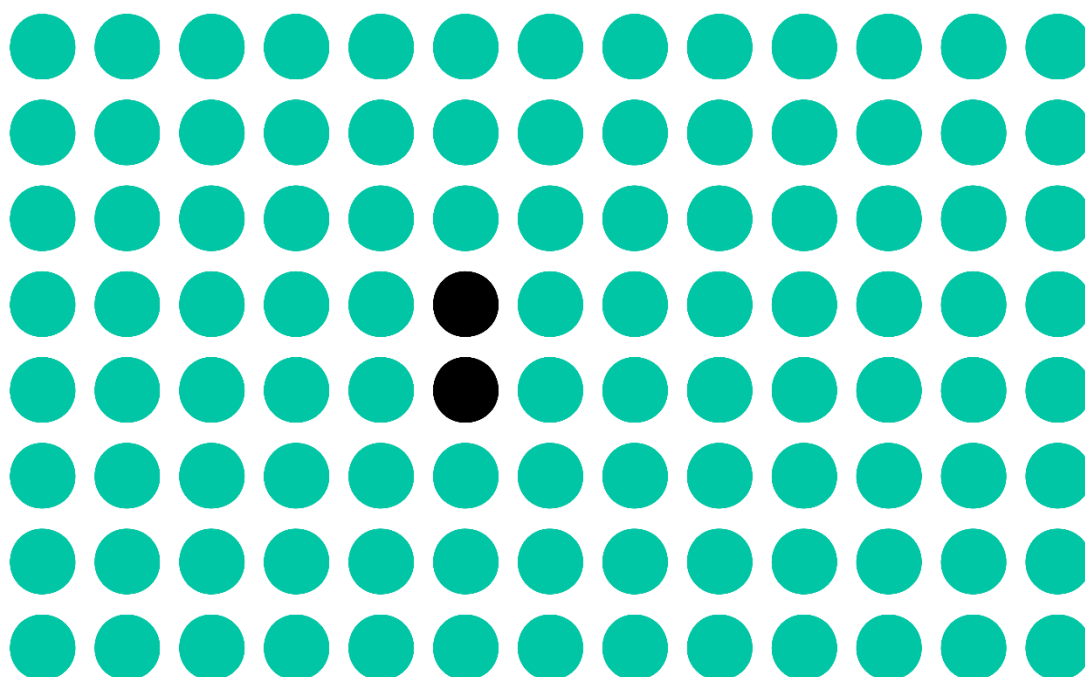




Instituto  
de Medicina  
Molecular

João  
Lobo  
Antunes

## Scientific Report 2023



Lisbon, April 2024

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## Organization and Structure

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

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

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

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

### iMM Associated Members

Universidade de Lisboa

Faculdade de Medicina da Universidade de Lisboa

Centro Hospitalar Universitário Lisboa Norte – Hospital de Santa Maria

Associação para a Investigação e o Desenvolvimento da Faculdade de Medicina

Fundação Oriente

### Board of Trustees

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

## Board of Directors

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

M. Carmo-Fonseca, MD, PhD  
President

Maria M. Mota, PhD  
Executive Director

Bruno Silva-Santos, PhD  
Vice-Director

## Council of Scientists

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

## Scientific Advisory Board

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

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

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

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

Yasmine Belkaid, PhD – National Institutes of Health, USA

## Industry Advisory Board

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

Daniela Couto – Biogeneration Ventures Fund

David Malta – Vesalius Biocapital

Isabel Ferreira – Versameb

Miguel Forte – Zelluna Immunotherapy

Pascale Redig – Janssen



## Societal Advisory Board

António Barreto, *Chairman* – Sociologist and Columnist

Graça Franco – Renascença Group

Paula Martinho da Silva – Lawyer

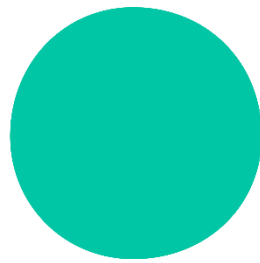
Diogo Lucena – NOVA School of Business and Economics

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

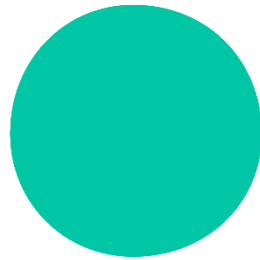
Henrique Leitão – Faculdade de Ciências da Universidade de Lisboa

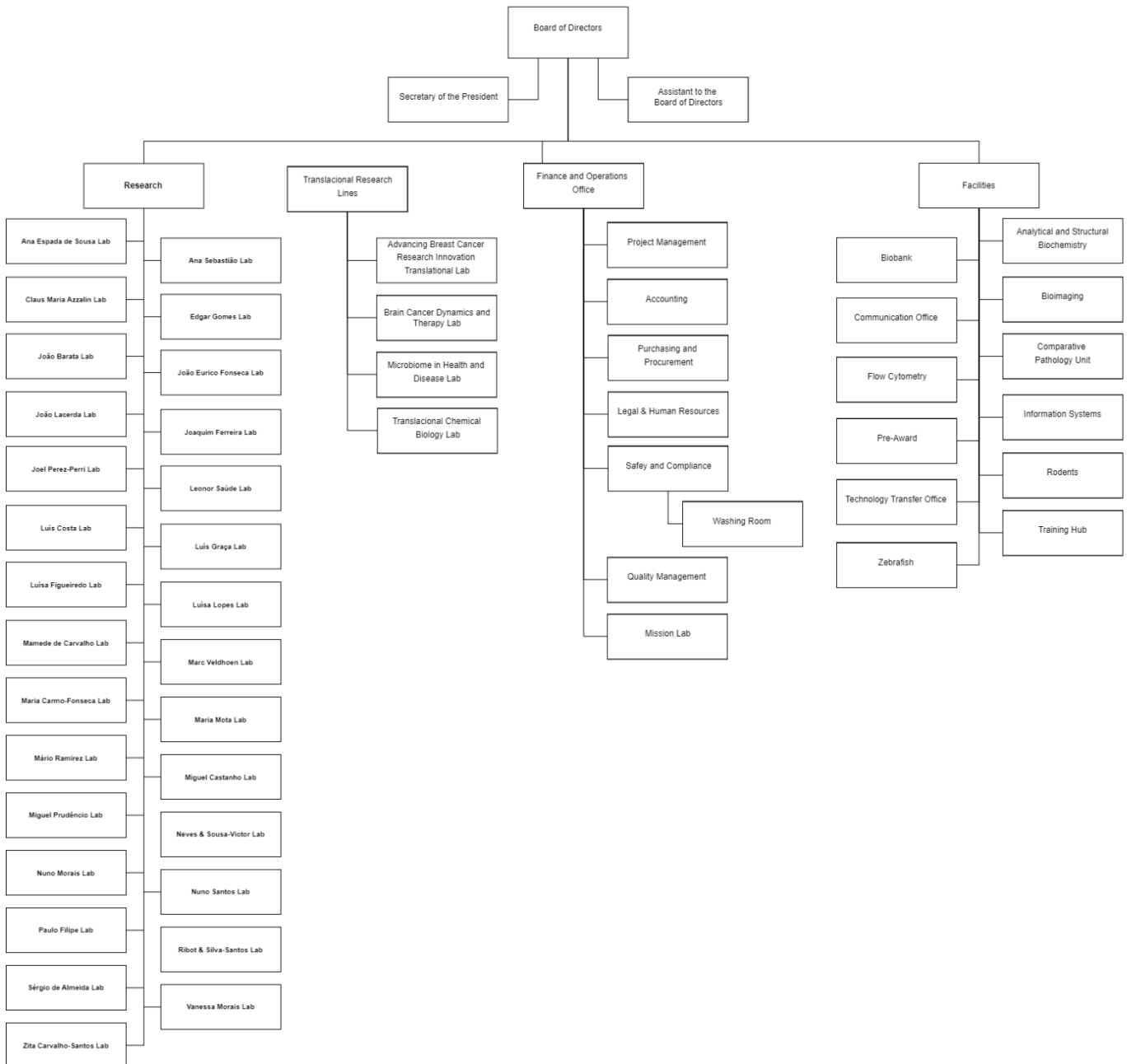
Pedro Norton – Finerge

Domília dos Santos – The dos Santos Group



# Organigram





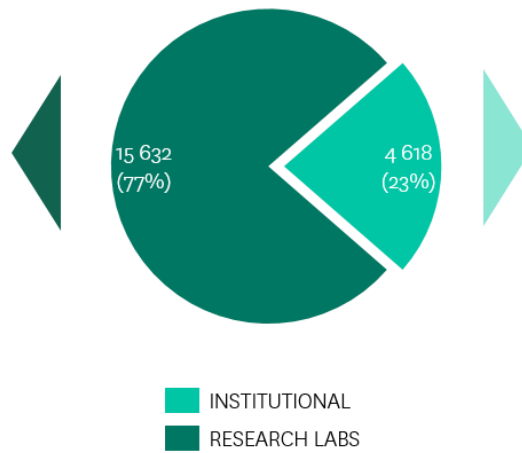


## Research Funding

### Expenditure in 2023

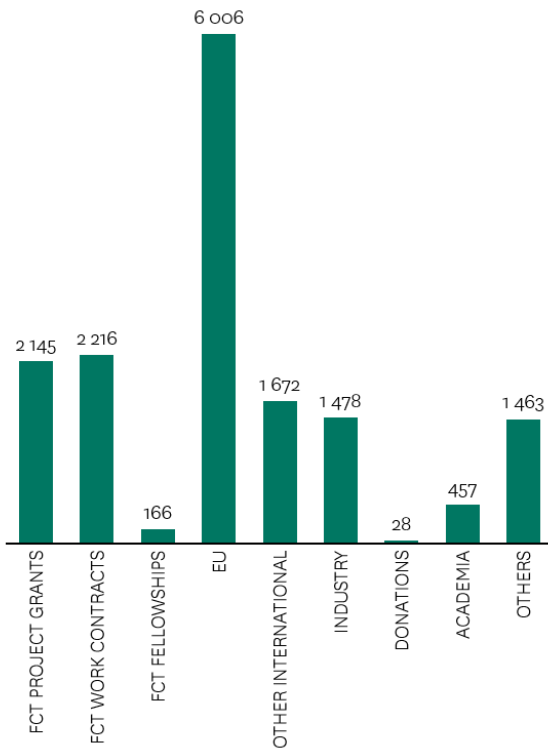
Total Expenditure: € 20.249.486<sup>1</sup>

Total Expenditures 20,3 M



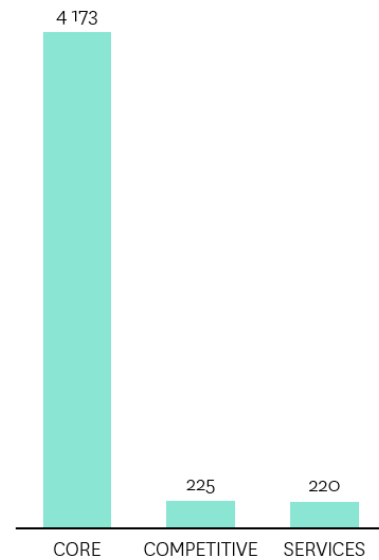
#### Research Labs

All Values in 000 Euros



#### Institutional

All Values in 000 Euros



<sup>1</sup> Includes total expenditures under specific institutional growth projects – EU Teaming and “Centro de Tecnologia e Inovação” and expenditures directed to core facilities and structure under indirect costs.

## Total Expenditures 2023

			(EUROS)
INSTITUTIONAL	CORE	4.173.328	
	COMPETITIVE SERVICES	224.665	
		219.625	4.617.618
RESEARCH LABS	FCT PROJECT GRANTS	2.145.103	
	FCT WORK CONTRACTS	2.216.433	
	FCT FELLOWSHIPS	165.503	
	EU	6.006.474	
	OTHER INTERNATIONAL	1.671.795	
	INDUSTRY	1.478.374	
	ACADEMIA	28.039	
	DONATIONS	456.747	
	OTHERS	1.463.399	15.631.868
TOTAL		20.249.486 <sup>2</sup>	

<sup>2</sup> Includes total expenditures under specific institutional growth projects – EU Teaming and “Centro de Tecnologia e Inovação” and expenditures directed to core facilities and structure under indirect costs.

### Number of Ongoing Research Grants in 2023

220 Research Grants:

Public National FCT: 64

Private National: 36

Public National Other: 8

Of which with the industry – 17

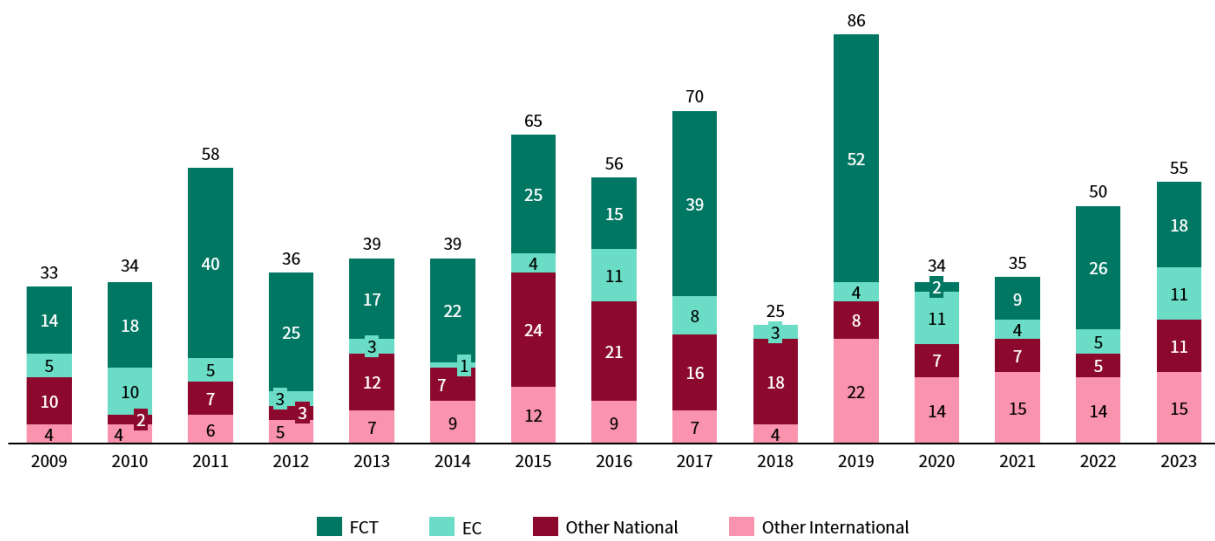
Public European Commission: 34

Private International: 78

Public International Other: 0

Of which with the industry – 40

### Number of Research Grants Initiated from 2009 to 2023



### Number of Research Funding Grants Initiated in 2023

55 Research Grants:

Public National: 18

Public International: 11

Private National: 11

Private International: 15

## Projects Initiated in 2023 through Competitive Funds

FUNDING AGENCY	RESEARCHER	iMM BUDGET	
"la Caixa" Foundation	Maria Rebelo	305 100,00 €	
	Luísa Lopes	50 000,00 €	
	Maria Mota	499 999,50 €	
	Pedro Victor	499 835,60 €	
European Commission	Gonçalo Bernardes	486 806,40 €	
	Gonçalo Bernardes	156 778,56 €	
	Edgar Gomes	150 000,00 €	
	iMM	39 750 000,00 €	
	João Eurico da Fonseca	907 186,25 €	
	Patrícia Costa Reis	490 039,00 €	
	Luisa Lopes	170 200,00 €	
	Maria Mota	2 467 196,25 €	
	Mário Ramirez	121 947,50 €	
	Pedro Silva	750 339,50 €	
	Zita Carvalho-Santos	1 481 513,00 €	
	Fundação para a Ciência e a Tecnologia (FCT)	Cláudia Faria	248 750,00 €
		Afonso Malheiro	50 000,00 €
Vasco Crispim Romão		50 000,00 €	
Isaura Martins		49 995,00 €	
Carmen de Sena Tomás		49 901,25 €	
Luís Costa		8 000,00 €	
Luís Graça		250 000,00 €	
Luísa Figueiredo		49 937,50 €	
Luisa Lopes		49 375,00 €	
Pedro Prudêncio		49 375,00 €	
Inês Bento		49 772,50 €	
Diana Fontinha		50 000,00 €	
Nuno Santos		50 000,00 €	
Ivo Martins		43 750,00 €	
Julie Ribot		249 982,50 €	
Anne-Valerie Gendrel		50 000,00 €	
Robert Manfred Martin		50 000,00 €	
Catarina Brás-Pereira		86 614,59 €	
Gilead Sciences, Lda		Karine Serre	10 000,00 €
		iMM	15 000,00 €
	João Lacerda	20 000,00 €	
	Maria Carmo-Fonseca	37 000,00 €	
ANI	iMM	6 412 725,76 €	

### Protocols, Donations and Awards<sup>3</sup>

FUNDING AGENCY	RESEARCHER	iMM BUDGET
University of Washington	Gonçalo Bernardes	174 488,25 €
Alchemab Therapeutics Ltd	Mamede Carvalho	20 031,25 €
Bristol Myers Squibb	Luís Costa	25 000,00 €
Chan Zuckerberg Initiative	Zita Carvalho-Santos	328 310,41 €
ETHRIS GmbH	Maria Carmo-Fonseca	102 911,00 €
GASOXMED Gases Medicinais SA	Luisa Lopes	3 500,00 €
Laboratórios Pfizer, Lda	iMM	5 000,00 €
Liga Portuguesa Contra o Cancro	Marta Sofia Martins	6 800,00 €
Takeda	Bruno Silva-Santos	1 835 625,00 €
Ministério da Defesa Nacional	Luisa Lopes	10 000,00 €
Morton Cure Paralysis Fund	Isaura Martins	27 665,08 €
Sociedade Portuguesa de Neurocirurgia	Luisa Lopes	2 500,00 €
The Michael J. Fox Foundation	Luisa Lopes	13 023,43 €
Several	Gonçalo Bernardes	87 827,50 €
Vifor Pharma Portugal SA	João Eurico da Fonseca	100 000,00 €

<sup>3</sup> Considered protocols, donations and awards that fund projects, infrastructures and seminars.

## IMM Applications and Secured Competitive Funding

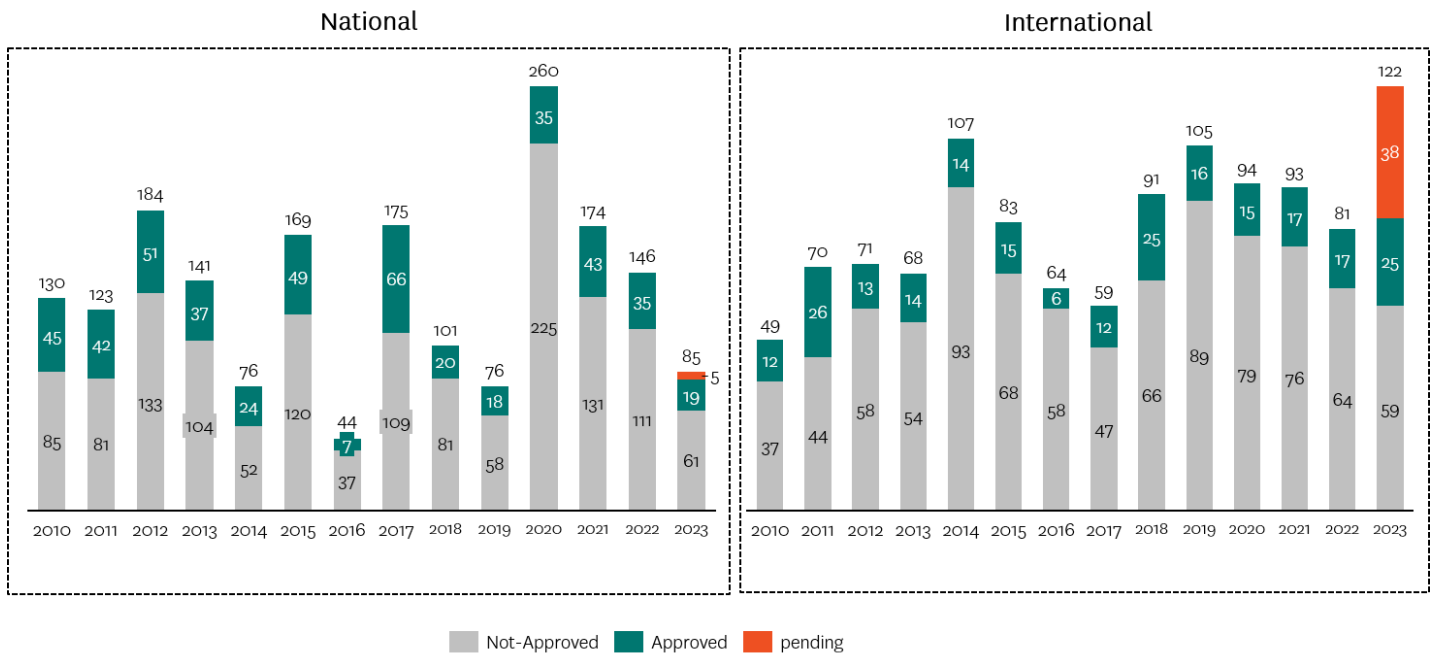


Figure 1: Submitted and approved applications to national and international competitive funding schemes since 2010. The number of submitted applications corresponds to those effectively communicated to the Pre-Award.

## Funds Secured<sup>4</sup>

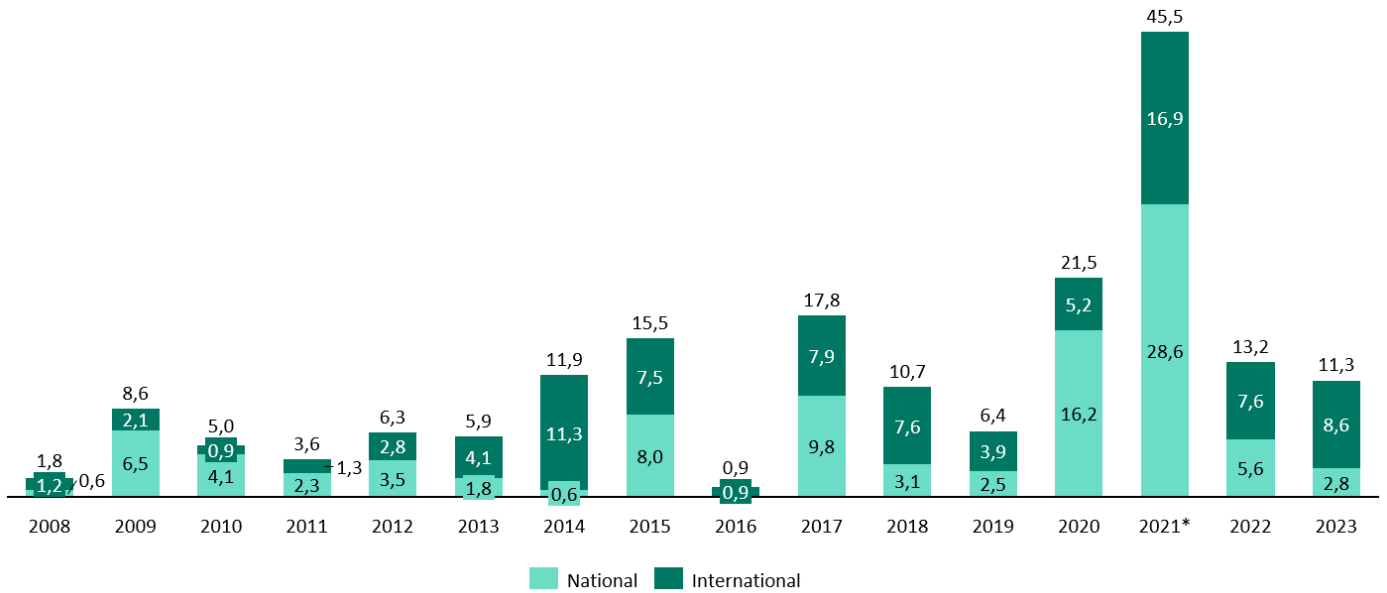


Figure 2: Total funds secured by iMM (in millions of €) in international and national competitive funding schemes since 2008. Secured funds per year correspond to the sum of the iMM budget of the approved applications submitted in the corresponding year (irrespective to the project starting date).

<sup>4</sup> Includes Teaming Proposal Secured funds for 6 Years – 15M EU; 15PT GOV: 2,75M FCT and 4M Private National Funds.

## Funding Sources of iMM Applications

In 2023, iMM researchers and staff have submitted grants to the following funding schemes:

INTERNATIONAL				
PRIVATE	PUBLIC			
AFM-Telethon	European Commission	European Research Council - ERC	ERC Advanced Grants	
Alzheimer's Association			ERC Consolidator Grants	
Beug Foundation		Pillar 2	Cluster 1 - Health	
Bristol Myers Squibb			Cluster 1 - Mission Cancer	
Chan Zuckerberg Initiative			Cluster 4 - Digital, Industry and Space	
Concern Foundation		Partnerships	IHI	
EMBO			Postdoctoral Fellowships	EuroHPC Joint Undertaking
			Installation Grants	EDCTP3
			Scientific Exchange Grants	THCS
European Association for Cancer Research			Interreg Sudoe	
EUROSPINE			COST	
Fight Kids Cancer		European Innovation Council - EIC	EIC Pathfinder	
Foundation for Research in Rheumatology			EIC Transition	
Hevolution Foundation		Marie Skłodowska-Curie Actions - MSCA	Staff Exchanges	
Impetus Grants			COFUND	
Johnson & Johnson			Postdoctoral Fellowships	
"la Caixa" Foundation		CaixaResearch Health	CITIZENS	
		CaixaImpulse Health Innovation	Widening	Doctoral Networks
		Postdoctoral Junior Leader Fellowships		Pathways to Synergy
Michelson Medical Reserach Foundation			Twinning	
Morton Cure Paralysis Fund			Hop-On	
Muscular Dystrophy Association				
Novartis				
The Branco Weiss Fellowship				
The New York Stem Cell Foundation				
Wings for Life				
Worldwide Cancer Research				



NATIONAL			
PRIVATE		PUBLIC	
BIAL	Maria de Sousa Award	Fundação para a Ciência e Tecnologia - FCT	CEEC Individual
Biocodex Microbiota Foundation Portugal			FCT RESTART
FLAD	Science Award Mental Health		
	Programa UP Ensino Superior		
Fundação Amélia de Mello	Prémios Alfredo da Silva		
Gilead Sciences	Program Génese		
Liga Portuguesa Contra o Cancro - LPCC	Colorectal Cancer		
	Oncologia LPCC-NRS		
	Prémio Liga Inovação		
MSD			
Pfizer   Sociedade das Ciências Médicas de Lisboa			
Sociedade Portuguesa de Doenças Metabólicas			
Sociedade Portuguesa de Hematologia			

### Funding Programmes

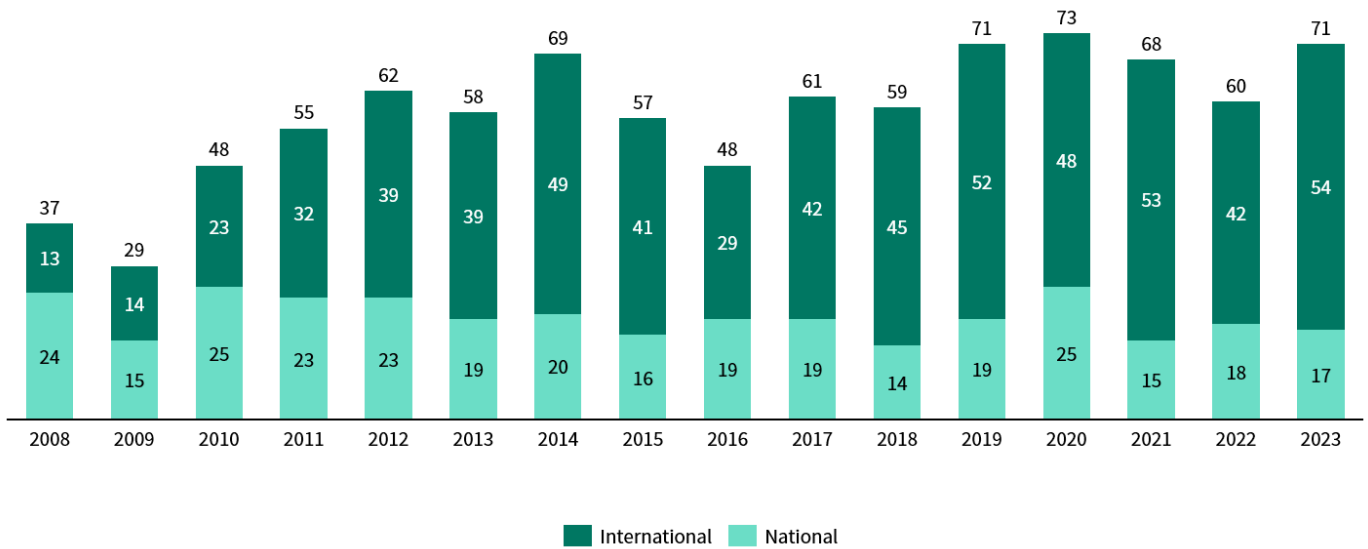


Figure 3: Evolution of the diversity of international and national funding schemes for which iMM researchers submitted applications from 2008 to 2023.

## 2023 Activities Highlights

### Human Resources

		2022	2023
<b>Researchers</b>	PhD	212	219
	PhD Students	122	110
	MSc Students	124	87
	Master	47	41
	Graduate	18	25
	Other	8	3
		<b>531</b>	<b>485</b>
<b>Technical Staff</b>	PhD	8	9
	Master	46	46
	Graduate	18	34
	Other	14	16
		<b>86</b>	<b>105</b>
<b>Administrative Staff</b>	PhD	13	16
	Master	19	16
	Graduate	17	19
	Other	11	7
		<b>60</b>	<b>58</b>
<b>TOTAL</b>		<b>677</b>	<b>648</b>

### Selection of Prizes and Awards

#### European Innovation Council Ambassador

Miguel Castanho (Group Leader)

#### European Research Council Proof of Concept Grant

Edgar Gomes (Group Leader)

#### 2022 Clinical Medicine Prizes by BIAL (Honorable Mention)

Cláudia Faria (iMM-CARE Translational Lab Director)

#### "la Caixa" Foundation Junior Leader Fellowship

Maria Rebelo (Gonçalo Bernardes Lab)

Sara Silva Pereira (Luísa Figueiredo Lab)

#### European Research Council Advanced Grant

Maria Mota (Group Leader)

#### Best Master Thesis Awards 2021/2022 (Announced in 2023)

João Fontela (João Barata Lab)  
Ana Fraga (Miguel Prudêncio Lab)  
Vicente Almeida (Ribot & Silva-Santos Lab)

#### European Federation for Medicinal Chemistry and Chemical Biological Awards 2023 for Excellence in Chemical Biology

Gonçalo Bernardes (Group Leader)

#### João Lobo Antunes PhD Merit Awards 2022/2023

Saumya Kumar (Luís Graça Lab)  
Henrique Machado (Luisa Figueiredo Lab)

#### Morton Cure Paralysis Fund Research Grant

Isaura Martins (Leonor Saúde Lab)

#### Prémio Universidade de Lisboa 2021 (Announced in 2023)

Maria Carmo-Fonseca (Group Leader)

#### EMBO Member

Luísa Figueiredo (Group Leader)

#### Lídia Silva Santos Postdoctoral Achievement Award 2023

Cong Tang (Gonçalo Bernardes Lab)  
Bruno Silva (Claus Azzalin Lab)

#### “la Caixa” Foundation CaixaImpulse Health Innovation Call 2023

Luísa Lopes (Group Leader)  
Pedro Soares-Castro (Nuno Santos Lab)

#### 9th Edition Gilead GÉNESE Program

Karine Serre (iMM-Laço Hub)  
João Barata (Group Leader)  
Diogo Gomes da Silva (João Lacerda Lab)

#### Chan Zuckerberg Initiative’s Measuring Metabolism across Scales Program

Zita Carvalho-Santos (Group Leader at iMM), and Ricardo Henriques and Jorge Carvalho (Instituto Gulbenkian de Ciência)

#### FCT Restart Program

Maria Rebelo (Gonçalo Bernardes Lab)

#### Pfizer Prize 2023

Luís Graça (Group Leader)

#### Scientific Prize by Universidade de Lisboa

Miguel Prudêncio (Group Leader)

Nuno Santos (Group Leader)

Joaquim Ferreira (Group Leader)

#### “la Caixa” Foundation Health Research Call 2023

Pedro Sousa-Victor (Group Leader)

Maria Mota (Group Leader)

#### European Research Council Consolidator Grant

Pedro Sousa-Victor (Group Leader)

#### Saúde Sustentável Award - Personalidade do Ano (initiative by Jornal de Negócios and Sanofi)

Maria Carmo-Fonseca (Group Leader)

#### Breakthrough Idea Grant 2023 Awards

João Barata (Group Leader)

Joana Neves and Pedro Sousa-Victor (Group Leaders)

Marc Veldhoen and Vanessa Morais (Group Leaders)

#### European Innovation Council Accelerator Program

TargTex

#### Sociedade Portuguesa de Hematologia Grant

Eduardo Espada and Ana Alho (João Lacerda Lab)

#### Call for Scientific Employment (CEEC)

Ana Raquel Coelho (Gonçalo Bernardes Lab)

Maria Rebelo (Gonçalo Bernardes Lab)

Ana Rita Cascão (Brain Cancer Dynamics and Therapy Translational Lab)

Pedro Sousa-Victor (Group Leader)

Elisabete Martins (Mário Ramirez Lab)

Sandra Trindade (Luísa Figueiredo Lab)

Ângelo Chora (Maria Mota Lab)

## Productivity at a Glance

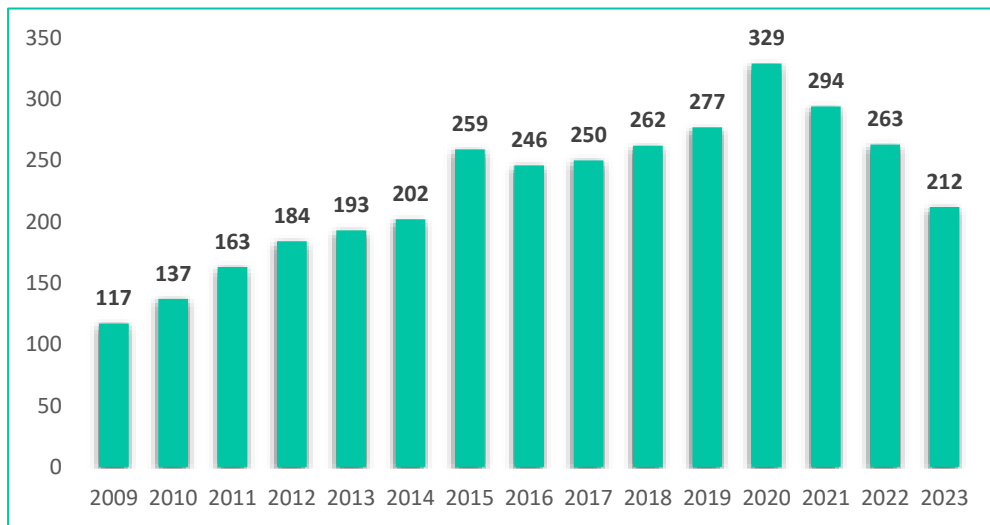
	2022	2023
Communications in International Conferences	364	320
Communications in National Conferences	233	209
Invited Lectures and Seminars	294	335
Organization of Conferences	88	77
Prizes and Honours	170	97
MSc Theses Completed	61	75
PhD Theses Completed	21	18

## Innovation

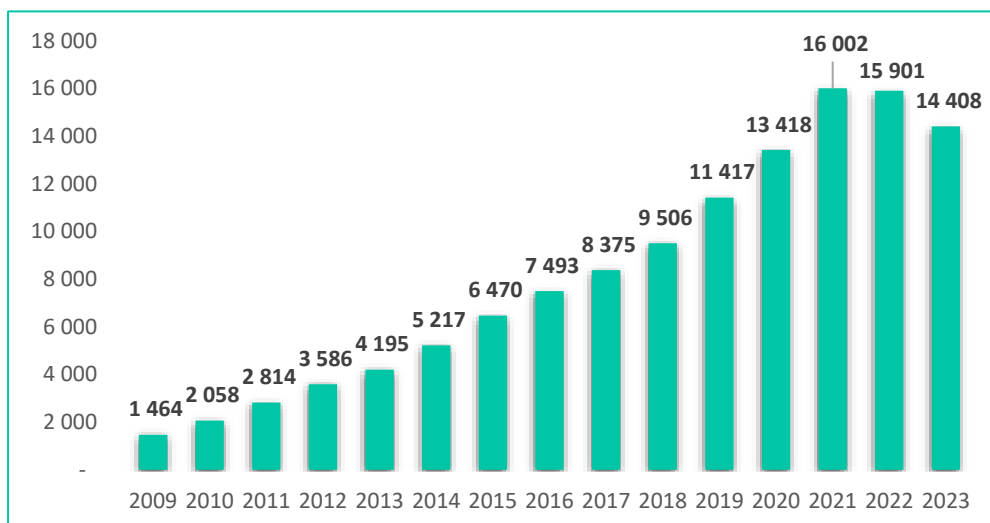
	2022	2023
New Inventions	29	22
License Agreements	8	10
Patents Filings	42	17
Industry & External Partners Collaborations	238	249

## Publications in International Journals

(Source: Web of Science™)



Published Items in Each Year: 2009-2023



Citations in Each Year: 2009-2023

Papers in 2023: **212**

Sum of the times cited: **106,235**

Average citations per item: **31.13**

h-index: **130**

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: 2009-2023. 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 2009-2023

(Source: Web of Science™)

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

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

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

Davatchi F, Assaad-Khalil S, Calamia KT, Crook JE, Sadeghi-Abdollahi B, Schirmer M, Tzellos T, Zouboulis CC, Akhlagi M, Al-Dalaan A, Alekberova ZS, Ali AA, Altenburg A, Arromdee E, Baltaci M, Bastos M, Benamour S, Ben Ghorbel I, Boyvat A, Carvalho L, Chen W, Ben-Chetrit E, Chams-Davatchi C, Correia JA, Crespo J, Dias C, Dong Y, Paixao-Duarte F, Elmuntaser K, Elonakov AV, Grana Gil J, Haghdoost A-A, Hayani RM, Houman H, Isayeva AR, Jamshidi AR, Kaklamanis P, Kumar A, Kyrgidis A, Madanat W, Nadji A, Namba K, Ohno S, Olivieri I, Vaz Patto J, Pipitone N, de Queiroz MV, Ramos F, Resende C, Rosa CM, Salvarani C, Serra MJ, Shahram F, Shams H, Sharquie KE, Sliti-Khanfir M, Tribolet de Abreu T, Vasconcelos C, Vedes J, Wechsler B, Cheng YK, Zhang Z, Ziaei N (2014). The International Criteria for Behcet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. **Journal of the European Academy of Dermatology and Venereology** 28(3):338-347.

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.

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.

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.



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

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.

Zerr I, Kallenberg K, Summers DM et al (2009). Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. **Brain** 132:2659-2668.

[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

Alpalhão M, Sousa D, Frade JV, Patrocínio J, Garrido PM, Correia C, Brazão C, Mancha D, Nuncio MS, Pelerito A, Borrego MJ, Filipe P (2023). [Human Immunodeficiency Virus infection may be a contributing factor to Monkeypox infection: analysis of a 42-case series](#). **Journal of the American Academy of Dermatology**, 88(3):720-722.

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## Seminars, Workshops and Events

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### Computational Biology and Bioinformatics Seminar

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January 18

“Impact of imperfect diagnosis in association analyses”

João Malato, Luís Graça Lab

January 25

“Cell Competition: Separating the Winners from the Losers”

Alexandre Afonso, Nuno Morais Lab

February 8

“Bioinformatics in academia and industry - a tale of two cities”

João Carriço, Biomérieux

February 22

“Identifying cells and clusters in an injured spinal cord by single cell RNA-seq”

Daniel Ribeiro, Leonor Saúde Lab

March 8

“Using scRNAseq to uncover new Trypanosoma brucei populations in vivo”

Lara López Escobar, Luísa Figueiredo Lab

March 22 (online)

“Identifying OXPHOS deficient skeletal myofibres in patients with m.3243A>G-related mitochondrial myopathy”

Conor Lawless, Wellcome Trust Centre for Mitochondrial Research

Host: Claus Azzalin Lab

April 5

“Systematic annotation of the short-lived transcripts in human iPSCs”

Rui Luís, Carmo-Fonseca Lab

April 12

“Knowledge-Based Informatics Framework to Support Medicine”

Margarita Sordo, Brigham and Women’s Hospital, Harvard Medical School

Host: IMM-Laço Hub

April 19

“Principles and practice of computer-aided drug design”

Francisco J. Enguita, IMM Analytical and Structural Biochemistry Unit

May 17

“RNAsum: implementing patients transcriptome profiling in precision oncology setting”

Jacek Marzec, Nuno Morais Lab

May 31

“Single-cell transcriptional landscape of circulating Tfh cells in COVID-19 patients”

Diogo Fonseca, Luís Graça Lab

June 14

“Single cell analysis of the spinal cord reveals a persistent, injury-induced neuronal cell state”

Daniel Ribeiro, Leonor Saúde Lab

June 21

“Uncovering human naive CD4 T cell biology one cell at a time”

Beatriz Moleirinho and Margarida Pedro, Ana Espada de Sousa Lab

July 12

“p16/ARF as a transcriptomic marker of cell senescence regulation”

Rita Silva, Nuno Morais Lab

November 8

“Lobo Roadmap and Best Practices”

Daniel Silva, IMM IT Director

December 6

Jacek Marzec, CoLAB AccelBio

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## Immunology Club

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March 22

“Investigating the impact of IL-17 in peripheral nerve regeneration”

André Luís Bombeiro, Bruno Silva-Santos Lab

April 5

“Dissecting the role of miR-34c-5p in human CD4+T cells”

Cláudia Estima, RNA Systems Biology Lab, BioISI

Host: Ana Espada de Sousa Lab

April 19

“Functional convergence of V $\delta$ 1+ and V $\delta$ 2+  $\gamma\delta$  T cells in response to SARS-CoV-2 infection”

Rui Vieira, Luís Graça Lab

May 3

“JAK-STAT signalling: a role in early arthritis?”

Rui Lourenço Teixeira, João Eurico da Fonseca Lab

May 17

“Homeostasis of CD4+ Regulatory T cells after allogeneic hematopoietic cell transplantation”

Ana Alho, João Lacerda Lab

May 31

“A role for AIP in the biology of T cells”

Gonçalo Malpica, Marc Veldhoen Lab

June 14

“Dissecting the cytokine-specific mRNome of gd T cells”

Anita Gomes, Ribot & Silva-Santos Lab

June 19

Special Immunology Club: “Scientific publishing at JEM: What, How and Why”

Montserrat Cols, Senior Scientific Editor, Journal of Experimental Medicine, Rockefeller University Press, NY

Host: Marc Veldhoen

June 28

“Modification of monoclonal antibodies towards reduction of immunogenicity”

Rodrigo Pedroso, Luís Graça Lab

July 12

“CCL28/CCR10 axis in ARDS: Friend or Foe?”

André Gomes, Ana Espada de Sousa Lab

October 25

“Interaction between dendritic cells and memory T cells beyond lymphoid organs”

Elena Hernández García, Ribot & Silva-Santos Lab

“Single-cell transcriptional landscape of circulating Tfh and Treg cells in COVID-19 patients”

Diogo Fonseca, Luís Graça Lab

November 8

“The aryl-hydrocarbon receptor interacting protein (AIP) in T cell biology”

Himadri Mukhopadhyay, Marc Veldhoen Lab

November 22

“Unveiling the role of CD1a in human regulatory T cell development”

Nicole Martins, Ana Espada de Sousa Lab

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## Internal Seminar

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February 1

“Placing gd T cells in Plasmodium Liver stage infection”

Ângelo Chora, Maria Mota Lab

“Science must go on, even during a pandemic”

Maria Mota, iMM Group Leader

February 15

“Shreds and Slivers of (my) Malaria Vaccine Research”

Helena Nunes Cabaço, Miguel Prudêncio Lab

“Splicing maths for dummies”

Nuno Morais, iMM Group Leader

March 1

“Immune dysfunction and regenerative failure in aging”

Joana Neves, iMM Group Leader

March 15

“A Selective SARS-CoV-2 Host-Directed Antiviral Targeting Stress Response to Reactive Oxygen Species”

Cong Tang, Gonçalo Bernardes Lab

“Our lab contribution towards readiness and preparedness for the next viral pandemic”

Miguel Castanho, iMM Group Leader

March 29

“Multi-dimensional cartography of healthy, pre-malignant and malignant breast tissues”

Karine Serre, iMM-Laço Hub/Bruno Silva-Santos Lab

“The Epidemic of Hybrid Immunity”

Luís Graça, iMM-Group Leader

April 12

“Developing strategies to achieve immunocompetence”

Afonso Almeida, Ana Espada de Sousa Lab

“A (short) trip through the healthy versus malignant thymus”

Bruno Silva-Santos, iMM Group Leader



May 24

“How to train your T cells: Development of CAR-T cells using DNA from Plasmodium as immunotherapy against cancer”

Diogo Silva, João Lacerda Lab

João Lacerda, iMM Group Leader

June 7

“Anti-HIV-1 activity and mode of action of pepRF1”

Ana Salomé Veiga, Miguel Castanho Lab

“Flavivirus capsid proteins interaction with host lipid systems and viral RNA”

Nuno Santos, iMM Group Leader

July 5

“Nuclear waste”

M. Carmo-Fonseca, iMM Group Leader

July 19

“Cerebral Venous Thrombosis- Does recanalization matter?”

Diana Aguiar de Sousa, Joaquim Ferreira Lab

“Breaking barriers in tissue tropism”

Luísa Figueiredo, iMM Group Leader

October 4

“Bioengineering Peptides for Nanotechnology”

Ivo Martins, Nuno Santos Lab

“Biomechanical regulation of membrane contact sites in skeletal muscle pathophysiology”

Edgar Gomes, iMM Group Leader

October 18

“The ups and downs of vascular biology”

Cláudio Franco, Católica Biomedical Research Centre, Instituto de Medicina Molecular

November 15

“Insights about the role of B cells and follicular T cells in Juvenile Idiopathic Arthritis”

Rita Moura, João Eurico da Fonseca Lab

“The microbiome as a new actionable tool in precision oncology”

Ana Margarida Almeida, iMM-CARE - Head of Microbiome in Health & Disease Translational Laboratory

Chair: Gonçalo Malpica (Marc Veldhoen Lab)

November 29

"Live-cell imaging of R-loops - a novel tool to detect DNA/RNA hybrids"

Robert Martin, Sérgio de Almeida Lab

"Novel players impacting IL-7R-mediated signaling and leukemia development"

João Barata, IMM Group Leader

Chair: Anwesha Ghosh (Ana Sebastião Lab)

December 13

"What determines Acute Myeloid Leukemia recognition by Delta One T cells?"

Sofia Mensurado, Ribot & Silva-Santos Lab

Chair: Beatriz Silva (Claus Azzalin Lab)

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## Monday Lecture

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January 9

"Reward and aversion in the brain: from genes to cells to circuits to behavior"

Ana João Rodrigues - ICVS, Universidade do Minho

Host: Sandra Vaz (Ana Serbastião Lab)

January 16

"Mosquito immune responses against malaria parasites"

Elena Levashina, Max Planck Institute for Infection Biology

Host: Luísa Figueiredo

January 23

"Synthetic reconstitution of cortical polarity in unpolarized cells"

Emmanuel Derivery, MRC Laboratory of Molecular Biology

Host: Edgar Gomes

January 30

"Discovery of a metal-driven signaling pathway that regulates cell plasticity"

Raphaël Rodriguez, Institut Curie

Host: Marta Marques (Gonçalo Bernardes Lab)

February 6

"Cellular senescence in cancer: a double-edged sword"

Juan Pedro Martinez-Barbera, Institute of Child Health, University College London

Host: Leonor Saúde

February 13

"The role of mitochondria in cellular homeostasis in cancer and aging disorders"

Christian Frezza, Cologne University

Host: Vanessa Morais

February 27

“Charting tissue diversity with bioinformatics”

Francesca Finotello, Universidade de Innsbruck

Hosts: Ana Espada de Sousa & Alexandre Raposo (Ana Espada de Sousa Lab)

March 13

“New therapeutic opportunities for breast cancer treatment”

Eva González-Suárez, Centro Nacional de Investigaciones Oncológicas

Host: Sandra Casimiro (Luís Costa Lab)

March 20

“Molecular Engineering of Safe and Efficacious Oral Protein Drugs”

Martin Münzel, Novonordisk

Host: Miguel Castanho

March 27

“Comparative approaches reveal regenerative mechanisms in the spinal cord”

Maysa Mokalled, Washington University School of Medicine

Host: Leonor Saúde

April 3

“Amino Acid Concentration Signatures: a novel platform for detecting multiple types of cancer from a blood test, and suggesting personalized treatment”

Emma Yates, Co-Founder & Chief Scientific Officer, Proteotype Diagnostic Company

Host: Cong Tang (Gonçalo Bernardes Lab) / Gonçalo Bernardes

April 17

“Huntington Disease as a neurodevelopmental disorder with adult-onset manifestations”

Sandrine Humbert, Grenoble Institute of Neuroscience

Host: Luísa Lopes

April 24

“Fighting Fire with Fire: Endogenous Retroviruses Boost Human Immunity”

Cédric Feschotte, Cornell University

Host: Nuno Morais

May 8

“Making the retina: from nuclear movements to fate choices”

Caren Norden, Instituto Gulbenkian de Ciência (IGC)

Host: Luísa Figueiredo

May 15

“The Impending Storm: Environmental inputs into epigenetic states during development and inheritance”

Miguel Ramalho-Santos, Lunenfeld-Tanenbaum Research Institute and University of Toronto

Host: Edgar Gomes

May 22

“Neuronal Specification from Neurogenesis”

Soraia Barão, John Hopkins University

Host: Vanessa Morais

May 29

“Towards improving synaptic transmission in the ageing brain”

Ira Milosevich, MIA Portugal

Host: Luísa Lopes

June 5

“Decoding host-microbiota interactions in the gut”

Patrick Varga-Weisz, University of Essex

Host: Jean-Christophe Lone (Luís Graça & Marc Veldhoen Labs)

June 19

“Investigating TERRA biology: from telomere-specific polyadenylation to its function in telomerase regulation”

Emilio Cusanelli, University of Trento, Italy

Host: Claus Azzalin

June 26

Klaas van Gisbergen, Champalimaud Centre

Host: Marc Veldhoen

July 3

“How does genome 3D organization direct alternative splicing”

Gil Ast, Tel Aviv University

Host: M. Carmo-Fonseca

July 10

“Stargazin in the etiology of neurodevelopmental disorders”

Ana Luísa Carvalho, CNC-Coimbra

Host: Luísa Lopes

July 17

Special João Lobo Antunes Merit PhD Thesis Award:

“Unveiling the regulation of germinal centre responses and antibody production by follicular T cells”

Saumya Kumar, Luís Graça Lab

“Impact of adipose tissue colonization by *Trypanosoma brucei* during infection”

Henrique Machado, Luísa Figueiredo Lab

Host: Training Hub

July 24

Special Lídia Silva Santos Postdoctoral Achievement Award

“A selective SARS-CoV-2 host-directed antiviral targeting stress response to reactive oxygen species”

Cong Tang, Gonçalo Bernardes Lab

“The alternative lengthening of telomeres mechanism jeopardizes telomere integrity if not properly restricted”

Bruno Silva, Claus Azzalin Lab

Host: Training Hub

September 25

"Follicular helper T cells in the control of humoral immunity"

Di Yu, Frazer Centre of Children's Immunotherapy Research, Australia

Host: Luís Graça

October 16

"Epigenomic programming of brain plasticity and disease risk by ovarian hormones."

Marija Kundakovic, Fordham University

Host: Zita Santos

October 23

"Biological design principles for controlling gene expression"

João Guimarães, Faculdade de Medicina da Universidade de Lisboa, iSTARS ERA Chair

Host: Nuno Morais

October 30

"Molecular insight into the poly(A) tail machinery"

Lori Passmore, LMB - Cambridge University

Host: Luísa Figueiredo

November 13

"T cells as regulators of germinal center kinetics"

Johanne Jacobsen, Laboratory of Immunoregulation and T Cell Biology, University of Oslo, Rikshospitalet, Norway

Host: Luís Graça

November 20

"Immunometabolism at the crossroad between inflammation and aging"

Maria Mittelbrunn, Center of Molecular Biology, Madrid

Hosts: Joana Neves & Pedro Sousa-Victor

November 27

"Mitotic errors as a new source of epigenetic instability"

Stamatis Papathanasiou, IMB Mainz

Host: Robert Martin (Sérgio de Almeida Lab)

December 4

"Road to persistence - how Plasmodium falciparum survives the dry season"

Silvia Portugal, Max Planck Institute for Infection Biology

Host: Maria Mota

December 11

"Reproducible science in an era of greater research complexity"

John Ioannidi, Stanford University

Host: Nuno Morais

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## Neurosciences Seminar

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January 9

"Characterization of adenosine and BDNF signaling pathways in the pre-symptomatic phase of Rett Syndrome"

Ana Laura Duarte – Ana Sebastião Lab

January 16

"Unravelling the role of dose and 5-HT<sub>2A</sub> receptor activation in the long-lasting effects of psilocybin"

Chloé Galipeau, Ana Sebastião Lab

"Role of astrocytes in the endocannabinoid-mediated long-term depression in the medial prefrontal cortex"

Leandro Freiras, Ana Sebastião Lab

January 23

"Landing into purinergic receptors and Alzheimer's disease"

Paloma Aivar Mateo, Universidad Europea de Madrid

February 6

"The transcriptional regulation of the human ADORA2A gene in aging and in Alzheimer's disease"

Joana Condesso, Luísa Lopes Lab

"Interaction between cannabinoid receptors and adenosine receptors: implication on synaptic plasticity in the hippocampus"

Madalena Gualdino, Ana Sebastião Lab

February 13

"Long-lasting neurobiological and antidepressant actions of psilocybin: transcriptomic modifications"

Ana Paula Condesso, Ana Sebastião Lab

March 6

"Mouse spinal cord vascular transcriptome analysis identifies CD9 and MYLIP as injury-induced players"

Isaura Martins, Leonor Saúde Lab

March 13

"NAD-5HT: New Advance in the treatment of Depression using Serotonin"

Ana Salomé Correia, ICBAS U. Porto/ CINTESIS U. Porto

March 20

"Efeitos da cafeína nos cotransportadores de cloreto durante o desenvolvimento da retina"

Amanda Alves Nascimento, Universidade Federal Fluminense/Brasil

March 27

"DBS for the treatment of Parkinson's Disease"

Pedro Batista, Luísa Lopes Lab

April 3

"The Science behind HBK-15: Exploring the Multimodal Compound's Antidepressant and Procognitive Effects"

Klaudia Lustyk, University of Jagiellonian, Krakow, Poland

April 17

"Cellular and subcellular targets of cannabinoids in the basal ganglia: from signaling to behavior and beyond"

Luigi Bellocchio, INSERM U1215 Neurocentre Magendie, Université de Bordeaux

April 24

“Unveiling the CB1R effect in glutamate transporters: the where matters”

Joana Ribeiro, Ana Sebastião Lab

May 8

“Role of mitochondrial dynamics and metabolism in postnatal neural stem cells differentiation”

Rita Soares, Ana Sebastião & Vanessa Morais Labs

May 15

“Using the Mouse Walker to Quantify Locomotor Dysfunction in a Mouse Model of Spinal Cord Injury”

Ana Isidro, Leonor Saúde Lab

May 22

“Bean There, Drank That: The impact of caffeine in adult neurogenesis and synaptogenesis”

João Moreira, Ana Sebastião & Luísa Lopes Labs

May 29

“DS12: a thiazolidinone past, present, and future”

Fernando Lopez Alvez, Ana Sebastião Lab

June 5

“Cognitive comorbidities of experimental absence seizures”

Mariana Sottomayor, Ana Sebastião Lab

June 26

“Mechanisms underlying the physiological role of Amyloid Precursor Protein in glutamatergic synapses”

Joana Saraiva, Luísa Lopes Lab

July 3

“Direct conversion of human skin fibroblasts into induced neurons: A model do study age-related synaptic dysfunctions”

Catarina Candeias Ferreira, Luísa Lopes Lab

July 10

“PhD pitch: BDNF receptor cleavage in Alzheimer’s disease: unveiling the impact on microglia”

Mafalda Manso, Ana Sebastião Lab

July 17

“Small compounds and TrkB-FL cleavage: a sum up of the last year”

Sara Oliveira, Ana Sebastião Lab



September 25

"Impact of manipulating the neuroinflammatory context in epileptic-like slices: Potential synergy between IL-10 and NLRP3 signaling pathway"

Ana Pereira, Ana Sebastião Lab

October 2

"A multimodal compound HBK-15 - the mechanisms behind its fast antidepressant-like and procognitive effects"

Karolina Pytka, Department of Pharmacodynamics, Faculty of Pharmacy, Jagiellonian University Medical College

October 9

"Run, brain, run! In vitro and in vivo modulation of adult oligodendrogenesis by BDNF"

Joana Mateus, Ana Sebastião Lab

October 16

"Pyroptotic Deadly Curse of Neurons in Alzheimer's Disease: Unravelling the role of NLRP3 Inflammasome Pathway"

Tiago Ferreira, Ana Sebastião Lab

October 23

"The Metabolic Profile of Synaptic Mitochondria"

Bernardo Cetra Antunes, Vanessa Morais Lab

November 6

"Therapeutic potential of cannabinoids in stress-related psychiatric disorders and their molecular mechanisms"

Sâmia Joca, Department of Biomedicine, Health Faculty, Aarhus University, Denmark

November 20

"Is the zebrafish spinal cord a glitch in the matrix?"

