/portugal-ambiciona-novo-premio-nobel-1890611>

MSc Theses

Inês Vicente, 12/11/2019, How do parasites remodel their metabolism?, Mestrado em Genética Molecular e Biomedicina, Universidade Nova de Lisboa - Faculdade de Ciências e Tecnologia. Supervisor: Luísa M. Figueiredo. Co-Supervisor: Sandra Trindade.

Luísa Lopes Lab

Major Interests / Objectives

Aging, stress and neurodegenerative diseases are among the conditions that contribute to the accelerated loss of cognitive function. Our group's work is focused on understanding the mechanisms inducing this "early-ageing", which render the hippocampus - the brain area related to learning and memory – particularly susceptible.

We focus on characterizing the molecular mechanisms associated to hippocampal loss of function and its outcome in behavior performance and synaptic function, using rodent models. We ensure the translation to the human brain, by testing these molecular imprints in healthy and diseased human brain tissue. We are currently focused into exploring the age-related alterations in glutamatergic synapses.

Head of Laboratory

Luísa Maria Vaqueiro Lopes, PhD

Team

Ana Inês Marques Morgado	Master Degree	PhD Student
Cátia Cristina Peixinho Reis	Master Degree	PhD Student
Joana Fernandes Esteves Soares Coelho	PhD	Senior Postdoctoral Researcher
Joana Gomes Ribeiro	Master Degree	PhD Student
Joana Isabel Rajão Saraiva	Master Degree	PhD Student
Mariana de Brito Morais	High School Diploma	MSc Student
Mariana Temido Mendes Ferreira	PhD	Postdoctoral Researcher
Raquel Lagoa Madruga da Costa	University Degree	MSc Student
Rui Artur Paiva Loureiro Gomes	PhD	Senior Postdoctoral Researcher

Laboratory Keywords / Research Areas

Neurosciences, Cognition, Aging, Hippocampus.

Major Scientific Achievements

- 1) Publications: The brain has long been considered to be a site of immune privilege; however, it is now increasingly appreciated that immune cells can enter the brain at steady state to exert important physiological effects. In a *Science Immunology* paper, we contributed to an important Neuroimmunology study led by J .Ribot (BSS lab) to find a distinctive population of V γ 6+ $\gamma\delta$ T cells in the mouse meninges, but not in the brain parenchyma, that support learning. Phenotypically, these $\gamma\delta$ T cells are the prominent producers of the cytokine IL-17 within the meninges but almost wholly lack production of the cytokine IFN- γ . Their steady-state production of IL-17 acts on glia — and potentially other cells of the brain parenchyma — to elicit production of the nerve growth factor BDNF. This signaling axis via $\gamma\delta$ T cell–produced IL-17 supports synaptic plasticity and short-term spatial memory acquisition.

- 2) Awards: Interstellar Initiative Award 2019 for the project “***Fast versus slow cognitive decline in aging***” - New York Academy of Sciences and Japan Agency for Medical Research and Development

Selected Publications

Ferreira DG, Temido-Ferreira M, Miranda HV, Batalha VL, Coelho JE, Szegö EM, Marques-Morgado I, Vaz SH, Rhee JS, Schmitz M, Zerr I, Lopes LV*, Outeiro TF* (2017). α -Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B. **Nature Neuroscience** **20(11):1569-1579**. *Co-senior author. (IF: 17.8, Citations: 33. Source: Web of Science).

Temido-Ferreira M, Ferreira DG, Batalha VL, Marques-Morgado I, Coelho JE, Pereira P, Gomes R, Pinto A, Carvalho S, Canas PM, Cuvelier L, Buée-Scherrer V, Faivre E, Baqi Y, Müller CE, Pimentel J, Schiffmann SN, Buée L, Bader M, Outeiro TF, Blum D, Cunha RA, Marie H, Pousinha PA, Lopes LV (2018). Age-related shift in LTD is dependent on neuronal adenosine A(2A) receptors interplay with mGluR5 and NMDA receptors. **Molecular Psychiatry**. (IF: 15.4, Citations: 8. Source: Web of Science).

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC (2019). Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. **Science Immunology** 4(40). (IF: 10.551. Citations: 2. Source Web of Science).

Batalha VL, Pego JM, Fontinha BM, Costenla AR, Valadas JS, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV (2013). Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. **Molecular Psychiatry** 18(3):320-31. (IF: 15.4, Citations 80. Source: web of Science).

Ongoing Research Projects

2019/2021: The physiological role of circadian rhythms in memory. Coordinator: Luísa Lopes. Funding Agency: Fundação BIAL. Reference: Bial Lopes. Amount: € 45 000,00. Total Amount: € 45 000,00.

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 Amount: € 175 000,00.

2016/2020: Targeting the glycation defenses as a protective strategy for Parkinson's disease. Coordinator: Luísa Lopes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/NEU-OSD/5644/2014. Amount: € 51 000,00. Total Amount: € 199 961,00.

2016/2019: Microglia dysregulation as trigger for chronic brain inflammation. Coordinator: Joana Coelho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MEC/4778/2014. Amount: € 195 035,00. Total Amount: € 195 035,00.

Other Projects

2018/2021: Hippocampal-cortical coordination and the mechanisms of cognition: the formation and retrieval of contextual memory during decision-making. 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.

2018/2021: Meningeal gd 17 T cells: impact on cognitive functions in health and disease. 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.

Publications in Peer Review Journals

Ribeiro M, Brigas HC, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Valente CA, Omenetti S, Stockinger B, Waisman A, Manadas B, Lopes LV, Silva-Santos B, Ribot JC (2019). Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory. **Science Immunology** 4(40). (IF: 10.551. Citations: 2. Source Web of Science).

Pousinha PA, Mouska X, Bianchi D, Temido-Ferreira M, Rajão-Saraiva J, Gomes R, Fernandez SP, Salgueiro-Pereira AR, Gandin C, Raymond EF, Barik J, Goutagny R, Bethus I, Lopes LV, Migliore M, Marie H (2019). The Amyloid Precursor Protein C-Terminal Domain Alters CA1 Neuron Firing, Modifying Hippocampus Oscillations and Impairing Spatial Memory Encoding. **Cell Reports** 29(2):317-331. (IF: 7.815. Citations: 0. Source: Web of Science).

Carvalho K, Faivre E, Pietrowski MJ, Marques X, Gomez-Murcia V, Deleau A, Huin V, Hansen JN, Kozlov S, Danis C, Temido-Ferreira M, Coelho JE, Mériaux C, Eddarkaoui S, Gras SL, Dumoulin M, Cellai L; NeuroCEB Brain Bank, Landrieu I, Chern Y, Hamdane M, Buée L, Boutillier AL, Levi S, Halle A, Lopes LV, Blum D (2019). Exacerbation of C1q dysregulation, synaptic loss and memory deficits in tau pathology linked to neuronal adenosine A2A receptor. **Brain** 142(11):3636-3654. (IF: 11.814. Citations: 0. Source: Web of Science).

Vaz RL, Chapela D, Coelho JE, Lopes LV, Ferreira JJ, Afonso ND, Sousa S, Outeiro TF (2019). Tapentadol Prevents Motor Impairments in a Mouse Model of Dyskinesia. **Neuroscience** 424:58-71. (IF: 3.244. Citations: 0. Source: Web of Science).

Temido-Ferreira M, Coelho JE, Pousinha PA, Lopes LV (2019). Novel Players in the Aging Synapse: Impact on Cognition. **Journal of Caffeine and Adenosine Research** 9(3):104-127. (IF:--, Citations:--).

Communications in International Conferences

Temido-Ferreira M, Saraiva J, Pousinha P, Lopes LV. Adenosine A_{2A} receptors as a risk factor in hippocampal neurodegeneration. The 14th International Conference on Alzheimer's & Parkinson's Diseases, Lisbon, Portugal, March 26-31, 2019. (*Oral Presentation*).

Brigas HC, Coelho JE, Ribeiro M, Gomez V, Carvalho K, Faivre E, Blum D, Silva-Santos B, Lopes LV, Ribot JC. Elucidating the Impact of $\gamma\delta$ T cells Alzheimer's Disease. The 14th International Conference on Alzheimer's & Parkinson's Diseases, Lisbon, Portugal, March 26-31, 2019 (*Poster Presentation*).

Communications in National Conferences

Ribeiro M, Brigas HC, Temido-Ferreira M, Santa C, Valente CA, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. Meningeal $\Gamma\delta$ T Cell-Derived IL-17 Controls Synaptic Plasticity and Cognitive Behaviour. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ferreira C, Coelho JE, Marques-Morgado I, Temido-Ferreira M, Miranda-Lourenço C, Fonseca-Gomes J, Belo RF, Tanqueiro SR, Marttinen M, Sebastião AM, Lopes LV, Mendonça A, Diógenes MJ, Hiltunen M. Ept5 Phosphorylation Status as Modulator of Synaptic Function in the Hippocampus. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Marques-Morgado I, Coelho JE, Dias M, Remondes M, Dawson N, Lopes LV. Impact of Circadian Shifting on Functional Brain Connectivity. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Ribeiro JG, Marques-Morgado I, Temido-Ferreira M, Coelho JE, Summavielle T, Remondes M, Lopes LV. Study of Midbrain-Hippocampal Connectivity Underlying Drug-Related Memory Formation. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Marques-Morgado I, Coelho JE, Lopes LV. Neuronal Adenosine A_{2A} Receptor Overexpression Promotes Changes In Glial Phenotype In The Hippocampus. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Brito DVC, Kupke J, Karaca KG, Zeuch B, Temido-Ferreira M, Gomes R, Lopes LV, Oliveira AMM. Bidirectional Dysfunction in GADD45 γ Expression during Mammalian Aging Impairs Cognition and Disrupts Activity-Dependent Gene Expression. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Saraiva JR, Temido-Ferreira M, de Almeida SF, Pousinha PA, Lopes LV. Modulation of NMDA Receptor Function by Amyloid Precursor Protein. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Brigas HC, Coelho JE, Ribeiro M, Gomez V, Carvalho K, Faivre E, Blum D, Silva-Santos B, Lopes LV, Ribot JC. Elucidating the Impact of gd T Cells on Cognition. Sociedade Portuguesa de Neurociências 2019, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Organization of Conferences

Brigas HC. XII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 23-25, 2019.

Lopes LV. Co-Organizer with Cláudia Faria. NeuroSeS (Neuroscience Seminar Series), Centro Académico de Medicina de Lisboa, Lisbon, Portugal, 2019.

Internationalization

Brigas HC. PhD Exchange Period in University of Lille, France. January-February, 2019.

Hosting of Aleix Marti Navia, University of Camerino, Italy. Effects of A1 agonists and A2A antagonists in neuroinflammation and neurodegenerative diseases. June 15-September 15, 2019.

Hosting ERASMUS+ program Felix Korbinian Schmidtner, University of Vienna, Austria. GFAP expression in the hippocampus of rats subjected to Maternal Separation. July 10-September 20, 2019.

Prizes, Honours and Awards

Lopes LV. Interstellar Initiative Award 2019, "Fast versus slow cognitive decline in aging", New York Academy of Sciences and Japan Agency for Medical Research and Development. New York, US, September 2019.

Lopes LV. Appointed as Director of the Course *Cognitive Ageing*, funded by the FENS Cajal School of Neurosciences, Bordeaux, France. March 2019.

Saraiva J. CAJAL Advanced Neuroscience Training Program Award for the course “Advanced Techniques for Synapse Biology”, University of Bordeaux, Bordeaux, France. October 2019.

Advanced Teaching

Lopes LV. Teaching at the Neurosciences PhD/MSc. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

Saraiva, J. Participant on CAJAL course “Advanced Techniques for Synapse Biology” of the CAJAL Advanced Neuroscience Training Program, Bordeaux Neurocampus, University of Bordeaux, Bordeaux, France, October 2019.

Science and Society

Lopes LV. Horizontes iMM: Uma Pergunta a Três Conference. June 19, 2019.

Lopes LV. iMM/Morais Leitão “Desafios do Envelhecimento” Conference. July 2, 2019.

Lopes LV. Round table about GAPIC projects, Noite Europeia dos Investigadores. September 27, 2019.

Lopes LV. MDS Conference "Saúde & Longevidade. October 3, 2019.

Lopes LV. Interview for the show “Admirável Mundo Novo SIC”. December 2019.

Several interviews for Portuguese newspapers, radio and TV shows.

MSc Theses Completed

Gonçalo Correia de Oliveira Ferreira, Functional role of the Oc2M cortical area in the processing of multimodal sensory inputs in rats’. Supervisor: Miguel Remondes. Co-Supervisor Luísa V. Lopes. Faculdade de Medicina de Lisboa, May 2019

Mariana Nunes, The role of Cdc42 GTPase during synaptic cooperation. Supervisor: Rosalina Fonseca. Co-Supervisor: Luísa V. Lopes. Faculdade de Medicina de Lisboa, September 2019

Mamede de Carvalho Lab

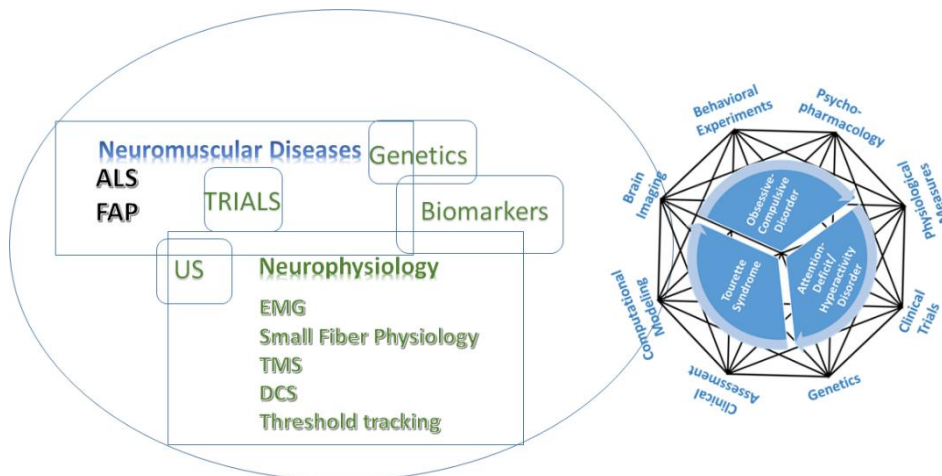
Major Interests/Objectives

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 and data mining in amyotrophic lateral sclerosis (ALS); and computational models in behavior 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.

Head of Laboratory

Mamede Alves de Carvalho, Full Professor of Physiology and Director of Physiology Institute, Unit Leader iMM, and Vice-Dean of the Faculdade de Medicina da Universidade de Lisboa, Neurologist and Neurophysiologist, head of the Neuromuscular Unit of Centro Hospitalar Universitário Lisboa-Norte.

Graphical Abstract



Team

Ana Catarina de Oliveira da Silva Pronto Laborinho	University Degree	PhD Student
Ana Catarina dos Santos Farinha	Master Degree	PhD Student
Ana Rita Mendes Londral Gamboa	MD/PhD	Clinical Researcher (Left February)
Anabela Leuschner Fernandes Cardoso Pinto Noronha Sanches	MD/PhD	Clinical Researcher
Andreia Leitão Tavares Ribeiro dos Santos		PhD Student
Ângelo Rodrigo Neto Dias	Master Degree	PhD Student
Anna Caroline Marques dos Anjos Braga	MD/PhD	Clinical Researcher
Bruno André e Silva Miranda	MD/Master Degree	Clinical Researcher
Bruno Daniel da Costa Gomes	PhD	Postdoctoral Researcher (Started April)
Cristiano Torres Tavares dos Santos	MD/Master Degree	Clinical Researcher
Fernando Manuel Pinto Ferreira Domingos	MD/PhD	Clinical Researcher
Francisco José Correia Graça Almeida	Master Degree	Trainee (Started October)
Gabriel Miltényi-Miltenberger	PhD	Staff Scientist
Isabel Maria dos Santos Conceição	MD/University Degree	Clinical Researcher
Isabel Martins de Castro	University Degree	Technician
João Daniel Galvão Antunes	Master Degree	MSc Student
José Filipe Oliveira Castro	Master Degree	Senior Technician
Lena Helene Ernst	PhD	Postdoctoral Researcher
Leonel Almeida Luis	MD/PhD	Clinical Researcher
Maria da Conceição Jonet de Azevedo Coutinho	MD/PhD	Clinical Researcher
Mariana Fernandes Alves Pereira	Master Degree	PhD Student
Marta Luisa Gromicho Morgado Silva	PhD	Senior Postdoctoral Researcher
Michael Swash	MD/PhD	Clinical Researcher
Pedro Miguel Tojais Rodrigues Alves	MD/University Degree	Clinical Researcher (Left February)
Sofia Isabel Ferro Pires	Master Degree	Lab Technician (Started February. Left September)
Sofia Rita Cardoso Fernandes	Master Degree	PhD Student
Susana Cristina da Costa Pinto	PhD	Visiting Researcher
Tiago Vaz Maia	PhD	Staff Scientist
Vasco Manuel Aranha da Conceição	Master Degree	PhD Student

Laboratory Keywords / Research Areas

Amyotrophic Lateral Sclerosis, Neurophysiology of Respiratory Function, hATTR Amyloidosis, Neurocomputational Modelling of Brain Disorders, Biological Signal Processing.

Major Scientific Achievements

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. Also, we published results on the genetic mutations and wet-biomarkers in ALS, clinical features of hATTR amyloidosis and electromyography. Our participation in competitive clinical trials in hATTR amyloidosis and ALS will promote additional future publications.

Selected Publications

Cavanagh SE, Malalasekera WN, Miranda B, Hunt, LT, Kennerley SW (2019). Visual fixation patterns during economic choice reflect covert valuation processes that emerge with learning. **Proceedings of the National Academy of Sciences of the United States of America** 116(45): 22795-22801. (IF: 9.58, Citations: 1. Source: Google Scholar).

González-Duarte A, Berk JL, Quan D, Mauermann ML, Schmidt HH, Polydefkis M, Waddington-Cruz M, Ueda M, Conceição IM, Kristen AV, Coelho T (2019). Analysis of autonomic outcomes in APOLLO, a phase III trial of the RNAi therapeutic patisiran in patients with hereditary transthyretin-mediated amyloidosis. **Journal of Neurology** 267(3):703-712. (IF: 3.783, Citations: 1. Source: Google Scholar).

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. **Journal of Neurology Neurosurgery and Psychiatry** 90(1):118-120. (IF: 8.272, Citations: 6. Source: Google Scholar).

Johnsen B, Pugdahl K, Fuglsang-Frederiksen A, Kollwe K, Paracka L, Dengler R, Camdessanché JP, Nix W, Liguori R, Schofield I, Maderna L, Czell D, Neuwirth C, Weber M, Drory VE, Abraham A, Swash M, de Carvalho M (2019). Diagnostic criteria for amyotrophic lateral sclerosis: a multicenter study of inter-rater variation and sensitivity. **Clinical Neurophysiology** 130(2):307-314. (IF: 3.675, Citations: 4. Google Scholar).

Pinto S, Gromicho M, Swash M, de Carvalho M (2019). Cervical Muscle Weakness Is a Marker of Respiratory Dysfunction in Amyotrophic Lateral Sclerosis. **Journal of Neurology Neurosurgery Psychiatry** 91(3):323-324. (IF: 8.272, Citations: 0. Source: Google Scholar).

Ongoing Research Projects

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.

2018/2019: Investigação Síndrome Tourette. Coordinator: Tiago Maia. Funding Agency: Ampastta. Reference: Investigação Síndrome Tourette. Amount: € 5 683,50. Total Amount: € 5 683,50.

2016/2019: Unravelling Prognostic markers in NEUROdegenerative diseases through CLINical and OMICS data integration. Coordinator: Mamede de Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EEI-SII/1937/2014. Amount: € 48 791,00. Total Amount: € 197 346,00.

Publications in Peer Reviewed Journals

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. **Journal of Neurology Neurosurgery and Psychiatry** 90(1):118-120. (IF: 8.272, Citations: 6. Source: Google Scholar). **Q1**

Swash M, Czesnik D, de Carvalho M (2019). Muscular cramp: causes and management. **European Journal of Neurology** 26(2):214-221. (IF: 4.387, Citations: 7. Source: Google Scholar). **Q1**

Alix JJP, Neuwirth C, Gelder L, Burkhardt C, Castro J, de Carvalho M, Gawel M, Goedee S, Grosskreutz J, Lenglet T, Moglia C, Omer T, Schrooten M, Nandedkar S, Stalberg E, Barkhaus PE, Furtula J, van Dijk JP, Baldinger R, Costa J, Otto M, Sandberg A, Weber W (2019). Assessment of the reliability of the motor unit size index (MUSIX) in multi-centre and single subject “round-robin” settings. **Clinical Neurophysiology** 130(5):666-674 (IF: 3.675, Citations: 0. Source: Google Scholar). **Q1**

Körner S, Kammeyer J, Zapf A, Kuzma-Kozakiewicz M, Piotrkiewicz M, Kuraszkiwicz B, Goszczyńska H, Gromicho M, Grosskreutz J, Andersen PM, de Carvalho M, Petri S (2019). Influence of environment and lifestyle on incidence and progress of Amyotrophic Lateral Sclerosis in a German ALS population. **Aging and Disease** 10(2):205-216. (IF: 4.232, Citations: 5. Source: Google Scholar). **Q1**

Tazelaar GH, Dekker AM, van Vugt JJ, van der Spek RA, Westeneng H-J, Kool LJ, Kenna KP, van Rheenen W, Pulit SL, McLaughlin RL, Sproviero W, Iacoangeli A, Hübers A, Brenner D, Morrison KE, Shaw PJ, Shaw CE, Panadés MP, Mora Pardina JS, Glass JD, Hardiman O, Al-Chalabi A, van Damme P, Robberecht W, Landers JE, Ludolph AC, Weishaupt JH, van den Berg LH, Veldink JH, van Es M.A, on behalf of the Project MinE ALS Sequencing Consortium (2019). Association of NIPA1 repeat expansions with amyotrophic lateral sclerosis in a large international cohort. **Neurobiology of Aging** 74:234e9-234e15. (IF: 4.398, Citations: 7. Source: Google Scholar). **Q1**

Campos CF, Viana P, Castro I, Castro J, de Carvalho M, Conceição I (2019). Non-invasive evaluation of sudomotor function in patients with Myasthenia Gravis. **Neurophysiologie Clinique-Clinical Neurophysiology** 49(1):81-86. (IF: 2.167, Citations: 0. Source: Google Scholar). **Q2**

Johnsen B, Pugdahl K, Fuglsang-Frederiksen A, Kollwe K, Paracka L, Dengler R, Camdessanché JP, Nix W, Liguori R, Schofield I, Maderna L, Czell D, Neuwirth C, Weber M, Drory VE, Abraham A, Swash M, de Carvalho M (2019). Diagnostic criteria for amyotrophic lateral sclerosis: a multicentre study of inter-rater variation and sensitivity. **Clinical Neurophysiology** 130(2):397-314. (IF: 3.675, Citations: 4. Source: Google Scholar). **Q1**

Pronto-Laborinho A, Pinto S, Gromicho M, Pereira M, Swash M, de Carvalho M (2019). Interleukin-6 and Amyotrophic Lateral Sclerosis. **Journal of the Neurological Sciences** 398:50-53. (IF: 2.651, Citations: 2. Source: Google Scholar). **Q2**

de Carvalho M, Pinto S, Swash, M (2019). Diaphragmatic Neurophysiology and Respiratory Markers in ALS. **Frontiers in Neurology** 10:143. (IF: 3.552, Citations: 2. Source: Google Scholar). **Q1**

Costa J, Streich L, Pinto S, Pronto-Laborinho A, Nimitz M, Conradt HS, de Carvalho M (2019). Exploring cerebrospinal fluid IgG N-glycosylation as potential biomarker for Amyotrophic Lateral Sclerosis. **Molecular Neurobiology** 56(8):5729–5739. (IF: 5.076, Citations: 2. Source: Google Scholar). **Q1**

de Carvalho M, Swash M (2019). Motor unit recruitment in myopathy: The myopathic EMG reconsidered. **Journal of Electromyography and Kinesiology** 45:41-45 (IF: 1.753, Citations: 1. Source: Google Scholar). **Q2**

de Carvalho M, Turkman A, Swash M (2019). Sensory modulation of fasciculation discharge frequency. **Muscle & Nerve** 59(6):688-693. (IF: 2.393, Citations: 0. Source: Google Scholar). **Q2**

Pinto S, de Carvalho M (2019). SVC is a marker of respiratory decline function, similar to FVC, in patients with ALS. **Frontiers in Neurology** 10:109. (IF: 3.552, Citations: 2. Source: Google Scholar).

van den Berg LH, Sorenson E, Gronseth G, Macklin EA, Andrews J, Baloh RH, Benatar M, Berry JD, Chio A, Corcia P, Genge A (2019). Revised Airlie House consensus guidelines for design and implementation of ALS clinical trials. **Neurology** 92(14):e1610-e1623. (IF: 8.320, Citations: 9. Source: Google Scholar). **Q1**

Pinto S, Gromicho M, de Carvalho M (2019). Assessing Upper Limb Function with ALSFRS-R in amyotrophic lateral sclerosis patients. **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 20(5-6):445-448. (IF: 2.883, Citations: 0. Source: Google Scholar). **Q1**

Campos CF, de Carvalho M (2019). Distal myopathy and rapidly progressive dementia associated with a novel mutation in the VCP gene: expanding Inclusion Body Myopathy with early-onset Paget Disease and Frontotemporal Dementia spectrum. **Journal of Clinical Neuroscience** 64:8-10 (IF: 1.593, Citations: 1. Source: Google Scholar). **Q3**

de Carvalho M, Swash, M (2019). The split hand in amyotrophic lateral sclerosis: a possible role for the neuromuscular junction. **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 20(5-6):368-375. (IF: 2.883, Citations: 1. Source: Google Scholar). **Q1**

de Carvalho M (2019). Guide the EMG Lines. **Clinical Neurophysiology** 130(9):1682-1683. Editorial (IF: 3.675, Citations: 0. Source: Google Scholar). **Q1**

Caetano A, Pereira M, de Carvalho, M (2019). A 15-minute session of direct current stimulation does not produce lasting changes in axonal excitability. **Neurophysiologie Clinique** 49(4):277-282. (IF: 2.167, Citations: 2. Source: Google Scholar). **Q2**

Swash M, de Carvalho M (2019). The neurophysiological index predicts survival in amyotrophic lateral sclerosis. **Clinical Neurophysiology** 130(9):1684-1685. Editorial (IF: 3.675, Citations: 0. Source: Google Scholar). **Q1**

Costa MR, Gromicho M, Pronto-Laborinho AC, Miltényi GM, de Carvalho M (2019). Novel TBK1 LoF variant in a family with upper motor neuron predominant motor neuron disease. **Journal of the Neurological Sciences** 403: 117-118 (IF: 2.651, Citations: 0. Source: Google Scholar). **Q2**

de Carvalho M, Swash M (2019). The ‘split-leg’ syndrome in ALS: specific or variable? **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 20(7-8): 615-616. (IF: 2.883, Citations: 0. Source: Google Scholar). **Q1**

Mora JS, Genge A, Chio A, Estol CJ, Chaverri D, Hernández M, Marín S, Mascias J, Rodriguez GE, Povedano M, Paipa A, Dominguez R, Gamez J, Salvado M, Lunetta C, Ballario C, Riva N, Mandrioli J, Moussy M, Kinet J-P, Auclair C, Dubreuil P, Arnold V, Mansfield CD, Hermine, C; on behalf of the AB10015 STUDY GROUP (2019). Masitinib as an add-on therapy to riluzole in patients with amyotrophic lateral sclerosis: a randomized clinical trial. **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 1-10 (IF: 2.883, Citations: 4. Source: Google Scholar). **Q1**

van der Spek R, van Rheenen W, Pulit SL, Kenna KP, van den Berg LH, Veldink JH, on behalf of the Project MinE ALS Sequencing Consortium (2019). The project MinE databrowser: bringing large-scale whole-genome sequencing in ALS to researchers and the public. **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 20(5-6): 432-440. (IF: 2.883, Citations: 2. Source: Google Scholar). **Q1**

Caetano A, Pereira P, Pereira M, de Carvalho M. Modulation of sensory nerve fiber excitability by transcutaneous cathodal direct current stimulation. **Neurophysiologie Clinique** 49(5):385-390 (IF: 2.167, Citations: 0. Source: Google Scholar). **Q2**

Swash M, de Carvalho M (2019). Testing electrolyte supplementation for muscle cramp. **Muscle & Nerve** 60(5):499-500. Editorial. (IF: 2.393, Citations: 0. Source: Google Scholar). **Q2**

Rezak M, de Carvalho M (2019). Disease modification in neurodegenerative diseases: not quite there yet. **Neurology** 94(1):12-13. Editorial. (IF: 8.320, Citations: 0. Source: Google Scholar). **Q1**

Fernandes SR, Pereira M, Salvador R, Miranda PC, de Carvalho, M (2019). Cervical Trans-Spinal Direct Current Stimulation: a modelling-experimental approach. **Journal of Neuroengineering and Rehabilitation** 16(1):123. (IF: 3.582, Citations: 0. Source: Google Scholar). **Q1**

Brenner D, Rosenbohm A, Yilmaz R, Muller K, Grehl T, Petri S, Meyer T, Grosskreutz J, Weydt P, Ruf W, Neuwirth C, Weber M, Pinto P, Claeys KG, Schrank B, Jordan B, Knehr A, 1 Gunther K, Hubers A, Zeller D, Kubisch C, Jablonka S, Sendtner M, Klopstock T, de Carvalho M, Sperfeld A, Borck G, Volk AE, Dorst J, Weis J, Otto M, Schuster J, Tredici KD, Braak H, Danzer KM, Freischmidt A, Meitinger T, Strom TM, Ludolph AC, Andersen PM, Weishaupt JH, and German ALS network MND-NET* (2019). Reply: Adult-onset distal spinal muscular atrophy: a new phenotype associated with KIF5A mutations (letter). **Brain: A Journal of Neurology** 142(12): 119-121. (IF: 11.814, Citations: 0. Source: Google Scholar). **Q1**

Shefner JM, Cudkovicz ME, Hardiman O, Cockcroft BM, Lee JH, Malik FI, Meng L, Rudnicki SA, Wolff AA, Andrews JA, & on behalf of the VITALITY-ALS STUDY GROUP (2019). A phase III trial of tirasemtiv as a potential treatment for amyotrophic lateral sclerosis. **Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration** 20:584–594. (IF: 2.883, Citations: 2. Source: Google Scholar). **Q1**

Pinto S, Gromicho M, Swash M, de Carvalho M (2019). Cervical Muscle Weakness Is a Marker of Respiratory Dysfunction in Amyotrophic Lateral Sclerosis. **Journal of Neurology Neurosurgery Psychiatry** 91(3):323-324. (IF: 8.272, Citations: 0. Source: Google Scholar).

Zapata-Zapata CH, Dáger EF, Aguirre-Acevedo DC, de Carvalho M, Solano J (2019). Prevalence, incidence and clinical-epidemiological characterization of amyotrophic lateral sclerosis in Antioquia – Colombia. **Neuroepidemiology**. (IF: 2.689, Citations: 0. Source: Google Scholar). **Q2**

Swash M, de Carvalho M (2019). Fasciculations: opening Pandora’s Box. **Clinical Neurophysiology** 131(1):239-240. Editorial. (IF: 3.675, Citations: 0. Source: Google Scholar). **Q1**

Silva C, Rodrigues FB, Duarte, GS, Costa J, de Carvalho M (2019). Prognostic value of phrenic nerve conduction study in Amyotrophic Lateral Sclerosis: a systematic review and meta-analysis. **Clinical Neurophysiology** 131(1):106-113. (IF: 3.675, Citations: 0. Source: Google Scholar). **Q1**

Inês M, Coelho T, Conceição I, Landeiro F, de Carvalho M, Costa J (2019). Societal costs and burden of hereditary transthyretin amyloidosis polyneuropathy. **Amyloid-Journal of Protein Folding Disorders** (IF: 2.167, Citations: 0. Source: Google Scholar). **Q2**

Farhan SMK, Howrigan DP, Abbott LE, Klim JR, Topp SD, Byrnes AE, Churchhouse C, Phatnani H, Smith BN, Rampersaud E, Wu G, Wu J, Shatunov A, Iacoangeli A, Al Khleifat A, Mordes DA, Ghosh S, ALSGENS Consortium, FALS Consortium, Project MinE Consortium, CReATe Consortium, Eggan K, Rademakers R, McCauley JL, Schüle R, Züchner S, Benatar M, Taylor JP, Nalls M, Gotkine M, Shaw PJ, Morrison KE, Al-Chalabi A, Traynor B, Shaw CE, Goldstein DB, Harms MB, Daly MJ, Neale BM (2019). Exome sequencing in amyotrophic lateral sclerosis implicates a novel gene, DNAJC7, encoding a heat-shock protein. **Nature Neuroscience** 22(12):1966-1974. (IF: 21.126, Citations: 0. Source: Google Scholar). **Q1**

Santos MO, Jacobsen AB, Tankisi H (2019). Multiple Point Stimulation MUNE in ALS: Toward a Faster Modification. **Journal of Clinical Neurophysiology** 36(3):220-223. (IF: 1.64, Citations: 0. Source: Google Scholar). **Q2**

Coelho P, Santos MO (2019). First Portuguese patient presenting with hereditary sensory and autonomic neuropathy type 1E associated with a novel mutation in DNMT1 gene. **Neurological Sciences** (IF: 1.45, Citations: 0. Source: Google Scholar). **Q2**

de Campos CF, Vidailhet M, Toutain A, de Becdelièvre A, Funalot B, Bonello-Palot N, Stojkovic T (2019). Hereditary Sensory Autonomic Neuropathy Type II: report of two novel mutations in the FAM134B gene. **Journal of the Peripheral Nervous System** 24(4):354-358. (IF: 1.49, Citations: 0. Source: Google Scholar). **Q1**

Miranda B*, Martins AI*, Jorge AF, Nunes C, Lemos J, Sousa L (2019). Paroxysmal Adduction After Internuclear Ophthalmoplegia. **Journal of Neuro-Ophthalmology** (*First Authors). (IF: 2.509, Citations: 0. Source: Google Scholar). **Q2**

Coelho T, Yarlak A, Waddington-Cruz M, White MK, Sikora Kessler A, Lovley A, Pollock M, Guthrie S, Ackermann EJ, Hughes SG, Karam C, Khella S, Gertz M, Merlini G, Obici L, Schmidt HH, Polydefkis M, Dyck PJB, Brannagan Iii TH, Conceição I, Benson MD, Berk JL (2019). Inotersen preserves or improves quality of life in hereditary transthyretin amyloidosis. **Journal of Neurology** (IF: 3.783, Citations: 0. Source: Google Scholar). **Q1**

Oliveira Santos M, Coelho P, Roque R, Conceição I (2019). Very late-onset limb-girdle muscular dystrophy type 2D: A milder form with a normal muscle biopsy. **Journal of Clinical Neurosciences** (IF: 1.593, Citations: 0. Source: Google Scholar) **Q3**

Conceição I (2019). Novel RNA-targeted therapies for hereditary ATTR amyloidosis and their impact on the autonomic nervous system. **Clinical Autonomic Research** 29(Sup 1):11-17. Review. (IF: 2.485, Citations: 1. Source: Google Scholar). **Q2**

Conceição I (2019). Response: Suhr OB: commentary to Isabel Conceição et al. early diagnosis through targeted follow-up of identified carriers of TTR gene mutations. **Amyloid** 26(4):248-249. (IF: 4.048, Citations: 0. Source: Google Scholar). **Q2**

Conceição I, de Castro I, Castro J (2019). Correlation between Sudoscan and COMPASS 31: assessment of autonomic dysfunction on hATTR V30M patients. **Amyloid** 26(Sup 1):23. (IF: 4.048, Citations: 0. Source: Google Scholar). **Q2**

de Campos CF, Conceição I, Castro I (2019). Early diagnostic tools in hereditary amyloidosis related to transthyretin (hATTR) V30M autonomic neuropathy. **Amyloid** 26(Sup1):35-36. (IF: 4.048, Citations: 0. Source: Google Scholar). **Q2**

Falcão de Campos C, Parreira S, Conceição I (2019). Misdiagnosis in late versus early onset hATTR amyloidosis patients: experience from a reference centre. **Amyloid** 26(Sup1):37-38. (IF: 4.048, Citations: 0. Source: Google Scholar). **Q2**

Conceição I, Coelho T, Rapezzi C, Parman Y, Obici L, Galán L, Rousseau A (2019). Assessment of patients with hereditary transthyretin amyloidosis - understanding the impact of management and disease progression. **Amyloid** 26(3):103-111. (IF: 4.048, Citations: 1. Source: Google Scholar). **Q2**

Conceição I, Damy T, Romero M, Galán L, Attarian S, Luigetti M, Sadeh M, Sarafov S, Tournev I, Ueda M (2019). Early diagnosis of ATTR amyloidosis through targeted follow-up of identified carriers of TTR gene mutations. **Amyloid** 26(1):3-9. (IF: 4.048, Citations: 10. Source: Google Scholar). **Q2**

Other International Publications

Costa MR, Maruta C, de Carvalho M (2019). Lambert-Eaton Myasthenic Syndrome plus. **Journal of Clinical Neuromuscular Disease** 21(2):119-121.

Falcão de Campos C, Oliveira Santos M, Roque R, Conceição I, de Carvalho M (2019). Mitochondrial neurogastrointestinal encephalomyopathy: novel pathogenic mutation in Thymidine Phosphorylase gene in a patient from Cape Verde Islands. **Case Reports in Neurological Medicine** 2019:5976410.

Miranda PC, Fernandes SR, de Carvalho M (2019). Electric field distribution during non-invasive electric and magnetic stimulation of the cervical spinal cord. *In* Proceedings of the 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society: 5898-5901.

Fernandes SR, de Carvalho M, Miranda PC (2019). Non-Invasive Spinal Cord Stimulation: Relevance of Modelling Studies in Clinical Protocol Design. *In* MEDICON 2019, IFMBE Proceedings 76 (15th Mediterranean Conference on Medical and Biological Engineering and Computing). J. Henriques et al. (Eds.): *Springer Nature* Switzerland AG 2020: 1767-1773.

Pires S, Gromicho M, Pinto S, de Carvalho M, Madeira SC (2019). Patient Stratification in Amyotrophic Lateral Sclerosis using Clinical and Patient Profiles. *In* Proceedings of the KDD Workshop on Applied Data Science for Healthcare.

Pereira T, Pires S, Gromicho, M, Pinto S, de Carvalho M, Madeira SC (2019). Predicting assisted ventilation in Amyotrophic Lateral Sclerosis using a mixture of experts and conformal predictors. *In* Proceedings of the KDD Workshop on Applied Data Science for Healthcare.

Matos J, Gromicho M, Pires S, de Carvalho M, Madeira SC (2019). Biclustering Electronic Health Records to Unravel Disease Presentation Patterns: a Case Study in ALS. *In* Proceedings of the EEE ICDM 2019 Workshop on Interpretable and Explainable Machine Learning for Healthcare.

Pires S, Gromicho M, Pinto S, de Carvalho M, Madeira SC (2019). Patient Stratification using Clinical and Patient Profiles: targeting personalized prognostic prediction in ALS. *In* Proceedings of the Workshop on Data Mining in Biomedical Informatics and Healthcare.

Conceição VA, Maia TV (*in press*). A computational perspective on Tourette syndrome. In P. Seriès (ed.), *Computational Psychiatry*, MIT Press.

Roberts AC, Goldstein RZ, Badre D, Balleine B, Critchley HD, Fotopoulou K, Frangou S, Friston KJ, Maia TV, Stein EA (in press). A systems-level perspective on intrusive thinking. In P. W. Kalivas and M. P. Paulus, *Intrusive Thinking across Neuropsychiatric Disorders*, Strüngmann Forum Reports, Cambridge, MA: MIT Press.

Other National Publications

Marinho A, Lopes A, Sousa G, Antunes H, Fonseca J, Mendes L, de Carvalho M, Veríssimo MT, Carvalho N, Alves P, Alves P (2019). A malnutrição associada à doença e as suas repercussões em Portugal. *Med Int* 26(1): 60-66.

Miranda B (2019). Vestibulopatia bilateral – Causas neurológicas. *Revista da XI Reunião de Inverno, APO, Lisboa.* 27-29.

Invited Lectures and Seminars

Maia TV. Tourette syndrome: dopamine and motor habits in overdrive. Center for Innovation in Mental Health, Department of Psychology, University of Southampton, Southampton, UK, February 11, 2019.

Miranda B. Vestibulopatia bilateral – Causas Neurológicas. XI Reunião de Inverno da Associação Portuguesa de Otoneurologia, Cascais, Portugal, February 23, 2019.

Maia TV. Using computational psychiatry to develop a rigorous and integrative understanding of psychiatric disorders. 7th Annual Neuroscience Virtual Conference, online conference, March 14, 2019.

Conceição I. Chronic inflammatory neuropathies. Autoantibodies as a phenotype marker. 7^o Congresso Nacional da Sociedade Portuguesa de Estudos de Doenças Neuromusculares, Tomar, Portugal, March 30, 2019.

Miranda B. Da clínica para a investigação básica e de volta à clínica. Programa de Formação em Investigação, Centro de Formação do HSM-CHULN, Lisbon, Portugal, May 22, 2019.

Miranda B. Vestibulopatia bilateral – Causas Neurológicas. Congresso Anual da Associação Portuguesa de Otoneurologia, Évora, Portugal, May 24, 2019.

de Carvalho M. PLS and ALS are two Different Diseases. The Second International PLS Conference, Philadelphia, USA, May 2019.

de Carvalho M. Chairman of the Session “Measuring PLS Disease Progression”. The Second International PLS Conference, Philadelphia, USA, May 2019.

Pronto-Laborinho AC. Keynote Speaker. Molecular Biomarkers Associated with Respiratory Insufficiency in Amyotrophic Lateral Sclerosis. 4th congress of CiiEM on “Health, Well-Being and Ageing in the 21st Century, Monte de Caparica, Portugal, June 2-5, 2019.

de Carvalho M. Muscle and Nerve Damage in Intensive Care: electrophysiological studies. Respiratory Muscles. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

de Carvalho M. Diagnosing Amyotrophic Lateral Sclerosis: clinical and electrophysiological criteria. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

de Carvalho M. Tips for Trainees Lectures: MND EMG. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

de Carvalho M. Chairman of the Session “Muscle and Nerve Damage in Intensive Care: electrophysiological studies”. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

Conceição I. Conventional neurophysiology options for the study of small fibers. Sympathetic skin response. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

Maia TV. Participant and discussant (by invitation only). Strungmann Forum on Intrusive Thinking across Neuropsychiatric Disorders, Frankfurt, Germany, June 14-19, 2019.

Conceição I. Clinical Follow Up of Asymptomatic Gene Carriers: Achieving the Earliest Diagnosis and Therapeutic Intervention. Pfizer Symposium: ATTR (Amyloid Transthyretin) Amyloidosis: The Source, the Impact, the Management. Peripheral Nerve Society 2019 Annual Meeting, Genova, Italy, June 23, 2019.

Conceição I. hATTR Amyloidosis: Tracing the Threads of a Multisystem Disease. Alnylam Symposium: Untangling the Mixed Symptoms: Identifying and treating hATTR Amyloidosis. Peripheral Nerve Society 2019 Annual Meeting, Genova, Italy, June 23, 2019.

Miranda B. Research path – neurociência translacional. Dia da Investigação, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, July 11, 2019.

de Carvalho M. Electrodiagnosis in ALS. 11th Oset Congress, Porto, Portugal, September 9-13, 2019.

Miranda B. Cortical stimulation for behavior and study in animal model. 11th International Organization for Societies for Electrophysiological Technology Congress, Porto, Portugal, September 9-13, 2019.

Conceição I. Embarking on a diagnostic journey: unusual suspects of hATTR. Clues for neurologists. hATTR Southern Europe Summit, Rome, Italy, October 11-12, 2019.

de Carvalho M. Doente informado e comprometido: o acesso a tratamentos em fase experimental. C-HEALTH Congress, Lisbon, Portugal, October 22, 2019.

Conceição I. Sistema Nervoso Autónomo. Quando e como avaliar. Curso de avaliação clínica e investigação do Sistema Nervoso Periférico e Sistema Nervoso Autónomo da SPN, Coimbra, Portugal, November 13, 2019.

Conceição I. Diagnosticar PAF. Quando diagnosticar quando referenciar. Simposium Akcea: atualização em Polineuropatia Amiloidotica Familiar, Congresso Nacional de Neurologia, Coimbra, Portugal, November 13, 2019.

Maia TV. Keynote Speaker. Using computational psychiatry to develop a rigorous and integrative understanding of psychiatric disorders. 9th International Conference on Aspects of Neuroscience, Warsaw, Poland, November 23, 2019.

de Carvalho M. OnWebDuals Project. JPND /JPco-fuND Symposium, Brussels, Belgium, November 2019.

de Carvalho M. Chairman of the Session “Clinical Electrophysiology”. 30th International Symposium on ALS/MND, Perth, Australia, December 4-6, 2019.

de Carvalho M. Chairman of the Session “Refining LMN features: imaging”. Gold Coast Consensus Meeting, Brisbane, Australia, 2019.

Communications in International Conferences

Dasgupta NR, Falk RH, Drachman BM, Maurer MS, Whelan CJ, Brannagan T, Coelho T, Waddington-Cruz M, Damy T, Hanna M, Berk JL, Merlini G, Conceição I, Hughes SG, Kwoh J, Jung SW, Guthrie S, Pollock M, Gertz M, Benson MD, Heitner S. Safety of Inotersen Treatment in Patients with Transthyretin Amyloid Cardiomyopathy. American College of Cardiology’s 68th Annual Scientific Session & Expo, New Orleans, USA, March 16-18, 2019. *(Poster Presentation)*.

Drachman BM, Brannagan T, Maurer MS, Heitner S, Whelan CJ, Coelho T, Waddington-Cruz M, Damy T, Berk JL, Merlini G, Conceição I, Hughes SG, Kwoh J, Jung SW, Guthrie S, Pollock M, Benson MD, Gertz M. NEURO-TTR Open-label Extension for Hereditary Transthyretin Amyloidosis: 2 year update. American College of Cardiology’s 68th Annual Scientific Session & Expo, New Orleans, USA, March 16-18, 2019. *(Poster Presentation)*.

Brannagan TH, Waddington-Cruz M, Wang AK, Polydefkis MJ, Dyck PJ, Khella S, Plante-Bordeneuve V, Berk JL, Barroso F, Merlini G, Conceição I, Hughes DG, Kwoh J, Shiangtung W, Jung SW, Pollock M, Benson MD, Gertz M, Coelho T. Long-Term Efficacy and Safety of Inotersen for Hereditary Transthyretin Amyloidosis: 2-Year Results From the NEURO-TTR Open-Label Extension Study. American Academy OF Neurology 71st Annual Meeting, Philadelphia, USA, May 4-10, 2019. *(Oral Communication)*.

Coutinho MCA, Cortez-Dias N, Cantinho G, Goncalves S, Guimarães T, Lima Da Silva G, Francisco AR, Santos L, Conceição I, Pinto FJ. Cardiac 99mTc-DPD uptake in transthyretin V30M amyloidosis depends on the age of disease onset. International Congress on Nuclear Cardiology and Cardiac CT, Lisbon, Portugal, May 12-13, 2019. *(Oral Communication)*.

Barć K, Nieporęcki K, Szacka, K, de Carvalho M, Gromicho M, Grosskreutz J, Petri S, Rödiger A, Steinbach R, Uysal H, Kuźma-Kozakiewicz M. The Emotional Liability at Disease Onset is a Prognostic Factor of Faster Disease Progression in Amyotrophic Lateral Sclerosis. ENCALS Meeting 2018, Tours, France, May 15-17, 2019. *(Poster Presentation)*.

Madeira SC, Pires S, Mueller M, Figueiral M, Gomicho M, de Carvalho M. Predicting disease progression in Amyotrophic Lateral Sclerosis using Machine Learning: Learning from longitudinal data using time windows and progression patterns. 53rd Annual Scientific Meeting of the European Society for Clinical Investigation: “The Clocks of Metabolism and Disease”. Coimbra, Portugal, May 22-24, 2019. (*Oral Communication*).

Pereira M, Fernandes SR, Miranda PC, de Carvalho M. Neuromodulation of Lower Limb Motor Pathways with Trans-spinal Direct Current Stimulation: an overview of current findings. Health, Well-Being and Ageing in the XXI Century, Monte de Caparica, Portugal, June 2-5, 2019. (*Poster Presentation*).

Pinto S, Gromicho M, Swash M, de Carvalho M. Cervical Muscle Weakness Correlates with Respiratory Function in Amyotrophic Lateral Sclerosis. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019. (*Oral Communication*).