Dalila Silva, Leonor Saúde Lab

November 27

"GDNF signaling pathways in Absence Seizures"

Klaudia Wojtal, Utrecht University

December 4

"Tonic GABA inhibition and absence seizures are distinguishably modulated by 5-HT<sub>2A</sub> receptors in normal and epileptic rats"

Tatiana Morais, Cardiff and Malta University, IMM Ana Sebastião Lab

December 11

"What happens when your support cells aren't so supportive? Astrocyte contribution to synaptic dysfunction in the SOD1G93A mice"

Sara Pinto, Ana Sebastião Lab

December 18

"Inter-hippocampal demyelination in the early onset of Alzheimer's disease"

Artemis Ftara, University of Valencia

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## Oncobiology Club

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January 18

"The integrity of adherens junctions is a key determinant for the success of resensitization to radioiodine therapy in metastatic thyroid cancer"

Micaella Miranda, Ana Luísa Silva Lab, ISAMB-Instituto de Saúde Ambiental

February 1

"Combined TLR3 and CD40 signalling triggers macrophage-dependent antitumour immunity"

Carolina Jardim, Bruno Silva-Santos Lab

March 1

"Splicing modulation to rescue the activity of a biallelic BRCA2 mutant in a patient derived cell line"

Beatriz Lima, Carmo-Fonseca Lab

March 15

"Cell Competition: Separating the Winners from the Losers"

Alexandre Afonso, Nuno Morais Lab

March 29

"Clinical Impact of Whole Exome Sequencing and RNAseq in Sarcoma Patients Care"

Tânia Peniche, Luís Costa Lab

April 12

"Characterizing the crosstalk between the Circadian Molecular Clock and the CK2-PI3K signaling axis in T-ALL"

Patrícia Amaral, João Barata Lab

April 26

"A positive feedback loop between IFN-g signaling and cholesterol uptake sustains PDL-1 expression in breast cancer cells"

Ana Magalhães, Sérgio Dias Lab

May 24 (online)

“Bioinspired human stomach-on-chip with in-vivo like function and architecture”

Daniel Ferreira, I3S

June 7

“RNAsum: implementing patients transcriptome profiling in precision oncology setting”

Jacek Marzec, AccelBio in collaboration with Nuno Morais Lab

June 21

“New arrivals at iMM: Two syngeneic models of Luminal breast cancer”

Sandra Casimiro, Luís Costa Lab

July 5

“Development of anti-IL-7R $\alpha$  antibodies as a targeted therapy for T-cell Acute Lymphoblastic Leukemia”

Mafalda Duque, João Barata Lab

August 4

“Fusion Oncoproteins as Drivers of Brain Tumor Development”

Steve Mack, St Jude's Hospital (Memphis USA)

Host: Cláudia Faria (João Barata Lab & Biobank)

October 4

"Precision weapons against cancer: Harnessing the potential of protein inhibitors and degraders"

Bárbara B. Sousa, Gonçalo Bernardes Lab

October 18

"Charting New Frontiers in Colorectal Cancer Immunotherapy with V $\delta$ 1 T Cells"

Rafael Blanco Dominguez, Ribot & Silva-Santos Lab

November 15

"Impact of cancer-associated mutations in the BRCA2 interactome"

Laura Cathleen Grzegorzec, Carmo-Fonseca Lab

November 29

"Efficacy of RANK pathway and CDK4/6 inhibition in immune competent Luminal breast cancer models"

Maria Martelo, Luís Costa Lab

December 13

"Transient activation of macrophages leads to tumour regression in a murine model of breast cancer"

Ana Marta Bica, Nuno Morais Lab

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## Other Events

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January 9

Special Seminar: "The Afterlife of the Adipocyte: Implications for Health and Disease"

Phil Scherer, U. Southwestern, Dallas, USA

Host: Luísa Figueiredo

January 11

Special Seminar: "Circulating Tumor Cells" (online)

Nicola Aceto, Swiss Federal Institute of Technology (ETH) Zurich

Host: Ana Magalhães (Sérgio Dias Lab)

January 11

Science Careers (online)

Cátia Janota, Business Data Analyst, Amgen

January 18

BLEND Art & Science Talks: "Digital Twin"

Sérgio Eliseu, University of Aveiro & ISCE DOURO (Institute of Educational Sciences of Douro)

January 26-27

RNA in Disease – IX ptRNA Meeting

January 30

Science Careers (online)

Joana C. Carvalho, Science Illustration and Visual Communication

February 3

CAML Rheumatology Series: "Musculoskeletal injections: ultrasound-guided versus conventional"

Esperanza Naredo, Hospital Universitario Fundación Jiménez Díaz, Madrid

February 7

Special Seminar

Laura Elo, University of Turku, Finland

Host: Jean-Christophe Lone (Luís Graça & Marc Veldhoen Labs)

February 9

Special Seminar: "Is there a herpesviruses-related antibody signature in patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome?"

Nuno Sepúlveda

Host: Luís Graça

February 14

Science Careers (online)

Joana Pinto Melo, Medical Writer, W4Research

February 23

Out of Our Box Seminar: "What do political scientists do?"

Pedro Magalhães, Institute of Social Sciences (ICS), University of Lisbon

February 28

"Controversial issues in Sjögren's syndrome"

Chiara Baldini, Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy

March 3

Special Seminar: "Synchronized Microscopy and Flow Cytometry: The exclusive advantages of the Imaging Flow Cytometer Amnis® Imagestream®x MK II for Multidisciplinary Research"

Alessandro Serra, Field Application Scientist, Luminex Corporation

Host: Mariana Fernandes (Flow Cytometry Unit) & José Rino (Bioimaging Unit)

March 7

CAML Rheumatology Series: "The human synovium in inflammatory arthritis: a single cell perspective"

Mojca Frank Bertoneclj, BioMed X, Heidelberg, Germany

March 9

FlowJo Workshop

Serena di Cecilia, Application Scientist, BD Biosciences

March 9

BLEND Art & Science Talks

Catarina Pombo Nabais, Science-Art-Philosophy Laboratory (SAP Lab)

March 10

Special Seminar: "The importance of water in receptor function"

Anthony Watts, University of Oxford

Host: Ivo Martins (Nuno Santos Lab)

March 15

Science Careers (online)

Adriana Temporão, Clinical Project Manager, Biofabri

March 28

NeuroSeS Seminar: "Behavior, stroke and neuroimaging - an analysis about spatial delusions and multimodal networks"

Pedro Alves, Hospital Santa Maria, Faculdade de Medicina da Universidade de Lisboa

March 29

FLxFlow Tech's Café: "The Bigfoot Cell Sorter – Flexibility and Performance, a legend come true!"  
Guerric Epron, Thermo Fisher Scientific

March 30

Out of Our Box Seminar: "Designing data with a 'Post-Infographic mindset'"  
Stephanie Posavec, Information designer, artist, author

April 13

Science Careers (online)  
Jorge Borbinha, E-detail Medical Sales Representative, IQVIA/Alnylam Pharmaceuticals

April 21

Debate Session: "Accelerating Science and Publication in Biology, step by step"  
Mafalda Pimentel, ASAPbio & Instituto Gulbenkian de Ciência

April 27

Out of Our Box Seminar: "Impact investment – mobilising capital for society's most pressing challenges"  
António Miguel, Managing Partner, MAZE

May 4

Special Seminar: "Tackling the complexity of ageing with systems approaches"  
João Pedro de Magalhães, Institute of Inflammation and Ageing, University of Birmingham  
Research Laboratories  
Host: Luísa Figueiredo Lab

May 5

Special Seminar: "Splicing as a drugging modality"  
Alejandro Reyes, Data Scientist, Novartis Institutes for BioMedical Research, Basel, Switzerland  
Host: Nuno Morais Lab

May 9

CAML Rheumatology Series: "Immune response produced by mRNA COVID-19 vaccine on rheumatic patients"  
João Gonçalves, Faculdade de Farmácia da Universidade de Lisboa

May 9-12

XVI CAML PhD Students Meeting

May 17

Special Seminar: "Peroxisome-organelle cooperation and dynamics in human health and disease"  
Michael Schrader, University of Exeter, UK  
Host: Vanessa Morais Lab

May 18

Science Careers (online)

Tânia Perestrelo, Key Account Manager (Health & Biotech), Izasa Scientific

May 25

Out of Our Box Seminar: "The development of decision-making across diverse cultural contexts"

Dorsa Amir, UC Berkeley Department of Psychology

May 26

Special Seminar: "Unpicking How the Tumor Microenvironment Sculpts Metastasis and Therapy Failure"

Erik Sahai, Francis Crick Institute

Host: Sérgio Dias

June 3, 4, 8, 10

Feira do Livro – Lisboa

Hands-on Activities and conferences

June 9

"Cellular quiescence uncouples the proteome from the transcriptome"

Rita Sousa-Nunes, King's College London

Host: M. Carmo-Fonseca

June 15

Seminar: "Quantitative, reproducible confocal fluorescence microscopy made easy"

Isabel Groß, PicoQuant - Application Specialist for Microscopy

Host: José Rino (Bioimaging Unit)

June 16 (online)

Science Careers

Bárbara Abreu, Postdoctoral Research Associate, Astex Pharmaceuticals

June 19

Launch iMM-CARE: Boosting Clinical Research for the Benefit of Society

June 20

CAML Rheumatology Series: "Clinical trials in Sjogren's: challenges and opportunities"

Benjamin Fisher, Institute of Inflammation and Ageing, University of Birmingham, United Kingdom

June 21

Special Seminar: "A new therapeutic approach to leverage vision restoration in glaucoma"  
Raquel Boia, Instituto de Investigação Clínica e Biomédica de Coimbra (iCBR) & VectorB2B - Drug Development

VectorB2B "a young successful story"

Teresa Duarte, VectorB2B - Drug Development  
Host: Miguel Castanho Lab

June 29

iMM Master's Day 2023

June 29

BLEND Laser Talk: "Imaginary Beings; three characters walk into the Bar LUCA..."  
Nigel Helyer

July 4

Science Careers  
Jorge Sampaio, Bioinformatics Engineer, Loka

July 10

Special Seminar: "Designing bioinspired peptides for products development"  
Octavio L. Franco, Universidade Católica de Brasília e Universidade Católica Dom Bosco  
Host: Nuno Santos

July 11

Special Seminar: "New frontiers in live imaging with the Zeiss Lattice lightsheet"  
Jonathan Shewring, ZEISS Application Specialist  
Host: José Rino (Bioimaging Unit)

September 12

CAML Rheumatology Series: "Use of biomarkers to improve therapeutics strategies in pediatric rheumatology"  
Dirk Föll, Department of Pediatric Rheumatology and Immunology, University of Münster, Germany

September 14

Out of Our Box Seminar: "Short-term rentals in Lisbon: recent research, shortcomings and question marks"  
Susana Peralta, NOVA School of Business and Economics

September 18-19

iMM Scientific Retreat



September 20 (online)

iMM Alumni Meeting

Elsa Abranches (Astrazeneca), Pedro Alves (i3S), Margarida Trindade (ITQB NOVA), Catarina Ramos (Champalimaud Foundation), Pedro Papotto (University of Manchester) and Helena Brigas (BIAL)

September 21

Special Seminar: "The peptidoglycan as a signaling molecule in host-microbe interactions"

Ivo Boneca, Institut Pasteur, Unit of Biology and Genetics of the bacterial cell wall

Host: Mário Ramirez

September 22

Special Seminar: "Impact of microbiota-derived peptidoglycan on infections by *Candida albicans*"

Qiao Yuan, Nanyang Assistant Professor, School of Chemistry, Chemical Engineering and Biotechnology, Nanyang Technological University, Singapore

Host: Claire Tang (Gonçalo Bernardes Lab)

September 28 (online)

Science Careers

Ana Sofia Brandão, Jr Data Team Lead, IQVIA

September 29

European Researchers' Night | RAISE

October 12-13

EMBO Young Scientists Forum

October 17

CAML Rheumatology Series: "Mendelian Lupus: A new and growing field"

Alexandre Belot, Pediatric Rheumatology Unit, Centre Hospitalier Universitaire de Lyon, France, National Reference Centre for Rare Rheumatic & Autoimmune Diseases in Children (Raise) & INSERM

October 17

CoLAB AccelBio Workshop: Navigating Intellectual Property Challenges in Pharma and Biotech

Anton Hutter, Venner Shipley

October 19

iMM Postdoc Day

October 19

Special Out of Our Box Seminar: "Changing the paradigm to overcome three major global crisis"

Francisco Ferreira, ZERO – Association for the Sustainability of the Earth System

Host: Green Team

October 24-30  
Semana da Mama 2023 (iMM-Laço Hub)

October 25  
Science Careers  
Bárbara Gomes, AccelBio

October 26  
Welcome Session for Master Students

October 26  
Out of Our Box Seminar: "'45 Graus' and the power of podcasts: stretching the boundaries of knowledge, stimulating critical thinking and communicating science"  
José Maria Pimentel, 45 Graus  
Host: Nuno Morais

October 31  
BLEND Art & Science Talks  
Rudolfo Quintas, Media Artist

November 2  
Biophysics Club: "Probing polarity and viscosity by time-dependent fluorescence shifts: Applications in enzyme and membrane studies"  
Martin Hof, Director of the J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences

November 3  
Special Seminar: "Ontogeny and stability of the Foxp3 regulatory T cell population"  
Benoit Solomon, Centre for Immunology and Microbial Infections, France  
Host: Luís Graça

November 7  
NeuroSeS Seminar: "Ageing transcriptomes and cognitive biases"  
Nuno Morais, iMM Group Leader

November 8  
FLxFlow Tech's Café: "Multiomics and TotalSeq Reagents"  
Jean-Baptiste Guillerme, BioLegend

November 16  
Special Seminar: "Regulation of gene expression and tumor suppression in high-risk leukemia"  
Sinisa Dovat, Pennsylvania State University  
Host: João Barata

November 23

Special Seminar: "Structural Basis of a Marginally Stable Client Recognition by an Hsp40/ JDP Chaperone"

Micael S. Silva, Department of Chemical and Structural Biology, Weizmann Institute of Science, Rehovot, Israel

Host: Nuno Santos

November 24

iMM Comparative Pathology Unit Annual Meeting

November 29

Bioimaging Users Meeting

November 30

Science Careers

André Jerónimo Santos, Medical Manager in Neurology & Immunology, Merck Group

December 4, 6 and 7

iMM Comparative Pathology Unit – Histology Crash Course

December 12

iMM Flow Cytometry Users Meeting

December 14

Biophysics Club: "Open technologies in the quest for nanoscale live-cell imaging"

Ricardo Henriques, Optical Cell Biology Laboratory, Instituto Gulbenkian de Ciência

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## Parasitology Club

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January 17

"Groups at increased risk of malaria disease and death: Status of safety and efficacy of chemopreventive strategies in these groups"

Emanuelle Bache, CERMEIL, Lambarene, Gabon

January 31

"Impact of a gammaherpesvirus on Plasmodium berghei infection in vivo"

Andreia Mósca, Miguel Prudêncio & Maria Mota Labs

February 7

"From zero to many. When Plasmodium replication meets damage!"

Inês Bento, Maria Mota Lab

February 14

"Molecular engineering of *Leishmania donovani* for the development of whole cell vaccine against Malaria and Leishmaniasis"

Akriti Srivastata, Miguel Prudêncio Lab

February 28

"What's the Me-tter with the poly(A) tail? – Finding the potential m6A Methyltransferase in *Trypanosoma brucei*"

Christoph Wenzl, Luísa Figueiredo Lab

March 7

"Heterogeneity of *T. brucei* among tissue populations"

Lara López Escobar, Luísa Figueiredo Lab

March 14

"Ivermectin hybrids - potential insecticidal and multistage antiplasmodial drugs for malaria control"

Diana Fontinha, Miguel Prudêncio Lab

March 21

"Keep your friends happy and your enemies happier!"

Ângelo Chora, Maria Mota Lab

March 28

"Madeira dengue outbreak - a follow up of symptomatic and asymptomatic infections"

Margarida Vigário, Maria Mota Lab

April 18

"Malaria Vaccination and Age"

Helena Nunes Cabaço, Miguel Prudêncio Lab

May 2

"Stem cell-derived microvascular infection models to study malaria pathogenesis"

François Korbmacher, EMBL Barcelona

May 16

Henrique Machado, Luísa Figueiredo Lab

May 23

"Plasmodium cross-stage interplay modulates parasite virulence"

Sónia Pereira, Maria Mota Lab

May 30 (online)

“Actin organization in *Toxoplasma gondii* is controlled by an unconventional myosin motor protein”

Aoife Heaslip, University of Connecticut

June 20

“m6A in the poly(A) tail: the next chapter”

Lúcia Serra, Luísa Figueiredo Lab

June 27

“De Novo Protein Decoys: from COVID-19 to Malaria”

Maria Rebelo, Gonçalo Bernardes Lab

July 4

“How do trypanosomes cytoadhere to the endothelium?”

Sara Silva Pereira, Luísa Figueiredo Lab

July 11

“The liver stage of *Plasmodium* infection - written in extracellular vesicles?”

Bárbara Teixeira, Miguel Prudêncio & Maria Mota Labs

September 26

"Effect of dosage on the protective efficacy of whole-sporozoite vaccines for immunization against malaria"

Diana Moita, Miguel Prudêncio Lab

October 10

"Impact of a gammaherpesvirus on *Plasmodium berghei* infection in vivo"

Andreia Mósca, Miguel Prudêncio & Maria Mota Labs

October 17

"Expanding the knowledge in liver stage *Plasmodium* replication"

Inês Bento, Maria Mota Lab

October 24

MSc Students Welcoming Session

Hugo Luiz, Maria Beatriz Câncio, Marta Matos and Mariana Sousa

October 31

“poly(A) me-TAILation – investigating mRNA stability in *T.brucei*”

Christoph Wenzl, Luísa Figueiredo Lab

November 7

“Whole-organism vaccines against *P. falciparum* for enhanced efficacy and scope”

Akriti Srivastata, Miguel Prudêncio Lab

November 14

"Forging New Frontiers: The Power of Academic-Industrial Collaboration in Malaria Research"  
Manuel Ruiz, MERCK

November 21

"Can motile cells be encapsulated with 10XGenomics microfluidic system?"  
Lara López Escobar, Luísa Figueiredo Lab

November 28

Masters Students Training Session

December 5

"Glucose and lipid handling in mice infected with *Trypanosoma brucei*"  
Abdulbasit Amin, Luísa Figueiredo Lab

December 12

Ângelo Chora, Maria Mota Lab

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## Pizza Seminar

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January 10

"R-loops as regulators of pre-mRNA processing"  
Madalena Almeida, Sérgio de Almeida Lab

January 24

"Imprinting fidelity in mouse iPSCs depends on sex of donor cell and medium formulation"  
Maria Arez, IST-iBB (Institute of Bioscience and Bioengineering)

"Autism: past, present and future perspectives"

Jorge Cardoso, Miguel Remondes Lab

February 7

"Development of small therapeutics for the treatment of metastatic breast cancer"  
Catarina Gonçalves, Miguel Castanho Lab

February 28

"Novel antiviral strategies: development and testing SARS-CoV-2 inhibitors"  
Inês Saraiva, Nuno Santos Lab

March 14

“Bean There, Drank That: The impact of caffeine in adult neurogenesis and synaptogenesis”

João Moreira, Ana Sebastião Lab

“m6A in the poly(A) tail: the next chapter”

Lúcia Serra, Luísa Figueiredo Lab

March 28

“Pieces of a complex puzzle: jaks and stats in early arthritis”

Rui Teixeira, João Eurico da Fonseca Lab

“(Not So) Fantastic Bacteria and How to Type Them: Bioinformatics Edition”

Rafael Mamede, Mário Ramirez Lab

April 11

“Novel TAT-TrkB compound in Alzheimer’s disease: Rescuing BDNF-mediated synaptic plasticity and cognitive behaviour in 5xFAD mice”

Tiago Coelho, Ana Sebastião Lab

“Deep Learning Approaches for the Analysis of 3D Microscopy Images”

Hemaxi Narotamo, Cláudio Franco Lab

May 2

“NPM1-mutated Acute Myeloid Leukemias - clinical and molecular relevance”

Marta Coelho, Gonçalo Bernardes Lab

“Developing targeted therapeutic approaches for MYBPC3 splicing mutations in Hypertrophic Cardiomyopathy”

Marta Furtado, Carmo-Fonseca Lab

May 16

“The role of Arp2/3 complex in skeletal muscle postnatal development”

Catarina Sequeira, Edgar Gomes Lab

“Go the extra mile: In vitro and in vivo modulation of adult oligodendrogenesis by BDNF”

Joana Mateus, Ana Sebastião Lab

May 30

“Replumbing the Central Nervous System - Macrophages as potential modulators of the vascular response after spinal cord injury in adult zebrafish”

Mariana Costa, Leonor Saúde Lab

“A role for AIP in T cell biology”

Gonçalo Malpica, Marc Veldhoen Lab

June 20

“1 year and 9 months at iMM”

Jean-Christophe Lone, Marc Veldhoen & Luís Graça Labs

July 4

“Mechanism of cell migration in Arteriogenesis”

Daniela Ramalho, Cláudio Franco Lab

“A Slice of Discovery: Unravelling the Mysteries of Circular RNAs”

André Gabriel, iMM Analytical and Structural Biochemistry Unit

October 3

"The zombie uprising: too early, too late or just right?-The role of senescent cells after SCI"

Ana Isidro, Leonor Saúde Lab

"Next generation nanotechnology based vaccines"

Deepanwita Ghosh, Luís Graça Lab

October 17

"Cardiac development: a journey through transcriptomic and splicing dynamics"

Beatriz Gomes da Silva, Carmo-Fonseca Lab

"iPSCs differentiation into mammary epithelial cells: a hit and miss story"

Alice Borges, Carmo-Fonseca Lab

October 31

“Data analysis pitfalls: the example of a cancer microbiome study”

Rafael Fresca Mamede, Mário Ramirez Lab

November 14

"BDNF as a beacon of trophic support: Extracellular vesicles mirror BDNF-TrkB dysfunction in Alzheimer's disease"

Tiago Costa Coelho, Ana Sebastião Lab



## Training Hub

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

### Team

Head of the Training Hub and Director of the LisbonBioMed PhD Program: Claus M. Azzalin, PhD

Executive Manager: Filipa Nunes, PhD

Training Hub Assistant and Alumni Community Manager: Mafalda Silva

Coordinator of MSc studies: Leonor Saúde, PhD

Coordinator of PhD Studies: Domingos Henrique, PhD

Coordinator of Postdoctoral Training: Vanessa Morais, PhD

### Advanced Training in Numbers

	2023
Postdoctoral Fellows	<b>72</b>
Started in 2023	7
PhD Students	<b>131</b>
Started in 2023	21
MSc Students	<b>144</b>
Started in 2023	50

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 – Centro Académico de Medicina de Lisboa), a consortium that provides an integrated form of education and training in Biomedicine and Clinical Research, combining multidisciplinary and internationalization.

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

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

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

In 2023, iMM hosted **6 PhD students from other Institutions/Universities**: Universidade do Porto (1), Universidade de Coimbra (1), Universidade NOVA de Lisboa (2), Faculdade de Ciências da Universidade de Lisboa (1), Instituto Superior Técnico da Universidade de Lisboa (1).

iMM also hosted 3 PhD students from **3 Innovative Training Networks (ITN) / Doctoral Networks (DN)** from the European Commission programme Marie Skłodowska-Curie Actions (MSCA), and 1 PhD student from the **“la Caixa” Foundation**.

In 2023, **18 iMM students concluded their PhD theses**, all of which were attributed by Faculdade de Medicina da Universidade de Lisboa (FMUL).

### Advanced Courses

**A total of 5 Advanced Courses were organized**

#### **LisbonBioMed Course: Towards a Creative and Critical Mind**

Organizer: Training Hub

Date: January 9 to March 3 (8 weeks)

This annual course includes lab seminars, lectures with invited speakers, workshops and other training activities, aiming to promote student integration, create an informal welcoming, foster team bonding and interaction with putative supervisors, introduce complementary skills training, and raise awareness of transversal competencies needed for a successful scientific career. In 2023, the course included 4 workshops: Biostatistics, Research Ethics and Scientific Integrity, Technology Transfer, Scientific Writing, and Equality, Diversity and Inclusion (EDI).

### **Statistical Thinking (Workshop)**

Organizer: Workshop group of the PhD Students Committee

Date: June 15

Speaker: Saghir Bashir, ilustat (data science company)

This workshop aims to provide participants with an overview of statistical thinking as applied to clinical research and medicinal sciences. Using the CONSORT Statement, participants are encouraged to interact and discuss what makes a clinical trial (or an experiment) good in the statistical sense. The focus is on asking questions and getting answers to understand the “statistical thinking” that goes into trials and experiments.

### **Graphical Design (Workshop)**

Organizer: Workshop group of the PhD Students Committee

Date: June 22

Speaker: Helena Pinheiro, iMM Communication Office

This workshop aims to develop the necessary techniques to elaborate scientific images, figures, schemes, and graphical abstracts for scientific communications (oral presentations, posters and publications). Participants have the opportunity to learn how to optimize the process of figure building, to make it more appealing without losing the focus on the main scientific conclusions. This is a very hands-on workshop, where everyone has the opportunity to improve figures/images/schemes related to their work and improve their knowledge on the use of the software Illustrator by Adobe.

### **CONGENTO Course on Laboratory Animal Science for Functions A+C+D**

Organizers: Iolanda Moreira (Rodent Facility) and Lara Carvalho (Zebrafish Facility)

Date: April 24 – May 26

The course was organized under the CONGENTO-harmonized programme and was targeted to Functions A + C + D (Performing Procedures and Euthanasia in Animals + Taking care of animals) for mouse/rat and/or zebrafish. The course provides theoretical and practical training for the use of animal models in scientific research. This course is a requirement to be able to work with animal models.

### **CONGENTO Course on Laboratory Animal Science for Functions A+C+D**

Organizers: Iolanda Moreira (Rodent Facility) and Lara Carvalho (Zebrafish Facility)

Date: October 20 – November 21

The course was organized under the CONGENTO-harmonized programme and was targeted to Functions A + C + D (Performing Procedures and Euthanasia in Animals + Taking care of animals) for mouse/rat and/or zebrafish. The course provides theoretical and practical training for the use of animal models in scientific research. This course is a requirement to be able to work with animal models.

### **Other Courses**

#### **Course for Supervisors: The art of supervising students - Skills for effective and empowering supervision**

Organizer: Training Hub

Date: November 9-10

Trainers: hfp consulting

In this practical course participants were able to:

- Improve their mentoring, coaching and communication skills
- Learn how to better guide students during the different phases of their PhD
- Practise tools to build and maintain a successful working relationship with their students
- Increase their awareness to their impact as mentors and supervisors
- Exchange their experiences as supervisors
- Be encouraged to build a peer support group to sustain the impact of the workshop
- Strengthen their network within the iMM community

#### **Responsible Research and Innovation (Workshop)**

Organizer: EpiEpiNet Twinning action

Date: April 17-19

Trainers: Chaperone

During the first two days of the workshop, participants got insight and discussed some of the pillars of Responsible Research and Innovation (RRI) including Gender Equality, Public Engagement, Open Science and Science Education, and Good Governance. On the last day of the workshop, participants discussed examples on how to implement RRI in institutions/projects and, particularly, in ongoing and future projects at iMM.

### **Portuguese Course (Foreign Language)**

Organizer: Training Hub and Postdoctoral Association (PDA)

Dates: Levels A1/A2 and B2/C1 (7th edition): November 2022 to June 2023 (45h, 1 class/level/week); Levels A1 and B1 (8th edition): November 2023 to June 2024 (45h, 1 class/level/week);

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

### **Other Events**

#### **Science Careers Sessions (online or hybrid)**

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

Organizer: Science Careers group of the PhD Students Committee

Dates: January 11; January 30; February 14; March 15; April 13; May 18; June 14; July 4; September 28; October 25; November 30.

Speakers: Cátia Janota, Business Data Analyst at Amgen; Joana C. Carvalho, Science Illustration and Visual Communication at EMBL; Joana Pinto Melo, Medical Writer at W4Research; Adriana Temporão, Clinical Project Manager; Jorge Borbinha, E-detail Medical Sales Representative for IQVIA/Alnylam Pharmaceuticals; Tânia Perestrelo, Key Account Manager (Health & Biotech) at Izasa Scientific; Bárbara Abreu, Postdoctoral Research Associate at Astex Pharmaceuticals; Jorge Sampaio, Bioinformatics Engineer at Loka; Ana Sofia Brandão, Jr Data Team Lead at IQVIA; Bárbara Gomes, CEO at AccelBio; André Jerónimo Santos, Medical Manager in Neurology & Immunology at the Merck Group.

#### **16th PhD Students Meeting**

Organizer: PhD Meeting group of the PhD Students Committee

Date: May 9-12

The annual PhD Students meeting is the place by excellence where students present their work to the iMM/CAML community. In 2023, the event included as keynote speakers Manuel Sobrinho Simões, Cecília Rodrigues, Francesca Nadalin, Elisabeth Bik and João Matos. It also included one roundtable discussion “From academia to a startup”, and a photo contest “A day in the life of a PhD student”.

### **PhD Students Retreat**

Organizer: PhD Retreat group of the PhD Students Committee

Date: June 16-17

During the two-day retreat at Peniche, Portugal, PhD students engaged in scientific and group activities fostering team spirit and social interaction.

### **Master's Day at iMM (targeted to all iMM MSc students)**

Organizer: Master Students Committee 22/23

Date: June 29

This one-day event is planned and organized by the Master Students Committee to foster scientific and social networking with iMM's students and researchers. In 2023, this event included the awarding ceremony of the Best Master Thesis 2021/2022, inspiring talks by Isabel Palmeirim and Daniel Correia, and a roundtable about "Artificial Intelligence Impact on Research". The afternoon session was dedicated to team-building activities among the iMM Master students, followed by the usual iMM Informal Monthly Gathering.

### **Thematic sessions**

Organizer: Postdoctoral Association (PDA)

The thematic sessions are informal meetings among Postdocs (but not exclusively) to troubleshoot, discuss, and learn among Postdocs regarding different techniques/subjects. The 2023 sessions took place on the 1st Friday of the month and included:

- (i) "Tech Transfer", June 2;
- (ii) "CRISPR", July 7;
- (iii) "Green Team", October 6;
- (iv) "Pre-Award", November 3.

### **Postdoc Day**

Organizer: Postdoctoral Association (PDA)

Date: October 19

The Postdoc Day is the opportunity for postdoctoral researchers to share their work with the iMM community. In 2023, the program included:

- (i) a scientific session, including 9 short talks by iMM Postdocs and a keynote lecture delivered by Brigitte Maria Städler, from iNANO, Aarhus University, Denmark;
- (ii) an Out of Our Box seminar, co-organized with iMM's GreenTeam, delivered by Francisco Ferreira, from ZERO – Association for the Sustainability of the Earth System;
- (iii) an evening session of social gathering.

### **Postdoc Retreat**

Organizer: Postdoctoral Association (PDA)

Date: October 20

In 2023, the iMM Postdocs came together at Convento da Arrábida to interact, connect and strengthen the community through roundtable and leisure activities.

### **Welcome Session for Master Students**

Organizer: Training Hub

Date: October 26

The purpose of this initiative is to welcome all new MSc Students to iMM. The second Welcome Session for Master Students started with a very enriching session by Leonor Saúde, Coordinator of Master Studies, followed by the scientific presentations of the Best Master Thesis Awardees 2021/2022, the testimony from one iMM Master Alumni who shared with us their experience at iMM and how their professional paths have been shaped since then, ending with a session “Doing a Master at iMM” by a 2nd-year Master student at iMM.

## CARE

The time between the emergence of innovations in healthcare and their practical application for the benefit of human health is too long. This statement is the result of complex and often disconnected processes to develop, test and implement novel healthcare solutions, across sectors and with an accumulation of missed opportunities along the way.

In a global setting of significant healthcare challenges, the COVID-19 pandemic and our cooperative response to it made it clear that, together, we can create and put into practice specific healthcare solutions within tangible timeframes, with iMM capable of taking on a proactive leadership role. This realization shifted our mindset and shaped our next strategic goal – to establish a Centre of Excellence in human-centered clinical and translational research: CARE.

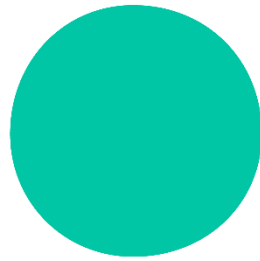
Launched in May 2023, CARE initiative teams up iMM with a strategic international partner – the Vall d’Hebron Barcelona Hospital Institute of Research (VHIR) – a world-leading healthcare complex with complementary expertise in clinical trials and training. Building on existent links with the Unidade Local de Saúde (ULS) de Santa Maria and Faculty of Medicine of the University of Lisbon (FMUL), CARE will create the framework and actions to catalyze a continuum across biomedical research, from bench to bedside and back again.

CARE brings together a Brain Trust of global key opinion leaders in science and health from various sectors to help guide our strategy, through proposing and elaborating disease-specific Missions, with citizens’ needs in mind. The Missions will address urgent health challenges in Portugal, and allow us to test solutions that can then be shared and scaled up to other countries with similar needs. Our goal is to tackle specific diseases where science is just “one step behind” and can offer vital information for a specific part of the solution. Investment will then be funneled to develop the operational setting that allows the solution to be scaled up rapidly, first as a proof of concept and then as part of future national policy guidelines. Alongside, CARE drives the digital transformation process and the upgrade of critical clinical research infrastructures, including the Biobank. CARE includes a significant number of cross-disciplinary co-creation opportunities geared towards open innovation, including tailored actions for patients and representatives, ensuring that key end users are included and empowered to actively participate in the R&I process.

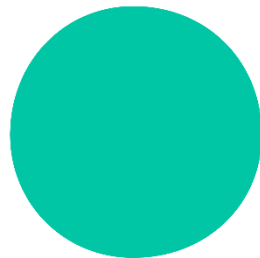


Our first mission, launched in 2023, is centered on improving colorectal cancer (CRC) screening, aiming to cover 50% of the Portuguese population in the age group 40-75. This broad mission is implemented alongside a specific research and innovation flagship aiming to develop a highly sensitive and affordable test for early detection of CRC, to improve detection of premalignant lesions and to stratify patients, assessing the risk of CRC severity, therapeutic resistance and recurrence. Through this first mission, CARE aims to showcase the societal impact of scientific research and tap into impact assessment and investment opportunities, preparing our team for many more missions to come.

CARE Centre of Excellence will receive significant investment (41.75M EUR), initially through iMM-CARE Teaming for Excellence EU project plus complementary public and private funding, with a long-term view to becoming a sustainable business unit of GIMM (Gulbenkian Institute for Molecular Medicine) to feed into CAML R&I ecosystem.



# 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:**

Sérgio de Almeida Lab
Claus M. Azzalin Lab
João Barata Lab
Maria Carmo-Fonseca Lab
Mamede de Carvalho Lab
Zita Carvalho-Santos Lab
Miguel Castanho Lab
Luís Costa Lab
Joaquim Ferreira Lab
Luísa Figueiredo Lab
Paulo Filipe Lab
João Eurico da Fonseca Lab
Cláudio Franco Lab
Edgar Gomes Lab
Luís Graça Lab
João Lacerda Lab
Luísa Lopes Lab
Nuno Morais Lab
Vanessa Morais Lab
Maria Mota Lab
Joel Perez-Perri Lab
Miguel Prudêncio Lab
Mário Ramirez Lab
Nuno Santos Lab
Leonor Saúde Lab
Ana Sebastião Lab
Ribot & Silva-Santos Lab
Ana Espada de Sousa Lab
Neves & Sousa-Victor Lab
Marc Veldhoen Lab

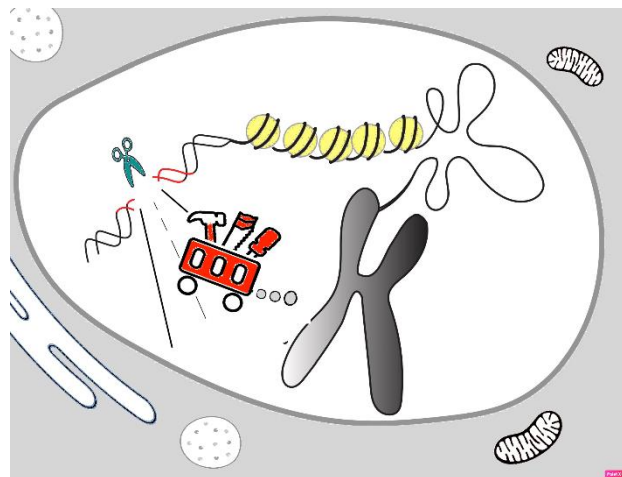
## Sérgio de Almeida Lab

**Head of Laboratory:** Sérgio de Almeida, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Associate Professor with Habilitation at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Rita Henriques Simões Marques	University Degree	Lab Technician (Left August)
André Jorge Balsinha	University Degree	MSc Student (Left November)
Anna Françoise Lucienne Le Breton	Master Degree	Lab Technician (Started January. Left December)
Anne-Valerie Gendrel	PhD	Senior Postdoctoral Researcher
Bilal Ahmad Naikoo	Master Degree	PhD Student (Started January. Left October)
Cristiana Marisa de Sousa Morgado	Master Degree	PhD Student
Ian Lopes Teixeira	University Degree	MSc Student (Left November)
Madalena Isabel Reto de Almeida	Master Degree	PhD Student
Margarida Pinho Gonçalves Bento de Bettencourt	University Degree	MSc Student (Left December)
Maria Soutilha Gonçalves da Conceição	University Degree	MSc Student (Started September. Left November)
Robert Manfred Martin	PhD	Senior Postdoctoral Researcher

### Graphical Abstract



*The DNA repair toolbox*

### Lab Interests

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

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

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

This year, our lab has made important contributions to our research field. We spearheaded the development of a cutting-edge genetically encoded sensor that can be used to image nucleic acid structures termed R-loops in live cells with high specificity and sensitivity (Martin et al. 2023). We filed a patent describing this novel sensor, which we will further explore as a tool to test novel anticancer therapies. We disclosed the adaptive changes in the DNA damage response during skeletal muscle cell differentiation (Faleiro et al. 2023). Our lab members communicated these and other findings in several national and international meetings.

### **Ongoing Projects**

2023/2024: New horizons for Rett syndrome: exploring the role of transposable elements using genetically engineered human stem cell models. Coordinator: Anne-Valerie Gendrel. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02195.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2023/2024: Investigating R-loops as important regulators of splicing. Coordinator: Robert Manfred Martin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.08846.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2023: Exploring the contribution of transposable element. Coordinator: Anne-Valerie Gendrel. Funding Agency: Rett Syndrome Foundation. Reference: International Rett Foundation 2021. Amount: 46 617,48€. Total Amount: 46 617,48€.

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

## Scientific Impact

### Selected Publications

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

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

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

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

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

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

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

**Relevance of the publication:** DSBs are repaired by two major pathways: non-homologous end joining (NHEJ) and homologous recombination (HR). NHEJ is rapid but error-prone (i.e. the repaired sequence is often mutated), whereas HR is slower but highly accurate. While mutations in the non-coding genome are probably less harmful than the persistence of a DSB, the same may not be true for protein-coding genes. In particular mutations in tumour suppressors or oncogenes could lead to cancer. Consistently, we found that DSBs in protein-coding genes are preferentially repaired by the error-free HR pathway. We observed that the H3K36me3 histone modification (found in all transcribed chromatin) recruits homologous recombination factors to active genes. This study revealed a hitherto unknown segregation of DNA repair pathways that is determined by the transcriptional status of the damaged sequence. Mechanistically, we found that H3K36me3 is necessary for the formation of RAD51 microfilaments at resected DNA ends.

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

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

### 2023 Publications in Peer-Reviewed Journals

Cardoso BA, Duque M, Gírio A, Fragoso R, (...), Neto JL, de Almeida SF, Van Vlieberghe P, Mullighan CG, Yunes JA, Langenau DM, Pflumio F, Barata JT (2023). CASZ1 upregulates PI3K-AKT-mTOR signaling and promotes T-cell acute lymphoblastic leukemia. *Haematologica* Dec 7.

Faleiro I, Afonso AI, Balsinha A, Lucas B, Martin RM, Gomes ER, de Almeida SF\* (2023). Adaptive changes in the DNA damage response during skeletal muscle cell differentiation. *Front Cell Dev Biol* 27:11:1239138.

Martin RM, de Almeida MR, Gameiro E, de Almeida SF\* (2023). Live-cell imaging unveils distinct R-loop populations with heterogeneous dynamics. *Nucleic Acids Research* 51(20) 11010-11023.

### Invited Lectures and Seminars

Sérgio de Almeida. Live-Cell Imaging of R-loops and Their Impact on Gene Expression. Dunn School of Pathology Research Seminars, UK, October 13, 2023.

Sérgio de Almeida. Live-Cell Imaging Unveils Distinct R-loop Populations with Heterogeneous Dynamics. Spanish/Portuguese Meeting for Advanced Optical Microscopy, Portugal, October 25, 2023.

### **Communications**

#### Communications in International Conferences:

Anne-Valerie Gendrel. Evaluating the cis-regulatory potential of full-length LINE-1 elements. Institute of Genetics, Reproduction and Development (iGReD), Clermont-Ferrand (France), May 23, 2023.

Anne-Valerie Gendrel. Exploring the contribution of transposable elements for the pathogenesis of Rett syndrome. 2023 IRSF Rett Syndrome Scientific Meeting, Nashville, USA, June 5, 2023. (Poster Presentation)

Anne-Valerie Gendrel. Evaluating the cis-regulatory potential of full-length LINE-1 elements: implications for X-chromosome inactivation. EMBO workshop: X-chromosome inactivation: New insights on its 60th anniversary, Berlin, Germany, June 19, 2023. (Poster Presentation)

Cristiana Morgado. Epigenetic determinants of replication stress regulation. 13<sup>th</sup> EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Robert Martin. Live-Cell Imaging Unveils Distinct R-loop Populations with Heterogeneous Dynamics. Spanish/Portuguese Meeting for Advanced Optical Microscopy, Faro, Portugal, October 25, 2023. (Poster Presentation)

#### Communications in National Conferences:

Madalena. R-loops as regulators of pre-mRNA processing. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Anna Le Breton. Epigenome editing as a tool to study the role of DNA methylation at the Zdbf2 locus. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Cristiana Morgado. Role of epigenetic modifications in telomere maintenance. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Cristiana Morgado. Epigenetic determinants of replication stress regulation. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 9, 2023. (Poster Presentation)



Anna Le Breton. iMM Green Team: Actions and Intentions. Green Labs Portugal Symposium, Coimbra, Portugal, September 22, 2023. (Poster Presentation)

### **Organization of Conferences**

Sérgio de Almeida, Co-Organizer, International RiboMed meeting - RNA in Disease, Lisbon, Portugal, January 26-27, 2023.

### **Networks and Research Infrastructures**

Sérgio de Almeida, RiboMed, Associated lab, European Union.

### **Advanced Teaching**

Sérgio de Almeida, Coordination of Master curricular unit, Master in Biomedical Research, Lisbon, Portugal.

Sérgio de Almeida, Coordination of PhD curricular unit, LisbonBioMed PhD program, Lisbon, Portugal.

Sérgio de Almeida, Lecture, Integrated Master in Medicine, Lisbon, Portugal.

Robert Martin, Supervision of “Rotation III” laboratory internship module, Lisbon, Portugal.

### **MSc Theses**

André Balsinha, DNA damage repair in skeletal muscle cells: role of nuclear autophagy and DASP in muscle repair, Supervisor: Sérgio de Almeida, Co-Supervisor: Ana Rita Grosso, FCT-NOVA, Lisbon, Portugal, November 16, 2023.

Ian Teixeira, Bit by bit: associating transcription to ageing, Supervisor: Sérgio de Almeida, Co-Supervisor: Ana Rita Grosso, FCT-NOVA, Lisbon, Portugal, November 22, 2023.

Margarida Bettencourt, Developing human stem cell models to explore the contribution of transposable elements for the pathophysiology of Rett syndrome, Supervisor: Anne-Valerie Gendrel, Co-Supervisor: Cláudia Lobato da Silva, Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal, November 28, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Intellectual Property Rights in 2023**

A Genetically Encoded Sensor for Live-Cell Imaging of R-loops. Inventors: Sérgio de Almeida and Robert Martin.

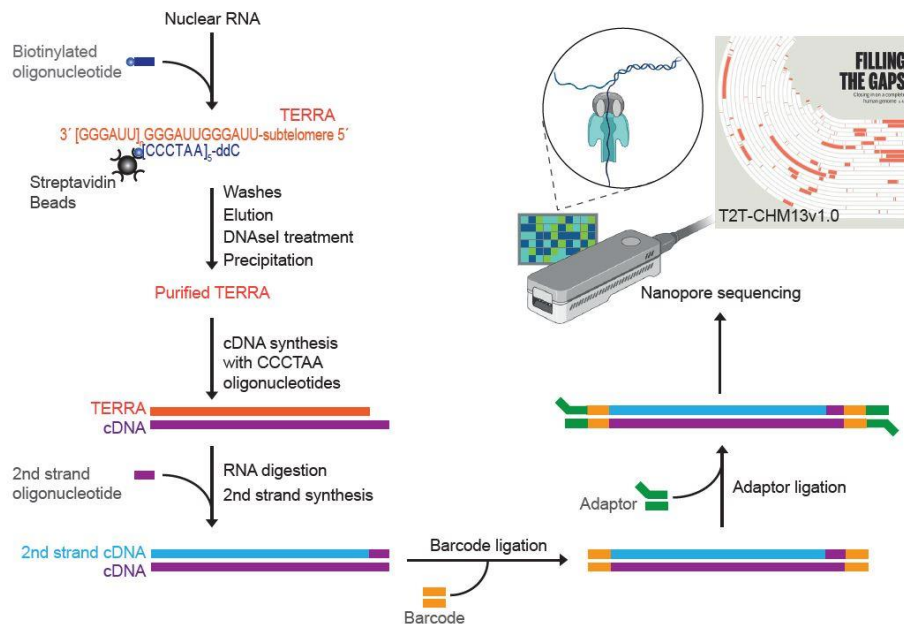
## Claus M. Azzalin Lab

**Head of Laboratory:** Claus Maria Azzalin, PhD, Group Leader and Director of Training Hub at Instituto de Medicina Molecular João Lobo Antunes and Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Beatriz Domingues Silva	Master Degree	PhD Student
Bruno Adriano de Sousa Silva	PhD	Senior Postdoctoral Researcher
Inês de Freitas Martins	University Degree	MSc Student (Started September)
Inês Vaz Fernandes Teixeira Justo	University Degree	MSc Student (Left November)
Joana Cristina Pedro Rodrigues	PhD	Postdoctoral Researcher
João Pedro Pina Rebelo	University Degree	MSc Student (Left December)
Luca Zardonì	PhD	Postdoctoral Researcher
Marta Andolfato	Master Degree	PhD Student
Patrícia Alexandra Lona Abreu	PhD	Lab Manager
Sara Barros Salgado	Master Degree	PhD Student
Valentina Riva	PhD	Postdoctoral Researcher

### Graphical Abstract



*Schematic representation of the TERRA purification and ONT sequencing pipeline developed for the study of TERRA biogenesis and expression. After TERRA sequencing using the long read Oxford Nanopore Technology, reads were mapped to the most recent telomere-to-telomere (T2T) genome reference, which has filled subtelomeric sequence gaps present in previous assemblies. Figure created with BioRender.com.*

### **Lab Interests**

Telomeres are nucleoprotein structures 'capping' the ends of linear eukaryotic chromosomes. Dysfunctional telomeres cause severe chromosome instability, which unleashes cellular reactions that are common hallmarks of human diseases including cancer and premature aging. We employ molecular biology, cell biology and biochemistry to understand how telomeres execute their protective functions and how telomeric dysfunctions are mechanistically linked to pathological conditions.

In particular, we study how the telomeric long noncoding RNA TERRA regulates telomere structure and functions in both normal and diseased human cells. In 2023, our research largely focused on the development of a pipeline to study TERRA biogenesis and expression, and the dissection of the molecular mechanism through which TERRA regulates the proper assembly of the telomeric protective cap in telomerase-positive and primary human cells.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

We developed a novel experimental pipeline for the study of human TERRA based on Oxford Nanopore Technology (ONT) long read sequencing (TERRA ONTseq) and combined it with the mapping to the most recent genome reference. Using TERRA ONTseq, we showed that the vast majority of human telomeres produce TERRA, we identified regions containing TERRA transcription start sites in more than half of human subtelomeres, and we isolated a novel TERRA promoter. Overall, the development of TERRA ONTseq provides a refined picture of human TERRA biogenesis and expression equips the scientific community with an invaluable tool for future studies.

Additionally, continued to explore the functional relevance of TERRA-mediated regulation of telomeric chromatin composition. Our data suggests that telomere transcription and TERRA can remodel telomere composition and render telomeres accessible to repair and elongation activities that are normally suppressed at chromosome ends.

### **Ongoing Projects**

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

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

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

2021/2023: Dissecting the composition and functions of the telomeric deoxyribo/ribonucleoprotein: the missing building block of the puzzle. Coordinator: Valentina Riva. Funding Agency: European Molecular Biology Organisation. Reference: EMBO - VALENTINA RIVA. Amount: 104 000,00€. Total Amount: 104 000,00€.

2020/2024: Tessellate Bio. Coordinator: Claus Azzalin. Funding Agency: Tessellate Bio BV. Reference: Tessellate Bio/Claus Lab. Amount: 498 850,00€. Total Amount: 498 850,00€.

## Scientific Impact

### Academic Collaborations

- Department of Biology, Institute of Molecular Systems Biology, ETH Zurich, Zürich, Switzerland.
- Lineberger Comprehensive Cancer Center and Departments of Microbiology and Immunology, and Biochemistry and Biophysics, University of North Carolina at Chapel Hill, United States.
- Institute of Human Genetics, UMR 9002 CNRS and Université de Montpellier, France.
- Institute of Molecular Genetics Luigi Luca Cavalli Sforza, National Research Council, Computational Biology Unit, Italy.

### Selected Publications

Silva B, Arora R, Azzalin CM (2022). [The alternative lengthening of telomeres mechanism jeopardizes telomere integrity if not properly restricted](#). *PNAS* 19 (39) e2208669119.

**Relevance of the publication:** We developed a tool for increasing telomere transcription in ALT cells. Using this tool, we demonstrated that increased TERRA transcription promotes ALT features and leads to rapid loss of telomeric DNA; this indicates that ALT activity can jeopardize telomere integrity if not properly regulated and suggests that TERRA might be a uniquely versatile target for therapy.

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

**Relevance of the publication:** We developed a novel cell biological tool for the suppression of telomere transcription in ALT cells. By employing this tool, we demonstrated that TERRA transcription is a major trigger of ALT activity; this answers a longstanding question in the field.

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

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

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

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

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

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

### Pre-Prints

Rodrigues J, Alfieri R, Bione S, Azzalin CM (2023). TERRA ONTseq: a long read-based sequencing pipeline to study the human telomeric transcriptome. bioRxiv. <https://doi.org/10.1101/2023.11.30.569384>.

### Invited Lectures and Seminars

Azzalin CM. Transcription remodels the composition of the telomeric nucleoprotein. Seminar at École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland, February 27, 2023.

Azzalin CM, Invited talk. Ins and outs of transcription at human chromosome ends. XVI Annual Congress of Biotechnology, Badajoz, Spain, July 13, 2023.

Azzalin CM, Invited speaker. LGBTQ+ representation in STEM. EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023.

Azzalin CM. The interplay between telomere transcription and shelterin at human telomeres. SFB 1361 & 4R-RTG Seminar, Institute of Molecular Biology, Mainz, Germany, December 7, 2023.

## **Communications**

### Communications in International Conferences:

Andolfato M. Structure and function of the TERRA long noncoding RNA in a vertebrate. 12th European Zebrafish Meeting, Krakow, Poland, July 10, 2023. (Poster Presentation)

Andolfato M. Structure and function of TERRA long noncoding RNA in a vertebrate. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Domingues-Silva B. Understanding the functions of telomeric repeat-containing RNAs at non-telomeric loci. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Riva V. TERRA regulates TRF1 and TRF2 interactions with telomeres. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Zardoni L. Characterization of new transcriptional regulators of TERRA. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

### Communications in National Conferences:

Riva V. TERRA regulates TRF1 and TRF2 interactions with telomeres. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Oral Presentation)

Abreu PL. In vitro analysis of the physical interactions of TRF2 with the long noncoding RNA TERRA. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Domingues-Silva B. Understanding the functions of telomeric repeat-containing RNAs at non-telomeric loci. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Rodrigues J. The human telomeric transcriptome RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Salgado S. SUB1 as a novel regulator in the Alternative Lengthening of Telomeres pathway. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

### **Organization of Conferences**

Azzalin CM, Co-Organizer, RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023.

Azzalin CM, Co-Organizer, 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023.

Azzalin CM, Co-Organizer, EMBO workshop 'Telomere function and evolution in health and disease' (to be held in May 06-11 2024), Rome, Italy.

### **Networks and Research Infrastructures**

Azzalin CM, RiboMed, Co-PI, Funding sources: H2020-WIDESPREAD-2018-2020.

### **Prizes and Honours**

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

Azzalin CM, Appointment as invited faculty member of the PhD program in Genetics and Molecular and Cellular Biology of the University of Pavia, Italy.

Silva B, Winner of the Lídia Silva Santos Postdoctoral Achievement Award.

### **Advanced Teaching**

Azzalin CM, Lecture, LisbonBioMed PhD Program, Towards a Creative and Critical Mind training module, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 9, 2023.

Azzalin CM, Lecture, Mestrado em Investigação Biomédica, IMM/ FMUL - "Advanced Techniques in Biomedical Research II" – RNA analysis and Chromosome labelling, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 1, 2023.

Azzalin CM, Zardoni L, Lecture, Mestrado em Investigação Biomédica, IMM/ FMUL - “Advanced Techniques in Biomedical Research II” (Rotações laboratoriais), Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 17, 2023.

Azzalin CM, Andolfato M, Lecture, Mestrado em Investigação Biomédica, IMM/ FMUL - “Advanced Techniques in Biomedical Research II” (Rotações laboratoriais), Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, June 19, 2023.

Azzalin CM, Abreu PL, Lecture, Curso livre experimental Introdução à investigação científica em biologia molecular da célula (unidade curricular optativa), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 11, 2023.

### **MSc Theses**

Inês Vaz Fernandes Teixeira Justo, Exploring the role of the ESCRT-III proteins in response to telomeric replication stress in ALT cancer cells, Supervisor: Claus Maria Azzalin, Co-Supervisor: Bruno Silva, Universidade NOVA de Lisboa, Faculdade de Ciências Médicas, Portugal, November 23, 2023.

João Pedro Pina Rebelo, TERRA-mediated recruitment of SMARCAL1 in response to Telomeric Replication Stress, Supervisor: Claus Maria Azzalin, Co-Supervisor: Pedro Viana Baptista, Universidade NOVA de Lisboa, Faculdade de Ciências e Tecnologia, Portugal, December 5, 2023.

### **PhD Theses**

Patrícia Alexandra Lona Abreu, Characterization of the physical and functional interactions between human TRF proteins and the telomeric long noncoding RNA TERRA, Supervisor: Claus Maria Azzalin, Faculdade de Medicina da Universidade de Lisboa, Portugal, March 23, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

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





### **Intellectual Property Rights in 2023**

Instituto de Medicina Molecular João Lobo Antunes and Faculdade de Medicina da Universidade de Lisboa, Inventors: Sérgio de Almeida, Cristiana Morgado and Claus Maria Azzalin, Induction of Cellular Lethality in Cancer.

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## João Barata Lab

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**Head of Laboratory:** João Pedro Taborda Barata, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Patrícia Cebola Cachucho	Master Degree	PhD Student
Ana Rita Freitas Martins de Matos Fragoso	PhD	Staff Scientist
Cláudia Maria Coelho de Faria	MD/PhD	Clinical Researcher
Hélio João dos Santos Crespo	PhD	Senior Postdoctoral Researcher
Joana Margarida Bartolomeu Cavaco	University Degree	MSc Student
João Bernardo Serrador Nunes	University Degree	MSc Student
João Paulo Rita Fontela	University Degree	Trainee (Started June)
Mafalda dos Santos Dias Duque	Master Degree	PhD Student
Maria Francisca Teixeira Correia da Silva	University Degree	MSc Student (Started September)
Marta Sofia Barbosa Fernandes	Master Degree	PhD Student
Patrícia Alexandra Martins Amaral	University Degree	Trainee (Started March)
Pedro Lino Rosado	University Degree	MSc Student
Sara Alexandra Barros da Gama	University Degree	MSc Student
Tatiana Vanessa Fernandes Araújo	Master Degree	Lab Manager

### Lab Interests

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

### Research Fields

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

### Major Scientific Achievements in 2023

Combining patient data, genetic modulation of cell lines, patient samples, different in vivo models, we showed that the conserved transcription factor CASZ1 is overexpressed in T-cell acute lymphoblastic leukemia (T-ALL). CASZ1 promotes T-ALL development and resistance to chemotherapy, in part, via upregulation of PI3K signaling (Cardoso, Duque et al, Haematologica).

How IL-7/IL-7R signaling promotes leukemia is a major lab interest. In 2023, we contributed to a study led by Stéphane Schurmans demonstrating that the phosphoinositide 5-phosphatase INPP5K controls the dynamic structure and thereby promotes optimal signaling of leukemia-associated IL-7R (Moes et al, Blood).

We revealed UBE2C as a key player in the development of brain metastatic disease and demonstrated that PI3K/mTOR inhibition prevents UBE2C-induced leptomeningeal metastases (Paisana et al, Neurooncol Adv). These studies were a great way to mark the transition of Cláudia Faria to her independent lab at IMM-Care.

### **Ongoing Projects**

2022/2026: Ba/F3 cell line. Coordinator: João Barata. Funding Agency: ANAVEON. Reference: Ba/F3 cell line – ANAVEON. Amount: 5 000,00€. Total Amount: 5 000,00€.

2022/2025: Expressão aberrante de IL7R nas células de cancro do pulmão: contribuição para tumorigénese, metastização e resistência a imunoterapia. Coordinator: João Barata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MEC-ONC/4606/2021. Amount: 249 921,25€. Total Amount: 249 921,25€.

2022/2023: A regulação recíproca entre o relógio molecular circadiano e a sinalização mediada por IL7/IL7R em Leucemia Linfoblástica Aguda de células T. Coordinator: Bruno Cardoso. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/MEC-HEM/0571/2021. Amount: 49 375,00€. Total Amount: 49 375,00€.

2022/2023: A microRNA-regulated cell death-inducing gene therapy for T-cell Acute Lymphoblastic Leukemia. Coordinator: João Barata. Funding Agency: European Commission. Reference: ERC-101069429 - miRToTALL – POC. Amount: 150 000,00€. Total Amount: 150 000,00€.

2021/2024: IL7R in lung cancer development, metastasis and resistance to immune checkpoint inhibitor therapy. Coordinator: João Barata. Funding Agency: “la Caixa” Foundation. Reference: La Caixa - HR21-00761 - IL7R in lung cancer. Amount: 489 158,00€. Total Amount: 489 158,00€.

2019/2023: Explore the role of chk1 and the importance of chk1 targeted therapy in aml. Coordinator: Leonor Sarmiento. Funding Agency: Sociedade Portuguesa de Hematologia. Reference: Sociedade Port. Hematologia - Leonor Sarmiento. Amount: 5 000,00€. Total Amount: 5 000,00€.

## Scientific Impact

### Academic Collaborations

- Filipa Rijo-Ferreira, University of California, Berkeley, United States of America.
- José Cabeçadas, Instituto Português de Oncologia de Lisboa Francisco Gentil EPE, Lisbon, Portugal.
- Manuel Valiente, Centro Nacional de Investigaciones Oncológicas, CNIO, Madrid, Spain.
- Rafael Roque, Neuropathology Department, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal.
- Teresa Pacheco, Oncology Department, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal.
- Isidro Cortes-Ciriano, EMBL-EBI, Cambridge, United Kingdom.
- Marc Remke, Department of Pediatric Oncology, Hematology and Clinical Immunology German Cancer Consortium (DKTK), University Hospital Düsseldorf, Düsseldorf, Germany.
- Jon Zugazagoitia, Hospital 12 de Octubre & CNIO, Madrid, Spain.
- Luis Alvarez-Vallina, Hospital 12 de Octubre, Madrid, Spain.
- David Langenau, Massachusetts General Research Institute (United States of America).
- J Andres Yunes, Boldrini Children's Center, Campinas, Brazil.
- Ben Seddon, UCL Institute of Immunity & Transplantation, London, United Kingdom.
- Jan Cools, KU Leuven, Belgium.
- Ana Rita Grosso, Departamento Ciências Vida - Universidade Nova de Lisboa, Portugal.
- Charles Mullighan, Department of Pathology and the Hematological Malignancies Program, St. Jude Children's Research Hospital, Memphis, Tennessee, United States of America.
- Nigel Pyne, Strathclyde Institute of Pharmacy & Biomedical Sciences (Sipbs), Glasgow, United Kingdom.
- Vasco Barreto, Nova Medical School, Lisbon, Portugal.
- Stéphane Schurmans, Laboratory of Functional Genetics, GIGA Research Centre, Université de Liège, Liège, Belgium.

## Selected Publications

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

**Relevance of the publication:** We previously showed that the gene that encodes the receptor for IL-7 (IL7R) is bona fide oncogene and gain-of-function mutations occur in T-cell acute lymphoblastic leukemia (T-ALL) patients (Zenatti et al, Nat Genet 2011). Here, using a combination of transgenic and knock-in animals and transcriptomics patient data, we demonstrated that mutational activation is not the only mechanism driving the oncogenic potential of IL7R. High levels of expression of non-mutated, wild type IL7R can also drive T-ALL. IL7R high T-ALLs can be therapeutically targeted by different inhibitors of IL-7R downstream signaling.

A. Almeida, J.L. Neto, A. Cachucho, M. Euzébio, X. Meng, R. Kim, M.B. Fernandes, B. Raposo, M.L. Oliveira, D. Ribeiro, R. Fragoso, P.P. Zenatti, T. Soares, M.R. de Matos, J. Ronchi Corrêa, M. Duque, K.G. Roberts, Z. Gu, C. Qu, S. Pyne, N.J. Pyne, V.M. Barreto, I. Bernard-Pierrot, E. Clappier, C.G. Mullighan, A.R. Grosso, J.A. Yunes, J.T. Barata (2021). [Interleukin-7 receptor  \$\alpha\$  mutational activation can initiate precursor B-cell acute lymphoblastic leukemia](#). **Nature Communications**. 12 (1): 7268

**Relevance of the publication:** Using conditional knock-in mice we demonstrate that IL7R mutational activation can not only contribute to leukemia development but actually also trigger the set of events that will result in leukemia. Our mouse model recapitulates many features of human acute lymphoblastic leukemia and can be exploited to uncover new biological features and test new therapeutic strategies in this disease.

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

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

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

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

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

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

### 2023 Publications in Peer-Reviewed Journals

Fernandes MB, Barata JT (2023). IL-7 and IL-7R in health and disease: An update through COVID times. *Adv Biol Regul*, 87:100940 doi: 10.1016/j.jbior.2022.100940.

Fernandes MB, Barata JT (2023). Surprise, surprise: STAT5 not enough to stop the steroids. *Haematologica*, 108(3):670-672 doi: 10.3324/haematol.2022.281369.

Cardoso BA, Duque M, Gírio A, Fragoso R, Oliveira ML, Allen JR, Martin LR, Correia NC, Silveira AB, Veloso A, Kimura S, Demoen L, Matthijssens F, Jeha S, Cheng C, Pui CH, Grosso AR, Neto JL, de Almeida SF, Van Vlierberghe P, Mullighan CG, Yunes JA, Langenau DM, Pflumio F, Barata JT (2023). CASZ1 upregulates PI3K-AKT-mTOR signaling and promotes T-cell acute lymphoblastic leukemia. *Haematologica*. doi: 10.3324/haematol.2023.282854. Online ahead of print.

Rita Cascão and Claudia C. Faria (2023). New insights into glioblastoma: diagnosis, therapeutics and theranostics, Chapter III.16 Optimizing the Role of Immunotherapy for the Treatment of Glioblastoma. Elsevier <https://doi.org/10.1016/C2021-0-00368-0>

Roque D, Cruz N, Ferreira HA, Reis CP, Matela N, Herculano-Carvalho M, Cascão R, Faria CC (2023). "Nanoparticle-Based Treatment in Glioblastoma". *J Pers Med*. 13(9):1328. doi: 10.3390/jpm13091328

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, David Pauck, Tânia Carvalho, Pedro Ruivo, Clara Barreto, Delfim Doutel, José Cabeçadas, Rafael Roque, José Pimentel, José Miguéns, Marc Remke, João T. Barata, Claudia C. Faria (2023). UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease. *Neurooncol Adv*. 5(1):vdad048. doi: 10.1093/noajnl/vdad048.

Cruz N, Herculano-Carvalho M, Roque D, Faria CC, Cascão R, Ferreira HA, Reis CP, Matela N (2023). Highlighted Advances in Therapies for Difficult-To-Treat Brain Tumours Such as Glioblastoma. *Pharmaceutics*. 15(3):928. doi: 10.3390/pharmaceutics15030928.

Ana Rita Garcia, Avilson Mendes, Carlos Custódia, Cláudia C Faria, João T Barata, Rui Malhó, Inês Figueira, Maria Alexandra Brito (2023). Abrogating Metastatic Properties of Triple-Negative Breast Cancer Cells by EGFR and PI3K Dual Inhibitors. *Cancers*. 15(15): 3973. doi: 10.3390/cancers15153973.

B. Moës, H. Li, P. Molina-Ortiz, C. Radermecker, A. Rosu, C.A. Vande Catsyne, S.A. Sayyed, J. Fontela, M. Duque, A. Mostafa, A. Azzi, J.T. Barata, R. Merino, C. Xu, C.J. Desmet, S. Schurmans (2023). INPP5K controls the dynamic structure and signaling of wild type and mutated, leukemia-associated IL7 receptors. *Blood* 141 (14): 1708-1717.

#### **Pre-Prints**

N. Moreno-Marin, G. Marteil, N. C. Fresmann, B.P. de Almeida, K. Dores, R. Fragoso, J. Cardoso, J.B. Pereira-Leal, J.T. Barata, S. Godinho, N.L. Barbosa-Morais, M. Bettencourt-Dias (2023). High prevalence and dependence of centrosome clustering in mesenchymal tumors and leukemia. bioRxiv 2023.03.13.532472; doi: <https://doi.org/10.1101/2023.03.13.532472>.

#### **Invited Lectures and Seminars**

João Taborda Barata, Signaling in Cancer. 24th JORTEC – Jornadas Tecnológicas, NOVA School of Sciences and Technology, Caparica, Portugal, February 14, 2023.

João Taborda Barata, MicroRNA-Regulated Gene Therapy Cell Death-inducing System for T-ALL. T-ALL Biology Special Interest Group, ALLTogether Consortium Annual General Meeting, University of Strathclyde Technology and Innovation Centre, Glasgow, United Kingdom, September 25, 2023.

#### **Communications**

##### Communications in International Conferences:

Rita Fragoso, Development of a gene therapy cell death-inducing system regulated by microRNAs for cancer. ESGCT 30th Annual Congress, Brussels, Belgium, April 24, 2023. (Poster Presentation)

Marta Fernandes, Sphingosine Kinases are essential positive modulators of IL7/IL-7R signaling in Acute Lymphoblastic Leukemia. 3rd Translational Research Conference: Acute Lymphoblastic Leukaemia, Berlin, Germany, May 19, 2023. (Poster Presentation)

Mafalda Duque, Development of anti-IL-7R $\alpha$  antibodies as a targeted therapy for T-cell Acute Lymphoblastic Leukemia. 3rd Translational Research Conference: Acute Lymphoblastic Leukaemia, Berlin, Germany, May 19, 2023. (Poster Presentation)

Mafalda Duque, Development of a gene therapy cell death-inducing system regulated by microRNAs for T-cell Acute Lymphoblastic Leukemia. 3rd Translational Research Conference: Acute Lymphoblastic Leukaemia, Berlin, Germany, May 19, 2023. (Poster Presentation)

Marta Fernandes, Sphingosine Kinases are essential positive modulators of IL7/IL-7R signaling in Acute Lymphoblastic Leukemia. European Hematology Association 2023 Hybrid Congress, Frankfurt, Germany, June 8, 2023. (Oral Presentation)

Mafalda Duque, Development of anti-IL-7R $\alpha$  antibodies as a targeted therapy for T-cell Acute Lymphoblastic Leukemia. European Hematology Association 2023 Hybrid Congress, Frankfurt, Germany, June 8, 2023. (Poster Presentation)

Mafalda Duque, Development of a gene therapy cell death-inducing system regulated by microRNAs for T-cell Acute Lymphoblastic Leukemia. European Hematology Association 2023 Hybrid Congress, Frankfurt, Germany, June 8, 2023. (Poster Presentation)

Marta Fernandes, Dependence of IL-7R-Mediated Signaling on Sphingosine Kinase Activity in Acute Lymphoblastic Leukemia, but Not Healthy Lymphoid Cells, Is an Exploitable Therapeutic Vulnerability. 65th American Society of Hematology Annual Meeting and Exposition, San Diego, California, USA, December 9, 2023. (Oral Presentation)

Communications in National Conferences:

Carlos Custódia, CCL2/CCR2 pathway as a therapeutic target in the treatment of meduloblastoma. XIII Congresso Nacional da Associação Portuguesa de Neuro-Oncologia, Vila Nova de Gaia, Portugal, February 3, 2023. (Oral Presentation)



Eunice Paisana, PI3K/mTOR inhibition decreases UBE2C-driven leptomeningeal dissemination. XIII Congresso Nacional da Associação Portuguesa de Neuro-Oncologia, Vila Nova de Gaia, Portugal, February 3, 2023. (Oral Presentation)

Ana Cachucho, Characterizing the risk for IL-7R-mediated malignancy in different stages of hematopoietic development. XLVIII Annual Meeting of Sociedade Portuguesa de Imunologia (SPI), Aveiro, Portugal, March 29, 2023. (Poster Presentation)

João Fontela, Histone deacetylase inhibition abrogates IL-7R-mediated signaling by downregulating IL7R and preventing mTORC1 activation. XLVIII Annual Meeting of Sociedade Portuguesa de Imunologia (SPI), Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Ana Cachucho, Characterizing the risk for IL-7R-mediated malignancy in different stages of hematopoietic development. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 9, 2023. (Oral Presentation)

Carlos Custódia, Dissecting the role of CCL2/CCR2 axis in metastatic meduloblastoma. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 9, 2023. (Poster Presentation)

João Fontela, Histone Deacetylase Inhibitors as therapeutic candidates against IL-7-responsive Acute Lymphoblastic Leukemia. IMM Master's Day 2023, Lisbon, Portugal, June 29, 2023. (Oral Presentation)

João Fontela, Histone Deacetylase Inhibitors as therapeutic candidates against IL-7-responsive Acute Lymphoblastic Leukemia. Master Student Welcome Session 2023, Lisbon, Portugal, October 26, 2023. (Oral Presentation)

### **Organization of Conferences**

Tatiana Araújo, Organizer, Oncobiology Club, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, since October 2023.

Rita Fragoso, Co-Organizer, IMM PostDoc Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 19, 2023.

Rita Fragoso, Co-Organizer, IMM PostDoc Retreat, Arrábida, Portugal, October 20, 2023.

### **Prizes and Honours**

Marta Fernandes, American Society of Hematology Abstract Achievement Award, Highlighted in the “Best of ASH 2023” - Dependence of IL-7R-Mediated Signaling on Sphingosine Kinase Activity in Acute Lymphoblastic Leukemia, but Not Healthy Lymphoid Cells, Is an Exploitable Therapeutic Vulnerability.

Marta Fernandes, Award for best PhD work in the Oncology and Precision Medicine category from University of Lisbon - Sphingosine Kinases are essential positive modulators of IL7/IL-7R signaling in Acute Lymphoblastic Leukemia.

Rita Fragoso, MDPI 2023 Reviewer Acknowledgment.

João Taborda Barata, Member of the Evaluation Committee of Institut Cochin, Paris, France, for the Haut Conseil de l'Évaluation de la Recherche et de l'Enseignement Supérieur (HCERES), France.

João Taborda Barata, Coordinator of the Reviewer Group for “Category 603 - Lymphoid Oncogenesis: Basic” of the 65th Annual Meeting of the American Society of Hematology, USA.

João Taborda Barata, Member of the Editorial Board of Leukemia.

João Fontela, iMM Best Master Thesis Award 2022/2023.

### **Advanced Teaching**

João Taborda Barata, Coordination of Master Curricular Unit, Signaling in Cancer module of the Oncobiology Master, Lisbon, Portugal, January 14, 2023.

Rita Fragoso, Lecture, Oncobiology Master Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 17, 2023.

Rita Fragoso, Lecture, Oncobiology Master Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 17, 2023.

João Taborda Barata, Lecture, Curso de Imunologia e Imunoterapia [Immunology and Immunotherapy course], SPFCS, Tomar, Portugal, March 25, 2023.

### **MSc Theses**

Sara Gama, Exploring the role of HoxA9 in IL7R-mediated B-Cell Leukemogenesis, Supervisor: João Taborda Barata, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 26, 2023.

João Fontela, Histone Deacetylase Inhibitors as therapeutic candidates against IL-7-responsive Acute Lymphoblastic Leukemia, Supervisor: João Taborda Barata, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 24, 2023.

Patrícia Amaral, Characterizing the role of the circadian molecular clock in T-ALL, Supervisor: João Taborda Barata, Co-Supervisor: Clara Gonçalves Dias, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, July 27, 2023.

Pedro Rosado, Study of the impact of the IL-7R on non-small cell lung cancer, Supervisor: João Taborda Barata, Co-Supervisor: Rita Fragoso, NOVA Medical School, Lisbon, Portugal, December 20, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Fairjourney Biologics, Development and characterization of antibodies for cancer treatment, Collaborative Research.

### **Science and Society in 2023**

Rita Fragoso was a mentor for the Ciência di Noz Manera (CNM) programme (2nd edition). CNM is a mentoring programme, currently running under the umbrella of RAISE - Researchers in Action for Inclusion in Science and Education. Its mission is to foster the inclusion of young people from under-represented communities in higher education and science. Rita Fragoso was a mentor at the Marquesa Alorna School in Lisbon, a school from the TEIP network - Priority Educational Intervention Territories.

João T. Barata participated in the round table on job perspectives for early career biomedical graduates. Dia da Escola de Saúde e Desenvolvimento Humano, University of Évora, 20 April.

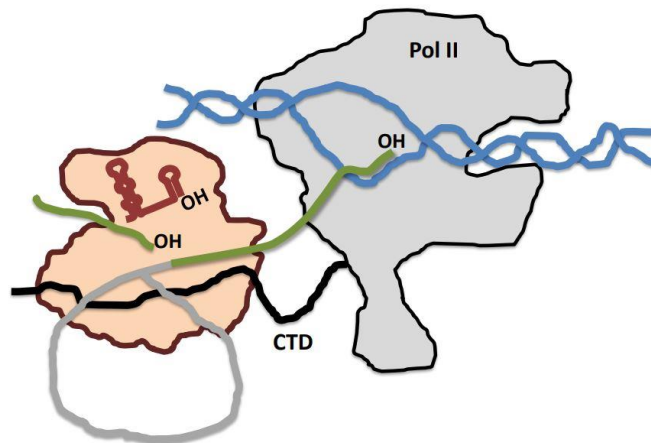
## Maria Carmo-Fonseca Lab

**Head of Laboratory:** Maria Carmo-Fonseca, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Full Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Alice da Cruz Madeira Borges	Master Degree	PhD Student
Ana Cláudia Bernardino Raposo	Master Degree	PhD Student
Ana Margarida Inácio Veloso	University Degree	MSc Student (Left December)
Ana Pereira de Brito Líbano Monteiro	University Degree	Lab Technician
André Miguel Ventura Gomes	University Degree	MSc Student
Bárbara Lopes dos Santos	University Degree	MSc Student (Left September)
Beatriz Alexandra Adrião Salvado	University Degree	MSc Student (Started March. Left October)
Beatriz Anjo Santos Lima	High School Diploma	Trainee (Left November)
Beatriz Dias Gomes da Silva	Master Degree	PhD Student
Beatriz Pinto Galvão	Master Degree	Lab Technician
Catarina Alves do Vale	Master Degree	PhD Student
Catarina Marta Gonçalves Bota	Master Degree	PhD Student (Started June)
Célia da Conceição Vicente Carvalho	PhD	Staff Scientist
Dinora Levy	University Degree	Administrative Technician
Evguenia Pavlovna Bekman	PhD	Senior Postdoctoral Researcher (Left June)
Ioana Militaru	PhD	Postdoctoral Researcher (Started December)
João Tiago Alves Prior Proença	PhD	Senior Postdoctoral Researcher
Kevin Pham	PhD	Postdoctoral Researcher (Left May)
Laura Cathleen Grzegorzek	University Degree	Lab Technician
Liliia Demianenko	Master Degree	Lab Technician (Left February)
Maria Joana Pinto Desterro	PhD	Staff Scientist
Maria Teresa Tenório Figueiredo Carvalho Gonçalves	PhD	Staff Scientist
Marta Isabel Brandão Furtado	Master Degree	PhD Student
Noélia Maria Fernandes Custódio	PhD	Staff Scientist
Patrícia Alexandra Veloso Napoleão	PhD	Senior Postdoctoral Researcher
Pedro António Pereira Prudêncio	PhD	Postdoctoral Researcher
Pedro Moisés Marques Silvestre		Lab Technician (Started April)
Pedro Santos Barbosa	Master Degree	PhD Student
Rui Gonçalo Viegas Russo da Conceição Martinho	PhD	Visiting Researcher
Rui Sérgio de Sousa Luís	Master Degree	PhD Student
Sandra Cristina Bento Penisga Martins	PhD	Senior Postdoctoral Researcher
Simão José Teixeira da Rocha	PhD	Invited Assistant Researcher
Susana Santos Lopes	PhD	Visiting Researcher

## Graphical Abstract



*Transcription and RNA splicing are tightly interwoven processes*

### Lab Interests

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

### Research Fields

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

### Major Scientific Achievements in 2023

We study RNA splicing using a combination of cutting-edge cell imaging and genome-wide approaches. We previously found that the developmentally regulated Zeb2 gene is activated by an intragenic antisense lncRNA (Zeb2-nat) that initiates within the first intron of Zeb2 (de Jesus et al., 2018). Our recent results show that promoter-proximal convergent antisense transcripts (PCATs) are a general feature of protein coding genes and that they display a positive role in the regulation of transcriptional initiation (Sousa-Luis et al., in preparation). We are also studying how RNA splicing is affected by genetic variation in the context of human disease (Barbosa et al., 2023), and how disease-associated mis-splicing could be therapeutically targeted. We are focusing on inherited heart disease, BRCA-associated cancer and leukemia.

As model systems, we are developing functional assays on cells differentiated in vitro from patient-derived induced pluripotent stem cells.

### **Ongoing Projects**

2023/2025: Identificação de neo-antígenos para imunoterapia preventiva de cancro da mama hereditário. Coordinator: M. Carmo-Fonseca. Funding Agency: Gilead Sciences, Lda. Reference: PROGRAMA GILEAD GÉNESE 2022 - CARMO FONSECA. Amount: 37 000,00€. Total Amount: 37 000,00€.

2023/2024: Mapping the spatial organization of co-transcriptional splicing. Coordinator: Pedro Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.01836.PTDC - PEDRO PRUDÊNCIO. Amount: 49 375,00€. Total Amount: 49 375,00€.

2022/2026: Cardiac Splicing as a Therapeutic Target (CASTT). Participating PI: M. Carmo-Fonseca. Funding Agency: Leducq Fondation for Cardiovascular Research. Reference: 21CVD02-(CASTT). Amount: 789 033,96€. Total Amount: 6 089 707,68€.

2022/2025: RNA Processing for Anti-Cancer Immunotherapy. Participating PI: M. Carmo-Fonseca. Funding Agency: European Commission. Reference: CANCERNA - Project 101057250. Amount: 550 625,00€. Total Amount: 5 999 381,25€.

2022/2024: Mutação BRCA2 fundadora Portuguesa: impacto na transcrição e identidade de células estaminais. Coordinator: M. Carmo-Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/3921/2021. Amount: 249 884,38€. Total Amount: 249 884,38€.

2021/2024: Non-coding BHF grant. Coordinator: M. Carmo-Fonseca. Funding Agency: University College London. Reference: Non-coding BHF grant. Amount: 66 440,65€. Total Amount: 66 440,65€.

2020/2024: AbbVie Inc - Material Transfer Agreement. Coordinator: M. Carmo-Fonseca. Funding Agency: AbbVie. Reference: AbbVie Inc - Material Transfer Agreement. Amount: 108 000,00€. Total Amount: 108 000,00€.

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

2019/2023: RNA in disease — RiboMed. Coordinator: M. Carmo-Fonseca. Funding Agency: European Commission. Reference: RiboMed - GA 857119. Amount: 424 750,00€. Total Amount: 799 750,00€.

## Scientific Impact

### Academic Collaborations

- University of Oxford, United Kingdom.
- MDC Berlin, Germany.
- University College of London, United Kingdom.

### Selected Publications

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

**Relevance of the publication:** A new methodology to purify and sequence RNA polymerase II-associated intact nascent transcripts reveals the kinetics of co-transcriptional splicing at a single molecule level.

Desterro J, Bak-Gordon P, Carmo-Fonseca M (2020). [Targeting mRNA processing as an anticancer strategy](#). *Nature Reviews Drug Discovery* 19:112-129.

**Relevance of the publication:** This commissioned review testifies our recognition in the field of splicing and its medical implications.

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

**Relevance of the publication:** We identified the transcription factor Zeb2 as a novel age-associated barrier to reprogramming.

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

**Relevance of the publication:** This review highlights the importance of studying variation in deep intronic sequence as a cause of monogenic disorders as well as hereditary cancer syndromes.

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

**Relevance of the publication:** This study provides the first genome-wide analysis of co-transcriptional RNA splicing at single-nucleotide resolution.

### 2023 Publications in Peer-Reviewed Journals

Carmo-Fonseca M (2023). Sweet splicing. *Cell* 186(1):10-11.

Carmo-Fonseca M (2023). A twist to splicing regulation in haematopoiesis. *Nature Cell Biology* 25(4):516-517.

Gotthardt M, Badillo-Lisakowski V, Parikh VN, Ashley E, Furtado M, Carmo-Fonseca M, Schudy S, Meder B, Grosch M, Steinmetz L, Crocini C, Leinwand L (2023). Cardiac splicing as a diagnostic and therapeutic target. *Nature Reviews Cardiology* 20(8):517-530.

Barbosa, P., Savisaar, R., Carmo-Fonseca, M., Fonseca, A (2023). Computational prediction of human deep intronic variation. *GigaScience*, Volume 12, giad085.

### Invited Lectures and Seminars

Carmo-Fonseca M. A investigação clínica em Portugal – perspetivas futuras. 1<sup>o</sup> Jornadas Investigação Clínica CUF, Lisbon, Portugal, January 20, 2023.

Carmo-Fonseca M. Tecnologia RNA na era da medicina de precisão. XXVIII Jornadas de Pediatria, Lisbon, Portugal, February 22, 2023.

Carmo-Fonseca M. Antisense transcription during cell fate commitment. University of Bern, Switzerland, April 3, 2023.

Carmo-Fonseca M. Antisense transcription during cell fate commitment. ETH Zurich, Switzerland, April 4, 2023.

Carmo-Fonseca M. Basic science and clinical medicine - the interface. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases, Lisbon, Portugal, May 9, 2023.

Carmo-Fonseca M. The timing of splicing: a unifying perspective. King's College London, UK, May 18, 2023.



Carmo-Fonseca M. The timing of splicing: a unifying perspective. RiboClub, Canada, September 28, 2023.

Carmo-Fonseca M. Exploring unresolved questions on co-transcriptional splicing. Louis Jeantet Symposium, Geneva, Switzerland, October 10, 2023.

## **Communications**

### Communications in International Conferences:

Sandra Martins. hiPSC model for the study of cardiac disease and its application to test splicing modulation using ASOs. 9th COST Action CardioRNA, Nicosia, Cyprus, February 22, 2023. (Oral Presentation)

Marta Furtado. An alternative splicing signature of genetic and ischemic dilated cardiomyopathy. 9th COST Action CardioRNA, Nicosia, Cyprus, February 22, 2023. (Oral Presentation)

Rui Sousa-Luís. Promoter-proximal convergent antisense transcription during cell fate commitment. The 28th Annual Meeting of the RNA Society - RNA 2023, Singapore, May 30, 2023. (Poster Presentation).

Marta Furtado. Splicing modulation using antisense oligonucleotides: a therapeutic opportunity for Hypertrophic Cardiomyopathy. 37th Annual Meeting of the International Society for Heart Research European Section, Porto, Portugal, July 10, 2023. (Oral Presentation)

Pedro Prudêncio. Dynamics of anti-sense transcription during iPSC differentiation. Cell Symposia – “The conceptual power of single cell biology”, San Diego, USA, August 28, 2023. (Poster Presentation).

Marta Furtado. Single-cell contractility assays in iPSC-derived models of hypertrophic cardiomyopathy. San Diego, USA, August 28, 2023. (Poster Presentation).

Marta Furtado. Developing targeted therapeutic approaches for MYBPC3 splicing mutations in Hypertrophic Cardiomyopathy. 13<sup>th</sup> EMBO Young Scientists’ Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Marta Ribeiro. Generation of patient-derived iPSCs from hypertrophic cardiomyopathy patients 13<sup>th</sup> EMBO Young Scientists’ Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Beatriz Gomes-Silva. Cardiac splicing during development in vivo and in vitro. 13<sup>th</sup> EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023. (Poster Presentation)

Noélia Custódio. Efficacy of indisulam in combination with venetoclax and azacitidine on cultured primary human AML cells. 6th ESH International Conference: Acute Myeloid Leukemia "Molecular and Translational": Advances in Biology and Treatment, Estoril, Portugal, October 29, 2023. (Poster Presentation)

André Ventura-Gomes. Roaming splicing neighbourhoods in the cell nucleus. 20th Annual Vienna BioCenter PhD Program Symposium – “A Mixtape of Science”, Vienna, Austria, November 10, 2023. (Poster Presentation)

#### Communications in National Conferences:

Marta Furtado. Alternative splicing is similarly dysregulated in genetic and ischemic cardiomyopathy. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Liliia Demianenko. CRISPR-mediated activation of MYBPC3 expression in cardiomyocytes derived from human induced pluripotent stem cells. RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Beatriz Gomes-Silva. Differences in the regulation of human cardiac splicing during development in vivo and in vitro RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

André Ventura-Gomes. Nascent RNA conformation RNA in Disease – IX ptRNA joint meeting, Lisbon, Portugal, January 26-27, 2023. (Poster Presentation)

Alice Borges. Vacina contra o cancro: um futuro próximo e tangível? 2º Congresso do cancro da mama do Algarve, Lagos, Portugal, February 17, 2023. (Oral Presentation)

#### **Prizes and Honours**

M Carmo-Fonseca, Prémio Universidade de Lisboa.

M Carmo-Fonseca, Prémio Personalidade do Ano - Jornal de Negócios/Sanofi.

### **Advanced Teaching**

Carmo-Fonseca M, Lecture, 1º Curso de genética médica aplicada a Neurologia, Lisbon, Portugal, March 10, 2023.

Carmo-Fonseca M, Lecture, 1ª Master Class em Terapêuticas Alvo, Coimbra, Portugal, March 31, 2023.

Pedro Prudêncio, Lecture, Master Course in Molecular and Microbial Biology, Universidade do Algarve, Portugal, November 16, 2023.

Carmo-Fonseca M, Lecture, Webinar da Liga Portuguesa contra o Cancro, Portugal, November 23, 2023.

### **MSc Theses**

Ana Pereira de Brito Líbano Monteiro, Unveiling co-transcriptional splicing kinetics using novel nascent transcriptomic techniques, Supervisor: M. Carmo-Fonseca, Master in Bioinformatics and Computational Biology, Faculdade de Ciências da Universidade de Lisboa, Portugal, April 20, 2023.

Laura Cathleen Grzegorzek, Impact of cancer-associated mutations in the BRCA2 interactome, Supervisor: M. Carmo-Fonseca, Master Program Freie Universität Berlin, Germany, July 10, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

AbbVie, Investigate the efficacy of ABT-199 in combination with azacitidine and splicing inhibitors in cultured primary human AML cells, Sponsored Research.

### **Science and Society in 2023**

Noélia Custódio and Sandra Martins participated in “Ciência di Noz Manera!”, RAISE - Researchers in Action for Inclusion in Science and Education, Instituto de Medicina Molecular João Lobo Antunes and Champalimaud Foundation, February 15, 2023.

M. Carmo-Fonseca, “Mulheres de Poder”, Cimeira Feminina 2023, Lisbon, Portugal. March 8, 2023.

M. Carmo-Fonseca, “Desafios da globalização”, Participar + Associação para a participação cívica, Lisbon, Portugal, September 18, 2023.

M. Carmo-Fonseca, “Desafios do século XXI”, 3º Encontro Luso Espanhol - Fundação D. Luís I e Fundación Duques de Soria de Ciencia e Cultura Hispánica, Cascais, Portugal, September 30, 2023.

M. Carmo-Fonseca, Sessão Inspiracional no lançamento do livro “A investigação nas organizações de saúde”, Lisbon, Portugal, November 9, 2023.

M. Carmo-Fonseca, Simpósio RNA Solutions to infectious and non-communicable, Porto, Portugal, November 27, 2023.

## Mamede de Carvalho Lab

**Head of Laboratory:** Mamede Alves de Carvalho, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full Professor of Physiology and Director of Physiology Institute at Faculdade de Medicina da Universidade de Lisboa and Graduated Senior Consultant, Neurologist and Clinical Neurophysiologist at Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria and Head of the ALS Clinic at Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria

### Team

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

### **Lab Interests**

This Unit aims to further develop the main areas where it has been highly competitive internationally. In particular: markers for early diagnosis, including wet biomarkers; epidemiology and treatment effectiveness/costs in hATTR amyloidosis; neurophysiology, phenotype-genotype 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 centers located in Europe and USA, promoting scientific development and higher output in topics of this Unit expertise.

### **Research Fields**

- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Prevention, Diagnosis and Treatment of Human Diseases

### **Major Scientific Achievements in 2023**

The team is committed to making strides in understanding the disease mechanism of ALS, using new research strategies, addressing several areas of knowledge.

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, predictors and wet-biomarkers in ALS, clinical/neurophysiological features and epidemiology of hATTR amyloidosis. Our participation in several competitive projects in ALS will promote additional future publications.

### **Ongoing Projects**

2023/2024: Achemab-ALS Patients Study (Biobanco-iMM/Prof. Mamede Carvalho collaboration). Coordinator: Mamede de Carvalho. Funding Agency: Alchemab Therapeutics Ltd. Reference: IMM ALCHEMAB COLLABORATION - MCARVALHO 50%. Amount: 20 031,25€. Total Amount: 20 031,25€.

2021/2026: ALS PROJECT - ONO PHARMA. Coordinator: Mamede de Carvalho. Funding Agency: National Institutes of Health (NIH). Reference: NIH - COLUMBIA UNIVERSITY. Amount: 41 038,61€. Total Amount: 41 038,61€.

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

2021/2024: BrainTeaser. Local Coordinator: Mamede de Carvalho. Funding Agency: European Commission. Reference: SC1-DTH-02-2020. Amount: 315 690,00€. Total Amount: 5 889 190,00€.

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

2018/2024: Investigação Síndrome Tourette. Coordinator: Tiago Maia. Funding Agency: Ampastta. Reference: Investigação Síndrome Tourette. Amount: 9 183,50€. Total Amount: 9 183,50€.

2017/2024: Computational Psychiatry Consulting on Pediatric Mental Illnesses. Coordinator: Tiago Maia. Funding Agency: National Institutes of Health (NIH). Reference: NIH - Reference 4464450 - Computational Psychiatry. Amount: 30 903,27€. Total Amount: 30 903,27€.

## **Scientific Impact**

### **Academic Collaborations**

- Amy Margolis-Columbia University, United States.
- Carles Soriano-Mas-Institut d'Investigació Biomèdica de Bellvitge and University of Barcelona, Spain.
- Klaas Stephan-ETH and University of Zurich, Switzerland.
- Hatice Tankisi-Aarhus University, Denmark.
- Sara Madeira- LASIGE, Faculdade de Ciências da Universidade de Lisboa, Portugal.
- Steve Vucic-University of Sydney, Australia.

- Adriano Chio-University of Turin, Italy.
- Paul Barkhaus-Medical College of Wisconsin, United States.
- Vincenzo Di Lazzaro - Campus Bio-Medico University, Rome, Italy.

### Selected Publications

de Carvalho M (2023). [Major research advances in amyotrophic lateral sclerosis in 2022](#). **Lancet Neurol**, 22(1):21-22.

**Relevance of the publication:** This work is highly relevant as it provides a comprehensive overview of recent advancements in understanding and treating Amyotrophic Lateral Sclerosis (ALS). The identification of potential genetic factors, insights into pathogenesis, and exploration of novel treatment avenues, such as splicing modulation and immune response modulation, offer hope for future therapeutic interventions. The findings on SOD1 mutations, FUS-associated ALS, and the sodium phenylbutyrate–taurursodiol coformulation present promising developments. This research is crucial for clinicians, researchers, and the ALS community, contributing to the ongoing quest for effective treatments and improving the lives of those affected by this debilitating neurodegenerative disease.

Conceição I, de Castro I, Diaz A, Castro J (2022). [Quantitative sensory testing: a good tool to identify subclinical neuropathy in ATTRV30M amyloidosis patients?](#) **Amyloid**, Dec 15:1-5.

**Relevance of the publication:** This study investigates the utility of quantitative sensory testing (QST) in detecting subclinical neuropathy in carriers of ATTRV30M amyloidosis. Assessing vibratory and cooling thresholds, along with heat pain responses, the research categorizes subjects into asymptomatic carriers, paucisymptomatic carriers, and stage 1 ATTRv-PN patients. Significant differences in QST parameters highlight its potential in identifying early neuropathic involvement. The findings, particularly regarding CDT and heat pain modalities, underscore the relevance of QST as a sensitive tool for detecting subclinical neuropathy in ATTRv amyloidosis carriers, contributing valuable insights for disease monitoring and intervention.

Pereira M, Fernandes SR, Miranda PC, De Carvalho M (2022). [Lumbar trans-spinal direct current stimulation: A modeling-experimental approach to dorsal root ganglia stimulation](#). **Front Neurosci**, 16.

**Relevance of the publication:** This research investigates transcutaneous spinal direct-current stimulation (tsDCS) effects on lumbar spinal cord (L-SC) responses. Computer modeling identified the most effective tsDCS montage, maximizing the electric field in the L-SC. In a blind crossover study, cathodal tsDCS applied to the L-SC and dorsal root ganglia increased H-reflex amplitude, suggesting modulation of synaptic efficiency and enhanced lower motor neuron response. The findings imply potential therapeutic applications for conditions involving altered spinal responses. Further studies will explore clinical implications, highlighting the relevance of this work in advancing non-invasive neuromodulation techniques.



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

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

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

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

### 2023 Publications in Peer-Reviewed Journals

Antunes M, Folgado D, Barandas M, Carreiro A, Quintão C, de Carvalho M, Gamboa H (2023). A Morphology-Based Feature Set for Automated Amyotrophic Lateral Sclerosis Diagnosis on Surface Electromyography. *Biomed Signal Process Control* 79:104011.

Soares M, Sequeira M, Oliveira T, Sequeira J, Lourenço J, Pronto-Laborinho A, de Carvalho M, Ladeira F (2023). Multiple Sclerosis associated with Amyotrophic Lateral Sclerosis: an unfortunate coincidence or a plausible concurrence? *Neuroimmunology Report*.

Schon M, Oliveira Santos M, Gromicho M, Pinto S, Swash M, de Carvalho M (2023). Wasted leg syndrome: an atypical slowly-progressive form of lower motor neuron disease. *Rev Neurol*.

Santos Silva C, Oliveira Santos M, Madureira J, Reimão S, de Carvalho M (2022). Novel compound heterozygous variants of SPG11 gene associated to amyotrophic lateral sclerosis. *Acta Neurol Belg*.

de Carvalho M (2023). Major research advances in amyotrophic lateral sclerosis in 2022. *Lancet Neurol*.

van Es MA, Tazelaar GHP, Hop PJ, Seelen M, ; van Vugt JJFA, van Rheenen R, Kool L, van Eijk KR, Gijzen M Dooijes D, Moisse M, Calvo A, Moglia C, Brunetti M, Canosa A, Nordin A, Pardina JSP, Ravits J; Al-Chalabi A, Chio A, McLaughlin RL, Hardiman O, Van Damme P, de Carvalho M, Neuwirth C, Weber M, Andersen PA, van den Berg LH, Veldink JH (2023). Whole genome sequencing analysis reveals post-zygotic mutation variability in monozygotic twins discordant for amyotrophic lateral sclerosis. *Neurobiol Aging*.

de Carvalho M (2022). Phlebology implications in amyotrophic lateral sclerosis. *Neurol Clin Pract* (Editorial).

Al Khleifat A, Iacoangeli A, Jones AR, Van Vugt JJFA, Moisse M, Shatunov A, Zwamborn RAJ, Van Der Spek RAA, Cooper-Knock J, Topp SD, Van Rheeën W, Kenna B, Van Eijk KR, Kenna K, Byrne R, Alonso VL, Opie-Martin S, Vural A, González Y, Weber M, Smith BN, Fogh I, Silani V, Morrison KE, Dobson RJB, A Van Es M, McLaughlin RL, Chio A, Corcia P, De Carvalho M, Gotkine M, Povedano M, Mora JS, Shaw PJ, Landers JE, Glass JD, Shaw CE, Basak NA, Hardiman O, Robberecht W, Van Damme P, Van Den Berg LH, Veldink J, Al-Chalabi A (2023). Telomere length analysis in amyotrophic lateral sclerosis using large-scale whole genome sequence data. *Front Cell Neurosci*.

Falcão de Campos C, Gromicho M, Uysal H, Grosskreutz J, Kuzma-Kozakiewicz M, Oliveira Santos M, Pinto S, Petri S, Swash M, de Carvalho M (2023). Trends in the diagnostic delay and pathway for ALS patients across different countries. *Frontiers Neurol*.

Adey BN, Cooper-Knock J, Al Khleifat A, Fogh I, Van Damme, Corcia P, Couratier P, Hardiman O, McLaughlin R, Gotkine M, Drory V, Silani V, Ticozzi N, Veldink JH, Van Den Berg LH, De Carvalho M, Pinto S, Pardina JM, Panades MP, Andersen, PM, Weber M, Başak NA, Shaw CE, Shaw PJ, Morrison KE, Landers JE, Glass JD, Vourc'h P, Dobson RJB, Breen J, Al-Chalabi A, Jones AR, Iacoangeli A (2023). Large-scale Analyses of CAV1 and CAV2 Suggest Their Expression is Higher in Post-mortem ALS Brain Tissue and Affects Survival. *Front Cell Neurosci* 17:1112405.

Castro J, Swash M, de Carvalho (2023). The cutaneous silent period as a measure of upper motor neuron dysfunction in amyotrophic lateral sclerosis. *Neurophysiol Clin* 53:102843.

Gromicho M, Oliveira Santos M, Pinto S, Swash M, de Carvalho M (2023). The flail-arm syndrome: the influence of phenotypic features. *Amyotr Lat Scler Frontotemporal Degener* 24:383-388.

de Carvalho M, Swash M (2023). Transcranial Magnetic Stimulation to monitor disease progression in ALS: a review. *Amyotr Lat Scler Frontotemporal Degener* 24:362-368.

Schon M, Domingues S, de Carvalho M, Oliveira Santos M (2023). Nusinersen treatment in a type 3 spinal muscular atrophy patient during early pregnancy. *Neurol Sci* 44:1803-1804.

Oliveira Santos M, Gromicho M, Pronto-Laborinho AC, de Carvalho M (2023). Sporadic Spinal-Onset Amyotrophic Lateral Sclerosis Associated with Myopathy in Three Unrelated Portuguese Patients. *Brain Sci* 13:220.

Castro J, Pedrosa T, de Castro I, Swash M, de Carvalho M (2023). Mirror movements – a simple algorithm for mirror activity signal processing and normative values. *Neurosci Lett* 803:137186.

Pinto S, Gromicho M, Oliveira Santos M, Swash M, de Carvalho M (2023). Respiratory phenotypes in ALS as determined by respiratory questions of the ALSFRS-R and their relation to respiratory tests. *Eur J Neuro* 30(6):1594-159.

Oliveira Santos M, Gromicho M, Pinto S, Pronto-Laborinho AC, de Carvalho M (2023). Clinical characteristics in amyotrophic lateral sclerosis with Sub-Saharan Africa ancestry – A Portuguese hospital-based cohort study. *Clin Neurol Neurosurg* 227:107674.

Henriques AR, Gromicho M, Grosskreutz J, Kuzma-Kozakiewicz M, Petri P, Uysal H, Pinto S, Antunes M, de Carvalho M, Ribeiro RM (2023). Association of the practice of contact sports with the development of amyotrophic lateral sclerosis. *Amyotr Lat Scler Frontotemporal Degener* 24:449-456.

Henriques AR, Gromicho M, Grosskreutz J, Kuzma-Kozakiewicz M, Petri P, Uysal H, Pinto S, Antunes M, de Carvalho M, Ribeiro RM (2023). Association of the practice of contact sports with the development of amyotrophic lateral sclerosis. *Amyotr Lat Scler Frontotemporal Degener* 24:449-456.

Soares DF, Henriques R, Gromicho M, de Carvalho M, Madeira SC (2023). Triclustering-based Classification of Longitudinal Data for Prognostic Prediction: Targeting Relevant Clinical Endpoints in Amyotrophic Lateral Sclerosis. *Sci Rep* 13:6182.

Gwathmey KG, Corcia P, McDermott CJ, Genge A, Sennfalt S, de Carvalho M, Ingre C (2023). Diagnostic delay in amyotrophic lateral sclerosis. *Eur J Neuro* 30:2595-2601.

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Berg LH, Al-Chalabi A, Veldink J, Van Damme P, on behalf of Project MinE Sequencing Consortium (2023). Genetic variability in known ALS genes in sporadic ALS patients. *Brain* 146: 3760–3769.

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### **Pre-Prints**

Conceição, V. A., Petzschner, F. H., Cole, D. M., Wellstein, K. V., Müller, D., Raman, S., & Maia, T. V. (2023). Serotonin Reduces Belief Stickiness. *bioRxiv*, 2023-12.

### **Invited Lectures and Seminars**

Mamede de Carvalho, *Semiologia das Doenças Neuromusculares. Curso de Terapêuticas Avançadas em Neurologia: Semiologia das Doenças Neuromusculares, Portugal, February 1, 2023.*

Mamede de Carvalho, *TMS-based neurophysiologic markers for ALS. 5th International Brain Stimulation Conference: On Demand Symposium on Transcranial Magnetic Stimulation in ALS, Portugal, February 2, 2023.*



Mamede de Carvalho, Clinical Perspectives and Pilot's Action. BRAINTEASER: Mid Term Workshop, Italy, February 3, 2023.

Isabel Conceição, Neuropatia Associada a Amiloidose ATTRv/Paramiloidose. Curso de Terapêuticas Avançadas em Neurologia Porquê, Quem, Quando e como Tratar, Portugal, February 4, 2023.

Isabel Conceição, Standardisation of monitoring in ATTRv Amyloidosis. Alnylam TTR Masterclass, Suisse, March 23, 2023.

Mamede de Carvalho, Motor Neuron Diseases. Advanced Health Education: Neurodegenerative Diseases - Advanced Course, Online, May 2, 2023.

Mamede de Carvalho, ICU-acquired weakness: Overview. 18th European Congress on Clinical Neurophysiology, France, May 5, 2023.

Mamede de Carvalho, Pulse Oximetry in ALS. Conference: Proposal for Creation of a Latin American Network for Research and Care in Amyotrophic Lateral Sclerosis, Online, June 7, 2023.

Mamede de Carvalho, Phrenic nerve stimulation. 9th Congress of the European Academy of Neurology, Hungary, June 12, 2023.

Isabel Conceição, When ATTR Amyloidosis Strikes a Nerve: Best Practices in Timely Suspicion, Diagnosis, and Management of ATTR-Polyneuropathy (Symposium Astra Zeneca). Peripheral Nerve Society Annual Meeting, Denmark, June 17, 2023.

Isabel Conceição, The importance of early treatment of transthyretin amyloidosis Symposium Pfizer Inc.). 9th Congress of the European Academy of Neurology, Hungary, July 15, 2023.

Mamede de Carvalho, Esclerose lateral amiotrófica: evaluación neurofisiológica. 29º Curso Internacional de Investigación en Neurociências, Peru, August 19, 2023.

Isabel Conceição, When to start treatment in TTR carriers? IV International Workshop in Cardiomyopathies, Hypertrophic Cardiomyopathy 2023, Spain, September 22, 2023.

Isabel Conceição, Small Fiber Neuropathy. Molecular and Neurophysiological Diagnosis. Congresso Português de Doenças Neuromusculares, Portugal, September 29, 2023.

Mamede de Carvalho, Biomarcadores na Esclerose Lateral Amiotrófica. XXIX Congresso Brasileiro de Neurofisiologia, Brasil, October 8, 2023.

Mamede de Carvalho, Neurophysiological Biomarkers for SBMA. European Neuromuscular Center - Workshop on SBMA, The Netherlands, October 15, 2023.

Mamede de Carvalho, Esclerose Lateral Amiotrófica. Serviço Regional de Saúde da Região Autónoma da Madeira, Portugal, October 17, 2023.

Isabel Conceição, Clinical Management of Patients with Hereditary Amyloidosis in a Reference Center. Meet the Global Neurologist Expert in ATTRv-PN (Astra Zeneca), Portugal, October 30, 2023.

Isabel Conceição, How to manage symptoms for in ATTR Amyloidosis? Central Neurological Manifestations and Pain, 4th European ATTR Amyloidosis Meeting for Patients and Doctors, Spain, November 2, 2023.

Isabel Conceição, Turning the tide: Therapeutic innovation in hATTR amyloidosis. Alnylam Symposium, 4th European ATTR Amyloidosis Meeting for Patients and Doctors, Spain, November 2, 2023.

Mamede de Carvalho, Esclerose Lateral Amiotrófica: Atualização. I Seminário Apela(R) para as Doenças Neurodegenerativas, Portugal, November 4, 2023.

### **Communications**

#### Communications in International Conferences:

Aidos H, The Intelligent Disease Progression Prediction Challenge. 45th European Conference on Information Retrieval (ECIR), Dublin, Ireland, April 3, 2024. (Oral Presentation)

Pedro Rocha, Smartphone-based cough data in amyotrophic lateral sclerosis: a potential predictor of functional disability. Annual International (bio) Medical Students Conference, Portugal, April 16, 2023. (Poster Presentation)

Ana Rita Henriques, Association of the practice of contact sports with the development of amyotrophic lateral sclerosis, 5th Statistics on Health Decision Making, Portugal, June 1, 2023. (Poster Presentation)

Marco Luigetti, Impact of Baseline Polyneuropathy Severity on Vutrisiran Treatment Response in the Phase 3 HELIOS-A Study. Peripheral Nerve Society Annual Meeting, Denmark, June 17, 2023. (Poster Presentation)

Elisa Vegezzi, Genetic modifiers in hereditary and acquired TTR amyloidosis: update on genome-wide association study. Peripheral Nerve Society Annual Meeting, Denmark, June 17, 2023. (Poster Presentation)

Markus Weiler, Eplontersen in Hereditary ATTR-polyneuropathy: Week 66 Final Analysis of the Phase 3 NEUROTTRansform. Peripheral Nerve Society Annual Meeting, Denmark, June 17, 2023. (Poster Presentation)

Cláudia Santos-Silva, Effects of ageing on hand muscles. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

M. Schon, Assessment of sympathetic sudomotor function in myotonic dystrophy type 1 with electrochemical skin conductance. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

M. Schon, Nusinersen treatment in a type 3 spinal muscular atrophy patient during early pregnancy. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Cláudia Santos-Silva, Atypical inflammatory myopathy mimicking amyotrophic lateral sclerosis 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

MD Costa, Type 2 and 3 spinal muscular atrophy patients under treatment with risdiplam: a small experience from a tertiary centre. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Pedro Rocha, Smartphone-based cough data in amyotrophic lateral sclerosis: a potential predictor of functional disability. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

C. Serrão, Nusinersen treatment in adult type 3 spinal muscular atrophy patients: data on motor and respiratory function at 22 and 42 months of treatment. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Miguel Oliveira-Santos, Glial fibrillary acidic protein and vascular endothelial growth factor in adult SMA patients treated with nusinersen. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Miguel Oliveira-Santos, Clinical characteristics in amyotrophic lateral sclerosis with Sub-Saharan Africa ancestry – A Portuguese hospital-based cohort study. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Isabel Conceição, Neurofilament light chain as a biomarker of disease activity in patients with hereditary ATTR-polyneuropathy in phase 3 NEURO-TTRransform. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Miguel Miranda, Clinical Progression in Acquired Amyloidosis after Domino Liver Transplantation: A Case-Control Study. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Oral Presentation)

Isabel Conceição, Transitioning from inotersen to eplontersen in patients with hereditary transthyretin amyloidosis polyneuropathy. 9th Congress of the European Academy of Neurology, Hungary, July 1, 2023. (Poster Presentation)

Auletta, E, LS stratification using patient similarity networks. International School and Conference on Network Science (NetSci 2023), Austria, July 10, 2023. (Oral Presentation)

Faggioli, G, Intelligent Disease Progression Prediction: Overview of iDPP@CLEF 2023. CLEF 2023: Conference and Labs of the evaluation forum information access evaluation meets multilinguality, multimodality, and visualization, Thessaloniki, Greece, September 18, 2023 (Oral Presentation)

Atzeni, M, Predicting Clinical Outcomes of Amyotrophic Lateral Sclerosis Progression using Logistic Regression and Deep-Learning Multilayer Perceptron. 18th Computational Intelligence Methods for Bioinformatics and Biostatistics Conference, Padua, Italy, September 6, 2023.

Miguel Oliveira Santos, Diaphragmatic weakness in late-onset Pompe disease: a complex interplay between lower motor neuron and muscle fibre degeneration. 28th International Annual Congress of the World Muscle Society, United States of America, October 7, 2023. (Oral Presentation)

Isabel Conceição, Transitioning from inotersen to eplontersen in patients with hereditary transthyretin amyloidosis polyneuropathy. 4th International ATTR Amyloidosis, Spain, November 2, 2023. (Oral Presentation)

Inês Alves, Assessing Disease Progression and Survival Patterns in ALS: A Study of Prognostic Subgroups and Deviations from Expected Outcomes. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Cláudia Santos Silva, C9orf7 gene repeat expansion profile of motor neuron disease patients in Portugal. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Ana Catarina Pronto Laborinho, Blood cells: unravelling their impact on respiratory outcome and survival in amyotrophic lateral sclerosis (ALS). 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Susana Pinto, Impact of age on the bulbar phenotype of ALS patients. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Marta Gromicho, Expanding the genotype-phenotype diversity of amyotrophic lateral sclerosis. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Miguel Oliveira Santos, Cerebral spinal fluid and plasma glial fibrillary acidic protein and vascular endothelial growth factor in adult spinal muscular atrophy patients treated with nusinersen. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Shefner, J, Title: Hospitalizations in COURAGE-ALS and their relationship to ALS. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Poster Presentation)

Shefner, J, COURAGE-ALS: Results of the Phase 3 Clinical Trial of Reldesemtiv in ALS. 34th International Symposium on ALS/MND, Basel, Switzerland, December 8, 2023. (Oral Presentation)

Communications in National Conferences:

Pedro Rocha, Home-based monitoring of patients with amyotrophic lateral sclerosis with mobile sensors. Rede Saúde Workshop O Desafio dos Dados: Uma Nova Fronteira nas Doenças Neurodegenerativas, Portugal, January 31, 2023. (Oral Presentation)

Inês Alves, BRAINTEASER: Bringing Artificial Intelligence at home for Better care of Amyotrophic Lateral Sclerosis (ALS) and Multiple Sclerosis (MS) patients. Rede Saúde Workshop O Desafio dos Dados: Uma Nova Fronteira nas Doenças Neurodegenerativas, Portugal, January 31, 2023. (Oral Presentation)

Beatriz de Carvalho, Body mass index as independent predictor of diaphragmatic function in amyotrophic lateral sclerosis. 6th Congress of the Egas Moniz Center for Interdisciplinary Research (CiiEM), Portugal, July 5, 2023. (Poster Presentation)

Diana Monteiro Lopes, Blood neutrophil-to-lymphocyte ratio predicts survival in amyotrophic lateral sclerosis patients. 6th Congress of the Egas Moniz Center for Interdisciplinary Research (CiiEM), Portugal, July 5, 2023. (Poster Presentation)

Ana Catarina Pronto Laborinho, Erythrocyte membrane properties in patients with ALS. 6th Congress of the Egas Moniz Center for Interdisciplinary Research (CiiEM), Portugal, July 5, 2023.

Pedro Rocha, Smartphone-based cough data in amyotrophic lateral sclerosis: a potential predictor of functional disability. 6th Congress of the Egas Moniz Center for Interdisciplinary Research (CiiEM), Portugal, July 5, 2023. (Poster Presentation)

Inês Alves, Demographic changes in a large motor neuron disease cohort in Portugal: a 27 year experience. 6th Congress of the Egas Moniz Center for Interdisciplinary Research (CiiEM), Portugal, July 5, 2023. (Poster Presentation)

Cláudia Santos Silva, Miopatia ocular em doentes infetados com o vírus de imunodeficiência humana sob terapêutica antirretroviral. 11º Congresso Português de Doenças Neuromusculares, Portugal, September 29, 2023. (Oral Presentation)

C Serrão, Polineuropatia desmielinizante em doente com Esclerose Múltipla: um exemplo de Desmielinização Central e Periférica Combinada? Reunião de Outono do Grupo de Estudos de Esclerose Múltipla, Portugal, October 21, 2023. (Poster Presentation)

Pedro Rocha, The impact of urban environment on spatial navigation in elderly people with mild cognitive impairment. Champalimaud Research Neuro Symposium 2023, Portugal, October 24, 2023. (Poster Presentation)

Sara Simão, Cognitive and behavioural changes and cognitive reserve in amyotrophic lateral sclerosis. Champalimaud Research Neuro Symposium 2023, Portugal, October 24, 2023. (Oral Presentation)

Pedro Rocha, Voice assessment in patients with amyotrophic lateral sclerosis and its relationship to bulbar and respiratory function. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Ana Catarina Pronto Laborinho, Red Cell Distribution Width (RDW) in ALS. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Cláudia Santos Silva, Perfil Fenotípico da Doença de Neurónio Motor Associada à Expansão do Gene C9ORF72 em Portugal. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Maria Fortuna Baptista, Preditores de Sobrevida na Fase Final da Doença Esclerose Lateral Amiotrófica. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Marta Gromicho, Expanding the Genotype-Phenotype Diversity of Amyotrophic Lateral Sclerosis. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Ana Catarina Pronto-Laborinho, Erythrocyte Membrane Properties in Patients with ALS Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Inês Alves, BRAINTEASER Project: Enhancing Amyotrophic Lateral Sclerosis Care through Remote Monitoring and Artificial Intelligence Integration. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Beatriz de Carvalho, Body Mass Index as Independent Predictor of Diaphragmatic Function in Amyotrophic Lateral Sclerosis. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)

Diana Monteiro Lopes, Blood Cells: Unravelling Their Impact on Respiratory Outcome and Survival in Amyotrophic Lateral Sclerosis (ALS). Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)

Diana Monteiro Lopes, Blood Neutrophil-to-Lymphocyte Ratio Predicts Survival in Amyotrophic Lateral Sclerosis Patients. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)

Cláudia Santos Silva, Forma familiar de doença do neurónio motor associada à mutação no gene VAPB – um genótipo de origem portuguesa numa família brasileira. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Ferrão, C, Nusinersen in adults with type 3 Spinal Muscular Atrophy: long-term outcomes on motor and respiratory function. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Miguel Oliveira Carvalho, Heterogeneidade fenotípica numa família portadora da variante c.110G>C (p.Arg37Pro) em homozigotia no gene HINT1. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation).