Castro J, de Carvalho M. The Cutaneous Silent Period (CSP) in Amyotrophic Lateral Sclerosis. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019. (*Poster Communication*).

Bell JM, Shibuya K, Caetano A, de Carvalho M, Kuwabara S, Jones KE. Feasibility of an International Normative Database for Nerve Excitability Studies. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019. (*Poster Communication*).

Caetano A, Pereira M, de Carvalho M. Changes in peripheral nerve excitability by transcutaneous direct currents in healthy subjects - a pilot study. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019. (*Poster Communication*).

José Castro, Bruno Miranda, Isabel de Castro, Isabel Conceição. Neurophysiological changes predates symptoms onset in hereditary amyloidosis related to transthyretin V30M. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019. (*Poster Communication*)

Obici L, Anan I, Ando Y, Coelho T, Conceição I, Cortese A, Dispenzieri A, Sarafov S, Tournev I, Wixner J, Serrano D, Iaconangelo C, Fang A, Kiszko J, Rill D, Stewart M, Sultan M, Mundayat R, Amass L, Waddington-Cruz M. Real-world Effectiveness of Tafamidis in Patients with Transthyretin Amyloidosis with Polyneuropathy in THAOS. 2019 PNS Annual Meeting, Genova, Italy, June 22-25, 2019. (*Poster Presentation*).

Brannagan TH, Cruz MW, Wang AK, Polydefkis MJ, Dyck PJ, Khella S, Plante-Bordeneuve V, Berk JL, Barroso F, Merlini G, Conceição I, Hughes SG, Kwoh J, Jung SW, Pollock M, Benson MD, Gertz M, Coelho T. Long-Term Efficacy and Safety of Inotersen for Hereditary Transthyretin Amyloidosis: 2-Year Results From the NEURO-TTR Open-Label Extension Study. 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Oral Communication)*.

A Yaras, A Sikora Kessler, A Lovley, SD Guthrie, M Pollock, T Coelho, I Conceicao, L Obici, MK White. The impact of disease and treatment on generic health-related quality of life in patients with hATTR amyloidosis: SF-36v2 results from a double-blind placebo controlled trial of inotersen. 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Communication)*.

Sotero FD, Campos C, Conceição I. Hereditary transthyretin amyloidosis V30M: intrafamilial phenotypic variability. 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Communication)*.

Yaras A, Lovley A, Guthrie SD, Pollock M, Kessler AS, Coelho T, Obici L, Conceição I, McCausland KL. The impact of disease and treatment on quality of life as assessed by the Norfolk Quality of Life Questionnaire in hereditary transthyretin amyloidosis relative to diabetic neuropathy. 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Communication)*.

Kyriakides T, Brannagan T, Lin H, Wang Y, Conceição I. Impact of baseline neuropathy stage in patients with hereditary transthyretin-mediated (hATTR) amyloidosis with or without patisiran treatment. 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019. *(Poster Communication)*.

Fernandes SR, Salvador R, de Carvalho M, Miranda P. Electric Field Distribution during Non-Invasive Electric and Magnetic Stimulation of the Cervical Spinal Cord. 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany, July 23-27, 2019. *(Oral Communication)*.

Miranda P, Fernandes SR, de Carvalho M. Modelling Studies of Transcutaneous Spinal Cord Direct Current Stimulation (tsDCS). 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany, July 23-27, 2019. *(Oral Communication)*.

Pires S, M Gromicho, Pinto S, de Carvalho M, Madeira SC. Patient Stratification in Amyotrophic Lateral Sclerosis using Clinical and Patient Profiles. 2019 KDD Workshop on Applied Data Science for Healthcare, Anchorage, USA, August 5, 2019. *(Poster Presentation)*.

Pereira T, Pires S, Gromicho M, Pinto S, de Carvalho M, Madeira SC. Predicting assisted ventilation in Amyotrophic Lateral Sclerosis using a mixture of experts and conformal predictors. 2019 KDD Workshop on Applied Data Science for Healthcare, Anchorage, USA, August 5, 2019. *(Oral Presentation)*.

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Changes on elasticity and morphology of erythrocytes from amyotrophic lateral sclerosis patients. AFM Biomed Conference, Munster, Germany, September 2-6, 2019. *(Poster Presentation)*.

Polydefkis M, Gillmore J, Dispenzieri A, Chen J, Sweetser MT, Vest J, Melanson M, Conceição I, Kristen A. Risk Factors for Mortality in Patients with Hereditary Transthyretin-Mediated Amyloidosis: Analysis of APOLLO and Global Open Label Extension Studies. HFSA 2019 23rd Scientific Meeting, Philadelphia, USA, September 13-16, 2019. *(Poster Presentation)*.

Fernandes SR, de Carvalho M, Miranda PC. Non-Invasive Spinal Cord Stimulation: Relevance of Modelling Studies in Clinical Protocol Design. MEDICON 2019, the 15th Mediterranean Conference on Medical and Biological Engineering and Computing, Coimbra, Portugal, September 26-28, 2019. *(Oral Communication)*.

Pinto S, Pinto A, de Carvalho M. Flail-Arm and Flail-Leg Syndromes: survival impact with non-invasive ventilation. 5th European Congress of Neurorehabilitation, Budapest, Hungary, October 9-12, 2019. *(Poster Presentation)*.

Pinto S, de Carvalho M, Lindsten H. Congenital insensitivity to pain – learning to live in a different reality. 5th European Congress of Neurorehabilitation, Budapest, Hungary, October 9-12, 2019. *(Poster Presentation)*.

Mauricio E, González-Duarte A, Conceição I, Brannagan TH, Dianna, Mezei M, Schmidt H, Wixner J, Dinh Q, Berber E, Sweetser MT, White MT, Wang JJ, Ueda M. Autonomic Manifestations of Hereditary Transthyretin-Mediated Amyloidosis: Long-term. Safety and Efficacy from the Patisiran Global Open-Label Extension Study. AANEM Congress, Austin, Texas. October 16-19, 2019. *(Poster Presentation)*.

Brannagan TH, Cruz MW, Wang AK, Polydefkis MJ, Dyck PJ, Khella S, Plante-Bordeneuve V, Berk JL, Barroso F, Merlini G, Conceição I, Hughes SG, Kwoh J, Jung SW, Pollock M, Benson MD, Gertz M, Coelho T. Long-Term Efficacy and Safety of Inotersen for Hereditary Transthyretin Amyloidosis: 2-Year Results From the NEURO-TTR Open-Label Extension Study. Ottawa International Conference on Neuromuscular Disease and Biology, Ottawa, Canada, October 17-19, 2019. *(Poster Presentation)*.

Matos J, Gromicho M, Pires S, de Carvalho M, Madeira SC. Biclustering Electronic Health Records to Unravel Disease Presentation Patterns: a Case Study in ALS. EEE ICDM 2019 Workshop on Interpretable and Explainable Machine Learning for Healthcare, Beijing, China, November 8, 2019. *(Oral Communication)*.

Pires S, Gromicho M, Pinto S, de Carvalho M, Madeira SC. Patient Stratification using Clinical and Patient Profiles: targeting personalized prognostic prediction in ALS. EEE ICDM 2019 Workshop on Interpretable and Explainable Machine Learning for Healthcare, Beijing, China, November 8, 2019. *(Oral Communication)*.

Costa J, Streich L, Pinto S, Laborinho-Pronto A, Nimtz M, Conradt H S, de Carvalho M. Phosphoneurofilament heavy chain and IgG N-glycosylation as cerebrospinal fluid biomarkers for ALS. 30th International Symposium on ALS/MND, Perth, Australia, December 4-6, 2019. *(Poster Presentation)*.

Grosskreutz J, Al-Chalabi A, van den Berg L, de Carvalho M, Chio A, Corcia P, Couratier P, van Damme P, Grehl T, Ingre C, Kiernan M, Koritnik B, Kuźma-Kozakiewicz M, Meyer T, Neuwirth C, Petri S, Talman P, Uysal H, Veldink J, Weber M, Wicks P, Zidar J. The world according to the D50 model of ALS progression. 30th International Symposium on ALS/MND, Perth, Australia, December 4-6, 2019. *(Poster Presentation)*.

Grosskreutz J, de Carvalho M, Fartmann F, Gromicho M, Kuźma-Kozakiewicz M, Petri S, Stubendorff B, Szacka K, Uysal H. Significant events during ALS progression according to the D50 model in the ONWebDUALS cohort. 30th International Symposium on ALS/MND, Perth, Australia, December 4-6, 2019. *(Poster Presentation)*.

de Carvalho M, Swash M. The split hand in ALS: A possible role for the neuromuscular junction. 30th International Symposium on ALS/MND, Perth, Australia, December 4-6, 2019. *(Oral Presentation)*.

Communications in National Conferences

Costa MR, Gromicho M, Pronto-Laborinho AC, de Carvalho M. Doença do Neurónio Motor Familiar Associada a Mutação do Gene TBK1. 7º Congresso Nacional da Sociedade Portuguesa de Estudos de Doenças Neuromusculares, Tomar, Portugal, March 30, 2019. *(Poster Presentation)*.

Fernandes SR, Pereira M, de Carvalho M, Miranda PC. Promoting Axonal Regeneration Using Non-Invasive Direct Current Stimulation. Encontro Ciência'19, Lisbon, Portugal, July 8-10, 2019. *(Poster Presentation)*.

Pereira M, Fernandes SR, Miranda PC, de Carvalho M. Neuromodulation of Lower Limb Motor Circuitry with Transcutaneous Lumbar Spinal Cord Direct Current Stimulation. Encontro Ciência'19, Lisbon, Portugal, July 8-10, 2019. *(Poster Presentation)*.

Costa J, Streich L, Pinto S, Pronto-Laborinho A, Nimitz M, Conradt HS, de Carvalho M. Exploring Cerebrospinal Fluid IgG N-Glycosylation as Potential Biomarker for Amyotrophic Lateral Sclerosis. 13ª Reunião do Grupo de Glúcidos, Porto, Portugal, September 3-5, 2019. *(Oral Communication)*.

Inês M, Coelho T, Conceição I, Ferreira L, de Carvalho M, Costa J. Health State Utility Values Estimation in Rare Diseases: the case of Hereditary Transthyretin Amyloidosis Polyneuropathy. 16ª Conferência Nacional de Economia da Saúde, Lisbon, Portugal, October 16-18, 2019. *(Poster Presentation)*.

Pisco AR, Gomes BC, Gromicho M, Pronto-Laborinho AC, Rueff J, de Carvalho M, Rodrigues AS. Assessment of microRNAs as Biomarkers of disease progression in amyotrophic lateral sclerosis. Jornadas Toxomics 2019, Lisbon, Portugal, November 9, 2019. *(Poster Presentation)*.

Pronto-Laborinho AC, Gromicho M, Pereira M, Pinto S, Swash M, de Carvalho M. Níveis de Interleucina-6 na Esclerose Lateral Amiotrófica. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Oral Communication)*.

Pronto-Laborinho AC, Lopes CS, Gromicho M, Santos NC, Carvalho FA, de Carvalho M. Alterações na Morfologia dos Eritrócitos na Esclerose Lateral Amiotrófica. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Oral Communication)*.

Pereira M, Swash M, de Carvalho M. Imobilidade e Ondas F: impacto na excitabilidade do 2º neurónio motor. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Poster Communication)*.

Marcolino A, de Carvalho M, Silveira F. Esclerose lateral amiotrófica com alterações sensitivas. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Poster Communication)*.

Coelho T, Conceição I, Polydefkis M, Gonzalez Duarte A, Santos M, Wixner J, A Kristen, Schmidt H, L Berk J, Alves C, Cardoso M, Dinh Q, Berber E, Sweetser M, White M, Wang JJ, Adams D. Long-term safety and efficacy of Patisiran in patients with hATTR amyloidosis: global OLE study. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Oral Communication)*.

Coelho P, Falcão de Campos C; Conceição I. Caracterização fenotípica da amiloidose hereditária relacionada com a TTR (hATTR): estudo retrospectivo do centro de referência HSM-CHULN. Congresso de Neurologia 2019, Coimbra, Portugal, November 14-16, 2019. *(Poster Communication)*.

de Carvalho, M. OnWebDuals Project. GAPIC – Dia da Investigação, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019. *(Poster Presentation)*.

Organization of Conferences

Conceição I. Member of the Steering Committee. Aria VIII Symposium. Advances and Research in ATTR Amyloidosis, Amsterdam, Netherlands, February, 22-23, 2019.

de Carvalho M. Member of the International Advisory and Scientific Board. 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

de Carvalho M. Co-Organizer. Comemorações do 70º Aniversário da atribuição do Prémio Nobel a Egas Moniz, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 2019.

Internationalization

Internationalization has been incremented by the leader position in the international consortium (OnWebDuals project, JPND); the collaboration in consortiums aimed to investigate genetic abnormalities in amyotrophic lateral sclerosis-ALS (Project Mine); the participation in multicenter clinical trials (ALL and FAP); the association with other centers for specific projects in psychiatric disorders for computational and imaging modeling in ALS (respiratory markers of disease progression, and in FAP (new treatments). Our groups play a pivotal international role in important research topics in our main areas: computational and imaging modeling in psychiatric disorders; phenotype-genotype interaction, disease spreading, assessment of respiratory function and neurophysiological changes in ALS; treatment impact, marker for early diagnosis and trials in FAP.

Prizes, Honors and Awards

de Carvalho, M. Publons Peer Review Awards 2019- Global Peer Review Awards, “for placing in the top 1% of reviewers in Neuroscience and Behavior”, September 2019.

de Carvalho, M. Publons Peer Review Awards 2019 - Global Peer Review Awards, “for placing in the top 1% of reviewers in each of the 22 Essential Science Indicators research fields”, September 2019.

de Carvalho, M. *Expertscape* – World Expert in EMG (*top 0.1% of scholars writing about Electromyography over the past 10 years*), 2019.

Industry Contract Research

We have been supported by Cytokinesis in small projects to approach specific scientific questions on the respiratory function in Amyotrophic lateral sclerosis.

Government/Organization Contract Research

National Institute of Mental Health (75N95B19P00153), USA, 2019-2020, PI: T. V. Maia.

Asociación Madrileña de Pacientes con Síndrome de Tourette y Trastornos Asociados, Spain, 2018-2019, PI: T. V. Maia

Ministerio de Ciencia, Innovación y Universidades, Spain, 2019-2021, PI: C. Soriano Mas, Co-I:
T. V. Maia

Advanced Teaching

De Carvalho M. Lectures. The Second International PLS Conference, Philadelphia, USA, May 2019.

De Carvalho M. Workshops in the 17th European Congress on Clinical Neurophysiology, Warsaw, Poland, June 5-8, 2019.

De Carvalho M. Workshops in the 5th Congress of European Academy of Neurology, Oslo, Norway, June 29-July 2, 2019.

Maia TV. Module. Computational neuroscience. Mestrado/Doutoramento em Neurociências, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 25-29, 2019.

Conceição I. Seminars and Lessons. Evoked Potentials. Master Degree and Doctoral Presentation Program on Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

Conceição I. Seminars and Lessons. Neuropathies: Transthyretin-Related Hereditary Amyloidosis. Master Degree and Doctoral Presentation Program on Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

De Carvalho M. Lectures. Master/PhD Degree of Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

Science and Society

Our Unit has developed interactions with different patient associations (Amyotrophic lateral sclerosis (ALS), Tourette, and Amyloidosis) in Portugal and other countries to share our projects and results, and to promote participation. Project MINE represents an international scientific project supported by the Portuguese ALS association. In addition, we have participated in various media initiatives to share scientific information with our society.

MSc Theses

João Afonso Morgadinho Martins, 06/2019, Creatinina, um Biomarcador de Prognóstico e Preditor da Função Respiratória, na Esclerose Lateral Amiotrófica, MIM, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

João Antunes, 11/12/2019, Building-up new approach tendencies in individuals with high versus low fear of contamination, Mestrado em Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Lena Ernst. Co-Supervisor: Tiago V. Maia.

Diogo Afonso de Lima, Ongoing, Hereditary Neuropathy with liability to Pressure Palsies, MIM, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Inês Alexandra Alves, Ongoing, Planeamento cognitivo episódico e semântico: evidência de populações clínicas, Mestrado em Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Miranda.

Renata Cruz, Ongoing, Role of the telencephalon in the maintenance of social dynamics of zebrafish in a free moving environment. Mestrado em Neurociências, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Bruno Miranda.

PhD Theses

Anna Caroline dos Anjos Braga, 06/2019, Amyotrophic Lateral Sclerosis: Exercise and Disease Progression, Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Anabela Pinto. Co-Supervisor: Mamede de Carvalho.

Sofia Rita Fernandes, 10/2019, Transcutaneous Spinal Direct Current Stimulation: Modelling the spinal electric field distribution and clinical relevance, Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Pedro C Miranda. Co-Supervisor: Mamede de Carvalho.

Mónica Sofia Inácio Duarte Inês Mestre, Health Economics of Hereditary Transthyretin Amyloidosis Polyneuropathy, CAML, Faculdade de Medicina da Universidade de Lisboa. Supervisor: João P Costa. Co-Supervisor: Mamede de Carvalho.

Ana Pronto-Laborinho, Biomarcadores Respiratórios na Abordagem Clínica da Esclerose Lateral Amiotrófica, CAML, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho. Co-Supervisor: Filomena Carvalho.

André Caetano, Ongoing, Changes in peripheral nerve excitability by transcutaneous direct currents - results with threshold tracking, Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Mariana Reis da Costa, Ongoing, 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, Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Lígia Sofia Ferreira, Ongoing, Predictors of successful treatment of Refractory Status Epilepticus, Neurociências, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Carla Bentes. Co-Supervisor: Mamede de Carvalho.

Pedro Pereira, Ongoing, Patologia das Neuropatias de Pequenas Fibras – estudos morfológicos, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Mariana Fernandes Alves Pereira, Ongoing, Neuromodulação dos circuitos motores espinhais através de estimulação transcutânea por corrente directa: implicações na Esclerose Lateral Amiotrófica, NeurULisbon-UL, Universidade de Lisboa. Supervisor: Mamede de Carvalho.

Sandra Lopes, Ongoing, Controlo cognitivo e motor na demência frontotemporal e na esclerose lateral amiotrófica, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Miranda.

Marc Veldhoen Lab

Major Interests/Objectives

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.

Head of Laboratory

Marc Veldhoen, PhD

Team

Annes Hilde Valckenaers	University Degree	BSc Student (Started February. Left June)
Birte Blankenhaus	PhD	Senior Postdoctoral Researcher
Cristina da Conceição Varandas Ferreira	PhD	Senior Postdoctoral Researcher
Joana Alexandra Lima Gonçalves	University Degree	MSc Student (Started September)
Leandro Joel Barros Fernandes	Master Degree	PhD Student
Marta Sofia Serra Baptista	Master Degree	Lab Technician
Nicole Nussbaum	Master Degree	MSc Student (Left August)
Patrícia Isabel Figueiredo Campos	Master Degree	PhD Student
Roos Haczewski	University Degree	Lab Technician
Silvia Ariotti	PhD	Postdoctoral Researcher
Spela Konjar	PhD	Senior Postdoctoral Researcher
Tomás Ochôa May Pereira da Cruz	University Degree	MSc Student (Started September)

Laboratory Keywords / Research Areas

Epithelial Immunology, T cell Activation, T cell Differentiation, Tissue Resident T cells
 Immunology, Infection, Vaccination.

Major Scientific Achievements

Preliminary data obtained over the past 3 years regarding the biology of tissue resident memory T cells was awarded funding via the Fundo iMM-Laço award and subsequently via the “la Caixa” Foundation Health Research program. The funding allowed us to speed up our investigation in the generation of tissue resident T cells, the cellular and molecular mechanisms involved in their generation. The first results are now under final revisions at *Nature Immunology*. 3 MSc students successfully submitted and defended their work.

Selected Publications

Fellows R, Denizot J, Stellato C, Cuomo, A., Jain, P., Stoyanova, E., Balazsi, S., Hajnady, Z., Liebert, A., Kazakevych, J., *et al.* (2018). Microbiota derived short chain fatty acids promote histone crotonylation in the colon through histone deacetylases. **Nature Communications** 9:105. (IF: 11878, Citations: 62. Source: Web of Science).

Konjar S, Frising U, Ferreira C, Hinterleitner R, Mayassi T, Blankenhaus B, Guedes J, Zhang Q, Haberman N, Loo Y, Baptista M, Innocentin S, Stange J, Strathdee D, Jabri B, Veldhoen M (2018). Mitochondria maintain controlled state of activation in epithelia resident T lymphocytes. **Science Immunology** 3(24):eaan2543. (IF: 10.551, Citations: 9. Source: Web of Science).

Brucklacher-Waldert V, Ferreira C, Stebegg M, Fesneau O, Innocentin S, Marie JC, Veldhoen M (2017). Cellular Stress in the Context of an Inflammatory Environment Supports TGF-beta-Independent T Helper-17 Differentiation. **Cell Reports** 19(11):2357-2370. (IF: 7.815, Citations: 20. Source: Web of Science).

Brucklacher-Waldert, V., Ferreira, C., Innocentin, S., Kamdar, S., Withers, D.R., Kullberg, M.C., and Veldhoen, M. (2016). Tbet or Continued RORgammat Expression Is Not Required for Th17-Associated Immunopathology. **Journal of Immunology** 196(12):4893-4904. (IF: 4.718. Citations: 11. Source: Web of Science).

Withers DR, Hepworth MR, Wang X, Mackley EC, Halford EE, Dutton EE, Marriott CL, Brucklacher-Waldert V, Veldhoen M, Kelsen J, Baldassano RN, Sonnenberg GF (2016). Transient inhibition of RORyt therapeutically limits intestinal inflammation by reducing TH17 cells and preserving group 3 innate lymphoid cells. **Nature Medicine** 22(3):319-23. (IF: 30.641, Citations: 96. Source: Web of Science).

Ongoing Research Projects

29019/2022: Enhancing Tissue Resident Immunity. Coordinator: Marc Veldhoen. Funding Agency: Fundación Bancaria "la Caixa". Reference: HR18-00104, "ETERNITY"- "ENHANCING TISSUE RESIDENT. Amount: € 497 158,00. Total Amount: € 497 158,00.

2019/2020: Fundo IMM-Laço. Coordinator: Marc Veldhoen. Reference: Marc Veldhoen. Reference: FUNDO LAÇO - MARC VELDHOEN. Amount: € 29 700,00. Total Amount: € 29 700,00.

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.

2015/2020: EXCELLtoINNOV: Leverage research EXCELLENce 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.

Other Projects

2015/2019: ENLIGHT-TEN: European Network linking informatics and genomics of helper T cells. Coordinator: Jochen Huhn, Marc Veldhoen. Funding Agency: European Commission. Reference: MSCA ITN 675395. Amount: € 433 512,72. Total Amount: € 3 354 685,20.

Publications in Peer Reviewed Journals

Ariotti S, Veldhoen M (2019). Immunology: Skin T Cells Switch Identity to Protect and Heal. **Current Biology** 29(6):R220-R223. (IF: 9.193. Citations: 0. Source: Web of Science).

Cossarizza A, Chang HD, Radbruch A, Acs A, Adam D, Adam-Klages S, Agace WW, Aghaeepour N, Akdis M, Allez M, *et al.* (2019). Guidelines for the use of flow cytometry and cell sorting in immunological studies (second edition). **European Journal of Immunology** 49(10):1457-1973. (IF: 4.695. Citations: 27. Source: Web of Science).

Konjar S, Veldhoen M (2019). Dynamic Metabolic State of Tissue Resident CD8 T Cells. **Frontiers in Immunology** 10:1683. (IF: 4.716. Citations: 3. Source: Web of Science).

Zhang S, Al-Maghout T, Cao I, Pelzl L, Salker M, Veldhoen M, Cheng A, Lang F, Singh Y (2019). Gut bacterial metabolite Urolithin A (UA) mitigates Ca²⁺ entry in T cells by regulating miR-10a-5p. **Frontiers in Immunology** 10:1737. (IF: 4.716. Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Toulouse University, Toulouse, France, February 2019.

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 2019.

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Francis Crick Institute, London, UK, October 2019.

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Technical University of Denmark, Lyngby, Denmark, November 2019.

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Universidade de Aveiro, Aveiro, Portugal, November 2019.

Communications in International Conferences

Veldhoen M. Co-Organizer and speaker. Epithelial barriers: Maintaining and generating resident T lymphocytes. EMBO Immunology sectorial meeting, Cambridge, UK, February 2019.

Veldhoen M. Speaker. Epithelial barriers: Maintaining and generating resident T lymphocytes. Portuguese Society for Immunology 2019, Coimbra, Portugal, May 2019.

Veldhoen M. Organizer and speaker. Epithelial barriers: Maintaining and generating resident T lymphocytes. ExceltoInnov CD8 T Cell Meeting, Lisbon, Portugal, May 2019.

Figueiredo-Campos P. How to activate non-conventional epithelial T cells. XLV Annual Meeting of Portuguese Society for Immunology, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, May 15-17, 2019. (*Poster Presentation*).

Figueiredo-Campos P. How to activate non-conventional epithelial T cells. PhD Summer School Host-Microbe Symbiosis: From genetics to metabolic interactions, Instituto Gulbenkian de Ciência, Oeiras, Portugal, July 14th-26th, 2019. (Poster presentation)

Veldhoen M. Speaker and session chair. Epithelial barriers: Maintaining and generating resident T lymphocytes. European Academy of Allergy and Clinical Immunology Congress 2019, June 2019.

Konjar S. Metabolic programming of epithelia resident T lymphocytes during activation. Tissue environment in health and disease, Champalimaud Foundation, Lisbon, Portugal, October 8-10, 2019. (*Poster Presentation*).

Konjar S. Metabolic reprogramming of epithelia resident CD8+ T lymphocytes during activation. Crosstalk of immunity and metabolism, Instituto Gulbenkian de Ciência, Oeiras, Portugal, 11-14 November, 2019. (*Oral Presentation*).

Communications in National Conferences

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. Instituto de Medicina Molecular João Lobo Antunes Scientific Retreat, Évora, Portugal, April 2019. (*Oral Presentation*)

Figueiredo-Campos P. How to activate non-conventional epithelial T cells. XIII Annual CAML PhD Students' Meeting, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Veldhoen M. Epithelial barriers: Maintaining and generating resident T lymphocytes. CONGENTO Meeting, Champalimaud Centre for the Unknown, Lisbon, Portugal, October 2019. (*Oral Presentation*).

Organization of Conferences

Veldhoen M. Co-Organizer and speaker. EMBO Immunology Sectorial Meeting, Cambridge, UK, February 2019.

Veldhoen M. Organizer and speaker. EXCELLtoINNOV CD8 T Cell Meeting, Lisbon, Portugal, May 2019.

Internationalization

We are part of several international collaborations, including France, UK, Germany and the US.

We participated in international meetings can be found under "conferences".

We have invited speakers as part of the ERA Chair project and the TwinnToInfect Twinning program. We are part of an H2020 ITN, annual meeting and summer school and are currently writing a new ITN project (January 2020). We are part of a European T-cell focus group, funded by EMBO, which organizes an annual meeting to exchange ideas and with additional funding from EFIS obtained in 2018.

In addition, as part of a consortium, we applied for NMBP23 2020: Next generation of organ on a chip (RIA LS) first round of funding. Lastly, M Veldhoen participated in several PhD examination, including in the UK, France and Denmark and the lab hosts many international students under the ERASMUS program.

Advanced Teaching

Veldhoen M. T cell biology. Mestrado em Biologia Molecular e Genética Fronteiras da Investigação em Biologia, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, April 16, 2019.

Ferreira C. T cell development. Mestrado em Biologia Molecular e Genética Fronteiras da Investigação em Biologia, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, April 16, 2019.

Veldhoen M. Imunidade Celular II, Tronco Comum IIa, Mestrado Integrado em Medicina, Universidade de Lisboa, Lisbon, Portugal, October 10, 2019.

Veldhoen M. Imunidade das Mucosas, Tronco Comum IIa Mestrado Integrado em Medicina, Universidade de Lisboa, Lisbon, Portugal, October 17, 2019.

Veldhoen M. T helper cell types and cytokines. Licenciatura Ciências da Nutrição, Universidade de Lisboa, Lisbon, Portugal, October 17, 2019.

Veldhoen M. T helper cell types and cytokines. Licenciatura Ciências da Nutrição, Universidade de Lisboa, Lisbon, Portugal, October 17, 2019.

Veldhoen M. Mucosal immunology (T cells and ILCs). Licenciatura Ciências da Nutrição, Universidade de Lisboa, Lisbon, Portugal, October 24, 2019.

Veldhoen M. T cell subsets, Host-Pathogen Interactions, PhD Immunology Course, NOVA Universidade de Lisboa, Instituto Gulbenkian de Ciência, Oeiras, Portugal, October 25, 2019.

Veldhoen M. Microbiota and immunity, Licenciatura Ciências da Nutrição, Universidade de Lisboa, Lisbon, Portugal, October 29, 2019.

Veldhoen M. Metabolism and Immunity, Licenciatura Ciências da Nutrição, Universidade de Lisboa, Lisbon, Portugal, November 5, 2019.

Veldhoen M. Mucosal immunology, MCEdIE | Imunologia fundamental, Universidade de Lisboa, Lisbon, Portugal, December 10, 2019.

Veldhoen M. The complexity of Thelper subsets. Master Immunology course, Pasteur Institute and Paris Universities, Paris, France, December 13, 2019.

Science and Society

Members of the lab, Birte Blankenhaus and Patricia Figueiredo Campos participated in the Immunology Day 2019 (29 of April). It was in the Egas Moniz Building and dedicated to school groups that would be able to do hands-on activities all related with the Immune system. Our stand was the "microbiota and immune system", where we isolated bacteria from the saliva of the kids and looked at them live under a microscope.

MSc Theses

Jona You, 11/04/2019, The Role of the AhR Interacting Protein in T cells, University of Applied Sciences FH Campus Vienna, Austria. Supervisor: Marc Veldhoen and Cristina Ferreira.

Annes Valckenaers, 06/2019, Mouse Microbiota Analysis upon Antibiotic Treatment and Eimeria Vermiformis Infection, Farmaceutische en biologische laboratoriumtechnologie, University of Ghent, Belgium. Supervisor: Marc Veldhoen and Patrícia Figueiredo-Campos.

Roos Haczewski, 17/06/2019, The role of AhR-interacting protein in lymphocytes, Hanze Hogeschool Groningen, The Netherlands. Supervisor: Marc Veldhoen.

Maria Carmo-Fonseca Lab

Major Interests/Objectives

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 the role of RNA in the regulation of gene expression in cancer, cardiac and neurological diseases, and we are exploring new therapeutic strategies targeting disease-causing RNA molecules.

Head of Laboratory

Maria do Carmo Salazar Velez Roque da Fonseca, MD/PhD, Full Professor

Graphical Abstract

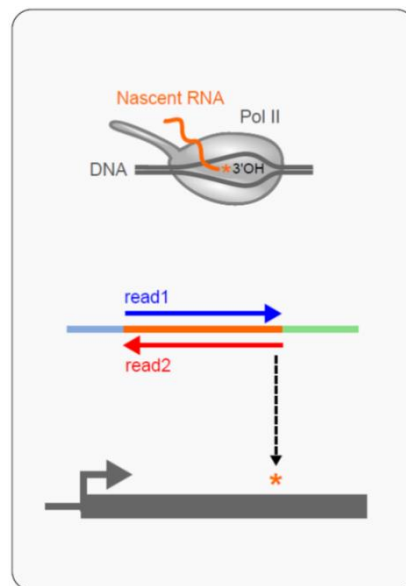


Figure 1: Genome-wide analysis of nascent transcripts

Team

Adriana Andrade Vieira	University Degree	MSc Student (Started September)
Ana Cláudia Bernardino Raposo	Master Degree	PhD Student
Beatriz Pinto Galvão	University Degree	MSc Student (Started October)
Carina Sofia Barradas Maranga	Master Degree	PhD Student
Carolina Correia de Figueiredo Abreu Pereira	Master Degree	Lab Technician (Left August)
Catarina Alves do Vale	Master Degree	Trainee
Catarina Guerra Ferreira	University Degree	MSc Student (Left December)

Célia da Conceição Vicente Carvalho	PhD	Staff Scientist
Christian Gomes da Silva Ramos	PhD	Senior Postdoctoral Researcher
Cláudia Raquel Estopa Gil	Master Degree	Lab Technician (Left December)
Cristiano Emanuel Ribeiro Esteves	University Degree	BSc Student
Dinora Levy	University Degree	Administrative Technician
Evguenia Pavlovna Bekman	PhD	Senior Postdoctoral Researcher
João Tiago Alves Prior Proença	PhD	Senior Postdoctoral Researcher (Started July)
Kenny Patrick Figueira Rebelo	Master Degree	Lab Technician (Left August)
Marcia Triunfol	PhD	Senior Postdoctoral Researcher
Maria Joana Pinto Desterro	PhD	Staff Scientist
Maria João de Andrade Terras Arez	Master Degree	Lab Technician
Maria Teresa Tenório Figueiredo Carvalho Gonçalves	PhD	Staff Scientist
Marta Isabel Brandão Furtado	University Degree	MSc Student
Miguel Francisco Cruz Romano Guedes	University Degree	MSc Student (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 (Started November)
Pedro António Pereira Prudêncio	Master Degree	PhD Student
Pedro Ervilha Pereira	Master Degree	Lab Technician (Left May)
Pedro Galhardo Bak-Gordon	High School Diploma	MSc Student
Pedro Santos Barbosa	Master Degree	PhD Student
Renata Inês Proença Casimiro	Master Degree	Lab Technician (Left September)
Rita Catarina Vaz Drago	PhD	Postdoctoral Researcher (Left October)
Rosina Savisaar	PhD	Postdoctoral Researcher (Started August)
Rui Gonçalo Viegas Russo da Conceição Martinho	PhD	Visiting Researcher
Rui Sérgio de Sousa Luís	Master Degree	PhD Student (Started February)
Samantha Mancino	PhD	Postdoctoral Researcher (Started July)
Sandra Cristina Bento Penisga Martins	PhD	Senior Postdoctoral Researcher
Sandrina Nóbrega Pereira	PhD	Senior Postdoctoral Researcher (Started July)
Sara Patricia Henriques Castro	Master Degree	Lab Technician
Simão José Teixeira da Rocha	PhD	Staff Scientist
Tajda Klobucar	University Degree	MSc Student (Started May)
Teresa Maria Pereira da Silva	Master Degree	Postdoctoral Researcher
Tomás Miguel Custódio dos Santos	High School Diploma	MSc Student

Laboratory Keywords / Research Areas

Laboratory Keywords: RNA Biology, Gene Regulation, Splicing, RNA in Disease.

Research Areas: Cell and Molecular Biology, Human Genetics, Cancer.

Major Scientific Achievements

Our lab is known for studies on RNA splicing using a combination of cutting-edge cell imaging and genome-wide approaches. Our previous work indicated that reciprocal interconnectivity between the different steps required for gene activation plays a critical role ensuring efficiency and fidelity of gene expression. 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; Prudêncio, Rebelo *et al.* 2019). Using this methodology, we have unraveled unanticipated dynamic links between Pol II and the spliceosome (Nojima, Rebelo, *et al.*, 2018). In parallel, our lab is developing stem-cell derived cellular models to study the role of RNA molecules in cardiac and neurological diseases, and we are testing drugs that target defects in mRNA splicing as an anticancer strategy (Desterro, *et al.*, 2019).

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. (IF: 14.55, Citations: 21. Source: Google Scholar).

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. (IF: 36.22, Citations: 254. Source: Google Scholar).

Martin RM, Rino J, Carvalho C, Kirchhausen T, Carmo-Fonseca M (2013). Live-cell visualization of pre-mRNA splicing with single-molecule sensitivity. **Cell Reports** 4(6):1144-1155. (IF: 7.81, Citations: 102. Source: Google Scholar).

de Almeida SF, Grosso AR, Koch F, Fenouil R, Carvalho S, Andrade J, Levezinho H, Gut M, Eick D, Gut I, Andrau JC, Ferrier P, Carmo-Fonseca M (2011). Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36. **Nature Structural & Molecular Biology** 18(9):977-983. (IF: 12.59, Citations: 201. Source: Google Scholar).

Grosso AR, Gomes AQ, Barbosa-Morais NL, Caldeira S, Thorne NP, Grech G, von Lindern M, Carmo-Fonseca M (2008). Tissue-specific splicing factor gene expression signatures. **Nucleic Acids Research** 36(15):4823-4832. (IF: 11.15, Citations: 149. Source: Google Scholar).

Ongoing Research Projects

2019/2022: RNA in disease – RiboMed. Coordinator: Maria Carmo-Fonseca. Funding Agency: European Commission. Reference: RiboMed - GA 857119. Amount: € 424 750,00. Total Amount: € 799 795,00.

2019/2020: Homenagem Prof. Fernando Lopes da Silva. Coordinator: Maria Carmo-Fonseca. Funding Agency: Fundação BIAL. Reference: Homenagem Prof. Fernando Lopes da Silva. Amount: € 5 000,00. Total Amount: € 5 000,00.

2019/2019: Meeting - Lessons from targeted deep sequencing. Coordinator: Maria Carmo-Fonseca. Funding Agency: Celgene. Reference: Meeting - Lessons from targeted deep sequencing. Amount: € 2 245,18. Total Amount: € 2 245,18.

2019/2019: Catalysing transcriptomics research in cardiovascular disease (CardioRNA). Coordinator: Maria Carmo-Fonseca. Funding Agency: Cost Action. Reference: COST - CA17129 – CardioRNA. Amount: € 10 000,00. Total Amount: € 10 000,00.

2018/2021: O papel dos RNAs não-codificantes longos (lncRNAs) na adaptação molecular e metabólica do cancro da mama. Coordinator: Maria Carmo-Fonseca. Reference: RNAMETCANCER - LISBOA-01-0145-FEDER-028534. Amount: € 238 213,92. Total Amount: € 238 213,92.

2018/2021: CEREBREX: Desenvolvimento de organóides cerebelares para investigação de ataxias. Coordinator: Maria 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.

2018/2021: BRCA_RNA: Organóides com edição génica para estudar o impacto funcional de mutações BRCA1 e BRCA2. Coordinator: Maria 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: As barreiras epigenéticas do envelhecimento na reprogramação celular. Coordinator: Simão Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-MOL/29320/2017. Amount: € 239 555,22. Total Amount: € 239 555,21.

2018/2019: Identification of genes involved in DNA repair that may be used to develop novel targeted therapies for breast cancer. Coordinator: Rui Martinho. Funding Agency: Fundo iMM-Laço. Reference: Fundo iMM-Laço. Amount: € 25 000,00. Total Amount: € 25 000,00.

2017/2024: The Discoveries CTR: Implementation of the discoveries centre for regenerative and precision medicine, a new centre of excellence in Portugal. Coordinator: Maria Carmo-Fonseca. Funding Agency: European Commission. Reference: Teaming 739572. Amount: € 1 001 137,50 (Lisbon University). Total Amount: € 14 996 606,25.

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

2016/2019: The non-coding transcriptome in stemness and aging. Coordinator: Bruno Jesus. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MED/0032/2014. Amount: € 188 175,00. Total Amount: € 188 175,00.

2016/2019: Molecular constraints to pre-mRNA splicing in fast dividing cells. Coordinator: Rui Martinho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BID/0395/2014. Amount: € 98 888,00. Total Amount: € 198 831,00.

2016/2019: Making sense of antisense transcription. Coordinator: Maria Carmo-Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BCM/5899/2014. Amount: € 200 000,00. Total Amount: € 200 000,00.

2016/2019: Comprehensive study of the dynamics of epigenetic processes involving lncRNAs during iPSC reprogramming. Coordinator: Simão Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BCM/2612/2014. Amount: € 157 880,00. Total Amount: € 157 880,00.

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

2015/2020: Exploring the role of lncRNAs and chromatin modifying complexes for the establishment of defined chromatin states. Coordinator: Simão Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00242/2014/CP1236/CT0009. Amount: € 50 000,00. Total Amount: € 50 000,00.

Publications in Peer Reviewed Journals

Sousa AC, Silveira C, Janeiro A, Malveiro S, Oliveira AR, Felizardo M, Nogueira F, Teixeira E, Martins J, Carmo-Fonseca M (2019). Detection of rare and novel EGFR mutations in NSCLC patients: implications for treatment-decision. **Lung Cancer** 139:35-40. (IF: 3.96).

Desterro J, Bak-Gordon P, Carmo-Fonseca M (2019). Targeting mRNA processing as an anticancer strategy. **Nature Reviews Drug Discovery** 19(2):112- Review. (IF: 57.62, Citations: 1. Source: Web of Science).

Prudêncio P, Rebelo K, Grosso AR, Martinho RG, Carmo-Fonseca M (2019). Analysis of mammalian native elongating transcript sequencing (mNET-seq) high-throughput data. **Methods**. (IF: 3.78, Citations:--. Source: Web of Science).

Silva TP, Cotovio JP, Bekman E, Carmo-Fonseca M, Cabral JMS, Fernandes TG (2019). Design principles for pluripotent stem cell-derived organoid engineering. **Stem Cells International** 4508470. Review. (IF: 3.90, Citations: 4. Source: Web of Science).

da Rocha ST, Gendrel AV (2019). The influence of DNA methylation on monoallelic expression. **Essays in Biochemistry** 63(6):663-676. Review (IF: 3.338, Citations: 0. Source: Web of Science).

Bousard A, Raposo AC, Żylicz JJ, Picard C, Pires VB, Qi Y, Gil C, Syx L, Chang HY, Heard E, da Rocha ST (2019). The role of Xist-mediated Polycomb recruitment in the initiation of X-chromosome inactivation. **EMBO Reports** 20(10):e48019. (IF: 8.749, Citations: 1. Source: Web of Science).

Żylicz JJ, Bousard A, Žumer K, Dossin F, Mohammad E., da Rocha ST, Schwalb B, Syx L, Dingli F, Loew D, Cramer P, Heard E (2019). The implication of early chromatin changes in X chromosome inactivation. **Cell** 176(1-2):182-197. (IF: 31.298, Citations: 21. Source: Web of Science).

Sousa-Franco A, Rebelo K, da Rocha ST, Bernardes de Jesus B (2019). LncRNAs regulating stemness in aging. **Aging Cell** 18(1):e12870. Review. (IF: 7.627, Citations: 4. Source: Web of Science).

Other International Publications

Gomes CPC *et al.*, on behalf of the EU-CardioRNA COST Action (2019). Catalyzing transcriptomics research in cardiovascular disease: the EU-CardioRNA COST Action (CA17129). **Noncoding RNA** doi: 10.3390/ncrna5020031.

Silveira C, Triunfol M, Carmo-Fonseca M (2019). RNA sequencing: a complementary tool kit for the diagnosis of Mendelian disorders. **AACC/Clinical Laboratory News** <https://www.aacc.org/publications/cln/articles/2019/october/rna-sequencing>

Other National Publications

Carmo-Fonseca M. Prefácio do livro “A alma está no cérebro” de Eduardo Punset (D. Quixote).

Invited Lectures and Seminars

Carmo-Fonseca M. Conferência de receção aos novos Internos, Hospital Prof. Doutor Fernando Fonseca, Lisbon, Portugal, January 2, 2019.

Carmo-Fonseca M. Antisense transcripts as targets for rejuvenation interventions. RNA Meeting ptRNA, Porto, Portugal, January 24-25, 2019.

da Rocha ST. Epigenetic stability and long non-coding RNAs in stem cell biology. IBIMED, Universidade de Aveiro, Aveiro, Portugal, February 13, 2019.

Carmo-Fonseca M. The timing of splicing. Nuclear and Cytoplasmic Molecular Machines at Work, New York University Abu Dhabi, United Arab Emirates, April 8-10, 2019.

Carmo-Fonseca M. É possível reverter o envelhecimento? Congresso da Sociedade Portuguesa de Neurocirurgia, Lisbon, Portugal, May 25, 2019.

Carmo-Fonseca M. RNA and gene regulation. FEBS Advanced Course on Functional imaging of nuclear organization and signaling, Amsterdam, The Netherlands, June 10, 2019.

Carmo-Fonseca M. The timing of splicing. Keynote Lecture, Annual Meeting of the RNA Society, Kraków, Poland, June 11-16, 2019.

da Rocha ST. Epigenetic variability of iPSCs. Edith HEARD 17 years of e(Xist)ing at Curie, Institut Curie, Paris, France, June 28, 2019.

Carmo-Fonseca M. Splicing kinetics. The RNA localization and local translation conference, Snowmass Village, CO, USA, June 30-July 5, 2019.

Carmo-Fonseca M. Single-molecule live-cell imaging of mRNA life cycle. Biophysics Congress, Madrid, Spain, July 20-24, 2019.

Carmo-Fonseca M. Co-transcriptional splicing. Keynote Lecture, RNA Informatics, Wellcome Genome Campus, Hinxton, Cambridge, UK, September 9-11, 2019.

Carmo-Fonseca M. My career in science. PhD Program, NOVA Medical School, Lisbon, Portugal, September 13, 2019.

Carmo-Fonseca M. O médico como cientista. Congresso Nacional de Medicina, Porto, Portugal, September 27, 2019.

Carmo-Fonseca M. Live-cell analysis of pre-mRNA processing with single-molecule resolution. Spanish and Portuguese Advanced Optical Microscopy Meeting, Coimbra, Portugal, November 6-8, 2019.

Carmo-Fonseca M. Imaging the life cycle of mRNA with single molecule resolution. Symposium Imagerie et signalisation, Faculté de Médecine Paris-Sud, Paris, France, November 14, 2019.

Carmo-Fonseca M. Screening for mRNA biomarkers of response to cancer therapy. Targeting RNA, Frankfurt, Germany, November 26-27, 2019.

Carmo-Fonseca M. Sarcomeric cardiomyopathies: pathways from bench to bedside. International Post-graduate Learning Course on Cardiomyopathies in Clinical Practice, Lisbon, Portugal, November 28, 2019.

Carmo-Fonseca M. Medicina de precisão. Conferência de Abertura, Colóquio ANDAR, Lisbon, Portugal, November 29, 2019.

da Rocha ST. Epigenetic variability of iPSCs: consequences for disease modelling. Institut de Génétique Moléculaire de Montpellier (IGMM), CNRS & University of Montpellier, Montpellier, France, November 29, 2019.

Carmo-Fonseca M. Prevenção genética. Acrescentar conhecimento à saúde, Lisbon, Portugal, December 3, 2019.

Carmo-Fonseca M. Cancer development in mammary organoids from BRCA mutation carriers. DevBioMed Symposium, Champalimaud Center for the Unknown, Lisbon, Portugal, December 13, 2019.

Communications in International Conferences

Silva TP, Fernandes TG, Bekman E, Vaz SH, Rodrigues CAV, Hashimura Y, Jung S, Lee B, Carmo-Fonseca M, Cabral JMS. Scalable generation of cerebellar neurons from pluripotent stem cells. Advancing Manufacture of Cell and Gene Therapies VI, California, USA, January 27-31, 2019. (*Poster Presentation*).

da Rocha ST, Bousard A, Zylicz JJ, Raposo A, Picard C, Pires V, Qi Y, Syx L, Chang HY and Heard E. Exploring the role of Polycomb recruitment in Xist-mediated silencing of the X chromosome in ES cells. Keystone Symposium Conference on Epigenetics and Human Diseases (X5), Banff, Canada, March 18, 2019. (*Oral Presentation*).

Barbosa P, Ribeiro M, Garcia AB, Tavares J, Carmo-Fonseca M, Fonseca A. VETA: a framework to assess computational tools for predicting clinical significance of genetic variation. Intelligent Systems for Molecular Biology and European Conference on Computational Biology, Basel, Switzerland, July 21-25, 2019. (*Poster Presentation*).

Gil C, Raposo A, da Rocha ST. Functional Dissection of the Conserved Sequences within Xist lncRNA and Its Protein Interactors in X-Chromosome Inactivation. 3rd International Symposium on Frontiers in Molecular Science on RNA Regulatory Networks, Lisbon, Portugal, June 26-28, 2019. (*Poster Presentation*).

da Rocha ST, Bousard A, Zylicz JJ, Raposo A, Picard C, Pires V, Qi Y, Syx L, Chang HY and Heard E. Exploring the Role of Xist-mediated Polycomb Recruitment in the Initiation of Transcriptional Silencing of the X Chromosome. 3rd International Symposium on Frontiers in Molecular Science on RNA Regulatory Networks, Lisbon, Portugal, June 26-28, 2019. (*Poster Presentation*).

Pessoa J, Carvalho C, Rino J, Carmo-Fonseca M. Targeting catalytically dead Cas9 to a protein-coding gene without transcriptional interference. EMBO Young Scientists Forum, Prague, Czech Republic, June 27-28, 2019. (*Poster Presentation*).

Barbosa P. Predicting clinical significance of intronic variation in disease-causing genes. RNA Informatics, Wellcome Genome Campus, Hinxton, Cambridge, UK, September 9-11, 2019. (*Oral Presentation*).

Ribeiro M, Furtado M, Carvalho T, Martins S, Tavares J, Lopes L, Syrris P P, Akhtar M, Elliot P and Carmo-Fonseca M. An improved tissue engineering protocol to generate cardiomyocytes from patient iPSCs. Annual meeting of the ESC Working Group on Myocardial & Pericardial Diseases (M&PD 2019), Corunã, Spain, October 4-5, 2019. (*Poster Presentation*).

Silva TP, Fernandes TG, Bekman E, Vaz SH, Rodrigues CAV, Hashimura Y, Jung S, Lee B, Carmo-Fonseca M, Cabral JMS. Large scale production of cerebellar organoids from human pluripotent stem cells using the novel Vertical-Wheel single-use bioreactors. 7th International Conference on Stem Cell Engineering 2019, Barcelona, Spain, December 11-13, 2019. (*Poster Presentation*).

Communications in National Conferences

Bak-Gordon P, Luís R, Carmo-Fonseca M. Mining single-cell transcriptomic data for clues on tissue-specific expression of BRCA genes. RNA meeting ptRNA, Porto, Portugal, January 24-25, 2019. (*Poster Presentation*).

da Rocha ST, Arez M, Raposo A. Epigenetic variability in iPSCs: causes and consequences. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10, 2019. (*Oral Presentation*).

Arez M, Eckersley-Maslin M, da Rocha ST. Comprehensive Evaluation of Genomic Imprinting Stability in Mouse iPSCs. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10, 2019. (*Poster Presentation*).

Raposo AC, Luís R, Cadere FT, Esteves C, da Rocha ST. Stability of X-inactivation in female hiPSCs. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Lisbon, Portugal, October 10, 2019. (*Poster Presentation*).

Silva TP. Novel bioengineering strategies for modeling cerebellar ataxias. Lisbon Area Postdoc Meeting 2019, Costa da Caparica, November 14-15, 2019. (*Oral Presentation*).

Carvalho C, Custódio N, Dias P, Porto B, Sousa AB, Carmo-Fonseca M. A BRCA2 intronic variant of uncertain significance alters pre-mRNA splicing. 23rd Annual Meeting of the Portuguese Society of Human Genetics, Coimbra, Portugal, November 14-16, 2019. (*Poster Presentation*).

Santos T, Carvalho C. Exploring the connection between the glycolytic pathway and the proliferation capacity in TN breast cancer cells. Dia da Investigação, GAPIC, Faculdade de Medicina de Lisboa da Universidade de Lisboa, Lisbon Portugal, December 11, 2019. (*Poster Presentation*).

Pais ACC, Carvalho C. Accurate measurement of BRCA1 gene expression on mononucleated blood cells using droplet digital PCR: development of a screening test for rare variants of BRCA1 mutations. Dia da Investigação, GAPIC, Faculdade de Medicina de Lisboa da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019. (*Poster Presentation*).

Organization of Conferences

Carmo-Fonseca M. Organizer. 2nd COST Action CardioRNA, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 13-15, 2019.

Carmo-Fonseca M. Organizer. First RNA in Disease (RiboMed) Meeting, Hotel Riviera, Carcavelos, Portugal, October 14-16, 2019.

Ramos CG. Organizer & member of the Scientific committee. Lisbon Area Postdoc Meeting 2019, Costa da Caparica, Portugal, November 14-15, 2019.

Internationalization

Carmo-Fonseca M. Coordinates an EU H2020 Research and Innovation Staff Exchange (RISE) programme entitled “LysoMod: Genetic and small molecule modifiers of lysosomal function”.

Carmo-Fonseca M. Participates in a EUH2020 Teaming Grant with the University College London entitled “Implementation of the Discoveries Centre for Regenerative and Precision Medicine, a new Centre of Excellence in Portugal”.

Carmo-Fonseca M. Participates in COST action CardioRNA: Catalysing transcriptomics research in cardiovascular disease.

Carmo-Fonseca M. Coordinates an EU H2020 Research and Innovation Twinning program entitled “RiboMed: RNA in disease”.

Da Rocha ST. Collaborates with Prof. Edith Heard at the Curie Institute on RNA-seq and ChIP-seq experiments on inducible Xist non-coding RNA mutants and their effects on X-linked gene inactivation.

Prizes, Honors and Awards

M. Carmo-Fonseca was considered one of the “Most influential women in Portugal” by the magazine Executiva, May 16, 2019. <https://executiva.pt/sao-as-mulheres-influentes-portugal-2018/>

M. Carmo-Fonseca was awarded Prémio Aboim Sande Lemos – Identidade Portuguesa/2018. Sociedade Histórica da Independência de Portugal. May 23, 2019.

M. Carmo-Fonseca was appointed member of the Conselho Geral do Instituto Politécnico de Bragança. June 24, 2019.

M. Carmo-Fonseca was appointed member of the Advisory Board for Lusíadas Saúde, SA. October 29, 2019.

M. Carmo-Fonseca was appointed member of the Scientific Advisory Board for Fundação Bial. November 22, 2019.

Catarina Alves-Vale was awarded the 16th “AstraZeneca Foundation/FMUL” Research Grant. December 2019.

M. Carmo-Fonseca chaired the Jury for the Bial Award in Biomedicine 2019.

Advanced Teaching

da Rocha ST. Epigenetic stability and long non-coding RNAs in stem cell biology Course in Frontiers in Biology Research, Master in Molecular Biology and Genetics, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, February 27, 2019.

da Rocha ST. Epigenetics and Gene Expression. PhD program IBIMED/Aveiro and Nova Medical School/Lisbon, Aveiro, Portugal, May 7, 2019.

Carvalho T. “Observação e caracterização de cardiomiócitos derivados de hiPSCs”. Practical laboratory session in the “Stem cell Master Course”, Master Program in Evolutionary and Developmental Biology, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 8, 2019.

Martins S. “Manipulação e diferenciação de células estaminais em cardiomiócitos”. Lecture. “Stem cell Master Course”, Master Program in Evolutionary and Developmental Biology, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 8, 2019.

Martins, S. and Carvalho T. Supervision of Laboratory rotation for International Medical students Yasmin Abdou (Egypt) and Daniel Dali de Anda Gallo (Mexico), “In Vivo Cellular Models of cardiomyopathies”, July 1-26, 2019.

Custódio N. Seminar. Transcription and RNA processing in human genetic diseases. Mestrado em Tecnologias Moleculares em Saúde, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, October 3, 2019.

Custódio N. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student Pedro Bak-Gordon. Looking beyond DNA: Characterizing the impact of the Portuguese BRCA2 founder mutation on mRNA processing using induced pluripotent stem cells.

Carvalho C. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical students Santos T, Carvalho C. Exploring the connection between the glycolytic pathway, the epithelial-mesenchymal transition and the growth capacity in TN breast cancer cells.

Carvalho C. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student Pais ACC. Accurate measurement of BRCA1 gene expression on mononucleated blood cells using droplet digital PCR: development of a screening test for rare variants of BRCA1 mutations.

Martins, S. Supervision of GAPIC (“Educação pela Ciência”) research project. Medical student João Sousa. In Vivo Cellular Models of cardiomyopathies.

Science and Society

Carmo-Fonseca M. Conferência Inovação e Conhecimento. Assembleia da República, Lisbon, Portugal, January 8, 2019.

da Rocha ST. Sustentabilidade e edição genética – desafios para a Biologia no século XXI. IX Congresso Associação Portuguesa de Professores de Biologia e Geologia (APPBG), Coimbra, Portugal, April 27, 2019.

Carmo-Fonseca M. O futuro da humanidade: a tecnologia vai salvar-nos ou matar-nos? Masterclasses COGITO, Oeiras, Portugal, September 17, 2019.

Carmo-Fonseca M. Will amortality be possible? 2019 Brokerslink Conference, Bordeaux, France, October 17-18, 2019.

MSc Theses

Cláudia Gil, 08/11/2019, Functional dissection of the Xist lncRNA conserved sequences in X-chromosome inactivation, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Simão Teixeira da Rocha.

Catarina Guerra Ferreira, 20/12/2019, Mammary organoids to study the functional impact of BRCA mutations, Mestrado em Ciências Biofarmacêuticas, Faculdade de Farmácia da Universidade de Lisboa (16 Valores). Supervisor: M. Carmo-Fonseca.

Miguel Francisco Cruz Romano Guedes, 18/12/2019, How the lncRNA Zeb2-NAT regulates the expression of Zeb2, Mestrado em Ciências Biofarmacêuticas, Faculdade de Farmácia da Universidade de Lisboa (16 Valores). Supervisor: Noélia Custódio.

Marta Isabel Brandão Furtado Furtado, 13/12/2019 “Developing gene-edited models to study mis-splicing in Hypertrophic Cardiomyopathy”, Master in Molecular Genetics and Biomedicine, Faculdade de Ciências e Tecnologia Universidade Nova de Lisboa (19 Valores). Supervisor: Sandra Martins. Co-Supervisor: Teresa Carvalho.

Maria Mota Lab

Major Interests/Objectives

Disease burden is disproportionally distributed around the globe. A direct contributor to such asymmetry is malaria – more than 200 million new infections and 400 thousand deaths still occur every year. Disease combat is impaired by a poor understanding of the factors that dictate the onset of severe disease and outcome of infection.

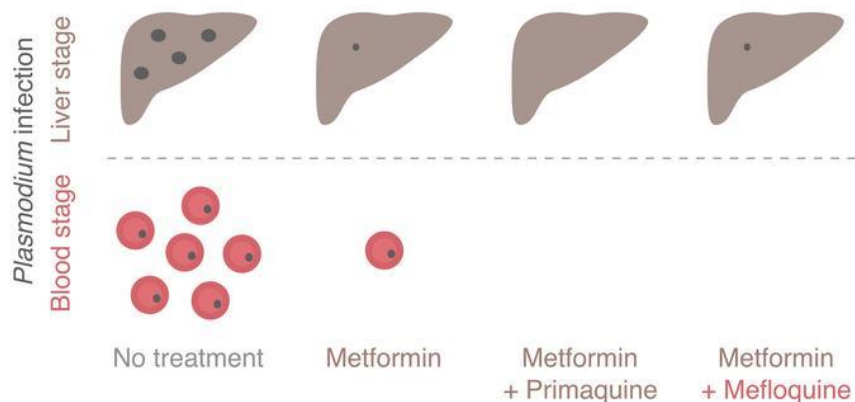
Our overall goal has been towards the elucidation of the most fundamental and conceptually innovative questions of Host-*Plasmodium* interactions. Our ongoing work indicates that the web of host-*Plasmodium* interactions is densely woven, with liver stage and the blood stage interacting towards pathology and disease severity. Moreover, we have identified a third-party determining disease – host microbiota!

We continue to pursue our long-lasting question – What is so special about the liver? Our data indicates that the liver special metabolism might be the key to modulate the ability of *Plasmodium* species that infect mammals to achieve extraordinary rates of replication.

Head of Laboratory

Maria Manuel Dias da Mota, PhD, Executive Director of iMM

Graphical Abstract



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	Master Degree	PhD Student
Camila Fernandes Mariano	University Degree	MSc Student
Catarina Alexandra Dinis de Andrade Pedro	University Degree	MSc Student
Cristina Fernández Arias	PhD	Senior Postdoctoral Researcher
Debanjan Mukherjee	Master Degree	PhD Student
Inês Fernandes Bento	PhD	Senior Postdoctoral Researcher
Joana Lisboa da Silva Gonçalves	Master Degree	PhD Student
João Tiago Carvalho Jordão de Mello Vieira	Master Degree	PhD Student
Maria Inês Moreira Oliveira Leite Marreiros	Master Degree	PhD Student
Sara de Jesus Santos Baptista	Master Degree	PhD Student
Sofia Pinto Guia Marques	PhD	Lab Manager
Sonali Setua	PhD	Postdoctoral Researcher
Sónia Maria Leite Pereira	Master Degree	PhD Student
Soraia Cristina Marques Caetano	PhD	Postdoctoral Researcher (Started June)
Vanessa Alexandra Zuzarte Luís	PhD	Senior Postdoctoral Researcher
Viriato M'Bana	Master Degree	PhD Student
Yash Girish Pandya	PhD	Postdoctoral Researcher (Started October)

Laboratory Keywords/Research Areas

Keywords:

Malaria, *Plasmodium*, Replication, Microbiota, Pathology.

Research Areas:

Liver Metabolism and Parasite Replication, Host-*Plasmodium*-Microbiota Interactions, Parasite Nutrient Sensing and Adaptation.

Major Scientific Achievements

While 2019 was a year with significant advances in several lines of research, we highlight an important study published this year (Vera *et al.*, JCI Insight).

We had previously demonstrated that AMPK negatively modulates hepatic infection by *Plasmodium* parasites and that several AMPK-activating drugs cause a reduction in the intracellular growth of rodent *P. berghei* parasites *in vitro*.

Following up on those observations, this year we report that prophylactic treatment with the widely used antidiabetic drug, metformin, impairs parasite liver stage development of both *P. berghei* and *P. falciparum* parasites. Moreover, metformin provided in combination with conventional antimalarial drugs further reduced the total burden of *P. berghei* infection and substantially lessened disease severity in mice. Together, our findings indicate that repurposing of metformin in a prophylactic regimen could be considered for malaria chemoprevention – a discovery that we have recently patented.

Selected Publications

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. (IF: 14.174, Citations: 15. Source: Web of Science).

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. (IF: 14.174, Citations: 19. Source: Web of Science).

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. (IF: 40.137, Citations: 33. Source: Web of Science).

Slavic K, Krishna S, Lahree A, Bouyer G, Hanson KK, Vera I, Pittman JK, Staines HM, Mota MM (2016). A vacuolar iron-transporter homologue acts as a detoxifier in *Plasmodium*. **Nature Communications** 7:10403. (IF: 12.124, Citations: 19. Source: Web of Science).

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. (IF: 29.886, Citations: 124. Source: Web of Science).

Ongoing Research Projects

2018/2021: Hepatic metabolism driving *Plasmodium* replication. Coordinator: Maria Manuel 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: Vias Metabólicas do Ferro em *Plasmodium*: deteção, aquisição e desintoxicação. 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: Modulação da malária pela interação entre as duas fases da infeção por *Plasmodium*. 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 Manuel Mota. Funding Agency: Fundación Bancaria "La Caixa". Reference: PoEMM: La Caixa. Amount: €499 950,00. Total Amount: € 499 950,00.

2018/2019: Sanofi - Institut Pasteur Awards 2018. Coordinator: Maria Manuel Mota. Funding Agency: Institut Pasteur. Reference: Sanofi - Institut Pasteur Awards 2018. Amount: € 150 000,00. Total Amount: € 150 000,00.

2018/2019: Prémio L'Oréal. Coordinator: Inês Bento. Funding Agency: L'Oréal Paris. Reference: PRÉMIO LOREAL - INÊS BENTO. Amount: € 13 500,00. Total Amount: € 13 500,00.

2016/2019: Evasão da autofagia da célula hospedeira: mecanismos de sobrevivência do *Plasmodium* na fase hepática da infeção. Coordinator: Maria Manuel Mota. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MEC/1342/2014. Amount: € 200 000,00. Total Amount: € 200 000,00.

Publications in Peer Reviewed Journals

Vera IM, Grilo Ruivo MT, Lemos Rocha LF, Marques S, Bhatia SN, Mota MM, Mancio-Silva L (2019). Targeting liver stage malaria with metformin. **JCI Insight** 4(24):e127441. (IF: 6.014, Citations: 0 Source: Web of Science).

Mukherjee D, Chora ÂF, Mota MM (2019). Microbiota, a Third Player in the Host-*Plasmodium* Affair. **Trends in Parasitology** 36(1):11-18. Review. (IF: 8.020, Citations: 0 Source: Web of Science).

Mota MM, Mello-Vieira J (2019). Parasitism: Anopheles Mosquitoes and *Plasmodium* Parasites Share Resources. **Current Biology** 29(13):R632-R634. (IF: 9.193, Citations: 0 Source: Web of Science).

de Menezes MN, Salles ÉM, Vieira F, Amaral EP, Zuzarte-Luís V, Cassado A, Epiphany S, Alvarez JM, Alves-Filho JC, Mota MM, D'Império-Lima MR (2019). IL-1 α promotes liver inflammation and necrosis during blood-stage *Plasmodium chabaudi* malaria. **Scientific Reports** 9(1):7575. (IF: 4.011, Citations: 0 Source: Web of Science).

Ribot JC, Neres R, Zuzarte-Luís V, Gomes AQ, Mancio-Silva L, Mensurado S, Pinto-Neves D, Santos MM, Carvalho T, Landry JJM, Rolo EA, Malik A, Silva DV, Mota MM, Silva-Santos B, Pamplona A (2019). $\gamma\delta$ -T cells promote IFN- γ -dependent *Plasmodium* pathogenesis upon liver-stage infection. **Proceedings of the National Academy of Sciences of the United States of America** 116(20):9979-9988. (IF: 9.58, Citations: 1 Source: Web of Science).

Other International Publications

Zuzarte-Luis V, Mota M.M. "The hepatocyte as a household for *Plasmodium* parasites." in "The Liver" 6th edition Wiley Library (2019). Chapter 86.

Invited Lectures and Seminars

Mota MM. The complexity and the simplicity of host-*Plasmodium* interaction. Microbiology and Immunology at Stanford University School of Medicine Seminar Series, Stanford, USA, February 12-14, 2019.

Mota MM. Host, *Plasmodium* and the Surrounding Environment. Gordon Research Conference (GRC) Tropical Infectious Diseases Gordon Research Conference, Texas, USA, March 24-29, 2019.

Mota MM. Overview of the Complexity of Malaria Biology. NIAID_BMGF malaria vaccine workshop, Rockville, USA, May 22-23, 2019.

Zuzarte-Luís V. Doenças Infeciosas: Passado, Presente e Futuro. XV Biologia na Noite, Universidade de Aveiro, Aveiro, Portugal, May 27, 2019.

Mota MM. The complexity and the simplicity of host-*Plasmodium* interactions. Keystone Symposia on Molecular and Cellular Biology, Addis Ababa, Ethiopia, October 30-November 3, 2019.

Communications in International Conferences

Mukherjee D, Ferreira-Chora A, Ramiro R, Gordo I, Mota MM. Microbiota- A new player in Host-*Plasmodium* affair. BioMalPar XV: Biology and Pathology of the Malaria Parasite, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany, May 28-30, 2019. (*Oral Presentation*).

Lahree A, Zuzarte-Luís V, Sundaramurthy V, Zerial M, Mota MM. Eve (EEF) and Apple (APPL1): Plucking a forbidden fruit of host endosomal signalling. BioMalPar XV: Biology and Pathology of the Malaria Parasite, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany, May 28-30, 2019. (*Poster Presentation*).

Lahree A, Zuzarte-Luís V, Sundaramurthy V, Zerial M, Mota MM. Eve (EEF) and Apple (APPL1): Impersonating a signalling endosome. 30th Annual Molecular Parasitology Meeting, Marine Biology Laboratory (MBL), University of Chicago, Woodshole, USA, September 15-19, 2019. (*Poster Presentation*).

M'Bana V, Lahree A, Slavic S, Mota MM. 30th Annual Molecular Parasitology Meeting, Marine Biology Laboratory (MBL), University of Chicago, Woodshole, USA, September 15-19, 2019. (*Poster Presentation*).

Communications in National Conferences

Lahree A, Zuzarte-Luís V, Sundaramurthy V, Zerial M, Mota MM. Eve (EEF) and Apple (APPL1): Impersonating a signaling endosome. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Baptista S, Mota MM, Zuzarte-Luís V. The K(ey) factor in *Plasmodium* liver stage infection. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Fernandez-Arias C, Fernandez C. How do red blood cells know when to die?. Tissue environment in health and disease. Champalimaud Foundation, Lisbon, Portugal. October 8-10, 2019. (*Oral Presentation*).

Marreiros MM, Zuzarte-Luís V, Mota MM. Establishing a blood-stage infection: The role of SAM in *Plasmodium* development. GABBA Annual Scientific Meeting, Instituto de Investigação e Inovação em Saúde, Porto, Portugal, December 20, 2019. (*Oral Presentation*).

Mukherjee D, Ferreira-Chora A, Ramiro R, Gordo I, Mota MM. Microbiota- A new player in Host-*Plasmodium* affair. XLV Portuguese Society for Immunology Meeting, Coimbra, Portugal, 2019. (*Oral Presentation*).

Organization of Conferences

Lahree A. Co-Organizer. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019.

Internationalization

The Mota Lab has developed over the years and strengthened in 2019 a network of international collaborations with multiple laboratories around the world. This strategy allows us to develop more interdisciplinary projects by bringing together our own interest and expertise on *Plasmodium* with that of others in different areas. Examples are liver metabolism (J. Mato, CIC, Biogune, Spain), metabolism of microbial pathogens (M. Barrett, Glasgow University, UK), *P. falciparum* epigenetics (A. Scherf, Institut Pasteur, France), *Plasmodium* transporters (S. Krishna and H. Staines, St. George's, University of London, UK), *Plasmodium* genetic technologies (O. Billker, Sanger Institute, UK), endosome biology and 3D tissue imaging (M. Zerial, Max Planck Institute, Germany) and human micro livers (S. Bhatia, MIT, USA).

Additionally, Debanjan Mukherjee visited Prof. Laurence Zitvogel lab in Villejuif, France to learn Fecal-Microbiota-Transplant experiments from humans to mice.

Prizes, Honors and Awards

Debanjan Mukherjee - Best oral communication award at the EMBL Conference: BioMalPar XV: Biology and Pathology of Malarial Parasite Meeting 45, 2019.

Debanjan Mukherjee - Best oral communication award at the XLV Portuguese Society for Immunology Meeting, 2019.

Debanjan Mukherjee - EMBO short-term fellowship, 2019.

Advanced Teaching

Mello-Vieira J, Mukherjee D, Mota MM. Lecturers. Biology and the Host-Microbe Interface PhD Program, Instituto de Medicina Molecular João Lobo Antunes/ITQB/IGC, Universidade de Lisboa, April 1, 2019.

Zuzarte-Luis V, Mello-Vieira Mota MM. Lecturers. Masters in Clinical Microbiology and Infectious Diseases, Malaria Module, Universidade de Lisboa, Lisbon, Portugal, May 29-30, 2019.

Science and Society

Bento I, Marques M. International Immunology Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 29, 2019.

Marques S, Parreira A. 4th grade students visit to Mota Lab, May 10, 2019.

Marques S, Parreira A. 12th grade students visit to Mota Lab, May 28, 2019.

Zuzarte-Luís V. Speaker. 100th anniversary of Sir Eddington's expedition to Principe, Sociedade de Geografia de Lisboa, Lisbon, Portugal, May 29, 2019.

Mota MM. O Futuro E A Esperança – Os desafios da ciência e o envolvimento da sociedade. Instituto Miguel Galvão Teles, Lisbon, Portugal, July 2, 2019.

Baptista S. Organizer. Next Einstein Forum Africa Science Week Cabo Verde 2019, Cabo Verde, September 23-October 8, 2019.

Zuzarte-Luís V, Bento I. Tutor. Teaching Science. African Science Week, Cabo Verde, October 03-07, 2019.

Mota MM. Curso Livre - Ciência, Democracia e Sociedade, Centro de Filosofia das Ciências da Universidade de Lisboa, Lisbon, Portugal, November 14, 2019.

Mota MM. Ciência e Universo - Encontro Fundação Francisco Manuel dos Santos, Portugal, November 16, 2019.

MSc Theses

Camila Mariano, 25/11/2019, Characterization of *Plasmodium* replication throughout its life cycle, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Inês Bento.

Catarina Pedro, 29/11/2019, *Plasmodium* exploitation of host methionine metabolism, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Vanessa Alexandre Zuzarte-Luís.

Mário Ramirez Lab

Major Interests / Objectives

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 bacterial genomics, microbial typing data sharing, data analysis and visualization tools is ongoing. The development of novel laboratory methodologies for the diagnosis of infectious diseases is also an active area of research.

Head of Laboratory

Mário Nuno Ramos d'Almeida Ramirez, MD/PhD

Team

Ana Carolina Santos Rodrigues de Castro	University Degree	MSc Student
Ana Catarina da Silva e Costa	PhD	Postdoctoral Researcher
Ana Isabel de Aquino Friães	PhD	Senior Postdoctoral Researcher
Ana Rita de Oliveira Rosado Freire da Silva	High School Diploma	MSc Student (Started October)
Ana Teresa Fernandes Alegre Branco	University Degree	Trainee (Left April)
Andreia das Neves Horácio	Master Degree	PhD Student (Left March)
Andreia Isabel Pais Santos	University Degree	MSc Student (Started November)
Beatriz Gonçalves Esteves	University Degree	MSc Student
Beatriz Vicente dos Santos	University Degree	MSc Student (Started September)
Bruno Brandão de Capistrano	University Degree	MSc Student (Started December)
Bruno Filipe Ribeiro Gonçalves	Master Degree	PhD Student
Catarina Ferreira Duarte	Other	BSc Student (Left September)
Catarina Inês Marques de Sousa Mendes	Master Degree	PhD Student
Cezar Vinícius Würdig Riche	Master Degree	PhD Student (Left August)
Elisabete Raquel Ferreira Martins	PhD	Senior Postdoctoral Researcher
Francisca Baptista Vieira Melo	High School Diploma	Trainee (Started October. Left December)

Inês Maria Marques Teodoro	University Degree	MSc Student
Joana Catarina Ferreira da Silva	High School Diploma	MSc Student (Started February)
Joana Filipa Gomes da Silva	Master Degree	Lab Technician
Joana Rita Sebastião Ferreira da Costa	University Degree	MSc Student
João André Nogueira Custódio Carriço	PhD	Staff Scientist
José Augusto Gamito Melo Cristino	MD/PhD	Clinical Staff Scientist
Marcos Daniel Caetano Borges de Pinho	PhD	Postdoctoral Researcher
Maria Antónia Couto Viana Lomba	Other	Administrative Technician (Left December)
Miguel Paulo Machado	Master Degree	Lab Technician (Left January)
Pedro Miguel Festas Marinho	Master Degree	Trainee
Pedro Rafael Vila Cerqueira	Master Degree	Lab Technician (Started April)
Rafael Fresca Mamede	Master Degree	Lab Technician (Started July)
Rui David Ferro Pedrosa	University Degree	MSc Student
Sara Mateus Mahomed	Other	MSc Student
Soraia Isabel da Silva Guerreiro	Master Degree	Lab Technician (Left May)
Thomas Hanscheid	MD/PhD	Clinical Staff Scientist
Tiago Miguel Garcia Ferreira	High School Diploma	Trainee (Started October. Left December)

Laboratory Keywords / Research Areas

Population Biology and Genomics, Bioinformatics, Detection of Antimalarial Drug Resistance, Molecular Epidemiology, Diagnostic Tools, Antibiotic Resistance.

Major Scientific Achievements

Found that short-term increases emm types in invasive disease caused by *Streptococcus pyogenes* were associated with distinct super antigen profiles.

Identified and characterized the first penicillin nonsusceptible *Streptococcus agalactiae* in Europe.

Found that vaccine serotypes are still major causes of pediatric invasive pneumococcal disease in Portugal.

Established the importance of molecular diagnostic methods for an accurate picture of the serotypes causing pediatric invasive pneumococcal disease.

Found that *Streptococcus canis* are a single population infecting multiple hosts.

Established a novel *P. falciparum in vitro* culture protocol.

Selected Publications

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. (IF: 7.185, Citations: 14. Source: Web of Science).

Lopes E, Fernandes T, Machado MP, Carriço JA, Melo-Cristino J, Ramirez M, Martins ER, The Portuguese Group For The Study Of Streptococcal Infections (2018). Increasing macrolide resistance among *Streptococcus agalactiae* causing invasive disease in non-pregnant adults was driven by a single capsular-transformed lineage, Portugal, 2009 to 2015. **EuroSurveillance** 24(7):1307-1314. (IF: 7.421, Citations: 3. Source: Web of Science).

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. **Microbial Genomics** 4(3):000166. (IF: 4.853, Citations: 12. Source: Web of Science).

Pato C, Melo-Cristino J, Ramirez M, Friães A, Portuguese Group for the Study of Streptococcal Infections (2018). *Streptococcus pyogenes* causing skin and soft tissue infections are enriched in the recently emerged *emm89* clade 3 and are not associated with abrogation of CovRS. **Frontiers of Microbiology** 9:2372. (IF: 4.259, Citations: 2. Source: Web of Science).

Pinho MD, Erol E, Ribeiro-Gonçalves B, Mendes CI, Carriço JA, Matos SC, Preziuso S, Luebke-Becker A, Wieler LH, Melo-Cristino J, Ramirez M (2016). Beta-hemolytic *Streptococcus dysgalactiae* strains isolated from horses are a genetically distinct population within the *Streptococcus dysgalactiae* taxon. **Scientific Reports** 6: 31736. (IF: 4.011, Citations: 3. Source: Web of Science).

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. (IF: 4.868, Citations: 2. Source: Web of Science).

Ongoing Research Projects

2019/2020: Pediatric complicated pneumonia – the importance of molecular methods in the etiological diagnosis. Coordinator: Catarina Silva-Costa. Funding Agency: Sociedade Portuguesa de Doenças Infecciosas e Microbiologia Clínica (Bolsa de Estudo Dr. Mário Nunes da Costa/Alere). Total Amount: € 5 000,00.

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.

2017/2020: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Ramirez. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

2016/2019: The changing pneumococci: adapting to vaccination and transitioning between colonization and disease. Coordinator: José Melo Cristino. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-EPI/1555/2014. Amount: € 179 000,00. Total Amount: € 179 000,00.

2016/2019: An integrated system for bacterial genome tracking using high throughput sequencing technology: from identification to visualization. Coordinator: João Carriço. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: TUBITAK/0004/2014. Amount: € 61 572,00. Total Amount: € 98 721,22.

Publications in Peer Review Journals

Friães A, Melo-Cristino J, Ramirez M, Portuguese Group for the Study of Streptococcal Infections (2019). Changes in emm types and superantigen gene content of *Streptococcus pyogenes* causing invasive infections in Portugal. **Scientific Reports** 9:18051. (IF: 4.011, Citations: 0. Source: *Web of Science*).

Fleres G, Couto N, Schuele L, Chlebowicz M A, Mendes C I, van der Sluis L W M, Rossen J W A, Friedrich A W, García-Cobos S (2019). Detection of a novel mcr-5.4 gene variant in hospital tap water by shotgun metagenomic sequencing. **Journal of Antimicrobial Chemotherapy** 75(2):3626–3628. (IF: 5.113, Citations: 0. Source: *Web of Science*).

Espadinha D, Sobral RG, Mendes CI, Méric G, Sheppard SK, Carriço JA, de Lencastre H, Miragaia M (2019). Distinct phenotypic and genomic signatures underlie contrasting pathogenic potential of *Staphylococcus epidermidis* clonal lineages. **Frontiers of Microbiology** 10:1971. (IF: 4.259, Citations: 0. Source: Web of Science).

Duque-Valencia J, Forero-Muñoz NR, Díaz FJ, Martins E, Barato P, Ruiz-Saenz J (2019). Phylogenetic evidence of the intercontinental circulation of a Canine distemper virus lineage in the Americas. **Scientific Reports** 9:15747. (IF: 4.011, Citations: 0. Source: Web of Science).

Hänscheid T, Grobusch MP (2019). Coenzyme Q10 and cerebral malaria in mice: Questionable interpretations, improbable usefulness in humans. **Parasitology International** 74:101969. (IF: 4.011, Citations: 0. Source: Web of Science).

Dias O, Saraiva J, Faria C, Ramirez M, Pinto F, Rocha I (2019). iDS372, a phenotypically reconciled model for the metabolism of *Streptococcus pneumoniae* Strain R6. **Frontiers of Microbiology** 10:1283. (IF: 4.259, Citations: 0. Source: Web of Science).

Barkham T, Zadoks RN, Azmai MNA, Baker S, Bich VTN, Chalker V, Chau ML, Dance D, Deepak RN, van Doorn HR, Gutierrez RA, Holmes MA, Huong LNP, Koh TH, Martins E, Mehershahi K, Newton P, Ng LC, Phuoc NN, Sangwichian O, Sawatwong P, Surin U, Tan TY, Tang WY, Thuy NV, Turner P, Vongsouvath M, Zhang D, Whistler T, Chen SL (2019). One hypervirulent clone, sequence type 283, accounts for a large proportion of invasive *Streptococcus agalactiae* isolated from humans and diseased tilapia in Southeast Asia. **PLoS Neglected Tropical Diseases** 13(6):e0007421. (IF: 4.487, Citations: 1. Source: Web of Science).

Caneiras C, Lito L, Melo-Cristino J, Duarte A (2019). Community- and hospital-acquired *Klebsiella pneumoniae* urinary tract infections in Portugal: virulence and antibiotic resistance. **Microorganisms** 7(5):138. (IF: 4.167, Citations: 1. Source: Web of Science).

Caneiras C, Lito L, Mayoralas-Alises S, Díaz-Lobato S, Melo-Cristino J, Duarte A (2019). Virulence and resistance determinants of *Klebsiella pneumoniae* isolated from a Portuguese tertiary university hospital centre over a 31-year period. **Enfermedades Infecciosas Y Microbiología Clinica** 37(6):387–393. (IF: 1.685, Citations: 2. Source: Web of Science).

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. **Frontiers of Microbiology** 10:631. (IF: 4.259, Citations: 1. Source: Web of Science).

Silva-Costa C, Brito MJ, Aguiar SI, Lopes JP, 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 (2019). Dominance of vaccine serotypes in pediatric invasive pneumococcal infections in Portugal (2012-2015). **Scientific Reports** 9:6. (IF: 4.011, Citations: 0. Source: Web of Science).

Echániz-Aviles G, Guerreiro SI, Silva-Costa C, Mendes CI, Carriço JA, Carnalla-Barajas MN, Soto-Noguerón A, Velazquez-Meza ME, Melo-Cristino J, Luévanos-Velazquez A, Martínez-Medina L, Vázquez-Larios MDR, Ramirez M (2019). Streptococcus pneumoniae serotype 3 in Mexico (1994 to 2017): decrease of the unusual clonal complex 4909 lineage following PCV13 introduction. **Journal of Clinical Microbiology** 57(1):e01354-18. (IF: 4.959, Citations: 0. Source: Web of Science).

Pinto M, González-Díaz A, Machado MP, Duarte S, Vieira L, Carriço JA, Marti S, Bajanca-Lavado MP, Gomes JP (2019). Insights into the population structure and pan-genome of Haemophilus influenzae. **Infection Genetics and Evolution** 67:126–135. (IF: 2.611, Citations: 3. Source: Web of Science).

Jesus TF, Ribeiro-Gonçalves B, Silva DN, Bortolaia V, Ramirez M, Carriço JA (2019). Plasmid ATLAS: plasmid visual analytics and identification in high-throughput sequencing data. **Nucleic Acids Research** 47:D188–D194. (IF: 11.147, Citations: 2. Source: Web of Science).

Björnsdóttir ES, Martins ER, Erlendsdóttir H, Haraldsson G, Melo-Cristino J, Ramirez M, Kristinsson KG (2019). Group B Streptococcal Neonatal and Early Infancy Infections in Iceland, 1976-2015. **Pediatric Infectious Disease Journal** 38(6):620–624. (IF: 2.317, Citations: 0. Source: Web of Science).

Hanscheid T, Schlagenhauf P, Grobusch MP (2019). Atovaquone/proguanil for malaria chemoprophylaxis - Could a difference in susceptibility during hepatic development explain the need to continue drug intake for 7 days post-exposure? **Travel Medicine and Infectious Disease** 21:101527. (IF: 4.868, Citations: 0. Source: Web of Science).

Huizenga E, van der Ende J, Zwinkels N, Jimissa A, van der Ende-Bouwman C, van Rooijen R, Kargbo B, Agnandji ST, Hanscheid T, Goorhuis A, Grobusch MP (2019). A Modified Case Definition to Facilitate Essential Hospital Care During Ebola Outbreaks. **Clinical Infectious Diseases** 68(10):1763-1768. (IF: 9.117, Citations: 0. Source. Web of Science).

Hanscheid T, Grobusch MP (2019). Could antibiotic treatment of traveller's diarrhoea even prolong elimination of pathogens? **Travel Medicine and Infectious Disease** 28:104. (IF: 4.868, Citations: 0. Source. Web of Science).

Hanscheid T (2019). A Simple Method to Test Microscope Objectives Using a Laser Pointer. **Microscopy Today** 27(5):32-34. (IF:--, Citations:--).

Invited Lectures and Seminars

Ramirez M. Streptococcus - definitely more than the pneumococcus. 4th Annual Dubai International Conference on Infectious Diseases and Vaccination, Dubai, UAE, April 25-27, 2019.

Ramirez M. Maturing pneumococcal vaccination programs in children: implications for adult and at-risk group vaccination. 4th Annual Dubai International Conference on Infectious Diseases and Vaccination, Dubai, UAE, April 25-27, 2019.

Carriço JA, Ramirez M. INNUENDO platform overview and data management. WGS-based surveillance: a cog-wheel workshop to detect links and promote collaboration among OHEJP projects and external initiatives, Dubrovnik, Croatia, September 16-17, 2019.

Carriço JA, Ramirez M. Pipelines of the INNUENDO platform. WGS-based surveillance: a cog-wheel workshop to detect links and promote collaboration among OHEJP projects and external initiatives, Dubrovnik, Croatia, September 16-17, 2019.

Carriço JA, Ramirez M. UI/UX of the INNUENDO platform WGS-based surveillance: a cog-wheel workshop to detect links and promote collaboration among OHEJP projects and external initiatives, Dubrovnik, Croatia, September 16-17, 2019.

Carriço JA, Ramirez M. Future directions of the INNUENDO platform. WGS-based surveillance: a cog-wheel workshop to detect links and promote collaboration among OHEJP projects and external initiatives, Dubrovnik, Croatia, September 16-17, 2019.

Ramirez M. Using next generation sequencing in clinical microbiology. Illumina Users Group Meeting, Oeiras, Portugal, October 9, 2019.

Communications in International Conferences

Mendes CI. Workflow automation with Nextflow and Flowcraft. 3rd Meeting Bioinformatics in Medical Microbiology NL, Utrecht, Netherlands, March 11, 2019.

Pinho MD, Castro AC, Melo-Cristino J, Ramirez M. Diversity of emm types among *Streptococcus dysgalactiae* subspecies equisimilis isolates recovered from invasive and non-invasive human infections in Portugal. 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Poster Presentation*).

Martins ER, Costa J, Fernandes T, Lopes E, Melo-Cristino J, Ramirez M. Expansion of a macrolide-resistant lineage of Group B streptococci causing skin and soft tissue infections among adults in Portugal (2005-2016). 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Oral Presentation*).

Mendes CI, Lizarazo E, Machado MP, Silva DN, Tami A, Ramirez M, Couto N, Rossen JWA, Carriço JA. DEN-IM: dengue virus identification from metagenomic sequencing data. 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Oral Presentation*).

Espadinha D, Sobral R, Mendes CI, Méric G, Sheppard SK, Carriço JA, De Lencastre H, Miragaia M. Strategies of adaptation of *Staphylococcus epidermidis* lineages to commensal and pathogenic lifestyle. 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Oral Presentation*).

Belas A, Aboim C, Leal R, Mendes CI, Carbonetto MB, Marques C, Carriço JA, Pomba MC. 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Poster Presentation*).

Friães A, Marrão G, Ramirez M, Melo-Cristino J. Low macrolide resistance and minimal clonal diversity among *Streptococcus pyogenes* causing pharyngitis in Portugal. 29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 13-16, 2019. (*Poster Presentation*).

Mendes CI, Lizarazo E, Machado MP, Silva DN, Tami A, Ramirez M, Couto N, Rossen JWA, Carriço JA. Identification and Characterization of Dengue Virus Directly from Metagenomic and Amplicon Sequencing Data. Applied Bioinformatics for Public Health Microbiology (ABPHM), Wellcome Genome Campus, United Kingdom, June 5-6, 2019. (*Poster Presentation*).

Mendes CI, Silva DN, Jesus TF, Ribeiro-Gonçalves B, Ramirez M, Carriço. FlowCraft: build, monitor and report Nextflow pipelines made easy (B14, Bioinformatics Demo). Applied Bioinformatics for Public Health Microbiology (ABPHM), Wellcome Genome Campus, United Kingdom, June 5-6, 2019.

Caneiras C, Lito L, Melo-Cristino J, Duarte A. Antimicrobial resistance in Gram-negative bacteria: the epidemiology of carbapenemase-producing *K. pneumoniae* isolates in Portugal. IC2AR 2019 - 3rd International Caparica Conference in Antibiotic Resistance, Caparica, Portugal, June 10-13, 2019.

Silva-Costa C, Gomes-Silva J, Guerreiro SI, Prados L, Brito MJ, 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. Serotypes 3, 8 and 10A dominate among pediatric invasive pneumococcal infections in Portugal (2015-2018). 14th European Meeting on the Molecular Biology of the Pneumococcus, Greifswald, Germany, June 11-14, 2019. (*Oral Presentation*).

Silva-Costa C, Pinho MD, Friães A, Gomes-Silva J, Guerreiro SI, Brito MJ, Ramirez M, Melo-Cristino J, Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Invasive Pneumococcal Disease of the Paediatric Infectious Disease Society. Three years after PCV13 introduction in the National Immunization Plan serotype 3 is still the main cause of complicated pneumonia in Portugal (P46). 14th European Meeting on the Molecular Biology of the Pneumococcus, Greifswald, Germany, June 11-14, 2019.

Ribeiro Gonçalves B, Machado M, Silva M, Silva D, Rossi M, Ana D, Francisco A, Ramirez M, Carriço JA. ONEIDA-INNUENDO - A bioinformatic platform for the integration of genomics in surveillance and outbreak detection. 12th International Meeting on Microbial Epidemiological Markers (IMMEM XII), Dubrovnik, Croatia, September 18–21, 2019. (*Oral Presentation*).

González Díaz A, Machado M, Càmara J, Yuste J, Varon E, Domenech M, Del Grosso M, Marimon Ortiz de Zarate J, Cercenado E, Larrosa N, Quesada M, Fontals D, Cubero M, Carriço JA, Marti S, Ramirez M, Ardanuy Tisaire C. A double multi-fragment recombination event originated the *Streptococcus pneumoniae* serotype 11A-PMEN3 clone that is spreading in Southwest Europe (P177). 12th International Meeting on Microbial Epidemiological Markers (IMMEM XII), Dubrovnik, Croatia, September 18–21, 2019.

Silva-Costa C, Pinho M, Friães A, Gomes-Silva J, Guerreiro S, Brito M, Ramirez M, Melo-Cristino J. Molecular diagnostics reveals persistence of serotype 3 as the main cause of pediatric complicated pneumonia in Portugal despite extensive PCV13 use (P263). 12th International Meeting on Microbial Epidemiological Markers (IMMEM XII), Dubrovnik, Croatia, September 18–21, 2019.

Gomes-Silva J, Silva-Costa C, Ramirez M, Melo-Cristino J. Characterization of the genetic lineages responsible for pediatric invasive pneumococcal disease in Portugal (1999-2015) (P267). 12th International Meeting on Microbial Epidemiological Markers (IMMEM XII), Dubrovnik, Croatia, September 18–21, 2019.

Mendes C, Lizarazo E, Machado M, Silva D, Tami A, Ramirez M, Couto N, Rossen J, Carriço JA. Identification and typing of dengue viruses directly from patient samples with DEN-IM (P286). 12th International Meeting on Microbial Epidemiological Markers (IMMEM XII), Dubrovnik, Croatia, September 18–21, 2019.

Communications in National Conferences

Branco AT, Mahomed S, Hanscheid T. Fatores no sangue que influenciam a taxa de proliferação do *Plasmodium falciparum*, para além da imunidade. 8^o Congresso de Pandemias, Coimbra, Portugal, Maio 30-31, 2019.

Internationalization

Collaboration in shotgun metagenomics for clinical diagnostics with Dr. John Rossen, Head of the Molecular Unit and Principal Investigator Genomics for Infection Prevention, Department of Medical Microbiology, University of Groningen, University Medical Center Groningen.

Participation in an international projects in collaboration with Turkish colleagues.

Advanced Teaching

Carricho JA, Friães A, Häscheid T, Melo Cristino J, Pinho M, Ramirez M, Silva-Costa C. Organizers and lecturers. Second cycle course of Clinical Microbiology and Emerging Infectious Diseases, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Friães A, Häscheid T, Melo Cristino J, Pinho M, Ramirez M, Silva-Costa C. Participation on the second cycle course of Microbiology (responsible for the course on Medical Microbiology). Instituto Superior Técnico da Universidade de Lisboa in collaboration with Faculdade de Medicina da Universidade de Lisboa, Faculdade de Ciências da Universidade de Lisboa and Faculdade de Medicina Veterinária da Universidade de Lisboa, Lisbon, Portugal.

Carricho JA. Participation on the second cycle course of Computational Biology/Bioinformatics for Master and PhD programmes (responsible for the module on Molecular Phylogenetics). Instituto Superior Técnico da Universidade de Lisboa in collaboration with the Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

MSc Thesis Completed

Pedro Miguel Festas Marinho, 22/11/2019, Improved acid-fast stain and histology methods for the detection of mycobacteria in tissue samples, Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Thomas Häscheid.

PhD Thesis Completed

Andreia das Neves Horácio, 15/03/2019, Characteristics of pneumococci causing disease in adults in Portugal in a time of private use of pneumococcal conjugate vaccines in children, Doutoramento em Ciências e Tecnologias da Saúde, especialidade em Microbiologia, Faculdade de Medicina da Universidade de Lisboa. Supervisor: José Melo-Cristino.

Jorge Diamantino-Miranda, 01/10/2019, Understanding pherotype specificity and its influence on the genetic structure of *Streptococcus pneumoniae*, Doutoramento em Ciências e Tecnologias da Saúde, especialidade em Microbiologia, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mário Ramirez. Co-Supervisor: J.A. Hermoso.

Miguel Castanho Lab

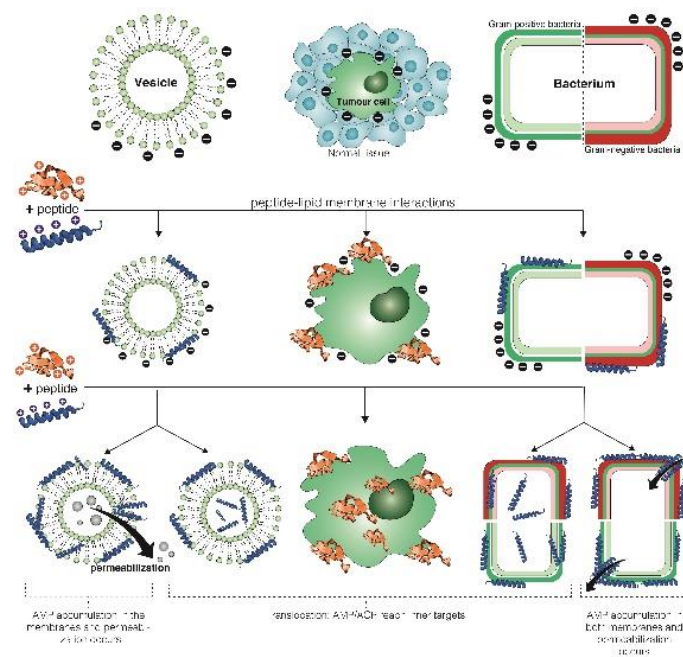
Major Interests/Objectives

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, Zika and Dengue viruses are of particular interest), analgesia and translocation of the blood-brain barrier, as well as in the development of antimicrobial and anticancer drugs. We are interested not only in drug targets and drug discovery itself, but also in the molecular-level mechanism of action of efficient and safe drugs.

Head of Laboratory

Miguel A. R. B. Castanho, PhD, Full Professor

Graphical Abstract



Team

Abeda Hanif Haji Ahmad	Master Degree	MSc Student (Left October)
Ana Filipa Daniel da Cruz	Master Degree	PhD Student (Left October)
Ana Rosa Miranda dos Santos Silva Herdade	PhD	Assistant Professor
Ana Salomé Rocha Nascimento Veiga	PhD	Assistant Professor
Carla Íris Cadima Couto	PhD	Senior Postdoctoral Researcher
Catarina Isabel Parente Chaparro	Master Degree	PhD Student (Started October)
Christine Cruz Oliveira	PhD	Senior Postdoctoral Researcher (Started April)
Diana Maria Diez Gaspar	PhD	Senior Postdoctoral Researcher (Left September)
Diogo Alexandre de Mendonça	Master Degree	PhD Student
Filipa Dias de Oliveira	Master Degree	PhD Student
Iara Sofia Mota Lima da Silva	Master Degree	Researcher
João Filipe Lopes da Cruz Morais	Master Degree	Researcher (Started March. Left September)
Julia Michalina Skalska	Master Degree	PhD Student
Liliana Faia Carvalho	Master Degree	Lab Manager
Marco Calvinho Cavaco	Master Degree	PhD Student
Miguel de Almeida Fuzeta	Master Degree	PhD Student (Left October)
Rita Isabel Pedro Aroeira	PhD	Postdoctoral Researcher (Started March)
Susana Filipa Almeida Dias	Master Degree	PhD Student
Tiago Nascimento Figueira	PhD	Postdoctoral Researcher (Left December)
Vera Luísa Santos Neves	PhD	Staff Scientist

Laboratory Keywords / Research Areas

Drug Discovery, Antimicrobials/Anticancer Drugs, Antiviral Peptides, Viruses, HIV, Zika, Inflammation, Blood-brain Barrier.