José Castro, A neurophysiological approach to mirror movements in Amyotrophic Lateral Sclerosis. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Beatriz de Carvalho, Body mass index as independent predictor of diaphragmatic function in amyotrophic lateral sclerosis. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)

Sara Simão, Cognitive and behavioural changes and cognitive reserve in amyotrophic lateral sclerosis Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)



Catarina Serrão, Nusinersen in Adults with Type 3 Spinal Muscular Atrophy. Long-term outcomes on motor and respiratory function. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Oral Presentation)

Miguel Schön, Insuficiência respiratória aguda como manifestação inaugural de miopatia congénita numa doente octogenária. Congress of Neurology, Portuguese Society of Neurology, Portugal, November 9, 2023. (Poster Presentation)

### **Organization of Conferences**

Mamede de Carvalho, Moderator and Co-Organizer, Workshop “O Desafio dos Dados: uma nova fronteira das doenças neurodegenerativas” by redeSAÚDE” - Universidade de Lisboa, Portugal, January 16, 2023.

Mamede Alves de Carvalho, Moderator and Co-Organizer, Demand Symposium on Transcranial Magnetic Stimulation in ALS, 5th International Brain Stimulation Conference, Portugal, February 15, 2023.

Mamede de Carvalho, Moderator and Organizer, ICU-Acquired weakness: Clinical and electrophysiological aspects, promoted by European Chapter on Clinical Neurophysiology-European Chapter on Clinical Neurophysiology, 17th European Congress of Clinical Neurophysiology, France, May 5, 2023.

Mamede de Carvalho, Moderator, European Chapter on Clinical Neurophysiology, 17th European Congress of Clinical Neurophysiology), France, May 5, 2023.

Mamede de Carvalho, Member of the Organising Committee, 7ª Conferência Anual da redeSAÚDE da ULisboa, “Viver em Qualidade: Valor em Saúde e Bem-Estar”, Portugal, September 17, 2023.

Mamede de Carvalho, Moderator, Hot Topics Session: Neuromuscular, Congresso da Sociedade Portuguesa de Neurologia, Porto, Portugal, November 6, 2023.

Mamede de Carvalho, Moderador, Symposium Anylam Session, Congresso da Sociedade Portuguesa de Neurologia, Porto, Portugal, November 6, 2023.

Isabel Conceição, Organizer, XII Encontro Nacional de Paramiloidose para Técnicos de Saúde, Portugal, November 17, 2023.

### **Prizes and Honours**

Beatriz de Carvalho, Best Poster, 6th CiiEM International Congress.

Ana Catarina Pronto Laborinho, Referee for journals: - Journal of Neuroinflammation (springer nature) - MDPI Journal - Scientific Reports (Nature Group) - Frontiers in Neurology - BMC Medical Genomics - Neurology Research International - Case Reports in Medicine.

Marta Gromicho, Referee for journals: - Frontiers in Neurology - Current Research in Neurobiology - Journal of Neurology - Journal of the Neurological Sciences – Biomolecules.

Vasco Conceição, Referee for journals: - Reviewer for Scientific Reports (Nature).

Mamede de Carvalho, Member of the Editorial Board of the journals (revised articles): “Clinical Neurophysiology”, 2004-2010 and 2020- ... (346). “Amyotrophic Lateral Sclerosis”, since 2007 (136). “Neurophysiologie Clinique”, since 2008 (45). “Journal of Neurological Sciences-Turkish”, since 2017 “Neurology”, since 2021 (78) “Clinical Neurology and Neurosurgery”, since 2021 (61) “Brain Sciences”, since 2021 (9).

Mamede de Carvalho, Associate Editor of Journals: “Case Reports in Medicine”, since 2009. “Neurology Research International”, since 2009. “BMC Neurology”, since 2018. “Sinapse”, since 2020. “Frontiers of Neurology”, since 2021.

### **Advanced Teaching**

Vasco Conceição, Lecture, Mestrado/Doutoramento em Neurociências – 2º e 3º ciclo (Módulo de Neurociências Computacionais), Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2, 2023.

Vasco Conceição, Lecture, Mestrado Integrado em Engenharia Biomédica (1º Ano – 1º Semestre) – 2º ciclo (Bioeletricidade), Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2, 2023.

Vasco Conceição, Lecture, Mestrado Integrado em Engenharia Biomédica (2º Ano – 2º Semestre) – 2º ciclo (Fisiologia dos Sistemas), Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2, 2023.

Vasco Conceição, Lecture, Mestrado Integrado em Medicina (2º Ano – 2º Semestre) – 2º ciclo, Tronco Comum em Neurociências – (Neuro)Fisiologia, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2, 2023.

Vasco Conceição, Lecture, Mestrado Integrado em Medicina (1º Ano – 1º Semestre) – 2º ciclo-  
Módulo II.I – Fisiologia, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal,  
January 2, 2023.

Vasco Conceição, Lecture, Mestrado Integrado em Medicina (1º Ano – 2º Semestre) – 2º ciclo-  
Módulo II.II – Fisiologia, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2,  
2023.

Vasco Conceição, Lecture, Mestrado Integrado em Medicina (2º Ano – 1º Semestre) – 2º ciclo-  
Módulo II.III – Fisiologia, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2,  
2023.

José Castro, Lecture, Mestrado Integrado em Medicina (2º Ano – 2º Semestre) – 2º ciclo, Tronco  
Comum em Neurociências – (Neuro)Fisiologia, Portugal, January 2, 2023.

Mariana Pereira, Lecture, Mestrado Integrado em Medicina (2º Ano – 2º Semestre) – 2º ciclo,  
Tronco Comum em Neurociências – (Neuro)Fisiologia, Portugal, January 2, 2023.

Ana Catarina Oliveira Silva Pronto Laborinho, Lecture, Mestrado Integrado em Medicina (1º Ano  
– 2º Semestre) – 2º ciclo-Módulo II.I – Fisiologia, Faculdade de Medicina da Universidade de  
Lisboa, Portugal, January 2, 2023.

Mamede de Carvalho, Coordination of Master Curricular Unit, Mestrado em Neurociências,  
Portugal, January 2, 2023.

Isabel Conceição, Lecture, Neuroscience Master-Seminar – Neuropathology of TTR  
Transthyretin-Related Hereditary Amyloidosis, Lisbon, Portugal, February 2, 2023.

Ana Catarina Oliveira Silva Pronto Laborinho, Lecture, Ciências da Nutrição, Portugal, February  
6, 2023.

Isabel Conceição, Lecture, Evoked Potentials and Small Fibers Neurophysiology, University of  
Lisbon - Neuroscience Master, Lisbon, Portugal, February 22, 2023.

Ana Catarina Oliveira Silva Pronto Laborinho, Lecture, Mestrado Integrado em Medicina (1º Ano  
– 2º Semestre) – 2º ciclo-Módulo II.II – Fisiologia, Faculdade de Medicina da Universidade de  
Lisboa, Portugal, March 6, 2023.

Ana Catarina Oliveira Silva Pronto Laborinho, Lecture, Mestrado Integrado em Engenharia Biomédica (2º Ano – 2º Semestre) – 2º ciclo (Fisiologia dos Sistemas), Faculdade de Medicina da Universidade de Lisboa, Portugal, May 31, 2023.

Mamede de Carvalho, Coordination of Master Curricular Unit, Mestrado Integrado em Medicina (2º Ano – 1º Semestre) – 2º ciclo- Módulo II.III, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 1, 2023.

Tiago Maia, Coordination of PhD Curricular Unit, Module Coordination: Computational Neuroscience. Mestrado/Doutoramento em Neurociências, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 10, 2023.

### **MSc Theses**

Bernardo Machado Antunes, Diagnostic delay in sporadic ATTRv amyloidosis, Supervisor: Mamede de Carvalho, Co-Supervisor: Isabel Conceição, Faculdade de Medicina da Universidade de Lisboa, Portugal, May 18, 2023.

Miguel Afonso N Lopes, Low intensity F-wave stimulation as a marker of excitability of lower motor neurons innervating hand muscles, Supervisor: Mamede de Carvalho, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 14, 2023.

Gonçalo LX Mendes Pechirra, The senile hand: age effects on intrinsic hand muscle CMAP amplitudes influence split-hand index calculations, Supervisor: Mamede de Carvalho, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 14, 2023.

Nuno Peixinho Elias, Identification of de-regulated circulating microRNAs as putative biomarkers in Amyotrophic Lateral Sclerosis, Supervisor: Mamede de Carvalho, Co-Supervisor: Marta Gromicho, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 14, 2023.

João Farinha Correia, Creatine Kinase and Respiratory Decline in Amyotrophic Lateral Sclerosis: friend or foe?, Supervisor: Mamede de Carvalho, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 18, 2023.

Carla Freitas da Costa, Exercício físico pré-mórbido e declínio da função respiratória em Esclerose Lateral Amiotrófica, Supervisor: Mamede de Carvalho, Co-Supervisor: Marta Gromicho, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 18, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

- Cytokinetics Inc, Clinical Project, Sponsored Research.
- Biogen Inc, Collaborative Research.
- Ono Pharmaceutical, Contract Research.
- COURAGE-ALS (A Phase 3, Multi-Center, Double-blind, Randomized, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Reldesemtiv in Patients with ALS) , Clinical Trial (Mamede de Carvalho – Coordinator).
- PHOENIX (A Phase III, randomized, double blind, placebo controlled, multicenter trial to evaluate the safety and efficacy of AMX0035 versus placebo for 48 week treatment of adult patients with ALS) – 2021, Clinical Trial (Mamede de Carvalho-Coordinator).
- ADORE (ALS Deceleration with ORal Edaravone) - multicenter, randomized, double-blind, placebo-controlled study to investigate the efficacy and safety of FAB122 in patients with ALS– 2021, Clinical Trial (Mamede de Carvalho-Coordinator).

### **Science and Society in 2023**

Mamede de Carvalho:

- President of the Scientific Committee of the Associação Portuguesa de Esclerose Lateral Amiotrófica - APELA, since 1997.
- Responsible for the Neurodegenerative Diseases Working Group of the Rede Saúde da Universidade de Lisboa since 2021.
- Collaboration with APELA (Portuguese Association of patients with Amyotrophic Lateral Sclerosis), target population patients and caregivers, concerning science advances sharing, in particular regarding treatments, and sharing undergoing scientific projects.

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## Zita Carvalho-Santos Lab

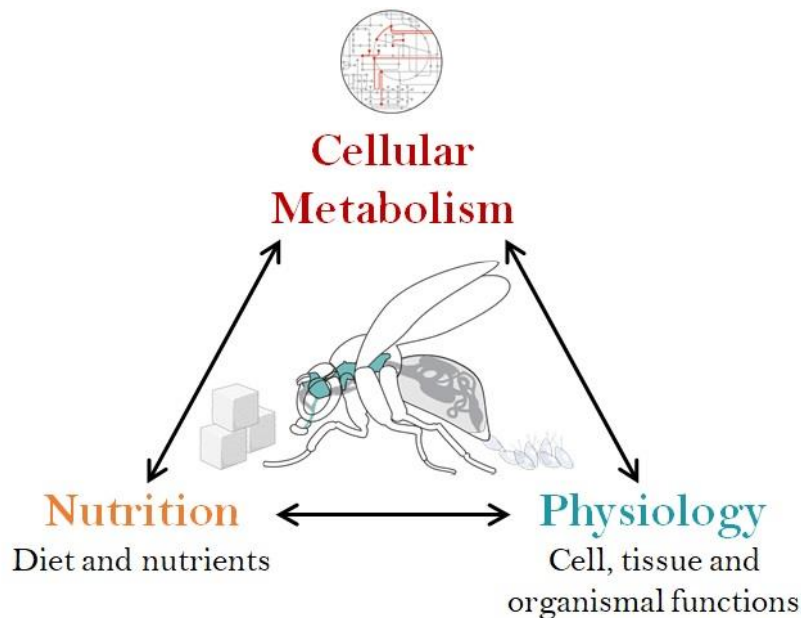
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**Head of Laboratory:** Zita Carvalho-Santos, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes (Started January)

### Team

Ana Patrícia Tomé Francisco	PhD	Lab Manager/Researcher (Started March)
Catarina Alexandra Brás Simões Pereira	PhD	Senior Postdoctoral Researcher (Started October)
Raquel Rebocho Nóbrega	University Degree	Master Student (Started September)

### Graphical Abstract



### Lab Interests

Metabolic processes are core to all cellular functions. Unraveling the mechanisms that enable animals to address the metabolic demands of various tissues, and understanding how cell-specific metabolic programs impact overall animal physiology, is a fundamental question to understand all biological systems. Our laboratory's primary goal is to understand how cellular metabolism regulates animal physiology. We aim at revealing the mechanisms that allow animals to integrate dietary nutrient availability with cell-specific metabolic processes, thereby influencing cellular functions that resonate throughout the entire animal. Given the complexity of this question, which spans diverse scientific domains, we use a systems biology approach combined with a highly tractable model system—the fruit fly—to tackle this question.

Leveraging the adaptable nature of the germline, we investigate the impact of diet-metabolism interactions on ovary homeostasis, female fertility, and feeding behavior.

### **Research Fields**

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging

### **Major Scientific Achievements in 2023**

Established in January 2023, our laboratory embarked on an exciting journey over the past year. Our primary focus during this period has been the establishment of the laboratory infrastructure, the recruitment of new collaborators, and the initiation and advancement of the inaugural experiments conducted within the Organismal Metabolic Physiology lab. As we look forward, our aspiration is to make numerous compelling discoveries in the coming year, and we anticipate sharing more insights in the near future.

### **Ongoing Projects**

2023/2027: The impact of germline metabolic reprogramming on reproduction and physiology. Coordinator: Zita Carvalho-Santos. Funding Agency: European Commission. Reference: ERC-101043068-SWEETEGGS. Amount: 1 481 513,00€. Total Amount: 1 481 513,00€.

2023/2025: Sub-cellular Metabolic Compartmentalization during Oocyte Development. Coordinator: Zita Carvalho-Santos. Funding Agency: Chan Zuckerberg Initiative. Reference: CZI - MEASURING METABOLISM ACROSS SCALES. Amount: 328 310,41€. Total Amount: 442 790,05€.

2023/2024: The role of healthy cells on the elimination of premalignant cells. Coordinator: Catarina Brás-Pereira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-CEL/3594/2020. Amount: 86 614,59€. Total Amount: 231 875,00€.

## **Scientific Impact**

### **Academic Collaborations**

- Instituto Gulbenkian de Ciência, Portugal.
- INESC-ID Universidade de Lisboa, Portugal.

## Selected Publications

Li H, Janssens J, De Waegeneer M, Kolluru SS, Davie K, Gardeux V, Saelens W, David F, Brbić M, Leskovec J, McLaughlin CN, Xie Q, Jones RC, Brueckner K, Shim J, Tattikota SG, Schnorrer F, Rust K, Nystul TG, Carvalho-Santos Z, Ribeiro C, Pal S, Przytycka TM, Allen AM, Goodwin SF, Berry CW, Fuller MT, White-Cooper H, Matunis EL, DiNardo S, Galenza A, O'Brien LE, Dow JAT, Jasper H, Oliver B, Perrimon N, Deplancke B, Quake SR, Luo L, Aerts S, FCA Consortium. [Fly Cell Atlas: a single-cell transcriptomic atlas of the adult fruit fly](#) (2022). *Science* 375(6584):eabk2432.

**Relevance of the publication:** The *Drosophila melanogaster* serves as a leading model organism. The integration of state-of-the-art single-cell sequencing with robust genetic tools in fruit flies provides an opportunity to delve into fundamental and evolutionarily conserved biological mechanisms. This study unveils a comprehensive single-cell atlas of the entire adult fly, serving as a valuable resource for the *Drosophila* community to explore genetic perturbations and diseases with unprecedented single-cell resolution.

Carvalho-Santos Z, Cardoso-Figueiredo R, Elias AP, Tastekin I, Baltazar C, Ribeiro C†. [Cellular metabolic reprogramming controls sugar appetite in \*Drosophila\*](#) (2020). *Nat Metab.* 2(9):958-973.

**Relevance of the publication:** In this study, we investigated the dietary and metabolic demands of the female germline and their implications for animal physiology. We uncovered that the germline undergoes metabolic reprogramming involving the transcriptional upregulation of genes in the pentose phosphate pathway. We found that this process regulates both female fertility and the animal's appetite for sugary foods. These findings demonstrate how metabolism of specific cellular subsets can influence broader animal functions.

Carvalho-Santos Z, Ribeiro C (2017). [Gonadal ecdysone titers are modulated by protein availability but do not impact protein appetite](#). *J Insect Physiol.*

**Relevance of the publication:** The amount of ingested dietary protein impacts animal reproduction. Upon dietary protein deprivation, insects rapidly stop producing eggs and develop a strong appetite for protein-rich foods. Our findings demonstrate that the levels of ovarian hormone in mated females reflect the physiological state of the ovaries and that while this hormone is unlikely to instruct the brain to develop a yeast appetite upon protein deprivation, it may contribute to the overall control of food intake.

Leitão-Gonçalves R\*, Carvalho-Santos Z\*, Francisco AP\*, Fioreze GT, Anjos M, Baltazar C, Elias AP, Itskov PM, Piper MDW, Ribeiro C (2017). [Commensal bacteria and essential amino acids control food choice behavior and reproduction](#). *PLoS Biol* 15(4): e2000862.

**Relevance of the publication:** Nutrient intake influences animal life-history traits but the mechanisms governing feeding decisions for nutrient homeostasis remain poorly understood. We discovered that deprivation of single essential amino acids boosts the appetite for protein-rich food while drastically impairing female fertility. Remarkably, specific gut bacterial combinations lead rescues both protein appetite and fertility during amino acid deprivation. This study highlights the influence of gut microbes on food choice.

## Invited Lectures and Seminars

Zita Carvalho-Santos, Metabolic Tango: Gut Bacteria and Dietary Nutrients Dance Together to Regulate Host Food Choices and Reproduction. ABC-RI International Forum, Online, April 18, 2023.



## Communications

### Communications in International Conferences:

Zita Carvalho-Santos, Metabolic remodeling as a trigger for female fertility decay. GCRLE Scholars Symposium, USA, February 5, 2023. (Oral Presentation)

Zita Carvalho-Santos, How cellular metabolic reprogramming shapes nutrient utilization by the germline and impacts female fertility. European Drosophila Research Conference, France, October 21, 2023. (Poster Presentation)

Patricia Francisco, Marmite defines a novel conserved neuropeptide family mediating nutritional homeostasis. European Drosophila Research Conference, France, October 23, 2023. (Oral Presentation)

### Communications in National Conferences:

Zita Carvalho-Santos, How germline cellular metabolic reprogramming impacts female fertility and whole animal physiology. Building Bridges in Biology Symposium, Portugal, March 1, 2023. (Oral Presentation)

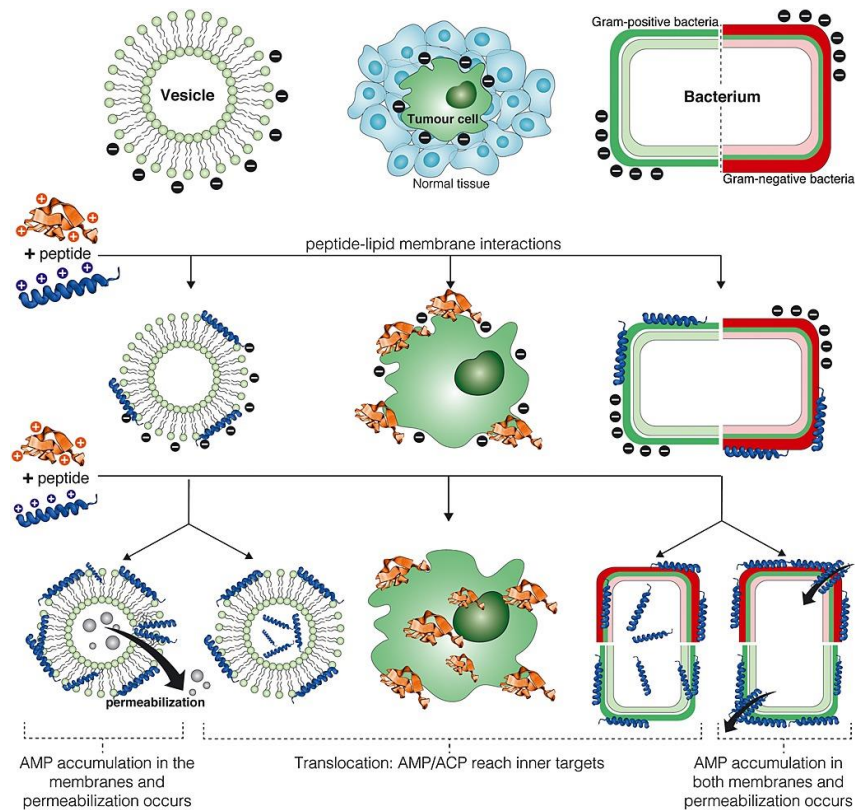
## Miguel Castanho Lab

**Head of Laboratory:** Miguel Castanho, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Full Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Alexandra Lopes Leal Afonso	Bachelor Degree	Trainee (Started September)
Ana Carolina Carvalho Buga	Master Degree	PhD Student
Ana Isabel Machado Roque	PhD	Project Manager
Ana Rosa Miranda dos Santos Silva Herdade	PhD	Senior Postdoctoral Researcher
Ana Salomé Rocha do Nascimento Veiga	PhD	Staff Scientist
António Alexandre Riachos Camarão	PhD	Postdoctoral Researcher (Started December)
Beatriz Lopes Dias Vieira da Silva	Master Degree	Researcher (Started October)
Beatriz Traguedo Simões	Master Degree	Researcher
Catarina de Jesus Pinto Gonçalves	Master Degree	PhD Student
Catarina Isabel Parente Chaparro	Master Degree	PhD Student
Christine Cruz Oliveira	PhD	Senior Postdoctoral Researcher
Cyan Zoey Kort	Bachelor Degree	MSc Student (Started September)
Diogo Alexandre de Mendonça	Master Degree	PhD Student (Left October)
Joana Azevedo Felice Lopes	University Degree	MSc Student (Left July)
Liliana Faia Carvalho	Master Degree	Lab Manager
Marco Calvino Cavaco	PhD	Postdoctoral Researcher
Mariana Viegas Farinha Lemos Parada	University Degree	MSc Student (Left December)
Milena Bellei Cherene	Master Degree	PhD Student (Left February)
Patrícia Alexandra Branco Fraga	Master Degree	PhD Student (Started February)
Rodrigo Castel-Branco de Avelar Osório de Alarcão	University Degree	MSc Student (Left December)
Tiago André Afonso dos Santos	PhD	Postdoctoral Researcher
Vera Luísa Santos Neves	PhD	Staff Scientist

## Graphical Abstract



*Permeabilization of vesicles and bacteria usually demands saturation of membranes. In standard antibacterial activity assays, this occurs in or above micromolar concentration ranges. In bacteria, saturation of outer membranes leads to permeabilization and AMP interaction with the inner membrane. Some AMPs are able to translocate membranes at lower concentrations and reach the interior of vesicles or bacteria. In these cases, killing may occur by interaction with intracellular targets. This mechanism is more often associated with ACP. Freire, JM, Gaspar D, Veiga AS, Castanho MA. Shifting gear in antimicrobial and anticancer peptides biophysical studies: from vesicles to cells. *J Pept Sci.* 2015 Mar;21(3):178-85. doi: 10.1002/psc.2741.*

## Lab Interests

Numerous biological processes rely on the interplay between peptides/proteins and membrane lipids, including viral fusion, translocation across epithelia, and innate immune defense. Some inspire the creation of therapeutic tools. Our goal is to unravel the physical principles governing lipid-peptide interactions, specifically in viral fusion (HIV, SARS-CoV-2, Zika and Dengue viruses) and blood-placental/blood-brain barrier translocation, fostering anti-infective and antimetastatic cancer drug development.

To achieve our goals, we've identified proprietary drugs and carriers while developing tailored spectroscopic and imaging methodologies. These advances contribute to our holistic approach in identifying the molecular determinants of peptide drug mechanism, positioning us at the forefront of innovative therapeutic research with potential applications in infectious diseases and cancer treatment.

### Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Neuroscience and Disorders of the Nervous System
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

### Major Scientific Achievements in 2023

In 2023, we secured EU approval for two HORIZON projects, focusing on Antiviral Therapeutics. One of the projects, EvaMobs in collaboration with ITQB/NOVA, uses a multidisciplinary approach to design next-gen antiviral biologics. Another project, AVITHRAPID, consists of a collaboration with academic and industry partners to develop Antiviral Therapeutics for Rapid Response Against Pandemic Infectious Diseases.

During 2023, we published 10 papers on rational discovery and development of bioactive peptides. Our commitment to advancing knowledge was also evident in active participation in National (e.g., Encontro Ciência 2023, ESN-ISN Neurochemistry School – Faro) and International (e.g., APS Symposium 2023) Conferences. These platforms showcased groundbreaking findings, reinforcing leadership in antiviral therapeutics research and consolidating our role in shaping the future of this crucial field.

### Ongoing Projects

2022/2025: *Lentes oculares inteligentes para o tratamento de doenças do olho diabético*. Coordinator: Ana Herdade. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CTM-CTM/2353/2021. Amount: 31 875,00€. Total Amount: 249 920,00€.

2022/2025: *Desenvolvimento de fragmentos de anticorpos potentes e amplamente neutralizantes para COVID-19 derivados de gatos domésticos naturalmente infectados com SARS-CoV-2*. Coordinator: Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CVT-CVT/0149/2021. Amount: 22 500,00€. Total Amount: 249 328,24€.

2022/2025: The BioPlaTTar platform for the tailored and rapid development of antiviral biopharmaceuticals. Coordinator: Ana Salomé Veiga. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - HR22-00722 – BIOPLATTAR. Amount: 174 680,00€. Total Amount: 1 000 000,00€.

2022/2025: *Desenvolvimento de uma nanopartícula translocadora da barreira hematoencefálica para o diagnóstico precoce da doença de Alzheimer.* Coordinator: Vera Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BTM-MAT/2472/2021. Amount: 177 505,63€. Total Amount: 210 005,63€.

2022/2024: *Uma abordagem molecular e nano direcionada à interface RANK-TRAF6 para tratamento de metástases ósseas.* Coordinator: Vera Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QUI-OUT/3854/2021. Amount: 65 000,00€. Total Amount: 248 329,40€.

2021/2024: TRESPASS2TREAT: uma abordagem inovadora na farmacoterapia de pacientes com metástases cerebrais de cancro de mama. Coordinator: Miguel Castanho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-BQM/5027/2020. Amount: 77 500,00€. Total Amount: 127 500,00€.

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

2021/2023: NOSTRESS: New functional foods to reduce the effects of stress in aquaculture. Coordinator: Miguel Castanho. Funding Agency: Portugal 2002. Reference: ALG-01-0247-FEDER-047122. Amount: 165 634,74€. Total Amount: 995 958,32€.

2019/2024: "One size fits all" unique drug to eradicate multiple viral species simultaneously from the central nervous system of co-infected individuals - NOVIRUSES2BRAIN. Coordinator: Miguel Castanho. Funding Agency: European Commission. Reference: GA 828774 - H2020-FETOPEN-2018. Amount: 2 113 125,00€. Total Amount: 3 933 965,63€.

2014/2024: Neuropore Therapies. Coordinator: Miguel Castanho. Funding Agency: Neuropore Therapies, Inc. Reference: NEUROPORE THERAPIES. Amount: 20 000,00€. Total Amount: 20 000,00€.

## Scientific Impact

### Academic Collaborations

- Andrea Da Poian, Instituto de Bioquímica Médica Leopoldo de Meis, Federal University of Rio de Janeiro, Brazil.
- Charles Lawrie, Asociación Instituto Biodonostia, Spain.
- Cláudio M. Soares, Instituto de Tecnologia Química e Biológica António Xavier, da Universidade Nova de Lisboa (ITQB NOVA), Portugal.
- David Andreu, Proteomics and Protein Chemistry Unit, Department of Experimental and Health Sciences, Pompeu Fabra University, Spain.
- Diana Lousa, Instituto de Tecnologia Química e Biológica António Xavier, da Universidade Nova de Lisboa (ITQB NOVA), Portugal.
- Frederico Aires-da-Silva, Faculty of Veterinary Medicine, CIISA-Centre for Interdisciplinary Research in Animal Health, University of Lisbon, Portugal.
- João D. G. Correia, Centro de Ciências e Tecnologias Nucleares and Departamento de Engenharia e Ciências Nucleares, Instituto Superior Técnico da Universidade de Lisboa, Portugal.
- João P. Borges, i3N/CENIMAT, Department of Materials Science, NOVA School of Science and Technology, NOVA University of Lisbon, Campus de Caparica, Portugal.
- Jordi Llop, CIC biomaGUNE Donostia, Spain.
- Katia da Conceição, Universidade Federal de São Paulo: São José dos Campos, Brazil.
- Maja Katalinić, Institute for Medical Research and Occupational Health, Portugal.
- Mária A Deli, Department of Biophysics, Biological Research Centre, Hungarian Academy of Sciences, Hungary.
- Michael Burnet, Synovo GmbH, Tübingen, Germany.
- Paula I.P. Soares, i3N/CENIMAT, Department of Materials Science, NOVA School of Science and Technology, NOVA University of Lisbon, Campus de Caparica, Portugal.
- João Gonçalves, Faculdade de Farmácia da Universidade de Lisboa, Portugal.
- Manuel Melo, Instituto de Tecnologia Química e Biológica António Xavier da Universidade Nova de Lisboa (ITQB NOVA), Lisboa, Portugal.
- João Vicente, Instituto de Tecnologia Química e Biológica António Xavier da Universidade Nova de Lisboa (ITQB NOVA), Lisboa, Portugal.
- Isabel Abreu, Instituto de Tecnologia Química e Biológica António Xavier da Universidade Nova de Lisboa (ITQB NOVA), Lisboa, Portugal.

- Maria João Amorim, Instituto Gulbenkian de Ciência e do Católica Biomedical Research Centre, Lisboa, Portugal.

### Selected Publications

Dias SA, Pinto SN, Silva-Herdade AS, Cavaco M, Neves V, Tavares L, Oliveira M, Andreu D, Coutinho A, Castanho MARB, Veiga AS (2023). [Quantitative Imaging of the Action of vCPP2319, an Antimicrobial Peptide from a Viral Scaffold, against Staphylococcus aureus Biofilms of a Clinical Isolate](#). *ACS Infect Dis.* 9(10):1889-1900.

**Relevance of the publication:** In this work, we show that vCPP2319, a polycationic peptide derived from the capsid protein of Torque teno douroucouli virus, is active against preformed Staphylococcus aureus biofilms produced by both a reference strain and a clinical strain isolated from a diabetic foot infection, mainly by the killing of biofilm-embedded bacteria.

Valério M, Mendonça DA, Morais J, Buga CC, Cruz CH, Castanho MARB, Melo MN, Soares CM, Veiga AS, Lousa D (2022). [Parainfluenza Fusion Peptide Promotes Membrane Fusion by Assembling into Oligomeric Porelike Structures](#). *ACS Chem Biol.* 17(7):1831-1843.

**Relevance of the publication:** We uncovered the crucial mechanisms for the entry of parainfluenza viruses into the host's cells. This discovery can contribute to unveiling ways to inhibit entrance and prevent infection.

Todorovski T, Mendonça DA, Fernandes-Siqueira LO, Cruz-Oliveira C, Guida G, Valle J, Cavaco M, Limas FIV, Neves V, Cadima-Couto Í, Defaus S, Veiga AS, Da Poian AT, Castanho MARB, Andreu D (2022). [Targeting Zika Virus with New Brain- and Placenta-Crossing Peptide-Porphyrin Conjugates](#). *Pharmaceutics* 14(4):738.

**Relevance of the publication:** We reported one conjugate, PP-P1, able to cross both blood-placental and/or blood-brain barriers, and has shown to be effective against Zika Virus.

Dias SA, Pinto SN, Silva-Herdade AS, Cheneval O, Craik DJ, Coutinho A, Castanho MARB, Henriques ST, Veiga AS (2022). [A designed cyclic analogue of gomesin has potent activity against Staphylococcus aureus biofilms](#). *J Antimicrob Chemother.* 77(12):3256-3264.

**Relevance of the publication:** Our results suggest that the 3D structure of [G1K,K8R]cGm and its stabilization by disulphide bonds are essential for its antibacterial and antibiofilm activities. Moreover, our findings support the potential application of this stable cyclic antimicrobial peptide to fight bacterial biofilms.

Caccuri F, Neves V, Gano L, Correia JDG, Oliveira MC, Mazzuca P, Caruso A, Castanho M (2022). [The HIV-1 Matrix Protein p17 Does Cross the Blood-Brain Barrier](#). *J Virol.* 96(1):e0120021.

**Relevance of the publication:** We showed the ability of the p17 to cross the BBB and to reach the CNS, thus playing a crucial role in neuronal dysfunction in HIV-1-associated neurocognitive disorder (HAND).

### 2023 Publications in Peer-Reviewed Journals

Chaparro CIP, Simões BT, Borges JP, Castanho MARB, Soares PIP, Neves V. (2023). A Promising Approach: Magnetic Nanosystems for Alzheimer's Disease Theranostics. *Pharmaceutics*. 15(9):2316.

Vieira-da-Silva B, Castanho MARB (2023). The structure and matrix dynamics of bacterial biofilms as revealed by antimicrobial peptides' diffusion. *J Pept Sci*. 29(6):e3470.

Mota-Silva I, Castanho MARB, Silva-Herdade AS. (2023). Towards Non-Invasive Intravital Microscopy: Advantages of Using the Ear Lobe Instead of the Cremaster Muscle. *Life (Basel)*. 13(4):887.

Vieira-da-Silva B, Castanho MARB (2023). Resazurin Reduction-Based Assays Revisited: Guidelines for Accurate Reporting of Relative Differences on Metabolic Status. *Molecules*. 28(5):2283.

Strandberg E, Wadhvani P, Bürck J, Anders P, Mink C, van den Berg J, Ciriello RAM, Melo MN, Castanho MARB, Bardají E, Ulmschneider JP, Ulrich AS (2023). Temperature-Dependent Re-alignment of the Short Multifunctional Peptide BP100 in Membranes Revealed by Solid-State NMR Spectroscopy and Molecular Dynamics Simulations. *Chembiochem*. 24(4).

Cherene MB, Taveira GB, Almeida-Silva F, da Silva MS, Cavaco MC, da Silva-Ferreira AT, Perales JEA, de Oliveira Carvalho A, Venâncio TM, da Motta OV, Rodrigues R, Castanho MARB, Gomes VM (2023). Structural and Biochemical Characterization of Three Antimicrobial Peptides from *Capsicum annum* L. var. *annuum* Leaves for Anti-Candida Use. *Probiotics Antimicrob Proteins*.

Dias SA, Pinto SN, Silva-Herdade AS, Cavaco M, Neves V, Tavares L, Oliveira M, Andreu D, Coutinho A, Castanho MARB, Veiga AS (2023). Quantitative Imaging of the Action of vCPP2319, an Antimicrobial Peptide from a Viral Scaffold, against *Staphylococcus aureus* Biofilms of a Clinical Isolate. *ACS Infect Dis*. 9(10):1889-1900.

André AS, Dias JNR, Aguiar SI, Leonardo A, Nogueira S, Amaral JD, Fernandes C, Gano L, Correia JDG, Cavaco M, Neves V, Correia J, Castanho M, Rodrigues CMP, Gaspar MM, Tavares L, Aires-da-Silva F. (2023) Panobinostat-loaded folate targeted liposomes as a promising drug delivery system for treatment of canine B-cell lymphoma. *Front Vet Sci*. 10:1236136.



Zandona A, Madunić J, Miš K, Maraković N, Dubois-Geoffroy P, Cavaco M, Mišetić P, Padovan J, Castanho M, Jean L, Renard PY, Pirkmajer S, Neves V, Katalinić M. (2023) Biological response and cell death signaling pathways modulated by tetrahydroisoquinoline-based aldoximes in human cells. *Toxicology*. 494:153588.

André AS, Dias JNR, Aguiar S, Nogueira S, Bule P, Carvalho JI, António JPM, Cavaco M, Neves V, Oliveira S, Vicente G, Carrapiço B, Braz BS, Rütgen B, Gano L, Correia JDG, Castanho M, Goncalves J, Gois PMP, Gil S, Tavares L, Aires-da-Silva F. (2023) Rabbit derived VL single-domains as promising scaffolds to generate antibody-drug conjugates. *Sci Rep*. Mar 13(1):4837.

### **Invited Lectures and Seminars**

Miguel Castanho, NOVIRUSES2BRAIN: Developing broad spectrum brain-targeting drugs against flaviviruses and other envelope viruses. Symposium Cell-Based Research in Toxicology and Drug Design, Croatia, January 26, 2023.

Vera Neves, Peptide Shuttles for receptor independent transport across the BBB. Symposium Cell-Based Research in Toxicology and Drug Design, Croatia, January 26, 2023.

Miguel Castanho, Beating the blood-brain barrier to target Alzheimer's and other brain diseases. 2nd Symposium on Alzheimer's Disease, Portugal, February 10, 2023.

Miguel Castanho, Our Lab contribution towards readiness and preparedness for the next pandemic. Internal Seminar iMM, Portugal, March 15, 2023.

Miguel Castanho, EIC Pathfinder Outlook, Name of meeting: Info day Horizon Europe, Portugal, March 29, 2023.

Miguel Castanho, One Health: A new challenge for health education and research. II Jornadas de Saúde - One Health, Portugal, May 24, 2023.

Miguel Castanho, Deep tech entrepreneurship - for innovative, resilient, and competitive internal market. Swedish presidency of the Council of the EU - 2023, Sweden, June 1, 2023.

Miguel Castanho, Getting prepared for the next big pandemic - is it possible? Biophysics for Global health and sustainability - International year of basic sciences for development, IUPB, France, June 5, 2023.

Miguel Castanho, Transition from postdoc to starting a faculty position - careful considerations and challenges. Biophysical Society Webinar "Postdoc to Faculty Q&A", USA, July 13, 2023.

Miguel Castanho, A broad spectrum antiviral peptide-drug conjugate targeting the brain, from design to in vivo activity. IMAP2023, University of Trieste, Italy, September 8, 2023.

Miguel Castanho, Chair - Session 4: AMPs/HDPs in Immunomodulation. IMAP2023, University of Trieste, Italy, September 8, 2023.

Miguel Castanho, Portugal Healthcare innovation summit 2023. Bamberg Health, Portugal, September 27, 2023.

Miguel Castanho, SP20: Vaccines and new frontiers of life (HALL D). Global Health Forum - Cascais, Portugal, September 29, 2023.

Miguel Castanho, Rethinking the Innovation Pathway. Global Health Forum - Cascais, Portugal, September 30, 2023.

Miguel Castanho, Symposium Chair, XVIII Iberian Peptide Meeting, Portugal, November 29, 2023.

## **Communications**

### Communications in International Conferences:

Miguel Castanho, NOVIRUSES2BRAIN: Developing broad spectrum brain-targeting drugs against Flaviviruses and other envelope viruses. BPS 2023 - 67th Biophysical Society Annual Meeting, USA, February 18, 2023. (Oral Presentation)

Vera Neves, Peptide shuttles to assist the transport of therapeutics across the blood-brain barrier. Cerebral Vascular Biology - CVB 2023 conference, Sweden, June 18, 2023. (Poster Presentation)

Vera Neves, Blood-brain barrier peptide shuttles to improve therapeutics action in the central nervous system. 28th American Peptide Symposium, APS2023, USA, June 24, 2023. (Poster Presentation)

Ana Salomé Veiga, Design and discovery of pepRF1, a new potent CXCR4-targeted inhibitor of HIV-1 entry. 28th American Peptide Symposium, APS2023, USA, June 24, 2023. (Oral Presentation)

Ana Salomé Veiga, Design and discovery of pepRF1, a new potent CXCR4-targeted inhibitor of HIV-1 entry. 28th American Peptide Symposium, APS2023, USA, June 24, 2023. (Poster Presentation)

Miguel Castanho, Developing broad spectrum brain-targeting peptide-drug conjugates against flaviviruses and other envelope viruses. 28th American Peptide Symposium, APS2023, USA, June 26, 2023. (Oral Presentation)

Carolina Buga, Unveiling the molecular mechanism of membrane fusion mediated by the parainfluenza fusion peptide. European Biophysical Societies' Association (EBSA) Congress 2023, Sweden, July 31, 2023. (Oral Presentation)

Carolina Buga, Unveiling the molecular mechanism of membrane fusion mediated by the parainfluenza fusion peptide. European Biophysical Societies' Association (EBSA) Congress 2023, Sweden, July 31, 2023. (Poster Presentation)

Catarina Chaparro, Development of magnetic-polymeric nanoparticles as a theranostics strategy for Alzheimer's disease. 33rd Annual Conference of the European Society for Biomaterials (ESB 2023), Switzerland, September 4, 2023. (Poster Presentation)

Beatriz Tragedo Simões, Development of a nanoparticle for early diagnosis of Alzheimer's disease. 33rd Annual Conference of the European Society for Biomaterials (ESB 2023), Switzerland, September 4, 2023. (Poster Presentation)

Carolina Buga, Molecular insights into membrane fusion mediated by the parainfluenza fusion peptide. EMBO Workshop - Mechanisms of membrane fusion, Germany, September 18, 2023. (Poster Presentation)

Catarina Gonçalves, Inhibition of Cancer Stem Cell Migration in Triple Negative Breast Cancer. 13th EMBO Young Scientists' Forum 2023, Portugal, October 12, 2023. (Poster Presentation)

Catarina Gonçalves, New approach to target triple negative breast cancer brain metastasis. Cancer Immunology, Tumor Microenvironment and Metastasis, Portugal, October 27, 2023. (Poster Presentation)

Patrícia Fraga, Unlocking the gateway to the brain: Innovative strategies for therapeutic delivery across the blood-brain barrier peptides. 2nd Belgian Brain Barrier Symposium, Belgium, November 13, 2023. (Poster Presentation)

Patrícia Fraga, Unlocking the gateway to the brain: Innovative strategies for therapeutic delivery across the blood-brain barrier peptides. Periphery-brain Interplay and CNS Disease, Belgium, November 14, 2023. (Poster Presentation)

Carolina Buga, Molecular insights into membrane fusion mediated by the parainfluenza fusion peptide. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Poster Presentation)

Beatriz Vieira da Silva, Unravelling the factors that govern the ability of antiviral peptide-porphyrin conjugates to translocate the blood-brain barrier. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Poster Presentation)

Beatriz Vieira da Silva, Unravelling the factors that govern the ability of antiviral peptide-porphyrin conjugates to translocate the blood-brain barrier. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Oral Presentation)

Marco Cavaco, The use of a selective, nontoxic dual-acting peptide for breast cancer patients with brain metastasis. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Poster Presentation)

Marco Cavaco, The use of a selective, nontoxic dual-acting peptide for breast cancer patients with brain metastasis. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Oral Presentation)

Vera Neves, Peptide Shuttles to improve therapeutic action in the central nervous system. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Oral Presentation)

Ana Salomé Veiga, Activity and mode of action of pepRF1, a new CXCR4-targeted HIV inhibitor. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Oral Presentation)

Ana Herdade, Bioactive peptides in functional foods can mitigate stress behaviors in zebrafish (*Danio rerio*). EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Poster Presentation)

Ana Herdade, Bioactive peptides in functional foods can mitigate stress behaviors in zebrafish (*Danio rerio*). EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Oral Presentation)

Christine Cruz Oliveira, Targeting arboviral infections in the central nervous system with peptide-porphyrin conjugates. EPI 2023 - XVIII Iberian Peptide Meeting, Portugal, November 27, 2023. (Poster Presentation)

Communications in National Conferences:

Patrícia Fraga, Peptides for brain drug delivery. 2nd edition of AD Symposium - Porto, Portugal, February 10, 2023. (Poster Presentation)

Catarina Chaparro, Magnetic-polymeric nanoparticles as a platform for brain drug delivery. VIII Annual Meeting - Jornadas i3N (Instituto de Nanoestruturas, Nanomodelismo e Nanofabricação) 2023, Portugal, March 3, 2023. (Oral Presentation)

Catarina Chaparro, Peptide mediation of nanoparticles to cross the blood-brain barrier – a platform for brain drug delivery. Encontro Ciência 2023, Portugal, July 5, 2023. (Poster Presentation)

Marco Cavaco, Tratamento de metastases cerebrais com um péptido seletivo e não tóxico. 5º Encontro Nacional de Jovens Investigadores em Oncologia, Portugal, September 22, 2023. (Poster Presentation)

Marco Cavaco, Tratamento de metastases cerebrais com um péptido seletivo e não tóxico. 5º Encontro Nacional de Jovens Investigadores em Oncologia, Portugal, September 22, 2023. (Oral Presentation)

Beatriz Tragedo Simões, Nanoparticles as a drug delivery system of therapeutics for brain diseases. Spanish and Portuguese Advanced Optical Microscopy Conference, Portugal, October 25, 2023. (Poster Presentation)

Patrícia Fraga, Unlocking the gateway to the brain: Innovative strategies for therapeutic delivery across the blood-brain barrier peptides. ESN-ISN Neurochemistry School - Faro, Portugal, October 29, 2023. (Poster Presentation)

### **Networks and Research Infrastructures**

Catarina Chaparro, FCT/NKFIH, 2019/2020 Development of a blood-brain barrier shuttle platform for applicability in Alzheimer's disease, Participant/Investigator/Partner, Cooperation between Portugal and Hungary funded by FCT and NKFIH from Hungary.

Catarina Chaparro, PTDC/BTM MAT/2472/2021 Towards the development of a nanoparticle for early diagnosis of Alzheimer's Disease, based, Participant/Investigator/Partner, Fundação para a Ciência e Tecnologia (FCT).

### **Prizes and Honours**

Patrícia Fraga, 2nd edition of AD Symposium, Porto - Best Poster.

Beatriz Vieira da Silva, EPI 2023 - XVIII Iberian Peptide Meeting - Second place for best flash talk.

### **Advanced Teaching**

Ana Salomé Veiga, Lecture, 2023 LisbonBioMed PhD Program, Portugal, January 30, 2023.

Christine Cruz Oliveira, Lecture, 2023 LisbonBioMed PhD Program, Portugal, January 30, 2023.

Miguel Castanho, Lecture, Curso de Formação em Educação Médica (DEM) - Como estruturar e apresentar uma aula teórica, Portugal, April 30, 2023.

Ana Herdade, Lecture, Curso de Formação em Educação Médica (DEM) - Como lecionar uma aula prática no laboratório, Portugal, April 30, 2023.

Miguel Castanho, Lecture, Workshop de Iniciação Pedagógica - "Como manter os estudantes acordados", Portugal, September 13, 2023.

Vera Neves, Lecture, Master/PhD in Neurosciences Faculdade de Medicina da Universidade de Lisboa (FMUL), Portugal, October 18, 2023.

Miguel Castanho, Coordination of Master Curricular Unit, Curricular unit "Brain Barriers in drug development" master's degree in biopharmaceutical sciences, Portugal, November 2, 2023.

### **MSc Theses**

Joana Lopes, Characterization of models of young and mature bacterial biofilms to study the activity and mechanism of action of a designed cyclic analog of gomesin, Supervisor: Ana Salomé Veiga, Co-Supervisor: Miguel Castanho, Universidade Nova de Lisboa, Instituto de Higiene e Medicina Tropical, Portugal, July 27, 2023.

Beatriz Vieira da Silva, Unravelling the factors that influence the ability of antiviral peptideporphyrin conjugates to translocate the blood-brain barrier, Supervisor: Miguel Castanho, Faculdade de Ciências da Universidade de Lisboa, Portugal, October 19, 2023.

### **PhD Theses**

Susana Dias, Towards the development of antimicrobial peptides active against bacterial biofilms, Supervisor: Ana Salomé Veiga, Faculdade de Medicina da Universidade de Lisboa, Portugal, May 16, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

VectorB2B, Collaboration to provide highly qualified services of drug discovery and development from the bench to bedside, VectorB2B, a Drug Developing Association for Research in Biotechnology, Collaborative Research.

Dompé farmaceutici S.p.A., Collaboration to provide highly qualified services of Drug Design and Discovery Platform, Collaborative Research.

SPAROS, Lda., NoSTRESS - New functional foods to reduce the effects of stress in aquaculture project, Collaborative Research.

### **Intellectual Property Rights in 2023**

ANTI-INFECTIVE CONJUGATE FOR USE IN THE TREATMENT OF ZIKA VIRUS INFECTION. Publication Number: WO/2023/161311; Publication Date: 31.08.2023; International Application No.PCT/EP2023/054489; International Filing Date: 23.02.2023

### **Science and Society in 2023**

Miguel Castanho, Interview. Brain Awareness Week, “Impedir que metástases do cancro da mama e vírus cheguem ao cérebro e façam estragos: Os dois projetos que um investigador português tem em mãos”. Visão magazine, March 3, 2023.

Miguel Castanho, Interview. Internacional da Saúde Feminina. “Está a ser preparado um “medicamento inteligente” que ajuda a proteger o cérebro em doentes com cancro da mama”. CNN, May 28, 2023.

Miguel Castanho Lab in collaboration with iMM Communication Office. Project BREAST-BRAIN-N-BBB Website. May 29, 2023.

MCastanho Lab, Students visit to our lab, Medical Study Association Rotterdam (the Netherlands), IMM, June 5, 2023.

Miguel Castanho, Interview. Dia Mundial do Mosquito. Mosquitos que propagam Dengue e Zika “já se instalaram na Europa”. Healthnews, August 18, 2023.

Miguel Castanho, Interview. “Surgiu na Ásia, é “ainda mais transmissível”, mas não é certo que seja mais perigosa: Éris, a nova variante da covid-19”. CNN, August 21, 2023.

Miguel Castanho, Opinion Article. A Inteligência Artificial é um gato. Visão. September 9, 2023.

Beatriz Vieira-Silva, Beatriz Simões, Rodrigo Alarcão, Christine Oliveira, Ana Herdade, Patrícia Fraga and Ana Roque. Participation in European Researchers’ Night, September 30, 2023.

Miguel Castanho, Interview. “Dengue está a surgir em áreas onde nunca vimos”: os esforços científicos para tratamentos eficazes”. SIC Notícias, November 12, 2023.

Miguel Castanho, Interview. Portugueses combatem próxima pandemia. “Futuro Hoje”, SIC, December 5, 2023.

MCastanho Lab, Students visit to our lab, 12th Edition of Research Day, IMM, December 13, 2023.

MCastanho Lab, Study visit from 23 students from Vilamoura International School to our lab, 12th Edition of Research Day, IMM, November 7, 2023.

**POLICY:**

Miguel Castanho, EIC ambassador.

Miguel Castanho, Biochemistry Society UK ambassador.

Miguel Castanho, Biophysics Society US ambassador.

Miguel Castanho, Specialty Chief Editor Pharmaceutical Innovation.

Miguel Castanho, Universidade de Lisboa, Senate member.



## Luís Costa Lab

**Head of Laboratory:** Luis Costa, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa and Director of Serviço de Oncologia and Centro de Investigação Clínica at Centro Hospitalar Universitário Lisboa Norte- Hospital de Santa Maria

### Team

Ana Cláudia Martins Cavaco	PhD	Study Coordinator
Ana Ferro Espadanal Torres Luísa Magalhães Canha	PhD	Senior Postdoctoral Researcher
André Miguel Branco Mansinho	MD/Master Degree	Clinical Researcher
Andreia Sofia de Sá Barreira Cordeiro	University Degree	MSc Student (Started September)
Carolina Lopes Melo	University Degree	MSc Student (Left July)
Érica Beatriz Alves Martins	University Degree	MSc Student (Started September)
Inês Fernandes Gomes	Master Degree	PhD Student (Left May)
Isabel Cristina Ferreira Fernandes Borges da Costa	MD/PhD	Clinical Researcher (Left September)
Joana Filipa da Silva Santos	Master Degree	PhD Student (Started November)
Joana Lourenço Martins	University Degree	MSc Student (Started September)
João Pedro Coelho Monteiro	University Degree	MSc Student (Left September)
Lina Marcela Gallego Paéz	PhD	Senior Postdoctoral Researcher
Manuel Sérgio Sokolov Ravasqueira	University Degree	MSc Student
Maria Marques Martelo	University Degree	MSc Student
Marta Sofia Alves Martins	PhD	Staff Scientist
Miguel Filipe Portugal do Canto e Costa	Master Degree	Trainee
Miguel Maria Escoval Lopes Esperança Martins	MD/Master Degree	PhD Student
Patrícia Borges Alves	Master Degree	Clinical Study Coordinator (Left April)
Patrícia Isabel Martins Corredeira	Master Degree	Lab Technician
Raquel Filipa Rodrigues Neto	University Degree	MSc Student (Left October)
Raquel Sofia Cruz Duarte	Master Degree	PhD Student (Left April)
Rita Alexandra Vieira Soares	University Degree	MSc Student
Rúben Duarte Dos Santos Vilela	University Degree	MSc Student (Left August)
Rúben Marcelo Simão Nunes	University Degree	MSc Student (Left September)
Sandra Cristina Cara de Anjo Casimiro	PhD	Staff Scientist
Sara Filipa Silva Pestana	Master Degree	Trainee (Left September)
Sérgio Jerónimo Rodrigues Dias	PhD	Visiting Researcher
Tânia Carneiro Peniche	University Degree	MSc Student
Teresa Raquel Duarte Pacheco	PhD	Senior Postdoctoral Researcher
Tito Miguel Palmela Leitão	MD/University Degree	PhD Student

### **Lab Interests**

Metastases are the hallmark of cancer lethality. They represent a unique and complex phenomenon, associated not only with genomic alterations in cancer cells, but also with a heterotypic signaling between cancer cells and host tissues. Our main goal is to better understand the molecular mechanisms driving tumor progression at the metastatic site (using bone metastases as a paradigm); and to unravel molecular signatures of organotropism through identification of “leader gene signatures” common to the primary tumor and corresponding metastasis (using colorectal cancer (CRC) as a model). We also focus on the identification of the mechanisms involved in resistance to therapy in the metastatic setting, as well as in finding new therapeutic strategies to overcome such resistance. It is also our objective to interpret the dynamics of metastatic cancer progression by comprehensive analysis of clonal evolution and host immune and humoral response.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

We have shown that RANK pathway is involved in breast cancer (BC) resistance to CDK4/6i, overcome by RANKL inhibitors. From a research perspective, a clinical trial with patients could be designed at once.

The Oncodynamics prospective collection of liquid biopsies from metastatic solid tumors achieved the recruitment of 248 patients, and is being used to longitudinally evaluate tumor clonal evolution and heterogeneity, host immune response and circulating biomarkers. In collaboration with GBernardes Lab, we could demonstrate that amino acid residue biomarkers provide a cancer-specific signature, which is also predictive of response to CDK4/6i in advanced BC patients.

Another milestone was the conclusion of DNA/RNA sequencing of 566 tumors in the Multicancer Profile Project, from patients with breast, endometrial and non-small cell lung cancers or sarcomas. This unique genomic and clinical dataset is now being investigated for biological and clinical relevant information.

### Ongoing Projects

2023/2026: Oncology Research. Coordinator: Luís Costa. Funding Agency: Bristol Myers Squibb. Reference: ONCOLOGY - BMS. Amount: 25 000,00€. Total Amount: 25 000,00€.

2023/2024: Innovative approaches for pancreatic cancer: Decoding and manipulating immune response to short sialylated O-glycans. Coordinator: Luís Costa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.04607.PTDC. Amount: 8 000,00€. Total Amount: 247 347,08€.

2023/2024: PLCg1 expression in circulating tumour cells as a biomarker of cetuximab responses in metastatic colorectal cancer. Coordinator: Marta Sofia Martins. Funding Agency: Liga Portuguesa Contra o Cancro. Reference: MARTA MATINS – LPCC. Amount: 6 800,00€. Total Amount: 6 800,00€.

2023/2023: Young adult cancers. Funding Agency: Vários. Reference: YOUNG ADULT CANCERS. Amount: 2 670,00€. Total Amount: 2 670,00€.

2022/2024: Desenvolvimento de bebidas vegetais de tremço e grão como alimento funcional para o cancro retal. Coordinator: Luís Costa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/OCE-ETA/4836/2021. Amount: 162 007,00€. Total Amount: 218 291,00€.

2022/2024: FRONTAL- ROCHE - CLARUM ONCOLOGY PORTUGAL. Coordinator: Luís Costa. Funding Agency: Roche Farmacêutica. Reference: FRONTAL- ROCHE - CLARUM ONCOLOGY PORTUGAL. Amount: 122 000,00€. Total Amount: 122 000, 00€.

2021/2023: CDki. Coordinator: Sandra Casimiro. Funding Agency: Laboratórios Pfizer, Lda. Reference: CDKI. Amount: 25 000,00€. Total Amount: 25 000,00€.

2020/2023: Metabolómica em Sarcomas. Coordinator: Isabel Fernandes. Funding Agency: PharmaMar. Reference: Metabolómica em Sarcomas. Amount: 20 000,00€. Total Amount: 20 000,00€.

2020/2023: MCPP- Illumina. Coordinator: Luís Costa. Funding Agency: Illumina. Reference: MCPP- Illumina. Amount: 36 000,00€. Total Amount: 36 000,00€.

2017/2025: Oncodynamics. Coordinator: Luís Costa. Funding Agency: Several (Industry).  
Reference: ODB. Amount: 428 109,00€. Total Amount: 428 109,00€.

2012/2023: Cancer Genomic Consortium. Coordinator: Luís Costa. Funding Agency: Several  
(Clinical Research). Reference: GCGC. Amount: 665 655,00€. Total Amount: 665 655,00€.