Major Scientific Achievements

In 2019 we have:

- Developed a nanocarrier consisting of large unilamellar vesicles for combined delivery of two HIV-1 entry inhibitors, enfuvirtide and protoporphyrin IX. We showed that the combination of the two entry inhibitors potentiated the synergy against HIV-1 entry.
- Investigated the effect of PvD1, a plant defensin, on the formation of exosomes by breast cancer cells. We revealed that PvD1 has a dual effect on exosomes by attenuating the recruitment of CD63 and CD9 to exosomes intracellularly and by binding to the mature exosomes in the extracellular environment.

- Explored the mechanism of action of pepR, a multifunctional peptide, against *Staphylococcus aureus* biofilms. We showed that pepR is able to prevent staphylococcal biofilm formation due to a fast killing of planktonic bacteria and kill biofilm-embedded bacteria, shedding new light on the antibiofilm mechanism of action of antimicrobial peptides.

Selected Publications

Petrin THC, Fadel V, Martins DB, Dias SA, Cruz A, Sergio LM, Arcisio-Miranda M, Castanho MARB, Dos Santos Cabrera MP (2019). Synthesis and Characterization of Peptide-Chitosan Conjugates (PepChis) with Lipid Bilayer Affinity and Antibacterial Activity. **Biomacromolecules** 20(7):2743-2753. (IF: 5.667, Citations: 0. Source: Web of Science).

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS (2019). The mechanism of action of pepR, a viral-derived peptide, against *Staphylococcus aureus* biofilms. **Journal of Antimicrobial Chemotherapy** 74(9):2617-2625. (IF: 5.113, Citations: 2. Source: Web of Science).

Skalska J, Oliveira FD, Figueira TN, Mello ÉO, Gomes VM, McNaughton-Smith G, Castanho MARB, Gaspar D (2019). Plant defensin PvD1 modulates the membrane composition of breast tumour-derived exosomes. **Nanoscale** 11(48):23366-23381. (IF: 6.97, Citations: 0. Source: Web of Science).

Ongoing Research Projects

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: € 2 113 125,00 €.

2019/2020: Desenvolvimento de uma plataforma trans-barreira hematoencefálica com aplicação na doença de Alzheimer. Coordinator: Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: COOPERAÇÃO CIENTIFICA E TECNOLOGICA FCT/NKFIH, 201. Amount: € 2 000,00. Total Amount: € 2 000,00.

2018/2021: Seleção de fármacos líder anti-virus zika capazes de translocar as barreiras hemato-placentária e hemato-encefálica. Combinando péptidos translocadores inovadores e eficazes com novos antivirais para alcançar o vírus Zika através de barreiras. 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.

2016/2019: Peptides for blood-brain barrier transmigration and drug delivery - novel therapies for the central nervous system. Coordinator: Vera Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-NAN/1578/2014. Amount: € 140 090,00. Total Amount: € 190 090,00.

2016/2019: Towards the development of innovative highly effective dual action anti-HIV peptides. Coordinator: Ana Salomé Veiga. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/4412/2014. Amount: € 143 133,00. Total Amount: € 193 123,00.

2016/2019: Cell-cell communication in metastatic breast cancer: a control point that can lead to breast cancer treatment. Coordinator: Diana Gaspar and Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BQB/1693/2014. Amount: € 187 151,00. Total Amount: € 187 151,00.

2015/2019: INPACT: Innovative peptides against cancer and pathogenic bacteria, with advances in science, biopharmaceutical drug development, product market targeting, training, and communication. Coordinator: Miguel Castanho. Funding Agency: European Commission. Reference: MSCA RISE 644167. Amount: € 463 500,00. Total Amount: € 1 390 500,00.

Other Projects

2018/2021: ADC1.1: Desenvolvimento de uma nova classe de moléculas de conjugados de anticorpos para o tratamento do cancro. Coordinator: Frederico Aires-Silva. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: ADC1.1 - LISBOA-01-0145-FEDER-032085. Amount: € 12 500,00. Total Amount: € 239 638,46.

2018/2021: Validação polifásica de péptidos antimicrobianos como tratamento alternativo para infeções do pé diabético. Coordinator: Manuela Oliveira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/SAU-INF/28466/2017. Amount: € 5 765,20. Total Amount: € 239 655,75.

2018/2021: Dadores de gasotransmissores NO e H₂S terapêuticos baseados em materiais nanoporosos. Coordinator: Moisés Pinto. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-QUI/28721/2017. Amount: € 6 000,00. Total Amount: € 227 943,25.

2018/2021: Fighting Zika virus with antiviral peptides and conjugates translocating blood-placental and blood-brain barriers. Coordinator: David Andreu Martinez. Funding Agency: Fundación Bancaria "la Caixa". Reference: NOZIKA project. Amount: € 254 650,00. Total Amount: € 777 250,00.

2018/2021: Combinando métodos computacionais e experimentais para obter uma caracterização genérica dos péptidos de fusão de vírus. Coordinator: Diana Lousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CCI-BIO/28200/2017. Amount: € 54 975,00. Total Amount: € 239 648,06.

2016/2019: Alzheimer3D: Trifunctional Conjugates for the Selective Drug Delivery in Alzheimer's Disease. Coordinator: Rudi Oliveira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/5512/2014. Amount: € 12 000,00. Total Amount: € 198 364,00.

2016/2019: Overcoming the Brain Drug Delivery Bottleneck: Development of single domain antibodies for brain targeting and drug delivery across the Blood-Brain Barrier. Coordinator: Frederico Aires-Silva. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BIO/0508/2014. Amount: € 19 800,00. Total Amount: € 192 320,00.

2015/2020: Engineering protease-resistant alpha-beta for broad-spectrum antivirals. Coordinator: Nuno Santos. Funding Agency: National Institute of Health. Reference: 5R01AI114736. Amount: € 300 000,00. Total Amount: € 1 225 000,00.

Publications in Peer Reviewed Journals

de Andrade VM, Bardají E, Heras M, Ramu VG, Junqueira JC, dos Santos JD, Castanho MARB, Conceição K (2019). Antifungal and anti-biofilm activity of designed derivatives from kyotorphin. **Fungal Biology** <https://doi.org/10.1016/j.funbio.2019.12.002>. (IF: 2.699, Citations: 0. Source: *Web of Science*).

Faustino AF, Barbosa GM, Silva M, Castanho MARB, Da Poian AT, Cabrita EJ, Santos NC, Almeida FCL, Martins IC (2019). Fast NMR method to probe solvent accessibility and disordered regions in proteins. **Scientific Reports** 9(1):1647. (IF: 4.011, Citations: 1. Source: *Web of Science*).

Pérez-Peinado C, Dias SA, Mendonça DA, Castanho MARB, Veiga AS, Andreu D (2019). Structural determinants conferring unusual long life in human serum to rattlesnake-derived antimicrobial peptide Ctn[15-34]. **Journal of Peptide Science** 25(8):e3195. (IF: 2.081, Citations: 1. Source: *Web of science*).

Petrin THC, Fadel V, Martins DB, Dias SA, Cruz A, Sergio LM, Arcisio-Miranda M, Castanho MARB, Dos Santos Cabrera MP (2019). Synthesis and Characterization of Peptide-Chitosan Conjugates (PepChis) with Lipid Bilayer Affinity and Antibacterial Activity. **Biomacromolecules** 20(7):2743-2753. (IF: 5.667, Citations: 0. Source: *Web of Science*).

Philippe GJ, Gaspar D, Sheng C, Huang YH, Benfield AH, Condon ND, Weidmann J, Lawrence N, Löwer A, Castanho MARB, Craik DJ, Troeira Henriques S (2019). Cell Membrane Composition Drives Selectivity and Toxicity of Designed Cyclic Helix-Loop-Helix Peptides with Cell Penetrating and Tumor Suppressor Properties. **ACS Chemical Biology** 14(9):2071-2087. (IF: 4.374, Citations: 0. Source: *Web of Science*).

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS (2019). The mechanism of action of pepR, a viral-derived peptide, against *Staphylococcus aureus* biofilms. **Journal of Antimicrobial Chemotherapy** 74(9):2617-2625. (IF: 5.113, Citations: 2. Source: *Web of Science*).

Santa-Maria AR, Walter FR, Valkai S, Brás AR, Mészáros M, Kincses A, Klepe A, Gaspar D, Castanho MARB, Zimányi L, Dér A, Deli MA (2019). Lidocaine turns the surface charge of biological membranes more positive and changes the permeability of blood-brain barrier culture models. **Biochimica et Biophysica Acta - Biomembranes** 1861(9):1579-1591. (IF: 3.79, Citations: 0. Source: *Web of Science*).

Sousa DC, Leal I, Moreira S, do Vale S, Silva-Herdade AS, Aguiar P, Dionísio P, Abegão Pinto L, Castanho MARB, Marques-Neves C (2019). A Protocol to Evaluate Retinal Vascular Response Using Optical Coherence Tomography Angiography. **Frontiers in Neuroscience** 13:566. (IF: 3.648, Citations: 0. Source: Web of Science).

Skalska J, Oliveira FD, Figueira TN, Mello ÉO, Gomes VM, McNaughton-Smith G, Castanho MARB, Gaspar D (2019). Plant defensin PvD1 modulates the membrane composition of breast tumour-derived exosomes. **Nanoscale** 11(48):23366-23381. (IF: 6.97, Citations: 0. Source: Web of Science).

Vernen F, Harvey PJ, Dias SA, Veiga AS, Huang YH, Craik DJ, Lawrence N, Troeira Henriques S (2019). Characterization of Tachyplesin Peptides and Their Cyclized Analogues to Improve Antimicrobial and Anticancer Properties. **International Journal of Molecular Sciences** 20(17): 4184. (IF: 4.183, Citations: 0. Source: Web of Science).

Other International Publications

Cavaco M, Pérez-Peinado C, Gaspar D, Andreu D, Castanho MARB, Neves V (2019). Targeting brain metastases with a peptide conjugate. **FEBS OPEN BIO** 9: 372.

Figueira TN, Mendonça DA, Gaspar D, Melo MN, Moscona A, Porotto M, Castanho MARB, Veiga AS (2019). Linking Structure, Stability and Function in the Anti-Measles Virus Action of Tocopherol-Derivatized Peptide Nanoparticles. **European Biophysics Journal with Biophysics Letters** 48: S158-S158.

Lousa D, Pinto ART, Campos SRR, Baptista AM, Veiga AS, Castanho MARB, Soares CM (2019). Effect of pH on the influenza fusion peptide structure and activity: A constant-pH molecular dynamics approach. **European Biophysics Journal with Biophysics Letters** 48: S47-S47.

Mendonça DA, Figueira TF, Melo M, Harder O, Niewiesk S, Moscona A, Porotto M, Castanho MARB, Veiga AS (2019). The efficacy of designed anti-measles virus peptides depends on the stability of self-assembled clusters. **European Biophysics Journal with Biophysics Letters** 48: S81-S81.

Oliveira FD, Figueira TN, Napoleão P, Andreu D, Castanho MARB, Gaspar D (2019). Anticancer activity of a novel cell -penetrating peptide, vCPP2319, and its interaction with breast cancer cells' derived exosomes. **European Biophysics Journal with Biophysics Letters** 48: S116-S116.

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS (2019). Insights into the mechanism of action of pepR, a viral-derived peptide, against *Staphylococcus aureus* biofilms. **European Biophysics Journal with Biophysics Letters** 48: S117-S117.

Silva-Herdade AS, Saldanha C, Ha N, Hou I, Castanho MARB, Roy S (2019). Effects of Diabetes on Microcirculation in Non-Ocular Tissues: Insights into Hemodynamic Alterations in Diabetic Retinopathy. **Journal of Vascular Research** 56(1):101.

Skalska J, Oliveira FD, Figueira TN, Mello EO, Gomes VM, Castanho MARB, Gaspar D (2019). Novel mechanism of action of natural plant defensin Pvd1 involves a modulatory effect of CD63 and CD9 expression level in breast cancer cells derived exosomes. **FEBS OPEN BIO** 9:325.

Invited Lectures and Seminars

Castanho MARB. A scientific career in biochemistry: what the future holds and what to hold in the future. 1st Meeting of the Master in Biochemistry, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, February 15, 2019.

Castanho MARB. What's hidden in viral proteins? Lessons from Dengue virus capsid. CEDOC Seminars, CEDOC, Lisbon, Portugal, February 20, 2019.

Castanho MARB. Membrane-targeting peptides: from antimicrobial to anticancer. Center for Cancer Research, National Cancer Institute, National Institutes of Health, USA, March 7, 2019.

Castanho MARB. From the Periodic Table to Biochemistry: A Chemical Reflection on Life and Its Origin. International Year Periodic Table 2019, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 9, 2019.

Veiga AS. From Dengue virus capsid protein to bioactive peptides – the mechanism of action of pepR, a viral-derived peptide, against biofilms. Special Seminar, Center for Cancer Research, National Cancer Institute, National Institutes of Health, USA, June 17, 2019.

Oliveira FD, Figueira TN, Napoleão P, Andreu D, Castanho MARB, Gaspar D. Coupling Cell-Penetrating Peptides to exosomes: a promising strategy to target metastatic breast cancer. iMM Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 25, 2019.

Castanho MARB. Peptide drugs and lipid membranes: Biophysical tales of love and hate. Centre of Physics of the University of Minho and Porto, Universidade do Minho, Braga, Portugal, September 19, 2019.

Castanho MARB. UFRJ-FMUL Bridges in Medical Biochemistry: examples in research, teaching and extension. Symposium on Medical Exchange, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 13, 2019.

Castanho MARB. Chasing bacteria in biofilms – Killing straight, killing fast, killing deep. 1st Annual Meeting in Pharmaceutical Sciences, Faculdade de Farmácia, Universidade de Coimbra, Coimbra, Portugal, November 15, 2019.

Castanho MARB. Studying the neuropeptide kyotorphin: from pain to Alzheimer's, from mouse to man. CAML Session, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 28, 2019.

Communications in International Conferences

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS. Insights into the mechanism of action of pepR, a viral-derived peptide, against *Staphylococcus aureus* biofilms. Gordon Research Conference on Antimicrobial Peptides, Lucca (Barga), Italy, February 24-March 1, 2019. (*Oral Presentation*).

Cavaco M, Aguiar S, Gaspar D, Frutos S, Vila-Perelló M, Andreu D, Aires da Silva F, MARB Castanho, Neves V. Overcoming the Blood-Brain barrier with peptide-conjugates. EMBO Workshop: Current advances in protein translocation across membranes, Sant Feliu, Spain, March 23-27, 2019. (*Poster Presentation*).

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião AM, Neves V, Castanho M, Diógenes MJ. Amidated-Kyotorphin neuroprotective effect on Alzheimer's Disease. The 14th International Conference on Alzheimer's & Parkinson's diseases, Centro de Congressos de Lisboa, Lisbon, Portugal. March 26-31, 2019. (*Poster Presentation*).

Silva-Herdade AS, Calado A, Saldanha C, Ha N, Hou I, Castanho M, Roy S. Effects of diabetes on microcirculation in non-ocular tissues: insights into hemodynamic alterations in diabetic retinopathy. 3rd joint ESM-EVBO Meeting 2019, Maastricht, Netherlands, April 15-18, 2019. (*Poster Presentation*).

Oliveira FD, Skalska J, Figueira TM, Napoleão P, Mello EO, Andreu D, Gomes VM, Castanho MARB, Gaspar D. Design of an exosome-based drug delivery system transporting anticancer peptides for targeting breast metastases in the brain. Annual Meeting ISEV 2019, Miyakomesse, Kyoto, Japan, April 24-28, 2019. (*Poster Presentation*).

Oliveira FD, Skalska J, Figueira TM, Napoleão P, Mello EO, Andreu D, Gomes VM, Castanho MARB, Gaspar D. Peptides targeting breast tumor derived exosomes as a therapeutic strategy for metastatic breast cancer. 26th American Peptide Symposium, Monterey, California, USA, June 22-27, 2019. (*Poster Presentation*).

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS. Insights into the mechanism of action of pepR, a viral-derived peptide, against Staphylococcus aureus biofilms. 26th American Peptide Symposium, Monterey, California, USA, June 22-27, 2019. (*Poster Presentation*).

Cavaco M, Pérez-Peinado C, Gaspar D, Andreu D, Castanho MARB, Neves V. Targeting brain metastases with a peptide conjugate. The 19th FEBS Young Scientists' Forum, Krakow, Poland, July 3-6, 2019. (*Oral Presentation*).

Cavaco M, Pérez-Peinado C, Gaspar D, Andreu D, Castanho MARB, Neves V. Targeting brain metastases with a peptide conjugate. The 44th FEBS Congress, Krakow, Poland, July 6-11, 2019. (*Poster Presentation*).

Skalska J, Oliveira FD, Figueira TN, Mello ÉO, Gomes VM, McNaughton-Smith G, Castanho MARB, Gaspar D. Novel mechanism of action of natural plant defensin PvD1 involves a modulatory effect of CD63 and CD9 expression level in breast cancer cells derived exosomes. The 44th FEBS Congress, Krakow, Poland, July 6-11, 2019. (*Poster Presentation*).

Figueira TN, Mendonça DA, Gaspar D, Melo MN, Moscona A, Porotto M, Castanho MARB, Veiga AS. Linking Structure, Stability and Function in the Anti-Measles Virus Action of Tocopherol-Derivatized Peptide Nanoparticles. 12th European Biophysics Congress and 10th International Conference on Biological Physics, Madrid, Spain, July 20-24, 2019 (*Oral and Poster Presentation*).

Mendonça DA, Figueira TF, Melo MN, Harder O, Niewiesk S, Moscona A, Porotto M, Castanho MARB, Veiga AS. The efficacy of designed anti-measles virus peptides depends on the stability of self-assembled clusters. 12th European Biophysics Congress and 10th International Conference on Biological Physics, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Oliveira FD, Figueira TN, Napoleão P, Andreu D, Castanho MARB, Gaspar D. Anticancer activity of a novel cell-penetrating peptide, vCPP2319, and its interaction with breast cancer cells' derived exosomes. 12th European Biophysics Congress and 10th International Conference on Biological Physics, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS. Insights into the mechanism of action of pepR, a viral-derived peptide, against *Staphylococcus aureus* biofilms. 12th European Biophysics Congress and 10th International Conference on Biological Physics, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Neves V, Cavaco M, Ahmad A, Aires-da-Silva F, Gan, L, Corte-Real S, Correi, JDG, Castanho MARB. Peptide Delivery Systems to Overcome the Blood-brain Barrier to Treat Brain Diseases: Focus On Alzheimer's Disease. Controlled Release Society Annual Meeting & Exposition in Valencia, Spain, July 21-24, 2019. (*Poster Presentation*).

Cruz AF, Freire JM, Pinto SN, Coutinho A, Andreu D, Castanho MARB, Veiga AS. Design and development of short and stable pepR-derived antibacterial peptides. 9th International Meeting on Antimicrobial Peptides, Utrecht, Netherlands, August 28-30, 2019. (*Poster Presentation*).

Dias SA, Freire JM, Pinto SN, Cavaco M, Neves V, Coutinho A, Castanho MARB, Veiga AS. Studying the antibacterial and antibiofilm activities of the viral-derived peptide vCPP 2319. 9th International Meeting on Antimicrobial Peptides, Utrecht, Netherlands, August 28-30, 2019. (*Poster Presentation*).

Pinto SN, Dias SA, Cruz AF, Mil-Homens D, Fernandes F, Valle J, Andreu D, Prieto M, Castanho MARB, Coutinho A, Veiga AS. PepR, a viral-derived peptide, is efficacious against *Staphylococcus aureus* biofilms. 6th European Congress on Biofilms, Glasgow, Scotland, September 3-6, 2019. (*Poster Presentation*).

Aguiar SI, Silva M, Martins D, André AS, Neves V, Dias JNR, Carrapiço B, Gano L, Galamba J, Tavares L, Gonçalves J, Castanho M, Aires-da-Silva F. Overcoming the BBB: in vivo selection of single domain antibodies for brain targeting and drug delivery. 11th Annual PEGS EUROPE, Lisbon, Portugal, November 18-22, 2019. (*Poster Presentation*).

Communications in National Conferences

Mota da Silva I. Kyotorphin impact on the microvascular lesions of diabetes and its application on diabetic retinopathy. Jornadas Intercalares das Dissertações Anuais dos Mestrados do DQ e do DCV, Monte da Caparica, Almada, Portugal, February 14-15, 2019. *(Oral Presentation)*.

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião A, Neves V, Castanho M, Diógenes MJ. The neuroprotective effect of Amidated-Kyotorphin on Alzheimer's Disease. XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. *(Oral Presentation)*.

Cavaco M, Aguiar S, Gaspar D, Frutos S, Vila-Perelló M, Andreu D, Aires da Silva F, MARB Castanho, Neves V. Overcoming the Blood-Brain barrier with peptide-conjugates. . XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. *(Poster Presentation)*.

Dias SA, Freire JM, Pinto SN, Cavaco M, Neves V, Coutinho A, Castanho MARB, Veiga AS. Novel membrane-targeting antibacterial and antibiofilm peptides derived from viral capsid proteins. XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. *(Oral Presentation)*.

Mendonça DA, Figueira TF, Melo MN, Harder O, Niewiesk S, Moscona A, Porotto M, Castanho MARB, Veiga AS. The efficacy of designed anti-measles virus peptides depends on the stability of self-assembled clusters. XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. *(Poster Presentation)*.

Oliveira FD, Figueira TN, Napoleão P, Andreu D, Castanho MARB, Gaspar D. Cell-penetrating peptide interactions with breast cells-derived exosomes followed with surface plasmon resonance. XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019. *(Poster Presentation)*.

Belo RF, Fonseca-Gomes J, Miranda HV, Outeiro TF, Sebastião A, Neves V, Castanho M, Diógenes MJ (2019). The neuroprotective effect Amidated-Kyotorphin on Alzheimer's Disease. XVI Meeting of the Portuguese Society for Neuroscience, Tryp Hotel Lisboa Aeroporto, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Cavaco M, Gaspar D, Valle J, Andreu D, Castanho MARB, Neves V. Brain metastases elimination with a peptide-conjugate. 5th Meeting of the Mind-Brain College of the University of Lisbon and 17th Meeting of Biomedical Engineering Instituto Superior Técnico/Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 12-13, 2019. (*Poster Presentation*).

Organization of Conferences

Oliveira F, Cavaco M, Dias SA. Co-Organizers. XIII CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 15-17, 2019.

Veiga AS. Co-Organizer. 4th Meeting of the College of Chemistry of ULisboa (4ECQUL), Chemistry: Shaping the Future & 2019 Summer School, Reitoria da Universidade de Lisboa, Lisbon, Portugal, July 16-19, 2019.

Internationalization

Our expertise is the development and application of biophysical techniques to dissect the molecular mechanisms of action of membrane-active peptides directly in viruses, bacteria or cells. Peptides are from 3 sources: i) Organic synthesis, for which we have collaborations with labs in Spain, ii) Natural products, for which we have collaborations in Brazil, and iii) Pharma products during development phase.

It is worth highlighting that Miguel Castanho coordinates a H2020 – FET Open project involving 3 partners aimed at developing drugs to clear viral species from brain.

In 2019 we have co-authored papers with the following international groups:

- i) Laboratório de Bioquímica de Peptídeos – Universidade Federal de São Paulo, São José dos Campos, Brazil.
- ii) Instituto de Bioquímica Médica Leopoldo de Meis, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.

- iii) Departamento de Química e Ciências Ambientais and Departamento de Física, Instituto de Biociências Letras e Ciências Exatas (Ibilce), Universidade Estadual Paulista (Unesp), Campus São José do Rio Preto, São José do Rio Preto, São Paulo, Brazil.
- iv) Laboratório de Fisiologia e Bioquímica de Microrganismos do Centro de Biociências e Biotecnologia da Universidade Estadual do Norte Fluminense Darcy Ribeiro, Rio de Janeiro, Brazil.
- v) Sorbonne Université, École Normale Supérieure, PSL University, CNRS, Laboratoire des Biomolécules, Paris, France.
- vi) Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona Biomedical Research Park, Barcelona, Spain.
- vii) CEAMED - Centro Atlántico del Medicamento, S.A., San Cristobal de La Laguna, S/C Tenerife, Spain.
- viii) Institute for Molecular Bioscience, The University of Queensland, Queensland, Australia.
- ix) Institute of Biophysics, Biological Research Centre, Hungarian Academy of Sciences, Szeged, Hungary.

Prizes, Honors and Awards

Miguel Castanho. Scientific Award Universidade de Lisboa/Caixa Geral de Depósitos 2018 in the scientific area of Biomedical Sciences. Universidade de Lisboa, Lisbon, Portugal. April 8, 2019.

Marco Cavaco. Best oral presentation (3rd prize), The 19th FEBS Young Scientists' Forum, Krakow, Poland, July 3-6, 2019.

Tiago Figueira. SPBf Young Biophysicist 2019 prize. Portuguese Biophysical Society, Portugal, July 21, 2019.

Miguel Castanho. Pedagogical Merit Award of Prof. Doutor J. Gomes-Pedro, Faculdade de Medicina da Universidade de Lisboa, Portugal, November, 2019.

Miguel Castanho appointed Chief Editor of Pharmaceutical Innovation, a speciality journal of Frontiers in Medical Technology, Springer Nature Publishing Group. November 2019. (<https://www.frontiersin.org/journals/medical-technology/sections/pharmaceutical-innovation>)

Industry Contract Research

Miguel Castanho Lab is a partner of VectorB2B, a Drug Developing Association for Research in Biotechnology that provides highly qualified services of drug discovery and development from the bench to bedside. (<http://vectorb2b.com/>)

Patents/Prototypes

Casado V, Moreno E, Maldonado R, Andreu D, Gallo M, Castanho M, Neves V, Cavaco M. Peptide compounds for reducing side effects of CB1 receptor agonists. European Patent Office 19382856.3- 110, November 26, 2019.

Advanced Teaching

Castanho MARB. Lecturer. Translation academy-industry in Health. Pós-Graduação em Avaliação Económica das Tecnologias e Intervenções em Saúde. Post-graduation in Economic Assessment of Technologies and Interventions in Health, Instituto Superior de Economia e Gestão da Universidade de Lisboa, Lisbon, Portugal, February 21, 2019.

Veiga AS. Lecturer. Innovative Antimicrobial Approaches in Veterinary Medicine. Integrated Master in Veterinary Medicine, Faculdade de Medicina Veterinária da Universidade de Lisboa, Lisbon, Portugal, February, 2019.

Castanho MARB. Lecturer. Peptides and lipid membranes: passionate tales of love and hate. FCUL Biochemistry Masterclass Seminars, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 16, 2019.

Neves, V. Lecturer. Blood Brain barrier: Challenges to develop new therapeutic tools to act in the brain. Master's and PhD degrees in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 25, 2019.

Science and Society

- Castanho MARB. HIV. Advances are positive but it is "premature" to speak in healing, Antena1, March 5, 2019.

- Castanho MARB. End of HIV transmission may be in sight, RTP, May 3, 2019.

- Castanho MARB. Use and refuse science in being and knowing. Círculo Cultural Sacalabitano, Santarém, May 24, 2019.
- Castanho MARB. Canal Saúde+: Raio X, May, 2019.
- Cadima-Couto I. What does an investigator do? Esc. Bás. São Francisco, Alcochete. May, 2019.
- Our group participated in European Researchers' Night, Lisbon, September 27, 2019.
- Castanho MARB. What we already know about viruses and what we don't know yet, Fighting viruses that attack the brain, Antena2, October, 2019.
- Our group organized an Open Day at Miguel Castanho Lab, IMM, October 24, 2019.
- Castanho MARB. Why is the flu vaccine only valid for one year?, Visão, November 18, 2019.
- Aroeira RI and Cadima-Couto I. HIV Research - Where, How and Why? Esc. Sec. António Damásio, Lisbon. December 3, 2019.
- Castanho MARB. Research studies methods for combating Zika viruses in brain. 90 segundos de Ciência – Antena1, December 3, 2019.

MSc Theses

Abeda Hanif Haji Ahmad, 25/10/2019, Blood-based biomarkers for Alzheimer's disease – an *In vitro* proof of concept, Universidade Nova de Lisboa - Faculdade de Ciências e Tecnologia. Supervisor: Miguel Castanho. Co-Supervisor: Vera Neves.

Iara Sofia Mota Lima da Silva, 25/10/2019, Kyporphan impact on the microvascular lesions of diabetes and its application on diabetic retinopathy, Universidade Nova de Lisboa - Faculdade de Ciências e Tecnologia. Supervisor: Miguel Castanho. Co-Supervisor: Ana Silva-Herdade.

PhD Theses

Tiago Figueira, 5/6/2019, Targeting enveloped virus entry into cells. Self-delivery and other strategies against HIV and Measles virus, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Salomé Veiga.

Miguel Prudêncio Lab

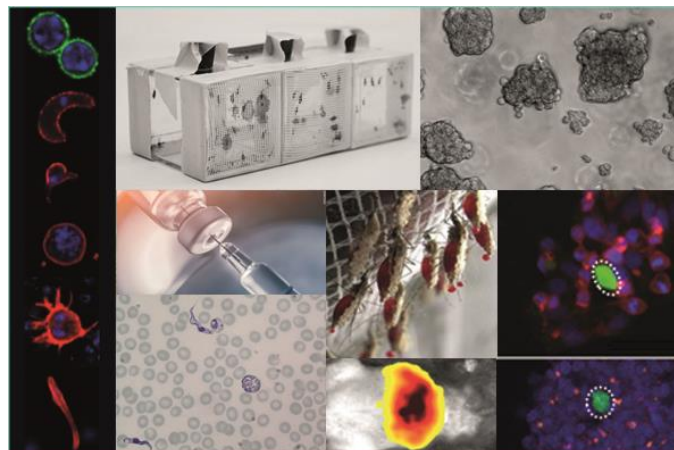
Major Interests/Objectives

Malaria is an infectious disease caused by *Plasmodium* parasites. The combat against this disease, which exerts a particularly heavy burden in the poorest regions of the globe, constitutes not only a major scientific challenge but also a moral and social imperative. The Prudêncio Lab's Mission is to contribute to this endeavor through harnessing the underexplored potential of the hepatic stage of *Plasmodium* infection to develop new anti-plasmodial intervention strategies. Among our major interests are the elucidation of novel aspects of the biology of *Plasmodium* infection of liver cells, the discovery of novel host-parasite interactions, the investigation of co-infections between *Plasmodium* and other parasites, and the development of new drug- and vaccine-based anti-malarial strategies.

Head of Laboratory

Miguel Prudêncio, PhD, Invited Associate Professor of Faculdade de Medicina da Universidade de Lisboa

Graphical Abstract



Team

Adriana Beatriz Oliveira Temporão	Master Degree	PhD Student
Américo José dos Santos Alves	Master Degree	PhD Student
Ana Filipa Gonçalves Teixeira	Master Degree	Lab Technician
Ana Margarida Roque Sanches Vaz	Master Degree	PhD Student
Andreia Cunha Barreto	University Degree	MSc Student (Left December)
António Manuel Barbeiro Mendes	PhD	Senior Postdoctoral Researcher

Carolina dos Santos Vinagreiro	PhD	PhD Student
Daniela Cristina de Henriques Brás	Master Degree	PhD Student (Started September)
Denise Rodrigues Francisco	Master Degree	Lab Technician
Diana Alves Moita	Master Degree	PhD Student
Diana Marisa Pinto Freire Fontinha	PhD	Postdoctoral Researcher
Francisca Maria de Andrade Terras Arez	Master Degree	PhD Student
Helena Isabel Marques Nunes Cabaço	PhD	Senior Postdoctoral Researcher
Isabel Margarida Meneses Moules	University Degree	MSc Student (Started June)
Jorge Henrique Ferreira Grilo	PhD	PhD Student
Luciano Gonçalo Nogueira Seabra Pereira	University Degree	MSc Student (Started July)
Patrícia dos Santos Meireles	PhD	Postdoctoral Researcher (Left January)
Pedro Gil Gameiro Eloy Sena Rego	Master Degree	PhD Student
Rafael Costa de Sousa	Master Degree	Lab Technician (Left December)
Raquel Alves de Azevedo	Master Degree	PhD Student
Teresa Gonçalves Carreira Maia	University Degree	MSc Student (Left October)

Laboratory Keywords / Research Areas

Malaria, *Plasmodium*, Vaccines, Host-Pathogen Interactions, Hepatic Infection, Co-Infections, Anti-Plasmodial Drugs.

Major Scientific Achievements

Among other scientific achievements, we have completed the first-in-humans evaluation of *PbVac*, the first malaria vaccine candidate against malaria based on the use of rodent *P. berghei* sporozoites genetically modified to express antigens of the human-infective *P. falciparum*. Additionally, we characterized for the first time the *P. berghei* EXP1 protein throughout the parasite's life cycle, showing that its C-terminal region is essential for its localization to the parasitophorous vacuole membrane and for its function during hepatic infection. We further established a new 3-D cell platform for drug screening against the liver stage of *Plasmodium* infection, demonstrating that it phenocopies the action of antiplasmodial compounds *in vivo*. Moreover, we investigated the impact of co-infection between *Plasmodium* and *Trypanosoma* parasites, showing that an ongoing infection by the latter protects the host from a subsequent infection with the malaria parasite. Finally, we employed a newly developed bioluminescence-based method to show for the first time that the insecticidal drug ivermectin inhibits the mosquito stages of *Plasmodium* development.

Additionally:

- We engaged in science outreach activities, dedicated to youngsters and to the general public;

- We entered the PCT phase of two patent applications regarding our novel 3D cell platform for drug screening assays, and a new class of compounds with anti-plasmodial activity;
- We had several media appearances in relation to our scientific activities.

Selected Publications

Sanches-Vaz M, Temporão A, Luis R, Nunes-Cabaço H, Mendes AM, Goellner S, Carvalho T, Figueiredo LM, Prudêncio M (2019). Trypanosoma brucei infection protects mice against malaria. **PLoS Pathogens** 15(11). (IF: 6.463. Citations: 0. Source: Web of Science).

Azevedo R, Mendes AM, Prudêncio M (2019). Inhibition of Plasmodium sporogonic stages by ivermectin and other avermectins. **Parasites & Vectors**. 12(1):594. (IF: 3.031. Citations: 0. Source: Web of Science).

Wolanin K, Fontinha D, Sanches-Vaz M, Nyboer B, Heiss K, Mueller AK, Prudêncio M (2019). A crucial role for the C-terminal domain of exported protein 1 during the mosquito and hepatic stages of the Plasmodium berghei life cycle. **Cellular Microbiology** 21(10). (IF: 4.288. Citations: 0. Source: Web of Science).

Arez F, Rebelo S, Fontinha D, Simão D, Martins TR, Machado M, Fischli C, Oeuvray C, Badolo L, Carrondo MJT, Rottmann M, Spangenberg T, Brito C, Greco B*, Prudêncio M*, Alves PM* (2019). Flexible 3D cell-based platforms for the discovery and profiling of novel drugs targeting Plasmodium hepatic infection. **ACS Infectious Diseases** 5(11):1831-1842. (IF: 4.911. Citations: 0. Source: Web of Science). (* Corresponding authors)

Mendes AM, Reuling IJ, Andrade CM, Otto TD, Machado M, Teixeira F, Pissarra J, Gonçalves-Rosa N, Bonaparte D, Sinfrônio J, Sanders M, Janse CJ, Khan SM, Newbold CI, Berriman M, Lee C, Wu Y, Ockenhouse CF, Sauerwein RW, Prudêncio M (2018). Pre-Clinical Evaluation of a P. berghei-Based Whole-Sporozoite Malaria Vaccine Candidate. **NPJ Vaccines** 3(54). (IF: 5.02. Citations: 0. Source: Web of Science).

Mendes AM, Machado M, Gonçalves-Rosa N, Reuling IJ, Foquet L, Marques C, Salman AM, Yang ASP, Moser KA, Dwivedi A, Hermsen CC, Jiménez-Díaz B, Viera S, Santos JM, Albuquerque I, Bhatia SN, Bial J, Angulo-Barturen I, Silva JC, Leroux-Roels G, Janse CJ, Khan SM, Mota MM, Sauerwein RW, Prudêncio M (2018). A Plasmodium berghei Sporozoite-Based Vaccination Platform Against Human Malaria. **NPJ Vaccines** 3(33). (IF: 5.02. Citations: 3. Source: Web of Science).

Machado M, Sanches-Vaz M, Cruz JP, Mendes AM, Prudêncio M (2017). Inhibition of Plasmodium hepatic infection by antiretroviral compounds. **Frontiers in Cellular Infection Microbiology** 7(729). (IF: 3.518. Citations: 4. Source: Web of Science).

Azevedo R, Markovic M, Machado M, Franke-Fayard B, Mendes AM, Prudêncio M (2017). A bioluminescence method for in vitro screening of Plasmodium transmission-blocking compounds. **Antimicrobial Agents Chemotherapy** 61(6). (IF: 4.715. Citations: --. Source: Web of Science).

Cunha CS, Nyboer B, Heiss K, Sanches-Vaz M, Fontinha D, Wiedtke E, Grimm D, Przyborski JM, Mota MM, Prudêncio M, Mueller AK (2017). P. berghei EXP-1 Interacts with Host Apolipoprotein H during Plasmodium Liver Stage Development. **Proceedings of the National Academy of Sciences of the United States of America** 114:E1138-E1147. (IF: 9.58. Citations: 11. Source: Web of Science).

Mendes AM, Albuquerque IS, Machado M, Pissarra J, Meireles P, Prudêncio M (2017). Inhibition of Plasmodium liver infection by ivermectin. **Antimicrobial Agents Chemotherapy** 61(2). (IF: 4.715. Citations: 15. Source: Web of Science).

Meireles P, Sales-Dias J, Andrade CM, Mello-Vieira J, Mancio-Silva L, Simas JP, Staines HM, Prudêncio M (2017). GLUT1-mediated glucose uptake plays a crucial role during Plasmodium hepatic infection. **Cellular Microbiology** 19(2). (IF: 4.288. Citations: 14. Source: Web of Science).

Liehl P, Meireles P, Albuquerque IS, Pinkevchy M, Baptista F, Mota MM, Davenport MP, Prudêncio M (2015). Innate immunity induced by Plasmodium liver infection inhibits malaria reinfections. **Infection and Immunity** 83(3):1172-1180. (IF: 3.16. Citations: 22. Source: Web of Science).

Ongoing Research Projects

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 Tecnologia. Reference: SporoMalVac LISBOA-01-0145-FEDER- 029550. Amount: € 215 464,63. 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.

2016/2019: Improving whole-organism vaccines against malaria by genetic modification. Coordinator: António Mendes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BMD/2695/2014. Amount: € 197 648,00. Total Amount: € 197 648,00.

Publications in Peer Reviewed Journals

Arez F, Rebelo S, Fontinha D, Simão D, Martins TR, Machado M, Fischli C, Oeuvray C, Badolo L, Carrondo MJT, Rottmann M, Spangenberg T, Brito C, Greco B*, Prudêncio M*, Alves PM* (2019). Flexible 3D cell-based platforms for the discovery and profiling of novel drugs targeting Plasmodium hepatic infection. **ACS Infectious Diseases** 5(11):1831-1842. (IF: 4.911. Citations: 0. Source: Web of Science). (* Corresponding authors)

Sanches-Vaz M, Temporão A, Luis R, Nunes-Cabaço H, Mendes AM, Goellner S, Carvalho T, Figueiredo LM, Prudêncio M (2019). Trypanosoma brucei infection protects mice against malaria. **PLoS Pathogens** 15(11). (IF: 6.463. Citations: 0. Source: Web of Science).

Azevedo R, Mendes AM, Prudêncio M (2019). Inhibition of Plasmodium sporogonic stages by ivermectin and other avermectins. **Parasites & Vectors**. 12(1):594. (IF: 3.031. Citations: 0. Source: Web of Science).

Pavić K, Rubinić B, Rajić Z, Fontinha D, Prudêncio M, Uzelac L, Kralj M, Held J, Zorc B (2019). Primaquine homodimers as potential antiplasmodial and anticancer agents. **Bioorganic & Medicinal Chemistry Letters** 29(19). (IF: 2.448. Citations: 0. Source: Web of Science).

Wolanin K, Fontinha D, Sanches-Vaz M, Nyboer B, Heiss K, Mueller AK, Prudêncio M (2019). A crucial role for the C-terminal domain of exported protein 1 during the mosquito and hepatic stages of the *Plasmodium berghei* life cycle. **Cellular Microbiology** 21(10). (IF: 4.288. Citations: 0. Source: Web of Science).

Beus M, Fontinha D, Held J, Rajić Z, Uzelac L, Kralj M, Prudêncio M, Zorc B (2019). Primaquine and chloroquine fumardiamides as promising antiplasmodial agents. **Molecules** 24(15). (IF: 3.06. Citations: 0. Source: Web of Science).

Beus M, Fontinha D, Held J, Rajić Z, Prudêncio M, Zorc B (2019). Synthesis and antiplasmodial evaluation of novel mefloquine-based fumardiamides. **Acta Pharmaceutica** 69(2):233-248. (IF: 1.405. Citations: 1. Source: Web of Science).

Aguiar L, Machado M, Sanches-Vaz M, Prudêncio M, Vale N, Gomes P (2019). Coupling the cell-penetrating peptides Transportan and Transportan 10 to primaquine enhances its activity against liver-stage malaria parasites. **MedChemComm** 10(2):221-226. (IF: 2.394. Citations: 3. Source: Web of Science).

Mayoka G, Njoroge M, Okombo J, Gibhard L, Sanches-Vaz M, Fontinha D, Birkholtz LM, Reader J, van der Watt M, Coetzer TL, Lauterbach S, Churchyard A, Bezuidenhout B, Egan TJ, Yeates CL, Wittlin S, Prudêncio M, Chibale K (2019). Structure-activity relationship studies and *Plasmodium* life cycle profiling identifies pan-active N-aryl-3-trifluoromethyl pyrido[1,2-a]benzimidazoles which are efficacious in an in vivo mouse model of malaria. **Journal of Medicinal Chemistry** 62(2):1022-1035. (IF: 6.054. Citations: 0. Source: Web of Science).

Kumar M, Okombo J, Mambwe D, Taylor D, Lawrence N, Reader J, Watt MV, Fontinha D, Sanches-Vaz M, Bezuidenhout B, Lauterbach S, Liebenberg D, Birkholtz LM, Coetzer TL, Prudêncio M, Egan TJ, Wittlin S, Chibale K (2019). Multistage Antiplasmodium Activity of Astemizole Analogues and Inhibition of Hemozoin Formation as a Contributor to Their Mode of Action. **ACS Infectious Diseases** 5(2):303-315. (IF: 4.911, Citations: 1. Source: Web of Science).

Invited Lectures and Seminars

Prudêncio M. Um Regresso às Origens na Busca de uma Vacina Contra a Malária. Pint of Science Portugal, Lisbon, Portugal, May 20, 2019.

Prudêncio M. Clinical Evaluation of a New Vaccine against Malaria. IGC Institutional Seminar, Instituto Gulbenkian de Ciência, Oeiras, Portugal, June 21, 2019.

Prudêncio M. *Plasmodium berghei* Sporozoites Expressing PfCSP as a Whole-Sporozoite-Based Malaria Vaccine Candidate. Sanaria Inc., Rockville, MD, USA, September 18, 2019.

Prudêncio M. PbSPZ-PfCSP (PbVac) - Results of Clinical Trial and Future Plans. International PfSPZ Consortium Meeting, Rockville, MD, USA, November 19, 2019.

Prudêncio M. Development and Clinical Evaluation of a New Vaccine against Malaria. Seminar in Master's in Biomedical Engineering, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 16, 2019.

Prudêncio M. Development and Clinical Evaluation of a New Vaccine against Malaria. Seminar in Master's in Human Biology and Environment, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, November 27, 2019.

Prudêncio M. A Journey through Friendship and Science in the Quest for a Vaccine against Malaria. Scientific Symposium in Memory of Dr. Shahid Khan, Leiden, The Netherlands, December 6, 2019.

Communications in International Conferences

Prudêncio M. Development and Clinical Evaluation of a New Vaccine against Malaria. 1st International Conference on Integrative Chemistry, Biology & Translational Medicine, Delhi, India, February 25-26, 2019. (*Plenary Lecture*).

Sanches-Vaz M, Luis R, Temporão A, Mendes AM, Goellner S, Carvalho T, Prudêncio M, Figueiredo LM. Interferon- γ mediates inhibition of *Plasmodium* hepatic infection by *Trypanosoma brucei*. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, MA, USA, April 27- May 1, 2019. (*Poster Presentation*).

Mendes A. PbVac: an open label randomized Phase 1/2a safety and efficacy trial. Malaria Vaccines for the World Conference, Oxford, UK, 8-10 May 2019. (*Oral Presentation*).

Arez F, Rebelo S, Fontinha D, Simão D, Martins T, Machado M, Fischli C, Oeuvray C, Badolo L, Carrondo M, Rottmann M, Spangenberg T, Brito C, Greco B, Prudêncio M, Alves PM. Flexible human 3D cell-based platforms for preclinical assessment of anti-plasmodial drugs targeting *Plasmodium* hepatic infection. 7th International Conference on *Plasmodium vivax* Research (ICPvR), Paris, France, June 26-28, 2019. (*Poster Presentation*).

Rajic Z, Perkovic I, Rajic-Malic S, Marinovic M, Poje G, Prudêncio M, Fontinha D, Held J. Harmicines as novel antiplasmodial leads. 11th Joint Meeting on Medicinal Chemistry 2019, Prague, Czech Republic, June 27-30, 2019. (*Poster Presentation*).

Reuling IJ, Mendes AM, de Jong GM, Fabra-García A, Nunes-Cabaço H, van Gemert GJ, Graumans W, Coffeng L, de Vlas S, Yang ASP, Lee C, Wu Y, Birkett AJ, Ockenhouse CF, Koelewijn R, van Hellemond JJ, van Genderen PJJ, Sauerwein RW, Prudêncio M. Safety and efficacy of a genetically modified rodent malaria parasite against *Plasmodium falciparum* malaria : an open-label randomized phase 1/2a trial. ASTMH 68th Annual Meeting, National Harbor, MA, USA, November 20-24, 2019. (*Poster Presentation*).

Miyazaki Y, Marin-Mogollon C, Imai T, Sturn A, van Pul FJA, Miyazaki S, Ramesar J, van Schuijlenburg R, Kroeze H, Chevalley-Maurel S, Salman AM, Reyes-Sandoval A, Mendes AM, Decherig KJ, Prudêncio M, Franke-Fayard B, Janse CJ, Khan SM. Generation of genetically modified *P. falciparum* parasites expressing *P. vivax* circumsporozoite(CSP) protein for malaria vaccine development. ASTMH 68th Annual Meeting, National Harbor, MA, USA, November 20-24, 2019. (*Poster Presentation*).

Communications in National Conferences

Prudêncio M. Aquecimento Global e Ressurgimento da Malária - Perspetivas para Portugal. XII Congresso Científico do Núcleo de Estudantes de Farmácia da Associação Académica de Coimbra, Coimbra, Portugal, March 7, 2019. (*Seminar*).

Temporão A, Sanches-Vaz M, Prudêncio M, Figueiredo LM. Unraveling the role of Trypanosoma brucei proteins in the impairment of *Plasmodium* infection. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Azevedo R, Markovic M, Franke-Fayard B, Mendes AM, Prudêncio M. Evaluation of avermectins' *Plasmodium* transmission blocking activity. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Kocken C, Nunes-Cabaço H, Prudêncio M. Evaluation of tissue-associated cellular immune responses to PbVAC, a *P. berghei*-based whole-sporozoite malaria vaccine candidate, in rhesus macaques. XLV Annual Meeting Sociedade Portuguesa de Imunologia, Coimbra, Portugal, May 15-17, 2019. (*Poster Presentation*).

Maia T, Duarte M, Moita D, Nunes-Cabaço H, Mendes AM, Prudêncio M. New malaria vaccine candidate against *Plasmodium vivax* using genetically modified rodent *Plasmodium* parasites. XLV Annual Meeting Sociedade Portuguesa de Imunologia, Coimbra, Portugal, May 15-17, 2019. (*Poster Presentation*).

Prudêncio M. Aquecimento Global e Ressurgimento da Malária - Perspetivas para Portugal. Instituto de Saúde Ambiental - Os efeitos da alteração dos ambientes na saúde humana, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 27, 2019. (*Seminar*).

Alves AJS, Soares MIL, Lopes SMM, Prudêncio M, Taveira N, Pinho e Melo TMVD. Synthesis of Novel Chiral Spiro-Lactams from Alkylidene-Lactams. International Symposium on Synthesis and Catalysis 2019 (ISySyCat2019), Évora, Portugal, September 3-6, 2019. (*Poster Presentation*).

Internationalization

The lab has an extensive network of collaborations with leading national and international researchers, including:

Catarina Brito, Paula Alves – iBET;

Joana Carneiro da Silva – University of Maryland;

Kelly Chibale – University of Cape Town;

Thomas Hanscheid - Instituto de Medicina Molecular João Lobo Antunes;

Paula Gomes – Universidade do Porto;

Chris Janse and Shahid Khan - Leiden University;

Clemens Kocken - Biomedical Primate Research Centre, Rijswijk;

Rui Moreira, Francisca Lopes and Ana Ressurreição – Faculdade de Farmácia da Universidade de Lisboa; Ann-Kristin Mueller - Universtity of Heidelberg;

Robert Sauerwein - University of Nijmegen;
Bogdan Solaja - Faculty of Chemistry, Belgrade;
Branka Zorc – University of Zagreb.

Patents/Prototypes

Prudêncio M, Mendes A. Genetically modified rodent *Plasmodium* parasites as platforms for a whole-organism malaria vaccine, (WO 2013156949 A1, also published as CN104302313A, EP2838554A1, US20150071966.

Provisional application (Portugal) No. 20121000030819, filed 17/04/2012.

PCT international application PCT/IB2013/053050, submitted 17/04/2013, published 24/10/2013.

Patent applications filed in Angola, Australia, Brazil, China, India, Japan, Mozambique, South Africa, United States, and European Patent (Euro-PCT), November 2014.

Patent granted in India (07/08/2015), Mozambique (17/08/2015), South Africa (23/12/2015), Japan (2015), Australia (03/02/2017), USA (15/02/2017), China (20/11/2017), Europe (11/05/2018) and Hong-Kong (20/07/2018).

Prudêncio M, Fontinha D. Infected cell cultures, European Patent Office application EP 17 160 277.4, filed on 10/03/2017. PCT application number PCT/EP2018/055717 (08/03/2018).

Prudêncio M. 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.

Advanced Teaching

Prudêncio M. MSc Class. Vaccination against malaria - Development and clinical evaluation of a new vaccine. Masters in Clinical Microbiology and Emerging Infectious Diseases, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21, 2019.

Prudêncio M, Mendes A, Nunes-Cabaço H. Malaria vaccination. PhD Course. Design, characterization and (pre-) clinical evaluation of a new vaccine against malaria. Biology at the Host Microbe Interface PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 3, 2019.

Prudêncio M, Mendes A, Nunes-Cabaço H. MSc Class. Malaria: the quest for an effective vaccine. Frontiers of Research in Biology - Masters in Molecular Biology and Genetics, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 24, 2019.

Prudêncio M. MSc Class. Biomolecular methods for malaria research & Development of a new vaccine against malaria. Masters in Clinical Biochemistry, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Lisbon, Portugal, June 5, 2019.

Prudêncio M. MSc Class. Basic principles of writing a scientific article. Masters in Molecular Biology and Genetics, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, September 30-October 2, 2019.

Science and Society

Prudêncio M. Scientific research and the fight against malaria. 8th and 9th grades (14-15 years old) - Grémio de Instrução Liberal Campo de Ourique, Semana da Ciência 2019, Lisbon, Portugal, April 4, 2019.

MSc Theses

Teresa Maia, 2019, Comparative immunological analyses of whole-sporozoite malaria vaccines, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Lisbon, Portugal. Supervisor: António Mendes. Co-Supervisor: Miguel Prudêncio.

Andreia Barreto, 2019, Evaluation of humoral and cellular immune responses to *P. berghei*-based whole-sporozoite malaria vaccination in rhesus macaques, Instituto de Higiene e Medicina Tropical, Lisbon, Portugal. Supervisor: Helena Nunes-Cabaço. Co-Supervisor: Miguel Prudêncio.

Raquel Mestre, 2019, Targeting p53 with indole-based compounds, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal. Supervisor: Maria Santos. Co-Supervisor: Miguel Prudêncio.

Miguel Remondes Lab

Major Interests/Objectives

Cognitive deficits present in Alzheimer's Disease, Anhedonia, Depression, and Schizophrenia, have been mapped to neuropathological changes in midline cortical structures, such as the anterior cingulate cortex, necessary for appropriate decision-making, the retrosplenial cortex, critically involved in visual-spatial processing, and the hippocampal formation, critical for episodic memory and any mental function therein dependent. To understand such disorders, it is imperative that we identify the structures and mechanisms underlying the behaviors they affect. In our research group we model memory and therein behaviors in the rodent as the formation of episodic memories whose components drive goal-directed choices on a maze of variable complexity, while we dissect the neural circuits forming memories in the hippocampus and for bringing such mnemonic information to cingulate (CG) and retrosplenial (RSC) cortices. In parallel, we collaborate in human subject studies aimed at understanding decisions under higher cognitive loads such as conflicts. By dissecting neural mechanisms underlying memory and cognition, our research and its results can be leveraged to understand mental illness, and to develop mechanistically-targeted therapies.

Head of Laboratory

Armando Miguel Caseiro Pires Remondes, PhD, Principal Investigator at Instituto de Medicina Molecular João Lobo Antunes, Invited Auxiliary Professor at Faculdade de Medicina da Universidade de Lisboa

Team

Ana Inês Marques Morgado	Master Degree	PhD Student
Ana Raquel Rosa Pereira	University Degree	MSc Student (Left December)
Ana Sofia Carvalho Cruz	Master Degree	PhD Student
Bárbara Pinto Correia	Master Degree	PhD Student
Emanuel Ferreira Fernandes	Master Degree	PhD Student
Gonçalo Aires de Oliveira	PhD	Postdoctoral Researcher
Gonçalo Correia de Oliveira Ferreira	University Degree	MSc Student (Left December)
Joana Gomes Ribeiro	Master Degree	PhD Student
Jorge Miguel Claro Cardoso	Master Degree	PhD Student
Marcelo Francisco Vieira Dias	Master Degree	PhD Student

Raquel Filipa Rodrigues Ferreira	University Degree	MSc Student (Left December)
Thabelo Mmamatseliso Khoboko	Master Degree	PhD Student (Left June)

Laboratory Keywords / Research Areas

Cognitive Function and Dysfunction, Spatial-temporal Cognitive Mapping, Goal Directed Behavior and Decision-making, Electrophysiological Recording and Neural Manipulation of Defined Neural Circuits, Rodent Models of Human Behavior.

Major Scientific Achievements

Goal directed behaviours (GDB) require that a cognitive map is made available to medial mesocortical (MMC) regions, anterior cingulate cortex (CG) through retrosplenial cortex (RSC), responsible for decision-making, and dysfunctional in Autism spectrum disorder, and Schizophrenia. Besides reporting state-dependent communication between hippocampal formation (HIPPF) and CG, we have recently identified the synapses connecting the two structures, which we are currently manipulating, to assess their role in HIPPF-MMC communication during GDB. We have reported the anatomical and functional connectivity *in vitro* and *in vivo* between HIPP and MMC divisions in behaving animals.

To study time processing by HIPPF neurons we recently developed a behavioural task – Waiting to Trajectory Task (WTT) - in which rats are rewarding for waiting motionless for a specific self-generated time lapse. We are currently analysing the results of such neural/behavioural recording while rats process time lapses. Within this project, we have disturbed the activity in the HIPPF circuitry and found that this manipulation significantly impaired behavioural performance in the novel WTT and showing the necessity of information processed in the HIPPF-EC axis for time processing, and time-lapse-dependent GDB.

We have identified a sensory-mnemonic-decisional neural circuit we are currently monitoring and manipulating, in order to dissect neural mechanisms underlying cognition. Our results can be leveraged to understand the neural basis of cognitive dysfunction, and to develop mechanistically-targeted therapies.

Selected Publications

Ferreira-Fernandes E, Quintino C, Remondes M* (2019). A Gradient of Hippocampal Inputs to the Medial Mesocortex. **Cell Reports** 29(10):3266-3279. (IF: 7.815, Citations: 0. Source: Web of Science).

Remondes M*, Wilson M (2015). Slow-gamma rhythms coordinate cingulate cortical responses to hippocampal sharp-wave ripples during choice behavior. **Cell Reports** 13(7):1327-1335. (IF: 7.870, Citations: 17. Source: Web of Science).

Remondes M*, Wilson M (2013). Cingulate-hippocampus Coherence and Trajectory Coding in a Sequential Choice Task. **Neuron** 81(5):1277-89. (IF: 15.982, Citations: 39. Source: Thomson Reuters).

Wilson M*, Varela C, Remondes M* (2015). Phase organization of network computations. **Current Opinion in Neurobiology** 31:250-253. Review. (IF: 6.373, Citations: 19. Source: Thomson Reuters).

Remondes M, Schuman EM (2004). Role for a cortical input to hippocampal area CA1 in the consolidation of a long-term memory. **Nature** 431(709):699-703. (IF: 32.182, Citations: 344. Source: Thomson Reuters).

Remondes M, Schuman EM (2002). Direct Cortical Input Modulates Plasticity and Spiking in CA1 Pyramidal Neurons. **Nature** 416(6882):736-740. (IF: 30.432, Citations: 211. Source: Thomson Reuters).

Ongoing Research Projects

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.

2014/2019: Cingulate-hippocampal interactions during decision-making. Coordinator: Miguel Remondes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00201/2013/CP1170/CT0002. Amount: € 50 000,00. Total Amount: € 50 000,00.

Publications in Peer Reviewed Journals

Ferreira-Fernandes E, Quintino C, Remondes M* (2019). A Gradient of Hippocampal Inputs to the Medial Mesocortex. **Cell Reports** 29(10):3266-3279. (IF: 7.815, Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Remondes M. Sensory integration in memory-driven choice behaviors. Leibniz Institute for Neurobiology, Magdeburg, Germany, January 15, 2019.

Remondes M. Sensory integration in memory-driven choice behaviors. V Bioengineering Week IST, Instituto Superior Técnico, Lisbon, Portugal, March 22, 2019.

Remondes M. Neural recordings in awake-behaving animals. NOVA Medical School Biomedical Science MSc, NOVA Medical School, Lisbon, Portugal, March 27, 2019.

Remondes. Workshop on Neuroengineering (WoN) organized by the EU H2020 Widespread project “The Discoveries CTR”, Portuguese Universities and University College London, Porto, Portugal, April 8, 2019.

Remondes M. Session Chair. Meeting of the Portuguese Society for Neuroscience, Spanish Society of Neuroscience symposium – Neural Circuits, Lisbon, Portugal, May 30-June 1, 2019.

Remondes M. Hippocampal-medial mesocortex interactions during choice behaviors. Spring Hippocampal Research Conference, Taormina, Sicily, Italy, June 2-7, 2019.

Remondes M. Demystifying the Brain. Live Podcast on Art, Culture and Science, Zénite Bar Galeria, Lisbon, Portugal, June, 2019.

Remondes M. Patient HM, Beyond Epilepsy Onto the Mechanisms of Memory. NOVA Medical School PhD Program “Critical Skills in Research”, NOVA Medical School, Lisbon, Portugal, September, 2019.

Remondes M. Neural Bases of Memory-driven Choice Behavior. NeuroSeS | Neuroscience Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November, 2019.

Remondes M. Invited Seminar. Sensory integration in memory-driven choice behaviors. Cajal Institute (for Neuroscience), Madrid, Spain, November 28, 2019.

Remondes M. Seminar. Cortico-hippocampal neural circuits in Memory-driven Choice Behaviors. MIT-Portugal PhD Program in Bio-Engineering Neuroscience Course 2019, Center for Neuroscience and Cell Biology, Universidade de Coimbra, Coimbra, December 2019.

Remondes M. Seminar. Cortico-hippocampal neural circuits in Memory-driven Choice Behaviors. MIT-Portugal PhD Program in Bio-Engineering Neuroscience Course 2019, Center for Neuroscience and Cell Biology, Universidade de Coimbra, Coimbra, December 2019.

Remondes M. Seminar. Sensory integration in memory-dependent choice behaviors. FMUL PhD Program in Neuroscience, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2019.

Remondes M. Memory, Choice and Self-determination, Are We Free?. Pint of Science Lisbon, O'Gilins Irish Pub, Lisbon, Portugal, 2019.

Remondes M. Speaker. Using the Brain with Fun, Wonder Science, Brain Awareness Week 2019, Lisbon, Portugal, 2019.

Communications in International Conferences

Remondes M. Hippocampal-medial mesocortex interactions during choice behaviors. Spring Hippocampal Research, Taormina, Sicily, Italy, June 2-7, 2019. (*Oral Presentation*).

Communications in National Conferences

Remondes M. Meeting of the Portuguese Society for Neuroscience, Spanish Society of Neuroscience symposium – Neural Circuits, Lisbon, Portugal, May 30-June 1, 2019. (*Session Chair*).

Internationalization

Lab members were participants at the **Spring Hippocampal Research Conference, Taormina, Sicily, Italy, June 2-7, 2019.**

Lab members have engaged in Summer schools abroad, and graduate students seek international scientists as thesis committee members.

The lab is part of the network "Neurologic and Psychiatric Disorders: from synapses to networks (SynaNet)", which includes labs from the United Kingdom, Finland, Italy and France.

Prizes, Honors and Awards

Remondes M. Co-Investigator with Luísa V. Lopes. The Physiological Role of Circadian Rhythms in Memory, BIAL Award 2019.

Advanced Teaching

Remondes M. Member. Doctoral Programme in Experimental Biology and Biomedicine, Center for Neuroscience and Cell Biology, Universidade de Coimbra, Coimbra, Portugal.

Remondes M. Member and Lecturer. MSc Programme Neurasmus ERASMUS Mundus Programme and MIT-Portugal PhD Programme in Bioengineering.

Remondes M. Member and Lecturer. IMM/FMUL PhD programme in Biomedicine – LisbonBioMed. Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Remondes M. Member and Lecturer. FMUL PhD Programme in Neuroscience – lecture on Neuronal Circuits, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Remondes M. Lecture on Neuronal Circuits. NOVA Medical School PhD Program “Critical Skills in Research”, NOVA Medical School, Lisbon, Portugal, 2019.

Remondes M. Patient HM, Beyond Epilepsy onto the Mechanisms of Memory. NOVA Medical School PhD Program “Critical Skills in Research”, NOVA Medical School, Lisbon, Portugal, September 2019.

Science and Society

- Live Podcast on Art, Culture and Science, Zénite Bar Galeria, "Demystifying the Brain", June 2019.
- Speaker at the outreach activity "Pint of Science" talk entitled "Memory, Choice and Self-determination, Are We Free?", organized by Pint of Science Lisbon in 2019, held at O'Gilins Irish Pub (Cais do Sodré, Lisbon).
- Speaker at the outreach activity "Using the Brain with Fun" organized by Wonder Science, during the Brain Awareness Week 2019, held at LX Factory (Alcântara, Lisbon)
- Collaborations with news media (several).

MSc Theses

Raquel Ferreira, 12/18/2019, Hippocampal Time, the Neural Substrate of Time in Memory Systems, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Miguel Remondes. Co-Supervisor: Alexandre Andrade.

PhD Theses

Emanuel Ferreira Fernandes, A Gradient of Hippocampal Inputs to the Medial Mesocortex, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Miguel Remondes. Co-Supervisor: Luísa V. Lopes.

Nuno Morais Lab

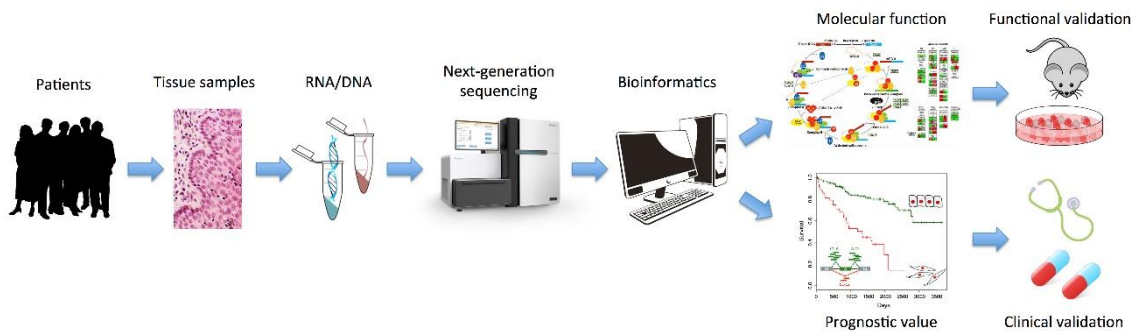
Major Interests/Objectives

We have a long-term interest in the systems-level transcriptional regulation underlying mammalian cell specification, often perturbed in disease. We employ computational biology approaches for the analysis of next-generation sequencing data to find disease-specific transcriptomic signatures, aiming to understand how the regulation of transcription and splicing is affected in pathologies associated with ageing, like cancer and neurodegenerative disorders, and thereby to identify molecular targets for functional exploration *in vitro* and *in vivo*. We also combine molecular and clinical information for the unveiling of novel diagnostic and prognostic factors, as well as of innovative therapeutic strategies.

Head of Laboratory

Nuno Luís Barbosa Morais, PhD

Graphical Abstract



Team

Ana Marta Fernandes Bica	Master Degree	MSc Student
Ana Sofia Galrinho Borges	Master Degree	Trainee (Started March)
Arthur Louis François Schneider	Master Degree	MSc Student
Joel Amaque da Silva Indi	Master Degree	PhD Student
Mariana Ascensão Ferreira	Master Degree	PhD Student
Marie Catherine Bordone	Master Degree	PhD Student
Nuno Daniel Saraiva Agostinho	Master Degree	PhD Student
Sara Rodrigues Mendes	University Degree	MSc Student (Left September)

Laboratory Keywords / Research Areas

Alternative Splicing, Transcriptional Regulation, Aging, Neurodegenerative Disease, Cancer, Transcriptomics, Computational Biology.

Major Scientific Achievements

We published in *PLoS Computational Biology* our work showing the pan-cancer association of a centrosome amplification gene expression signature with genomic alterations and clinical outcome.

The article about *psichomics*, our R/Bioconductor package for the integrated analysis of alternative splicing from large transcriptomic datasets, was published in its print version in *Nucleic Acids Research*. We were invited by Springer Methods to write a book chapter on using *psichomics* to analyze alternative splicing in stem cell differentiation, to be published in *Methods in Molecular Biology* in 2020.

Our latest collaboration with the lab of David Elliott (IGM Newcastle) on androgen regulation of alternative splicing in prostate cancer was published in *eLife* (with Nuno Morais as co-corresponding author).

Collaborations with the labs of Henrique Veiga-Fernandes (CCU Lisbon) and Gonçalo Bernardes (iMM) also yielded publications in *Nature*, *Bioorganic & Medicinal Chemistry*, and *Chemical Communications*.

Selected Publications

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. (IF: 7.551, Citations: 0. Source: eLife).

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. (IF: 4.428, Citations: 3. Source: Scopus).

Saraiva-Agostinho N, Barbosa-Morais NL (2019). *psichomics: graphical application for alternative splicing quantification and analysis*. **Nuclei Acids Research** 47(2):e7. (IF: 11.147, Citations: 4. Source: Web of Science).

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. (IF: 3.930, Citations: 23. Source: Crossref).

Barbosa-Morais NL, Irimia M, Pan Q, Xiong HY, Gueroussov S, Lee LJ, Slobodeniuc V, Kutter C, Watt S, Colak R, Kim T, Misquitta-Ali CM, Wilson MD, Kim PM, Odom DT, Frey BJ, Blencowe BJ (2012). The evolutionary landscape of alternative splicing in vertebrate species. **Science** 338(6114):1587-93. (IF: 41.063, Citations: 432. Source: Web of Science).

Ongoing Research Projects

2017/2021: GENOME Portugal. Coordinator: Nuno Morais. Funding Agency: Portugal 2020. Reference: PINFRA/22134/2016. Amount: € 123 711,00. Total Amount: € 826 226, 00.

2016/2019: PERSEIDS: Personalização de Terapêuticas Oncológicas através de modelação integrada e decisão. Nuno Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EMS-SIS/0642/2014. Amount: € 70 408,00. Total Amount: € 199 997,00.

2015/2020: Transcriptomic landscapes of cancer: 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.

2015/2019: RNA regulation in cancer: defining the transcriptional etiology of metastasis its implications on personalized therapeutics. Coordinator: Nuno Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00595/2014/CP1236/CT0002. Amount: € 50 000,00. Total Amount: € 50 000,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Godinho-Silva C, Domingues RG, Rendas M, Raposo B, Ribeiro H, da Silva JA, Vieira A, Costa RM, Barbosa-Morais NL, Carvalho T, Veiga-Fernandes H (2019). Light-entrained and brain-tuned circadian circuits regulate ILC3s and gut homeostasis. **Nature** 574(7777):254-258. (IF: 43.070, Citations: 6. Source: Crossref).

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. (IF: 7.551, Citations: 0. Source: eLife).

Rodrigues T, de Almeida BP, Barbosa-Morais NL, Bernardes GJL (2019). Dissecting celastrol with machine learning to unveil dark pharmacology. **Chemical Communications** 55(45):6369-6372. (IF: 6.164, Citations: 0. Source: Crossref).

Baker C, Rodrigues T, de Almeida BP, Barbosa-Morais NL, Bernardes GJL (2019). Natural product-drug conjugates for modulation of TRPV1-expressing tumors. **Bioorganic & Medicinal Chemistry** 27(12):2531-2536. (IF: 2.793, Citations: 1. Source: ScienceDirect).

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. (IF: 4.428, Citations: 3. Source: Scopus).

Saraiva-Agostinho N, Barbosa-Morais NL (2019). psychomics: graphical application for alternative splicing quantification and analysis. **Nuclei Acids Research** 47(2):e7. (IF: 11.147, Citations: 4. Source: Web of Science).

Invited Lectures and Seminars

Barbosa-Morais N. Bioinformatics in the translation of cancer transcriptomics. V Semana da Bioengenharia, Instituto Superior Técnico, Lisbon, Portugal, March 18, 2019.

Barbosa-Morais N. Bioinformatics in the translation of cancer transcriptomics. Biozentrum, University of Basel, Switzerland, May 21, 2019.

Barbosa-Morais N. What transcriptomes tell us about disease. Department of Bioengineering, Instituto Superior Técnico, Lisbon, Portugal, May 21, 2019.

Communications in International Conferences

Saraiva-Agostinho N, Barbosa-Morais NL. psichomics: a bioinformatics application for the quantification, analysis and visualisation of alternative splicing from large transcriptomic datasets. EMBO VIZBI 2019, Heidelberg, Germany, March 13-15, 2019. (*Poster Presentation*).

Bordone MC, Barbosa-Morais NL. Decoupling cellular composition and gene expression alterations in Alzheimer's and Parkinson's brains. The 14th International Conference on Alzheimer's & Parkinson's Diseases 2019, Lisbon, Portugal, March 30, 2019. (*Oral Presentation*).

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. 24th Annual RNA Society Meeting - RNA 2019, Krakow, Poland, June 11-16, 2019. (*Poster Presentation*).

Saraiva-Agostinho N, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. 24th Annual RNA Society Meeting - RNA 2019, Krakow, Poland, June 11-16, 2019. (*Poster Presentation*).

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. International Cell Senescence Association 2019 Conference: Cellular Senescence - the bright & dark side, Athens, Greece, September 9-12, 2019. (*Poster Presentation*).

Bica M, Serre K, Barbosa-Morais NL. Single-cell transcriptomics in unravelling the cellular diversity and molecular signature that govern anti-tumour functions of myeloid cells *in vivo*. Basel Life Conference, Basel, Switzerland, September 9-12, 2019. (*Poster Presentation*).

Barbosa-Morais NL. What transcriptomes tell us about ageing and associated diseases. RiboMed Kickoff Meeting, Carcavelos, Portugal, October 15, 2019. (*Oral Presentation*).

Communications in National Conferences

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. VIII National RNA Meeting: ptRNA2019, i3S Porto, Portugal, January 25, 2019. (*Oral Presentation*).

Barbosa-Morais NL. CELF2 at the core of a prognostic alternative splicing signature in colorectal cancer. VIII National RNA Meeting: ptRNA2019, i3S Porto, Portugal, January 25, 2019. (*Oral Presentation*).

Saraiva-Agostinho N, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. VIII National RNA Meeting: ptRNA2019, i3S Porto, Portugal, January 25, 2019. (*Poster Presentation*).

Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations and phenotype-targeting compounds from differential expression data. GenomePT Symposium, CIBIO-InBIO Vairão, Portugal, May 10, 2019. (*Oral Presentation*).

Ascensão-Ferreira M, Barbosa-Morais NL. Profiling the alternative splicing landscape of senescent cells. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Saraiva-Agostinho N, Barbosa-Morais NL. cTRAP: identification of candidate causal perturbations from differential expression data. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Bica M, Serre K, Barbosa-Morais NL. Single-cell transcriptomics in unravelling the cellular diversity and molecular signature that govern anti-tumour functions of myeloid cells *in vivo*. AstraZeneca Foundation Innovate Competition - iMed Conference 11.0, Lisbon, Portugal, October 16-20, 2019. (*Oral Presentation*).

Schneider A, Barbosa-Morais NL. Modelling of ageing-associated gene expression alterations. AstraZeneca Foundation Innovate Competition - iMed Conference 11.0, Lisbon, Portugal, October 16-20, 2019. (*Oral Presentation*).

Rodrigues-Mendes S, Barbosa-Morais NL. How much Alzheimer have Alzheimer's disease mouse models? AstraZeneca Foundation Innovate Competition – iMed Conference 11.0, Lisbon, Portugal, October 16-20, 2019. (*Poster Presentation*).

Barbosa-Morais NL. Tumor transcriptomes reveal a prognostic alternative splicing signature in colorectal cancer. 23rd Annual Meeting of the Portuguese Human Genetics Society, Fundação Bissaya Barreto, Coimbra, Portugal, November 15, 2019. (*Oral Presentation*).

Internationalization

Our collaboration with David Elliott (Newcastle University) on alternative splicing in prostate cancer yielded a publication in eLife.

We carried on our collaborations with Jesus Gil (Imperial College London, England) on the role of alternative splicing in cell senescence, George Garinis (FORTH Crete, Greece) on the impact of TC-NER perturbations on splicing, and Professor Sir Bruce Ponder, on the interaction between genetic background and smoking in lung cancer.

Nuno Morais was the main examiner of a PhD thesis defense at the Pompeu Fabra University in Barcelona (Spain).

Nuno Morais was invited by the lab of Mihaela Zavolan to give a lecture at the Biozentrum of the University of Basel, Switzerland, in May.

Several lab members presented work in scientific meetings in Germany, Greece, Poland and Switzerland.

Prizes, Honors and Awards

Ascensão-Ferreira M. Young ICSA Poster Award: 1st Place, Young International Cell Senescence Association, Greece. September 12, 2019.

Schneider A. Best Master Thesis Award: 2nd Place, Instituto de Medicina Molecular João Lobo Antunes, Lisbon Portugal. December 3, 2019.

Barbosa-Morais NL. Assistant Researcher Grant, FCT Scientific Employment Stimulus, Portugal. December 2019.

Advanced Teaching

Barbosa-Morais NL. Lecture. Bioinformatics - Computational biology in the translation of cancer 'omics'. Masters in Biopharmaceutical Sciences and Integrated Masters in Pharmaceutical Sciences, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 8, 2019.

Barbosa-Morais NL. Lecture. Disease transcriptomics. PhD Programs Plants for Life and Molecular Biosciences, ITQB-NOVA, Oeiras, Portugal, October 8, 2019.

Barbosa-Morais NL. Lecture. Bioinformatics - Computational biology in the translation of cancer 'omics'. Masters in Biomedical Research, NOVA Medical School, Lisbon, Portugal, October 18, 2019.

Barbosa-Morais NL. 20% of semestral course. Bioinformatics. Integrated Masters in Biomedical Engineering, Instituto Superior Técnico, Lisbon, Portugal, December, 2019.

Science and Society

Nuno Morais participated in the promotion video of book “Cientistas Portugueses” by David Marçal, published by Fundação Francisco Manuel dos Santos (February 2019).

Nuno Morais participated in a “speed dating” session with secondary school students, as part of the “Little iMMers” outreach event at iMM (July 5, 2019).

Marta Bica gave an oral presentation on “What is cancer?” at the Fundo iMM-Laço Breast Cancer Awareness session in Lisbon, Portugal (November 6, 2019).

MSc Theses

Marta Bica, 22/10/2019, Single-cell transcriptomics in unravelling the molecular complexity of immunity in human disease, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Nuno Barbosa Morais. Co-Supervisor: Fernanda Diamantino.



Arthur Schneider, 10/10/2019, Modelling of ageing-associated gene expression alterations, Instituto Superior Técnico, Universidade de Lisboa. Supervisor: Nuno Barbosa Morais. Co-Supervisor: Tiago Fernandes.

Nuno Santos Lab

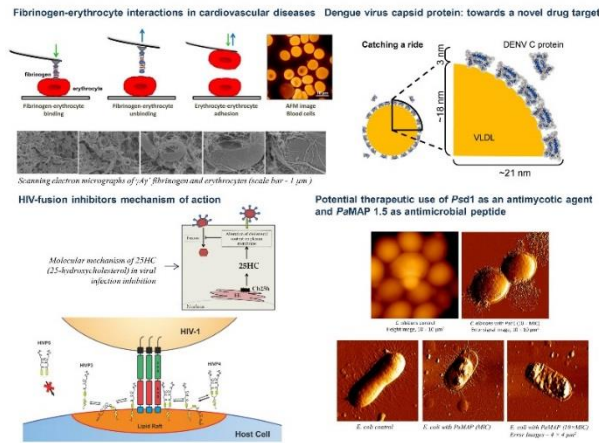
Major Interests/Objectives

Biochemical and biophysical processes occurring in membranes of human cells, as well as of their viral and bacterial pathogens. Study of the two steps of the life cycle of enveloped viruses (HIV-1, dengue, West Nile, Zika and pediatric respiratory viruses) that involve biomembranes – the entrance of the virus or its content into the target cell (including its inhibition) and the assembly of new virions. Study of the binding of fibrinogen to erythrocytes as a determinant for cardiovascular risk. Pre-clinical evaluation of the membrane activity and mechanism of action of antimicrobial (AMP) and anticancer (ACP) peptides. Also, on the Nanomedicine area, we are interested in the development of biosensor systems using innovative protein-ligand interactions (nanoparticles and amyloid-based biosensors).

Head of Laboratory

Nuno Fernando Duarte Cordeiro Correia dos Santos, PhD and Habilitation, Associate Professor

Graphical Abstract



Team

Ana de Souto Martins	Master Degree	PhD Student
Catarina Isabel de Sousa Lopes	Master Degree	PhD Student
Filomena Maria Dias Almeida Carvalho	PhD	Staff Scientist
Francisca Lidiane Linhares de Aguiar		PhD Student (Started February. Left August)
Ítala Cristine Silva	Master Degree	PhD Student
Ivo Cristiano da Rocha Martins	PhD	Staff Scientist
Joana Cristina Pacheco Barbosa	Master Degree	PhD Student (Started January. Left December)
Marcin Makowski	Master Degree	PhD Student
Marco André Manso Domingues	PhD	Staff Scientist
Maria Constança Gomes Redinha Pais do Amaral	Master Degree	PhD Student
Maria Teresa Damásia Freitas Santos	High School Diploma	Lab Technician
Mário Nuno Romão Felício	Master Degree	PhD Student (Left March)
Miriam Raquel Figueiredo Arrulo	University Degree	MSc Student (Left November)
Nelly Marine Carreira da Silva	Master Degree	PhD Student (Started December)
Nina Elisabeth Karguth	University Degree	MSc Student (Left September)
Patrícia Isabel Duarte Montês Carvalho	Master Degree	PhD Student
Patrícia Morgado da Silva	Master Degree	PhD Student
Sofia Antunes Angélico Pinto Nabais	University Degree	MSc Student (Left June)
Sónia Gonçalves Abreu	PhD	Staff Scientist

Laboratory Keywords / Research Areas

Nanomedicine, HIV, Dengue, West Nile, Zika and Respiratory Viruses, Peptide-based Therapies (AMPs, ACPs, pep14-23), Atomic Force Microscopy (AFM), Biomarkers of Cardiovascular Diseases.

Major Scientific Achievements

The capsid protein of West Nile virus interacts with host lipid systems, namely, lipid droplets and very low-density lipoproteins, in a potassium ion dependent manner. The interactions of the capsid proteins of West Nile, Zika and dengue virus with lipid systems induce allosteric changes in those proteins that lead to specific binding to viral RNA. These interactions are essential for viral replication and viral particle assembly, and could lead to the identification of new drug targets, as previously done in our Lab for the dengue virus.

A designed lipopeptide inhibitor of HIV-1, C34-25-hydroxycholesterol, interacts preferentially with human peripheral blood mononuclear cells, potentially targeting CD4⁺ cells.

Higher fibrinogen-erythrocyte binding forces and increased erythrocyte stiffness in essential arterial hypertension patients, together with patients' altered hemorheological parameters, may lead to changes in the whole blood flow and trigger erythrocyte aggregation, increasing cardiovascular risk.

Selected Publications

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. (IF: 37.490, Citations: 22. Source: Web of Science).

Vigant F, Santos NC, Lee B (2015). Broad-spectrum antivirals against viral fusion. **Nature Reviews Microbiology** 13(7):426-437. (IF: 31.851, Citations: 59. Source: Web of Science).

Faustino AF, Carvalho FA, Martins IC, Castanho MARB, Mohana-Borges R, Almeida FC, Da Poian AT, Santos NC (2014). Dengue virus capsid protein interacts specifically with very low-density lipoproteins. **Nanomedicine (NBM)** 10:247-255. (IF: 6.500, Citations: 34. Source: Web of Science).

Hauser CA, Maurer-Stroh S, Martins IC (2014). Amyloid-based nanosensors and nanodevices. **Chemical Society Reviews** 43(15):5326-5345. (IF: 40.182, Citations: 85. Source: Web of Science).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC (2010). Atomic force microscopy-based molecular recognition of a fibrinogen receptor on human erythrocytes. **ACS Nano** 4:4609-4620. (IF: 13.709, Citations: 108. Source: Web of Science).

Ongoing Research Projects

2018/2021: When the host cell is not so cosy anymore? A drop off in energy or an increase in toxicity? Coordinator: Filomena Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/28456/2017. Amount: € 47 064,00.

2018/2021: iDNArT - Intelligent DNA nanostructures aimed at brain therapeutics. Coordinator: Nuno C. Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/NAN-MAT/30898/2017. Amount: € 7 812,00.

2017/2020: VIH_TRANFERSOME: Inibidor de fusão veiculado em Transfersomas para libertação transdérmica. Funding Agency: Gilead Génese Project. Reference: PGG/006/2016. Amount: € 23 000,00.

2016/2020: Between Atom and Cell: Integrating Molecular Biophysics Approaches for Biology and Healthcare. National Responsible: Nuno Santos Funding Agency: COST Project. Acronym: MOBIEU. Reference: OC-2015-1-19651. Total Amount: € 520 000,00.

2016/2019: Broad-spectrum antiviral peptides against respiratory viruses. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BQB/3494/2014. Amount: € 197 839,00. Total Amount: € 197 839,00.

2016/2019: Molecular interactions of circulating fibrinogen as a risk factor for cardiovascular and cerebrovascular pathologies. Coordinator: Filomena Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BMD/6307/2014. Amount: € 184 965,00. Total Amount: € 184 965,00.

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: Horizon 2020 (EU). Reference: GA 814607 – SAFE-N-MEDTECH. Amount: € 714 815,00. Total Amount: € 14 588 286,50.

2015/2019: INPACT: Innovative peptides against cancer and pathogenic bacteria, with advances in science, biopharmaceutical drug development, product market targeting, training, and communication. Coordinator: Miguel Castanho. Funding Agency: European Commission. Reference: MSCA RISE 644167. Amount: € 463 500,00. Total Amount: €1 390 500,00.

Publications in Peer Reviewed Journals

Meneguetti BT, Cardoso MH, Ribeiro CFA, Felício MR, Pinto IB, Santos NC, Carvalho CME, Franco OL (2019). Neuropeptide receptors as potential pharmacological targets for obesity. **Pharmacology & Therapeutics** 196:59-78. (IF: 7.731, Citations: 1. Source: Web of Science).

Gomes B, Sanna G, Madeddu S, Hollmann A, Santos NC (2019). Combining 25-hydroxycholesterol with a HIV fusion inhibitor peptide: interaction with biomembrane model systems and human blood cells. **ACS Infectious Diseases** 5(4):582-591. (IF: 4.911, Citations:--. Source: Web of Science).

Figueira TN, Domingues MM, Illien F, Cadima-Couto I, Todorovski T, Andreu D, Sagan S, Castanho MARB, Walrant A, Veiga AS (2019). Enfuvirtide-protoporphyrin IX dual-loaded liposomes: in vitro evidence of synergy against HIV-1 entry into cells. **ACS Infectious Diseases** 6(2):224-236. (IF: 4.911, Citations: 1. Source: Web of Science).

Faustino AF, Martins AS, Karguth N, Artilheiro V, Enguita FJ, Ricardo JC, Santos NC, Martins IC (2019). Structural and functional properties of the capsid protein of Dengue and related Flavivirus. **International Journal of Molecular Sciences** 20(16):3870. (IF: 4.183, Citations: 1. Source: Web of Science).

Irazazabal LN, Porto WF, Fensterseifer ICM, Alves ESF, Matos CO, Menezes ACS, Felício MR, Gonçalves S, Santos NC, Ribeiro SM, Humblot V, Lião LM, Ladram A, Franco OL (2019). Fast and potent bactericidal membrane lytic activity of PaDBS1R1, a novel cationic antimicrobial peptide. **Biochimica et Biophysica Acta-Biomembranes** 1861(1):178-190. (IF: 4.402, Citations: 3. Source: Web of Science).

Faustino AF, Barbosa GM, Silva M, Castanho MARB, Da Poian AT, Cabrita EJ, Santos NC, Almeida FCL, Martins IC (2019). Fast NMR method to probe solvent accessibility and disordered regions in proteins. **Scientific Reports** 9:1647. (IF: 4.011, Citations: 1. Source: Web of Science).

Amaral VSG, Fernandes CM, Felício MR, Valle AS, Quintana PG, Almeida CC, Barreto-Bergter E, Gonçalves S, Santos NC, Kurtenbach E (2019). Psd2 pea defensin shows a preference for mimetic membrane rafts enriched with glucosylceramide and ergosterol. **Biochimica et Biophysica Acta-Biomembranes** 1861(4):713-728. (IF: 4.402, Citations: 3. Source: Web of Science).

Guedes AF, Moreira C, Nogueira JB, Santos NC, Carvalho FA (2019). Fibrinogen-erythrocyte binding and hemorheology measurements on the assessment of essential arterial hypertension patients. **Nanoscale** 11(6):2757-2766. (IF: 6.970, Citations:--. Source: Web of Science).

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. (IF: 3.518, Citations: 1. Source: Web of Science).

Maillard APVF, Gonçalves S, Santos NC, Mishima BAL, Dalmasso PR, Hollmann A (2019). Studies on interaction of green silver nanoparticles with whole bacteria by surface characterization techniques. **Biochimica et Biophysica Acta-Biomembranes** 1861(6):1086-1092. (IF: 4.402, Citations:--. Source: Web of Science).

Martinez M, Gonçalves S, Felício MR, Maturana P, Santos NC, Semorile L, Hollmann A, Maffía PC (2019). Synergistic and antibiofilm activity of the antimicrobial peptide P5 against carbapenem-resistant *Pseudomonas*. **Biochimica et Biophysica Acta-Biomembranes** 1861(7):1329-1337. (IF: 4.402, Citations: 1. Source: Web of Science).

Fensterseifer ICM, Felício MR, Alves ESF, Cardoso MH, Torres MDT, Matos CO, Silva ON, Lu TK, Freire MV, Neves NC, Gonçalves S, Lião LM, Santos NC, Porto WF, Fuente-Nunez C, Franco OL (2019). Selective antibacterial activity of the cationic peptide PaDBS1R6 against Gram-negative bacteria. **Biochimica et Biophysica Acta-Biomembranes** 1861(7):1375-1387. (IF: 4.402, Citations: 4. Source: Web of Science).

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** 8:e45853. (IF: 7.551, Citations: 2. Source: Web of Science).

Makowski M, Silva ÍC, Amaral CP, Gonçalves S, Santos NC (2019). Advances in lipid and metal nanoparticles for antimicrobial peptide delivery. **Pharmaceutics** 11(11):588. (IF: 4.773, Citations:--. Source: Web of Science).

Barros E, Gonçalves RM, Cardoso MH, Santos NC, Franco OL, Cândido ES (2019). Snake venom cathelicidins as natural antimicrobial peptides. **Frontiers in Pharmacology** 10:1415. (IF: 3.845, Citations: 0. Source: Web of Science).

Eaton P, Amaral CP, Couto SCP, Oliveira MS, Vasconcelos AG, Borges TKS, Kückelhaus SAS, Leite JRSA, Muniz-Junqueira MI (2019). Atomic Force Microscopy Is a Potent Technique to Study Eosinophil Activation. **Frontiers in Physiology** 10:1261. (IF: 3.201, Citations: 0. Source: Web of Science).

Other International Publications

Santos NC, Carvalho FA (2019). Atomic Force Microscopy. Springer / Humana Press, New York (ISBN: 978-1-4939-8893-8).

Domingues MM, Felício MR, Gonçalves S (2019). Antimicrobial peptides: effect on bacterial cells. In: Santos NC, Carvalho FA (eds.) Atomic Force Microscopy. pp. 233-242. Springer / Humana Press, New York.

Invited Lectures and Seminars

Santos NC. Cardiovascular patients' evaluation by force spectroscopy. XXI Annual Linz Winter Workshop – Advances in Single-Molecule Research for Biology & Nanoscience, Linz, Austria, February 1-4, 2019.

Santos NC. Using the force at the nanoscale for cardiovascular risk evaluation. X Jornadas Nacionais de Ciências Biomédicas, Aveiro, Portugal, March 13-16, 2019.

Martins IC. A startup company journey. 11th Workshop on Biomedical Engineering, Lisbon, Portugal, April 6, 2019.

Carvalho FA. Force Spectroscopy: Biological and Biomedical Applications. REQUIMTE BIO-AFM Hands-on Workshop, Porto, Portugal, April 16, 2019.

Domingues M. Quantitative Imaging in Biological Applications. REQUIMTE BIO-AFM Hands-on Workshop, Porto, Portugal, April 17, 2019.

Santos NC. Cardiovascular patients' evaluation by AFM-based force spectroscopy measurements. Centre de Biochimie Structurale (CBS), INSERM, CNRS, Montpellier, France, May 16, 2019.

Carvalho FA. Role of fibrinogen-erythrocyte and erythrocyte-erythrocyte adhesion on cardiovascular pathologies. 4th International Congress of CiiEM – Health, Well-Being and Ageing in the XXI Century, Monte da Caparica, Portugal, June 2-5, 2019.

Santos NC. Evaluation of heart failure and hypertension patients cardiovascular risk by atomic force microscopy. Asylum Research Lisbon AFM Workshop, Monte da Caparica, Portugal, July 2, 2019.

Carvalho FA. Fibrinogen-erythrocyte interactions as a biomarker for the early detection of (cardio)vascular thrombotic events. 9th AFM BioMed Conference, Münster, Germany, September 2-6, 2019.

Santos NC. Measuring forces at the nanoscale for cardiovascular risk evaluation. UC-Biotech, CNC and Biocant, Cantanhede, Portugal, October 2, 2019.

Santos NC. Nanoscale evaluation of cardiovascular risk. Workshop New Advances in Nanomedicine, Ribeirão Preto, Brazil, October 15, 2019.

Felício MR, Gonçalves S, Franco OL, Santos NC. Peptides with dual activity against multiresistant bacteria and cancer cells. XLIV Congresso da Sociedade Brasileira de Biofísica, Santos, Brazil, October 17-20, 2019.

Guedes AF, Sargento L, Braz-Nogueira J, Lousada N, Moreira C, Carvalho FA, Santos NC. Measuring forces at the nanoscale for cardiovascular risk evaluation. SMS (Smart Materials and Surfaces) 2019 / EGF (European Graphene Forum) 2019 / NanoMed (NanoMedicine) 2019 Joint International Conferences and Exhibition, Lisbon, Portugal, October 23-25, 2019.

Carvalho FA. Evaluating the risk for cardio/cerebrovascular diseases in patients by atomic force microscopy. 2nd Course of Atomic Force Microscopy applied to life sciences, I3S, Porto, Portugal, November 6-8, 2019.

Santos NC. Oportunidades de cooperação Portugal-Brasil: um trajeto por 6 estados. Simpósio sobre Intercâmbio em Medicina, Lisbon, Portugal, November 13-14, 2019.

Santos NC. Measuring forces at the nanoscale for cardiovascular risk assessment. J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, Prague, Czech Republic, November 20, 2019.

Santos NC. Nanoscale evaluation of cardiovascular risk. CEDOC, Lisbon, Portugal, November 27, 2019.

Communications in International Conferences

Felício MR, Gonçalves S, Franco OL, Santos NC. Efficient antimicrobial peptides against multiresistant bacteria presenting also anticancer activity. ARBRE-MOBIEU 3rd Plenary Meeting – Molecular biophysics: ABC of the puzzle of life, Zagreb, Croatia, March 18-20, 2019. (*Oral Presentation*).

Guedes AF, Sargento L, Braz-Nogueira J, Lousada N, Moreira C, Carvalho FA, Santos NC. AFM as a nanotool to evaluate cardiovascular risk in heart failure and hypertension patients. NanoMed Europe Conference 2019, Braga, Portugal, June 17-19, 2019. (*Oral Presentation*).

Makowski M, Felício MR, Franco OL, Gonçalves S, Melo MN, Santos NC. Exploring the mechanism of action of EcAMP1R2, a designed antimicrobial peptide. 19th FEBS (Federation of European Biochemical Societies) Young Scientists' Forum, Krakow, Poland, July 3-6, 2019. (*Oral Presentation*).

McPherson H, Duval C, Asquith NL, Baker SR, Hindle MS, Domingues MM, Ridger VC, Connel SD, Naseem KM, Philippou H, Ajjan RA, Ariëns RAS. The fibrin α C region is critical for mechanical strength, resistance to fibrinolysis and the formation of a stable whole blood clot. International Society on Thrombosis and Homeostasis (ISTH), Melbourne, Australia, July 6-10, 2019. (*Poster Presentation*).

Makowski M, Felício MR, Franco OL, Gonçalves S, Melo MN, Santos NC. Exploring the mechanism of action of EcAMP1R2, a designed antimicrobial peptide. 44th FEBS (Federation of European Biochemical Societies) Congress – From Molecules to Living Systems, Krakow, Poland, July 6-11, 2019. (*Poster Presentation*).

Silva PM, Eaton P, Santos NC. The interaction of viral fusion inhibitor lipopeptides with biomembranes is improved by PEG linker length. Joint 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Martins AS, Carvalho FA, Faustino AF, Nascimento AR, Enguita FJ, Santos NC, Martins IC. Flavivirus capsid proteins and their ability to interact with host lipid systems. Joint 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Silva I, Pereira E, Franco OL, Santos NC, Gonçalves S. Antimicrobial activity of peptide-conjugated silver nanoparticles. Joint 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Amaral CP, Leite JR, Santos NC, Eaton P. Caiman crocodilus blood-derived peptides as potential anticancer and antimicrobial therapeutic agents. Joint 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Makowski M, Felício MR, Franco OL, Gonçalves S, Melo MN, Santos NC. Studies of the non-porogenic activity of the antimicrobial peptide EcAMP1R2 against E. coli. Joint 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Felício MR, Franco OL, Santos NC, Gonçalves S. PaMAP's family: antimicrobial peptides efficient against multi-resistant bacteria show evidence of anticancer activity. 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Carvalho PM, Teixeira M, Sequeira D, Santos NC, Domingues MM. A Lipid-based nanoparticle design and activity for targeted delivery of a fibrinolytic agent. 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. (*Poster Presentation*).