## Scientific Impact

### Academic Collaborations

- Lorena Dieguez, International Iberian Nanotechnology Laboratory, Portugal.
- Marília Antunes, Faculdade de Ciências da Universidade de Lisboa Portugal.
- Ana Rita Grosso, FCT-NOVA, Portugal.
- Susana Vinga, INESC-ID, IST, Portugal.
- Bruno Silva-Santos, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Nuno Barbosa-Morais, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Ricardo Ferreira, Instituto Superior de Agronomia, Portugal.
- Helena Florindo, Faculdade de Farmácia da Universidade de Lisboa, Portugal.
- João Galamba, Instituto Superior Técnico, Portugal.
- Eva Gonzalez Suarez, CNIO, Spain.
- Rakesh Kumar, Rutgers New Jersey Medical School, USA.
- Allan Lipton, Penn State Hershey Medical Center, USA.

### Selected Publications

Inês Gomes, Lina M Gallego-Páez, Maria Jiménez, Patricia G Santamaria, André Mansinho, Rita Sousa, Catarina Abreu, Eva González Suárez, Luis Costa and Sandra Casimiro (2023). [Co-targeting RANK pathway treats and prevents acquired resistance to CDK4/6 inhibitors in luminal breast cancer](#). *Cell Reports Medicine* 4(8):101120.

**Relevance of the publication:** CDK4/6i and endocrine therapy are the first-line treatment for advanced luminal breast cancer. Gomes et al. show that the RANK pathway is involved in resistance to CDK4/6i, via interferon response and alternative cell cycle mediators. Moreover, RANKL inhibitors concomitant with CDK4/6i can increase therapy efficacy and delay acquired resistance.

Raquel Cruz-Duarte, Cátia Rebelo de Almeida, Magda Negrão, Afonso Fernandes, Paula Borralho, Daniel Sobral, Lina M. Gallego-Paez, Daniel Machado, João Gramaça, José Vílchez, Ana T. Xavier, Miguel Godinho Ferreira, Ana R. Miranda, Helder Mansinho, Maria J. Brito, Teresa R. Pacheco, Catarina Abreu, Ana Lucia-Costa, André Mansinho, Rita Fior, Luís Costa, Marta Martins (2022). [Predictive and Therapeutic Implications of a Novel PLCy1/SHP2-Driven Mechanism of Cetuximab Resistance in Metastatic Colorectal Cancer](#). *Clin Cancer Res* 28(6) 1203–1216.

**Relevance of the publication:** Our discoveries reveal the potential of PLCy1 as a predictive biomarker for cetuximab responses and suggest an alternative therapeutic approach to circumvent PLCy1-mediated resistance to cetuximab in patients with RAS WT mCRC. In this way, this work contributes to the development of novel strategies in the medical management and treatment of patients with mCRC.

Coleman RE, Croucher PI, Padhani AR, Clézardin P, Chow E, Fallon M, Guise T, Colangeli S, Capanna R, Costa L. (2020) [Bone metastases](#). *Nature Reviews Disease Primers*. 6(1):83.

**Relevance of the publication:** This PrimeView, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, describes the epidemiology, pathophysiology and clinical features of metastatic bone disease, and highlights the specific treatment approaches to prevent and treat bone metastases from solid tumours as well as myeloma bone disease.

Body JJ, Casimiro S, Costa L (2015). [Targeting bone metastases in prostate cancer: improving clinical outcome](#). *Nature Reviews Urology* 12: 340-56. Review

**Relevance of the publication:** This Review, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, describes the latest developments in the treatment of bone metastases in prostate cancer, and is an important tool for clinicians and scientists in the field.

Henry D, Costa L, Goldwasser F, Hirsh V, Hungria V, Prausova J, Scagliotti GV, Sleeboom H, Spencer A, Vadhan-Raj S, von Moos R, Willenbacher W, Woll PJ, Wang J, Jiang Q, Jun S, Dansey R, Yeh H (2011). [A randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer \(Excluding Breast and Prostate Cancer\) or Multiple Myeloma](#). *Journal of Clinical Oncology* 9(9):1125-1132

**Relevance of the publication:** This paper, written by world experts in the biology and clinics of bone metastases, including Dr. Costa, reported the results of the pivotal clinical trial that has demonstrated that Denosumab was a potential novel treatment option with the convenience of subcutaneous administration and no requirement for renal monitoring or dose adjustment.

### 2023 Publications in Peer-Reviewed Journals

Fortuna, A., Nobre Carvalho, A., Soares de Pinho, I., Lopes-Brás, R., Patel, V., Esperança-Martins, M., Gonçalves, L., Freitas, R., Simão, D., Roldán Galnares, M., Fernandes, I., Artacho Criado, S., Gamez Casado, S., Baena Cañada, J., Saffie Vega, I.M., Costa, J., Fernandes, A.S., Teixeira de Sousa, R., Costa, L., Luz, P (2023). A Brain Relapse in HER-2 Positive Breast Cancer after Neoadjuvant Treatment: An International Multicentric Study. *Neuro-Oncology*. 25(2):ii86.

M.B. Menezes, L. Goncalves, I.Q. Dunões, P. Semedo, S.L. Lobo Martins, A.G. da Silva Oliveira, G.M. Baió, C. Alvim, I.S. Soares de Pinho, T. Barroso, V.D.C. Patel, M. Esperanca-Martins, R.L. Brás, A.R. Teixeira Sousa, A.B. Mansinho, S. Torres, M.M. Inácio, L. Costa, R.D. Dinis (2023). 1122P Neutrophil/lymphocyte ratio and systemic inflammatory index as prognostic biomarkers in metastatic melanoma patients under immune checkpoint inhibitors: Could any of them be used? *Annals of Oncology*, Volume 34, Supplement <https://doi.org/10.1016/j.annonc.2023.09.2256>.

M.H. Voss, B. Garmezzy, S.H. Kim, J.P. Maroto Rey, A.B. Mansinho, A. Rodriguez-Vida, J. Oliveira, M. van Dongen, L. Medina Rodríguez, S. Negrier, B. Tran, B.A. Carneiro, E. Castanon Alvarez, S.Y. Rha, Y. Wang, S.D. Gainer, Z. Tang, I. Achour, J.M. Asare, L. Albiges (2023). 1883MO MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first-line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC), *Annals of Oncology*, Volume 34, Supplement 2, <https://doi.org/10.1016/j.annonc.2023.09.1113>.

L. Gonçalves, M. Pinho, R. Brás, V. Lobo, I. Pinho, T. Barroso, V. Patel, C. Lopes, A. Mansinho, S. Torres, R. Luís, C. Alvim, L. Costa (2023). P-28 Locally advanced gastric cancer under FLOT – real-world data on efficacy of patients with dMMR, *Annals of Oncology*, Volume 34, Supplement 1, Page S23, <https://doi.org/10.1016/j.annonc.2023.04.084>

Mário Fontes-Sousa, Helena Magalhães, Ricardo Leão, André Mansinho, Mariana Malheiro, Alina Rosinha, Margarida Carrolo, Paula Borralho, Joaquina Mauricio, Margarida Brito, Jose Luis C Passos-Coelho, Antonio Quintela (2023). A multicenter prospective validation study of the 3-cm cut-off in stage I seminoma (S3MI-PT). *JCO* 41, TPS435-TPS435. DOI:10.1200/JCO.2023.41.6\_suppl.TPS435.

Mansinho A, Cruz A, Marconi L, Pinto C, Augusto I. Avelumab as First-Line Maintenance Treatment in Locally Advanced or Metastatic Urothelial Carcinoma (2023). *Adv Ther.* 40(10):4134-4150. doi: 10.1007/s12325-023-02624-9. Epub 2023 Aug 22. PMID: 37608243.

Esperança-Martins, M., Melo-Alvim, C., Dâmaso, S., Lopes-Brás, R., Peniche, T., Nogueira-Costa, G., Abreu, C., Luna Pais, H., Teixeira de Sousa, R., Torres, S., Gallego-Paez, L.M., Martins, M., Ribeiro, L., Costa, L (2023). Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Agressive Entities. *Cancers*. 15:3933.

Esperança-Martins, M., Roque, D., Barroso, T., Abrunhosa-Branquinho, A., Belo, D., Simas, N., Costa, L (2023). Multidisciplinary Approach to Spinal Metastases and Metastatic Spinal Cord Compression – A new integrative flowchart for patient management. *Cancers*. 2023; 15: 1796.

Esperança-Martins, M., Dâmaso, S., Carreira, N., Pena, B., Correia, C., Aguado-Lobo, M., Espinosa-Lara, P., Soares-de-Almeida, L., Abreu Ribeiro, L., Costa, L (2023). Taxane and antiHER2 treatment-associated dermatomyositis: a rare adverse event? *Dermatology Online Journal*. 29(2)4.

Soares do Brito, J., Esperança-Martins, M., Goes, R., Spranger, A., Almeida, P., Fernandes, I., Portela, J (2023). Closed-incision negative-pressure wound therapy (ciNPWT) to minimize wound-related complications in lower limb reconstruction after bone tumor resection: Preliminary proof-of-concept study. *European Journal of Orthopaedic Surgery and Traumatology*. 33:2895-2902.

Soares de Pinho, I., Luz, P., Alves, L., Lopes-Brás, R., Patel, V., Esperança-Martins, M., Gonçalves, L., Freitas, R., Simão, D., Roldán Galnares, M., Fernandes, I., Artacho Criado, S., Gamez Casado, S., Baena Canãda, J., Saffie Veja, I.M., Costa, J.G., Fernandes, A.S., Teixeira de Sousa, R., Costa, L (2023). Anthracyclines versus No Anthracyclines in the Neoadjuvant Strategy for HER2+ Breast Cancer: Real World Evidence. *Clinical Drug Investigation*. 43: 691-698.

Soares do Brito, J., Esperança Martins, M., Goes, R., Spranger, A., Almeida, P., Fernandes, I., Portela, J (2023). Clinical features and management strategies for primary bone sarcomas: experience of a Portuguese Sarcoma Center. *Revista Portuguesa de Oncologia*. 6(2):68-75.

Gonçalves L, Gonçalves D, Esteban-Casanelles T, Barroso T, Soares de Pinho I, Lopes-Brás R, Esperança-Martins M, Patel V, Torres S, Teixeira de Sousa R, et al (2023). Immunotherapy around the Clock: Impact of Infusion Timing on Stage IV Melanoma Outcomes. *Cells*. 12(16):2068. <https://doi.org/10.3390/cells12162068>.

Marques D, Costa AL, Mansinho A, Quintela A, Pratas E, Brito-da-Silva J, Cruz J, Félix J, Rodrigues J, Mota M, Teixeira AR, Dâmaso S, Pinheiro S, Andreozzi V, Costa L, Barros AG (2023). The REWRITE Study - REal-WoRld effectiveness of TrifluridinE/tipiracil in Patients with Previously Treated Metastatic Colorectal Cancer. *Clin Oncol (R Coll Radiol)*. 35(10):665-672. doi: 10.1016/j.clon.2023.07.004. Epub 2023 Jul 14. PMID: 37487914.

Costa Luís, Alexandre Teresa, Mansinho André, Sousa Rita, Vieira Cláudia, Hughes Robert, Roediger Alexander, Pereira Sónia Matos, Araújo António (2023). Health outcomes and budget impact projection of anti-PD-(L)1s in cancer care in Portugal. *Frontiers in Public Health*, 11, 10.3389/fpubh.2023.1133959.

Leitão, T. P., Corredeira, P., Kucharczak, S., Rodrigues, M., Piairo, P., Rodrigues, C., Alves, P., Cavaco, A., Miranda, M., Antunes, M., Ferreira, J., Reis, J., Lopes, T., Diéguez, L., Costa, L. (2023). Clinical Validation of a Size-Based Microfluidic Device for Circulating Tumor Cell Isolation and Analysis in Renal Cell Carcinoma. *International Journal of Molecular Sciences*, 24(9):8404.

Inês Gomes, Catarina Abreu, Luis Costa and Sandra Casimiro (2023). The Evolving Pathways of the Efficacy of and Resistance to CDK4/6 Inhibitors in Breast Cancer. *Cancers*, 15, 4835. <https://doi.org/10.3390/cancers15194835>.

Tiago Barroso, Cecília Melo-Alvim, Leonor Ribeiro, Sandra Casimiro, Luís Costa (2023). Targeting Apoptosis Proteins to Overcome Chemotherapy Resistance - A Marriage between Targeted Therapy and Cytotoxic Chemotherapy. *International Journal of Molecular Science*, 24, 13385. <https://doi.org/10.3390/ijms241713385>.

Inês Gomes, Lina M Gallego-Páez, Maria Jiménez, Patricia G Santamaria, André Mansinho, Rita Sousa, Catarina Abreu, Eva González Suárez, Luis Costa and Sandra Casimiro (2023). Co-targeting RANK pathway treats and prevents acquired resistance to CDK4/6 inhibitors in luminal breast cancer. *Cell Reports Medicine* 4 (8), 101120. <https://doi.org/10.1016/j.xcrm.2023.101120>.

Carolina Peixoto, Marta B. Lopes, Marta Martins, Sandra Casimiro, Daniel Sobral, Ana Rita Grosso, Catarina Abreu, Daniela Macedo, Ana Lúcia Costa, Helena Pais, Cecília Alvim, André Mansinho, Pedro Filipe, Pedro Marques da Costa, Afonso Fernandes, Paula Borralho, Cristina Ferreira, João Malaquias, António Quintela, Shannon Kaplan, Mahdi Golkaram, Michael Salmans, Nafeesa Khan, Raakhee Vijayaraghavan, Shile Zhang, Traci Pawlowski, Jim Godsey, Alex So, Li Liu, Luís Costa & Susana Vinga (2023). Identification of biomarkers predictive of metastasis development in early-stage colorectal cancer using network-based regularization. *BMC Bioinformatics* 24, 17. <https://doi.org/10.1186/s12859-022-05104-z>.

Nóbrega-Pereira S et al, Dias S (2023). Mitochondrial Metabolism Drives Low-density Lipoprotein-induced Breast Cancer Cell Migration. *Cancer Research Communications*, 3(4):709–724.



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Rego IB, Coelho S, Semedo PM, Cavaco-Silva J, Teixeira L, Sousa S, Reis J, Dinis R, Schmitt F, Afonso N, Fougho JL, Pavão F, Baptista Leite R, Costa L (2023). 360 Health Analysis (H360)-A Comparison of Key Performance Indicators in Breast Cancer Management across Health Institution Settings in Portugal. *Curr Oncol*. 30(7):6041-6065. doi: 10.3390/currncol30070451.

Esperanca-Martins M, Damaso S, Carreira N, Pena B, Correia C, Aguado-Lobo M, Espinosa-Lara P, Soares-de-Almeida L, Abreu Ribeiro L, Costa L (2023). Paraneoplastic or treatment-associated dermatomyositis: a diagnostic challenge. *Dermatol Online J*. 29(2). doi: 10.5070/D329260768.

#### **Pre-Prints**

Tito Palmela Leitão, Patrícia Corredeira, Carolina Rodrigues et al (2023). Circulating tumor and mesenchymal cell release in no-touch radical nephrectomy: a randomized controlled trial, 28 October 2023, PREPRINT (Version 1) available at Research Square [<https://doi.org/10.21203/rs.3.rs-3376872/v1>].

#### **Invited Lectures and Seminars**

André Mansinho, Trending Topics in Renal Cancer. Trending Topics in GU Cancer, Spain, January 20, 2023.

André Mansinho, Doença metastizada: presente e futuro. Encontros da Primavera, Portugal, March 25, 2023.

Sandra Casimiro, Co-targeting RANK Pathway treats and prevents acquired resistance to CDK4/6 inhibitors in Luminal Breast Cancer. Sessões Educativas do Serviço de Oncologia Médica – Hospital Santa Maria – Centro Hospitalar Universitário Lisboa Norte, Portugal, April 26, 2023.

Inês Gomes, Targeting RANKL as an opportunity to overcome resistance to CDK4/6 inhibitors in breast cancer. ENBDC (European Network of Breast Development and Cancer) Seminar Series, Online, June 6, 2023.

Sérgio Dias. Round Table European Health Data Space, Portugal, June 19, 2023.

Sandra Casimiro, New arrivals at iMM: Two syngeneic models of Luminal breast cancer. Oncobiology Club iMM, Portugal, June 21, 2023.

Sérgio Dias, 2023 USA-Portugal Leaders in Cancer Research, Portugal, July 20, 2023.

André Mansinho, Best practice for the long-term management of advanced prostate cancer. APEX Meeting, Portugal, September 8, 2023.

Luis Costa, Highlighting the Benefits of a Multidisciplinary Team. Oncology Academy, Portugal, September 9, 2023.

Luís Costa, Como evoluiu a ciência nos últimos 50 anos e como será o futuro. 50 Anos Roche Portugal, Portugal, October 9, 2023.

André Mansinho, Novas terapêuticas no Cancro Esófago-gástrico. 19º Congresso Nacional de Cancro Digestivo, Portugal, October 13, 2023.

Luis Costa, Current and Future Challenges in Cancer Immunotherapy. 1st Immuno-Oncology SPO/SPI Joint Meeting, Portugal, October 28, 2023.

Luis Costa, Breast Cancer in the Young Woman: what to do more? BRIGHT AWARENESS DAY - BRIGHT Consortium, Sweeden, November 8, 2023.

André Mansinho, A view into Academic Institutes for Success. SCRS - Breakout Session, Portugal, November 13, 2023.

André Mansinho, Immunotherapy in invasive bladder cancer. GPGU, Portugal, November 18, 2023.

André Mansinho, Tumores NTRK: como os identificar na prática clínica. 20º Congresso Nacional de Oncologia, Portugal, November 24, 2023.

Luis Costa, New approaches in cancer treatment: facts and expectations with medical radionuclides. Workshop "Challenges in Nuclear Medicine", Portugal, November 28, 2023.

Maria Martelo, Efficacy of RANK pathway and CDK4/6 inhibition in immune competent Luminal breast cancer models. Oncobiology Club iMM, Portugal, November 29, 2023.

Ana Magalhães, A positive feedback loop between IFN-g signaling and cholesterol uptake sustains PDL-1 expression in breast cancer cells. Oncobiology Club IMM, Portugal, December 26, 2023.

Miguel Esperança-Martins, Avelumab maintenance in bladder cancer. XXVIII Workshop de Urologia Oncológica do Grupo Português Génito-Urinário, Portugal.

Miguel Esperança-Martins, Integrated bioinformatic analysis of clinical and genomic data for systemic treatment optimization. 2º Encontro Ibérico de Atualização no Tratamento de Sarcomas, Portugal.

Miguel Esperança-Martins, Eflúvio capilar secundário a tratamentos oncológicos. 1ªs Jornadas de Tricologia e Patologias Cutâneas, Portugal.

### **Communications**

#### Communications in International Conferences:

Mario Fontes-Sousa\*, Helena Magalhães, Ricardo Leão, André Mansinho, Mariana Malheiro, Alina Rosinha, Margarida Carrolo, Paula Borralho, Joaquina Mauricio, Margarida Brito, Jose Luis C Passos-Coelho, Antonio Quintela, A multicenter prospective validation study of the 3-cm cut-off in stage I seminoma (S3MI-PT). 2023 ASCO Genitourinary Cancers Symposium, USA, February 16, 2023. (Poster Presentation)

M.B. Menezes\*, L. Goncalves, I.Q. Dunões, P. Semedo, S.L. Lobo Martins, A.G. da Silva Oliveira, G.M. Baió, C. Alvim, I.S. Soares de Pinho, T. Barroso, V.D.C. Patel, M. Esperanca-Martins, R.L. Brás, A.R. Teixeira Sousa, A.B. Mansinho, S. Torres, M.M. Inácio, L. Costa, R.D. Dinis, Neutrophil/lymphocyte ratio and systemic inflammatory index as prognostic biomarkers in metastatic melanoma patients under immune checkpoint inhibitors: Could any of them be used? 2023 ASCO Genitourinary Cancers Symposium, USA, February 16, 2023. (Poster Presentation)

Cong Tang\*, Wesley Sukdao, Patrícia Corredeira, Sandra Casimiro, Luís Costa, Emma Yates, Gonçalo J. L. Bernardes, Amino Acid Concentration Signatures (AACS) for Disease Detection - A novel platform for detecting multiple types of cancer from a blood test, suggesting personalised treatment. Gordon Research Conference - Bioorganic Chemistry, USA, June 11, 2023. (Poster Presentation)

L. Gonçalves\*, M. Pinho, R. Brás, V. Lobo, I. Pinho, T. Barroso, V. Patel, C. Lopes, A. Mansinho, S. Torres, R. Luís, C. Alvim, L. Costa, Locally advanced gastric cancer under FLOT – real-world data on efficacy of patients with dMMR. ESMO 25th World Congress on Gastrointestinal Cancer, Spain, June 28, 2023. (Poster Presentation)

M.H. Voss\*, B. Garmez, S.H. Kim, J.P. Maroto Rey, A.B. Mansinho, A. Rodriguez-Vida, J. Oliveira, M. van Dongen, L. Medina Rodríguez, S. Negrier, B. Tran, B.A. Carneiro, E. Castanon Alvarez, S.Y. Rha, Y. Wang, S.D. Gainer, Z. Tang, I. Achour, J.M. Asare, L. Albiges, MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first-line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC). ESMO Congress 2023, Spain, October 20, 2023. (Oral Presentation)

Miguel Costa\*, Ana Cavaco, Luis Costa, Type I procollagen carboxyterminal propeptide plays a role in the innate immune system dynamics and immune evasion in triple negative breast cancer. III ASPIC-ASEICA International Meeting – Cancer Immunology, Tumor Microenvironment and Metastasis, Portugal, October 26-27, 2023. (Poster Presentation)

Pedro Marreiros, Daniela Botinas, Diogo Coutinho, Luís Costa, Ana Magalhães\*, Sérgio Dias, A positive feedback loop between IFN-g signaling and cholesterol uptake sustains PDL-1 expression in breast cancer cells. III ASPIC-ASEICA International Meeting – Cancer Immunology, Tumor Microenvironment and Metastasis, Portugal, October 26-27, 2023. (Poster Presentation)

Maria Martelo\*, Rúben Vilela, Inês Gomes, Carolina Jardim, Karine Serre, Luis Costa, Sandra Casimiro, Therapy-induced immunomodulation in breast cancer allografts treated simultaneously with CDK4/6 and RANKL inhibitors. III ASPIC-ASEICA International Meeting – Cancer Immunology, Tumor Microenvironment and Metastasis, Portugal, October 26-27, 2023. (Poster Presentation)

Sérgio Dias, How LDL cholesterol promotes breast cancer progression. III ASPIC-ASEICA International Meeting – Cancer Immunology, Tumor Microenvironment and Metastasis, Portugal, October 26-27, 2023. (Oral Presentation)

Pedro Marreiros, Daniela Botinas, Diogo Coutinho, Luís Costa, Ana Magalhães\*, Sérgio Dias, A positive feedback loop between IFN-g signaling and cholesterol uptake sustains PDL-1 expression in breast cancer cells metastasis. CNIO-CaixaResearch Frontiers Meeting, Spain, November 6, 2023. (Poster Presentation)

Luis Costa\*, Cong Tang, Emma Yates, Qi Shi, Wesley Sukdao, Patrícia Corredeira, Gonçalo Costa, Helena Pais, Catarina Abreu, Leonor Ribeiro, Rita Sousa; Sofia Torres, André Mansinho, Sandra Casimiro, Ana Cavaco, Patrícia Alves, Ângela Rodrigues, Lisiana Szeneszi, Gonçalo Bernardes, Immune Activation Signatures for predicting CDKi primary response in advanced breast cancer patients. 2023 SABCS, USA, December 5, 2023. (Poster Presentation)

Fortuna, A.\*, Nobre Carvalho, A., Soares de Pinho, I., Lopes-Brás, R., Patel, V., Esperança-Martins, M., Gonçalves, L., Freitas, R., Simão, D., Roldán Galnares, M., Fernandes, I., Artacho Criado, S., Gamez Casado, S., Baena Cañada, J., Saffie Vega, I.M., Costa, J., Fernandes, A.S., Teixeira de Sousa, R., Costa, L., Luz, P, A Brain Relapse in HER-2 Positive Breast Cancer After Neoadjuvant Treatment: An International Multicentric Study. 18th Meeting of the European Association of Neuro-Oncology, The Netherlands. (Poster Presentation)

Boavida, J.\*, Soares de Pinho, I., Barroso, T., Patel, V., Gonçalves, L., Esperança Martins, M., Lopes Brás, R., Teixeira de Sousa, R., Costa, L., Correia, M.L., Androgen receptors in metastatic triple negative breast cancer. 35th European Congress of Pathology, Ireland. (Poster Presentation)

#### Communications in National Conferences:

Gonçalves, L.\*, Bairos Menezes, M., Barroso, T., Soares de Pinho, I., Patel, V., Esperança Martins, M., Araújo, J., Santos, A.R., Mansinho, A., Sousa, A.R., Torres, S., Costa, L., Melanoma da cabeça e pescoço sob imunoterapia paliativa: uma casuística multicêntrica nacional. 13<sup>o</sup> Simpósio Nacional de Cancro da Cabeça e Pescoço, Portugal. (Poster Presentation)

### **Organization of Conferences**

Luis Costa and André Mansinho, Organizer, Challenging melanoma: Facts beyond controversies, Portugal, April 15, 2023.

Luis Costa, Co-Organizer, 5<sup>a</sup> Conferência Anual de Saúde Pública DA REDESAÚDE, Portugal, May 18, 2023.

Luis Costa and André Mansinho, Organizer, New Frontiers in Uro-Oncology 2023, Online, September 29, 2023.

Luis Costa, Co-Organizer, Innovation in Breast Cancer – Lisbon Edition 2023, Online, November 13, 2023.

Luis Costa, Co-Organizer, Workshop “Challenges in Nuclear Medicine”, Portugal, November 28, 2023.

### **Networks and Research Infrastructures**

Luis Costa, Global Consortium for Breast Cancer in Young Women, Scientific Director.

Sandra Casimiro, ERASMUS+, Supervisor.

Sérgio Dias, National Biobank Network, Coordinator.

Sérgio Dias, Mesa da Assembleia Geral da ASPIC (Associação Portuguesa de Investigação do Cancro), President.

### **Prizes and Honours**

Sandra Casimiro, Guest Editor, Signaling Pathways of Breast Cancer in Cancers.

Marta Martins, Co-Guest Editor, Signaling Pathways of Breast Cancer in Cancers.

### **Advanced Teaching**

Marta Martins, Thesis arguer, Joana Mota: “Deflamin, an edible anti-inflammatory and anticancer protein isolated from legume seeds”, PhD in Biology, Instituto Superior de Agronomia (school of Agriculture), Universidade de Lisboa, Portugal, January 18, 2023.

Sandra Casimiro, Jury President, João Pedro Vilar Miguel Patrício: “NTRK Gene Fusions, Entrectinib and Larotrectinib: a Narrative Review of Clinical Evidence”, Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 23, 2023.

Luis Costa, Thesis arguer, Sara Filipa Fernandes de Almeida, Doutoramento em Ciências Farmacêuticas, Universidade de Coimbra, Portugal, June 27, 2023.

Sandra Casimiro, Jury President, Patrícia Amaral: “Characterizing the role of the Circadian Molecular Clock in T-ALL”, Masters in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 27, 2023.

Sandra Casimiro, Thesis arguer, Masters defense, Ana Isabel Aguiar Encarnação: “Immune Modulation of Skeletal Muscle Regeneration”, Masters in Biomedical Engineering, Instituto Superior Técnico, Portugal, December 6, 2023.

Luis Costa, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Luis Costa, Lecture, Curricular Unit: Principles of Cancer Biology, Masters in Biomedical Research, Portugal.

Luis Costa, Course organization, Faculdade de Medicina da Universidade de Lisboa Masters in Oncobiology, Portugal.

Luis Costa, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Discovery and Development of New Drugs in Oncology, Masters in Oncobiology, Portugal.

Luis Costa, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Discovery and Development of New Drugs in Oncology, Masters in Oncobiology, Portugal.

Luis Costa, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Oncobiology, Masters in Oncobiology, Portugal.

Luis Costa, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Oncobiology, Masters in Oncobiology, Portugal.

Luis Costa, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Seminars in Oncobiology, Masters in Oncobiology, Portugal.

Luis Costa, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Cancer Therapeutics, Masters in Oncobiology, Portugal.

Luis Costa, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Cancer Therapeutics, Masters in Oncobiology, Portugal.

Luis Costa, Coordination of Master Curricular Unit, Curricular Unit Oncology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Lecture, Theoretical Class on “Biobanking”, “Research Techniques and Methodologies”, PhD Program, Universidade de Coimbra, Portugal.

Sérgio Dias, Lecture, Theoretical Class on “Biobanking and GDPR: the Portuguese experience”, PhD Program of Faculty of Medicine of Algarve University, Portugal.

Sérgio Dias, Lecture, “Angiogenesis and Cancer” Class. Master Program in Molecular and Cell Biology of Cancer, Faculdade de Ciências da Universidade de Lisboa, Portugal.

Sérgio Dias, Lecture, "Signaling and Cancer" Classes (4 hours), Master Program in Oncobiology, University of Algarve, Portugal.

Sérgio Dias, Lecture, Curricular Unit: Principles of Cancer Biology, Masters in Biomedical Research, Portugal.

Sérgio Dias, Coordination of Master Curricular Unit, Principles of Cancer Biology, Masters in Biomedical Research, Portugal.

Sérgio Dias, Lecture, “Developmental Biology and Cancer” Module, Master Program in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Coordination of Master Curricular Unit, “Developmental Biology and Cancer” Module, Master Program in Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Lecture, “The Biology of Cancer” Module, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Coordination of PhD Curricular Unit, “The Biology of Cancer” Module, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sérgio Dias, Lecture, Class on “Metabolism and Cancer”, ITQB (PhD Program), Portugal.

Sandra Casimiro, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Sandra Casimiro, Lecture, Curricular Unit: Principles of Cancer Biology, Masters in Biomedical Research, Portugal.



Sandra Casimiro, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Discussion of Articles, Masters in Oncobiology, Portugal.

Sandra Casimiro, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Discussion of Articles, Masters in Oncobiology, Portugal.

Sandra Casimiro, Lecture, MUL – UL, Curricular Unit: Discovery and Development of New Drugs in Oncology, Masters in Oncobiology, Portugal.

Sandra Casimiro, Coordination of Master Curricular Unit, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Laboratory Rotations, Masters in Oncobiology, Portugal.

Sandra Casimiro, Course organization, Faculdade de Medicina da Universidade de Lisboa Masters in Oncobiology, Portugal.

Marta Martins, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Teresa Pacheco, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Teresa Pacheco, Lecture, Curricular Unit Oncology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Miguel Esperança-Martins, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Miguel Esperança-Martins, Lecture, Licenciatura em Ciências da Nutrição da Faculdade de Medicina da Universidade de Lisboa, Portugal.

Miguel Esperança-Martins, Lecture, Curricular Unit Oncology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

André Mansinho, Lecture, Curricular Unit Oncobiology, Faculdade de Medicina da Universidade de Lisboa, Portugal.

André Mansinho, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Discovery and Development of New Drugs in Oncology, Masters in Oncobiology, Portugal.

André Mansinho, Lecture, Faculdade de Medicina da Universidade de Lisboa, Curricular Unit: Clinical Trials, Masters in Oncobiology, Portugal.

André Mansinho, Lecture, Mestrado em Investigação e Ensaio Clínicos, Curricular Unit: Ensaio de Iniciativa do Investigador, Portugal.

### **MSc Theses**

Daniela Botinas, High systemic cholesterol and IFN- $\gamma$  response in breast cancer cells, Supervisor: Sérgio Dias, Co-Supervisor: Ana Magalhães, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 29, 2023.

Rúben Nunes, In human evidence of the therapeutic efficacy of CDK4/6 inhibitors plus RANK pathway inhibition in Triple Negative Breast Cancer, Supervisor: Sandra Casimiro, Co-Supervisor: Célia Gomes, Coimbra Medical School, University of Coimbra, Portugal, October 25, 2023.

João Coelho, ONCODYNAMICS - An integrated analysis of the host response to cancer, Supervisor: Ana Cavaco, Co-Supervisor: Célia Gomes, Coimbra Medical School, University of Coimbra, Portugal, October 27, 2023.

Carolina Melo, Prognostic significance of PLC $\gamma$ 1 in Luminal a Breast Cancer: insights into cell cycle regulation and estrogen signalling, Supervisor: Marta Martins, Co-Supervisor: Salomé Lourenço, Coimbra Medical School, University of Coimbra, Portugal, October 27, 2023.

Tânia Peniche, Clinical Impact of High Throughput Molecular Data in Sarcomas Patient Care, Supervisor: Marta Martins, Co-supervisor: Lina Gallego, Universidade Nova de Lisboa, Portugal, November 21, 2023.

João Gaio, RANK pathway mediates a dual response to TRAIL in Luminal breast cancer, Supervisor: Sandra Casimiro, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 29, 2023.

Raquel Neto, From cells to mice: Investigating the role of PLC $\gamma$ 1 in triple-negative breast cancer, Supervisor: Marta Martins, Universidade Nova de Lisboa, Portugal, December 12, 2023.

### **PhD Theses**

Raquel Duarte, Phospholipase C signalling in resistance to anti-RTK therapy, Supervisor: Marta Martins, Co-Supervisor: Luis Costa, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 23, 2023.

Inês Gomes, RANK signaling pathway as a mediator of resistance to targeted therapies in breast cancer, Supervisor: Sandra Casimiro, Co-Supervisor: Luis Costa, Faculdade de Medicina da Universidade de Lisboa, Portugal, December 13, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

PharmaMar, Study of Sarcomas' metabolomics, Sponsored Research.

Lilly Portugal, Oncodynamics, Sponsored Research.

Astellas Farma, Lda, Oncodynamics, Sponsored Research.

Bristol-Myers Squibb, Oncodynamics, Sponsored Research.

Illumina, INC., MCPP - Multi-Cancer Profile Project, Collaborative Research.

Pfizer, IFN-mediated immune response in patients with metastatic breast cancer under CDK4/6 inhibitors (CDK4/6i) plus endocrine therapy (ET), Contract Research

Amgen, Inc., Rank Pathway Inhibitors in Combination with CDK Inhibitors, Sponsored Research.

### **Science and Society in 2023**

Luís Costa was regularly invited by the media (TV, radio, journals) to comment and discuss oncology-related news and events. He also acted as QoL for several patient advocate associations and pharma companies.

Sérgio Dias is the Coordinator of all Science Communication activities and those aimed at raising awareness to the importance of Science and Breast cancer Research, within the framework of the iMM-Laço Hub Laboratory.

## Joaquim Ferreira Lab

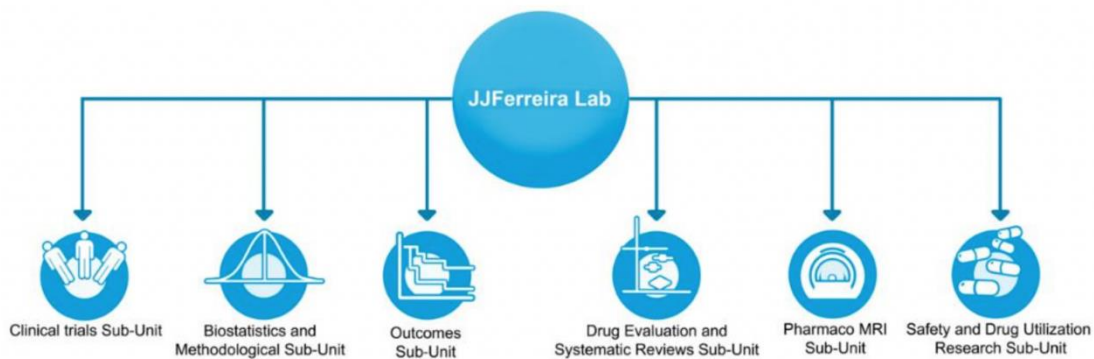
**Head of Laboratory:** Joaquim Ferreira, MD/PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Neurologist, Associate Professor and Head of Laboratory of Clinical Pharmacology and Therapeutics at Faculdade de Medicina da Universidade de Lisboa and Head of CNS - Campus Neurológico Sénior

### Team

Ana Catarina Gaspar Fonseca	MD/PhD	Clinical Researcher
Ana Cristina Brito Almeida Sampaio Cruz	MD/ PhD with Habilitation	Clinical Researcher
Ana Cristina Veloso Luís	PhD	Clinical Researcher
Ana Raquel Duque Gonçalves Fernandes	Master Degree	Clinical Researcher
Ana Teresa Martins Sousa Santos	PhD	Lab Manager
Anabela Ferreira Valadas	MD/PhD	Clinical Researcher
Carla Filipa Pestana Leão Guerreiro	MD/Master Degree	Clinical Researcher
Carolina Pires Maruta	PhD	Clinical Researcher
Catarina Filipa Severiano e Sousa	PhD	Clinical Researcher
Cláudio Virgílio Antunes David	MD/ Master Degree	Clinical Researcher
Constança Maria Abecasis Jalles	MD/Master	Clinical Researcher
Daisy Andreina Vieira de Abreu	PhD	Clinical Researcher
Daniel Gomes Caldeira	MD/PhD	Clinical Researcher
Fátima Vanessa Santos Carvalho	MD/Master Degree	Clinical Researcher
Inês Marques de Matos Dias	Master Degree	Clinical Researcher
Isabel Cristina Ramos Peixoto Guimarães	PhD	Clinical Researcher
Joana Filipa dos Santos	Master Degree	Clinical Researcher
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Clinical Researcher
Lucas Wilfried Lopes Naumann	Master Degree	Clinical Researcher
Luís António Garcez Duarte da Costa Ferreira	Master Degree	Clinical Researcher
Luísa Maria Russo Prada	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 Atouguia	MD/ University Degree	Clinical Researcher
Maria Isabel Segurado Pavão Martins Catarino Petiz	MD/PhD	Clinical Researcher
Maria João Bettencourt Pereira Forjaz	PhD	Clinical Researcher
Maria Leonor Brito de Arriaga Correia Guedes Möller Miranda	MD/PhD	Clinical Researcher
Mariana da Cruz Alves	MD/PhD	Clinical Researcher
Mário Miguel Coelho da Silva Rosa	MD/PhD	Clinical Researcher
Marta Almeida e Silva Granadeiro	Master Degree	Clinical Researcher
Miguel Vilhena Soares Coelho	MD/PhD	Clinical Researcher
Raquel de Queirós Bouça Ribeirinho Machado	PhD	Clinical Researcher
Raquel José Ladeira Lobo	Master Degree	Clinical Researcher

Ricardo Miguel Ribeiro Marques Cunha Fernandes	MD/PhD	Clinical Researcher
Sara Alexandra Neves Dias	Master Degree	Clinical Researcher
Sofia Cristina Pereira Coutinho Reimão	MD/PhD	Clinical Researcher
Sofia Esteves Bélico de Velasco	Master Degree	Psychologist (Started April)
Tiago Alexandre Mestre	MD/PhD	Clinical Researcher
Tiago Heleno Mendes	Master Degree	Clinical Researcher
Tiago Rodrigues Teodoro	MD/PhD	Clinical Researcher
Vanda Viseu Filipa Cândido de Freitas	Master Degree	Clinical Researcher

### Graphical Abstract



### Lab Interests

The main mission 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. It also envisions 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.

### Research Field

- Neuroscience and Disorders of the Nervous System
- Prevention, Diagnosis and Treatment of Human Diseases

## Major Scientific Achievements in 2023

We are participating in the design and conduction of a European Union Horizon 2020 program funded large clinical validation study to gather information on a variety of potential digital measures captured with different devices and their ability of reflecting sleep disturbances or fatigue. With the other international partners, 1,000 individuals have already been recruited, accounting for 50% of the proposed sample of participants with Parkinson's Disease (PD), Huntington's Disease (HD), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Primary Sjögren's Syndrome (PSS), Inflammatory Bowel Disease and controls.

We have also presented very important results on the cognitive and psychiatric characteristics of advanced and late stage PD patients. This is even more relevant given the scarcity of data on these clinical domains in such a late and difficult-to-evaluate group.

## Ongoing 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: 289 500,0€. Total Amount: 20 997 522,50€.

2018/2024: A Prospective Registry Study in a Global Huntington's Disease Cohort. Coordinator: Joaquim Ferreira. Funding Agency: CHDI Foundation, Inc. Reference: ENROLL-HD PROTOCOL. Amount: 104 021,64€. Total Amount: 104 021,64€.

2013/2024: Prestação de serviços de realização de exames de avaliação neurocomportamental. Coordinator: Joaquim Ferreira. Funding Agency: Centro Hospitalar Lisboa Norte, E.P.E. Reference: INDUSTRIA. Amount: 141 928,00€. Total Amount: 141 928,00€.

2008/2023: Euro HD – registry. Coordinator: Joaquim Ferreira. Funding Agency: Euro Huntington's disease network. Reference: EURO HD – REGISTRY. Amount: 75 065,00€. Total Amount: 75 065,00€.

## Scientific Impact

### Academic Collaborations

- Instituto Superior Técnico da Universidade de Lisboa, Portugal.

### Selected Publications

Outeiro, T. F., Alcalay, R. N., Antonini, A., Attems, J., Bonifati, V., Cardoso, F., Chesselet, M., Hardy, J., Madeo, G., McKeith, I., Mollenhauer, B., Moore, D. J., Rascol, O., Schlossmacher, M. G., Soreq, H., Stefanis, L., & Ferreira, J. J. (2023). [Defining the Riddle in Order to Solve It: There Is More Than One “Parkinson’s Disease”](#). **Movement Disorders**, mds.29419. <https://doi.org/10.1002/mds.29419>.

Mestre, T. A., McDermott, M. P., Lobo, R., Ferreira, J. J., & Lang, A. E. E. (2023). [The Lessebo Effect in Disease Modification Trials in Parkinson’s Disease](#). **Movement Disorders**. <https://doi.org/10.1002/mds.29414>.

Machado T, Mainoli B, Caldeira D, Ferreira JJ, Fernandes RM (2023). [Data monitoring committees in pediatric randomized controlled trials registered in ClinicalTrials.gov](#). **Clinical Trials** doi:10.1177/17407745231182417.

Soares GM, Bouça-Machado R, Abreu D, Ferreira JJ (2023). [Contributory Factors to Caregiver Burden in Parkinson's Disease](#). **Mov Disord Clin Pract**. 10(10):1507-1518. doi: 10.1002/mdc3.13868. PMID: 37868922; PMCID: PMC10585976.

Bakkum, M. J., Verdonk, P., Thomas, E. G., van Rosse, F., Okorie, M., Papaioannidou, P., Likic, R., Sanz, E. J., Christiaens, T., Costa, J. N., Dima, L., de Ponti, F., van Smeden, J., van Agtmael, M. A., Richir, M. C., Tichelaar, J., & for the EurOPE consortium. (2023). [A Clinical Pharmacology and Therapeutics Teacher’s Guide to Race-Based Medicine, Inclusivity, and Diversity](#). **Clinical Pharmacology & Therapeutics**, 113(3), 600–606. <https://doi.org/10.1002/cpt.2786>.

### 2023 Publications in Peer-Reviewed Journals

Bublitz, S. K., Brandstötter, C., Fegg, M., Ferreira, J. J., Odin, P., Bloem, B. R., Meissner, W. G., Dodel, R., Schrag, A., & Lorenzl, S. (2023). Meaning in Life in Late-Stage Parkinson’s Disease: Results from the Care of Late-Stage Parkinsonism Study (CLaSP) in Six European Countries. *Journal of Religion and Health*. <https://doi.org/10.1007/s10943-023-01962-w>.

Araújo, R., Kole, J.J., Ferreira, J.J. and Bloem, B.R. (2023), Ethical Considerations of Unsolicited Medical Opinion in Movement Disorders. *Mov Disord Clin Pract*, 10: 1470-1475. <https://doi.org/10.1002/mdc3.13870>.

Branco, D. R., Alves, M., Severiano E Sousa, C., Costa, J., Ferreira, J. J., & Caldeira, D. (2023). Direct oral anticoagulants vs vitamin K antagonist on dementia risk in atrial fibrillation: Systematic review with meta-analysis. *Journal of Thrombosis and Thrombolysis*, 56(3), 474–484. <https://doi.org/10.1007/s11239-023-02843-5>.

Agurto-Ramírez A, Pino-Rosón C, Ayala A, Falcón M, Rodríguez-Blázquez C, Forjaz MJ and Romay-Barja M (2023). Association between Pandemic Fatigue and Disease Knowledge, Attitudes, Concerns, and Vaccination Intention at Two Key Moments of the COVID-19 Pandemic. *Int J Public Health* 68:1606049. doi: 10.3389/ijph.2023.1606049.

Marques, A., Caldeira, D., Alegria, S., Pereira, A. R., João, I., & Pereira, H. (2023). Glossopharyngeal neuralgia with cardioinhibitory syncope: Is a permanent pacemaker required? *Revista Portuguesa de Cardiologia*, 42(9), 805–809. <https://doi.org/10.1016/j.repc.2019.12.013>.

Gangas, P., Judica, E., Marin, M., Bouça-Machado, R., Ferreira, J. J., Louro, C., Brach, M., Linnane, D., Ahmed, M., Bentlage, E., Semerci, Y. C., Proença, J. P., & Alfonso, J. (2023). PROCare4Life lessons learned. *Open Research Europe*, 3, 147. <https://doi.org/10.12688/openreseurope.16304.1>.

Gouveia, M., Borges, M., Costa, J., Lourenço, F., Fiorentino, F., Rodrigues, A. T., Teixeira, I., Guerreiro, J. P., Caetano, P., & Carneiro, A. V. (2023). Measuring the value of solidarity: The abem financial assistance program for out-of-pocket payments on pharmacy medicines in Portugal. *Journal of Health Services Research & Policy*, 13558196231196384. <https://doi.org/10.1177/13558196231196384>.

Soares GM, Bouça-Machado R, Abreu D, Ferreira JJ (2023). Contributory Factors to Caregiver Burden in Parkinson's Disease. *Mov Disord Clin Pract*. 10(10):1507-1518. doi: 10.1002/mdc3.13868. PMID: 37868922; PMCID: PMC10585976.

Judica, E., Tropea, P., Bouça-Machado, R., Marín, M., Calarota, E., Cozma, L., Badea, R., Ahmed, M., Brach, M., Ferreira, J. J., & Corbo, M. (2023). Personalized Integrated Care Promoting Quality of Life for Older People: Protocol for a Multicenter Randomized Controlled Trial. *JMIR Research Protocols*, 12, e47916. <https://doi.org/10.2196/47916>.

Silva, D.P., Coelho, M., Soares, T., Vale, T.C., Correia Guedes, L., Maciel, R.O.H., Antunes, A.P., Camargos, S.T., Valadas, A., Godinho, C., Maia, D.P., Pita Lobo, P., Maia, R.D., Teodoro, T., Rieder, C.R., Velon, A.G., Tumas, V., Barbosa, E.R., Teive, H.A.G., Ferraz, H.B., Rosas, M.J., Calado, A., Lampreia, T., Simões, R., Vila-Chã, N., Costa, M.M., Rodrigues, A.M., Caniça, V., Cardoso, F., Ferreira, J.J. and (2023), Handicap as a Measure of Perceived-Health Status in Parkinson's Disease. *Mov Disord Clin Pract*, 10: 1172-1180. <https://doi.org/10.1002/mdc3.13826>.



Araújo, R., Kole, J.J., Ferreira, J.J. and Bloem, B.R. (2023), Ethical Considerations of Unsolicited Medical Opinion in Movement Disorders. *Mov Disord Clin Pract*, 10: 1470-1475. <https://doi.org/10.1002/mdc3.13870>.

Monge-Martín D, Caballero-Martínez F, Forjaz MJ, Castillo MJ, Rodríguez-Blázquez C (2023). Health state perception of people close to retirement age: Relationship with lifestyle habits and subjects' characteristics. *Heliyon* 9:e17995. <https://doi.org/10.1016/j.heliyon.2023.e17995>.

Pereira S C, Abrantes A L, António P S, Morais P, Sousa C, David C, Pinto F J, Almeida A G, Caldeira D (2023). Infective endocarditis risk in patients with bicuspid aortic valve: Systematic review and meta-analysis. *IJC Heart & Vasculature* 47. 28:47:101249. <https://doi.org/10.1016/j.ijcha.2023.101249>.

Chendo, I., Fabbri, M., Godinho, C., Simões, R. M., Sousa, C. S., Coelho, M., Voon, V., & Ferreira, J. J. (2023). High frequency of Depressive Disorders and Suicidal Phenomena in Late-Stage Parkinson's Disease – A Cross-Sectional Study. *Journal of Geriatric Psychiatry and Neurology*, 36(4), 336–346. <https://doi.org/10.1177/08919887221135556>.

Bouça-Machado, R., Leitão, M., Benedetti, A., & Ferreira, J. J. (2023). The Efficacy and Safety of Physiotherapy in People with Dementia: A Systematic Review. *Journal of Alzheimer's Disease*, 1–9. <https://doi.org/10.3233/JAD-230463>.

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Fernandes A, David C, Pinto F J, Costa J, Ferreira J J, Caldeira D (2023). The effect of catheter-based sham renal denervation in hypertension: systematic review and meta-analysis. *BMC Cardiovascular Disorders* 23(1):1-13. <https://doi.org/10.1186/s12872-023-03269-w>.

Monje, M., Grosjean, S., Srp, M., Antunes, L., Bouça-Machado, R., Cacho, R., Domínguez, S., et al. (2023). Co-Designing Digital Technologies for Improving Clinical Care in People with Parkinson's Disease: What Did We Learn? *Sensors*, 23(10), 4957. MDPI AG. Retrieved from <http://dx.doi.org/10.3390/s23104957>.

Outeiro, T. F., Alcalay, R. N., Antonini, A., Attems, J., Bonifati, V., Cardoso, F., Chesselet, M., Hardy, J., Madeo, G., McKeith, I., Mollenhauer, B., Moore, D. J., Rascol, O., Schlossmacher, M. G., Soreq, H., Stefanis, L., & Ferreira, J. J. (2023). Defining the Riddle in Order to Solve It: There Is More Than One “Parkinson’s Disease”. *Movement Disorders*, mds.29419. <https://doi.org/10.1002/mds.29419>.

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Teodoro, T., Koreki, A., Chen, J., Coebergh, J., Poole, N., Ferreira, J. J., Edwards, M. J., & Isaacs, J. D. (2023). Functional cognitive disorder affects reaction time, subjective mental effort and global metacognition. *Brain*, 146(4), 1615–1623. <https://doi.org/10.1093/brain/awac363>.

Moreno-Juste A, Gimeno-Miguel A, Poblador-Plou B, Calderón-Larrañaga A, Cano del Pozo M, Forjaz MJ, Prados-Torres A, Gimeno-Feliú LA (2023). Multimorbidity, social determinants and intersectionality in chronic patients. Results from the EpiChron Cohort. *J Glob Health* 13 04014. doi: 10.7189/jogh.13.04014.

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### **Invited Lectures and Seminars**

Ferreira, JJ. Simpósio Abbvie - Qual o papel das terapêuticas infusionais na doença de Parkinson?, Congresso Anual SPDMov, Portugal, March 17, 2023.

Rosa MM. A doença de Parkinson deveria ser diagnosticada antes dos sintomas motores?, Congresso Anual SPDMov, Portugal, March 17, 2023.

Ferreira JJ, Doença de Parkinson: da causa aos remédios. I Congresso Nacional do Doente de Parkinson, Ciência para Todos, Portugal, April 11, 2023.

Ascensão R, Investigação em Cuidados Primários de Saúde. The Stepping Stone to Clinical Research, Portugal, April 26, 2023.

Ferreira JJ, Early symptoms. 9th Congress of the Italian Society Parkinson and Movement Disorders/LIMPE-DISMOV, Italy, May 5, 2023.

Ferreira, JJ, Updates in essential tremor. XXVIII World Congress on Parkinson's Disease and Related Disorders, USA, May 14, 2023.

Ferreira JJ, Viver com Parkinson: relacionamentos e sexualidade. Bootcamp YPP 2023, Portugal, May 18, 2023.

Ferreira JJ, New treatments in the pipeline for the management of PD. Bulgarian Neurology, Bulgaria, May 19, 2023.

Ferreira JJ, Multidisciplinary care for the management of Parkinson's Disease. Bulgarian Neurology, Bulgaria, May 20, 2023.

Ferreira JJ, Painel temático: Intervenções Inovadoras na Demência: O papel das novas tecnologias na reabilitação. Apresentação Pública dos Resultados do Projeto: Reabilitação Cognitiva com Robot PEPE, Portugal, May 22, 2023.

Ferreira, JJ, Como nos preparamos para o envelhecimento? 5 Décadas de Democracia, Portugal, June 20, 2023.

Ferreira JJ, The Fundamentals of Clinical Trials. MDS Congress 2023, Denmark, August 30, 2023.

Rosa MM, The role of biomarkers in drug development and regulatory decision making. Biomarkers in Drug Development for Perinatal Asphyxia. Conect4children Multi-Stakeholder Meeting on Perinatal Asphyxia, Italy, September 18, 2023.

Ferreira JJ, How to translate the best drug development data into clinical practice. 5ª Edição do Moving on Series – “Interdisciplinaridade na Doença de Parkinson”, Portugal, September 23, 2023.

Ferreira JJ, Innovation in Research and Care of Parkinson’s Disease: what we can expect in the next 10 years? Parkinson National Center of Excellence in Research, NCER-PD Consortium Meeting, Luxembourg, September 26, 2023.

Ferreira JJ, Os direitos Humanos através das gerações: ontem, hoje e amanhã. A 80 Saúde Sénior, Portugal, September 30, 2023.

Ferreira JJ, Qual o modelo de cuidados no futuro na Enxaqueca. Reabilitação pós-AVC e Doença de Parkinson, NeuroConnect, Portugal, October 14, October 14, 2023.

Ferreira JJ, Investigação na Medicina. X Congresso Nacional de Estudantes em Medicina, Portugal, October 15, 2023.

Correia Guedes L, What do PwP know about the genetics of Parkinson’s disease? Bial PD Summit 2023, Portugal, October 20, 2023.

Ferreira JJ, Introducing Kynmobi, Bial PD Summit 2023, Portugal, October 20, 2023.

Ferreira JJ, Why multidisciplinary is a must. Bial PD Summit 2023, Portugal, October 20, 2023.

Sampaio C, Artificial intelligence – a new member of the multidisciplinary team? Bial PD Summit 2023, Portugal, October 21, 2023.

Ferreira JJ, Levodopa + Opicapona = ? Congresso Nacional de Neurologia, Portugal, November 9, 2023.

Ferreira JJ, International keynote: multiprofessional Parkinson's Disease treatment. 4th German Parkinson's Network Congress, Germany, December 1, 2023.

### **Communications**

#### Communications in International Conferences:

Ghattas J, Makovski TT, Monnier-Besnard S, Cavillot L, Ambrožová M, Vašinová B, Feteira-Santos R, Bezzegh P, Ponce Bollmann F, Cottam J, Haneef R, Speybroeck N, Nogueira PJ, Forjaz MJ, Coste J, Carcaillon-Bentata L, Devleeschauwer B., Etiological and prognostic roles of socioeconomic characteristics in the development of SARS-CoV-2 infection and related severe health outcomes: a systematic review of population-based studies. 17th World Congress on Public Health, Italy, May 2, 2023. (Poster Presentation)

Prieto-Flores ME, Forjaz MJ, Bernal-Alonso A, Rodriguez-Blazquez C, Personas mayores cuidadoras: apoyo social percibido e intensidad de cuidados prestados. 63 Congreso de la Sociedad Española de Geriatría y Gerontología, Spain, June 6, 2023 (Poster Presentation)

Fernandez-Mayoralas G, Rojo-Perez F, Molina-Martinez MA, Rodriguez-Blazquez C, Forjaz MJ, Rodriguez-Rodriguez V, Rojo-Abuin JM, Edadismo percibido y calidad de vida entre población mayor institucionalizada en tiempos de COVID-19. 63 Congreso de la Sociedad Española de Geriatría y Gerontología, Spain, June 6, 2023 (Poster Presentation)

Rodriguez Rodriguez V, Rojo Perez F, Perez De Arenaza Escribano C, Fernandez-Mayoralas Fernandez G, Forjaz Mj, Rodriguez Blázquez C, Realización de actividades por las personas mayores en residencias durante la pandemia por COVID-19. 63 Congreso de la Sociedad Española de Geriatría y Gerontología, Spain, June 6, 2023 (Poster Presentation)

Rojo-Perez F, Rodriguez-Rodriguez V, Fernandez-Mayoralas G, Forjaz MJ, Rodríguez-Rodríguez C, Cárdenas Soriano P, Martín García S, Calidad de vida y factores asociados en población mayor en residencias durante la pandemia por COVID-19. 63 Congreso de la Sociedad Española de Geriatría y Gerontología, Spain, June 6, 2023 (Poster Presentation)

Rodriguez-Blazquez C, Forjaz MJ, Martin-Garcia S, Rojo-Perez F, Fernandez-Mayoralas G, Perez de Arenaza C, Rodriguez-Rodriguez C, Estado de salud y satisfacción con los cuidados sanitarios en personas mayores que vivían en residencias durante la pandemia de COVID-19. 63 Congreso de la Sociedad Española de Geriatría y Gerontología, Spain, June 6, 2023 (Poster Presentation)

C Rodríguez-Blázquez, F Rojo-Perez, V Rodríguez-Rodríguez, M J Forjaz, G Fernandez-Mayoralas, S Martin, Loneliness, ageism and mental wellbeing in nursing homes during the COVID-19 pandemic. European Public Health Conference, Ireland, November 8, 2023. (Oral Presentation)

Martins ME., Lopes AA., Santos HF., Rosado M.L, Guimarães I., Paquete P., Almeida P., Lopes AF., Carrillo E., Vilaró J., Järvinen STS., Kozakiewicz M., Kędziora-Kornatowska K., Hoxha A., Pekarić J., Gruneberg C, Projeto SIENHA – Rede europeia estratégica e inovadora para a educação no envelhecimento saudável [SIENHA-Strategic Innovative Educational Network for Healthy Ageing]. 4ª Reunião Internacional da Rede Académica das Ciências da Saúde da Lusofonia, Angola, November 25, 2023. (Oral Presentation)

R. Barbosa, P Pita Lobo, A. Valadas, P. Bastos, S. Alberto, L Correia Guedes, M. Rosa, R. Matias, M. Coelho, Unveiling The Role of Subthalamic Nucleus Stimulation on Freezing of Gait in Parkinson Disease Using Wearable sensors. International Congress of Movement Disorders and Parkinson's Disease, Denmark. (Oral Presentation)

Miguel de Oliveira Carvalho, Maria Begoña Cattoni, Leonor Correia Guedes, Herculano Carvalho, Patricia Pita Lobo, Luisa Albuquerque, Vanda Freitas, Inês Chendo, Sofia Reimão, Ana Castro Caldas, Anabela Valadas, Margherita Fabbri, Catarina Godinho, Raquel Barbosa, Pedro Baptista, Joaquim J Ferreira, A Gonçalves Ferreira, Mário Miguel Rosa, Miguel Coelho, Reasons for exclusion from Deep Brain Stimulation (DBS) for Parkinson's Disease. 9th Congress of the European Academy of Neurology, Budapest. (Oral Presentation)

### **Organization of Conferences**

Ferreira, JJ, Organizer, Curso Multidisciplinar de Doenças do Movimento, Centro Neurológico Sénior, Portugal, March 24, 2023.