Lopes CS, Guedes AF, Fonseca AC, Ferro JM, Santos NC, Carvalho FA. Fibrinogen-erythrocyte binding as a new cerebrovascular risk factor on stroke patients. 12th EBSA (European Biophysical Societies' Association) & 10th ICBP-IUPAP (International Conference on Biological Physics – International Union of Pure and Applied Physics) Biophysics Congress, Madrid, Spain, July 20-24, 2019. *(Poster Presentation)*.

Lopes CS, Pronto-Laborinho AC, Carvalho M, Santos NC, Carvalho FA. Changes on elasticity and morphology of erythrocytes from amyotrophic lateral sclerosis patients. 9th AFM BioMed Conference, Münster, Germany, September 2-6, 2019. *(Poster Presentation)*.

McPherson H, Duval C, Baker SR, Hindle MS, Cheah LT, Asquith NL, Domingues MM, Ridger VC, Connel SD, Naseem KM, Philippou H, Ajjan RA, Ariëns RAS. Role of the fibrin α C region in mechanical strength, resistance to fibrinolysis and the formation of a stable whole blood clot. European Congress on Thrombosis and Homeostasis, Glasgow, UK, October 2-4, 2019. *(Poster Presentation)*.

Martins AS, Faustino AF, Karguth N, Santos NC, Martins IC. Combining wet lab experiments with in silico data to understand Zika, West Nile and Dengue virus capsid protein. AMMA Molecular Modelling Conference 2019, Bintan Island, Indonesia, December 5-8, 2019. *(Oral Presentation)*.

Communications in National Conferences

Pinheiro J, Lopes CS, Carvalho FA, Santos NC. Avaliação hemorreológica em atletas de alta competição: Dados preliminares. XVIII Congresso de Nutrição e Alimentação – O Valor da Nutrição, Porto, Portugal, May 16-17, 2019. *(Poster Presentation)*.

Karguth N, Martins AS, Santos NC, Martins IC. Biophysical studies of dengue virus capsid protein interaction with nucleic acids. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. *(Poster Presentation)*.

Faustino F, Barbosa GM, Silva M, Castanho MARB, Da Poian AT, Cabrita EJ, Santos NC, Almeida FCL, Martins IC. How to test solvent accessibility in protein disordered regions. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. *(Poster Presentation)*.

Amaral CP, Leite JR, Baptista PV, Santos NC, Eaton P. Caiman crocodilus blood-derived peptides as potential anticancer and antimicrobial therapeutic agents. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Arrulo MF, Amaral CP, Marani MM, Cancelarich NL, Santos NC, Eaton P. Anticancer and antimicrobial properties of host-defence peptides from Patagonian amphibians. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Lopes CS, Guedes AF, Fonseca AC, Ferro JM, Santos NC, Carvalho FA. Fibrinogen-erythrocyte binding as a new cerebrovascular risk factor on stroke patients. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Makowski M, Felício MR, Franco OL, Gonçalves S, Melo MN, Santos NC. Studies of a non-porogenic, fusogenic antimicrobial peptide. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Martins AS, Carvalho FA, Faustino AF, Nascimento AR, Enguita FJ, Santos NC, Martins IC. Flavivirus capsid proteins and their ability to interact with host lipid systems. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Silva I, Pereira E, Franco, OL Santos NC, Gonçalves S. Peptide-conjugated silver nanoparticles: a promising antimicrobial agent. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Silva PM, Eaton P, Santos NC. The interaction of viral fusion inhibitor lipopeptides with biomembranes is improved by PEG linker length. Chemistry: Shaping the Future – 4th Meeting of the College of Chemistry, Lisbon, Portugal, July 16-19, 2019. (*Poster Presentation*).

Karguth N, Martins AS, Santos NC, Martins IC. Dengue virus capsid protein and its interaction with nucleic acids. NOVA Biophysica, Lisbon, Portugal, September 4-6, 2019. (*Oral Presentation*).

Organization of Conferences

Domingues MM. Chair at the XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019.

Santos NC. Co-Organizer. Beyond MEd – Educational Assessment, Lisbon, Portugal, October 23, 2019.

Internationalization

Collaborative publications and/or funded projects with groups from Dom Bosco Catholic University (Campo Grande, Brazil), Catholic University of Brasília (Brazil), University of Brasília (Brazil), University of Cagliari (Italy), CONICET (Buenos Aires, Argentina), University of Buenos Aires (Argentina), University of Santiago del Estero (Argentina), University of Quilmes (Argentina), Sorbonne Université (France), PSL University (France), National Center for Scientific Research (France), Pompeu Fabra University (Barcelona, Spain), Federal University of Goiás (Brazil), State University of Goiás (Brazil), Federal University of Grande Dourados (Brazil), Federal University of Rio de Janeiro (Brazil), Stony Brook University (USA), Massachusetts Institute of Technology (MIT, USA), and University of Pennsylvania (USA).

Advanced Teaching

Carvalho FA. PhD Program in Medicines and Pharmaceutical Innovation (i3DU). Atomic force microscopy - Biological and biomedical applications. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, January 9, 2019.

Domingues MM. PhD Program in Medicines and Pharmaceutical Innovation (i3DU). Light scattering applications in biotechnology. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, January 9, 2019.

Santos NC. Mestrado em Biologia Estrutural. Atomic force microscopy. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, March 25, 2019.

Santos NC. Mestrado em Biologia Molecular e Genética. Usando a força à nanoescala – da avaliação do risco cardiovascular ao combate a infeções virais. Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, March 26, 2019.

Carvalho FA. Mestrado em Biologia Estrutural. Role of fibrinogen-erythrocyte and erythrocyte-erythrocyte adhesion on cardiovascular pathologies. Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, March 29, 2019.

Santos NC. Programa de Doutoramento em Ciências da Saúde. Fibrinogen-erythrocyte interaction as a cardiovascular risk. Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, May 9, 2019.

Santos NC. Mestrado em Bioquímica. Biological and biomedical applications of AFM-based force spectroscopy. Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica, Portugal, May 10, 2019.

Santos NC. PhD Program in Medicines and Pharmaceutical Innovation (i3DU) Molecular interactions probed by AFM-based force spectroscopy. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 29, 2019.

Santos NC. Programa Doutoral em Molecular Biosciences (MolBioS). Atomic Force Microscopy. ITQB, Oeiras, Portugal, September 26, 2019.

Santos NC. Programas de Pós-Graduação em Física e Química (both Master and PhD Programs). Curso de Microscopia de Força Atômica. Universidade de São Paulo, Ribeirão Preto, Brazil, October 9-11, 2019.

Science and Society

With the aim of promoting the interest in science among young students, our Lab organized visits for undergraduate students via presentations and “speed-dating” style contact with the different components in the Unit’s Research work. In 2019, the visits were from students of:

- Comissão Organizadora da JORTEC de Bioquímica de 2019 | Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, February 1, 2019;
- Dia do Candidato da Faculdade de Medicina da Universidade de Lisboa, April 30, 2019;
- Escola Básica e Secundária Ibn Mucana, June 5, 2019.

Makowski M. O planeta vivo (i): o grande evento de oxigenação. @ the pop-science site bit2geek. March 2019. (Science popularization).

Carvalho PM. Startup representative at iMM Summit, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 16-17, 2019.

Carvalho PM. Interview for Canal S+ (PPS – Produtos Portugueses de Saúde – T03 E004). (<http://www.saudemais.tv/video/61571-pps-produtos-portugueses-de-saude-t03-e004>)

MSc Theses

Sofia Antunes Angélico Pinto Nabais, 06/06/2019, Studying the molecular interactions of fibrinogen with erythrocytes in carotid artery disease. Instituto Superior Técnico da Universidade de Lisboa. Supervisor: Filomena Carvalho. Co-Supervisor: Fábio Monteiro Fernandes.

Nina Karguth, 11/09/2019, Study of Dengue virus capsid protein in the context of its interaction with nucleic acids, Universidade Nova de Lisboa - Faculdade de Ciências e Tecnologia. Supervisor: Ivo C. Martins. Co-Supervisor: Nuno C. Santos.

Miriam Arrulo, 27/11/2019, Antibacterial, antiparasitic and anticancer properties of host-defence peptides from Argentinian amphibians, Universidade Nova de Lisboa – Instituto de Higiene e Medicina Tropical. Supervisor: Peter Eaton. Co-Supervisor: Celso Cunha.

Ana Sofia Antunes Silvestre, 20/12/2019, Developing a method for a rapid immunoassay Kit to detect *Salmonella spp.* bacteria, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Ivo C. Martins.

Paulo Filipe Lab

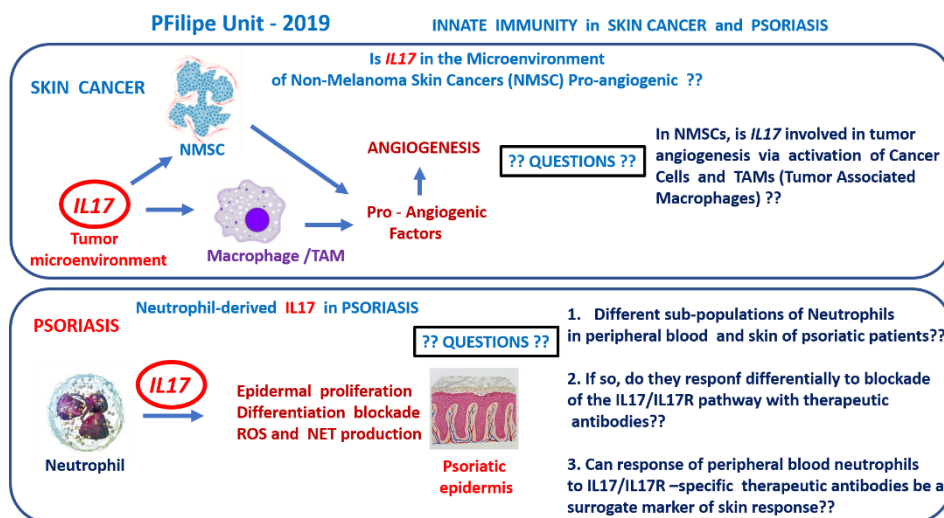
Major Interests/Objectives

1. We are committed to understand how host immune responses influence the outcome of Non-Melanoma Skin Cancers (NMSCs), namely Basal Cell carcinomas and Squamous Cell carcinomas. Also, how host responses mediated by macrophages (innate immunity) influence progression of NMSCs.
2. We are interested in understanding how another innate immunity cell type – the neutrophil – is involved in the pathogenesis of psoriasis. Also, in psoriasis we are currently focusing our efforts on validating complement Factor H as a potential biomarker of therapeutic response and disease recurrence. Of note, Factor H has been recently identified by us as a potential biomarker in a proteomics screening.
3. As subsidiary aims, we are devoting efforts to understand how the cell cycle dynamics influences skin carcinogenesis and hair follicle senescence, and to identify the photoproducts of widely used drugs that act as photo-carcinogens (e.g. thiazides) and their mechanisms of skin carcinogenesis.

Head of Laboratory

Paulo Manuel Leal Filipe, MD, PhD, Associate Professor of Dermatology

Graphical Abstract



Team

João António Augusto Ferreira	MD/PhD	Staff Scientist
João Borges da Costa	PhD	Clinical Researcher
João Nuno Maia Rodrigues Silva	MD/PhD	Clinical Researcher
Luís Miguel dos Santos Reis Soares de Almeida	PhD	Clinical Researcher
Maria Clara Gomes da Fonseca Pedro Bicho	MD/PhD	Clinical Researcher

Laboratory Keywords / Research Areas

Keywords:

Psoriasis, NMSC (Non-Melanoma Skin Cancer), Phototoxicity, Inflammation, Cell Cycle.

Research Areas:

IL17 in Psoriasis, IL17 in NMSCs, Carcinogenesis.

Major Scientific Achievements

1. We have characterized the inflammatory infiltrate of two types of high incidence non-melanoma skin cancers (NMSCs), namely Basal Cell Carcinomas (BCCs) and Squamous Cell Carcinomas. Using large cohorts of patients (and matched healthy controls), we have found evidence for a predominant Th1-mediated immune response, contradicting common belief in the area. Moreover, we have found that IL17-producing inflammatory cells comprise a significant proportion of these infiltrates.
2. We have identified complement factor H as a putative marker of psoriasis response to biologicals (therapeutic antibodies) through serum proteomics (mass spectrometry approach).
3. We have identified the photo-degradation products of Voriconazole, a triazole commonly prescribed for treatment and prophylaxis of severe fungal infections.
4. We have set-up a novel, fast methodology for cell cycle analysis that allows the absolute estimation (time units) of the duration of all cell cycle stages.

Selected Publications

Queirós C, Filipe P, Soares-Almeida L (2019). Cutaneous Metastases from Solid Neoplasm in the 21st Century: A Retrospective Study from a Portuguese Tertiary Care Centre. **Journal of the European Academy of Dermatology and Venereology**. (IF: 5.113, Citations: 0. Source: Thomson Reuters).

Morlière P, Silva AMS, Seixas RSGR, Boscá F, Mazière J-C, Ferreira J, Santus R, Filipe P (2018). Photosensitisation by voriconazole-N-oxide results from a sequence of solvent and pH-dependent photochemical and thermal reactions. **Journal of Photochemistry & Photobiology B: Biology** 187: 1-9. (IF: 3.165, Citations: 1. Source: Thomson Reuters).

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. (IF: 5.168, Citations: 8. Source: Thomson Reuters).

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. (IF: 4.081, Citations: 4. Source: Thomson Reuters).

Morlière P, Hug GL, Patterson LK, Mazière JC, Ausseil J, Dupas JL, Ducroix JP, Santus R, Filipe P (2014). Chemistry of free radicals produced by oxidation of endogenous aminoketones. A study of 5 aminolevulinic acid and aminoacetone by fast kinetics spectroscopy. **Biochimica et Biophysica Acta** 1840 (10): 3190-7. (IF: 5.12, Citations: 1. Source: Thomson Reuters).

Pinheiro T, Silva R, Fleming R, Gonçalves A, Barreiros MA, Silva JN, Morlière P, Santus R, Filipe P (2014). Distribution and quantitation of skin iron in primary haemochromatosis: correlation with total body iron stores in patients undergoing phlebotomy. **Acta Dermo-Venereológica** 94(1):14-9. (IF: 3.531, Citations: 7. Source: Thomson Reuters).

Outgoing Research Projects

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.

2016/2020: 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.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria do Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Queirós C, Filipe P, Soares-Almeida L (2019). Cutaneous Metastases from Solid Neoplasm in the 21st Century: A Retrospective Study from a Portuguese Tertiary Care Centre. **Journal of the European Academy of Dermatology and Venereology** (IF: 5.113, Citations: 0. Source: Thomson Reuters).

Pimenta R, Oliveira A (2019). Dermoscopic and confocal microscopic presentation of linear lichen planus. **Skin Research and Technology** 25(5):765-767. (IF: 1.657, Citations: 0. Source: Thomson Reuters).

Roda Â, Travassos AR, Soares-de-Almeida, Kutzner H (2019). Lupus erythematosus mimicking mycosis fungoides: CD123+ plasmacytoid dendritic cells as a useful diagnostic clue. **Journal of Cutaneous Pathology** 46(2):167-170. (IF: 1.532, Citations: 0. Source: Thomson Reuters).

Oliveira A, Alpalhão M, Filipe P, Maia-Silva J (2019). The role of Janus kinase inhibitors in the treatment of alopecia areata: A systematic review. **Dermatologic Therapy** 32(5):1-9. (IF: 1.74, Citations: 2. Source: Thomson Reuters).

Alpalhão M, Borges-Costa J, Filipe P (2019). Psoriasis in HIV infection: an update. **International Journal of STD & AIDS** 30(6): 596-604. Review. (IF: 1.501, Citations: 3. Source: Thomson Reuters).

Granulomatous Skin Diseases in a Tertiary Care Portuguese Hospital: A 10-year Retrospective Study. Queirós C, Uva L, Soares Almeida L, Filipe P (2019). **American Journal of Dermatopathology** (CME article). (IF: 1.106, Citations: 0. Source: Thomson Reuters).

Roda Â, Marcos-Pinto A, Pimenta R, Maia-Silva J (2019). Earlobe reconstruction with a superiorly based bilobed infra-auricular flap. **Journal of Cutaneous and Aesthetic Surgery** 12(3):201-202. (IF: 0.83, Citations: 0. Source: Thomson Reuters).

Aguiar-Ricardo I, Nunes-Ferreira A, Roda Â, Brás-Rosário L (2019). Omalizumab induced Takotsubo syndrome: case report. **European Heart Journal: Case Reports** 3:1-5. (IF:--, Citations: 0. Source: Thomson Reuters).

Pimenta R, Borges-Costa J (2019). Successful Treatment with Fusidic Acid in a Patient with Folliculitis Decalvans. **Acta Dermatovenerologica Croatica** 27(1):49-50. (IF: 0.855, Citations: 0. Source: Thomson Reuters).

Queirós C, Uva L, Soares Almeida L, Filipe P (2019). Multiple eruptive dermatofibromas associated with early pregnancy: case report and literature review. **Dermatology Online Journal** 25(5):12. (IF: 0.21, Citations: 1. Source: Thomson Reuters).

Mendes R, Ortins-Pina A, Fraga A, Marques T, Viveiros M, Machado D, Soares-Almeida L, Freitas J, Filipe P (2019). *Mycobacterium marinum* lymphocutaneous infection. **Dermatology Online Journal** 25(2):10-16. (IF: 0.21, Citations: 2. Source: Thomson Reuters).

Mendonça-Sanches M, Rolim I, Cabeçadas J, Rafael M (2019). An Unusual Presentation of Metastatic Breast Carcinoma. **European Journal of Case Reports in Internal Medicine** 6(4):001089. (IF: 0.101, Citations: 0. Source: Thomson Reuters).

Sanches M, Rolim I, Costa-Rosa J, Caldas G, Moura C (2019). Eruptive junctional nevi appearing during Langerhans cell histiocytosis treatment. **European Journal of Case Reports in Internal Medicine** 6(6):001088. (IF: 0.101, Citations: 0. Source: Thomson Reuters).

Other National Publications

Roda Â, Pinto A, Filipe AR, Travassos AR, Freitas JP, Filipe P (2019). Clinical and laboratory factors associated with prolonged hospital stay among patients with cellulitis/erysipelas. **Acta Médica Portuguesa** 32(6):448-452. (IF: 0.581, Citations: 0. Source: Web of Science).

Sanches MM, Pimenta R, Roda Â, Leal-Filipe P, Freitas JP (2019). Cutaneous manifestations of diabetes mellitus and prediabetic state. **Acta Médica Portuguesa** 32(6):459-465. (IF: 0.581, Citations:--. Source: Web of Science).

Queirós C, Borges da Costa J (2019). Oral Transmission of Sexually Transmissible Infections: A Narrative Review. **Acta Médica Portuguesa** 32(12):776-781. (IF: 0.581, Citations:--. Source: Web of Science).

Sanches M, Roda Â, Pimenta R, Filipe P, Freitas JP (2019). Cutaneous Manifestations of Diabetes Mellitus. **Acta Médica Portuguesa**. 32(6):459-465. (IF: 0.581, Citations:--. Source: Web of Science).

Mendes R, Sanches M, Soares-Almeida L, Correia I (2019). A case of African Tick Bite Fever. **Journal of the Portuguese Society of Dermatology and Venereology** 77(3):261-264. (IF:--., Citations:--).

Mendes R, Ortins-Pina A, Marques T, Viveiros M, Machado D Lito L, Freitas JP, Filipe P (2019). A case Report of Multibacillary Leprosy Presenting with Multiple Outbreaks of Erythema Nodosum Leprosum. **Journal of the Portuguese Society of Dermatology and Venereology**, 77(1):67-72. (IF:--., Citations:--).

Queirós C, Borges da Costa J (2019). Gonorrhoea: Antimicrobial Resistance and New Drugs. **Journal of the Portuguese Society of Dermatology and Venereology**, 77(3):233-238. (IF:--., Citations:--).

Invited Lectures and Seminars

Filipe P. Punctate palmoplantar keratoderma: Characterization of three families with aagab mutation. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019.

Soares-Almeida L. Differentiating the Undifferentiated. XL Symposium of the International Society of Dermatopathology, Lisbon, Portugal, September 19-21, 2019.

Filipe P. Reflectance confocal microscopy of skin infections and infestations. XL Symposium of the International Society of Dermatopathology, Lisbon, Portugal, September 19-21, 2019.

Communications in International Conferences

Roda Â, Travassos AR, Soares-de-Almeida L, Filipe P (2019). Cholesterol emboli mimicking necrotizing vasculites. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Roda Â, Travassos AR, Uva L, Soares-de-Almeida L, Filipe P (2019). Squamous cell dysplasia in patients treated with hydroxyurea: a series of 4 patients. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Pimenta R, Filipe P (2019). Pembrolizumab-associated sarcoidosis. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Oral Presentation)*.

Queirós C, Uva L, Soares-Almeida L, Filipe (2019). Granulomatous skin diseases in a tertiary care Portuguese hospital: a 10-year retrospective study. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Mendes R, Sanches M, Soares-Almeida L, Correia I (2019). Africa Souvenirs: A case of African thick bite fever. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Mendes R, Correia I (2019). Non-Ablative, Fractional Erbium Glass Laser Therapy for the Treatment of Trauma Scars. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Mendes R, Correia I (2019). Combined treatment of keloids with Intense Pulsed Light, Cryotherapy and CO2 Laser. 24th World Congress of Dermatology, Milan, Italy, June 10-15, 2019. *(Poster Presentation)*.

Queirós C, Soares-Almeida L (2019). Cutaneous metastasis from solid neoplasms: a retrospective study in a tertiary care Portuguese hospital. XL Symposium of the International Society of Dermatopathology, Lisbon, Portugal, September 19-21, 2019. *(Oral Presentation)*.

Queirós C, López-Presa D, Soares-Almeida L (2019). Cutaneous leiomyosarcoma: a single center 20-year retrospective study. XL Symposium of the International Society of Dermatopathology, Lisbon, Portugal, September 19-21, 2019. (*Oral Presentation*).

Roda Â, Pimenta R, Soares-de-Almeida L, Ferreira J, Filipe P, Borges-Costa J (2019). Generalized cutaneous candidiasis in a renal transplant recipient with Crohn's disease. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Roda Â, Marcos-Pinto A, Soares-de-Almeida L, Filipe P, Maia-Silva J (2019). Lipomembranous panniculitis associated with subcutaneous injection of progesterone. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Pimenta R, Soares-Almeida L, Filipe P, Oliveira AL (2019). Epidermolysis bullosa simplex with mottled pigmentation. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Alpalhão M, Antunes J, Soares-Almeida L, Filipe P (2019). Koebner phenomenon induced by a computer mouse: A rare etiology for a common phenomenon. 28th EADV Congress, Madrid, Spain, October 9-13, 2019.

Alpalhão M, Antunes J, Soares-Almeida L, Filipe P (2019). Erosive pustular dermatosis of the scalp: An underdiagnosed condition. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Alpalhão M, Morlière P, Antunes J, Nourry V, Amado FM, Domingues PM, Guerreiro AC, Ferreira J, Maia-Silva J, Mazière JC, Santus RC, Filipe P (2019). Complement factor H as a potential biomarker for disease severity and clinical response to treatment in psoriasis. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Oral Presentation*).

Mendes R, Ortins-Pina A, Soares-Almeida L (2019). Granuloma faciale during pregnancy. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Correia I (2019). Multinucleated Cell Angiohistiocytoma. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Poster Presentation*).

Mendes R, Correia I (2019). Combined treatment of fractional nonablative Erbium-Glass laser and Picosend Laser for acne scar. 28th EADV Congress, Madrid, Spain, October 9-13, 2019. (*Oral Presentation*).

Communications in National Conferences

Queirós C, Borges da Costa J. Proctite a *Mycoplasma genitalium*: caso clínico. VII Jornadas de Atualização em IST, Porto, Portugal, April 13, 2019. *(Oral Presentation)*.

Pimenta R, Fonseca I, Camacho M, Gomes M, Oliveira A, Soares Almeida L, Filipe P. Doença de Erdheim-Chester: Relato de um caso. Reunião da Primavera da SPDV, Curia, Portugal, May 24 - 25, 2019. *(Oral Presentation)*.

Sanches M. Tilosina – um alérgeno de contacto airborne na indústria veterinária. Reunião da Primavera da SPDV, Curia, Portugal, May 24 -25, 2019. *(Oral Presentation)*.

Sanches M. Linfoma/Leucemia de células T do adulto. Reunião da Primavera da SPDV, Curia, Portugal, May 24 -25, 2019. *(Oral Presentation)*.

Mendes R, Soares-Almeida, Correia I. Líquen escleroso vulvar e morfeia. Mera coincidência? Reunião da Primavera da SPDV, Curia, Portugal, May 24 -25, 2019. *(Oral Presentation)*.

Mendes R, Marques T, Soares-Almeida L, Correia I. Éctima gangrenoso. Reunião da Primavera da SPDV, Curia, Portugal, May 24 -25, 2019. *(Poster Presentation)*.

Queirós C, Pimenta R, Ortins-Pina A, Soares-Almeida L, Filipe. Penfigóide gestacional: um diagnóstico simples, uma abordagem desafiante. 2ª Academia de Dermatologia Almirall, Figueira da Foz, Portugal, October 19-20, 2019. *(Oral Presentation)*.

Queirós C, Cerejeira A. Dermatoses bolhosas: comentário. 2ª Academia de Dermatologia Almirall, Figueira da Foz, Portugal, October 19-20, 2019. *(Oral Presentation)*.

Mendes R, Soares-Almeida L, Correia I, Freitas JP, Filipe P. Caso Clínico: Dermatomiosite. 2ª Academia de Dermatologia Almirall, Figueira da Foz, Portugal, October 19-20, 2019. *(Oral Presentation)*.

Mendes R. Pênfigo Vulgar em idade pediátrica. 2ª Academia de Dermatologia Almirall, Figueira da Foz, Portugal, October 19-20, 2019. *(Oral Presentation)*.

Pimenta R, Martins A, Esteves G, Raposo J, Kempf W, Soares Almeida L, Filipe P. Linfoma epidermotrópico de células T associado a EBV. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Pimenta R, Sousa V, Garrido P, Laureano A. Técnicas não invasivas no diagnóstico de larva migrans – Descrição de 3 casos. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Pimenta R, Arzberger E, Soares Almeida L, Oliveira AL. (Re)definição dermatoscópica da doença de Bowen Pigmentada. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Alpalhão M. Caso Clínico: Herpes Simplex tipo 1 a mimetizar pioderma gangrenoso clássico. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Queirós C. Agentes anti-TNF no Síndrome de Lyell: a propósito de um caso clínico. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Queirós C, Borges Da Costa J, Lito L, Filpe P, Melo-Cristino J. Infecções por N.gonorrhoeae num Hospital Terciário: estudo retrospectivo de 10 anos da evolução do número de casos e das resistências aos antimicrobianos. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Mendes R, Garrido P, Kutzner H, Soares-Almeida L, Correia I. Eritema Elevatum Diutinum em áreas de cicatriz pós-queimadura. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Oral Presentation)*.

Alpalhão M, Antunes J, Soares-Almeida L, Filipe P. Reacção liquenoide tardia a pigmento exógeno de tatuagem. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Poster Presentation)*.

Queirós C, Cardoso JC, Laureano-Oliveira A. Acantoma de células claras: a importância do reconhecimento de um padrão dermatoscópico. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Poster Presentation)*.

Soares-Almeida L, Filipe P. Fluconazol oral no tratamento da leishmaniose cutânea: caso clínico. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Poster Presentation)*.

Queirós C, Soares-Almeida L, Filipe P. Miíase cutânea em idade pediátrica: caso clínico. XIX Congresso Nacional SPDV, Porto, Portugal, December 6-8, 2019. *(Poster Presentation)*.

Internationalization

The group maintains an active collaboration in the area of photobiology with Professors René Santus, Patrice Morlière and J-C Mazière, INSERM, Amiens, France, which has resulted in several collaborative research articles in reputed Journals in the area. Also, there is an ongoing collaboration with Professor Heinz Kutzner, Institute of Dermatopathology, Friedrichshafen, Germany in the area of skin cancer.

Prizes, Honors and Awards

Pimenta R. SPDV Prize for best presentation. Portuguese Society of Dermatology and Venereology, Portugal, Porto, December 8, 2019.

Advanced Teaching

Ferreira J. Masters in Oncobiology – Gene Expression Module, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October-December, 2019.

Science and Society

Cutaneous Cancer Screening – in collaboration with “Santa Casa da Misericórdia”, Lisbon, Portugal.

MSc Theses

Mariana Rodrigues Rebelo, 30/9/2019, Líquen plano e esquema terapêutico: estudo epidemiológico no Centro Hospitalar Lisboa Norte (HSM) referente ao período 2008-2017, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paulo Leal Filipe.

José Pereira, 27/9/2019, Análise estatística e epidemiológica de variáveis clinico-patológicas de uma série de melanomas do laboratório de Dermatopatologia do CHULN, Faculdade de Medicina da Universidade de Lisboa. Supervisor: L Soares de Almeida.

Adriana Caixinha. 4/10/2019, The influence of ultraviolet radiation in the prevalence of psoriasis, Faculdade de Medicina da Universidade de Lisboa. Supervisor: J Borges da Costa.

Ana Beatriz Oliveira. 8/11/2019, What’s new? – a systematic review of the literature, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Miguel Alpalhão.

Pedro Sousa-Victor Lab

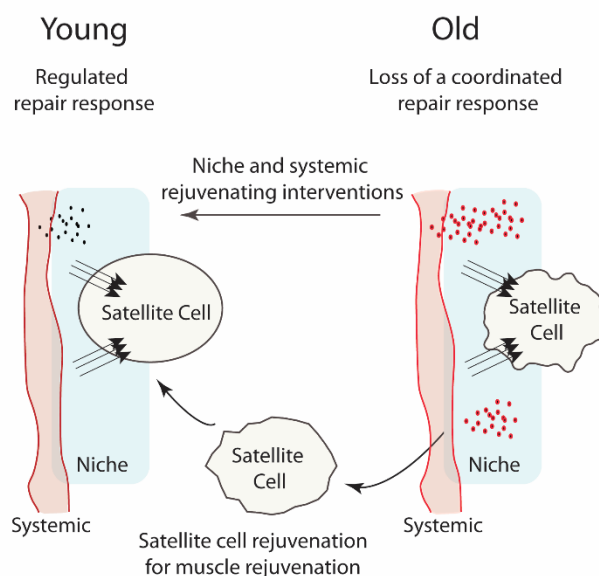
Major Interests/Objectives

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 ageing 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.

Head of Laboratory

Pedro Miguel Sousa Corado Victor, PhD (Started April)

Graphical Abstract



Team

Inês Curado Batista Antunes	Master Degree	Lab Manager (Started June)
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Laboratory Keywords / Research Areas

Stem Cell, Regeneration, Muscle, Ageing, Sarcopenia.

Major Scientific Achievements

This year we moved our main research lines from the Buck Institute for Research on Aging to the iMM, initiating new projects that address our central scientific questions. We have also contributed with two review articles where we provide our vision on the state of the art and scientific challenges in the field of stem cell aging.

Selected Publications

Munoz-Canoves P**, Neves J, Sousa-Victor P** (2019). Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells. **FEBS Journal** 287(3):406416. Review (*IF: 4.739, Citations: 0. Source: Google Scholar*).

Neves J**, Sousa-Victor P** (2019). Regulation of inflammation as an anti-aging intervention. **FEBS Journal** 287(2020):43–52. Perspective. (*IF: 4.739, Citations: 1. Source: Google Scholar*).

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. (*IF: --, Citations: 4. Source: Google Scholar*).

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. (*IF: 7.815, Citations: 20. Source: Google Scholar*).

Neves J*, Sousa-Victor P*, Jasper H (2017). Rejuvenating Strategies for Stem Cell-Based Therapies in Aging. **Cell Stem Cell** 20(2):161-175. Review. (*IF: 21.464, Citations: 54. Source: Google Scholar*).

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. (IF: 43.070, Citations: 471. Source: Google Scholar).

*equal contribution

**Corresponding author

Ongoing Research Projects

2019/2022: New mechanisms driving stem cell aging. Coordinator: Pedro Sousa-Víctor. Funding Agency: "la Caixa" Foundation. Reference: la Caixa - Junior Leader Fellowships Programme. Amount: € 297 900,00. Total Amount: € 297 900,00.

Publications in Peer Reviewed Journals

Munoz-Canoves P**, Neves J, Sousa-Victor P** (2019). Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells. **FEBS Journal** 287(3):406-416. Review. (IF: 4.739, Citations: 0. Source: Google Scholar).

Neves J**, Sousa-Victor P** (2019). Regulation of inflammation as an anti-aging intervention. **FEBS Journal** 287(2020):43–52. Perspective. (IF: 4.739, Citations: 1. Source: Google Scholar).

Korzelius J, Azami S, Ronnen-Oron T, Koch P, Baldauf M, Meier E, Rodriguez-Fernandez IA, Groth M, Sousa-Victor P, Jasper H (2019). The WT1-like transcription factor Klumpfuss maintains lineage commitment of enterocyte progenitors in the Drosophila intestine. **Nature Communications** 10(1):1-13. (IF: 11.880, Citations: 1. Source: Google Scholar).

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. (IF: --, Citations: 4. Source: Google Scholar).

*equal contribution

**Corresponding author

Communications in International Conferences

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 immune homeostasis in ageing and protects against liver damage. Nature Conference 2019 on Ageing, Health and Rejuvenation, Rotterdam, Netherlands, June 23-26, 2019. (*Poster presentation with pitch talk*).

Prizes, Honors and Awards

Sousa-Victor P. Poster Prize from Nature Review Molecular Cell Biology, Nature Conference 2019 on Ageing, Health and Rejuvenation, Rotterdam, Netherlands, June 23-26, 2019.

Pedro Simas Lab

Major Interests / Objectives

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.

Head of Laboratory

João Pedro Monteiro e Louro Machado de Simas, PhD

Team

Andreia Filipa Bonecas Mósca	PhD	Postdoctoral Researcher
Anita Marisa Pinto Sousa	University Degree	MSc Student (Left September)
Beatriz Gonçalves Arede	High School Diploma	BSc Student (Started September)
Catarina Neves Costa	University Degree	MSc Student
Marta Pires de Miranda	PhD	Senior Postdoctoral Researcher
Nelly Marine Carreira da Silva	Master Degree	MSc Student (Left September)
Tânia Alexandra da Cruz Rodrigues	University Degree	Trainee (Left September)

Laboratory Keywords / Research Areas

Herpes Virus, B-lymphocytes, Chronic Infection, Kaposi Sarcoma Herpesvirus (KSHV), B Cell and Lymphomas, MuHV-4, Animal Model of Infection.

Major Scientific Achievements

We found that despite 60 million years of evolutionary divergence, kLANA and mLANA act reciprocally on TR DNA and kLANA can rescue mLANA deficient virus to enable chimeric virus to establish latent infection in mice. This novel model system is now being used to investigate molecular functions of kLANA *in vivo* upon infection of laboratory mice.

This work is of broad interest as it successfully tests the concept of functional substitution of a human pathogen gene into a model pathogen to allow *in vivo* investigation. Previously, such chimeric viruses were felt to be non-viable due to evolutionary divergence, and have not been used. Importantly, these findings have the potential to be applied to other human pathogens, which lack small animal models.

Selected Publications

Habison AC, de Miranda MP, Beauchemin C, Tan M, Cerqueira SA, Correia B, Ponnusamy R, Usherwood EJ, McVey CE, Simas JP, Kaye KM (2017). Cross-species conservation of episome maintenance provides a basis for *in vivo* investigation of Kaposi's sarcoma herpesvirus LANA. **PLoS Pathogens** 13(9):e1006555. (IF: 6.608, Citations: 3. Source: Web of Science).

Decalf J, Godinho-Silva C, Fontinha D, Marques S, Simas JP (2014). Establishment of Murine Gammaherpesvirus Latency in B Cells Is Not a Stochastic Event. **PLoS Pathogens** 10(7):e1004269. (IF: 6.608, Citations: 5. Source: Web of Science).

Godinho-Silva C, Marques S, Fontinha D, Stevenson PG, Simas JP (2014). Defining Immune Engagement Thresholds for *in vivo* Control of virus-driven Lymphoproliferation. **PLoS Pathogens** 10(6):e1004220. (IF: 6.608, Citations: 1. Source: Web of Science).

Correia B, Cerqueira SA, Beauchemin C, Pires de Miranda M, Li S, Ponnusamy R, Rodrigues L, Schneider TR, Carrondo MA, Kaye KM, Simas JP, McVey CE (2013). Crystal structure of the gamma-2 herpesvirus LANA DNA binding domain identifies charged surface residues, which impact viral latency. **PLoS Pathogens** 9(10):e1003673. (IF: 6.608, Citations: 18. Source: Web of Science).

Rodrigues L, Popov N, Kaye KM, Simas JP (2013). Stabilization of Myc through Heterotypic Poly-Ubiquitination by mLANA is Critical for Herpesvirus Lymphoproliferation. **PLoS Pathogens** 9(8):e1003554. (IF: 6.608, Citations: 6. Source: Web of Science).

Ongoing Research Projects

2018/2021: Investigação de um gene tumoral viral num modelo de infeção 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.

2017/2020: CONGENTO - Consortium for Genetically Tractable Organisms. Coordinator: Pedro Simas. Funding Agency: Fundação para a Ciência e a Tecnologia/Portugal2020. Reference: 027947/2017. Amount: € 560 086,20. Total Amount: € 3 408 283,80.

2016/2019: Chimera virus model to investigate the pathogenesis of Kaposi's sarcoma herpesvirus in laboratory mice. Coordinator: Pedro Simas. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/IMI-MIC/0980/2014. Amount: € 199 998,00. Total Amount: € 199 998,00.

Publications in Peer Review Journals

Lawler C, Simas JP, Stevenson PG (2019). Vaccine protection against murid herpesvirus-4 is maintained when the priming virus lacks known latency genes. **Immunology and Cell Biology** 98(1)67-68. (IF: 3.947. Citations: 0. Source: Web of Science). 2019;10.1111/imcb.12299.

MSc Theses

Catarina Neves Costa, Tiago Pestana, 20/11/2019, Study of SUMO-2-interacting motifs in Kaposi's sarcoma-associated herpesvirus, Universidade Nova de Lisboa - Faculdade de Ciências e Tecnologia. Supervisor: Pedro Simas.

Anita Marisa Pinto Sousa, 22/11/2019, Investigation of LANA: a Human Virus Tumor Gene, Faculdade de Farmácia da Universidade de Lisboa. Supervisor: Pedro Simas.

Tânia Alexandre da Cruz Rodrigues, 29/11/2019, Evaluation of the therapeutic potencial of several compounds in Human Herpesvirus 8 using a Chimera Virus Mouse Infection Model, Faculdade de Farmácia da Universidade de Lisboa. Supervisor: Pedro Simas.

Sérgio de Almeida Lab

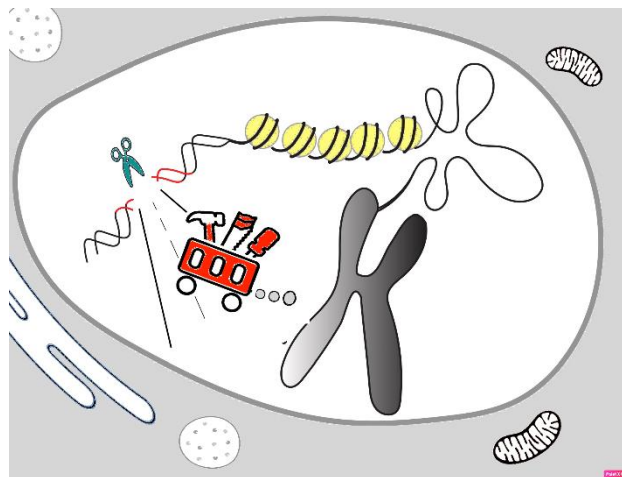
Major Interests / Objectives

Our research focuses on the mechanisms that regulate chromatin dynamics during transcription and DNA damage repair and how they coordinate to safeguard the genome integrity. Our general aims are twofold: first, we aim at investigating the epigenetic regulation of transcription; in addition, we study the molecular mechanisms that sense, signal and repair DNA damage. A major goal of our research is to understand how changes in transcription and DNA repair are linked to cancer development.

Head of Laboratory

Sérgio Fernandes de Almeida, PhD

Graphical Abstract



Team

Alda Filipa Queirós Oliveira e Silva	Master Degree	Lab Technician (Left December)
Ana Isabel Afonso Duarte	Master Degree	Trainee
Ana Rita Fialho Grosso	PhD	Visiting Researcher
Anne Valerie Gendrel	PhD	Visiting Researcher (Started October)
Cristiana Marisa de Sousa Morgado	Master Degree	Lab Technician
Diana Reckendorfer	Highschool Diploma	BSc Student (Started January. Left May)
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	Lab Technician
Maria João Rodrigues da Silva	PhD	Postdoctoral Researcher (Started October)

Naike Salvador Moreno	PhD	Postdoctoral Researcher (Started May)
Robert Manfred Martin	PhD	Senior Postdoctoral Researcher
Srchaiyanya Sridhara	PhD	Postdoctoral Researcher (Left June)

Laboratory Keywords / Research Areas

DNA Repair, Chromatin, Gene Expression, Cancer, Molecular Biology, Epigenetics, Oncobiology.

Major Scientific Achievements

During 2019, our lab disclosed novel aspects of the crosstalk between transcription and DNA damage. We co-authored a study describing a novel pathway involving RNA polymerase II in the activation of ATR, a key factor well known for its participation in DNA damage and replication stress signaling (Landsverk *et al.*, 2019). In addition, we spearheaded the development of a set of cutting-edge reporter genes that allow the direct visualization of transcription with single-molecule resolution upon the controlled induction of a unique DNA lesion in live cells (Vitor *et al.*, 2019).

During this year, we also investigated the determinants of intratumor genetic heterogeneity (ITH), the main obstacle to effective cancer treatment and a major mechanism of drug resistance. Our systematic pan-cancer analysis of thousands of genomic datasets revealed novel epigenetic drivers of ITH, which may be useful as predictive biomarkers or therapeutic targets to improve cancer treatment (Matos *et al.*, 2019).

Selected Publications

Vitor 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** 5(1):eaau1249. (IF: 12.8, Citations: 3 Source: Web of Science/JCR).

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** 18(2):334-343. (IF: 8.282, Citations: 31. Source: Web of Science/JCR).

Grosso AR, Leite AP, Carvalho S, Matos MR, Martins FB, Vítor AC, Desterro JM, Carmo-Fonseca M, de Almeida AF (2015). Pervasive transcription read-through promotes aberrant expression of oncogenes and RNA chimeras in renal carcinoma. **eLife** 4:09214. (IF: 7.725, Citations: 42. Source: *Web of Science/JCR*).

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** 3:02482. (IF: 7.725, Citations: 101. Source: *Web of Science/JCR*).

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** 41(5):2881-2893. (IF: 10.162, Citations: 73. Source: *Web of Science/JCR*).

Ongoing Research Projects

2019/2020: Targeted DNA Damage as a novel tumor suppressor tool. Coordinator: Sérgio de Almeida. Funding Agency: Fundo iMM-Laço. Reference: Fundo iMM-Laço. Amount: € 30 000,00. Total Amount: € 30 000,00.

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.

2018/2021: Papel fisiológico de inativação 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.

2018/2019: The inhibition of such R-loop suppressor enzymes leads to the selective killing of estrogen-dependent breast cancer cells. Coordinator: Sérgio de Almeida. Funding Agency: Fundo iMM-Laço. Reference: Fundo iMM-Laço. Amount: € 29 325,00. Total Amount: € 29 325,00.

2016/2019: Novel tumorigenic mechanisms of aberrant epigenetic regulation in clear cell renal cell carcinoma. Coordinator: Sérgio de Almeida. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-ONC/0016/2014. Amount: € 199 944,00. Total Amount: € 199 944,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Matos MR, Posa I, Carvalho FS, Morais VA, Grosso AR, de Almeida SF* (2019). A systematic pan-cancer analysis of genetic heterogeneity reveals associations with epigenetic modifiers. **Cancers** 11(3):391. (IF: 6.2, Citations: 2 Source: Web of Science/JCR)

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** 5(1):eaau1249. (IF: 12.8, Citations: 3 Source: Web of Science/JCR).

Landsverk HB, Sandquist LE, Sridhara SC, Rødland G, Sabino JC, de Almeida SF, Grallert B, Trinkle-Mulcahy L, Syljuåsen RG. (2019). Regulation of ATR activity via the RNA polymerase II associated factors CDC73 and PNUTS-PP1. **Nucleic Acids Research** 47(4):1797-1813. (IF: 11.147, Citations: 1. Source: Web of Science/JCR).

Da Rocha ST, Gendrel A-V (2019). The influence of DNA methylation on monoallelic expression. **Essays in Biochemistry** 63(6):663-676. Review. (IF: 4.8 Source: Web of Science/JCR).

Invited Lectures and Seminars

de Almeida SF. Reciprocal regulatory links between transcription and DNA repair. Research Seminar, IFOM-IEO, Milan, Italy, April 1, 2019.

de Almeida SF. Imaging DNA Break-Induced Transcription in Live Cells. Spatial Genome Organization Conference - The Nucleome in Basic Biology and Disease, Nassau, Bahamas, February 25-28, 2019.

de Almeida SF. Single-molecule imaging of transcription at damaged chromatin. RNA meeting, ptRNA, Porto, Portugal, January 24-25, 2019.

de Almeida SF. Live cell imaging of DNA Break-Induced Transcription. Research Seminar, Jinan University, Guangzhou, China, January 11, 2019.

Communications in International Conferences

Martin RM. Single-molecule Imaging of Transcription at Damaged Chromatin. 3rd International Symposium on Frontiers in Molecular Science – RNA regulatory networks, Lisbon, Portugal, June 26-28, 2019. (*Oral Presentation*).

de Almeida SF. Imaging DNA Break-Induced Transcription in Live Cells. Spatial Genome Organization Conference - The Nucleome in Basic Biology and Disease, Nassau, Bahamas, February 25-28, 2019. (*Oral Presentation*).

Communications in National Conferences

Faleiro I, Afonso AI, Lucas B, Martin RM, Gomes ER, de Almeida SF. Unveiling the DNA damage response in multinucleated cells. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Sabino JC, Almeida MR, Sridhara SC, Abreu PL, Domingues MM, Santos NC, Grosso AR, de Almeida SF. Unraveling the impact of epigenetics on R-loop-mediated genomic instability. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Martin RM, Vítor AC, Sridhara SC, Sabino JC, Afonso AI, Grosso AR, de Almeida SF. Single-molecule Imaging of Transcription at Damaged Chromatin. Annual Postdoc Meeting 2019, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 25, 2019. (*Oral Presentation*).

Organization of Conferences

Sabino JC. Co-Organizer. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019.

Internationalization

During this year we published three original research papers and one review manuscript in international journals and presented our work in five international conferences and seminars. We maintained collaborative projects with the Oslo University and initiated a new collaboration with the Weizmann Institute.

Our lab is one of the members of the international RiboMed Twinning project. This 2019 EU-funded project includes partners from the University of Oxford (UK), the Weizmann Institute of Science (Israel) and The Max Delbrück Center for Molecular Medicine (MDC, Germany).

Prizes, Honors and Awards

Silva MJ. Les Grandes Avancées en Biologie, Académie des Sciences – Institut de France, France. 2019.

Sabino JC. 3rd Year Second Best Poster Presentation, Instituto de Medicina Molecular João Lobo Antunes, Portugal. May 17, 2019.

MSc Theses

Alda Silva, 13/11/2019, Single-molecule imaging of transcription Dynamics, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Robert M. Martin.

Madalena Almeida, 19/09/2019, Deciphering the role of DNA secondary structures in HIF1-mediated transcription, University of Copenhagen, Denmark. Supervisor: Sérgio F. de Almeida.

Diana Reckendorfer, 06/2019, DNA damage as a tumor suppressor tool, FH Campus Wien, Austria. Supervisor: Sérgio F. de Almeida.

Sérgio Dias Lab

Major Interests/Objectives

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.

Head of Laboratory

Sérgio Jerónimo Rodrigues Dias, PhD, Associate Professor

Team

Ana Luísa Ferro Espadanal Torres Magalhães	PhD	Senior Postdoctoral Researcher
Ana Patrícia Quintino Lopes	University Degree	MSc Student (Left September)
Catarina Isabel de Melo Pinheiro	High School Diploma	MSc Student (Left September)
Catarina Marçal da Costa	Master Degree	Trainee (Started February. Left August)
Diogo Da Silva Coutinho	University Degree	Trainee (Started November)
Emanuel Estevez de Oliveira	High School Diploma	MSc Student (Started January)
Mariana de Jesus Pimpão Luís	University Degree	BSc Student (Started February. Left July)
Sandrina Nóbrega Pereira	PhD	Senior Postdoctoral Researcher (Left June)
Sofia Dalla Volta	University Degree	MSc Student (Started May)
Teresa Laura Mendes Serafim	PhD	Senior Postdoctoral Researcher

Laboratory Keywords / Research Areas

Angiogenesis, Tumour Metastasis, Metabolism.

Major Scientific Achievements

We established a novel line of research at iMM, focused on cancer metabolism and its importance for cancer onset and progression in 2017. In 2019, we focused on our projects dealing with breast cancer metabolism and the importance of vascular mimicry. As a result, we presented our findings in several 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 (Bruno Costa Silva, Champalimaud Foundation) collaborations, we established fruitful collaborations with several Labs at iMM, including Vanessa Morais, Edgar Gomes, Luís Costa, and Bruno Silva-Santos.

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 γ 9V δ 2 T Cells. **Cancer Immunology Research** 6(4):448-457 (IF: 9.188, Citations: 3. Sources: Web of Science and Scopus).

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 (IF: 9.13, Citations: 9. Source: Web of Science).

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. (IF: 2.7, Citations 75. Source: Web of Science).

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. (IF: 9.13, Citations: 25. Source: Web of Science).

Gomes AL, Carvalho T, Torre C, Serpa J, Dias S (2010). Hypercholesterolemia promotes bone marrow cell mobilization by perturbing the SDF1:CXCR4 axis. **Blood** 115(19):3886-94. (IF: 15.13, Citations: 105. Source: Web of Science).

Ongoing Research Projects

2018/2021: Como o colesterol promove a metastização em cancro de mama. Coordinator: Sérgio Dias. Funding Agency: Fundação para a Ciência e Tecnologia. Reference: PTDC/MED-ONC/30436/2017. Amount: € 190 615,32. Total Amount: € 190 615,32.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Review Journals

Gomes CP, Nóbrega-Pereira S, Domingues-Silva B, Rebelo K, Alves-Vale C, Marinho SP, Carvalho T, Dias S, Bernardes de Jesus B (2019). An antisense transcript mediates MALAT1 response in human breast cancer. **BMC Cancer** 19(1):771 (IF: 2.933, Citations: 0. Source: Web of Science).

Other Publications

Magalhães A, Dias S (2019). Angiogenesis – Vessels Recruitment by Tumor Cells. *Molecular and Cell Biology of Cancer - when cells break the rules and hijack their own planet. Book Chapter. Springer.*

Invited Lectures and Seminars

Dias S. Metabolic Shifts in Cancer. First Joint Symposium of Jinan University, Guangzhou, China and Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 11-13, 2019.

Dias S. Metabolic alterations underlying phenotypic modifications in cancer cells. Center for Neuroscience and Cell Biology, Universidade de Coimbra, Coimbra, Portugal, March 12, 2019.

Communications in International Conferences

Serafim T, Dias S. Metabolic reprogramming of pulmonary metastasis. 2nd FEBS Advanced Course in Oncometabolism, Luso, Portugal, September 1-6, 2019. (*Poster Presentation*).

Magalhães A, Cesário V, Pinheiro C, Domingues G, Dias S. LDL-cholesterol favors vascular invasion by breast cancer cells. EACR-MRS Conference on Seed and Soil: Mechanisms of Metastasis, Berlin, Germany, October 7-9, 2019. (*Poster Presentation*).

Dias S. Mitochondrial dynamics underlie phenotypic shifts induced by hypercholesterolemia. Cell Symposia, Hallmarks of Cancer, Seattle, USA, November 17-19, 2019. (*Poster Presentation*).

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:

- Programa de Doutoramento em Ciências Químicas, Biológicas e Engenharia (ITQB, Nova Universidade de Lisboa).
- Programa Doutoral em Biologia Experimental e Biomedicina (Universidade de Coimbra).
- Programa de Doutoramento em Medicina (FCM, Nova Universidade de Lisboa).

And of the following Master Programs:

- Mestrado em Biologia Humana e Ambiente (Faculdade de Ciências da Universidade de Lisboa).

Science and Society

We participated in several initiatives organized by the Communication Office, throughout 2019.

Highlight: 5th December 2019. Lisbon. Annual Conference of Portuguese Insurance Companies/associations.

MSc Theses

Catarina Pinheiro, 27/06/2019, Systemic Factors and tumor progression, Universidade de Trás-os-Montes e Alto Douro. Supervisor: Sérgio Dias.

Ana Patrícia Lopes, 20/03/2019, Mitochondrial Adaptations in Breast Cancer during cell migration: Influence of lipid environments and response to Taxanes, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sérgio Dias.

PhD Theses

Neidy Varela Rodrigues, 27/11/2019, Impact of metabolic resources and infiltrating immune cells on protective responses against solid tumors, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sérgio Dias. Co-Supervisor: Bruno Silva-Santos.

Vanessa Morais Lab

Major Interests/Objectives

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 demands of energy generation during synaptic activity. Our research interests aim at deciphering the intrinsic properties of synaptic mitochondria and to further scrutinize their relevance for the diseased brain, and to unveil how the disruption of these acquired mechanisms contributes to neurodegeneration. Additionally, we intend to unravel the impact of mitochondria DNA mutations upon overall brain function. Ultimately, we seek to clarify the reciprocal crosstalk between the host cell – the neuron – and the powerhouse organelle – the mitochondria.

Head of Laboratory

Vanessa Alexandra dos Santos Morais Epifânio, PhD, Group Leader

Graphical Abstract

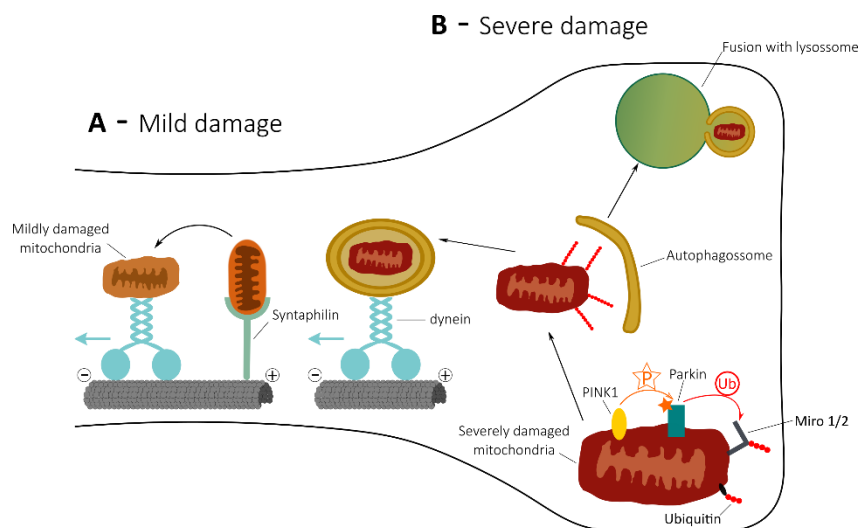


Figure 2: VMoraisLab_Mitochondria Quality Control at Synapse

Team

Ana Beatriz Marta Ferreira Madeira Ramos	University Degree	MSc Student (Started September)
Andreia Sofia Faria Pereira	Master Degree	PhD Student
Bernardo Cetra Antunes	Master Degree	Lab Technician (Started March)
Carlos Eduardo Cardanho dos Ramos	Master Degree	PhD Student
Elvira Pequeno Leites	Master Degree	PhD Student
Filipa Alexandra Barroso Gonçalves	Master Degree	PhD Student
Filipa Sofia Libório Carvalho	PhD	Postdoctoral Researcher (Left December)
Filipe Carlos Pereira dos Reis Cortes Figueiredo	Master Degree	PhD Student
Jonathan Verduyck	High School Diploma	BSc Student (Started February, Left May)
Rita Abrunhosa Soares	Master Degree	PhD Student
Rúben Filipe Alves Simões	High School Diploma	MSc Student (Started December)

Laboratory Keywords / Research Areas

Keywords:

Mitochondria, Mitochondrial DNA, Neurodegeneration, Synapse, Parkinson's Disease.

Research Areas:

Cell Biology, Neurobiology, Metabolism.

Major Scientific Achievements

A proper mitochondrial function is of utmost importance in neurons as their energy supply relies mostly on oxidative phosphorylation. 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 mitochondrial quality control processes and crosstalk between different neural types. Additionally, we have observed that modulating mitochondrial dynamics can be a powerful approach to regulate neural stem cell fate. And, in order to understand the impact of mitochondrial DNA heterogeneity on overall brain function, we have developed an algorithm for variant level determination.

Our research findings are driving exciting hypotheses and yielding promising molecular targets that will enable us to address key unanswered questions, stratify the importance of mitochondrial function for synapse biology, and overall brain homeostasis.

Selected Publications

Vos M, Geens A, Böhm C, Deaulmerie L, Swerts J, Rossi M, Craessaerts K, Leites E, Seibler P, Rakovic A, Lohnau T, De Strooper B, Fendt SM, Morais VA, Klein C, Verstreken P (2017). Cardiolipin promotes electron transport between ubiquinone and Complex-I to rescue PINK1 deficiency. **Journal of Cell Biology** 216:695-708. (IF: 9.8, Citations: 20. Source: Web of Science).

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. (IF: 4.5, Citations: 51. Source: Web of Science).

Morais VA*, Haddad D, Craessaerts K, De Bock P, Swerts J, Vilain S, Aerts L, Overbergh L, Grünwald 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. (IF: 34, Citations: 204. Source: Web of Science). *shared corresponding authors.

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. (IF: 14, Citations: 62. Source: Web of Science). *shared corresponding authors.

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. (IF: 9, Citations: 305. Source: Web of Science).

Ongoing Research Projects

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.

2018/2019: Unravelling longitudinal mitochondrial DNA mutations in Multiple Sclerosis: association with disease activity and progression. Coordinator: Vanessa Morais. Funding Agency: National Multiple Sclerosis Society. Reference: NATIONAL MULTIPLE SCLEROSIS SOCIETY-PP-1712-29466. Amount: € 32 193,76. Total Amount: € 32 193,76.

2016/2021: Synaptic Mitochondria: 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.

2016/2020: Homeostasis and Maintenance of Synaptic Mitochondria. Coordinator: Vanessa Morais. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG VMorais. Amount: € 150 000,00. Total Amount: € 150 000,00.

2015/2020: Maintaining Mitochondria Healthy: The Molecular Checkpoints involved in Mitochondrial Quality Control in Neurons. Coordinator: Vanessa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01693/2014/CP1236/CT0003. Amount: € 50 000,00. Total Amount: € 50 000,00.

Other Projects

2016/2019: PRECISE: Accelerating progress toward the new era of precision medicine. Coordinator: Maria do Carmo-Fonseca. Funding Agency: Portugal 2020. Reference: Lisboa-01-0145-FEDER-016394. Amount: € 1 199 140,10. Total Amount: € 2 499 827,92.

Publications in Peer Reviewed Journals

Cardanho-Ramos C, Faria-Pereira A, Morais VA (2019). Orchestrating mitochondria in neurons: Cytoskeleton as the conductor. **Cytoskeleton**. Review. (IF: 3.07. Citations: 0. Source: Web of Science).

de Matos MR, Posa I, Carvalho FS, Morais VA, Grosso AR, de Almeida SF (2019). A Systematic Pan-Cancer Analysis of Genetic Heterogeneity Reveals Associations with Epigenetic Modifiers. **Cancers** 20(3):11. (IF: 6.1, Citations: 3. Source: Web of Science).

Spinazzi M, Radaelli E, Horr  K, Arranz AM, Gounko NV, Agostinis P, Maia TM, Impens F, Morais VA, Lopez-Lluch G, Serneels L, Navas P, De Strooper B (2019). PARL deficiency in mouse causes Complex III defects, coenzyme Q depletion, and Leigh-like syndrome. **Proceedings of the National Academy of Sciences of the United States of America** 116(1):277-286. (IF: 9.6, Citations: 2. Source: Web of Science).

Invited Lectures and Seminars

Morais VA. Parkinson's Disease: the importance of mitochondria for brain homeostasis. ADPD meeting - 14th International Conference on Alzheimer's and Parkinson's Diseases, Lisbon, Portugal, March 2019.

Morais VA. Importance of Mitochondria Homeostasis for Brain Function. Invited Lecture, DMBR – Department for Biomedical Research, University of Berne, Berne, March 2019.

Morais VA. Synaptic mitochondria: in search of its functional fingerprint. Synaptic function, dysfunction and Repair Workshop, UCL Discoveries Centers - Nova School of Medicine CEDOC, Lisbon, Portugal, April 2019.

Morais VA. The importance of Mitochondria Homeostasis for Brain Function. Invited Lecture, VIB - Center for Brain & Disease Research, Leuven, Belgium, June 2019.

Morais VA. Metabolic Disorders: therapeutic options and future perspectives. Portuguese Society for Metabolic Disorders Meeting - *Centro de Forma o CHULN: Doenas Mitocondriais - um abordagem multidisciplinar*, Lisbon, Portugal, June 2019.

Morais VA. Role of Mitochondria in brain homeostasis. Invited Lecture, Charit  – Medical University of Berlin, Berlin, Germany, July 2019.

Morais VA. The importance of Mitochondria Homeostasis for Synapse Function. CAJAL Course - Advanced Techniques for Synapse Biology, Bordeaux, France, October 2019.

Communications in International Conferences

Cortes-Figueiredo F, Asseyer S, Carvalho FS, Gieß RM, Bellmann-Strobl J, Paul F, Morais VA. Unravelling longitudinal mitochondrial DNA mutations in Multiple Sclerosis: association with disease activity and progression. 3rd Annual NeurULisboa Meeting, Lisbon, Portugal, March 21-22, 2019. (*Oral Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Role of Mitochondrial Dynamics in directing neural stem cell differentiation: relevance for neurological disorders. AD/PD Conference2019, Lisbon, Portugal, March 27-31, 2019. (*Oral Presentation*).

Cardanho-Ramos C, Faria-Pereira A, Morais VA. Mitochondrial dynamics and turnover: impact on synaptic activity and neurodegeneration. AD/PD Conference2019, Lisbon, Portugal, March 27-31, 2019. (*Poster Presentation*).

Gonçalves FB, Monteiro JT, Enguita FJ, Morais VA. Unravelling PINK1 mutations: a linkage between Mitochondrial dysfunctions and Parkinson's Disease. AD/PD Conference2019, Lisbon, Portugal, March 27-31, 2019. (*Poster Presentation*).

Leites EP, Craessaerts K, de Strooper B, Morais VA. PINK1's impact in different neural cells. AD/PD Conference2019, Lisbon, Portugal, March 27-31, 2019. (*Poster Presentation*).

Faria-Pereira A, Spinazzi M, Craessaerts K, Savas J, De Strooper B, Morais VA. Unraveling the proteomic fingerprint of synaptic mitochondria. JCS Conference – Cell dynamics: organelle-cytoskeleton interface, Lisbon, Portugal, May 19-22, 2019. (*Poster Presentation*).

Cardanho-Ramos C, Faria-Pereira A, Morais VA. Unveiling the impact of mitochondrial dynamics and turnover at the synapse. JCS Conference - Cell dynamics: Organelle-cytoskeleton interface, Lisbon, Portugal, May 19-22, 2019. (*Flash Oral Presentation and Poster*).

Cardanho-Ramos C, Faria-Pereira A, Morais VA. Mitochondrial dynamics: impact on synaptic activity and neurodegeneration. EMBO workshop - Emerging roles of the neuronal cytoskeleton, Villarica, Chile, April 14-18, 2019. (*Poster Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Characterizing the role of mitochondrial dynamics in adult neural stem cells differentiation. 2019 Eurogenesis Meeting, Bordeaux, France, June 11-13, 2019. (*Poster Presentation*).

Cortes-Figueiredo F, Asseyer S, Carvalho FS, Gieß RM, Bellmann-Strobl J, Paul F, Morais VA. Mitochondrial DNA mutations in Multiple Sclerosis: untangling genotype, immunometabolism and disease activity. ECTRIMS 2019 Meeting, Stockholm, Sweden, September 11-13, 2019. (*Poster Presentation*).

Soares R, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target that modulates adult neural stem cell fate. EMBO|FEBS Lecture course - Mitochondria in life, death and disease, Herceg Novi, Montenegro, September 24-28, 2019. (*Poster Presentation*).

Gonçalves FB, Monteiro JT, Enguita FJ, Morais VA. Is PINK1 dictating mitochondrial functions in PD? EMBO|FEBS Lecture course - Mitochondria in life, death and disease, Herceg Novi, Montenegro, September 24-28, 2019. (*Poster Presentation*).

Cardanho-Ramos C, Faria-Pereira A, Morais VA. The life cycle of mitochondria at the synapse, 1st Annual Meeting in Pharmaceutical Sciences, Coimbra, Portugal, November 15, 2019. (*Oral Presentation*).

Communications in National Conferences

Soares R, Sebastião AM, Xapelli S, Morais VA. Unveiling the role of mitochondrial dynamics in the regulation of postnatal neural stem cell fate. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Faria-Pereira A, Spinazzi M, Craessaerts K, Savas J, De Strooper B, Morais VA. Searching for synaptic mitochondria's identity. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Cardanho-Ramos C, Faria-Pereira A, Morais VA. The birth life and death of mitochondria at synapse. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Cortes-Figueiredo F, Asseyer S, Carvalho FS, Gieß RM, Bellmann-Strobl J, Paul F, Morais VA. Are mitochondrial DNA mutations linked to Multiple Sclerosis? Insights from a longitudinal clinical study. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Oral Presentation*).

Gonçalves FB, Monteiro JT, Enguita FJ, Morais VA. Unravelling PINK1 mutations: a linkage between Mitochondrial dysfunctions and Parkinson's Disease. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Leites EP, Craessaerts K, de Strooper B, Morais VA. The Role of PINK1 in Mitochondrial Quality Control and Neurodegenerative Diseases. XIII Annual CAML PhD Students' Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 15-17, 2019. (*Poster Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target for regulation of adult neural stem cell fate. IV Symposium of the Portuguese Glial Network, Lisbon, Portugal, May 29, 2019. (*Poster Presentation*).

Soares R, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target for neural stem cell fate regulation, XVI Meeting of the Portuguese Society for Neuroscience, Lisbon, Portugal, May 30-June 1, 2019. (*Poster Presentation*).

Soares R, Verduyck J, Sebastião AM, Xapelli S, Morais VA. Mitochondrial Dynamics: a target that regulates adult neural stem cell fate. 11th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies (SPCE-TC), Lisbon, Portugal, October 10-12 October, 2019. (*Poster Presentation*).

Internationalization

Our projects involve collaborations with international research groups in Europe and USA. Current international collaborators include:

In Europe - Bart de Strooper (VIB, Belgium); Patrik Verstreken (VIB, Belgium); Christine Klein (University Luebeck, Germany); Friedemann Paul (Charité | MDKZ, Berlin, Germany).

In USA - Jeffrey Savas (North Western University, Chicago).

Prizes, Honors and Awards

Soares R. Travel grant of 900€ from the International Brain Research Organization to attend the Eurogenesis Meeting, Bordeaux, France, June 2019.

Cardanho-Ramos C. Travel grant of 500€ from EMBO to attend an EMBO Workshop, Villarica, Chile, April 14-18, 2019.

Cortes-Figueiredo F. Travel grant of 400€ from ECTRIMS to attend the ECTRIMS 2019 Meeting, Stockholm, Sweden, September 11-13, 2019.

Advanced Teaching

Morais VA. Member of the Scientific Advisory Board of the Instituto de Medicina Molecular João Lobo Antunes Training Hub.

Morais VA. Lecture in Master Program - Biochemistry of Neurodegeneration Course. Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, October 2018.

Morais VA. Instructor at the CAJAL Course - Advanced Techniques for Synapse Biology, Bordeaux, France, October 2019.

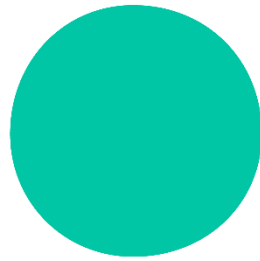
Morais VA. Lecture for 1st year medical students – Molecular and Cellular Biology Discipline, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 2018.

Science and Society

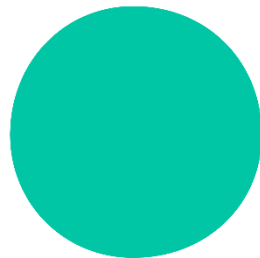
Soares R. Participated in the Jobshop AEIST 2019, Técnico IST, Lisbon, Portugal, May 7, 2019.

Morais VA and all the members of her research group participated in the “Noite Europeia dos Investigadores”, Lisbon, Portugal, September 27, 2019.

Soares R. Participated in the JobFest 2019, Faculdade de Ciências, NOVA Universidade de Lisboa FCT/UNL, Lisbon, Portugal, October 8, 2019.



Technical Facilities



Biobank Unit

Major Interests/Objectives

Biobanco-iMM CAML is a research infrastructure, which aims at promoting national and international collaborative research projects using human samples. It currently stores thousands of samples, including whole blood, serum, saliva, DNA, cerebrospinal fluid and tumor tissue, with detailed clinical information.

We provide support for biomedical research projects aiming at fostering national and international collaboration between researchers, namely through their participation in consortia and in international research networks.

We believe this facility creates a unique opportunity to promote synergies between partners, maximizing efficacy and minimizing costs.

Directors

Cláudia Maria Coelho de Faria, MD/PhD

Sérgio Jerónimo Rodrigues Dias, PhD

Team

Ângela Maria Cerqueira Coelho Afonso	Master Degree	Biobank Unit Area Manager
Fabiana Cândida da Rocha Rodrigues	Master Degree	Technician
Susana Raquel Salsinha Ferreira	Master Degree	Technician

Keywords / Research Areas

Biobank, Human Samples, Clinical Information, Biomedical Research

Major Achievements

In 2019, we had 57 active collections in Biobanco-iMM CAML covering all the main clinical areas. We received 47 sample requests which were used for different purposes, being the largest number of samples requested to the “Rheumatoid Arthritis” collection. Last year, 104 researchers requested samples and used our services, including cell culture and nucleic acid extraction.

In 2019, Biobanco-iMM CAML consolidated itself as an international partner, evidenced by the sharing of samples worldwide.

Biobanco-iMM CAML is certified with ISO 9001 Quality Management System by TÜV Rheinland Portugal, as part of the iMM Certification.

Selected Publications

Rosa N, Marques J, Esteves E, Fernandes M, Mendes VM, Afonso Â, Dias S, Pereira JP, Manadas B, Correia MJ, Barros M (2016). Protein Quality Assessment on Saliva Samples for Biobanking Purposes. **Biopreservation and Biobanking** 14(4):289-97. (IF: 1.698, Citations: 4. Source: *ResearchGate*).

Afonso A, Polido-Pereira J, Dias S (2014). Biobank Profile: Biobanco-iMM, Lisbon Academic Medical Centre. **Biopreservation and Biobanking** 12: 433-434. (IF: 1.698, Citations: 0. Source: *ResearchGate*).

Publications in Peer Reviewed Journals

Sánchez-Maldonado J *et al.* (2019). Steroid hormone-related polymorphisms associate with the development of bone erosions in rheumatoid arthritis and help to predict disease progression: Results from the REPAIR consortium. **Scientific Reports** 9:14812. (IF: 4.011, Citations: 0. Source: *ResearchGate*).

Rodrigues AM *et al.* (2019). Low serum levels of DKK2 predict incident low-impact fracture in older women. **JBMR Plus** 3(7): e10179. (IF: 6.284, Citations:---. Source: *ResearchGate*).

Soares MV, *et al.* (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** 10:334. (IF: 4.716, Citations: 1. Source: *ResearchGate*).

Invited Lectures and Seminars

Dias S. Biobanco-iMM CAML: a nossa experiência. Unidade Curricular Biobancos e gestão de amostras Biológicas, Mestrado em Gestão de Investigação Clínica, Universidade Nova e Universidade de Aveiro, NOVA Medical School - Faculdade de Ciências Médicas, Lisbon, Portugal, May 24, 2019.

Dias S. Biobancos. Programa de Doutoramento | Metodologias e Técnicas de Investigação, Universidade de Coimbra, Coimbra, Portugal, October 1, 2019.

Faria C. Investigação e Medicina. Congresso Nacional de Estudantes de Medicina, ISCTE – Instituto Universitário de Lisboa, Lisbon, Portugal, November 16, 2019.

Faria C. Biobank-iMM CAML, a tool for translational medicine. Sessão do Núcleo de Investigação do Departamento de Pediatria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, December 19, 2019.

Communications in International Conferences

Faria C. The basics of research and options in translational research. 1st European Combined Neuro-Oncology Course of the European Society for Pediatric Oncology - Brain Tumour Group (SIOPE BTG), Budapest, Hungary, April 2-4, 2019.

Communications in National Conferences

Faria C. Biobank. 1st Joint Meeting of Life Science Institutes in the Lisbon Area, Lisbon, Portugal, April 24, 2019.

Organization of Conferences

Faria C. Co-Organizer. ASPIC Conference “Research on Pediatric Cancer”, Lisbon, Portugal, November 8, 2019.

Faria C. Organizer. “Dia da Investigação da FMUL” with GAPIC, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2019.

Internationalization

During 2019, samples from Biobanco-iMM CAML were shared with researchers from Germany, Belgium, France and North America. With this, we will contribute to foster research in areas such as, rheumatology, neurosurgery and neurology.

Biobanco-iMM CAML is the national node for a pioneering EU project that aims to lead to new diagnostic tests to assess patients with non-alcoholic fatty liver disease (NAFLD) and identify those at risk for developing severe inflammation and liver scarring.

Moreover, Biobanco-iMM CAML is part of the EuroPDX Consortium, an international platform that gathers multiple institutions involved in the generation of patient-derived xenografts from multiple tumor types.

Advanced Teaching

Faria C. Lecture. Patient-derived xenografts of brain metastases – a tool for translational medicine. Curso Prático de Endocrinologia Molecular, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 8, 2019.

Faria C. Lecture. Biomedical research and Biobank. Programa de Formação em Investigação do Centro Hospitalar Lisboa Norte, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 22, 2019.

Science and Society

Faria C., organized the participation of the Brain Tumor Team (BTT) in Corrida Saúde + Solidária on April 28, 2019. The run/walk event is yearly organized by the students of the Lisbon Medical School (AEFML). The BTT gathered health care professionals, scientists, patients and their families aiming to support cancer research and to create hope for the future of patients affected with brain cancer.

MSc Thesis

Fabiana Rodrigues, 23/09/2019, Avaliação da qualidade das amostras de biópsias líquidas de pacientes com tumores urológicos, colhidas e armazenadas no Biobanco-iMM, CAML, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sérgio Dias.

Bioimaging Unit

Major Interests/Objectives

The Bioimaging Unit acts as a support structure to carry out and nurture research done with Light Microscopy inside the institute. Besides managing resources, we provide IMM scientists and visitors with excellence in scientific know-how and expertise in using light microscopy methods for their research. We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques and foster interactions and collaborations between microscopy users at the IMM.

Director

José Miguel Rino Henriques, PhD

Graphical Abstract



Team

Aida Andreia Pereira Pires Lima dos Santos	Master Degree	Technician (Started June)
Ana Margarida Santos do Nascimento	Master Degree	Senior Technician
António Francisco Pinção Loução Homem Temudo	Master Degree	Senior Technician
José Pedro Serrado Monteiro Marques	Master Degree	Technician (Left February)

Keywords / Research Areas

Microscopy, Confocal, Lightsheet, Multiphoton, Image Processing

Major Achievements

In 2019, the Bioimaging Unit services were used by 208 users from 36 different research labs, 5 of which from outside the iMM. During the year, we trained 84 new users in at least one microscopy system. The Bioimaging Unit is a Zeiss labs@location Partner, integrating a community of leading research facilities with expertise in specific applications of technologies that provide in depth knowledge and scientific support to Zeiss customers community. In 2019, the Bioimaging Unit organized a Super-Resolution Microscopy Workshop at the iMM for 20 selected participants.

Selected Publications

Martin RM*, Rino J*, Carvalho C*, Kirchhausen T, Carmo-Fonseca M (*these authors have contributed equally to this work) (2013). Live-Cell Visualization of Pre-mRNA Splicing with Single-Molecule Sensitivity. **Cell Reports** 4(6):1144-1155. (IF: 8.652, Citations: 74. Source: *Web of Science*).

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** 41(5):2881-2893. (IF: 10.727, Citations: 73. Source: *Web of Science*).

Martins SB*, Rino J*, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M (*these authors have contributed equally to this work) (2011). Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. **Nature Structural Molecular Biology** 18:1115. (IF: 12.65, Citations: 54. Source: *Web of Science*).

Domingues I, Rino J, Demmers JA, de Lanerolle P, Santos SC (2011). VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. **PLoS One** 6: e25668. (IF: 3.337, Citations: 50. Source: *Web of Science*).

Henriques CM, Rino J, Nibbs RJ, Graham GJ, Barata JT (2010). IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R alpha in T cells. **Blood** 115:3269-77. (IF: 13.206, Citations: 69. Source: *Web of Science*).

Ongoing Research Projects

2017/2020: PPBI – Plataforma Portuguesa de Bioimagem. Coordinator: José Henriques. Funding Agency: Portugal 2020. Reference: PINFRA/22122/2016. Amount: € 306 178,00. Total Amount: € 865 695,43.

Publications in Peer Reviewed Journals

Marques FG, Poli E, Rino J, Pinto MT, Diegues I, Pina F, Rosa Santos SC (2019). Low Doses of Ionizing Radiation Enhance the Angiogenic Potential of Adipocyte Conditioned Medium. **Radiation Research** 192(5):517-526. (IF: 2.943, Source: Web of Science).

Cabral Campello MP, Palma E, Correia I, Paulo PMR, Matos A, Rino J, Coimbra J, Pessoa JC, Gambino D, Paulo A, Marques F (2019). Lanthanide complexes with phenanthroline-based ligands: insights into cell death mechanisms obtained by microscopy techniques. **Dalton Transactions** 48(14):4611-4624. (IF: 3.813, Source: Web of Science).

Invited Lectures and Seminars

Rino J. Live Cell Imaging of pre-mRNA Biogenesis with Single-molecule Sensitivity. Lisbon Area Postdoc Meeting, Caparica, Portugal, November 14, 2019.

Internationalization

The Bioimaging Unit is a Zeiss labs@location Partner, integrating a community of leading research facilities with expertise in specific applications of technologies that provide in depth knowledge and scientific support to Zeiss customers community.

Advanced Teaching

Rino J. Lecturer (both theoretical lectures and hands-on sessions). Fluorescence Microscopy. Microscopy Workshop, Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, February 22, 2019.

Rino J. Lecturer. (both theoretical lectures and hands-on sessions). Light scatter in biological tissue + Imaging cleared tissue. Tissue clearing workshop, Centro de Neurociências e Biologia Celular, University of Coimbra, Coimbra, Portugal, March 2022, 2019.

Rino J. Organizer and Lecturer (both theoretical lectures and hands-on sessions). Overview of super-resolution techniques (SMLM, STED, SIM). Super-resolution Microscopy Workshop, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 4-5, 2019.

Temudo A, Nascimento A. Faculty (hands-on sessions). Super-resolution Microscopy Workshop, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 4-5, 2019.

Rino J. Lecturer (both theoretical lectures and hands-on sessions). Live cell imaging: F-techniques + Introduction to Image Analysis with FIJI. Syn2psy Network School 1: Basic concepts on imaging tools and data analysis. Centro de Neurociências e Biologia Celular, University of Coimbra, Coimbra, Portugal, September 30-October 4, 2019.

Science and Society

The MICRODIA | Open Microscopy Day, on May 5th 2019, integrated the commemoration of the International Microscopy Day and was an initiative of the PPBI (Portuguese Platform of Bioimaging). The Bioimaging Unit received 50 external visitors (students and teachers) for several activities including how to build a microscope at home, operating some of our high-end microscopes and finding out more about zebrafish development.

Flow Cytometry Unit

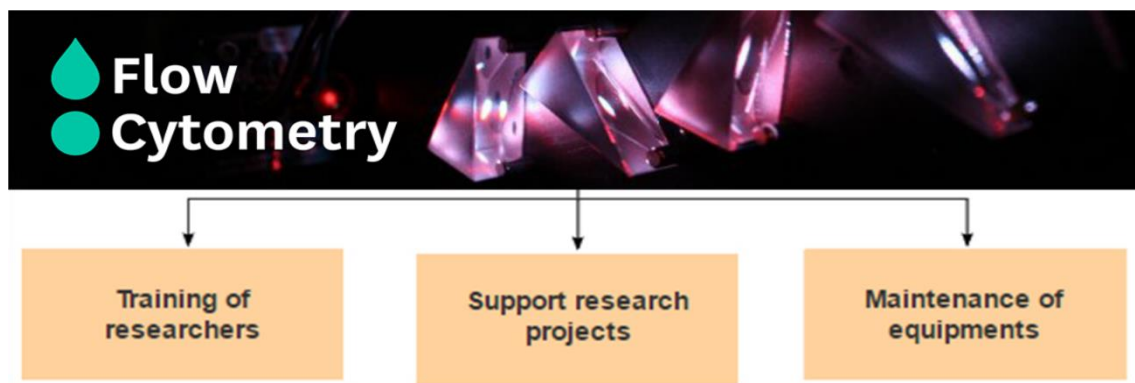
Major Interests/Objectives

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 4 cell analyzers (1 BD LSRFortessa X-20, 2 BD LSRFortessa - one of them equipped with a High Throughput Sampler - and 1 BD Accuri C6), 2 cell sorters (BD FACSAria IIu and BD FACSAria III) and one imaging flow cytometer (Amnis ImageStreamX). Besides a cell sorting service, our staff ensures quality control and maintenance procedures on all instruments and the implementation of the Quality Management System, according to ISO 9001.

Director

José Miguel Rino Henriques, PhD

Graphical Abstract



Team

Andreia Sofia Ramalho dos Santos	Master Degree	Technician
Bárbara Xavier Louro de Oliveira	Master Degree	Technician (Left March)
Joana Mafalda de Almeida Vaz Monteiro	University Degree	Technician (Started June, Left October)
Rute Regina Ferreira Gonçalves	Master Degree	Technician

Keywords / Research Areas

Flow Cytometry, Cell Sorting, Imaging Flow Cytometry

Major Achievements

In 2019, a total of 176 users from 37 research labs, 8 of them from outside the iMM, used the Flow Cytometry Unit. During the year, we trained 59 new users in at least one flow cytometry analyzer. The Flow Cytometry Unit is one of the founders of FLxFlow - a Portuguese network for Flow Cytometry created in 2017, which aims at bringing together the know-how of 4 core flow cytometry facilities in the Lisbon area, enabling advanced training and access to cutting-edge applications to the scientific community.

Selected Publications

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(25):40514-40532. (IF: 5.312, Citations: 4. Source: Web of Science).

Advanced Teaching

Rino J. Lecturer. Principles of Flow Cytometry + Fluorochromes, Brightness and Detection. Flow Cytometry Workshop, i3S – Instituto de Investigaçao e Inovacao em Saude, Porto, Portugal, October 7-10, 2019.

Comparative Pathology Unit

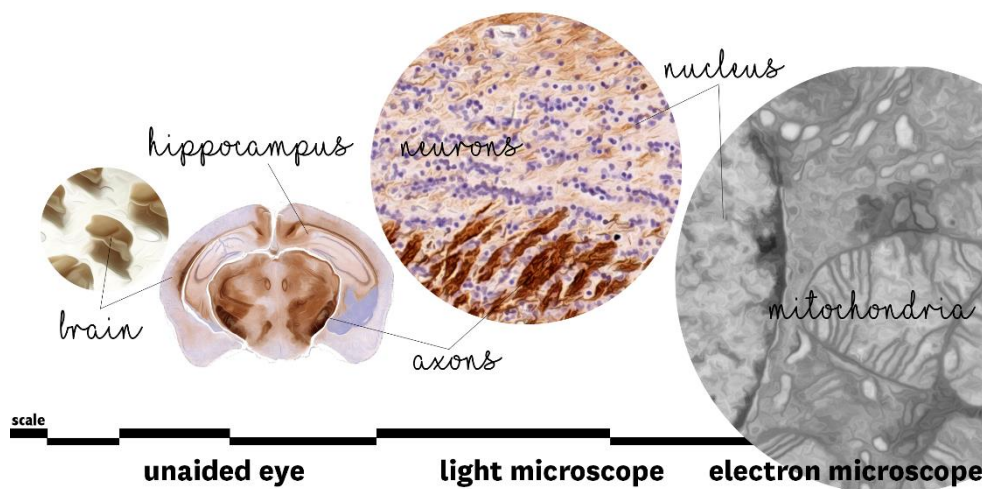
Major Interests/Objectives

Our mission is to achieve the highest level of quality in supporting researchers through: (1) training dissection skills and basic recording of macroscopic findings; (2) preparing the samples through state of the art histology and transmission electron microscopy services, including routine technique, paraffin, resin and cryo-embedding and sectioning, special stains, immunohistochemistry and immuno-EM; and (3) creating meaningful data from gross pathology observations and histopathology, with pathology reporting and document review for pathology content. Originality, integrity, and productivity while maintaining the highest level of technical proficiency and ethical principles is our motto; and we hope to keep up with your pace in the years to come.

Director

Tânia Carvalho, DVM, PhD, Experimental Pathologist

Graphical Abstract



Team

Ana Margarida Biscaia Fernandes dos Santos	Master Degree	Senior Technician
Ana Margarida Pereira Cristóvão Pinto	University Degree	Senior Technician
Ana Rita Varanda Correia Pires	Master Degree	Senior Technician
Pedro Jorge Filipe Pereira	Master Degree	Senior Technician
Pedro Reis Ruivo	Master Degree	Veterinarian

Keywords / Research Areas

Histology, Experimental Pathology, Transmission Electron Microscopy, Immunohistochemistry, Laboratory Animals.

Major Achievements

Quality and performance of our Unit was boosted by a reconfiguration of our histology and experimental pathology teams, which included the addition of two new members: Ana Margarida Cristóvão and Pedro Ruivo. This allowed us to build-up on important key performance indicators (KPI), like our turnaround time: we are currently with a turnaround time of 2 weeks from sample (in) to slide (out), for average sample size requests. Best ever!

Another important KPI is the number of projects that we are engaged with and the work that is published by our researchers that includes pathology data: 2019 summed a total of 11 papers of co-authorship.

Publications in Peer Reviewed Journals

Sanches-Vaz M, Temporão A, Luís R, Nunes-Cabaço H, Mendes AM, Goellner S, Carvalho T, Figueiredo LM, Prudêncio M (2019). *Trypanosoma brucei* infection protects mice against malaria. **PLoS Pathogens** 15(11): e1008145. (IF: 6.463, Citations: 0. Source: Web of Science).

Caiado F, Maia-Silva D, Jardim C, Schmolka N, Carvalho T, Reforço C, Faria R, Kolundzija B, Simões AE, Baubec T, Vakoc CR, da Silva MG, Manz MG, Schumacher TN, Norell H, Silva-Santos B (2019). Lineage tracing of acute myeloid leukemia reveals the impact of hypomethylating agents on chemoresistance selection. **Nature Communications** 10(1):4986. (IF: 11.878, Citations: 0. Source: Web of Science).

Godinho-Silva C, Domingues RG, Rendas M, Raposo B, Ribeiro H, da Silva JA, Vieira A, Costa RM, Barbosa-Morais NL, Carvalho T, Veiga-Fernandes H (2019). Light-entrained and brain-tuned circadian circuits regulate ILC3s and gut homeostasis. **Nature** 574(7777): 254-258. (IF: 43.07, Citations: 0. Source: Web of Science).

Freitas RF, Basto A, Almeida SCP, Santos RF, Gonçalves CM, Corria-Osorio J, Carvalho T, Carmo AM, Oliveira VG, Leon K, Graca L (2019). Modulation of CD4 T cell function via CD6-targeting. **EBioMedicine** 47:427-435. (IF: 6.68, Citations: 0. Source: Web of Science).

Carvalho T, Santos AM, Figueiredo LM (2019). Detection of Extravascular Trypanosoma Parasites by Fine Needle Aspiration. **Journal of Visualized Experiments - JoVE**(150): e59798. (IF: 1.108, Citations: 0. Source: Web of Science).

Gomes CP, Nóbrega-Pereira S, Domingues-Silva B, Rebelo K, Alves-Vale C, Marinho SP, Carvalho T, Dias S, Bernardes de Jesus B (2019). An antisense transcript mediates MALAT1 response in human breast cancer. **BMC Cancer** 19(1):771. (IF: 2.933, Citations: 0. Source: Web of Science).

Gil Marques F, Poli E, Malaquias J, Carvalho T, Portêlo A, Ramires A, Aldeia F, Ribeiro RM, Vitorino E, Diegues I, Costa L, Coutinho J, Pina F, Mareel M, Constantino Rosa Santos S (2019). Low doses of ionizing radiation activate endothelial cells and induce angiogenesis in peritumoral tissues. **Radiotherapy and Oncology** 141:256-261. (IF: 5.252, Citations: 0. Source: Web of Science).

Weis S, Heindl M, Carvalho T, Jentho E, Lorenz J, Sommerer I, Mössner J, Hoffmeister A (2019). Azithromycin does not improve disease severity in acute experimental pancreatitis. **PLoS One** 14(5):e0216614. (IF: 2.776, Citations:--. Source: Web of Science).

Ribot JC, Neres R, Zuzarte-Luís V, Gomes AQ, Mancio-Silva L, Mensurado S, Pinto-Neves D, Santos MM, Carvalho T, Landry JJM, Rolo EA, Malik A, Silva DV, Mota MM, Silva-Santos B, Pamplona A (2019). $\gamma\delta$ -T cells promote IFN- γ -dependent Plasmodium pathogenesis upon liver-stage infection. **Proceedings of the National Academy of Sciences of the United States of America** 116(20):9979-9988. (IF: 9.58, Citation:--. Source: Web of Science).

Di Lorenzo B, Simões AE, Caiado F, Tieppo P, Correia DV, Carvalho T, da Silva MG, Déchanet-Merville J, Schumacher TN, Prinz I, Norell H, Ravens S, Vermijlen D, Silva-Santos B (2019). Broad Cytotoxic Targeting of Acute Myeloid Leukemia by Polyclonal Delta One T Cells. **Cancer Immunology Research** 7(4):552-558. (IF: 8.619. Citations: 3. Source: Web of Science).

Akkapeddi P, Fragoso R, Hixon JA, Ramalho AS, Oliveira ML, Carvalho T, Gloger A, Matasci M, Corzana F, Durum SK, Neri D, Bernardes GJL, Barata JT (2019). A fully human anti-IL-7R α antibody promotes antitumor activity against T-cell acute lymphoblastic leukemia. **Leukemia** 33(9):2155-2168. (IF: 9.944. Citations: 1. Source: Web of Science).

Information Systems Unit

Major Interests/Objectives

Our mission is to help researchers reach their maximum productivity by using adequate Information Technology resources. Our aims are:

- Provide state-of-the-art information technology infrastructure and support services
- Contribute to improve productivity of researchers and research outcomes
- Facilitate and optimize management business processes

We intervene mainly in the following areas:

- Information Technology (IT) support to iMM users
- Planning, implementation and maintenance of the infrastructure that stores, processes and protects research data
- Design, implement and integrate information systems to facilitate scientific and management processes

Director

Pedro Miguel Bernardino Eleutério, Graduate (Left November)

Nuno Luís Barbosa Morais, PhD (Interim, December)

Team

André Filipe Cardoso Gonzalez Fragoso	High School Diploma	Information Systems Senior Technician
Pedro André Lozano Luiz de Castro	High School Diploma	Information Systems Senior Technician
Ricardo da Silva Martinho	University Degree	Information Systems Technician

Keywords/Research Areas

IT Support Data Protection, Information Integration, Web Services, Applications.

Major Achievements

We concluded implementing UNIT4 Business World HR management software, containing the institutional information about all iMM collaborators that feeds the newly developed iMM website, whose proper deployment to our servers we ensured.

We provide support on the new GDPR-compliant time clock system with biometric authentication and its control software.

We installed a new Dell 100TB storage system to meet the needs of Labs AESousa and NMorais.

We created a new Windows operating system image, based on the latest Microsoft build available, that uses fewer system resources and allows for faster configuration of new computers. We also created new templates for Windows Server 2016 and 2019.

We upgraded to a new version the entire IT virtualization platform, including three new servers, thereby improving stability and security, and increasing the performance available to the most demanding, and operationally critical, iMM services.

Advanced Teaching

Fragoso A, Luiz de Castro P, Eleutério P. 3-day course. Bioinformatics Cluster Usage. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, July 8-12, 2019.

Rodents Unit

Major Interests/Objectives

The aim of the Rodent Facility is to support 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 providing training and education in Laboratory Animal Science. In addition to normal husbandry routines, the Rodent Unit also provides specialized services such as colony management, rederivations of mouse lines, sperm and embryo cryopreservation, sample collections and surgical and experimental support to all research activities inside the animal facility.

Director

João Pedro Louro Machado Simas, DVM, PhD

Team

Ana Filipa Peixoto da Cunha	University Degree	Caretaker (Started July)
Ana Patrícia da Silva Almeida	Master Degree	Technician
Bruno Miguel da Conceição Novais	Master Degree	Technician (Left April)
Cecília Gonçalves Simão	University Degree	Caretaker
Daniel Corte Real Gomes da Costa	Master Degree	Veterinarian
Felícia Maria Augusto Ramos	University Degree	Caretaker
Filipe Fernandes Delgado	University Degree	Technician
Hugo de Barros Nogueira	Master Degree	Caretaker (Left December)
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 (Started October)
Mihaela Elena Morari	High School Diploma	Caretaker
Olena Pavlovska Borges Pinho	High School Diploma	Caretaker
Pedro Manuel Nogueira Santos	High School Diploma	Senior Technician
Sara Ghirelli	High School Diploma	Caretaker (Left September)
Sérgio Costa Miguel Gongo	University Degree	Caretaker (Started March, Left November)

Keywords/Research Areas

Rodents, Laboratory Animal Science, Animal Welfare.

Major Achievements

The implementation of a sperm cryopreservation program, providing a method to permanently preserve the genetic integrity of animal colonies. This is a cost-effective means to safeguard valuable lines and thereby avoid unnecessary breeding and being on line with the 3R-principle.

The development of a project aiming to improve the operation of the support infrastructure.

Ongoing Research Projects

2017/2020: CONGENTO - Consortium for Genetically Tractable Organisms. Coordinator: João Pedro Simas. Funding Agency: Portugal 2020. Reference: 027947/2017. Amount: € 560 086,20. Total Amount: € 1 363 313,52.

Invited Lectures and Seminars

Gareus R. Immune System Humanized Mice for Preclinical Research, Lisbon, Portugal, November 18, 2019.

Keck J. Sophisticated Humanized Mouse Models to Investigate the Mechanisms of Cancer, Lisbon, Portugal, November 18, 2019.

Advanced Teaching

Course. 1st Edition of the Laboratory Animal Science Course for Function A (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 17-July 31, 2019.

Course. 2nd Edition of the Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program - Researchers carrying out procedures on animals, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 18-November 18, 2019.



Science and Society

Launch of online access of Rodents Unit Virtual Tour.

Zebrafish Unit

Major Interests/Objectives

Provide a fully functional facility to be used by the iMM research laboratories.

Offer technical assistance to facilitate the use of zebrafish in a wide range of research areas.

Director

Maria Leonor Tavares Saúde, PhD, Invited Associate Professor

Team

Aida Gonçalves Lino Barros	High School Diploma	Senior Technician
Ana Fiipa Carvalho Marques Dias	PhD	Postdoctoral Researcher
Lara Margarida Marques Saraiva de Carvalho	Master Degree	Zebrafish Unit Area Manager
Mariana Antas Rebocho da Costa	Master Degree	Technician

Keywords/Research Areas

Zebrafish, Development, Regeneration, Disease Models, Small-Molecule Screening.

Major Achievements

Implementation of a new technique that allows the injection of tumor cell lines in zebrafish larvae.

Ongoing Research Projects

2017/2020: CONGENTO - Consortium for Genetically Tractable Organisms. Coordinator: João Pedro Simas. Funding Agency: Portugal 2020. Amount: € 560 086,20. Total Amount: € 1 363 313,52.

Invited Lectures and Seminars

Barros A. The health of Zebrafish. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Barros A. Handling and procedures in Zebrafish- Practical Model. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Carvalho L. Zebrafish Anesthesia and Euthanasia. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Carvalho L. Maintenance and Husbandry in Zebrafish. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Carvalho L. Zebrafish Transport. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Carvalho L. Zebrafish anatomy and Procedures. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Carvalho L. Procedures in Zebrafish- Practical Model. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Costa M. Handling and procedures in Zebrafish- Practical Model. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Dias AF. Zebrafish Behavior and Welfare. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Dias AF. Handling and procedures in Zebrafish- Practical Model. Module in CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Organization of Conferences

Zebrafish Unit. Co-Organizer. CONGENTO Course on Laboratory Animal Science Course for Function A (+D) (former FELASA Category B) CONGENTO-harmonized program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June and November, 2019.