Ferreira, JJ, Organizer, 5º Congresso CNS, Centro Neurológico Sénior, Portugal, April 22, 2023.

Ferreira, JJ, Co-Organizer, Congresso Nacional de Neurologia, Portugal, November 9, 2023.



### **Prizes & Honours**

Ferreira JJ, Prémio Científico Universidade de Lisboa/Caixa Geral de Depósitos na área da saúde – Edição 2023.

Ferreira JJ, Publicação de Louvor em Diário da República. Louvor nº 83/2023.

Ferreira JJ, President's distinguished Service Award, International Congress of Parkinson's Disease and Movement Disorders.

### **Advanced Teaching**

Rosa MM, Lecture, Terapêuticas Avançadas em Doenças do Movimento. Curso de Terapêuticas Avançadas em Neurologia, Portugal, February 10, 2023.

Ferreira JJ, Lecture, Abordagem farmacológica da doença de Parkinson e síndromes parkinsonianas atípicas, "Curso Multidisciplinar de Doenças do Movimento", Centro Neurológico Sénior, March 24, 2023.

Ferreira JJ, Lecture, O que ainda estamos a tratar? "Como estamos a tratar a Doença de Parkinson", 5º Congresso CNS, Centro Neurológico Sénior, Portugal, April 22, 2023.

Ferreira JJ, Lecture, Multidisciplinary care for management of PD, 12th International Movement Disorders Teaching Course, Romania, April 27, 2023.

Ferreira JJ, Lecture, How to best take levodopa in Parkinson's Disease, 12th International Movement Disorders Teaching Course, Romania, April 27, 2023.

Ferreira JJ, Lecture, 9th Congress of the Italian Society Parkinson and Movement Disorders/LIMPE-DISMOV, Italy, May 5, 2023.

Ferreira JJ, Lecture, Updates in essential tremor, XXVIII World Congress on Parkinson's Disease and Related Disorders, USA, May 14, 2023.

Ferreira JJ, Lecture, New treatments in the pipeline for the management of PD, Bulgaria, May 19, 2023.

Ferreira JJ, Lecture, Multidisciplinary care for the management of Parkinson's Disease, Bulgaria, May 20, 2023.

Ferreira JJ, Lecture, The Fundamentals of Clinical Trials, MDS Congress 2023, Denmark, August 30, 2023.

Ferreira JJ, Lecture, How to translate the best drug development data into clinical practice, 5ª Edição do Moving on Series – “Interdisciplinaridade na Doença de Parkinson”, Portugal, September 23, 2023.

Ascensão R, Lecture, Tipos de estudos clínicos, Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 4, 2023.

Ferreira JJ, Lecture, Introdução ao módulo: o que é a investigação clínica? Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 4, 2023.

Ascensão R, Lecture, Fundamentos de Bioética aplicados à IC, Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 11, 2023.

Alarcão J, Lecture, Desenvolvimento e validação de dispositivos médicos? Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 11, 2023.

Forjaz MJ, Lecture, Construção e avaliação de questionários e investigação qualitativa, Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 17, 2023.

Fernandes R, Lecture, Outcomes e instrumentos de avaliação clínica, Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 17, 2023.

Gonçalves N, Lecture, Desenvolvimento e avaliação de testes de diagnóstico, Mestrado Integrado em Investigação Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, November 18, 2023.

Ferreira JJ, Lecture, International keynote: multiprofessional Parkinson’s Disease treatment, 4th German Parkinson’s Network Congress, Germany, December 1, 2023.

### **PhD Theses**

Inês Chendo, The neuropsychiatric symptoms and syndromes in late-stage Parkinson's disease study, Supervisor: Joaquim Ferreira, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 10, 2023.

Tiago Teodoro, Unifying the neurobiology of functional neurological symptoms: the role of attention, Supervisor: Joaquim Ferreira, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 27, 2023.

Catarina Filipa Severiano e Sousa, Cognitive Disorders in Late-Stage Parkinson's Disease, Supervisor: Joaquim Ferreira, Faculdade de Medicina da Universidade de Lisboa, Portugal, May 2, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Grunenthal, Sponsored Research.

### **Science and Society in 2023**

Ferreira JJ, Interview, Dia Mundial da Doença de Parkinson, Jornal Médico, April 11, 2023.

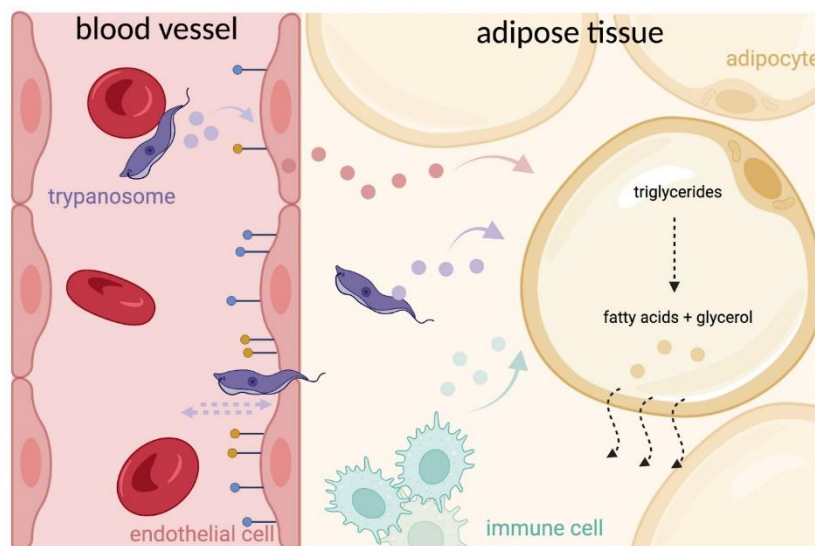
## Luísa Figueiredo Lab

**Head of Laboratory:** Luísa Figueiredo, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Abdulbasit Amin	PhD	Postdoctoral Researcher
Christoph Josef Wenzl	Master Degree	PhD Student
Daniel Filipe Silva Ribeiro	PhD	Postdoctoral Researcher (Started April)
David Filipe Valente Ferreira	University Degree	Lab Technician
Henrique Pedro Pereira da Silva Amaral Machado	PhD	Researcher (Left October)
Hugo Miguel da Costa Luiz	University Degree	MSc Student (Started September)
Idálio de Jesus Contreiras Viegas	PhD	Postdoctoral Researcher (Left July)
Lara López Escobar	Master Degree	PhD Student
Leonor Duarte Pinho	Master Degree	Lab Manager
Lúcia Branco Serra	Master Degree	PhD Student
Marta Valido Narciso	Master Degree	Lab Technician (Left November)
Michal Grzegorz Malecki	PhD	Postdoctoral Researcher (Started May)
Sandra Isabel Gonçalves Trindade	PhD	Senior Postdoctoral Researcher
Sara Silva Pereira	PhD	Postdoctoral Researcher (Left August)

### Graphical Abstract



*Parasite biology and adaptation to micro environment*

### **Lab Interests**

The African *trypanosome*, a single-celled parasite, causes sleeping sickness in humans and nagana in cattle. Sleeping sickness is fatal in humans. Nagana is a major obstacle to development of the rural areas in Sub-Saharan Africa. Our group aims to understand the disease mechanisms of these parasites.

TISSUE TROPISM - We have discovered that adipose tissue is an important parasite reservoir in mouse infections, with parasites functionally adapting to the tissue microenvironment. We are studying how parasites interact with host vasculature to invade tissues, the interface with adipocytes, the consequences of parasite heterogeneity and the impact of tissue tropism on immune evasion, host metabolism and ultimately disease progression.

POST-TRANSCRIPTIONAL GENE REGULATION - We focus on the role of RNA modifications and non-coding RNAs in gene regulation in African *trypanosomes*.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

In 2023, we published a novel important discovery conducted by Henrique Machado that adipocyte lipolysis protects mice against *Trypanosoma brucei* infection.

Luísa Figueiredo was elected as a new EMBO Member. The nomination and election by the other EMBO Members is a testament to the exceptional contributions in the parasitology field, specifically on the seminal research on the many facets of *Trypanosoma brucei* infection.

Appointment of Sara Silva-Pereira a previous lab postdoc to group leader in Católica Biomedical Research Centre (CBR).

### **Ongoing Projects**

2023/2024: Characterisation of *Trypanosoma* sequestration to endothelial cells. Coordinator: Sara Silva Pereira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02187.PTDC. Amount: 49 937,50€. Total Amount: 49 937,50€.

2022/2023: Prémio Maria de Sousa – Bial. Coordinator: Sara Silva Pereira. Funding Agency: Bial. Reference: Prémio Maria de Sousa – Bial. Amount: 25 000,00€. Total Amount: 25 000,00€.

2022/2023: BIG 2022 LFIGUEIREDO. Coordinator: Luísa Figueiredo and Claus Azzalin. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: BIG 2022 LFIGUEIREDO. Amount: 75 000,00€. Total Amount: 75 000,00€.

2021/2025: TrypM6A: Mechanism and function of epitranscriptomic poly(A) tail modifications in African trypanosomes. Coordinator: Luísa Figueiredo. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - TRYPM6A - HR20-00361 - LFIGUEIREDO. Amount: 499 400,00€. Total Amount: 499 400,00€.

2019/2024: 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€.

2018/2024: 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€.

2010/2023: Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes - PIRG06-GA-2009-256299. Coordinator: Luísa Figueiredo. Funding Agency: European Commission. Reference: HistoneH1Tryp. Amount: 99 718,39€. Total Amount: 99 718,39€.

## **Scientific Impact**

### **Academic Collaborations**

- Cláudio Franco, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Claus Azzalin, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Ed Bergstrom, University of York, United Kingdom.
- Samie Jaffrey, Weill Cornell Medicine, USA.
- Shulamit Michaeli, The Bar-Ilan University, Israel.
- Catarina Gadelha, University of Nottingham, United Kingdom.
- Frederic Bringaud, University of Bordeaux, France.

- Lori Passmore, University of Cambridge, United Kingdom.
- Rudolph Zechner, University of Graz, Austria.
- Philipp Scherer, University of Texas Southwestern, USA.

### Selected Publications

Machado H, Hofer P, Zechner R, Smith TK & Figueiredo LM (2023). [Adipocyte lipolysis protects mice against \*Trypanosoma brucei\* infection](#). **Nature Microbiology** 8(11):2020–2032.

**Relevance of the publication:** In this work we show that activation of lipolysis in adipose tissue protects mice during *T. brucei* infection, by extending host survival and by eliminating parasites through a lipotoxic accumulation of free fatty acids. Modulation of this metabolic pathway or its trypanocidal mechanism may be useful in future treatments for African *trypanosomiasis*.

Viegas IJ, de Macedo JP, Serra L, De Niz M, Temporão A, Silva Pereira S, Mirza AH, Bergstrom E, Rodrigues JA, Aresta-Branco F, Jaffrey SR, Figueiredo LM (2022). [N6-methyladenosine in poly\(A\) tails stabilize VSG transcripts](#). **Nature** 604(7905):362-370.

**Relevance of the publication:** In this work, which can be conceptually located at the intersection of post-transcriptional gene regulation and antigenic variation in *T. brucei*, we find that the presence of m6A in the poly(A) tail stabilizes the mRNA of the variant surface glycoprotein (VSG). This is a molecule central to parasite growth and immune evasion. Therefore, for the antigenic variation field, this was an important discovery adding a new mechanism to the current model. Additionally, for the field of RNA processing, it was the first chemical modification of the poly(A) tail found, opening up the possibility of a new regulatory mechanism for mRNA stability regulation.

Silva Pereira S, De Niz M, Serre K, Ouarné M, Coelho JE, Franco CA, Figueiredo LM (2022). [Immunopathology and \*Trypanosoma congolense\* parasite sequestration cause acute cerebral trypanosomiasis](#). **eLife** 5;11:e77440.

**Relevance of the publication:** *Trypanosoma congolense* is an animal pathogen that poses a significant threat for African livestock. In this study, we developed a novel mouse model of acute cerebral trypanosomiasis. We showed that parasite cyto-adhesion to brain vasculature triggers a CD4+ T cell dependent, lethal immunological response. This paper will prime further studies of the previously overlooked mechanism of parasite cyto-adhesion.

Guegan F, Rajan KS, Bento F, Pinto-Neves D, Sequeira M, Gumińska N, Mroczek S, Dziembowski A, Cohen-Chalamish S, Doniger T, Galili B, Estévez AM, Notredame C, Michaeli S, Figueiredo LM (2022). [A long non-coding RNA controls parasite differentiation in African \*trypanosomes\*](#).

**Science Advances** 17;8(24):eabn2706.

**Relevance of the publication:** In this work, we did not only identified the full repertoire of long non-coding RNA (lncRNA) genes in *T. brucei* but also characterized the first lncRNA function ever described in this parasite. We found that grumpy lncRNA is a key regulator that promotes parasite differentiation into the quiescent stumpy form, which ultimately led to a reduction in parasitemia and an improvement of the disease outcome in mice. Which was ultimately leading to a reduction parasitemia and the improvement of the disease outcome in mice.

Trindade S & Rijo-Ferreira F, Carvalho T, Pinto-Neves D, Guegan F, Aresta-Branco F, Bento F, Young SA, Pinto A, Van Den Abbeele J, Ribeiro RM, Dias S, Smith TK, Figueiredo LM (2016). [Trypanosoma brucei parasites occupy and functionally adapt to the adipose tissue in mice](#). **Cell Host & Microbe** 19(6):837-848.

**Relevance of the publication:** This work revealed for the first time that *T. brucei* preferentially accumulates in the adipose tissue. In this tissue, *T. brucei* adapts its metabolism to catabolize fatty acids.

### 2023 Publications in Peer-Reviewed Journals

Machado H, Hofer P, Zechner R, Smith TK & Figueiredo LM (2023). Adipocyte lipolysis protects mice against *Trypanosoma brucei* infection. *Nature Microbiology* 8(11):2020–2032.

### Invited Lectures and Seminars

Luisa M Figueiredo, A small RNA modification that prolongs the life of a messenger RNA. RNA IN DISEASE-IX ptRNA Meeting, Portugal, January 26, 2023.

Luisa M Figueiredo, Invasion and Adaptation: Exploring *Trypanosoma brucei*'s Phenotypic Flexibility in Host Tissues. Biomedical Science Seminars, United Kingdom, May 12, 2023.

Luisa M Figueiredo, Uncovering the unusual biology of trypanosomes. EMBO members' meeting, Germany, October 26, 2023.

Luisa M Figueiredo, Unveiling the impact of trypanosome infection on adipose tissue. MicroBUP Webinar, France, November 22, 2023.

Luisa M Figueiredo, Learning new biology by studying an ancient parasite. Journée du Département Sciences Biologiques et Médicales, France, December 11, 2023.

Luisa M Figueiredo, Hidden wonders in *Trypanosoma* biology. Université de Montpellier, France, December 12, 2023.

### Communications

#### Communications in International Conferences:

Sara Silva Pereira, Cytoadhesion of *Trypanosoma congolense* to bioengineered 3D bovine microvessels. 34th Molecular Parasitology Meeting, USA, September 19, 2023. (Oral Presentation)



Lúcia Serra, You shall not pass: the role of N6-methyladenosine in blocking poly(A) tail deadenylation. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Communications in National Conferences:

Lúcia Serra, You shall not pass: the role of N6-methyladenosine in blocking poly(A) tail deadenylation. RNA IN DISEASE-IX ptRNA meeting, Portugal, January 26, 2023. (Poster Presentation)

**Organization of Conferences**

Luisa M Figueiredo, Co-Organizer, MSCA ITN Cell2Cell Summer School in “Chromatin and infection Biology at the Single-Cell Level”, Portugal, September 24, 2023.

**Networks and Research Infrastructures**

Luisa M Figueiredo, ITN Cell2Cell, European Union.

Luisa M Figueiredo, COBALT, Wellcome Trust Collaborative Award in Science.

Luisa M Figueiredo, EMBO Member Community, EMBO.

**Prizes and Honours**

Luisa M Figueiredo, EMBO Member.

**Advanced Teaching**

Luisa M. Figueiredo & Henrique Machado, Lecture, PhD program in Molecular Biosciences, Portugal, April 19, 2023.

Luisa M Figueiredo, Coordination of PhD Curricular Unit, MSCA ITN Cell2Cell Summer School, Portugal, September 25, 2023.

Luisa M. Figueiredo & Sandra Trindade, Lecture, Masters in Biomedicine, Portugal, October 23, 2023.

Luisa M Figueiredo, Coordination of PhD Curricular Unit, Universidade de São Paulo, Brazil, December 1, 2023.

### **MSc Theses**

Marta Narciso, How similar are freshly isolated *Trypanosoma brucei* parasites from the ones extensively used in the laboratory?, Supervisor: Luisa M. Figueiredo and Henrique Machado, Faculdade de Ciências da Universidade de Lisboa, Faculdade de Medicina da Universidade de Lisboa, Instituto de Medicina Molecular João Lobo Antunes, Portugal, September 5, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

One-week internship from April 17 to 21st 2023 to introduce the world of biomedical research to Tomás Reis, a student in the 9th grade from Liceu Francês Charles Lepierre.

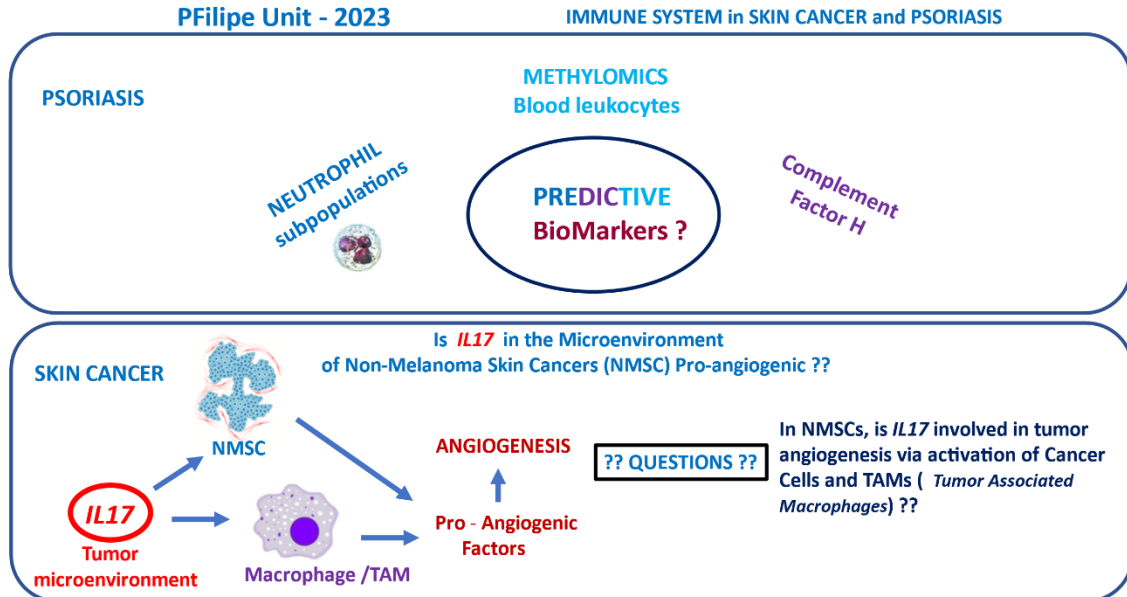
## Paulo Filipe Lab

**Head of Laboratory:** Paulo Filipe, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Associate Professor at Faculdade de Medicina da Universidade de Lisboa and Director of the Department of Dermatology at Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria

### Team

Ana Daniela Casimiro Cunha	Master Degree	PhD Student
David José Roxo Botequim	PhD	Postdoctoral Researcher
João António Augusto Ferreira	MD/PhD	Staff Scientist
João Borges da Costa	MD/PhD	Clinical Researcher
João Nuno Maia Rodrigues da Silva	MD/PhD	Clinical Researcher
Luís Miguel dos Santos Reis Soares de Almeida	MD/PhD	Clinical Researcher
Maria Clara Gomes da Fonseca Pedro Bicho	MD/PhD	Clinical Researcher
Miguel Duarte Botas Alpalhão	Master Degree	Trainee

### Graphical Abstract



### **Lab Interests**

Our research is focused in understanding the role of the immune system in susceptibility to infections affecting the skin and in progression of inflammatory skin diseases, namely psoriasis, and non-melanoma skin cancers (NMSCs). Our research shall elucidate functional links between innate and adaptive immunity in psoriasis and NMSCs. We are also searching for predictive biomarkers for psoriasis among components of the innate immune system (complement Factor H, neutrophil subpopulations) and epigenetic alterations in immune cells using high-end technologies and innovative clinical trials.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

As part of a multi-institutional, collaborative study combining genomic and epidemiological data on the 2022 outbreak of Mpox in Portugal our efforts provided a better understanding of the dynamics of viral emergence, diversification, and transmission. This may lead to better real-time monitoring and control of Mpox epidemics in the future. Our group also showed that HIV co-infection aggravates the clinical features of Mpox infection, and that Mpox genomes persisted in skin lesions longer than anticipated, which may lead to a change in currently recommended rules and standards for personal contact eviction. On the clinical side, we also contributed to better compose the spectrum of skin manifestations associated with the Mpox and SARS-CoV-2 viruses.

In skin psoriasis, we made significant advancements in establishing subpopulations of neutrophils as potential predictive biomarkers.

### **Ongoing Projects**

2020/2024: Apoio Janssen. Coordinator: Paulo Filipe. Funding Agency: Janssen - Cilag Farmacêutica, Lda. Reference: Acordo Janssen. Amount: 67 928,40€. Total Amount: 67 928,40€.

2016/2023: Th9-IL9R axis: a role in tissue memory in plaque-type psoriasis? Coordinator: Paulo Filipe. Funding Agency: Vários. Reference: Th9-IL9-IL9R axis. Amount: 105 000,00€. Total Amount: 105 000,00€.

## Scientific Impact

### Academic Collaborations

- Faculdade de Medicina Veterinária da Universidade de Lisboa, Portugal.
- Muséum National d'Histoire Naturelle, Alliance Sorbonne-Université, Paris, France.
- Department of Chemistry, University of Aveiro, Portugal.
- Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### Selected Publications

Correia C, Alpalhão M, de Sousa D, Vieitez-Frade J, Pelerito A, Cordeiro R, Lopes de Carvalho I, Nuncio MS, Ferreira J, Filipe P (2023). [Detection of mpox using polymerase chain reaction from the skin and oropharynx over the course of infection: A prospective study](#). *J Am Acad Dermatol.*, 89(4):822-823. DOI: 10.1016/j.jaad.2023.05.071

**Relevance of the publication:** In this research the Authors show that genomes from the mpox virus are shed from the skin and oropharynx for much longer than previously anticipated. This may lead to alteration of currently held transmission prevention measures.

Alpalhão M, Sousa D, Frade JV, Patrocínio J, Garrido PM, Correia C, Brazão C, Mancha D, Nuncio MS, Pelerito A, Borrego MJ, Filipe P (2023). [Human Immunodeficiency Virus infection may be a contributing factor to Monkeypox infection: analysis of a 42-case series](#). *J Am Acad Dermatol.*, 88(3):720-722. DOI:10.1016/j.jaad.2022.09.029

**Relevance of the publication:** In this research the Authors show that genomes from the mpox virus are shed from the skin and oropharynx for much longer than previously anticipated. This may lead to alteration of currently held transmission prevention measures.

Borges V, et al., (2023). [Viral genetic clustering and transmission dynamics of the 2022 mpox outbreak in Portugal](#). *Nat Med.*, 29(10):2509-2517. DOI: 10.1038/s41591-023-02542-x

**Relevance of the publication:** In this research genomic and epidemiological data on the 2022 Mpox outbreak in Portugal were combined to identify the predominant viral sublineages to better understand their dynamics of emergence, diversification, and transmission. This collaborative study highlighted the role played by sexual networks and the relevance of genomic epidemiology as a tool for real-time monitoring and control of the Mpox epidemics.

Queirós C, Filipe P, Soares-Almeida L (2020). [Cutaneous Metastases from Solid Neoplasms in the 21st Century: A Retrospective Study from a Portuguese Tertiary Care Centre](#). *J Eur Acad Dermatol Venereol.*, 34(6):1218-1224. DOI: 10.1111/jdv.16120

**Relevance of the publication:** This retrospective study was one of the largest published analyses on the topic of cutaneous metastasis from solid tumours (n= 164 patients). The Authors found that melanoma and breast cancer comprise the most frequent sources of cutaneous metastases, followed by lung cancer. This study consolidated the clinical landscape on this relevant topic. Our group was the exclusive contributor to this piece of research.

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. DOI: 10.18632/oncotarget.17121

**Relevance of the publication:** We described a novel technology of cell cycle analysis that, in contrast to precedent flow cytometric methodologies, allows the determination of both relative and absolute durations of all the cell cycle stages. Our group is the main contributor to this research, with collaborations from the groups of René Santus (University of Sorbonne, Paris, France) and Ana Espada-Sousa (iMM-JLA, Lisbon, Portugal). This research was very welcome within the scientific community working on the cell cycle, resulting in an invitation to contribute to the prestigious monographic series “Methods in Molecular Biology”.

### 2023 Publications in Peer-Reviewed Journals

Correia C, Alpalhão M, de Sousa D, Vieitez-Frade J, Pelerito A, Cordeiro R, Lopes de Carvalho I, Nuncio MS, Ferreira J, Filipe P (2023). Detection of mpox using polymerase chain reaction from the skin and oropharynx over the course of infection: A prospective study. *J Am Acad Dermatol.*, 89(4):822-823. DOI: 10.1016/j.jaad.2023.05.071

Brazão C, Garrido PM, Alpalhão M, Roda Â, Vieitez-Frade J, Ferreira JA, Pelerito A, Carvalho IL, Nuncio MS, Cordeiro R, Borrego MJ, Filipe P (2023). Monkeypox virus infection in HIV-1-coinfected patients previously vaccinated against smallpox: A series of 4 cases from Portugal. *J Eur Acad Dermatol Venereol.*, 37(3):e319-e321. DOI: 10.1111/jdv.18655

de Sousa D, Filipe P (2023). Comment on 'Monkeypox: key pointers for dermatologists'. *Clin Exp Dermatol.*, 48(6):696-697. DOI: 10.1093/ced/llad049

Mancha D, Brazão C, Filipe P (2023). Oro-mammary inoculation pathway of monkeypox in a female patient. *J Eur Acad Dermatol Venereol.*, 37(5):e636-e637. DOI: 10.1111/jdv.18672

Borges V, et al. (2023). Viral genetic clustering and transmission dynamics of the 2022 mpox outbreak in Portugal. *Nat Med.*, 29(10):2509-2517. DOI: 10.1038/s41591-023-02542-x

Frade JV, Sousa I, Marques T, Filipe P (2023). Acute paronychia: An atypical presentation of Monkeypox infection. *Enferm Infecc Microbiol Clin.*, 41(5):317-318. DOI: 10.1016/j.eimc.2022.09.003

Brazão C, Mancha D, Soares-de-Almeida L, Filipe P (2023). Sweet syndrome following SARS-CoV-2 infection: A unique bullous photo-distributed presentation. *J Eur Acad Dermatol Venereol.*, 37(7):e828-e830. DOI: 10.1111/jdv.19038

Mancha D, Antunes J, Soares-de-Almeida L, Borges-Costa J, Filipe P (2023). Localized Vitiligo and Post-Inflammatory Hypopigmentation at the Injection Site of a COVID-19 mRNA Vaccine. *Dermatol Pract Concept*. 13(1):e2023023. DOI: 10.5826/dpc.1301a23

Sun L, Brazão C, Mancha D, Soares-de-Almeida L, Filipe P (2023). Reply to: 'Severe bullous pemphigoid following Covid-19 vaccination resistant to rituximab and successfully treated with dupilumab' by Baffa et al. *J Eur Acad Dermatol Venereol*. 37(5):e578-e580. DOI: 10.1111/jdv.18893

Brazão C, Filipe P (2023). The Data on Scabies Cases during COVID-19 Pandemic: A Two-Year Analysis from the Largest Portuguese Tertiary Teaching Hospital. *Actas Dermosifiliogr.*, 114(1):88-89. DOI: 10.1016/j.ad.2022.06.005

Leitão TP et al. (2023). Clinical Validation of a Size-Based Microfluidic Device for Circulating Tumor Cell Isolation and Analysis in Renal Cell Carcinoma. *Int. J. Mol. Sci.*, 24, 8404. DOI: 10.3390/ijms24098404

Valente S, Nascimento C, Gameiro A, Ferreira J, Correia J, Ferreira F (2023). TIM-3 Is a Potential Immune Checkpoint Target in Cats with Mammary Carcinoma. *Cancers*, 15, 384. DOI:10.3390/cancers15020384

Alpalhão M, Botequim D, Ferreira J, Santus R, Filipe P (2023). Photosensitization of human skin fibroblasts by vemurafenib promotes pleiotropic effects on membrane-enclosed organelles and apoptosis. *J Photochem Photobiol B*. 238:112600. DOI: 10.1016/j.jphotobiol.2022.112600

Brazão C, Alpalhão M, Filipe P (2023). The clinical spectrum of response to narrowband-UVB therapy in chronic plaque psoriasis: The lower limbs are the most difficult-to-treat body region. *Photodermatol Photoimmunol Photomed.*, 39(5):529-531. DOI: 10.1111/phpp.12877

Mancha D, Filipe P (2023). Phototherapy in the artificial intelligence era. *Photodermatol Photoimmunol Photomed.*, 39(5):538-539. DOI: 10.1111/phpp.12890

Sun L, Alpalhão M, Filipe P (2023). Analysis of dermatology emergency consultations in a pediatric population: One-year retrospective audit from the largest Portuguese tertiary teaching hospital. *Pediatr Dermatol.*, 40(1):139-141. DOI: 10.1111/pde.15189

### **Invited Lectures and Seminars**

Filipe P, Unmet needs na psoríase - Gaps na investigação. A iluminar a vida dos doentes com psoríase (Pavilhão do Conhecimento), Portugal, February 3, 2023.

Filipe P, Inovação no Cuidado da Pele. Conferências do Estoril, Portugal, September 26, 2023.

Filipe P, Future of Change; the role of technology in shaping clinical practice. Derma Talks, Portugal, December 15, 2023.

### **Communications**

#### Communications in International Conferences:

Sun L, A case of lichen planus pigmentosus-inversus after COVID-19 vaccination: cause or coincidence? 18th Symposium of the European Academy of Dermatology and Venereology, Spain, May 18, 2023. (Poster Presentation)

Mancha D, An unusual autoimmune blistering disorder. 18th Symposium of the European Academy of Dermatology and Venereology, Spain, May 18, 2023. (Poster Presentation)

Sun L, Dermatofibrosarcoma protuberans: A 25-year retrospective study from a large metropolitan academic center. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

Sun L, Pyogenic granuloma-like Kaposi sarcoma as the initial presentation of HIV. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

Sun L, Punctate palmoplantar keratoderma type I: case report. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

Mancha D, Peripheral cutaneous T-cell lymphoma, NOS: a case report. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

Mancha D, Generalized bullous fixed drug eruption caused by iodinated contrast media. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)



Mancha D, Paracetamol-induced generalized fixed drug eruption. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

Mancha D, Reconstruction of an Anterior Auricular Defect through a Tunnelized Preauricular Transposition Flap. 32nd Congress of the European Academy of Dermatology and Venereology, Germany, October 11, 2023. (Poster Presentation)

#### Communications in National Conferences:

Sun L, Dermatofibrosarcoma protuberans – estudo retrospectivo de 25 anos de um Hospital Terciário. Reunião da Primavera da Sociedade Portuguesa de Dermatologia e Venereologia, Portugal, June 2, 2023. (Oral Presentation)

Mancha D, Dermatite de contato alérgica e Dermatite atópica - Resultados de um estudo retrospectivo de três anos. 22º Congresso Nacional de Dermatologia e Venereologia, Portugal, November 24, 2023. (Oral Presentation)

#### **Organization of Conferences**

Filipe P, Organizer, Reunião da Primavera, Sociedade Portuguesa de Dermatologia e Venereologia, Portugal, June 2, 2023.

Filipe P, Organizer, 22º Congresso Nacional de Dermatologia e Venereologia, Portugal, November 24, 2023.

#### **Networks and Research Infrastructures**

Filipe P, METHYLOMIC- HORIZON-HLTH-2022-TOOL-11-01 (Proposal ID: 101095449) (DOI: 10.3030/101095449), Research.

#### **Prizes and Honours**

Paulo Filipe, Invited referee for the following Journals: British Journal of Dermatology, Journal of Dermatology, Journal of European Academy of Dermato-Venereology, Molecular Diagnosis & Therapy, Photochemical and Photobiological Sciences, Rheumatology and Wound Repair and Regeneration.

João Ferreira, Invited referee for the following Journals: Veterinary Sciences, Frontiers in Immunology, Molecular Biology Reports, Journal of Pharmacy and Pharmacology, Cancers and International Journal of Molecular Sciences.

### **Advanced Teaching**

João Ferreira, Lecture, Diagnóstico laboratorial de fungos dermatófitos, Mestrado em Análises Clínicas, Faculdade de Farmácia da Universidade de Lisboa, Portugal, June 20, 2023.

Paulo Filipe, Workshop Organization, VII Jornadas de Dermatologia do Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Portugal, November 2, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Postdoctoral Fellowship (ref., IMM/BIPD/18-2021), JANSSEN – CILAG Farmacêutica Lda, Portugal, Sponsored Research.

Elucidate the effects of Brodalumab on neutrophils in psoriasis, LEO Farmacêuticos Lda, Portugal, Sponsored Research.

Elucidate the role of IL-23/IL-17 axis in skin cancer angiogenesis, ALMIRALL, S.A., Barcelona, Spain, Sponsored Research.

## João Eurico da Fonseca Lab

**Head of Laboratory:** João Eurico da Fonseca, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full Professor, Dean, Director of Instituto de Semiótica Clínica and of Clínica Universitária de Reumatologia at Faculdade de Medicina da Universidade de Lisboa, Director of the Rheumatology Department at Centro Hospitalar Universitário Lisboa Norte - Hospital de Santa Maria, President of the Centro Académico de Medicina de Lisboa

### Team

Adriana Andrade Vieira	Master Degree	Lab Manager
Afonso Maria Vilaça Delgado Vieira Gonçalves	MD/Master Degree	Clinical Researcher
Ana Filipa Brojo Lopes de Oliveira Ramos Cordeiro	PhD	Postdoctoral Researcher
Ana Patrícia Costa Reis	MD/PhD	Postdoctoral Researcher
Ana Rita da Cruz Machado	MD/Master Degree	Clinical Researcher
Ana Rita Faísca Mariano	University Degree	MSc Student (Left December)
Ana Teresa Freire de Melo	MD/Master Degree	Clinical Researcher (Left June)
Ângelo Miguel Silva Calado	PhD	Senior Postdoctoral Researcher
Beatriz Viana Pimpão Graça	Bachelor Degree	Trainee (Started January. Left December)
Bruno Miguel Costa Vidal	PhD	Postdoctoral Researcher
Catarina Alexandra Morais Fernandes da Costa Bento	University Degree	MSc Student
Catarina Mendes Cândido	Master Degree	MSc Student (Started September)
Catarina Sofia Melo Tomé	Master Degree	PhD Student
Cristina Dias Botelho da Ponte	MD/PhD	Postdoctoral Researcher
Eduardo Jorge Dourado Domingues	MD/Master Degree	Clinical Researcher (Left June)
Elsa Cristina Vieira de Sousa	MD/PhD	Postdoctoral Researcher
Estela Leite Nogueira	MD/University Degree	Clinical Researcher
Fernando Manuel Diamantino Saraiva	MD/University Degree	Clinical Researcher
Inês Cardoso Leal	PhD	Postdoctoral Researcher (Started January)
Inês de Almada Correia	University Degree	MSc Student
Inês Sá da Costa Pereira Borges	Master Degree	Clinical Study Coordinator – Technician (Started October)
Joana Rita Carrulo Inácio	University Degree	MSc Student (Started September)
Joaquim Miguel Polido Pereira	MD/University Degree	PhD Student
Manuel Quaresma Jorge Silvério António	MD/Master Degree	Clinical Researcher
Margarida Lucas Serrão André Rocha	Master Degree	Clinical Researcher (Started April. Left December)
Maria Helena Regalo da Fonseca	MD/PhD	Senior Postdoctoral Researcher
Maria José Parreira dos Santos	MD/PhD	Senior Postdoctoral Researcher
Maria Sara de Almeida Gonçalves Galezowski	MD/PhD	Senior Postdoctoral Researcher (Started November)
Matilde José Sousa Bandeira	MD/Master Degree	Clinical Researcher
Miguel Batista Lyon de Castro	University Degree	MSc Student (Left June)
Nikita Khmelinskii	MD/Master Degree	Clinical Researcher

Pedro Manuel Ávila Ribeiro	MD/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
Susana Paula Leonardo Dias Abreu Capela	MD/University Degree	Clinical Researcher
Vasco Madeira Crispim Romão	MD/PhD	Postdoctoral Researcher

### Lab Interests

The Rheumatology Research Unit (RRU) results from a partnership between the Instituto de Medicina Molecular João Lobo Antunes/Faculdade de Medicina da Universidade de Lisboa and the Rheumatology Department of the Santa Maria Hospital, Centro Hospitalar Universitário Lisboa Norte in the context of the Lisbon Academic Medical Centre. Basic scientists and clinicians closely work together to promote translational research and clinical excellence in the field of Rheumatology. Our research objective is the study of rheumatic diseases (such as Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Spondyloarthritis (SpA), Diffuse Connective Tissue Diseases and Vasculitis) in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies.

### Research Fields

- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

### Major Scientific Achievements in 2023

1. Demonstration that later initiation of biologics in juvenile idiopathic arthritis is associated with a greater physical disability, worse quality of life, and lower chance of drug-free remission in adulthood.
2. Demonstration of an activation profile of B and Th17-like Tfh cells in the pathogenesis of extended oligoarticular and polyarticular juvenile idiopathic arthritis, but not of persistent oligoarticular juvenile idiopathic arthritis.
3. The development and validation of the new module for myositis patients in Reuma.pt.
4. Demonstration that anti-SRP antibodies are predictors of cardiac involvement in myositis patients.
5. Demonstration that higher adherence to mediterranean diet is associated with lower disease activity, lower impact of disease, and lower functional disability in rheumatoid arthritis patients.

6. The development and validation of Uveitis.pt.

7. A positive Doppler signal on shoulder tendons can be a marker for a better prognosis in shoulder pain.

### **Ongoing Projects**

2023/2029: Stratification of Rheumatoid Arthritis: CompuTational models to personalise mAnagement strategies for difficult-to-Treat disease. Coordinator: João Eurico da Fonseca. Funding Agency: European Commission. Reference: HORIZON-HLTH 101080243 STRATA-FIT. Amount: 907 186,25€. Total Amount: 6 346 985,00€.

2023/2026: Systemic Endotoxemia as the driver of chronic inflammation: Biomarkers and novel therapeutic targets for Arthritis. Coordinator: Patrícia Costa Reis. Funding Agency: European Commission. Reference: ENDOTARGET. Amount: 490 039,00€. Total Amount: 6 997 820,00€.

2023/2024: Unraveling the molecular events of immune dysregulation leading to lymphoma associated with Sjögren's syndrome. Coordinator: Vasco Romão. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.05498.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2023/2023: Develop and adapt the current PT vasculitis registry to the registry of patients with AAV. Coordinator: João Eurico da Fonseca. Funding Agency: Vifor Pharma Portugal SA. Reference: GRANT CSL VIFOR. Amount: 100 000,00€. Total Amount: 100 000,00€.

2022/2026: DNA methylation markers to predict treatment success of biologicals in Crohn's disease. Coordinator: Vasco Romão. Funding Agency: European Commission. Reference: METHYLOMIC. Amount: 456 250,00€. Total Amount: 10 368 972,00€.

2022/2025: Exploring the link between diet, microbiome, gut permeability, metabolomics and disease activity in systemic lupus erythematosus. Coordinator: Patrícia Costa Reis. Funding Agency: Fundação Amélia da Silva de Mello. Reference: BOLSA D. MANUEL DE MELLO. Amount: 50 000,00€. Total Amount: 50 000,00€.

2022/2023: X-Chromosome Inactivation in Systemic Lupus Erythematosus. Coordinator: Patrícia Costa Reis. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/MED-OUT/1517/2021. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2023: EARLY\_JAKi: JAK-STAT signaling pathway as key to chronic arthritis onset. Coordinator: João Eurico da Fonseca. Funding Agency: AbbVie Inc. Reference: IIS EARLY JAKi – ABBVIE. Amount: 139 422,05€. Total Amount: 139 422,05€.

2019/2024: 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€.

2019/2023: Prémio L'oreal Women in Science. Coordinator: Patrícia Costa Reis. Funding Agency: L'oreal Paris. Reference: PCR - PRÉMIO L'OREAL: WOMEN IN SCIENCE. Amount: 14 600,00€. Total Amount: 14 600,00€.

## Scientific Impact

### Academic Collaborations

- Cristiana Barbosa, Hospital de Santa Maria, Portugal.
- Marta Arese, Hospital de Santa Maria, Portugal.
- Manuel Ramos-Casals, Department of Medicine, Universitat de Barcelona, and Department of Autoimmune Diseases, ICMiD, Hospital Clínic, Barcelona, Spain.
- Martin Stradner, Division of Rheumatology and Immunology, Medical University Graz, Graz, Austria.
- Divi Cornec, Rheumatology, Brest University Hospital, France.
- Raphaelle Seror, Rheumatology Department, Université Paris-Saclay, Institut National de la Santé et de la Recherche Médicale (INSERM) U1184, Hôpital Bicêtre, Assistance Publique–Hôpitaux de Paris (APHP), Paris, France.
- Gaetane Nocturne, Rheumatology Department, Université Paris-Saclay, Institut National de la Santé et de la Recherche Médicale (INSERM) U1184, Hôpital Bicêtre, Assistance Publique–Hôpitaux de Paris (APHP), Paris, France.
- Xavier Mariette, Rheumatology Department, Université Paris-Saclay, Institut National de la Santé et de la Recherche Médicale (INSERM) U1184, Hôpital Bicêtre, Assistance Publique–Hôpitaux de Paris (APHP), Paris, France.
- Samuel Bitoun, Rheumatology Department, Université Paris-Saclay, Institut National de la Santé et de la Recherche Médicale (INSERM) U1184, Hôpital Bicêtre, Assistance Publique–Hôpitaux de Paris (APHP), Paris, France.

## Selected Publications

Vieira-Sousa E, Alves P, Rodrigues AM, Teixeira F, Tavares-Costa J, Bernardo A, Pimenta S, Pimentel-Santos FM, Gomes JL, Aguiar R, Pinto P, Videira T, Catita C, Santos H, Borges J, Sequeira G, Ribeiro C, Teixeira L, Ávila-Ribeiro P, Martins FM, Canhão H, McInnes IB, Ribeiro RM, Fonseca JE (2020). [GO-DACT: a phase 3b randomised, double-blind, placebo-controlled trial of Golimumab plus methotrexate \(MTX\) versus placebo plus MTX in improving DACTylitis in MTX-naive patients with psoriatic arthritis](#). *Ann Rheum Dis*. Apr;79(4):490-498.

**Relevance of the publication:** This paper was the first randomized, double blind, multicentric clinical trial led by IMM. The end result clarified the role of anti TNF treatment (and specifically golimumab) as an effective and safe treatment of dactylitis, a major incapacitating manifestation of psoriatic arthritis.

Romão VC, Polido-Pereira J, Barros R, Luís R, Vidal B, Vieira-Sousa E, Vitorino E, Humby F, Kelly S, Pitzalis C, Saraiva F, Fonseca JE (2020). [Efficacy, Safety, and Sample Quality of Ultrasound-Guided Synovial Needle Biopsy in Clinical Practice and Research: A Prospective Observational Study](#). *Arthritis Care Res (Hoboken)*. 72(10):1497-1505.

**Relevance of the publication:** This paper was led by IMM, in the context of a collaboration with Pitzalis C in London that set the ultrasound guided synovial biopsy as a clinical standard procedure, both reliable for diagnostic and research purposes and safe.

Oliveira-Ramos F, Eusébio M, M Martins F, Mourão AF, Furtado C, Campanilho-Marques R, Cordeiro I, Ferreira J, Cerqueira M, Figueira R, Brito I, Canhão H, Santos MJ, Melo-Gomes JA, Fonseca JE (2016). [Juvenile idiopathic arthritis in adulthood: fulfilment of classification criteria for adult rheumatic diseases, long-term outcomes and predictors of inactive disease, functional status and damage](#). *RMD Open* 2(2):e000304.

**Relevance of the publication:** This paper was led by IMM, in the context of a national wide collaboration, being an example of the inbuilt resource Reuma.pt (developed at IMM on behalf of the Portuguese Society of Rheumatology). This was one of 2 pivotal papers (the second published in 2021 and listed in the current year publications) that helped to differentiate polyarticular and extended oligoarticular juvenile idiopathic arthritis (JIA) from persistent JIA and aligned with the pattern of rheumatoid arthritis.

Moura RA, Cascão R, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2011). [Cytokine pattern in early Rheumatoid arthritis favors B cell activation and survival](#). *Rheumatology* 50(2), 278-82.

**Relevance of the publication:** This paper was fully developed at IMM in close collaboration with Graça L lab. This was one of 2 pivotal papers for understanding the contribution of B cells for the development of very early Rheumatoid Arthritis. Later on, these results helped to better understand the phenotype of polyarticular and extended oligoarticular juvenile idiopathic arthritis as being aligned with that of rheumatoid arthritis.

Moura RA, Weinmann P, Pereira PA, Caetano-Lopes J, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Graça L, Fonseca JE (2010). [Alterations on peripheral blood B-cell subpopulations in very early arthritis patients](#). *Rheumatology (Oxford)* 49(6):1082-92.

**Relevance of the publication:** This paper was fully developed at IMM in close collaboration with Graça L lab. This was one of 2 pivotal papers for understanding the contribution of B cells for the development of very early Rheumatoid Arthritis. Later on these results helped to better understand the phenotype of polyarticular and extended oligoarticular juvenile idiopathic arthritis as being aligned with that of rheumatoid arthritis.

### 2023 Publications in Peer-Reviewed Journals

Tomé C, Oliveira-Ramos F, Campanilho-Marques R, Mourão AF, Sousa S, Marques C, Melo AT, Teixeira RL, Martins AP, Moeda S, Costa-Reis P, Torres RP, Bandeira M, Fonseca H, Gonçalves M, Santos MJ, Graça L, Fonseca JE, Moura RA (2023). Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. *RMD Open* 9(3):e002901. doi: 10.1136/rmdopen-2022-002901.

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Inês Leal, Vanda Nogueira, Diogo Bernardo Matos, Joana Araújo, Olga Berens, Margarida Ribeiro, Maria João Furtado, Marco Liverani, Marta Inês Silva, Marta Guedes, Miguel Cordeiro, Miguel Ribeiro, Patrícia José, Rafael Barão, Rui Nunes Ferreira, Sofia Fonseca, Sofia Mano, Susana Pina, Maria José Santos, João Eurico Fonseca, Cristina Fonseca & Luís Figueira (2023). Design and Development of a Web-Based Prospective Nationwide Registry for Ocular Inflammatory Diseases: UVEITE.PT – The Portuguese Ocular Inflammation Registry, *Ocular Immunology and Inflammation*, DOI: 10.1080/09273948.2023.2171891.

Louise Linde, Lykke M Ørnbjerg, Stylianos Georgiadis, Simon H. Rasmussen, Ulf Lindström, Johan Askling, Brigitte Michelsen, Daniela Di Giuseppe, Johan K Wallman, Bjorn Gudbjornsson, Thorvardur Jon Love, Dan C Nordström, Timo Yli-Kerttula, Lucie Nekvindová, Jiří Vencovský, Florenzo Iannone, Alberto Cauli, Anne Gitte Loft, Bente Glintborg, Karin Laas, Ziga Rotar, Matija Tomšič, Gary J Macfarlane, Burkhard Möller, Marleen van de Sande, Catalin Codreanu, Michael J Nissen, Merih Birlik, Sukran Erten, Maria J Santos, Elsa Vieira-Sousa, Merete L Hetland, Mikkel



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#### **Pre-Prints**

Reuma.pt/myositis – the Portuguese registry of inflammatory myopathies Journal: ARP Rheumatology Authors: Eduardo Dourado, Ana Teresa Melo, Patrícia Martins, Matilde Bandeira, Vanessa Fraga, José Luís Ferraro, André Saraiva, Marlene Sousa, Hugo Parente, Catarina Soares, Ana Margarida Correia, Diogo Esperança Almeida, Sara Paiva Dinis, Ana Sofia Pinto, Filipe Pinheiro, Maria Rato, Tiago Beirão, Beatriz Samões, Bernardo Santos, Ana Carolina Pereira, Ana Chícharo, Margarida Faria, Agna Neto, Helena Lourenço, Luísa Brites, Marília Rodrigues, Joana Dinis, João Madruga Dias, Filipe Araújo, Nádia Martins, Maura Couto, Ana Valido, Maria José Santos, Sofia Barreira, João Eurico Fonseca, Raquel Marques.

Beyond sicca: high prevalence and predictors of prevalent and incident systemic involvement in patients with Sjögren’s disease Journal: Submitted to Rheumatology Advances in Practice Authors: Matilde Bandeira, Manuel Silvério-António, Nikita Khmelinskii, João E. Fonseca, Vasco C. Romão.

Acute glomerular diseases: A retrospective cohort. Telma Pais; Renato Gonçalves; Marta Pereira; Iolanda Godinho; Paulo Fernandes; Estela Nogueira; Sofia Jorge; José António Lopes; Joana Gameiro.

Martins-Martinho J, Pintado Maury I, Leal I, Ponte C. Varicella zoster virus mimicking Giant Cell Arteritis: The importance of ultrasound in the differential diagnosis. *ARP Rheumatology* 2023 (submitted on the 14 October 2023).

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A challenging case of pulmonary arterial hypertension: never judge from appearances. *Journal: aguarda publicação na revista International Journal of Cardiovascular Sciences* Authors: Silvério António P, Silvério-António M, Lopes R, Guimarães T, Sa Pereira Y, Pinto F, Plácido R.

De Miguel E, Karalilova R, Macchioni P, et al. Subclinical giant cell arteritis increases the risk of relapse in polymyalgia rheumatica. *Annals of the Rheumatic Diseases* 2024;83:335-341.

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Miguel PJ, Moiteiro da Cruz R, Costa-Reis P, Sandes AR, Esteves da Silva J. Paracetamol Induced Acute Interstitial Nephritis: A Pediatric Case Report. *Acta Med Port.* 2024 Jan 3;37(1):67-69. doi: 10.20344/amp.20563. Epub 2024 Jan 3. PMID: 38183231.

Pedro J. Miguel, Patrícia Costa-Reis, Inês Leal, João Boavida, José Esteves da Silva. Severe tubulointerstitial nephritis and uveitis: a pediatric case report Portuguese. *Kidney Journal* 2024 Jan.

Ana Barbosa Rodrigues, Ana Raquel Claro, Pedro J. Miguel, Ana Sofia Vilardouro, Sara Costa, Ana Zagalo, Filipa Durão, Patrícia Costa-Reis, Ana Rita Sandes, José Esteves da Silva. Therapeutic adherence in kidney transplanted adolescents. *Portuguese Kidney Journal* 2024 Jan.

### **Invited Lectures and Seminars**

Rita Machado, Casos Clínicos em Reumatologia. VI – Curso de Internos de 2º ano (Reumatologia), Portugal, January 1, 2023.

Patrícia Costa-Reis, The role of ASCT and CAR-T cells in jSSc: the pediatric nephrology perspective. Juvenile Systemic Sclerosis Hamburg meeting, Germany, January 1, 2023.

Patrícia Costa-Reis, Hipofosfatasia ligada ao X: uma nova perspectiva quanto ao diagnóstico e à terapêutica. Reunião do Serviço de Nefrologia e Transplantação Renal do Hospital de Santa Maria, Portugal, January 1, 2023.

Patrícia Costa-Reis, How to do Medical Research. Jornadas de Educação Médica In2Me da Faculdade de Ciências da Saúde, Online, January 13, 2023.

Vasco C. Romão, História Clínica em Reumatologia. VII Curso de Internos do 2º Ano. Sociedade Portuguesa de Reumatologia, Portugal, January 27, 2023.

Inês Leal, Será Herpes? Webinar da Sociedade Portuguesa de Oftalmologia, tema “Uveítes Herpéticas”, Online, February 1, 2023.

Matilde Bandeira, Esclerose sistémica com envolvimento muscular – Caso clínico. Fórum Art & Treat 2023 - Curso de Atualização Multidisciplinar em Esclerose Sistémica, Portugal, February 1, 2023.

Raquel Marques, Tratamento Miopatias Inflamatórias. Fórum Art & Treat 2023 - Curso de Atualização Multidisciplinar em Esclerose Sistémica, Portugal, February 1,

Sofia Barreira, Doenças difusas do tecido conjuntivo. Curso de preparação para a prova nacional de seriação, Portugal, February 7, 2023.

Sofia Barreira, Casos Clínicos em Reumatologia. Curso de preparação para a prova nacional de seriação, Portugal, February 7, 2023.

Elsa Vieira-Sousa, “New perspectives on tumor necrosis factor inhibition for the treatment of psoriatic arthritis” in Bridging the gap - Comprehensive Clinical case presentation. Towards a Creative and Critical Mind Course of the LisbonBioMed PhD Program, Lisbon, Portugal, February 16, 2023.

Inês Leal, Sessão “Parece, mas não é”. 7ª Reunião Científica Internacional do Grupo de Estudos da Retina de Portugal, Portugal, February 24, 2023.

Inês Leal, The role of IL-6 & preclinical evidence of IL-6 targeting in uveitis macular edema. MEERKAT & SANDCAT (GR44277 & GR44278) Studies Investigator Meeting, Berlin, Germany, March 2, 2023.

Filipa O. Ramos, JIA after transition. JIR Academy Winter School, Chateaux D’Oex, Switzerland, March 4, 2023.

Nikita Khmelinskij, ANCA-vasculitis and interstitial lung involvement. XXX Congresso de Pneumologia do Norte e XXXVI Jornadas Galaico Durienses, Portugal, March 9, 2023.

Inês Leal, Uveitis: a tale of two challenging cases from CAML. Sessão Clínica do CAML, Portugal, March 9, 2023.

Elsa Vieira-Sousa, Principles of image techniques to Diagnose and Monitoring PsA. Clinical Cases simulator. PsA Diagnostic and Monitoring Image Online Course 2nd Master Class, Online, March 9, 2023.

Vasco C. Romão, Exploring RINVOQ. Dados de vida real e novas janelas de oportunidade na prática clínica. Reunião Abbvie, Portugal, March 15, 2023.

Joaquim Polido-Pereira, AR e doença intersticial pulmonar. Curso de Internos de Reumatologia, organizado pela Lilly, Portugal, March 16, 2023.

Nikita Khmelinskii, Workshop interativo – casos desafiantes. Escola de Pneumologia: Imagiologia em Interstício Pulmonar, Portugal, March 17, 2023.

Filipa O. Ramos, Tratamento das AIJ. Webinar WORD Day 2023, Online, March 18, 2023.

João Eurico Fonseca, Chasing the treatment of Arthritis. VIII Semana da Bioengenharia do IST, Portugal, March 20, 2023.

Cristina Ponte, AAV - Diagnosis vs classification and assessment of disease activity and damage. Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Cristina Ponte, Discussion of Vasculitis Clinical Cases. Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Cristina Ponte, Cryoglobulinemia - from diagnosis to treatment. Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Estela Nogueira, V with severe renal involvement - how to define the best treatment now and new insights for the future? Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Rita Machado, ANCA-associated vasculitis and steroids sparing approach - where are we now? Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Inês Leal, Cataract surgery in JIA-uveitis: leaving the child aphakic. The 14th Annual Congress of Controversies in Ophthalmology (COPHY), Portugal, March 24, 2023.

Inês Leal, Vogt Koyanagi Harada: Immunomodulatory treatment should be started at the first manifestation of VKH alongside with systemic corticosteroids. 14th Annual Congress of Controversies in Ophthalmology (COPHY), Portugal, March 24, 2023.

Ângelo Calado, Extracellular matrix in Rheumatoid Arthritis. GEMSTONE (Genomics of musculoskeletal traits translational network) COST Action WG4 Training School “Gene regulation of the bone extracellular matrix”, Portugal, March 24, 2023.

Sofia Barreira, Basic skills in MSK examination. AIMS Meeting, Portugal, April 13, 2023.

Vasco C. Romão, Sjögren’s essentials. ERN ReCONNET Webinar, Online, April 19, 2023.

João Eurico Fonseca, Biobanks and Registries: why we need them and what are we doing. 1st Reconnect Congress, Belgium, April 21, 2023.

João Eurico Fonseca, Registry and eHealth Working Group ERN ReCONNET. 1st Reconnect Congress, Belgium, April 23, 2023.