Science and Society

12th grade student's visit from Virgilio Ferreira Secondary School. January 23, 2019.

Experimental Biochemistry student's visit from Faculdade de Medicina da Universidade de Lisboa. February 21, 2019.

American student's visit from the Medical Biotechnology and Drug Development Course at Study Abroad in Scandinavia Program. March 6, 2019.

11th grade student's visit from Colégio Moderno. March 7, 2019.

AIMS workshop. March 14-15, 2019.

Master student candidates attending "Open Afternoon at iMM" initiative. March 28, 2019.

Greek national's visit under the European Twinning Project Mobility Program. May 3, 2019.

12th grade student's visit from Vila Nova de Gaia Secondary School. May 10, 2019.

PALOP Research Students in Science Management Course. May 22, 2019.

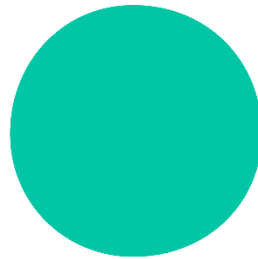
Students of the 2nd year of Colégio São João de Brito. May 28, 2019.

Students of the 4th year Rainha Dona Leonor EB1 School. May 29, 2019.

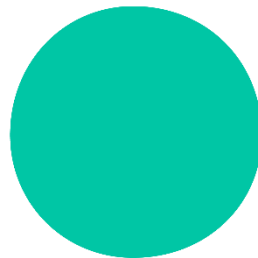
Students visit under the International Federation of Medical Students' Associations (IFMSA) scientific exchange program. July 22, 2019.

Teacher Visit with the objective of getting feedback on what they consider important to show students on study visits. July 3, 2019.

Science Club from Hospital de Santa Maria – Centro Hospitalar Lisboa Norte. October 13, 2019.



Administrative Facilities



Communication Office

Major Interests / Objectives

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.

Director

Ana Inês Jones Manteigas Domingues, PhD

Team

Ana Cláudia Marques da Silva	University Degree	Communication Officer
Maria Alexandra D'Abreu Pinto Sanfins	PhD	Trainee (Started June. Left September)

Keywords

Corporate and Institutional Communication, Science Communication, Public Affairs, Digital Communication, Social Media, Outreach, Science In and For Society.

Major Achievements

In 2019, we had:

- Media Office - 10 press releases; 700 clippings in national and international media outlets.
- School Visits - In 2019, 26 schools visited the institute with a total of 689 students and 57 teachers.
- Outreach Events – In 2019, we had four outreach events, such as Dia da Imunologia, MicroDia, Little iMMers and European Researchers’ Night with a total of 968 visitors. For these four events we had the collaboration of a 82 people from iMM.

Invited lectures and Seminars

Domingues I. SciCom PT, Aveiro, Portugal, May 30-31, 2019.

Domingues I. Chasing Questions. Excellence in Science Communication Workshop with ERC Host Institutions, Brussels, Belgium, October 17-18, 2019.

Domingues I. Lisbon Area PostDoc Meeting 2019, Caparica, November 14, 2019.

Organization of Conferences

Organization of Little iMMers, an event with different type of science activities dedicated to the children and family of iMM employees. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 5, 2019.

Science and Society

Co-Organization with Clara Artur (Assistant to the Board of Directors) of the Horizontes iMM: Uma Pergunta a Três, Lisbon, Portugal, February, March, June and October, 2019.

Co-Organization. Dia Internacional da Imunologia, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 29, 2019.

Co-Organization. Dia do Candidato FMUL, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 30, 2019.

Co-Organization. MICRODIA | Dia Nacional da Microscopia, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 22, 2019.

Co-Organization of the Instituto Miguel Galvão Teles Conference. Morais Leitão, Galvão Teles, Soares da Silva & Associados, Lisbon, Portugal, June 2, 2019.

Organization of the Tarde Aberta with the presence of a group of teachers to understand what is important for students and teachers on school visits. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 3, 2019.

Organization of the iMM presence at the European Researchers' Night 2019. National Museum of Natural History and Science, Lisbon, Portugal, September 27, 2019.

Finance and Operations Office

Major Interests/Objectives

Throughout the year of 2019, some very relevant steps for the organizational reshape of the Finance and Operations Office were put in place. In Q2 2019, the former Lab Management ceased to operate as a standalone facility to better align its activities with the overall iMM operations priorities with a new area Manager, Sara Santos. This action allowed to close the loop of the 360º Science Management Strategy designed and implemented at iMM. Additionally, two new managers were nominated in the Pre-Award (Joana Costa) and Project Management (Madalena Reis) departments. The Finance and Operations Office is now operating in a more agile organizational model with six departments - Pre-Award, Project Management, Purchases and Procurement, Accounting, Legal and Safety and Compliance each with an 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.

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 – Institutional and Researcher’s support; Main areas of expertise: Intellectual Property; Consortium Agreements; Public Law and Employment.

Core Services:

Preparation and revision of agreements and other acts (namely in the areas of labor commercial and public law, intellectual property and corporate & governance) and ensure the legal adequacy of processes, providing the optimum balance between the management promptness and efficiency with the legal utmost clarity and safety.

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.

Director

Fausto da Costa Santos Lopo de Carvalho, Master/MBA

Team

Assistant to the Board of Directors:

Ana Clara Pereira Faria Artur	University Degree	Assistant to the Board of Directors
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Pre-Award:

Joana Cristina Costa	PhD	Pre-Award Area Manager
Marija Petkovic Garcia	PhD	Grants Officer
Sílvia da Conceição Santos Pereira da Costa	PhD	Grants Officer (Started May)

Project Management:

Ana Maria Branco Alves	Master Degree	Project Manager (Started March)
Andreia Sofia Gonçalves Almeida Vaz Veiga	University Degree	Senior Project Manager
Eduarda Maria Seabra Rosmaninho	Master Degree	Project Manager
Madalena Gil Martins Reis	University Degree	Project Management Area Manager
Maria Fernanda Gonçalves da Veiga Vila-Chã	Other	Administrative Technician
Maria José Flores Marques Antunes	Master Degree	Senior Project Manager
Sara Marisa Caseiro Rebelo	University Degree	Project Manager (Left November)

Accounting:

Ana Filipa de Almeida Pereira	High School Diploma	Accounting Administrative Technician (Left April)
Jorge Manuel Pereira Lopes	University Degree	Treasurer (Started February, Left March)
Maria Elisabete Santos Liberato	University Degree	Senior Accounting Administrative Technician (Started January)
Maria José Serra da Silva	University Degree	Senior Accounting Administrative Technician (Started September)

Pedro Gaspar Rebelo Lopes Moura	Master Degree	Senior Accounting Administrative Technician (Left September)
Pedro Miguel da Rosa Santos	University Degree	Senior Accounting Administrative Technician
Sandra Paula da Silva Duarte	University Degree	Accounting Area Manager
Vera Cristina Felício da Conceição Rêgo	High School Diploma	Senior Accounting Administrative Technician

Purchasing and Procurement:

Alexandre Manuel Raposo de Jesus	Master Degree	Purchasing and Procurement Area Manager
Ana Rita Fonseca Vicente	Master Degree	Senior Purchasing Administrative Technician
Cláudia Sofia Palmeiro Alves da Costa	University Degree	Purchasing Administrative Technician (Moved to Safety and Compliance in February)
Lúcia Cristina Manso Alves	Master Degree	Purchasing Administrative Technician
Rita Santinho Grenho	Master Degree	Purchasing Administrative Technician (Left October)
Sandra Isabel Francisco Lopes	University Degree	Senior Purchasing Administrative Technician
Vânia Isabel Estevens Polido Marques Paula	University Degree	Senior Purchasing Administrative Technician

Legal:

Inês Bilé da Silva Plácido	Master Degree	Legal Counsel
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Safety and Compliance:

Ana Francisca Barroca Lemos	Master Degree	Technician
Cláudia Sofia Palmeiro Alves da Costa	University Degree	Technician
Maria Jardim Caramelo Dias Cabral	Master Degree	Technician
Sara Diana Pinheiro dos Santos	Master Degree	Safety and Compliance Area Manager

Washing Room:

Ana Cristina dos Santos Anunciação	High School Diploma	Senior Technician
Anilda Sofia Araújo Almeida	High School Diploma	Technician
Apolinário da Costa Gongo	High School Diploma	Technician
Bárbara Stefane Fernandes de Oliveira Paula	High School Diploma	Technician
Bashir Shamshudin Habib Alibhai	High School Diploma	Technician
Edna Neias Ferreira Gomes	High School Diploma	Senior Technician
Lucas Araújo da Silva	High School Diploma	Technician

Front Office:

Ana Rita Matos Dias	Master Degree	Administrative
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Keywords

Pre-Award	Project Management	Purchasing and Procurement	Accounting	Legal	Safety & Compliance
EXPERTISE	EXECUTION	SUSTAINABILITY	COMPLIANCE	SPECIALIZATION	SAFETY
<ul style="list-style-type: none"> ▪ New expertise building on RRI and “Broader impact” - Preparation actions to be put in place in 2020 regarding the starting year of HEU in 2021. New framework programme with significant differences from H2020 ▪ Team consolidation and uplift -H2020 closing calls will push team effort ▪ Joint actions with post award encouraged to continue 	<ul style="list-style-type: none"> ▪ Generate Internal control procedures for budget execution and budget transfers; ▪ Focus on project long term planning and forecasting to anticipate hurdles; ▪ Implement the full compliance plan for every project with special focus in EU and La Caixa funded projects ▪ Compliance with control dashboards 	<ul style="list-style-type: none"> ▪ Build sustainable long term relationships with main suppliers; ▪ Become a trusted partner inducing further price discounts and savings of 150K/year; ▪ Consolidate the account oriented suppliers plan; ▪ Build solid proposal for LXO cluster regarding joint actions for price discounts 	<ul style="list-style-type: none"> ▪ Month N closing around day 18 of month n+1 with rigorous focus on detail both on costs and revenue registering; ▪ Reshape of reimbursement procedures (blue ocean) ▪ Implementing and exporting SEPA file from Navision ▪ Implementation study for a document management system (digital invoicing) 	<ul style="list-style-type: none"> ▪ Evolve to a specialization model per area and topic; ▪ Streamline legal process flow per area of specialization especially on IP and Data protection with external consultants; ▪ Continue to focus on operational precision on “hands on” legal issues ▪ Continue to advise on 360° decision impact 	<ul style="list-style-type: none"> ▪ Planning and execution of legal demands on lab safety (license renewal 2019/20) ▪ Equipment listing and mapping per category, type and capacity model (usage) ▪ Laboratory design and remodeling with new processes allowing for better planning on overall impact ▪ Maintenance contracts and repairing with special focus on 2020

Major Achievements

In 2019, the Finance and Operations Office coordinated a study highlighting the impact of VAT costs in the budget availability of scientific projects, presenting a peer comparison with other European countries. Following this study, the IMM Executive Director Maria Mota launched the campaign NoVAT4Science and the Prime Minister of Portugal, António Costa, announced a reimbursement scheme for VAT in research projects as one of the actions to implement in 2020 for the Science Ministry.

Pre-Award:

Dissemination of 350+ funding opportunities; Support to 177 applications to 55 different International and 19 different National Funding Programmes, namely in eligibility, legal, technical and administrative aspects, as well as the ethics and data management requirements; Writing and proof-reading of institutional proposals to the H2020 Widening program; Support and management of *Fundo iMM-Laço* Research Grants call; 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:

Accounting records financial and fiscal documents in the respective projects, in compliance with the established deadlines (monthly closing at 15-20 of month n+1). A deeper financial analytics was implemented, by using Cod. Labs, which allows invoicing registering by facility or lab, including HR costs. The cash-flow dashboard is updated at a monthly basis to control the short-term cash needs, and helping with push actions with FCT. Besides this, the budget is followed-up in a quarterly basis and included on general quarterly presentations for the Board of Directors, and sent to the heads of facilities the checkpoint of each semester.

Purchasing and Procurement:

In 2019, the department changed from Purchasing Office to Purchasing and Procurement, showing the adjustment of strategy moving forward – a focus on negotiation and work with suppliers, resulting in financial savings for researchers. This work also led to partnerships with companies to reduce or reuse wrappings, improving sustainability on the supply chain. Tighter work with Safety and Compliance along with Projects resulted in a faster response time with less doubts regarding eligibility of equipments and amortizations. There was also a focus on simplifying the work for researchers, reducing double filling of paperwork and generating time savings to all involved.

Project Management:

The 360° iMM governance model has been fully adopted, with increased cooperation with the other F&O departments. Project submissions were assured in a timely and precise way with accuracy both in the deliverables and in the financial reports. Control Dashboards were implemented to monitor expense submission and deadlines compliance, contributing to overall iMM operation monitoring.

Project Management reshaped team was able to deal with demanding project audits, both to national and H2020 projects, providing all required information. Regular project management department meetings were set up, improving communication, internal knowledge and process standardization.

Legal:

The Legal department consolidated its strategy in 2019. The Legal Department of iMM is within the scope of the Finance and Operations Office and is set to provide advice in strategic issues and legal support to all the departments of the institution as well as to the Researchers, about all the legal questions regarding issues relevant for the work of the Institution. Besides the department specific activities, the Legal Counsel gives advice on impact of management-related actions planned by the Finance and Operations Director. As an example of a well-coordinated set of actions, iMM obtained the Estatuto de Utilidade Pública, in August of 2019.

Safety & Compliance:

Safety and Compliance department joined the Finance and Operations Office in the second quarter of 2019. In 2019, iMM underwent several modifications in lab spaces in different areas of the building. The Safety and Compliance department assured the full coordination of all works while maintaining focus on safety issues regarding lab management normal operations. The Safety and Compliance team rapidly integrated their actions with other departments of the Finance and Operations Office and synergies were extremely productive.

Quality Management System:

Successful audit in 2019, SWOT and annual satisfaction survey completed for iMM.

Human Resources Office

Major Interests/ Objectives

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 key iMM 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 the iMM 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.

Director

Sofia Isabel Lopes dos Santos Vicente dos Santos, University Degree

Team

André Daniel dos Santos Brás Pereira	University Degree	HR Administrative Technician
Cláudia Aurora Mira Soeiro	University Degree	Senior HR Administrative Technician
Mafalda Bettencourt Reinhardt da Costa Dias	Master Degree	Trainee (Started June. Left September)
Pedro Humberto Fernandes Monteiro Leite	Master Degree	Administrative Trainee (Started September)
Sérgio Miguel Cargaleiro Delgado Figueiredo Lopes	University Degree	Senior Administrative Technician (Started August)
Susana Isabel dos Santos Pedroso	High School Diploma	HR Administrative Technician (Left September)

Keywords/Research Areas

The Human Resources team has solid technical and soft skills that aim to promote Talent. Our goal is to select and support the most prepared candidates whether is a researcher or support staff.to maintain the excellence of iMM.

Major Achievements

The Human Resources Office in 2019 had six major achievements: 1. Conclusion of the implementation of the human resources management software - UNIT4; 2. *MyID Program* consolidation through *My Step* mentoring sessions; 3. Creation and implementation of the *All Aboard* project; 4. Implementation and installation of the integrated attendance management system (SmartStep); 5. Implementation and configuration of the Payroll Software; 6. Introduction of the new iMM Fellowship regulation.

During 2019, we have completed the implementation of the UNIT4 project, which was a demanding task for the HR Team but successfully accomplished due to their know-how and work capacity.

Regarding the *MyID Program* there were 6 sessions, reaching 22 participants, 27% of which were postdocs (while the others were distributed between PhD and Master Students).

The *All Aboard* Project aimed to promote the team spirit within the groups through the sharing of good practices, adapted to each group's dynamics and human resources. The *All Aboard* encounters took place over lunch, which allowed us to interact and get to know the Group Leaders and Head of Facilities and their teams. The initiative was also opened to Area Managers to assist them with leadership skills required for people management.

To improve the service provided we implemented softwares related to attendance management and payroll. This 'in-house' acquired capability permitted the adjustment to our activity.

Due to the legal compliance with FCT guidelines concerning the new research fellow statute, iMM put into effect the new fellowship regulation after approval by the competent entity (FCT).

Below we present the principal facts and figures related to the work developed all year round in comparison with previous years:

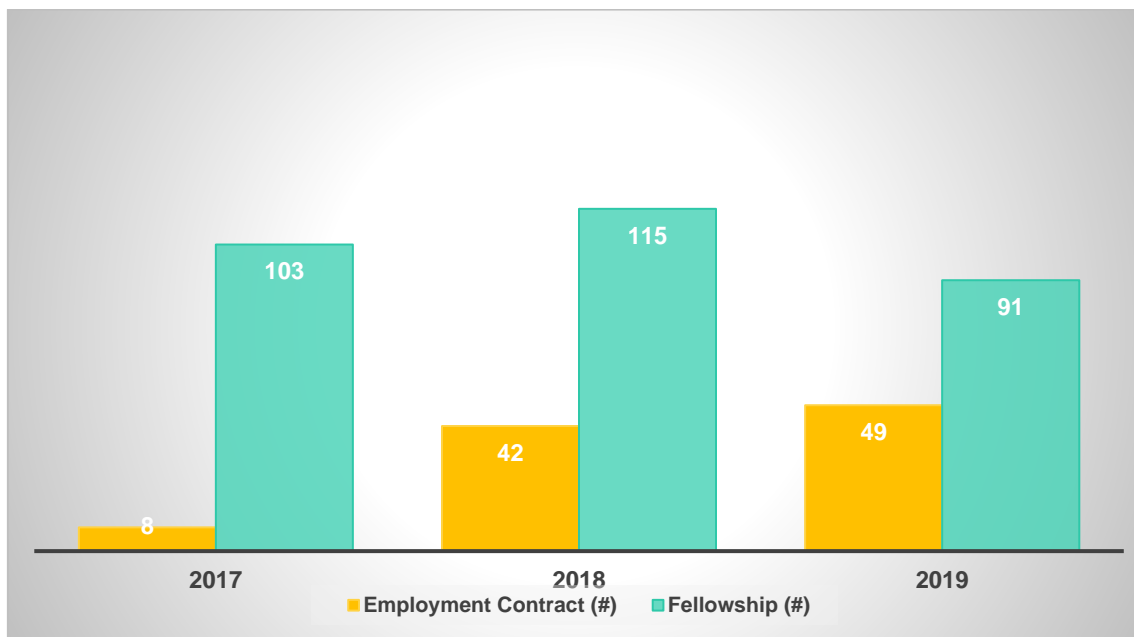
A) Number of Recruitment and Selection (R&S) interviews conducted

	1 st Interviews	2 nd Interviews	Final Interviews	Total
2018	27	15		27
2019	77	24	11	112

B) Number of Follow-up interviews conducted

	1 st Follow-up Interviews	2 nd Follow-up Interviews	3 rd Follow-up Interviews	Exit Interviews	Total
2017	4	3		3	10
2018	17	14	13	2	46
2019	45	34	10	6	95

Number of Employment and Fellowship Contract Calls per Year:



In the near future, all our new projects will continue to be guided by iMM’s main goal: “Institute that offers a vibrant scientific environment, aiming to nurture innovative ideas (...) leveraged by high-quality human resources, increasing expenditure in infrastructures and knowledge transfer to the society”.

Technology Transfer Office

Major Interests/Objectives

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 European networks and initiatives related with translational research (e.g.: EATRIS), open innovation (e.g.: Open Innovation Test Bed – “SAFE-N-MEDTECH”) and business acceleration (e.g.: Healthtech Translation Advisory Board and EIT Health).

Director

António Pedro Alves da Silva, University Degree

Team

Bárbara Sofia Lopes Gomes	PhD	Tech Transfer Officer
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Keywords / Research Areas

Technology Transfer, Innovation, Entrepreneurship, Intellectual Property, Business Development.

Major Achievements

Our IP portfolio was strengthened with 20 new inventions and 13 patents filed. 5 license agreements have been set with companies to exploit iMM IP. 7 start-up companies were supported, and 2 of them (TargTex and LiMM Therapeutics) were created and secured seed rounds close to 4 million Euros. To the best of our knowledge, iMM is the first Portuguese research institute to have an equity position in a VC-backed start-up.

150 collaborations with external organizations were promoted, including 126 collaborations with industry. As a result, 54 collaborations are already formalized (37 with industry).

Our industry outreach was reinforced with the attendance of key industry events (e.g. Bio-Europe and BioFIT) and the creation of a catalogue of research capacities to promote collaboration with industry.

The iMM Inventor Guide was created in collaboration with the Communication Office to raise the awareness of our research community about tech transfer.

Industry Advisory Boards have been established with key industry profiles to guide our innovation efforts.

Organization of Conferences

We have organized visits of industry to iMM, including:

- MSD (March);
- Evotec (May);
- Swedish and Danish companies (October) – in collaboration with HCP and AICEP;
- Neolpharma (November) – in collaboration with AICEP.

Training Hub

Major Interests/Objectives

General Aim: To provide training opportunities for a successful science-related career to researchers at different stages in their careers.

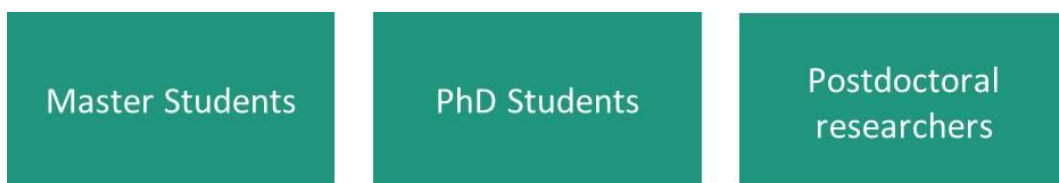
Specific Objectives:

- Ensure full running of ongoing Master, PhD, and Postdoctoral Programs: launch calls; administrative execution; managerial support to PhD students/Postdoctoral researchers' activities; support MSc/PhD students and Postdoctoral researchers throughout their training;
- Manage the "Master Program @ iMM";
- Coordinate the "Training Program for the Next Step";
- Run CAML Advanced Courses: cover all organizational aspects in articulation with IFA, FMUL;
- Organize Courses, Workshops, Seminars;
- Coordinate the Monday Lectures seminar series;
- Support candidate's applications to PhD fellowships at iMM (FCT, "la Caixa" Foundation);
- Coordinate university students' visits (e.g. Job Shadowing Days) and traineeships at iMM (summer internships, CoLabs).

Director

Ana Filipa Duarte Nunes Almeida, PhD

Graphical Abstract



Team

Domingos Manuel Pinto Henrique	PhD	Director of Studies
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Keywords

Advanced-Training, Master Program, PhD Program, Postdoctoral Program, Courses/Workshops.

Major Achievements

Specific Achievements:

- Overall managerial and administrative execution of the LisbonBioMed PhD Program, including the production of overall metrics, and reporting;
- Coordination of the iMM activities under the Biology at the Host Microbe Interface PhD Program: selection process, annual meetings, courses, lab rotations, admission and renewals;
- “Master Program @ iMM”: assembly and dissemination of iMM’s Master project proposals/vacancies; “Open Afternoon”; “Best Master Thesis” Awards;
- “Training Program for the Next Step”: personalized reviewing of full applications (including cover letters, research projects and CVs) and mock interviews for PhD, postdoctoral, and group leader positions;
- Organization of courses, seminars, visits, and traineeships at iMM.

Transversal managerial support to:

- FCT fellowships: applications, renewals, periods abroad, thesis committees and defenses, general queries;
- PhD students/Postdocs-driven initiatives.

Internationalization

Participation in the Kickoff meeting of the project RNA IN DISEASE (RiboMED), Carcavelos, Portugal, October 14-16, 2019.

Advanced Teaching

Nunes F. Organizer. Scientific Writing Course: Structuring and writing a hypothesis-driven research paper. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 26-December 12, 2019. (Twelve classes of three hours each, plus written exam).

Nunes F. Organizer. Career Seminar. Science to Medicine at Regeneron: Human Genetics, and Curing Ebola using New Technologies, by Neil Stahl (Executive VP Research and Development, Regeneron Pharmaceuticals), Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 14, 2019.

Science and Society

“Open Afternoon at iMM” (targeted to 1st year Master students). Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 28, 2019.

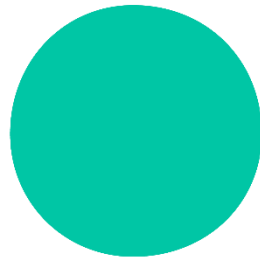
Job Shadowing for One Day, organized in collaboration with the Núcleo de Engenharia Biológica do Instituto Superior Técnico, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 11, 2019 (four students) and October 17, 2019 (five students).

31.^a Jobshop - Think the Future, Feira de Engenharia e Tecnologia do IST, Instituto Superior Técnico - Campus Alameda, Lisbon, Portugal, May 7, 2019.

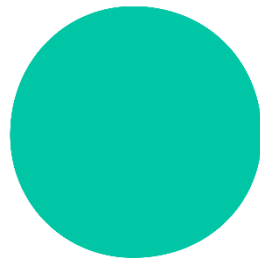
Visit to iMM in the context of the International Federation of Medical Students' Associations (IFMSA)'s scientific exchange program, July 2, 2019 (eight foreign medical students).

JobFest 2019 - Feira de Empregabilidade e Empreendedorismo da FCT-UNL, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Lisbon, Portugal, October 8, 2019.

Job Shadowing Day, one student from Colégio de S. Tomás, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, December 20, 2019.



Spin-offs



Genomed | Diagnósticos de Medicina Molecular SA

Major Interests/Objectives

GenoMed is a spin-off company of iMM created in 2004. GenoMed’s mission is to provide cutting-edge technology transfer services relevant for medical applications. Currently, GenoMed offers more than 800 different tests that are used in diagnosis, prognosis and therapeutic follow-up. The main medical areas covered include Oncology, Hematology, Cardiology, Neurology, Gastroenterology/Hepatology, Nephrology, Endocrinology/Metabolic diseases, Obstetrics/Gynecology, Pneumology, Dermatology, Ophthalmology, Otorhinolaryngology, Pediatrics, Urology and Pharmacogenetics. Additionally, GenoMed provides parental and ancestry DNA testing.

Director

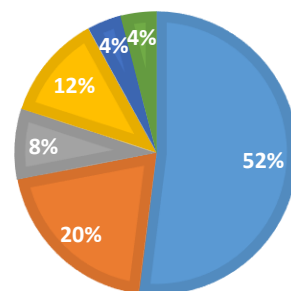
Teresa Porta Nova, MSc, Executive Director/Technical Director

Diana Antunes, MD, Clinical Director/Clinical Geneticist

Team

GENOMED'S TEAM ACADEMIC BACKGROUND

■ MSc ■ Graduated ■ PhD ■ Undergraduated ■ MD ■ PhD student (BDE)



Keywords / Research Areas

Molecular diagnosis, Oncology, Genetics, Rare Diseases.

Major Achievements

In 2019, we implemented 18 new NGS panels for various medical specialties as cardiology, neurology, among others. Those panels have been designed together with the clinicians and responding to their patient's needs.

GenoMed participated in the international collaborative study with the National Institute for Biological Standards and Control (NIBSC) for the evaluation of the first of the World Health Organization 1st International Standards for Cancer Genomes.

Genomed was recognized by EMQN for their Lung cancer clinical reports quality. Those reports will be used as educational tools on the EMQN website, as example of excellent reports.

Ongoing Research Projects

2018/Present: Next Generation Sequencing (NGS) to test BCR-ABL1 mutations in patients with CML and ALL Ph+ treated with TKIs. Incyte. Coordinator: Sónia Matos.

2018/Present: Molecular Profiles in Colorectal Cancer: Prognostic Value and Indicators for Tailored Therapies. Coordinator: Prof. Marília Cravo (HBA). Participants: Ana Carla Sousa.

2017/2019: MyCardioGeneTest, funded by Lisboa2020, Portugal2020 from European Regional Development Fund (FEDER).

2016/2019: Characteristics and frequency of IDH mutations in real world AML patients in Portugal. Celgene. Coordinator: Maria Carmo-Fonseca. Participants: Sónia Matos.

Publications in Peer Reviewed Journals

Sousa AC, Silveira C, Janeiro A, Malveiro S, Oliveira AR, Felizardo M, Nogueira F, Teixeira E, Martins J, Carmo-Fonseca M (2019). Detection of rare and novel EGFR mutations in NSCLC patients: Implications for treatment-decision. **Lung Cancer** 139:35-40. (IF: 4.599, Citations: 0. Source: Web of Science).

Silveira C, Triunfol M, Carmo-Fonseca M (2019). RNA Sequencing: A complementary tool kit for the diagnosis of Mendelian disorders. **AACC Clinical Laboratory News**.

Marchiò C, Da Cruz Paula A, Gularte-Mérida R, Basili T, Brandes A, da Silva EM, Silveira C, Ferrando L, Metovic J, Maletta F, Annaratone L, Pareja F, Rubin BP, Hoschar AP, De Rosa G, La Rosa S, Bongiovanni M, Purgina B, Piana S, Volante M, Weigelt B, Reis-Filho JS, Papotti M (2019). PAX8–GLIS3 gene fusion is a pathognomonic genetic alteration of hyalinizing trabecular tumors of the thyroid. **Modern Pathology** 32(12):1734-1743. (IF: 6.635, Citations: 1. Source: Web of Science).

Sebastiao APM, Pareja F, Kumar R, Brown DN, Silveira C, da Silva EM, Lee JY, Katabi N, Chiosea S, Weigelt B, Reis-Filho JS, Seethala RR (2019). Genomic analysis of recurrences and high-grade forms of polymorphous adenocarcinomas. **Histopathology** 75(2):193-201. (IF: 3.294, Citations: 1. Source: Web of Science).

Pareja F, Lee JY, Brown DN, Piscuoglio S, Gularte-Mérida R, Selenica P, Da Cruz Paula A, Arunachalam S, Kumar R, Geyer FC, Silveira C, da Silva EM, Li A, Marchiò C, Ng CKY, Mariani O, Fuhrmann L, Wen HY, Norton L, Vincent-Salomon A, Brogi E, Reis-Filho JS, Weigelt (2019). The genomic landscape of mucinous breast cancer. **Journal of the National Cancer Institute** 111(7):737-741. (IF: 10.211, Citations: 4. Source: Web of Science).

Cerveira N, Diamond J, Matos S, Amorim ML, Coucelo M, Bizarro S, Simões AT, Pierdomenico F, Lopes M, Ribeiro L, Carmo-Fonseca M, Guimarães JE, Almeida A, Teixeira AR (2019). Negative MR4.0 chronic myeloid leukemia and its implications for treatment-free remission. **British Journal of Haematology** 186(6):E181-E184. (IF: 5.206, Citations: 0. Source: Web of Science).

Other International Publications

Gomes CF, Sousa AC, Branco F, Palmela C, Rolim I, Henriques AR, Oliveira MH, Borralho P, and others (2019). Molecular Profiles in Colorectal Cancer. **Gastroenterology** 156(6):S-450-S1450. (IF: 19.809, Citations: 0. Source: Web of Science).

Invited Lectures and Seminars

Ribeiro A, Sousa AC. 6º Encontro de Pneumologia Oncológica do Sul – A importância da Anatomia Patológica e de Medicina Molecular na decisão terapêutica do CPNPC, Lisbon, Portugal, November 30, 2019.

Communications in International Conferences

Da Silva EM, Sebastião APM, Murray M, Silveira C, Pareja F, Weigelt B, Brogi E, Reis-Filho JS, Zhang H. Recurrent MED12 Exon 2 Mutations in Complex Fibroadenomas of the Breast. USCAP's (United States & Canadian Academy of Pathology) Annual Meeting, Maryland, USA, March 16-21, 2019. (*Poster Presentation*).

Sebastiao APM, Pareja F, Kumar R, Brown DN, Silveira C, da Silva EM, Lee JY, Katabi N, Chiosea S, Weigelt B, Reis-Filho JS, Seethala RR. Genomic analysis of recurrences and high-grade forms of polymorphous adenocarcinomas of the salivary gland. USCAP's (United States & Canadian Academy of Pathology) Annual Meeting, Maryland, USA, March 16-21, 2019. (*Poster Presentation*).

Silveira C, Sousa AC, Janeiro A, Carmo-Fonseca M. Detection of acquired T790M resistance mutation by liquid biopsy. EACR-ESMO Joint Conference on Liquid Biopsies, Bergamo, Italy, May 15-17, 2019. (*Poster Presentation*).

Cerveira N, Diamond J, Matos S, Amorim ML, Coucelo M, Bizarro S, Simões AT, Pierdomenico F, Lopes M, Ribeiro L, Carmo-Fonseca M, Guimarães JE, Almeida A, Teixeira AR. Negative MR4.0 Chronic Myeloid Leukemia and Its Implications for Treatment-Free Remission. EHA (European Hematology Association) Annual Meeting, June 13-16, 2019. (*Poster Presentation*).

Communications in National Conferences

Silveira C, Vendrell I, Carmo-Fonseca M. Detection of actionable mutations in ctDNA in advanced breast cancer patients. 1st GenomePT Symposium, CIBIO-InBIO, Vairão, Vila do Conde, May 10, 2019. (*Poster Presentation*).

Paulino R, Miranda F, Ranhel D, Azevedo AP, Silva C, Reis AB, Meireles F, Jorge A, Afonso C, Santos S. Um caso de Síndrome Mielodisplásica com uma alteração citogenética citogenética rara: t(1;3)(p36;q21). SPH Annual Meeting, Braga, Portugal, November 14-16, 2019. (*E-Poster Presentation*).

Macedo A, Caetano G, Guerra L, Lopes C, Polo B, Valle S, Mota A, Cabral R, Cunha M, Magalhães R, Santos MJ, Martins J, Santos P, Reichert A, Melo T, Coelho H, Montalvão A, Cerveira N, Matos S, Rodrigues J, Gírio A, Saraiva A. Efectividade e Segurança de Nilotinib no tratamento de LMC Recém-diagnosticada num contexto de “Vida Real”: Resultados Finais do Estudo PIANO-CML. SPH Annual Meeting, Braga, Portugal, November 14-16, 2019. (*Poster Presentation*).

Prizes, Honors and Awards

Silveira C. Meeting Bursary Award. EACR-ESMO Joint Conference on Liquid Biopsies, Bergamo, Italy, May 15-17, 2019.

Industry Contract Research

2018/Present: Next Generation Sequencing (NGS) to test BCR-ABL1 mutations in patients with CML and ALL Ph+ treated with TKIs. Incyte. Coordinator: Sónia Matos.

2016/2019: Characteristics and frequency of IDH mutations in real world AML patients in Portugal. Celgene. Coordinator: Maria Carmo-Fonseca. Participants: Sónia Matos.

Advanced Teaching

Silveira C, Matos S. Lecture. Next-Generation Sequencing aplicado ao diagnóstico molecular. Mestrado em Tecnologias Moleculares em Saúde, Escola Superior de Tecnologia da Saúde de Lisboa (ESTeSL), Lisbon, Portugal, February 28, 2019.

Silveira C. Lecture. Guidelines práticas de NGS em Oncologia: pesquisa de variantes de DNA. Pós-Graduação em Avanços em oncobiologia molecular aplicada ao diagnóstico e terapêutica. Escola Superior de Tecnologia da Saúde de Lisboa (ESTeSL), Lisbon, Portugal, November 22, 2019.

Santos S. Lecture. Genética Aplicada à Hemato-oncologia – Citogenética. Curso de Pós-Graduação em Medicina Laboratorial (4rd edition), Instituto de Ciências da Saúde da Universidade Católica Portuguesa and Centro de Medicina Laboratorial Germano de Sousa, Lisbon, Portugal, May 24, 2019.

Matos S. Lecture. Genética Aplicada à Hemato-oncologia – Biologia Molecular. Curso de Pós-Graduação em Medicina Laboratorial (4rd edition), Instituto de Ciências da Saúde da Universidade Católica Portuguesa and Centro de Medicina Laboratorial Germano de Sousa, Lisbon, Portugal, May 24, 2019.

Matos S. Lecture. Metodologias de Patologia Molecular aplicadas à clínica: PCR em Tempo Real aplicado ao Estudo de Doenças Oncológicas. Pós-graduação em Avanços em oncobiologia molecular aplicada ao diagnóstico e terapêutica, Escola Superior de Tecnologia da Saúde de Lisboa (ESTeSL), Lisbon, Portugal, November 9, 2019.

RoPlaVac

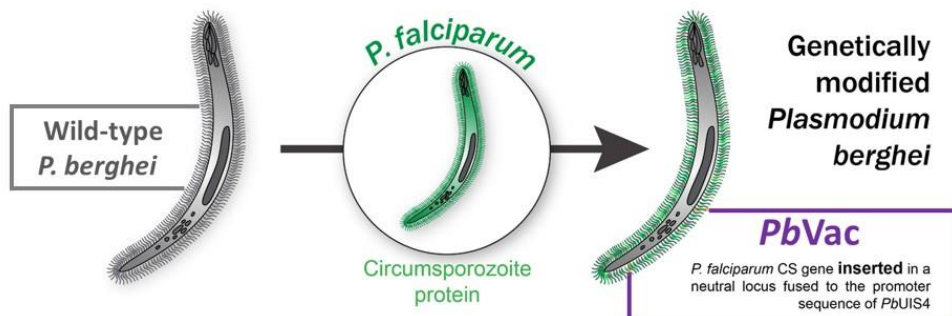
Major Interests/Objectives

We are a spin-off company of iMM, created in 2014. Our mission is to develop medical solutions against malaria, one of the most prevalent diseases worldwide. Malaria is caused by *Plasmodium* parasites, injected into their mammalian host as sporozoites, through the bite of an infected mosquito. Currently, RoPlaVac is engaged in three main endeavours: Vaccination-Development of a new whole-organism vaccine against malaria, based on the use of genetically modified rodent *Plasmodium* parasites; *Plasmodium* sporozoite cryopreservation- Development of an effective method to cryopreserve *Plasmodium* sporozoites for use in research and vaccination; In vitro *Plasmodium* sporozoite production- Development of a cell culture-based method to produce infective *Plasmodium* sporozoites for use in research and vaccination.

Director

Miguel Prudêncio, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes – Prudêncio Lab

Graphical Abstract



Team

António Manuel Barbeiro Mendes	PhD	Senior Postdoctoral Researcher
Maria Manuel Dias da Mota	PhD	Group Leader
Rui Miguel Prudêncio Cunha Pignatelli	PhD	Group Leader

Keywords / Research Areas

Malaria, *Plasmodium*, Vaccines, Liver Infection, Sporozoites, Cryopreservation.

Major Achievements

- Worldwide maintenance of patent covering RoPlaVac's novel vaccination strategy against malaria;
- Completion of first-in-humans clinical evaluation of the first vaccine candidate employing RoPlaVac's patented technology;
- An effective cryopreservation method for *Plasmodium* sporozoites is under optimization in collaboration with the company Smartfreez;
- A novel *in vitro* system for development of *Plasmodium* sporogonic stages was employed to assess the transmission-blocking activity of known insecticidal and antiretroviral compounds.

Selected Publications

Azevedo R, Mendes AM, Prudêncio M (2019). The impact of antiretroviral therapy on malaria parasite transmission. **Frontiers in Microbiology** 10:3048. (IF: 4.259, Citations: 0. Source: Web of Science).

Azevedo R, Mendes AM, Prudêncio M (2019). Inhibition of Plasmodium sporogonic stages by ivermectin and other avermectins. **Parasites & Vectors**. 12(1):594. (IF: 3.031. Citations: 0. Source: Web of Science).

Azevedo R, Markovic M, Machado M, Franke-Fayard B, Mendes AM, Prudêncio M (2017). A bioluminescence method for *in vitro* screening of *Plasmodium* transmission-blocking compounds. **Antimicrobial Agents Chemotherapy** 61(6). (IF: 4.302. Citations: 4. Source: Web of Science).

Mendes AM, Reuling IJ, Andrade CM, Otto TD, Machado M, Teixeira F, Pissarra J, Gonçalves-Rosa N, Bonaparte D, Sinfrônio J, Sanders M, Janse CJ, Khan SM, Newbold CI, Berriman M, Lee C, Wu Y, Ockenhouse CF, Sauerwein RW, Prudêncio M (2018). Pre-Clinical Evaluation of a *P. berghei*-Based Whole-Sporozoite Malaria Vaccine Candidate. **NPJ Vaccines** 3(54). (IF: 3.143. Citations: 0. Source: Web of Science and Scopus).

Mendes AM, Machado M, Gonçalves-Rosa N, Reuling IJ, Foquet L, Marques C, Salman AM, Yang ASP, Moser KA, Dwivedi A, Hermsen CC, Jiménez-Díaz B, Viera S, Santos JM, Albuquerque I, Bhatia SN, Bial J, Angulo-Barturen I, Silva JC, Leroux-Roels G, Janse CJ, Khan SM, Mota MM, Sauerwein RW, Prudêncio M (2018). A *Plasmodium berghei* Sporozoite-Based Vaccination Platform Against Human Malaria. **NPJ Vaccines** 3(33). (IF: 3.143. Citations: 1. Source: *Web of Science and Scopus*).

Ongoing Research Projects

2018/2021: Enabling strategies for enhanced whole-sporozoite malaria vaccines. Coordinator: Miguel Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Amount: € 234 000,00.

2017/2019: Production and maintenance of *Plasmodium*-infected mosquitoes. Coordinator: Miguel Prudêncio. Funding Agency: Merck. Amount: € 112 000,00.

2016/2019: Improving whole organism vaccines against malaria by genetic modification. Coordinator: António Mendes. Funding Agency: Fundação para a Ciência e a Tecnologia. Amount: € 197 648,00.

Publications in Peer Reviewed Journals

Azevedo R, Mendes AM, Prudêncio M (2019). The impact of antiretroviral therapy on malaria parasite transmission. **Frontiers in Microbiology** 10:3048. (IF: 4.259, Citations: 0. Source: *Web of Science*).

Azevedo R, Mendes AM, Prudêncio M (2019). Inhibition of *Plasmodium* sporogonic stages by ivermectin and other avermectins. **Parasites & Vectors**. 12(1):594. (IF: 3.031. Citations: 0. Source: *Web of Science*).

Invited Lectures and Seminars

Prudêncio M. *Plasmodium* Liver Infection and Antimalarial Strategies - Overview of Work from 2019. iMM Internal Seminar, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, December 11, 2019.

Prudêncio M. *Plasmodium berghei* Sporozoites Expressing PfCSP as a Whole-Sporozoite-Based Malaria Vaccine Candidate. Sanaria Inc., Rockville, MD, USA, September 18, 2019.

Communications in International Conferences

Prudêncio M. PbSPZ-PfCSP (PbVac) - Results of Clinical Trial and Future Plans. International PfSPZ Consortium Meeting, Rockville, MD, USA, November 19, 2019.

Internationalization

Joana Carneiro da Silva – University of Maryland;

Chris Janse and Shahid Khan - Leiden University;

Clemens Kocken - Biomedical Primate Research Centre, Rijswijk;

Robert Sauerwein - University of Nijmegen.

Patents/Prototypes

"Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine" (WO 2013156949 A1, also published as CN104302313A, EP2838554A1, US20150071966). Patent applications filed in Angola, Australia, Brazil, China, India, Japan, Mozambique, South Africa, United States, and European Patent (Euro-PCT), November 2014. Patent granted in India (07.08.2015), Mozambique (17.08.2015), South Africa (23.12.2015), Japan (2015), Australia (03.02.2017), USA (15.02.2017), China (20.11.2017), Europe (11.05.2018) and Hong-Kong (20.07.2018).

Advanced Teaching

Prudêncio M. Vaccination against malaria - Development and clinical evaluation of a new vaccine. Masters in Clinical Microbiology and Emerging Infectious Diseases, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21, 2019.

Prudêncio M. Malaria vaccination. Design, characterization and (pre)clinical evaluation of a new vaccine against malaria. Biology at the Host Microbe Interface PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 3, 2019.



Prudêncio M. Malaria: the quest for an effective vaccine. Frontiers of Research in Biology - Masters in Molecular Biology and Genetics, Faculdade de Ciências da Universidade de Lisboa, May 24, 2019.

Prudêncio M. Biomolecular methods for malaria research & Development of a new vaccine against malaria. Masters in Clinical Biochemistry, Faculdade de Ciências e Tecnologia, Universidade NOVA Lisboa, Lisbon, Portugal, June 5, 2019.

TechnoPhage SA

Major Interests/Objectives

TechnoPhage is a highly innovative drug discovery biopharmaceutical company focused on the development of proprietary biological drugs and repurposed compounds. Within the biologics arm, TechnoPhage is developing two classes of drugs, namely light-chain single-domain antibodies (sdAbs) and bacteriophage cocktails. TechnoPhage currently has 9 drug products into their development pipeline, each of which is being developed to treat medical indications such as diabetic foot ulcer infections, respiratory infections, Alzheimer's, age-related macular degeneration, plus other neurological and immunological disorders. We are in clinical stage with TP_102, a bacteriophage cocktail targeting diabetic foot ulcer infections.

Within the repurposing of chemical drugs, TechnoPhage has two chemical compounds ready to enter clinical trials, one that targets the on/off period related to Levo-DOPA induced dyskinesia and the other in spinal cord injury.

TechnoPhage has a strong IP position with over 65 patents granted and a total of over 140 patent applications in various jurisdictions.

QUADRO 1: INDICADOR GASTÃO CUNHA FERREIRA - EMPRESAS

Patenteamento internacional com origem portuguesa (prioridade portuguesa ou inventores residentes em Portugal) nos últimos 5 anos, resultados ordenados pelo acumulado dos últimos 5 anos:

	REQUERENTE	2014	2015	2016	2017	2018	TOTAL
1º	HOVIONE	28	29	44	51	50	202
2º	BIAL	30	52	56	33	24	195
3º	VENIAN		2	3	78	73	195
4º	BOSCH	20	30	15	22	66	153
5º	NOVADELTA	17	24	31	21	34	127
6º	TECNIMEDE	3	9	18	47	14	91
7º	BIOSURFIT	14	11	9	24	17	75
8º	TECHNOPHAGE	20	13	16	13	8	70
9º	OLI	17	10	5	9	13	54
10º	INL	2		12	8	25	47

Director

Miguel Garcia, PharmD, PhD, MBA

Team

Alexandra Wagner	MSc	Production scientist
Ana Almeida	BSc	Technician
Ana Isabel Guedelha da Silva Neves	MSc, Enginnering	IP and Legal Affairs Manager
Ana Raquel Martins Barbosa	MSc	Senior Scientist
Ana Filipa Martins	PhD	Scientist
Clara Isabel Rodrigues Leandro	MSc	Head of Infection
Daniela Jones-Dias	PhD	Head of Pre-clinical
Diana Sofia Chapela Duarte Pires	MSc	PhD Student
Helena Dordio	MSc	Quality
Manuel Garrido	PhD	Production Specialist
Manuela Teixeira	BSc	Financial Manager
Patricia Alexandra Norte Ferreira Pinto	BSc	Senior Technician
Roberta Zoppi	MSc	PhD Student
Sofia Volker Corte-Real	PhD	CSO
Susana Gonçalves	MSc	Operations Director

Keywords / Research Areas

Infection, Bacteriophages, Neuroscience, Small Domain Antibodies, Repurposing, GMP Manufacturing.

Major Achievements

Based on 14 years of R&D, TechnoPhage is now in a clinical stage company with a position to bring its products to commercial stage. In 2019 we put up and running a new facility for GMP manufacturing of biologics. Technophage also is now part of VectorB2B a nonprofit association with the mission to provide services from its partners.

Selected Publications

Chapela D, Sousa S, Martins I, *et al.* Author Correction: A zebrafish drug screening platform boosts the discovery of novel therapeutics for spinal cord injury in mammals. **Scientific Reports** 10(1):749. (IF: 4.011, Citations: 0. Source: Web of Science).

Ongoing Research Projects

Phage4BacID- PT2020 Co-Promoção coordinated by Technophage.

Patents/Prototypes

Main relevant patents of TechnoPhage filed in EU:

Patent Name	Number	Date of Filing
Phage 1: Antibacterial Phage, Phage Peptides and Methods of Use Thereof	10708834.6	05.02.2010
Phage 2: Antibacterial Phage, Phage Peptides and Methods of Use Thereof	11820825.5	15.03.2013
TP102: Compositions Comprising Cocktails of Antibacterial Phages and Uses Thereof For The Treatment Of Bacterial Infections	13725496.7	19.03.2013
TA101: Anti-Tumor Necrosis Factor-Alpha Agents and Uses Thereof	12783676.5	19.09.2012
CollectAB: Cell-Based Methods for Coupling Protein Interactions and Binding Molecule	14722391.1	03.03.2014
Technobodies: Engineered rabbit antibody variable domains and uses thereof	08753864.1	30.04.2008
Antibody molecules and peptide delivery systems for use in Alzheimer's disease and related disorders (collaborative shareholder FMUL)	WO2016120843 A1	29.01.2016