Elsa Vieira-Sousa, Diffuse idiopathic skeletal hyperostosis nad calcium pyrophosphate dihydrate crystal deposition disease (Differential Diagnosis). Sessão Clínica do Serviço de Neuroradiologia, Portugal, May 10, 2023.

Patrícia Costa-Reis, Lupus nephritis. VII Congresso Hispano-Português de Nefrologia Pediátrica e XLVI Congreso Español de Nefrologia Pediátrica, Portugal, May 18, 2023.

Inês Leal, O lado negro da investigação clínica: os problemas que não vêm nos livros e que temos de resolver. Quartas da SPO, Grupo Português de Investigação, Portugal, May 31, 2023.

Cristina Ponte, Imaging in the diagnosis and monitoring of LVV: Secondary LVV in rheumatoid arthritis and other rheumatic diseases. European Large Vessel Vasculitis Imaging Course (EULVIC) 2023, Austria, June 15, 2023.

João Eurico Fonseca, FMUL sustentável. XVIII Fórum de Auditoria Interna, Portugal, June 22, 2023.

Inês Leal, Navigating the Labyrinth of Serpiginous –like Choroiditis. Sessão Clínica do Hospital da Luz, Portugal, July 12, 2023.

João Eurico Fonseca, Rheumatology at Lisbon as a case study for the development of academic medical departments. Sino Luso International Medical Forum, China, July 16, 2023.

Raquel Marques, Tratamento Dermatomiosite Juvenil. Tratamento Dermatomiosite Juvenil, Portugal, September 1, 2023.

Inês Leal, Uveite.pt. International Ocular Inflammation Society, Germany, September 6, 2023.

Cristina Ponte, ANCA associated vasculitis and lungs: clinical aspects and screening. Lung involvement and Rheumatic disorders: from bench to bedside, from antigens to disease, Italy, September 7, 2023.

João Eurico Fonseca, Rheumatoid arthritis and lung: Issues on therapy. Lung involvement and Rheumatic disorders: from bench to bedside, from antigens to disease, Italy, September 8, 2023.

João Eurico Fonseca, Rheumatology Research at the Lisbon Academic Medical Center: A case study for how iMM can foster translational and clinical research and promote clinical excellence. iMM Scientific Retreat, Portugal, September 18, 2023.

João Eurico Fonseca, Rheumatology Research at the Lisbon Academic Medical Center. A case study for how iMM can foster translational and clinical research and promote clinical excellence. Medicina Genómica e de Precisão em Portugal: Horizontes e Desafios, Portugal, September 21, 2023.

Filipa O. Ramos, AIJ sistémica e Síndrome de Ativação Macrofágica. Curso Reumatologia Pediátrica para Internos, Portugal, September 21, 2023.

Cristina Ponte, Practical Considerations in the Management of Large Vessel Vasculitis. Open Rheum 2023, Spain, September 22, 2023.

Joaquim Polido-Pereira, Ultrasound-guided synovial biopsy procedures: large joints. 4th EULAR Course on Synovial Biopsy, Spain, September 22, 2023.

Cristina Ponte, Giant Cell Arteritis: Case Discussions. 5th EUVAS Vasculitis Course, Switzerland, September 28, 2023.



Patrícia Costa-Reis, Meet the expert: Lupus Nephritis. European Society of Pediatric Nephrology 55th Annual Meeting, Lithuania, September 28, 2023.

Patrícia Costa-Reis, Performing Clinical Research. European Society of Pediatric Nephrology 55th Annual Meeting, Lithuania, September 28, 2023.

Cristina Ponte, Imaging in giant cell arteritis - Ultrasound 5th EUVAS Vasculitis Course, Switzerland, September 29, 2023.

Inês Leal, Should we leave uveitis children with cataract aphakic? Emirates Uveitis and Retina Update (EUVRE) & Annual Meeting of the Uveitis Society (India), United Arab Emirates, September 29, 2023.

Raquel Marques, Diagnóstico em Idade Pediátrica mesmo que em idade adulta? XXV Congresso Português de Reumatologia, Portugal, October 1, 2023.

Manuel Silvério-António, Fraturas Osteoporóticas - que doentes referenciar? XXV Congresso Português de Reumatologia, Portugal, October 1, 2023.

Vasco C. Romão, Inovação na prevenção contra o Herpes Zoster. Reunião do Serviço de Reumatologia do Centro Hospitalar Universitário de Coimbra, Portugal, October 3, 2023.

Joaquim Polido-Pereira, Infiltrazione eco-guidate e blocchi nervosi arto inferiore (Ultrasound guided injection – lower limbs). Corso Teorico-Pratico di Ecografia in Reumatologia, Italy, October 5, 2023.

Fernando Saraiva, Ultrasound-guided synovial biopsy – state of the art. Corso Teorico-Pratico di Ecografia in Reumatologia, Italy, October 5, 2023.

João Eurico Fonseca, Rheumatoid arthritis: Back to basics. 1º Curso Monotemático de Artrite Reumatóide, SPR, Online, October 11, 2023.

Vasco C. Romão, What is new in Sjögren's Disease. 1st Annual Conference of Sjögren Patients, Greece, October 13, 2023.

Patrícia Costa-Reis e Inês Almada-Correia, Tudo começa no Intestino: Resultados do estudo Gut-Lupus. Sessão do Núcleo de Investigação do Departamento de Pediatria, Portugal, October 19, 2023.

Joaquim Polido Pereira, Perspetivas da Terapêutica Biológica nas Doenças Auto-imunes. Simpósio Científico da Ordem dos Farmacêuticos, Portugal, October 21, 2023.

João Eurico Fonseca, The story of JAK inhibitors in the past 10 years. XXV Congresso Português de Reumatologia, Portugal, October 23, 2023.

João Eurico Fonseca, Overview on Baricitinib relevant data: persistence on treatment. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Elsa Vieira-Sousa, Será que já conseguimos prevenir o aparecimento das doenças reumáticas inflamatórias crónicas? A artrite psoriática ao tratar mais efectivamente a psoríase ou nas fases pré-clínicas. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Elsa Vieira-Sousa, Momentos marcantes da ARP nos últimos 50 anos. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Cristina Ponte, Avacopan: Impact on the treatment of ANCA-associated vasculites. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Cristina Ponte, Algoritmo terapêutico atual na polimialgia reumática e na arterite de células gigantes. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Nikita Khmelinskii, Linfoma na síndrome de Sjögren – predição, monitorização e tratamento. XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Maria José Santos, Lúpus Eritematoso Sistémico juvenil: atualizações na classificação e tratamento. 23º Congresso Nacional de Pediatria, Portugal, October 25, 2023.

Vasco C. Romão, The impact of sicca syndrome: the role of pilocarpine. Curso Pré-Congresso "Atualização na Doença de Sjögren", XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Patrícia Costa-Reis, Intervention studies to address the gut-joint axis: WP4 results. ENDOTARGET meeting, Santiago de Compostela, Spain, October 25, 2023.

Inês Leal, Parece, mas não é! Sessão conjunta GER-GPRV, Grupo Português de Retina e Vítreo, Portugal, October 27, 2023.

Vasco C. Romão, Treatment of systemic manifestations of Sjögren's Disease in 2023. Curso Pré-Congresso "Atualização na Doença de Sjögren", XXV Congresso Português de Reumatologia, Portugal, October 28, 2023.

Vasco C. Romão, Can we prevent rheumatoid arthritis onset by treating pre-RA? XXV Congresso Português de Reumatologia, Portugal, October 28, 2023.

Fernando Saraiva, O papel da ecografia das glândulas salivares no diagnóstico da síndrome de Sjogren. XXXI Jornadas Internacionais do IPR, Portugal, November 1, 2023.

Estela Nogueira, Portuguese Vasculitis Registry. XXXVII Congresso Português de Nefrologia, o XV Congresso Luso-Brasileiro de Nefrologia, Portugal, November 1, 2023.

Rita Machado e Susana Capela, When hydroxychloroquine is not enough to prevent the recurrence of fetal atrio-ventricular block in a woman with anti-Ro/SSA antibodies. Webinar of the EULAR Study Group on Reproductive Health and Family Planning, Online, November 7, 2023.

Inês Leal, Desafios éticos nos primeiros anos do internato. 10ª Edição do Beyond MEd, Portugal, November 9, 2023.

Inês Leal, Ocular TB caused by TNFi? A mirage. 39º Congresso da Sociedade Portuguesa de Pneumologia, 4º Congresso Luso-PALOP de Pneumologia, 9th Union Europe Conference on Lung Health, Portugal, November 10, 2023.

João Eurico Fonseca, Médico académico e investigador. O futuro das carreiras médicas, Online, November 11, 2023.

Filipa O. Ramos, Transition in Portugal. SERPE 2023, Barcelona, Spain, November 13, 2023.

Rita A. Moura, Insights about the role of B cells and follicular T cells in Juvenile Idiopathic Arthritis. IMM Internal Seminar, Portugal, November 15, 2023.

Nikita Khmelinskii, A janela de oportunidade na Nefrite Lúpica – quando atuar para melhorar os outcomes renais? Almoço-Simpósio GSK, Encontro renal 2023, Portugal, November 16, 2023.

Cristina Ponte, Registo Português de Vasculites. Encontro renal 2023, Portugal, November 16, 2023.

João Eurico Fonseca, 75 anos no tratamento das doenças reumáticas – uma perspetiva histórica. Jornadas Internacionais do IPR, Portugal, November 23, 2023.

João Eurico Fonseca, How much we know about Pre-Clinical Rheumatoid Arthritis? International Conference of Chinese Rheumatologists (ICCR), China, November 26, 2023.

João Eurico Fonseca, Repurposing drugs: a 5,000-year story –Musculoskeletal diseases as a case study. Sino Luso International Medical Forum, China, November 26, 2023.

Vasco C. Romão, Baricitinib in a glance: EULAR & ACR 2023 update. Reunião do Serviço de Reumatologia do Centro Hospitalar Universitário de Coimbra, Portugal, November 28, 2023.

João Eurico Fonseca, The WG on Registries and eHealth tools. Training on “TogethERN ReCONNET Registry”, Online, November 29, 2023.

Sofia Barreira, Raquialgias. Rheumatology Insights, Portugal, December 12, 2023.

Sofia Barreira, Artrite Reumatóide e Espondilartrites. Rheumatology Insights, Portugal, December 12, 2023.

Cristina Ponte, What the Rheumatologist needs to know about the kidney. Consult the Expert - CSL Vifor Medical Activities EULAR Annual Congress 2023, Italy.

## **Communications**

### Communications in International Conferences:

Rui L. Teixeira, Peripheral blood leukocytes from early arthritis patients have an altered JAK-STAT signaling pathway activation profile. 42nd European Workshop for Rheumatology Research (EWRR), Ireland, February 9, 2023. (Poster Presentation)

Catarina Tomé, Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. 42nd European Workshop for Rheumatology Research (EWRR), Ireland, February 9, 2023. (Poster Presentation)

Catarina Tomé, Untreated early rheumatoid arthritis patients have an abnormal distribution B and follicular T helper cell subsets in peripheral blood. 42nd European Workshop for Rheumatology Research (EWRR), Ireland, February 9, 2023. (Poster Presentation)

Matilde Bandeira, Long-term outcomes of COVID-19 vaccination in patients with rare and complex connective tissue diseases: an ad-interim analysis of ERN-ReCONNET VACCINATE study. ERN ReCONNET Congress, Belgium, April 1, 2023.

Margarida Rocha, Testimonies from the ERN Exchange Programme. European Reference Network Plenary Meeting 2023, Belgium, April 22, 2023. (Poster Presentation)

Inês Almada-Correia, Gut permeability in lupus nephritis: results from the GUT-LUPUS study. VII Congresso Hispano-Português de Nefrologia Pediátrica 2023 and XLVI Congreso Español de Nefrologia Pediátrica 2023, Portugal, May 18, 2023. (Oral Presentation)

Inês Almada-Correia, Unraveling the mysteries of the connection between gut and the chronic activation of the immune system in Systemic Lupus Erythematosus. EULAR 2023 – Annual European Congress of Rheumatology, Italy, May 31, 2023. (Oral Presentation)

Catarina Tomé, Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. EULAR 2023 – Annual European Congress of Rheumatology, Italy, June 3, 2023. (Oral Presentation)

Estela Nogueira, Glomerulopathies during pregnancy: a ten-year single center experience. 60th ERA Congress, Italy, June 15, 2023. (Oral Presentation)

Estela Nogueira, Challenging management of nephrotic syndrome in pregnant diabetic women: maternal and fetal outcomes at a tertiary center. 60th ERA Congress, Italy, June 15, 2023. (Oral Presentation)

Estela Nogueira, Management of tubulointerstitial disease in pregnancy: ten-years experience of a nephron-obstetric clinic. 60th ERA Congress, Italy, June 15, 2023. (Oral Presentation)

Estela Nogueira, Pregnancy-related acute kidney injury: 10-years series of a nephro-obstetric clinic. 60th ERA Congress, Italy, June 15, 2023. (Oral Presentation)

Filipa Ramos, Clinical characteristics of a Portuguese cohort with Undefined Autoinflammatory diseases. 29th Paediatric Rheumatology European Society (PReS) Congress, Netherlands, September 27, 2023. (Poster Presentation)

Filipa Ramos, SAPHO SYNDROME: ARE THERE DIFFERENCES BETWEEN ADULTS AND CHILDREN? 29th Paediatric Rheumatology European Society (PREs) Congress, Netherlands, September 27, 2023. (Poster Presentation)

Filipa Ramos, Musculoskeletal manifestations of SARS-CoV-2 in a pediatric population – a Portuguese multicentric study. 29th Paediatric Rheumatology European Society (PREs) Congress, Netherlands, September 27, 2023. (Poster Presentation)

Catarina Tomé, Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. 29th Paediatric Rheumatology European Society (PREs) Congress, Netherlands, September 28, 2023. (Poster Presentation)

Inês Almada-Correia, Study of the Gut Microbiota and Permeability in Lupus Nephritis. ESPN 55th annual meeting, Lithuania, September 28, 2023. (Oral Presentation)

Adriana A. Vieira, X-Chromosome Inactivation in Systemic Lupus Erythematosus. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Margarida Rocha, Prevalence and Clinical Characteristics of Late Onset Axial Spondyloarthritis: Results from a Multicentre Nationwide Study. ACR Convergence 2023, USA, November 14, 2023. (Poster Presentation)

Communications in National Conferences:

Inês Almada-Correia, Microbiota, permeabilidade intestinal e endotoxémia no lúpus eritematoso sistémico. XXVIII Jornadas de Pediatria do Hospital de Santa Maria, Portugal, February 22, 2023. (Oral Presentation)

Rui L. Teixeira, Peripheral blood leukocytes from early arthritis patients have an altered JAK-STAT signaling pathway activation profile. XLVIII Annual Meeting of the Portuguese Society for Immunology (SPI), Portugal, March 29, 2023. (Poster Presentation)

Catarina Tomé, Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. XLVIII Annual Meeting of the Portuguese Society for Immunology (SPI), Portugal, March 29, 2023. (Poster Presentation)

Catarina Tomé, Untreated early rheumatoid arthritis patients have an abnormal distribution B and follicular T helper cell subsets in peripheral blood. XLVIII Annual Meeting of the Portuguese Society for Immunology (SPI), Portugal, March 29, 2023. (Poster Presentation)

Inês Almada-Correia, Com os olhos no intestino: Microbiota, Permeabilidade Intestinal e Dieta no Lúpus. XXV Congresso da Associação Portuguesa de Nutrição Entérica e Parentérica, Portugal, April 15, 2023. (Oral Presentation)

Margarida Rocha, Caso Clínico 5: Lupus Eritematoso Sistémico. IX edição das Jornadas de Reumatologia e Medicina Familiar do Algarve, Portugal, April 28, 2023. (Oral Presentation)

Margarida Rocha, Caso Clínico 6: Polimialgia Reumáticas. IX edição das Jornadas de Reumatologia e Medicina Familiar do Algarve, Portugal, April 28, 2023. (Oral Presentation)

Margarida Rocha, Impacto da Obesidade nas Doenças Reumáticas. IX edição das Jornadas de Reumatologia e Medicina Familiar do Algarve, Portugal, April 28, 2023. (Oral Presentation)

Manuel Silvério-António, Effectiveness evaluation of the Fracture Liaison Service - description of a single centre experience. XXV Congresso Português de Reumatologia, Portugal, October 1, 2023. (Poster Presentation)

Manuel Silvério-António, Anti-citrullinated protein antibodies in Sjögren's syndrome define a subset of patients with lower B cell activation markers and higher risk of lung involvement. XXV Congresso Português de Reumatologia, Portugal, October 1, 2023. (Poster Presentation)

Manuel Silvério-António, Leflunomide is a Safe and Effective Drug in Patients with Sjögren's Syndrome with Active Systemic Disease. XXV Congresso Português de Reumatologia, Portugal, October 1, 2023. (Poster Presentation)

Margarida Rocha, Manifestations and predictors of neurologic involvement in Behçet's disease: results from a monocentric study. XXV Congresso Português de Reumatologia 2023, Portugal, October 23, 2023. (Poster Presentation)

Rui L. Teixeira, Is JAK-STAT key to disease progression in early arthritis? XXV Congresso Português de Reumatologia 2023, Portugal, October 23, 2023. (Poster Presentation)

Catarina Tomé, Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. XXV Congresso Português de Reumatologia 2023, Portugal, October 25, 2023. (Poster Presentation)

Joaquim Polido-Pereira, Casos reais – AR e AIJ. XXV Congresso Português de Reumatologia 2023, Portugal, October 25, 2023. (Oral Presentation)

Joaquim Polido-Pereira, Na remissão clínica, a ecografia resolve as divergências de opinião entre médico e doente? XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Joaquim Polido-Pereira, How can we optimize therapeutic strategies in RA? XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Margarida Rocha, Fenómeno de Raynaud e úlceras digitais - Sessão IV. XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Rita Machado, COVID-19- doença e vacinação: origem e/ou agudização de um reumatismo inflamatório crónico? XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Fernando Saraiva, Efficacy and safety of ultrasound-guided muscle biopsy in the diagnosis of idiopathic inflammatory myopathies. XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Matilde Bandeira, Does age at diagnosis of giant cell arteritis influence the clinical phenotype and outcomes? XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Oral Presentation)

Matilde Bandeira, Clinical characterization of patients with Sjögren's Disease registered in Reuma.pt: PORTRESS — the PORTuguese REgistry of Sjögren's Syndrome. XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Poster Presentation)

Matilde Bandeira, Lymphopenia Fluctuation Patterns Determine the Trajectory of the Disease in Sjogren's Patients with Hematological Involvement. XXV Congresso Português de Reumatologia 2023, Portugal, October 26, 2023. (Poster Presentation)



Inês Leal, Health-Related Quality of Life and Work Productivity in Spondyloarthritis Patients with a History of Acute Anterior Uveitis Undergoing Treatment with Golimumab: 12-Month Results of the GO-VISION Observational Study. Grupo Português de Retina (GPRV)e Vítreo, Portugal, October 27, 2023. (Poster Presentation)

Joaquim Polido-Pereira, Pulmonary rheumatoid nodules in a patient treated with golimumab. XXXI Jornadas Internacionais do Instituto Português de Reumatologia, Portugal, November 22, 2023. (Poster Presentation)

Margarida Rocha, Prevalence and Clinical Characteristics of Late Onset Axial Spondyloarthritis: Results from a Multicentre Nationwide Study. XXXI Jornadas Internacionais do Instituto Português de Reumatologia, Portugal, November 22, 2023. (Oral Presentation)

Margarida Rocha, Beyond the skin: musculoskeletal manifestations of dystrophic epidermolysis bullosa disease. XXXI Jornadas Internacionais do Instituto Português de Reumatologia, Portugal, November 22, 2023. (Oral Presentation)

Joana Inácio, Systemic Lupus Erythematosus: The influence of the X-Chromosome. 27<sup>a</sup> Reunião Anual da Sociedade Portuguesa de Genética Humana, Portugal, November 23, 2023. (Poster Presentation)

Beatriz Graça, X-chromosome inactivation in Systemic Lupus Erythematosus. 26.º WORKSHOP “EDUCAÇÃO PELA CIÊNCIA”, Portugal, December 13, 2023. (Poster Presentation)

Beatriz Graça, X-chromosome inactivation in Systemic Lupus Erythematosus. 26.º WORKSHOP “EDUCAÇÃO PELA CIÊNCIA”, Portugal, December 13, 2023. (Oral Presentation)

### **Organization of Conferences**

Fernando Saraiva, Matilde Bandeira e Raquel Marques, Organizer, Ultrasound-guided muscle biopsy, Serviço de Reumatologia e DOM, Portugal, February 2, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Esperanza Naredo (Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain) - “Musculo-skeletal injections: ultrasound-guided versus conventional”, Portugal, February 3, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Chiara Baldini (Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy) - “Controversial issues in Sjögren’s syndrome”, Portugal, February 28, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Mojca Frank-Bertoncelj (BioMed X GmbH, Heidelberg, Germany) - “The human synovium in inflammatory arthritis: a single cell perspective”, Portugal, March 7, 2023.

Ângelo Calado, Co-Organizer, GEMSTONE (Genomics of musculoskeletal traits translational network) COST Action WG4 Training School, “Gene regulation of the bone extracellular matrix”, Portugal, March 22, 2023.

Inês Leal, Co-Organizer, 14th Annual Congress of Controversies in Ophthalmology (COPHY), Portugal, March 24, 2023.

Fernando Saraiva, Elsa Sousa e João Eurico Fonseca, Co-Organizer, MILES – Mesotherapy in Lateral Epicondylitis Study, Serviço de Reumatologia e DOM, Portugal, April 1, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Benjamin Fisher (Institute of Inflammation and Ageing, University of Birmingham Research Labs, University of Birmingham, UK) - “Clinical trials in Sjögren’s: challenges and opportunities”, Portugal, June 20, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Dirk Föll Department of Pediatric Rheumatology and Immunology, University of Münster, Germany - “Use of Biomarkers to improve therapeutic strategies in pediatric rheumatology”, Portugal, September 12, 2023.

Raquel Marques, Co-Organizer, Young Investigator Meeting do PReS, Netherlands, September 27, 2023.

Raquel Marques, Co-Organizer, Juvenile Dermatomyositis Working Party Meeting, Netherlands, September 29, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: Alexandre Belot, Pediatric Rheumatology Unit, Centre Hospitalier Universitaire de Lyon, France. National Reference Centre for Rare Rheumatic & Autoimmune Diseases in Children (Raise) & Inserm U1111 - “Mendelian Lupus: A new and growing field”, Portugal, October 17, 2023.

Cristina Ponte, Co-Organizer, XXV Congresso Português de Reumatologia, Portugal, October 25, 2023.

Estela Nogueira, Organizer, Congresso Nacional de Nefrologia, Encontro renal 2023, Portugal, November 16, 2023.

João Eurico da Fonseca Lab, Organizer, CAML Rheumatology Series: João Gonçalves (Faculdade de Farmácia, Universidade de Lisboa, Portugal) - “Immune response produced by mRNA COVID-19 vaccine on rheumatic patients”, Portugal.

### **Networks and Research Infrastructures**

Ângelo Calado and João Eurico Fonseca, GEMSTONE (Genomics of musculoskeletal traits translational network) COST Action, GEMSTONE members.

Sofia Barreira and Matilde Bandeira, Reuma.pt, Active members.

Sofia Barreira and Matilde Bandeira, European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET), Active members.

Sofia Barreira, Matilde Bandeira and Cristina Ponte, Grupo de trabalho de estudos de doenças reumáticas sistémicas da Sociedade Portuguesa de Reumatologia (GEDRESIS), Active members.

Sofia Barreira, Escola Portuguesa de Ecografia Musculo-Esquelética, Active member.

Sofia Barreira, Grupo de trabalho de Imagem Musculo-esquelética da Sociedade Portuguesa de Reumatologia (GoTime), Active member.

Sofia Barreira, European Reference Network on Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases, Active member.

Matilde Bandeira, European Reference Network RIT, Active member.

Matilde Bandeira, Grupo de trabalho de estudos da dor (GTDOR), Active member.

Matilde Bandeira, Grupo de trabalho de reumatologia pediátrica (GT Reumatologia Pediátrica), Active member.

Matilde Bandeira, Grupo de trabalho de Estudo das Espondilartrites (GESPA), Active member.

Matilde Bandeira, iMyos – International Myositis Society, Active member.

Cristina Ponte, European Vasculitis Study Group (EUVAS), Active member.

Cristina Ponte, OMERACT Ultrasound Large-Vessel Vasculitis Subtask Force, Active member.

Cristina Ponte, EMEUNET - EMerging EULAR NETWORK group, Active member.

Cristina Ponte, Grupo de trabalho de imagem músculo-esquelética – GoTIME, Active member.

Cristina Ponte, Steering Committee for the EULAR recommendations for the use of imaging in the diagnosis and management of large vessel vasculitis in clinical practice, Active member.

Vasco C. Romão, EULAR Research Study Group on Adherence to Therapy in RMDs, Active member.

Joaquim Pereira, European Synovitis Study Group, Speaker and Trainer of the Synovial Biopsy Courses; Researcher.

Joaquim Pereira, Study Group of Imaging of the Portuguese Society of Rheumatology - GoTIME, Coordinator.

Patrícia Costa-Reis, Sociedade Portuguesa de Nefrologia Pediátrica (SPNP), Vogal da Direção.

### **Prizes and Honours**

Rui L. Teixeira, Honourable Mention Award for Best Poster on the XXV Congresso Português de Reumatologia for the work “Is JAK-STAT key to disease progression in early arthritis? XXV Congresso Português de Reumatologia”.

Inês Almada-Correia, Best Portuguese Oral Communication Award on the VII Congresso Hispano-Português de Nefrologia Pediátrica and XLVI Congreso Español de Nefrologia Pediátrica 2023 for the work “Gut permeability in lupus nephritis: results from the GUT-LUPUS study”.

Catarina Tomé, EULAR Travel Bursary assigned by EULAR – European Alliance of Associations for Rheumatology to participate in EULAR 2023.

Margarida Rocha, "Emptying the threat: remission of giant pulmonary aneurysms in Behçet's syndrome", Honourable mention/prize for the Image Contest on the Congresso Português de Reumatologia 2023, October 2023.

Matilde Bandeira, EULAR scientific training grant for young fellows, received in the context of the fellowship in Birmingham from July to December 2023.

Fernando Saraiva, Prémio Reuméritis 2023 da Sociedade Portuguesa de Reumatologia; XXV Congresso Português de Reumatologia.

Inês Leal, Prémio Melhor Poster da Reunião Grupo Português de Retina e Vitreo for the work “Health-Related Quality of Life and Work Productivity in Spondyloarthritis Patients with a History of Acute Anterior Uveitis Undergoing Treatment with Golimumab: 12-Month Results of the GO-VISION Observational Study”.

Inês Leal. Prémio Melhor poster Retina on the 7ª Reunião Científica Internacional do Grupo de estudo da retina de Portugal for the work “Bull’S Eye Maculopathy in Near Infra-Red Reflectanceas an Early Sign of Hydroxychloroquine Toxicity”.

Beatriz Graça, Selected for oral presentation on the 26º Workshop “Educação pela Ciência”.

Patrícia Costa-Reis, Menção honrosa do Prémio Melhor Artigo da Sociedade Portuguesa de Nefrologia Pediátrica 2023 atribuído ao artigo “SARS-CoV-2 infection in pediatric kidney transplant recipients. Clin Transplant”.

Patrícia Costa-Reis, Primeiro Prémio Melhor Artigo da Sociedade Portuguesa de Nefrologia Pediátrica 2023 atribuído ao artigo “Urinary HER2, TWEAK and VCAM-1 levels are associated with new-onset proteinuria in paediatric lupus nephritis”.

Patrícia Costa Reis. Prémio “Best Portuguese Oral Communication” on the VII Congresso Hispano-Português de Nefrologia Pediátrica e XLVI Congreso Español de Nefrologia Pediátrica 2023 for the work “Gut permeability in lupus nephritis: results from the GUT-LUPUS study”.

Patrícia Costa-Reis, Prémio “Best Oral Communication” on the 55th Annual Meeting of the European Society for Paediatric Nephrology (ESPN), Vilnius, Lituânia for the work “Study of the Gut Microbiota and Permeability in Lupus Nephritis”.

Patrícia Costa-Reis, Prémio Jaime Salazar de Sousa 2023 atribuído ao artigo “Urinary HER2, TWEAK and VCAM-1 levels are associated with new-onset proteinuria in paediatric lupus nephritis”.

Inês Leal and Cristina Ponte, Best clinical case poster – Honorable mention on the XXV Congresso Português de Reumatologia for the work “Varicella zoster virus mimicking Giant Cell Arteritis: The importance of ultrasound in the differential diagnosis”.

### **Advanced Teaching**

Patrícia Costa-Reis, Course Organization, Lúpus Eritematoso Sistémico: revisão sobre diagnóstico e tratamento, Curso de Reumatologia Pediátrica da Sociedade Portuguesa de Reumatologia Pediátrica, Portugal, January 1, 2023.

Patrícia Costa-Reis, Course Organization, Exame Objectivo em Reumatologia Pediátrica: sessão prática; Curso de Reumatologia Pediátrica da Sociedade Portuguesa de Reumatologia Pediátrica, Portugal, January 1, 2023.

Estela Nogueira, Course Organization, Gravidez e Doença renal crónica. Curso final de preparação para o exame final de Nefrologia, Dioscope, Portugal, January 1, 2023.

Pedro Ávila-Ribeiro, Lecture, Rheumatology (practical classes, 5th year) and 6th year clinical rotations on the Integrated Masters in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 1, 2023.

Sofia Barreira, Coordination of Master Curricular Unit, Rheumatology fellowship for Physical Medicine and Rehabilitation residents, Portugal, January 1, 2023.

Ângelo Calado, Lecture, "Respostas metabólicas à hiperglicemia e à hipoglicémia", Master in Metabolic Diseases and Feeding Behavior (2022-23), Faculdade de Medicina da Universidade de Lisboa, Portugal, January 2, 2023.

Rita Machado, Lecture, "Casos Clínicos em Reumatologia" on the VI – Curso de Internos de 2º ano (Reumatologia), Portugal, January 2, 2023.

Cristina Ponte, Course Organization, Spanish Society of Nephrology - ANCA-vasculitis online course - 3rd edition, Online, January 25, 2023.

Vasco C. Romão, Lecture, "História Clínica em Reumatologia", VII Curso de Internos do 2º Ano, Sociedade Portuguesa de Reumatologia, Portugal, January 27, 2023.

Sofia Barreira, Lecture, "Principais DMARDs", VII Curso de Internos do 2º ano da SPR, Portugal, January 28, 2023.

Manuel Silvério-António, Course Organization, Curso intensivo de preparação para o exame de acesso ao Internato Médico – Academia da Especialidade – Módulo B - Reumatologia, Online, February 1, 2023.

Matilde Bandeira, Lecture, "Esclerose sistémica com envolvimento muscular – Caso clínico", Fórum Art & Treat 2023 - Curso de Atualização Multidisciplinar em Esclerose Sistémica, Portugal, February 1, 2023.

Sofia Barreira, Lecture, "Casos Clínicos em Reumatologia", Curso de preparação para a prova nacional de seriação, Portugal, February 2, 2023.

Raquel Marques, Course Organization, Art & Treat – Curso Miopatias Inflamatórias da SPR, Portugal, February 2, 2023.

Sofia Barreira, Lecture, "Doenças difusas do tecido conjuntivo", Curso de preparação para a prova nacional de seriação, Portugal, February 7, 2023.

Sofia Barreira, Workshop Organization, Workshop for Primary care physicians, Osteoporosis, from diagnosis to treatment, Portugal, February 15, 2023.

Elsa Vieira-Sousa, Lecture, "New perspectives on tumor necrosis factor inhibition for the treatment of psoriatic arthritis" in Bridging the Gap - Comprehensive Clinical case presentation on the Towards a Creative and Critical Mind Course of the LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Portugal, February 16, 2023.

Rita A. Moura, Lecture, "B cells, autoantibodies and cytokines in Rheumatoid Arthritis", Curso livre: Mecanismos fisiopatológicos das doenças reumáticas da auto inflamação à autoimunidade, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 21, 2023.

Patrícia Costa-Reis, Lecture, "Towards a Creative and Critical Mind Course", Bridging the Gap Seminar, Towards a Creative and Critical Mind Course of the LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Portugal, March 1, 2023

Manuel Silvério-António, Course Organization, Reumatologia nos Cuidados de Saúde Primários – a formação como estratégia para a melhoria dos cuidados aos doentes reumáticos, Online, March 1, 2023.

Sofia Barreira, Lecture, "Exploração ecográfica do joelho", Curso Básico de Ecografia Músculo-Esquelética, ESPER, Portugal, March 10, 2023.

Sofia Barreira, Lecture, "Course hands on supervision", Curso Básico de Ecografia Músculo-Esquelética, ESPER, Portugal, March 10, 2023.

Joaquim Polido-Pereira, "AR e doença intersticial pulmonar, Curso de Internos de Reumatologia, organized by Lilly, Portugal, March 16, 2023.

Estela Nogueira and Cristina Ponte, Course Organization, Curso de Nefro-Reumatologia: Expressão Renal de Doenças Reumáticas Sistémicas, Portugal, March 24, 2023.

Rita Machado, Lecture, "ANCA-associated vasculitis and steroids sparing approach - where are we now?", Curso de Nefro-Reumatologia – expressão renal de doenças reumáticas sistémicas, Portugal, March 24, 2023.

Sofia Barreira, Lecture, "SLE - new insights in disease mechanisms and new targets", Curso de Nefro-Reumatologia – expressão renal de doenças reumáticas sistémicas, Portugal, March 24, 2023.

Cristina Ponte, Lecture, "Cryoglobulinemia - from diagnosis to treatment", Curso de Nefro-Reumatologia – expressão renal de doenças reumáticas sistémicas, Portugal, March 24, 2023.

Cristina Ponte, Lecture, "Discussion of Vasculitis Clinical Cases", Curso de Nefro-Reumatologia – expressão renal de doenças reumáticas sistémicas, Portugal, March 24, 2023.

Matilde Bandeira, Workshop Organization, "Basic Skills in Musculoskeletal Examination", AIMS Meeting 2023, Portugal, April 1, 2023.

Fernando Saraiva, Course Organization, VI Curso Monotemático da ESPER – ecografia da anca, Portugal, April 1, 2023.

Pedro Ávila-Ribeiro, Lecture, "Exame objetivo músculo-esquelético – da teoria à prática" for the General Practice Residents (Postgraduate), Faculdade de Medicina da Universidade de Lisboa, Portugal. April 26, 2023.



Sofia Barreira, Lecture, "Ferramentas de avaliação das IIM", Curso de Miosites, Jornadas de Primavera da SPR, Portugal, May 5, 2023.

Cristina Ponte, Workshop Organization, Ultrasound of temporal arteries in healthy individuals, Austria, June 16, 2023.

Cristina Ponte, Workshop Organization, Ultrasound of temporal arteries in patients with GCA, Austria, June 16, 2023.

Cristina Ponte, Workshop Organization, Ultrasound of peripheral large arteries in healthy individuals and LVV patients, Austria, June 16, 2023.

Maria José Santos, Lecture, "Aplicação do Consentimento Informado" em Capacitar - Ações de formação e benchmarking AICIB, Online, July 4, 2023.

Sofia Barreira, Coordination of Master Curricular Unit, Rheumatology fellowship for Primary care residents, Portugal, August 1, 2023.

Raquel Marques, Course Organization, Curso de Reumatologia Pediátrica para Internos de Pediatria e de Reumatologia da SPR-SPRP, Portugal, September 1, 2023.

Elsa Vieira-Sousa, Course Organization, PsA Diagnostic and Monitoring Image Online Course, sponsored by Janssen, Online, September 1, 2023.

Raquel Marques, Course Organization, 1st PReS Juvenile Idiopathic Inflammatory Myopathies Course, Portugal, September 7, 2023.

Sofia Barreira, Lecture, "Auto-inflammation" on the Master in Medicine, Portugal, September 9, 2023.

Rita A. Moura, Lecture, "B cells, autoantibodies and cytokines in Rheumatoid Arthritis", Curso livre: Mecanismos fisiopatológicos das doenças reumáticas da auto inflamação à autoimunidade, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 20, 2023.

Filipa Ramos, Lecture, "AIJ sistémica e Síndrome de Activação Macrofágica", Curso Reumatologia Pediátrica para Internos, Portugal, September 21, 2023.

Maria José Santos, Lecture, "Poliartrite na criança: diagnóstico diferencial e abordagem terapêutica", Curso de Reumatologia Pediátrica SPRP/SPR, Portugal, September 21, 2023.

Joaquim Polido-Pereira, Lecture, "Ultrasound-guided synovial biopsy procedures: large joints", 4th EULAR Course on Synovial Biopsy, Spain, September 22, 2023.

Fernando Saraiva, Course Organization, IV Curso Intermédio de Ecografia da ESPER – Procedimentos ecoguiados, Portugal, October 1, 2023.

Fernando Saraiva, Course Organization, Corso Teorico-Pratico di Ecografia in Reumatologia, Italy, October 1, 2023.

Fernando Saraiva, Lecture, "Ultrasound-guided synovial biopsy – state of the art" on the Corso Teorico-Pratico di Ecografia in Reumatologia, Italy, October 5, 2023.

Joaquim Polido-Pereira, Lecture, "Infiltrazione eco-guidate e blocchi nervosi arto inferiore (Ultrasound guided injection – lower limbs)", Corso Teorico-Pratico di Ecografia in Reumatologia, Italy, October 5, 2023.

Sofia Barreira, Lecture, "Exploração ecográfica do punho e mão", Curso Intermédio de Ecografia Músculo-Esquelética da ESPER, Portugal, Portugal, October 12, 2023.

Sofia Barreira, Lecture, "Course hands on supervision", Curso Intermédio de Ecografia Músculo-Esquelética da ESPER, Portugal, Portugal, October 12, 2023.

Cristina Ponte, Course Organization, Match the guidelines 2022-2023, Online, October 14, 2023.

Fernando Saraiva, Course Organization, VII Curso Básico de Ecografia da ESPER – Projeção de Imagens ecográficas e identificação de estruturas, Portugal, November 1, 2023.

Fernando Saraiva, Course Organization, EULAR-endorsed Basic Musculoskeletal Ultrasound Course - Standardised scanning of the knee and basic pathological findings, Mexico, November 1, 2023.

Estela Nogueira and Cristina Ponte, Course Organization, Preceptorship in vasculitis, Portugal, December 15, 2023.

### **MSc Theses**

Miguel Castro, Study of Gut Permeability in Patients with Systemic Lupus Erythematosus, Supervisor: Patrícia Costa Reis, Co-Supervisor: Deodália Dias, Faculdade de Ciências da Universidade de Lisboa, Portugal, February 1, 2023.

Cristiana Barbosa, Quão única é a artrite reumatoide seronegativa?, Supervisor: Joaquim Polido-Pereira, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 4, 2023.

Marta Arese, Is ultrasound a good surrogate marker for remission in RA? Validation of Contrast-enhanced Doppler ultrasound as a valuable tool to detect minimal inflammation in Rheumatoid Arthritis patients, Supervisor: Maria Antonietta D'Agostino, Co-Supervisor: Joaquim Polido-Pereira, Facoltà di Medicina e Chirurgia "Agostino Gemelli", Italy, July 4, 2023.

Cláudio Guerreiro da Costa, Characterization of Damage in Patients with Longstanding Sjögren's Disease, Supervisor: Vasco C. Romão, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 17, 2023.

Maria Inês Arelo Manso da Fonseca, Imunogenicidade, eficácia e segurança da vacina da varicela – Revisão Sistemática, Supervisor: Patrícia Costa-Reis, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 26, 2023

Sofia de Aguiar Castilho Ramos Lopes, Estudo da qualidade de vida relacionada com a saúde em crianças e adolescentes submetidos a transplante renal, Supervisor: Patrícia Costa-Reis, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 27, 2023.

Catarina Bento, In vitro effect of upadacitinib and tofacitinib on peripheral blood leukocytes from patients with early and established rheumatoid arthritis, Supervisor: Rita Alexandra Pedra Aguiar de Moura, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, December 12, 2023.

Ana Rita Faísca, The role of JAK-STAT signaling pathway in early arthritis, Supervisor: Rita Alexandra Pedra Aguiar de Moura, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, December 18, 2023.

### **PhD Theses**

Filipa Ramos, Adult Outcomes of Juvenile Idiopathic Arthritis, Supervisor: João Eurico Fonseca, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 29, 2023.

## Valorization of Knowledge / Social and Economic Impact

### Partnerships with Industry in 2023

CSL Vifor, Development of the ANCA associated vasculitis registry, Sponsored Research.

GSK, Funding for the course of "Nefro-Reumatologia", Contract Research.

Merck Sharp & Dohme, Tutorial videos on rheumatology techniques.

Abbvie, Joaquim Pereira developed consulting activities as an expert in Rheumatoid arthritis.

Boehringer, Sponsored Clinical Sessions.

Pierre Fabre, Sponsored Clinical Sessions.

Menarini, Sponsored Clinical Sessions.

Theramex, Scientific communication: Workshops for primary care physicians.

MSD, Tutorial videos on procedures in rheumatology.

### Science and Society in 2023

Vasco C. Romão: Interview for "Saúde Online" and "Sapo" about Sjögren's syndrome and common symptomatology for lay people:

- <https://saudeonline.pt/sindrome-de-sjogren-reumatologista-alerta-para-sintomas-comuns-a-outras-patologias/>; [https://www.sapo.pt/noticias/saude/sindrome-de-sjogren-reumatologista-alerta\\_646f4d2fa68aa948e0137e08](https://www.sapo.pt/noticias/saude/sindrome-de-sjogren-reumatologista-alerta_646f4d2fa68aa948e0137e08)

Fernando Saraiva: Interview for the Sociedade Portuguesa de Reumatologia newsletter.

Filipa O. Ramos: Webinar for the Sociedade Portuguesa de Reumatologia Pediátrica and the Associação Nacional de Doentes com Artrites Infantis – ANDAI.

Joaquim Pereira: Member of the Direction of the Colégio da Especialidade de Reumatologia da Ordem dos Médicos, being the responsible of Secção Regional do Sul e Ilhas.

Rita Machado: Embassador for the FMUL Corrida Saúde+Solidária, organized by the Associação de Estudantes da Faculdade de Medicina de Lisboa, April 30, 2023.

Patrícia Costa-Reis: sessão de formação e discussão de ensaios clínicos em Pediatria com o grupo de jovens do departamento de pediatria do HSM.

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## Cláudio Franco Lab

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**Head of Laboratory:** Claudio Areias Franco, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa, and Associate Professor at Faculdade de Medicina da Universidade Católica Portuguesa

### Team

Ana Raquel Martins Figueiredo Fonseca	PhD	Postdoctoral Researcher
Andreia Alexandra Santos de Areosa Pena	Master Degree	PhD Student (Left December)
Daniela Maria Grou Ramalho	Master Degree	PhD Student
Hemaxi Narotamo	Master Degree	PhD Student
Lenka Henao Mišíková	Master Degree	Lab Manager
Marta Fernandes Pimentel Saraiva	University Degree	MSc Student
Nadine Vasconcelos Conchinha	PhD	Postdoctoral Researcher (Left February)

### Lab Interests

Our lab aims to understand the principles governing the formation and function of blood vessels and to integrate these concepts to reveal the aetiology of human vascular disorders. The questions we aim to solve are:

- i) How cells communicate with each other to generate supra-cellular structures?
- ii) How proliferation, migration and cell death are coordinated to control tissue size?
- iii) How physical and chemical cues are integrated at the single-cell level in space and time?

### Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Prevention, Diagnosis and Treatment of Human Diseases

### Ongoing Projects

2022/2023: Unveiling pericyte dynamics during vascular development. Coordinator: Cláudio Franco. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/MED-ANM/1616/2021. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2024: Mecanismos de arteriogénese dependentes da migração endotelial - Migration-based mechanisms of arteriogenesis. Coordinator: Cláudio Franco. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ANM/7695/2020. Amount: 249 950,00€. Total Amount: 249 950,00€.

2018/2023: ATTRACT: Arterial flow as attractor for endothelial cell migration. Coordinator: Cláudio Franco. Funding Agency: Fondation Leducq. Reference: ATTRACT. Amount. 25 424,99€. Total Amount: 5 000 000,00€.

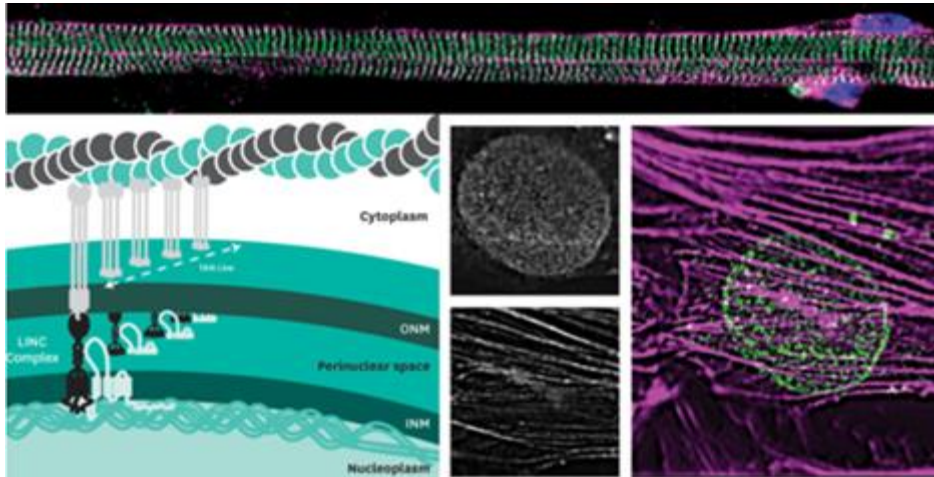
## Edgar Gomes Lab

**Head of Laboratory:** Edgar R. Gomes, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Associate Professor and Director of Instituto de Histologia e Biologia do Desenvolvimento at Faculdade de Medicina da Universidade de Lisboa

### Team

Afonso de Botelho Ferreira Braga Malheiro	PhD	Postdoctoral Researcher
Ana Margarida da Rosa Soares	PhD	Postdoctoral Researcher
Ana Raquel Ramos Pereira	PhD	Postdoctoral Researcher
Catarina Antunes Sequeira	Master Degree	PhD Student
Duarte Miguel Cancela de Amorim Candeias	University Degree	MSc Student
Francisco Javier Calero Cuenca	PhD	Postdoctoral Researcher
Gabriele Salvatore Motta	Master Degree	Lab Technician (Started September)
Hélia Cristina de Oliveira Neves	PhD	Senior Postdoctoral Researcher
Inês Correia da Silva Pires Faleiro	Master Degree	PhD Student
Inês Isabel Baltazar Belo Martins	Master Degree	Lab Technician (Left April)
Isabel da Conceição Alves Alcobia Principe Henriques	PhD	Senior Postdoctoral Researcher
João Pedro Nunes Paulo da Silva Martins	Master Degree	PhD Student (Left July)
Katharina Hennig	PhD	Postdoctoral Researcher
Mafalda Araújo e Sá Pereira	University Degree	MSc Student
Maria Judite Sousa da Costa	PhD	Lab Manager (Left January)
Marta Sofia Serra Baptista	Master Degree	Lab Manager
Sara Sofia Gasalho Ferreira	University Degree	Lab Technician
Silvia di Francescantonio	PhD	Postdoctoral Researcher
William Roman	PhD	Postdoctoral Researcher

## Graphical Abstract



Top: differentiated muscle cell with peripheral nuclei

Bottom left: scheme of interaction between nuclear envelope proteins and cytoskeleton

Bottom right: fluorescent image of nuclei in green and actin in purple

## Lab Interests

The cell nucleus is linked to the cytoskeleton and this connection is relevant for multiple cellular processes. Disruption of these connections result in several pathologies. Nuclear positioning within cell cytoplasm requires the connection between the nucleus and the cytoskeleton. We are interested in understanding the processes involved in these connections and the role for nuclear positioning in cell function. We study cell migration and skeletal myofiber formation, which involves the connection between the nucleus and the cytoskeleton and precise nuclear positioning. We also study the formation and maintenance of muscle triads, membrane structures that comprise the connection of a plasma membrane tubule with two sarcoplasmic reticulum cisternae, contiguous with the nuclear envelope. We use different molecular and cellular approaches in combination with time-lapse imaging analysis to address these questions.

## Research Fields

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Integrative Biology: From Genes and Genomes to Systems
- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Biotechnology and Biosystems Engineering



### **Major Scientific Achievements in 2023**

We designed a contractility assay based on optogenetics and particle image velocimetry. After in vitro exercise, myotubes contract faster, are more resistant and matured. We observed an upregulation in the expression of fast myosin heavy chain isoforms, which induced a shift towards a fast-twitch phenotype. This strategy can be used to study fiber specification and refine muscle disease modelling. (Henning et al 2023)

We co-cultured motor neurons differentiated iPSCs with primary muscle myofibers to determine the mechanisms of neuromuscular junction formation. We generated novel microdevices to mimic blood vessels with endothelial cells, motor neurons and myofibers (Myochip project, collaboration with Cláudio Franco Lab).

We found that myofibers transiently suppress transcription upon DNA damage and exhibit a long DNA damage response, in contrast to myoblasts. These findings provide a novel mechanism of DDR response in differentiated post-mitotic cells (Faleiro et al 2023, BIG grant with Sérgio de Almeida Lab).

### **Ongoing Projects**

2023/2024: A human skeletal muscle platform for disease modelling and high throughput drug screening. Coordinator: Edgar Gomes. Funding Agency: European Commission. Reference: MUSCLEPLATE - ERC-2022-POC2. Amount: 150 000,00€. Total Amount: 150 000,00€.

2023/2024: Development of a neuromuscular junction in vitro platform for amyotrophic lateral sclerosis (ALS) modelling. Coordinator: Afonso Malheiro. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02492.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2019/2025: ArpComplexity: Defining the role of Arp2/3 complex diversity at multiple scales of biology. Coordinator: Edgar Gomes. Funding Agency: European Commission. Reference: ERC SyG 810207. Amount: 3 207 935,00€. Total Amount: 10 715 153,00€.

2018/2023: A role for the microenvironment on nuclear positioning in myofibers. Coordinator: Edgar Gomes. Funding Agency: AFM Telethon. Reference: AFM Telethon. Amount: 98 000,00€. Total Amount: 98 000,00€.

2018/2023: Building a 3D innervated and irrigated muscle on a chip. Coordinator: Edgar Gomes.  
Funding Agency: European Commission. Reference: MYOCHIP - GA801423 - H2020-FETOPEN-2016-2017. Amount: 1 266 861,25€. Total Amount: 3 153 553,74€.

## Scientific Impact

### Academic Collaborations

- Bruno Cadot, Institut Myologie, France.
- Stephanie Decroix, Institut Curie, France.
- Miguel Bernabeu, United Kingdom.
- Fluigent, France.
- Michael Way, The Francis Crick Institute, United Kingdom.
- Carolyn Moores, The Francis Crick Institute, United Kingdom.
- Sérgio de Almeida, Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### Selected Publications

Janota CS, Pinto A, Pezzarossa A, Machado P, Costa J, Campinho P, Franco CA, Gomes ER (2022).

[Shielding of actin by the endoplasmic reticulum impacts nuclear positioning.](#) **Nature Communication.**

**Relevance of the publication:** We found that the endoplasmic reticulum shields actin cables to generate asymmetric nucleo-cytoskeleton connections for nuclear positioning.

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

**Relevance of the publication:** We found a complex between a nuclear envelope phosphatase (Ctdnep1) and an actin binding protein (Eps8L2) that is involved in nuclear movement.

Roman, W., Pinheiro, H., Pimentel, M.R., Segalés, J., Oliveira, L.M., García-Domínguez, E., Gómez-Cabrera, M.C., Serrano, A.L., **Gomes, E.R.**, and Muñoz-Cánoves, P. (2021). [Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction.](#) **Science**, 374, 355–359.

**Relevance of the publication:** We found a mechanism of self repair of muscle fibers involving nuclear movement and local translation at the site of injury.

Roman W, Martins J, Carvalho FA, Voituriez R, Abella JVG, Santos NC, Cadot B, Way M, Gomes ER (2017). [Myofibril contraction and cross-linking drive nuclear movement to the periphery of skeletal muscle](#). *Nature Cell Biology*, 1189–1201.

**Relevance of the publication:** We identify the mechanism of nuclear positioning at the periphery of skeletal muscle fibers. We found that nuclei are squeezed to the periphery and this process requires skeletal muscle contraction, myofiber crosslinking and activation of specific arp 2/# and actin isoforms

Sestina Falcone, William Roman, Karim Hnia, Vincent Gache, Nathalie Didier, Jeanne Lainé, Frederic Auradé, Isabelle Marty, Ichizo Nishino, Nicolas Charlet-Berguerand, Norma Beatriz Romero, Giovanna Marazzi, David Sassoon, Jocelyn Laporte, and Edgar R Gomes (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 Mol Med*. 6(11): 1455–1475.

**Relevance of the publication:** We found the first molecular that regulates nuclear positioning and triad formation in skeletal muscle and is disrupted in centronuclear myopathies.

### 2023 Publications in Peer-Reviewed Journals

Katharina Hennig, David Hardman, David M. B. Barata, Inês I. B. B. Martins, Miguel O. Bernabeu, Edgar R. Gomes and William Roman (2023). Generating fast-twitch myotubes in vitro using an optogenetic-based, quantitative contractility assay. *Life Science Alliance*.

Inês Faleiro, Ana I Afonso, André Balsinha, Beatriz Lucas, Robert M Martin, Edgar R Gomes, Sérgio F de Almeida (2023). Adaptive changes in the DNA damage response during skeletal muscle cell differentiation. *Front Cell Dev Biol* 11:1239138. doi: 10.3389/fcell.2023.1239138. eCollection 2023.

### Pre-Prints

David Hardman, Katharina Hennig, Edgar R Gomes, William Roman, Miguel O Bernabeu. An in vitro - agent-based modelling approach to optimisation of culture medium for generating muscle cells. doi: <https://doi.org/10.1101/2021.09.28.461963>

### Invited Lectures and Seminars

Edgar R. Gomes. Oxford University, United Kingdom.

Edgar R. Gomes, Nuclear positioning and membrane remodeling and during skeletal muscle formation. EMBO Workshop Cell polarity and membrane dynamics, Spain.

## **Communications**

### Communications in International Conferences:

Ana Soares, Arp2/3 complex regulate T-tubule formation and Triad assembly in Skeletal Muscle. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Mafalda Pereira, Dynamics of triad positioning during skeletal myofiber stretching and contraction. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Duarte Candeias, Microtubules Drive Mitochondrial Dynamics in Myofiber Formation. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Silvia Di Francescantonio, Rescue of dysferlin-deficient muscular dystrophy by gene-edited primary muscle stem cells. ESGCT 30th Annual Congress Brussels, Belgium, October 24, 2023. (Poster Presentation)

Silvia Di Francescantonio, The Arp2/3 complexes: the hidden role in skeletal muscle postnatal development and homeostasis. Frontiers in Myogenesis: Advances in Skeletal Muscle Growth, Repair and Disease, Brazil, November 6, 2023. (Oral Presentation)

Ana Raquel Pereira, T-tubule formation through membrane invagination is regulated by the Arp 2/3 complex and the cell cortex for membrane contact with the endoplasmic reticulum in skeletal muscle. ASCB EMBO, CellBio 2023, USA, December 6, 2023. (Poster Presentation)

### Communications in National Conferences:

Inês Faleiro, The DNA damage response in skeletal muscle cells. RNA in Disease - RiboMed and IX ptRNA joint meeting, Portugal, January 27, 2023. (Oral Presentation)

Ana Raquel Pereira, The Role of the Arp2/3 Complex in T-Tubule Membrane Localization and Dynamics in Skeletal Muscle Cells. JCS: Cell Dynamics: Imaging cell dynamics, Portugal, May 14, 2023. (Poster Presentation)

## **Organization of Conferences**

Edgar R Gomes, Co-Organizer, Cell Bio 2023 Meeting, Boston, USA, USA, December 6, 2023.

### **Networks and Research Infrastructures**

Edgar R Gomes, MyoChip Project a FetOpen project, Instituto de Medicina Molecular João Lobo Antunes is the Coordinator.

Edgar R Gomes, ArpComplecity is a ERC Synergy Grant, Instituto de Medicina Molecular João Lobo Antunes (Beneficiary).

### **Advanced Teaching**

Edgar R Gomes, Lecture, LisbonBioMed PhD Program, Portugal.

Edgar R Gomes, Coordination of Master Curricular Unit, Master of Biomedical Research, Portugal.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Fluigent, Build a 3D human skeletal muscle irrigated by vasculature and innervated by neurons, Collaborative Research.

### **Intellectual Property Rights in 2023**

Fluigent, Apparatus for Feeding a Liquid Medium to a Fluidic System Comprising Check valves.

Fluigent, Apparatus for Feeding a Liquid Medium to a Fluidic System Comprising Magnetic Agitation.

Fluigent, Apparatus for Feeding a Liquid Medium to a Fluidic System Having a Liquid Level Detection Capability.

Fluigent, Apparatus for Feeding a Liquid Medium to a Fluidic System Comprising a Cartridge and a Locking Mechanism.

### **Science and Society in 2023**

We participated in European Researchers Night with a showcase of a 3D muscle structure with multiple games from kids (September 30, 2023).

We were visited at IMM by students from 8th grade Colégio Sagrado Coração de Maria in April 2023. All the students had the possibility to interact with our 3D muscle model and observe muscle samples from different animals on the microscopes.

A senior group visited the lab and had the opportunity to interact with our 3D printed model and observe muscle samples from different animals on the microscopes. This visit was organized by the Municipality of Lisbon (February 14, 2023).

A visit of 120 students from Escola Marquesa de Alorna organized by the Program Ciência di Noz Manera that aims to reach students in a difficult social context. Our lab show them the 3D muscle model and microscope slides (February 15, 2023).

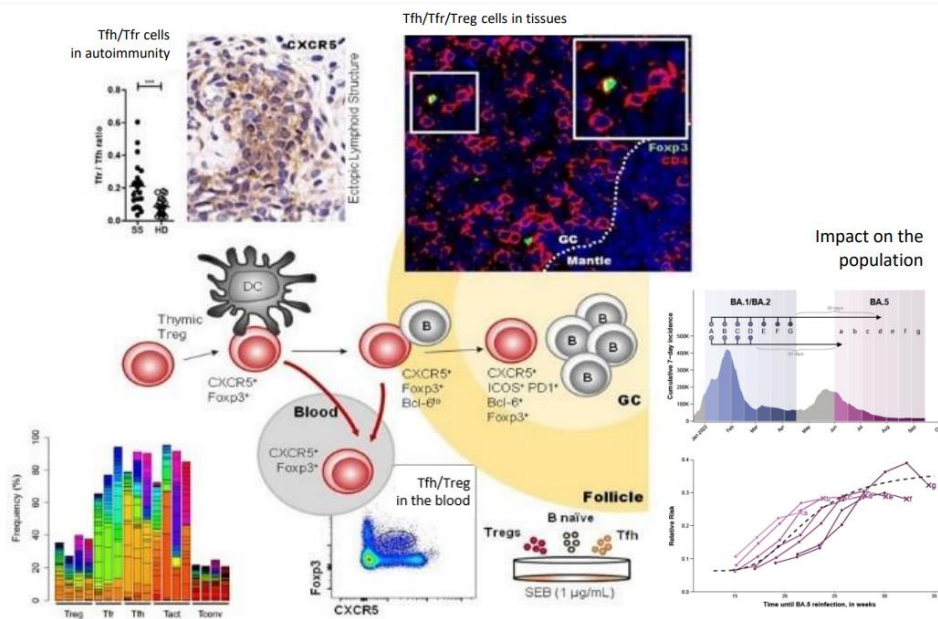
## Luís Graça Lab

**Head of Laboratory:** Luís Graça, MD, DPhil, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Full Professor and Vice-Dean at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Catarina Jorge Mendes	University Degree	Lab Manager (Left June)
Ana Isabel Neves de Matos	Master Degree	Trainee (Left December)
Ariana Santos Pina	Bachelor Degree	MSc Student (Started September)
Beatriz Guerreiro Filipe	Bachelor Degree	Lab Technician (Started May. Left December)
Deepanwita Ghosh	Master Degree	PhD Student
Diana Isabel Lourenço Matias	PhD	Postdoctoral Researcher
Diogo Alves Antunes	High School Siploma	MSc Student (Left November)
Diogo Martins Fonseca	University Degree	MSc Student (Left December)
Elisa Mastrantuono	Master Degree	PhD Student (Started September)
Filipa Ramos de Moura Ribeiro	Master Degree	PhD Student (Left December)
Jean-Christophe Lone	Master Degree	PhD Student
João Torrado Malato	Master Degree	PhD Student
Maria Miguel Pereira Serafim Rodrigues Cavaco	Master Degree	PhD Student (Started January)
Marta Pereira da Silva	University Degree	MSc Student (Started April)
Miguel Dinis Monteiro dos Santos	PhD	Postdoctoral Researcher (Started June)
Pedro Alexandre da Silva Gaspar	Master Degree	PhD Student
Pedro Manuel Ávila Ribeiro	MD/Master Degree	PhD Student
Rodrigo Balsinha Pedroso	Master Degree	PhD Student
Rui Pedro Oliveira do Amaral Vieira	Master Degree	PhD Student
Ruy Miguel Sousa Soeiro de Figueiredo Ribeiro	PhD	Senior Postdoctoral Researcher
Tomás Pires de Carvalho Gomes	PhD	Postdoctoral Researcher (Started July)
Válter Bruno Ribeiro Fonseca	PhD	Postdoctoral Researcher
Vanessa Alexandra Gonçalves de Oliveira Martins	MD/PhD	Clinical Researcher (Left November)
Vladimir Ghilas	University Degree	Lab Manager (Started June)

## Graphical Abstract



Our laboratory is interested in studying the different cell populations that regulate immune responses. We investigate the contribution of cell-mediated regulatory mechanisms in autoimmunity (top left), using various methods to assess the biology of those cells. These methods include computational approaches, namely to understand the receptor repertoire or transcriptome (bottom left), flow cytometry, and *in vitro* functional assays (bottom, middle), as well as the anatomic distribution of the different cells in the tissues (top right). Overall, these methods allow the identification of biological mechanisms (central diagram) and ultimately contribute to our understanding of the immune response in human populations (bottom right).

## Lab Interests

Our group studies mechanisms underlying the regulation of the immune response. In other words, we research methods to alter the balance of the immune response: reducing its action when the immune system is causing a disease, such as in autoimmunity, allergy, and transplant rejection, or enhancing the immune response to vaccines, cancer, or infection.

We are especially interested in defining the functional properties of lymphocytes that can regulate pathogenic immune responses. We have been studying how different types of lymphocytes with regulatory functions, such as T regulatory cells and T follicular regulatory cells, can be induced and modulated. In this respect, we have been interested in the regulation of germinal center responses and antibody production by T follicular cells.

In the foreseeable future, therapeutic strategies to modulate the immune system will significantly affect the quality of life of people suffering from immune-mediated diseases.



### **Research Field**

- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases
- Biotechnology and Biosystems Engineering

### **Major Scientific Achievements in 2023**

We defined the developmental pathways underlying the specialization of T follicular helper subsets induced within lymphoid tissue under distinct inflammatory environments, namely type-1 and -2 responses following immunization and infection.

A challenge in human immunology has been the unequivocal identification of T follicular regulatory (Tfr) cells. We characterized critical features of Tfr cells in human lymphoid tissue (manuscript in preparation).

We extended our work on immunity acquired following COVID-19 vaccination and infection (hybrid immunity) with the quantification of the stability of the hybrid immunity over time. These results, highlighted in the journal Nature, significantly impacted public health decisions regarding the best strategy for using COVID-19 vaccine booster doses.

### **Ongoing Projects**

2023/2026: Modulation of human antibody responses by T follicular helper subsets. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.04903.PTDC. Amount: 250 000,00€. Total Amount: 250 000,00€.

2022/2025: Nano-imunoterapia multifuncional para o tratamento de metastases cerebrais de melanoma. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BTM-SAL/4350/2021. Amount: 20 000,00€. Total Amount: 249 817,50€.

2022/2025: PolyMuTEs - Polymeric nanoparticles-based multivalent mABs against glioblastoma for T-cell engagement. Coordinator: Diana Matias. Funding Agency: “la Caixa” Foundation. Reference: “la Caixa” Postdoctoral Junior Leader - Diana Matias – PolyMuTEs. Amount: 286 900,75€. Total Amount: 286 900,75€.

2022/2025: The BioPlaTTAR Platform for tHarnessing germinal centre regulation for improved vaccines. Coordinator: Luís Graça. Funding Agency: “la Caixa” Foundation. Reference: HR22-00741 – GCVAX. Amount: 499 952,00€. Total Amount: 499 952,00€.

2022/2024: Protocolo MSD 2022. Coordinator: Luís Graça. Funding Agency: Merck Sharp & Dohme, Lda. Reference: LGRAÇA – MSD. Amount: 397 144,80€. Total Amount: 397 144,80€.

2022/2024: Innovative Alliance. Coordinator: Luís Graça. Funding Agency: Innovative Alliance. Reference: INNOVATIVE ALLIANCE – CUBA. Amount: 35 375,00€. Total Amount: 35 375,00€.

2022/2024: Ativação via TLR2 para o desenvolvimento de melhores vacinas veterinárias. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/CVT-CVT/4599/2021. Amount: 15 000,00€. Total Amount: 249 809,97€.

2022/2023: Regulação da produção de anticorpos protetores versus autoanticorpos em doenças autoimunes. Coordinator: Válter Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/MEC-MGI/1644/2021. Amount: 49 999,60€. Total Amount: 49 999,60€.

2021/2025: ENLIGHT-TENPlus. Coordinator: Luís Graça. Funding Agency: European Commission. Reference: H2020-MSCA-ITN-2020. Amount: 237 772,24€. Total Amount: 237 772,24€.

2021/2024: ALS PROJECT - ONO PHARMA. Coordinator: Luís Graça. Funding Agency: ONO PHARMA. Reference: ALS PROJECT - ONO PHARMA. Amount: 126 860,50€. Total Amount: 126 860,50€.

2021/2024: LiMM Therapeutics. Coordinator: Luís Graça. Funding Agency: LiMM Therapeutics. Reference: LIMM THERAPEUTICS. Amount: 5 000,00€. Total Amount: 5 000,00€.

2021/2023: SLE PROJECT - ONO PHARMA. Coordinator: Luís Graça. Funding Agency: ONO PHARMA. Reference: SLE PROJECT - ONO PHARMA. Amount: 126 593,75€. Total Amount: 126 593,75€.

2021/2023: Nanomateriais para desenho de novas vacinas. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: UTA-EXPL/NPN/0082/2019. Amount: 40 000,00€. Total Amount: 40 000,00€.

2020/2023: Thymic Abnormalities in Rare Immunological. Coordinator: Luís Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EJPRD/0003/2020. Amount: 150 000,00€. Total Amount: 150 000,00€.

2015/2023: Immune modulatory activity of CD6-targeting monoclonal antibodies. Coordinator: Luís Graça. Funding Agency: Center of Molecular Immunology. Reference: CUBA - CD6. Amount: 30 375,00€. Total Amount: 30 375,00€.

## Scientific Impact

### Academic Collaborations

- Ruy Ribeiro, Los Alamos National Laboratory, USA.
- Eliane Piaggio, Institut Curie, Paris, France.
- Yang Li, Hannover Medical Institute, Germany.
- Kathy O. Lui, The Chinese University of Hong Kong, China.
- Ana Caetano Faria, Universidade de Belo Horizonte, Brazil.

### Selected Publications

Malato J, Ribeiro RM, Leite PP, Casaca P, Fernandes E, Antunes C, Fonseca VR, Gomes MC, Graça L (2022). [Risk of BA.5 infection in individuals exposed to prior SARS-CoV-2 variants](#). **N Engl J Med**. 10.1056/NEJMc2209479.

**Relevance of the publication:** This study, based on Portuguese registries, evaluated protection against Omicron BA.5 infection in vaccinated people infected with previous SARS-CoV-2 variants. The study had a significant impact on public health policy, as adapted Omicron BA.1 vaccines were being developed and made available while the dominant subvariant was already BA.5.

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

**Relevance of the publication:** This is a study in which computational methods were used to address the differentiation of immune cells that regulate the production of antibodies within lymphoid tissue. We circumvented limitations to perform time-course experiments in humans using single-cell transcriptomics to establish the developmental trajectory of Tfh and Tfr cells in human lymph nodes and tonsils.

Fonseca VR, Romão VC, Água-Doce A, Santos M, López-Presa D, Ferreiras AC, Fonseca JE, Graça 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).

**Relevance of the publication:** Identification of biomarkers related to Tfh and Tfr cells (that regulate autoantibody production) that allow the stratification of patients with Sjögren's disease (SjD). This study relied on the study of paired samples from salivary gland biopsies and blood from a cohort of patients with primary SjD.

Fonseca VR, Água-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).

**Relevance of the publication:** This is the first comprehensive report on the ontogeny and function of human Tfr cells, using samples from human thymus, cord blood, paired peripheral blood and tonsil, vaccinated individuals, and B-cell deficient patients.

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 have different TCR-specificity](#). **Nature Communications** 8:15067. (IF: 12.353, Citations: 34. Sources: Web of Science and Scopus).

**Relevance of the publication:** This article used several approaches, including bioinformatics, to establish that the TCRs of Tfh and Tfr cells from the same GCs are different. The repertoire of Tfr cells is biased towards self-antigens, while the Tfh repertoire is specific to the immunizing antigen.

### 2023 Publications in Peer-Reviewed Journals

Coelho-Santos V\*, Matias D\*, Dubois G, Aran V, Moura-Neto V, Balça-Silva J (2023). Chapter 15- Glioblastoma heterogeneity and resistance: A glance in biology and therapeutic approach. Academic Press-Elsevier, Pages 319-344 doi.org/10.1016/B978-0-323-99873-4.00018-9

Malato J, Ribeiro RM, Fernandes E, Leite PP, Casaca P, Antunes C, Fonseca VR, Gomes MC, Graca L (2023). Stability of hybrid versus vaccine immunity against BA.5 infection over 8 months, The Lancet Infectious Diseases, 23(2):148--150, DOI: 10.1016/s1473-3099(22)00833-7

Malato J, Graca L, Sepúlveda N (2023). Impact of Misdiagnosis in Case-Control Studies of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Diagnostics, 13(3):531, MDPI AG, DOI: 10.3390/diagnostics13030531

Domingues TD, Malato J, Grabowska AD, Lee J-S, Ameijeiras-Alonso J, Biecek P, Graça L, Mouriño H, Scheibenbogen C, Westermeier F, Nacul L, Cliff JM, Lacerda E, Sepúlveda N (2023). Association analysis between symptomology and herpesvirus IgG antibody concentrations in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and multiple sclerosis, Heliyon, 9(7):e18250, Elsevier BV, DOI: http://dx.doi.org/10.1016/j.heliyon.2023.e18250

Machado IC, Nunes T, Maximino M, Malato J, Tavares L, Almeida V, Sepúlveda N, Gil S (2023). Epidemiologic Factors Supporting Triage of Infected Dog Patients Admitted to a Veterinary Hospital Biological Isolation and Containment Unit, *Veterinary Sciences*, 10(3):186, MDPI AG, DOI: 10.3390/vetsci10030186, URL: <http://dx.doi.org/10.3390/vetsci10030186>

Gaspar P, Farinha F, Sayar Z, Efthymiou M, Cohen H, Isenberg DA (2023). A one-point increase in the Damage Index for Antiphospholipid Syndrome (DIAPS) predicts mortality in thrombotic antiphospholipid syndrome. *Clin Exp Rheumatol.* 41(3):605-612. doi:10.55563/clinexprheumatol/0gs167

Gaspar P, Dias M, Parreira I, et al (2023). Predictors of Long-COVID-19 and its Impact on Quality of Life: Longitudinal Analysis at 3, 6 and 9 Months after Discharge from a Portuguese Centre. *Acta Med Port.* 36(10):647-660. doi:10.20344/amp.19047

Yang, K. Y., Liao, J., Ma, Z., Tse, H. F., Lu, L., Graça, L., & Lui, K. O. (2023). Single-cell transcriptomics of Treg reveals hallmarks and trajectories of immunological aging. *Journal of leukocyte biology*, 115(1):19–35. <https://doi.org/10.1093/jleuko/qiad104>

Tomé, C., Oliveira-Ramos, F., Campanilho-Marques, R., Mourão, A. F., Sousa, S., Marques, C., Melo, A. T., Teixeira, R. L., Martins, A. P., Moeda, S., Costa-Reis, P., Torres, R. P., Bandeira, M., Fonseca, H., Gonçalves, M., Santos, M. J., Graça, L., Fonseca, J. E., & Moura, R. A. (2023). Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. *RMD open*, 9(3):e002901. <https://doi.org/10.1136/rmdopen-2022-002901>

Rojas, G., Relova-Hernández, E., Pérez-Riverón, A., Castro-Martínez, C., Diaz-Bravo, O., Infante, Y. C., Gómez, T., Solozábal, J., DíazBravo, A. B., Schubert, M., Becker, M., Pérez-Massón, B., Pérez-Martínez, D., Alvarez-Arzola, R., Guirola, O., China, G., Graca, L., Dübel, S., León, K., & Carmenate, T. (2023). Molecular reshaping of phage-displayed Interleukin-2 at beta chain receptor interface to obtain potent super-agonists with improved developability profiles. *Communications biology*, 6(1):828. <https://doi.org/10.1038/s42003-023-05188-0>

Matos, A. I., Peres, C., Carreira, B., Moura, L. I. F., Acúrcio, R. C., Vogel, T., Wegener, E., Ribeiro, F., Afonso, M. B., Santos, F. M. F., Martínez-Barriocanal, Á., Arango, D., Viana, A. S., Góis, P. M. P., Silva, L. C., Rodrigues, C. M. P., Graca, L., Jordan, R., Satchi-Fainaro, R., & Florindo, H. F. (2023). Polyoxazoline-Based Nanovaccine Synergizes with Tumor-Associated Macrophage Targeting and Anti-PD-1 Immunotherapy against Solid Tumors. *Advanced science* (Weinheim, Baden-Wurttemberg, Germany), 10(25):e2300299. <https://doi.org/10.1002/advs.202300299>

Graça, L., Faria, A. C., & Ribeiro, R. M. (2023). Illuminating a blind spot in SARS-CoV-2 immunity. *Nature immunology*, 24(6), 889–890. <https://doi.org/10.1038/s41590-023-01518-w>

Graça, L., Jacobsen, J., & Kumar, S. (2023). The expanding family of T follicular regulatory cells. *Science immunology*, 8(82):eadg7526. <https://doi.org/10.1126/sciimmunol.adg7526>

### **Pre-Prints**

Barbieri V, González-Colsa J, Matias D, Duro-Castano A, Thapa A, Ruiz-Perez L, Albella P, Volpe G, Battaglia G, Designing thermoplasmonic polymersomes for photothermal therapy. arXiv, 2023, [doi.org/10.48550/arXiv.2307.16165](https://doi.org/10.48550/arXiv.2307.16165) (under review *Advanced Materials*)

Rodrigo Balsinha Pedroso et al., “Covid-19 Induces Senescence and Exhaustion of T Cells in Patients with Mild/Moderate and Severe Disease During a Seven-Day Interval” (medRxiv, January 18, 2023), <https://doi.org/10.1101/2023.01.16.23284612>

### **Invited Lectures and Seminars**

Diana Matias, Gateways to the brain: vascular glial-immune network. PGNET-neural and tumoral Immunobiology topics. PGNET-neural and tumoral Immunobiology topics, Brazil, January 1, 2023.

Luís Graça, Investigação em Autoimunidade. Curso Clínico de Autoimunidade, Portugal, March 9, 2023.

Rui do Amaral Vieira, Functional convergence of V $\delta$ 1+ and V $\delta$ 2+  $\gamma\delta$  T cells in response to SARS-CoV-2 infection. Instituto de Medicina Molecular João Lobo Antunes Immunology Club, Portugal, April 19, 2023.

Luís Graça, Regulation of antibody production: From cells to human populations. Departmental Seminar, University of Alabama in Birmingham, USA, April 20, 2023.

Luís Graça, Regulation of antibody production: From cells to human populations. Los Alamos National Laboratory, USA, May 9, 2023.

Rodrigo Balsinha Pedroso, Modification of monoclonal antibodies towards reduction of immunogenicity. XVI CAML PhD Students Meeting 2023, Portugal, May 10, 2023.

Luís Graça, Regulation of antibody production: From cells to human populations. Yale, Departmental Seminar, USA, May 30, 2023.

Rodrigo Balsinha Pedroso, Modification of monoclonal antibodies towards reduction of immunogenicity. Instituto de Medicina Molecular João Lobo Antunes Immunology Club, Portugal, June 28, 2023.

Luís Graça, Therapeutic manipulation of T cell regulation. University of Fudan, Shanghai, China, June 30, 2023.

Luís Graça, Regulation of antibody production. Arrábida Meeting, Portugal, July 6, 2023.

Luís Graça, Inteligência artificial, medicina e educação médica. CODEM, Brazil, July 14, 2023.

Luís Graça, Regulation of antibody production by specialized Tfh subsets. Congress of the Brazilian Society for Immunology, Brazil, October 4, 2023.

Filipa Ribeiro, The heterogeneity of T follicular cells within human lymphoid tissues. Instituto de Medicina Molecular João Lobo Antunes Scientific Retreat, Portugal, October 19, 2023.

Filipa Ribeiro, Identification of human blood and tissue T follicular regulatory cells by flow cytometry. IFlow Club – Sociedad Española de Inmunología, Online, November 15, 2023.

Luís Graça, RNA and immunology. FEBS seminar - RNA biology, Porto, November 27, 2023.

### **Communications**

#### Communications in International Conferences:

Filipa Ribeiro, PD-1 and ICOS are coherently expressed in T follicular helper cells but define three stages of maturation in T follicular regulatory cells. T and B cell collaboration in germinal centers and beyond Keystone Symposia, Canada, April 1, 2023. (Poster Presentation)

Pedro Gaspar, Stratification of Negative, Seroconverted and Persistently Positive Thrombotic Primary Antiphospholipid Syndrome Patients with Distinct Follicular Helper T Cells Subsets. European Congress of Rheumatology EULAR 2023, Italy, May 1, 2023, (Oral Presentation)

João Malato, Cellular Compartments in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Associated to Disease Trigger. 2nd International ME/CFS Research Conference, Charité, Germany, May 12, 2023. (Poster Presentation)

Rui do Amaral Vieira, The impact of severe respiratory viral infection in circulating Tfh and  $\gamma\delta$  T cell populations at single-cell resolution. T and B Cell Collaboration in Germinal Centers and Beyond Keystone Symposia, Canada, October 1, 2023.

Communications in National Conferences:

Rodrigo Balsinha Pedroso, COVID-19 induces senescence and exhaustion of T cells in patients with mild/moderate and severe disease during a seven-day interval. XLVIII Sociedade Portuguesa de Imunologia Annual Meeting 2023, Portugal, March 29, 2023. (Poster Presentation)

Pedro Gaspar, Stratification of Primary Antiphospholipid Syndrome Patients with distinct Follicular Helper T Cells Subsets according to Autoantibodies Profile. XLVIII Sociedade Portuguesa de Imunologia Annual Meeting 2023, Portugal, March 29, 2023. (Oral Presentation)

João Malato, Impact of Misdiagnosis in Case-Control Studies Of ME/CFS. XVI CAML PhD Students Meeting, Portugal, May 10, 2023. (Oral Presentation)

Rui do Amaral Vieira, Functional convergence of  $V\delta 1+$  and  $V\delta 2+$   $\gamma\delta$  T cells in response to viral infection. 10th International Gamma Delta T Cell Conference, Portugal, June 20, 2023. (Poster Presentation)

Pedro Gaspar, Dysregulation of circulating T follicular cells, but not clinical features, is associated with antiphospholipid antibodies positivity in patients with thrombotic primary antiphospholipid syndrome. Congresso Português de Reumatologia, Portugal, October 1, 2023. (Oral Presentation)



João Malato, The Magnitude and Stability of Protection Against Omicron SARS-CoV-2 Acquired by Hybrid Immunity. XXVI Congresso da Sociedade Portuguesa de Estatística, Portugal, October 14, 2023.

### **Networks and Research Infrastructures**

Diana Matias, Molecular bionics lab, IBEC- Spain, Synthesis and purification of PVP-PEG-PLA polymer, click chemistry of angiopep2-peg-pla.

Elisa Mastratuono, Molecular bionics lab, IBEC- Spain, Synthesis and purification of PVP-PEG-PLA polymer, click chemistry of angiopep2-peg-pla.

Luís Graça, Enlighten+, Beneficiary.

Luís Graça, T cell connect Europe (TCC-Europe), EFIS, Partner.

### **Prizes and Honours**

Luís Graça, Prémio Pfizer de Investigação Clínica.

Luís Graça, Medal of Merit, Alvalade Municipality.

### **Advanced Teaching**

Luís Graça, Course organization, Masters in Biomedical Research, Portugal, January 1, 2023.

Luís Graça, Lecture, Immunity and Infection, Portugal, January 19, 2023.

Diana Matias, Lecture, Programa de Pós-graduação em Neurociência Translacional, Brazil, July 1, 2023.

Luís Graça, Coordination of Master Curricular Unit, Immunity and Infection, Masters in Biomedical Research, Portugal, November 1, 2023.

### **MSc Theses**

Diogo Fonseca, Single-cell transcriptional landscape of circulating Tfh and Treg cells in COVID-19 patients, Supervisor: Luís Graça, Co-Supervisor: Saumya Kumar, Universidade Nova de Lisboa, Portugal, November 7, 2023.

## Valorization of Knowledge / Social and Economic Impact

### Science and Society in 2023

Luís Graça is the chair of the National COVID-19 and Influenza Vaccination Technical Advisory Group, Portuguese Health Authority (Direção-Geral da Saúde).

Luís Graça was present at the parliamentary health committee to inform MPs about the influenza and COVID-19 vaccination program.

Active participation of group members in activities to increase scientific literacy, especially among young people. These activities included podcasts (Falar de Ciência / Luís Graça), public lectures (LASER talk / Los Alamos, USA; Medical Museum, Copenhagen, Denmark; Cultivamos Cultura, Odemira, Portugal), and frequent appearances in the media (radio, television, and printed press). Collaboration with visual artists developing artworks exploring the interface between art and biomedical sciences. Artist Marta de Menezes was appointed “associate artist” in the group by the Medical School.

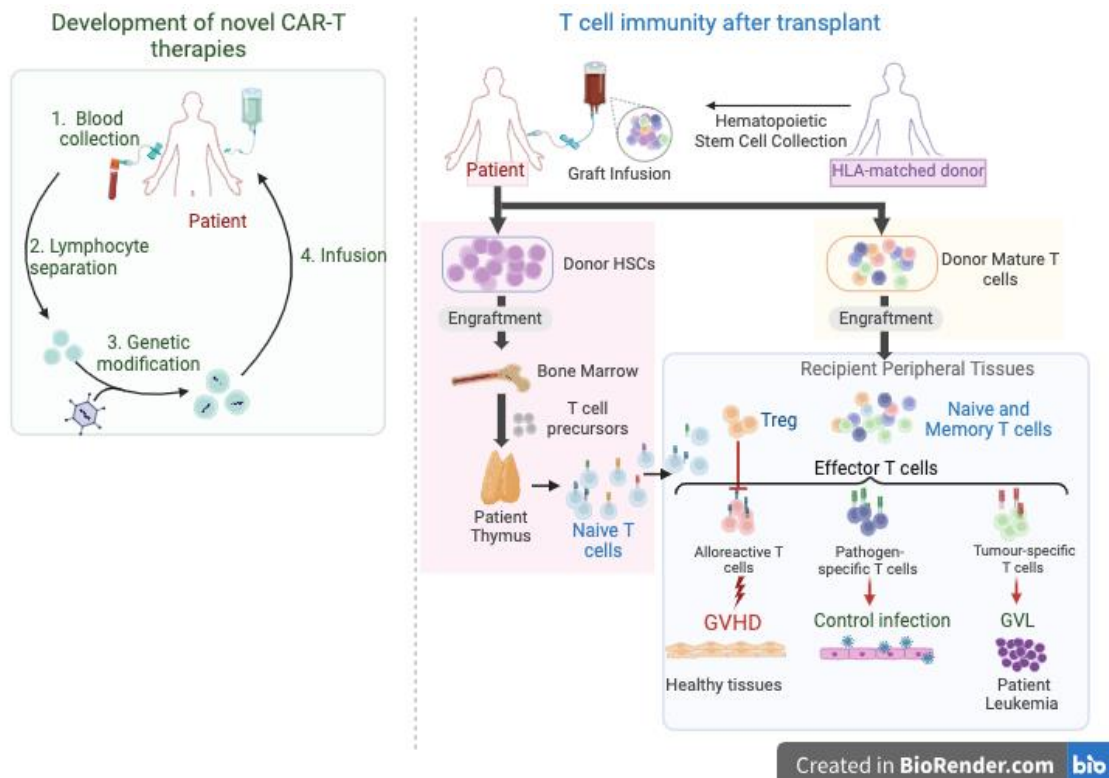
## João Lacerda Lab

**Head of Laboratory:** João Forjaz de Lacerda, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full Professor at Faculdade de Medicina da Universidade de Lisboa, Senior Attending, Hematology and Bone Marrow Transplant Service at Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria, President, Ethics Committee, Vice-President at Clinical Research Center at Lisbon Academic Medical Center

### Team

Ana Catarina Vagos Gomes Rodrigues da Mata	MD/Master Degree	Clinical Researcher/PhD Student
Ana Cristina Frazão Lopes Alho	MD/PhD	Clinical Researcher
Ana Teresa da Silva Pais	Master Degree	Lab Technician
Carolina Paulino Pacini	Master Degree	PhD Student
Diogo Gomes da Silva	PhD	Postdoctoral Researcher
Eduardo Lima da Silva Espada	MD/Master Degree	Clinical Researcher/PhD Student
Joana Brioso Infante	MD/Master Degree	Clinical Researcher/PhD Student
Maria Godinho Alves Vieira Duarte Soares	PhD	Senior Postdoctoral Researcher

### Graphical Abstract



### **Lab Interests**

The research projects in our lab look into the period that follows Hematopoietic Stem Cell Transplantation (HSCT), aiming to identify immunological risk factors and mechanisms involved in the most common complications, namely Graft-versus-Host Disease (GVHD), infection, and malignancy relapse. Hence our main goals are:

1. Study the clinical benefits of donor-derived polyclonal regulatory T cell (Treg) infusion in patients with steroid-resistant GVHD, while monitoring tissue regeneration markers and immunological parameters following Treg infusion.
2. Develop antigen-specific Tregs to treat GVHD whilst retaining leukemia-specific responses.
3. Tackle infection after HSCT by detailing virus-specific T cell responses after transplant, and dissecting the pattern of genetic propensities for the emergence invasive fungal infections.
4. Address malignancy relapse, using Chimeric antigen

### **Research Fields**

- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy
- Prevention, Diagnosis and Treatment of Human Diseases

### **Major Scientific Achievements in 2023**

In 2023 we have been preparing a joint publication with our partners detailing the final results of the Phase I/II clinical trial using donor Treg to treat cGVHD. We have performed the flow cytometry analysis in a centralized manner at iMM, in order to obtain consistent data on immune monitoring currently being prepared for publication.

Patient recruitment on the project that details CMV-specific responses after HSCT recruitment is close to completion and the flow cytometry analysis of CMV-specific cells advanced significantly in 2023.

Further, in 2023 we dedicated significant efforts to the development of a novel CAR T cell that elicits antitumor responses against an array of cancer cell lines in vitro, including triple negative breast cancer, glioblastoma, and various hematologic tumors. While requiring optimizations, we demonstrate the feasibility of this CAR T therapy, marking a milestone in our pursuit of innovative treatment modalities aiming towards clinical application.

## Ongoing Projects

2023/2024: Development of a Chimeric Antigen Receptor T cell therapy against oncologic-specific glycans. Coordinator: João Lacerda. Funding Agency: Gilead Sciences, Lda. Reference: PROGRAMA GILEAD GÉNESE 2023 - DIOGO SILVA. Amount: 20 000,00€. Total Amount: 40 000,00€.

2022/2024: Development of a Chimeric Antigen Receptor T cell therapy targeting oncological associated chondroitin sulfate as cancer treatment. Coordinator: Diogo Silva. Funding Agency: Liga Portuguesa Contra o Cancro. Reference: LPCC-NRS BOLSA INVESTIGAÇÃO. Amount: 10 000,00€. Total Amount: 10 000,00€.

2021/2024: T reguladores específicos para o receptor: seleção. Coordinator: João Lacerda. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MEC-HEM/5281/2020. Amount: 249 886,57€. Total Amount: 249 886,57€.

2020/2024: Projecto MSD 2019. Coordinator: João Lacerda. Funding Agency: Merck Sharp & Dohme, Lda. Reference: PROJECTO MSD 2019. Amount: 72 556,44€. Total Amount: 72 556,44€.

2020/2024: PRÉMIO SPH. Coordinator: João Lacerda. Funding Agency: Sociedade Portuguesa de Hematologia. Reference: PREMIO SPH. Amount: 25 000,00€. Total Amount: 25 000,00€.

2019/2024: Apoio Educacional – Janssen. Coordinator: João Lacerda. Funding Agency: Janssen-Cilag Farmacêutica, Lda. Reference: APOIO EDUCACIONAL – JANSSEN. Amount: 19 800,00€. Total Amount: 19 800,00€.

2019/2024: Ensaio Hematologia Prof. João Lacerda. Coordinator: João Lacerda. Funding Agency: Centro Hospitalar Lisboa Norte, E.P.E. Reference: ENSAIO HEMATOLOGIA PROF. JOÃO LACERDA. Amount: 3 542,22€. Total Amount: 3 542,22€.

## Scientific Impact

### Academic Collaborations

- José Antonio Pérez-Simón: Unidad de Hematología y Hemoterapia, Hospital Universitario Virgen del Rocío, Seville, and University of Seville, Spain.
- Marta Garcia-Finana: Department of Biostatistics, Faculty of Health & Life Sciences, University of Liverpool, United Kingdom.

- Agostinho Carvalho: Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal.
- Jerome Ritz, Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA.

### Selected Publications

Azevedo RI, Minskaia E, Fernandes-Platzgummer A, Vieira AIS, da Silva CL, Cabral JMS, Lacerda JF (2020). [Mesenchymal stromal cells induce regulatory T cells via epigenetic conversion of human conventional CD4 T cells \*in vitro\*](#). **Stem Cells** 38(8):1007-1019. Original article.

**Relevance of the publication:** In this paper we aimed to develop Treg expansion protocols to support future clinical trials, by exploring the potential of mesenchymal stromal cells (MSCs) to expand Treg *in vitro*. We report that while Treg do not proliferate in coculture with MSCs, we demonstrate that MSCs induce a Treg-like population from purified Tcon, which is functionally suppressive and displays a DNA methylation profile resembling that of nTreg. Our data shed light into the origin, function, and stability of MSC-induced Treg-like cells, paving the way for their potential clinical applicability.

Soares MV, Azevedo RI, Ferreira IA, Bucar S, Ribeiro AC, Vieira A, Pereira PNG, Ribeiro RM, Ligeiro D, Alho AC, Soares AS, Camacho N, Martins C, Lourenço F, Moreno R, Ritz J, Lacerda JF (2019). [Naive and stem cell memory T Cell subset recovery reveals opposing reconstitution patterns in CD4 and CD8 T cells in chronic graft vs host disease](#). **Frontiers in Immunology** 6(10):334. Original article.

**Relevance of the publication:** We studied immune reconstitution after allogeneic hematopoietic stem cell transplantation to find immunological correlates for cGVHD development. We observed increased naïve and SCM CD8 in patients who go on to develop cGVHD, thus suggesting a potential role for this population in cGVHD development.

Minskaia E, Saraiva BC, Soares MV, Azevedo RI, Ribeiro RM, Kumar SD, Vieira AIS, Lacerda JF (2018). [Molecular markers distinguishing T Cell subtypes with TSDR strand-bias methylation](#). **Frontiers in Immunology** 9: 2540. Original article.

**Relevance of the publication:** FOXP3 expression and TSDR demethylation are classically used for Treg lineage commitment and differentiation status, and for prognostic purposes in various disease settings. We describe a strand-specific methylation pattern that challenges current simplified interpretations of TSDR methylation and that can be instrumental in disclosing potential differences between subsets of Treg and Tcon. Such findings will directly impact on Treg research and on the clinical application of Treg therapies.

Alho AC, Kim HT, Chammas MJ, Reynolds CG, Matos TR, Forcade E, Whangbo J, Nikiforow S, Cutler CS, Koreth J, Ho VT, Armand P, Antin JH, Alyea EP, Lacerda JF, Soiffer RJ, Ritz J (2016). [Unbalanced recovery of regulatory and effector T cells after allogeneic stem cell transplantation contributes to chronic GVHD](#). *Blood* 127(5):646-657. Original article.

**Relevance of the publication:** This work carried out a prospective monitoring of T-cell reconstitution, revealing several homeostatic imbalances that appear to contribute to the development of chronic GVHD, namely Treg depletion, thus supporting the notion that selective interventions promote the generation, expansion, or persistence of CD4Tregs may improve the balanced recovery of effector and regulatory T-cell populations and promote immune tolerance after transplant.

Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Löffler M, Maertens JA, Bell AS, Almeida B, Sousa PS, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano I, Lupi M, Garlanda C, Mantovani A, Velardi A, Romani L, Carvalho A (2014). [Genetic PTX3 deficiency and aspergillosis in stem-cell transplantation](#). *The New England Journal of Medicine* 370(5): 421-432. Original article.

**Relevance of the publication:** We evaluated the impact of single-nucleotide polymorphisms (SNPs) in PTX3 to the development of invasive aspergillosis in hematopoietic stem cell transplantation. Using lung specimens from transplant recipients we observed that when donors had the homozygous haplotype in PTX3, transplant recipients had increased risk of infection, with impaired phagocytosis and clearance of the fungus. Hence, genetic deficiency of PTX3 affects the antifungal capacity of neutrophils and may contribute to the risk of invasive aspergillosis in patients treated with HSCT.

### 2023 Publications in Peer-Reviewed Journals

Bojanic I, Worel N, Pacini CP, Stary G, Piekarska A, Flinn AM, Schell KJ, Gennery AR, Knobler R, Lacerda JF, Greinix HT, Pulanic D, Crossland RE (2023). Extracorporeal photopheresis as an immunomodulatory treatment modality for chronic GvHD and the importance of emerging biomarkers. *Front Immunol*. 14:1086006. doi: 10.3389/fimmu.2023.1086006

Jia LJ, Rafiq M, Radosa L, Hortschansky P, Cunha C, Cseresnyés Z, Krüger T, Schmidt F, Heinekamp T, Straßburger M, Löffler B, Doenst T, Lacerda JF, Campos A Jr, Figge MT, Carvalho A, Kniemeyer O, Brakhage AA (2023). *Aspergillus fumigatus* hijacks human p11 to redirect fungal-containing phagosomes to non-degradative pathway. *Cell Host Microbe*. 31(3):373-388.e10. doi: 10.1016/j.chom.2023.02.002

Rodríguez-Gil A, Pérez-Simón JA, Ritz J, Lacerda JF, Soares MV (2023). Regulatory T cells in graft versus host disease. *Front Immunol*. 13:1085220. doi: 10.3389/fimmu.2022.1085220

Espada E, Ligeiro D, Trindade H, Lacerda JF (2023). HLA frequency distribution of the Portuguese bone marrow donor registry. *Front Immunol*. 14:1286001. doi: 10.3389/fimmu.2023.1286001

Minskaia E, Lacerda JF (2023). Analysis of FOXP3 DNA Methylation Patterns to Identify Functional FOXP3+ T-Cell Subpopulations. *Methods Mol Biol.* 2559:115-136. doi: 10.1007/978-1-0716-2647-4\_9

Schön M, Infante J, Pinho E Melo T, Lacerda JF, Ferro JM (2023). Cerebral venous thrombosis as a first presentation of a high-risk acute myeloid leukaemia. *Acta Neurol Belg.* doi: 10.1007/s13760-023-02467-9

Infante J, Esteves G, Raposo J, de Lacerda JF (2023). Predictors of very early death in acute promyelocytic leukemia: a retrospective real-world cohort study. *Ann Hematol.* 102(11):3031-3037. doi: 10.1007/s00277-023-05422-z

Sapinho G, Alves-Ribeiro L, Infante J, Jacinto-Correia C, Kalim S, Lacerda JF (2023). Full-Dose Azacitidine in 5 days versus 7 days with a weekend break in Myelodysplastic Syndromes: A retrospective cohort study. *Clin Lymphoma Myeloma Leuk.* S2152-2650(23)02131-6. doi: 10.1016/j.clml.2023.09.010

### **Invited Lectures and Seminars**

João Forjaz de Lacerda, Transplante haploidêntico. *Perspectivas em Hematologia*, Portugal, February 25, 2023.

João Forjaz de Lacerda, O doente com alterações hematológicas. 11º Curso de Atualização Geriatria/Geronotologia, Portugal, May 19, 2023.

João Forjaz de Lacerda, Novas Terapêuticas. Em: *Como se tratam os linfomas?* 1º Seminários Linfomas APCL, Portugal, November 18, 2023.

### **Communications**

#### Communications in National Conferences:

João Forjaz de Lacerda, A medula óssea no doente idoso. 43º Congresso Português de Geriatria e Gerontologia, Portugal, November 17, 2023. (Oral Presentation)

### **Prizes and Honours**

Diogo Silva, Gilead Génese “Development of a Chimeric Antigen Receptor T cell therapy against oncologic-specific glycans.



Diogo Silva, Individual Call to Scientific Employment Stimulus (CEEC) - 5th Edition Employment Contract.

Eduardo Espada, Bolsa de Investigação da Sociedade Portuguesa de Hematologia: "Multiparametric phenotypic characterization of CAR T cells and endogenous immune cells in patients with non-Hodgkin's lymphomas treated with CD19 CAR T cells".

Ana C. Alho, Bolsa de Investigação da Sociedade Portuguesa de Hematologia "Changes in stem cell memory T cell lymphocyte homeostasis associate with chronic GVHD development: possible therapeutic targets".

### **Advanced Teaching**

Diogo Gomes da Silva, Lecture, Optional Immuno-Oncology Course for Medical Students from Faculdade de Medicina da Universidade de Lisboa, Portugal, February 22, 2023.

Diogo Gomes da Silva, Lecture, Oncoimmunology Course for the Oncobiology Master of Faculdade de Medicina da Universidade de Lisboa, Portugal, March 15, 2023.

João Forjaz de Lacerda, Lecture, Programa Doutoral em Ciências da Saúde: Ongoing Development of CAR, Portugal, April 11, 2023.

### **MSc Theses**

João Bernardo Diogo Pereira, Insuficiência respiratória no doente imunossuprimido: revisão da literatura a propósito de um caso clínico, Supervisor: Ana Vagas Mata, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 27, 2023.

### **PhD Theses**

Ana C Alho, Homeostasis of CD4+ Regulatory T cells after allogeneic hematopoietic cell transplantation, Supervisor: João F. Lacerda, Co-Supervisor: Jerome Ritz, Faculdade de Medicina da Universidade de Lisboa, Portugal, March 7, 2023.

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## Luísa Lopes Lab

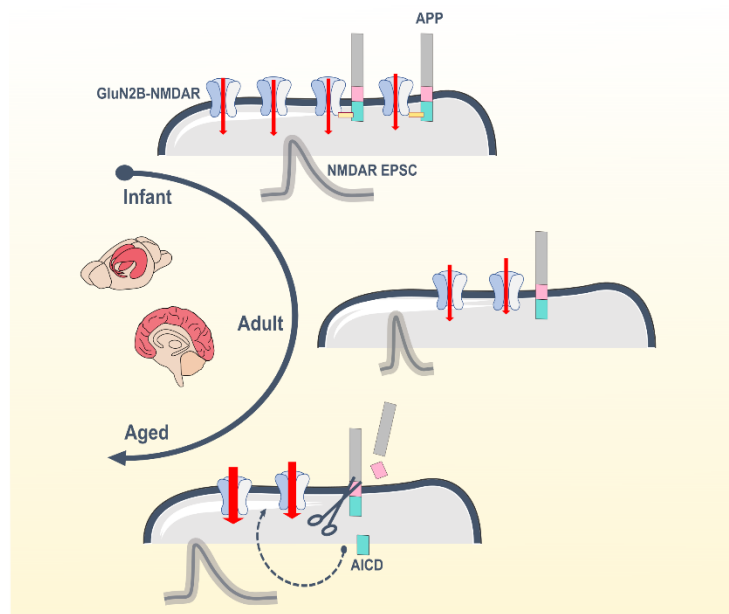
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**Head of Laboratory:** Luísa V. Lopes, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, and Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Inês Marques Morgado	Master Degree	PhD Student (Left December)
Ana Sofia Carvalho Cruz	Master Degree	PhD Student (Left June)
Armando Miguel Caseiro Pires Remondes	PhD	Staff Scientist
Catarina Candeias Ferreira	University Degree	MSc Student
Cátia Cristina Peixinho Reis	PhD	Postdoctoral Researcher
Gonçalo Aires de Oliveira	PhD	Postdoctoral Researcher (Left July)
Joana Bárbara Morais Condesso	University Degree	MSc Student
Joana Fernandes Esteves Soares Coelho	PhD	Senior Postdoctoral Researcher
Joana Gomes Ribeiro	Master Degree	PhD Student (Left December)
Joana Isabel Rajão Saraiva	Master Degree	PhD Student (Left July)
João Baptista Moreira	Master Degree	PhD Student
João Pedro Cláudio Agapito	University Degree	MSc Student (Left June)
Jorge Miguel Claro Cardoso	Master Degree	PhD Student
Manuel António Freire Dias da Silva	Master Degree	PhD Student (Started September)
Marcelo Francisco Vieira Dias	University Degree	PhD Student (Left December)
Marta Filipa Leite Luís	University Degree	MSc Student (Left June)
Nicolas Andres Morgenstern	PhD	Postdoctoral Researcher
Patrícia Morais Caldeira Rodrigues Bernardo	University Degree	MSc Student (Left April)
Pedro Filipe Duarte Pereira Batista	MD/Master Degree	Clinical Researcher
Rui Artur Paiva Loureiro Gomes	PhD	Senior Postdoctoral Researcher (Left December)

## Graphical Abstract



*We have identified the APP full-length protein as a regulator of glutamatergic transmission in immature synapses, by controlling GluN2B synaptic content and mediated currents during postnatal development. Upon aging, the APP amyloidogenic derived C-termi*

## Lab Interests

We run a translational neuroscience research program aimed at understanding the mechanisms inducing the "early-aging" of cognitive function, focusing on hippocampal circuitry and related behavior in rodent models.

The future research plan aims at implementing novel age-equivalent models using human-derived neurons to create improved aging models, in order to study early synaptic dysfunction and the mechanisms underlying resilience versus vulnerability in cognitive aging. This will allow going beyond and delving deeper into the mechanisms involved.

## Research Fields

- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System

## Major Scientific Achievements in 2023

- We've devised a rodent morphine-induced CPP protocol for MRI presentation, revealing a neural circuitry linking contextual cues, morphine, and memory. These findings, deposited on BioRxiv, may elucidate individual opioid sensitivity variations, crucial for understanding addiction. bioRxiv 2023.08.07.552221

- Using patch-clamp recordings, we've uncovered how amyloid-precursor protein (APP) modulates GluN2B-NMDARs across life stages. APP regulates synaptic GluN2B-NMDAR content and currents, with its amyloidogenic fragments implicated in age-related synaptic dysfunction. Our research, published in Aging Cell, suggests potential interventions to normalize GluN2B-NMDAR currents. <https://onlinelibrary.wiley.com/doi/full/10.1111/ace1.13778>

- Funded by “la Caixa” Impulse Innovation 2023 call, we're exploring a pre-clinical proof of concept aiming for a novel deep brain stimulation method. <https://caixaresearch.org/en/caixaimpulse-health-innovation-call-2023-project-luminopsins-parkinson>

### Ongoing Projects

2023/2026: The health benefits of deuterium depletion on synaptic function, regional metabolism, and behaviour. Partner: Luísa Lopes. Funding Agency: European Commission. Reference: PROJECT 101086453 — AQUA-SYNAPSE. Amount: 170 200,00€. Total Amount: 910 800,00€.

2023/2025: Luminopsins in Parkinson's disease stimulation. Coordinator: Luísa Lopes. Funding Agency: “la Caixa” Foundation. Reference: LUMINPD - CI23-10184. Amount: 50 000,00€. Total Amount: 50 000,00€.

2023/2024: Studying accelerated cognitive decline upon aging in human derived cholinergic neurons. Coordinator: Luísa Lopes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.03516.PTDC. Amount: 49 375,00€. Total Amount: 49 375,00€.

2023/2024: Insulin-degrading enzyme: a novel therapeutic target for Parkinson's disease. Co-Pi: Luísa Lopes. Funding Agency: The Michael J. Fox Foundation. Reference: MJFF-021400 - SPRING 2022 RFA. Amount: 13 023,43€. Total Amount: 13 023,43€.

2023/2024: Disrupção do Ritmo Circadiano Sono-Vigília em Militares Submarinistas: Caraterização da Dinâmica Disrupção-Recuperação e Identificação de Fatores Preditivos e Protetores. Coordinator: Cátia Reis. Funding Agency: Ministério da Defesa Nacional. Reference: MINISTÉRIO DEFESA NACIONAL - PROJECTO INVESTIGAÇÃO. Amount: 10 000,00€. Total Amount: 10 000,00€.

2023/2024: APOIO GASOXMED. Coordinator: Cátia Reis. Funding Agency: GASOXMED Gases Medicinais SA. Reference: APOIO GASOXMED. Amount: 3 500,00€. Total Amount: 3 500,00€.

2023/2024: Luminopsins for the Treatment of Parkinson's Disease. Coordinator: Pedro Batista. Funding Agency: Sociedade Portuguesa de Neurocirurgia. Reference: BOLSA DE INVESTIGAÇÃO DA SPNC 2022 - PEDRO BATISTA. Amount: 2 500,00€. Total Amount: 2 500,00€.

2021/2024: AgeIN. Coordinator: Luísa Lopes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/3890/2020. Amount: 218 050,00€. Total Amount: 218 050,00€.

2019/2024: NeuroSeS: Neuroscience Seminar Series. Coordinator: Luísa Lopes. Funding Agency: Roche Farmacêutica. Reference: NeuroSeS: NeuroscienEuropean Commission Seminar Series. Amount: 3 200,00€. Total Amount: 3 200,00€.

## Scientific Impact

### Academic Collaborations

- University of Côte d'Azur, Nice, France.
- CIBIT Coimbra, Portugal.
- Bordeaux Neurocampus, France.
- University of Wurzburg, Germany.
- University of Oxford, United Kingdom.
- i3S, Porto Portugal.

### Selected Publications

Blum D, Lopes LV (2021) [Stabilizing synapses](#). *Science*. doi: 10.1126/science.abm3902

**Relevance of the publication** Compelling evidence from our group and others demonstrates that the synaptic and neuronal up-regulation of adenosine A2AR in aging and neurodegeneration is instrumental to the decline of synaptic function and degeneration, presumably through neuron-glia dialog. Hereby, we put into the context the mechanism uncovered for synaptogenesis by Gomez-Castro (2021, *Science*) which may have broader implications—e.g., that of adenosine possibly playing a more general role as an activity detector, regulating synaptic dynamics and presumably synaptic loss, in the aged and diseased brain. Adenosine and A2AR would then regulate the fate of particular synapses in extreme stages of the brain life cycle. This supports a prime role for adenosine in synaptic allostasis (i.e., during brain adaptation to challenges), the controlling of brain network wiring, and cognitive function and emphasizes our contribution to this important physiological mechanism.

Mariana Temido-Ferreira, Diana G. Ferreira, Vânia L. Batalha, Inês Marques-Morgado, Joana E. Coelho, Pedro Pereira, Rui Gomes, Andreia Pinto, Sara Carvalho, Paula M. Canas, Laetitia Cuvelier, Valerie Buée-Scherrer, Emilie Faivre, Younis Baqi, Christa E. Müller, José Pimentel, Serge N. Schiffrmann, Luc Buée, Michael Bader, Tiago F. Outeiro, David Blum, Rodrigo A. Cunha, Hélène Marie, Paula A. Pousinha and Luísa V. Lopes (2020) [Age-related shift in LTD is dependent on neuronal adenosine A2A receptors interplay with mGluR5 and NMDA receptors](#), **Molecular Psychiatry**, 25(8):1876-1900.

**Relevance of the publication** Synaptic dysfunction plays a central role in Alzheimer's Disease (AD), since it drives the cognitive decline. An association between a polymorphism of the adenosine A2A receptor (A2AR) encoding gene - ADORA2A, and hippocampal volume in AD patients was recently described. In this study, we report, for the first time, a significant overexpression of A2AR in hippocampal neurons of aged humans, which is aggravated in AD patients. A similar profile of A2AR overexpression in rats was sufficient to drive age-like memory impairments in young animals and to uncover a hippocampal LTD-to-LTP shift. This is a consequence of an A2AR-induced increase in postsynaptic Ca<sup>2+</sup> influx via NMDAR, which is dependent on mGluR5 activation. We confirmed the same plasticity shift in memory-impaired aged rats and APP/PS1 mice modelling AD, which was rescued upon A2AR blockade. This A2AR/mGluR5/NMDAR interaction might prove a suitable alternative for regulating aberrant mGluR5/NMDAR signaling in AD without disrupting their constitutive activity.

Diana G. Ferreira, Mariana Temido-Ferreira, Hugo Vicente Miranda, Vânia L. Batalha, Joana E. Coelho, Éva M. Szegö, Inês Marques-Morgado, Sandra H. Vaz, Jeong Seop Rhee, Matthias Schmitz, Inga Zerr, Luísa V. Lopes\* and Tiago F. Outeiro\* (2017) [α-Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B](#). **Nature Neuroscience** 20(11):1569-1579.

**Relevance of the publication** Synucleinopathies, such as Parkinson's disease (PD) and dementia with Lewy bodies, are neurodegenerative disorders characterized by the accumulation of α-synuclein (αSyn) in intracellular inclusions. The main finding of this study is that αSyn oligomeric species physically interact with PrPC through mGluR5, activating SFK kinases and, subsequently, NMDAR2B, leading to neuronal calcium imbalance. We found for the first time, that genetic or antibody-mediated inactivation of PrPC prevented the toxic effects of αSyn on synaptic function. Finally, we confirmed the importance of this mechanism in vivo, by rescuing synaptic and cognitive deficits following blockade of mGluR5- evoked phosphorylation of NMDARs, in a mouse model overexpressing human αSyn. Together, these data support the hypothesis that a receptor-mediated mechanism, independent of pore formation and membrane leakage, is sufficient to trigger early synaptic damage induced by extracellular αSyn, which could occur as part of the normal biology of the protein or during the spreading of pathology in PD and other synucleinopathies.

VL. Batalha, JM. Pego B Fontinha, AR Costenla, J Valadas, Y Baqi, H Radjainia, C E. Müller, AM. Sebastião and Luísa V. Lopes (2013) [Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation](#). *Mol. Psychiatry*, 18, 320-331.

**Relevance of the publication** While the hippocampus is best known for its role in memory and spatial navigation, it's also extremely important in emotional responses. Neuronal growth in the hippocampus can come from enriched environments or chronic antidepressants, and death of those neurons can come from chronic stress. Chronic stress also disrupts the hypothalamic-pituitary-adrenal axis (the HPA axis). There are compelling evidences for a role of hippocampal adenosine A2AR in stress-induced modifications related to cognition. We assessed the therapeutic potential of a blocker of A2A receptors in stress-impaired animals and found that it reverted the behavior, electrophysiological and morphological impairments induced by stress. This mechanism is associated with restoration of the HPA-axis activity, as both the plasma corticosterone levels and hippocampal glucocorticoid receptor expression pattern returned to physiological-like status after the treatment. These results reveal that the HPA-axis dysfunction, as well as the long-lasting synaptic and behavioral effects of stress are associated to overactivation of A2A receptors. These findings provide novel evidence for the use of adenosine A2A receptor antagonists as potential therapy against psychopathologies.

### 2023 Publications in Peer-Reviewed Journals

Rajão-Saraiva J, Dunot J, Ribera A, Temido-Ferreira M, Coelho JE, König S, Moreno S, Enguita FJ, Willem M, Kins S, Marie H, Lopes LV, Pousinha PA (2023). Age-dependent NMDA receptor function is regulated by the amyloid precursor protein. *Aging Cell*. 22(3):e13778. doi: 10.1111/accel.13778

Oliveira GA, Remondes M, Garcia - Marques T (2023). Easy to process, hard to control: Transient and sustained processing fluency impairs cognitive control adjustments to conflict *Q J Exp Psychol (Hove)* DOI: 10.1177/17470218231159787

Matsui K, Chung F, Bjelajac AK, Merikanto I, Korman M, Mota-Rolim S, Cunha AS, Bjorvatn B, Xue P, Benedict C, Morin CM, Espie CA, Landtblom AM, Penzel T, De Gennaro L, Holzinger B, Hrubos-Strøm H, Leger D, Bolstad CJ, Nadorff MR, Plazzi G, Reis C, Chan NY, Wing YK, Yordanova J, Dauvilliers Y, Partinen M, Inoue Y (2023). Associations between changes in habitual sleep duration and lower self-rated health among COVID-19 survivors: findings from a survey across 16 countries/regions. *BMC Public Health* 23(1):2352. doi: 10.1186/s12889-023-17258-3

Berezin L, Waseem R, Merikanto I, Benedict C, Holzinger B, De Gennaro L, Wing YK, Bjorvatn B, Korman M, Morin CM, Espie C, Landtblom A, Penzel T, Matsui K, Hrubos-Strøm H, Mota-Rolim S, Nadorff MR, Plazzi G, Reis C, Chan RNY, Cunha AS, Yordanova J, Bjelajac AK, Inoue Y, Dauvilliers Y, Partinen M, Chung F (2023) Habitual short sleepers with pre-existing medical conditions are at higher risk of Long COVID. *Journal of Clinical Sleep Medicine* doi: 10.5664/jcsm.10818

Reis, C, Pilz LK, Kramer A, Lopes LV, Paiva T, Roenneberg T (2023). The impact of daylight-saving time (DST) on patients with delayed sleep-wake phase disorder (DSWPD). *Journal of Pineal Research*. e12867. doi: 10.1111/jpi.12867

Xue, P., Merikanto, I., Chung, F, Morin CM, Espie C, Bjorvatn B, Cedernaes J, Landtblom AM, Penzel T, De Gennaro L, Holzinger B, Matsui K, Hrubos-Strøm H, Korman M, Leger D, Mota-Rolim S, Bolstad CJ, Nadorff M, Plazzi G, Reis C, Chan RNY, Wing YK, Yordanova J, Bjelajac AK, Inoue Y, Partinen M, Dauvilliers Y, Benedict C (2023). Persistent short nighttime sleep duration is associated with a greater post-COVID risk in fully mRNA-vaccinated individuals. *Translational Psychiatry* 13, 32. doi:10.1038/s41398-023-02334-4

### **Pre-Prints**

Joana Gomes-Ribeiro, João Martins, José Sereno, Samuel Deslauriers-Gauthier, Teresa Summavielle, Joana E. Coelho. Mapping functional traces of opioid memories in the rat brain. doi: <https://doi.org/10.1101/2023.08.07.552221>

### **Invited Lectures and Seminars**

Luísa Lopes, Neurobiology of aging. EBBS, Portugal, January 12, 2023.

Luísa Lopes. Job2b, Portugal, March 7, 2023.

Luísa Lopes, Porque e como envelhecemos. Reitoria 2023, Portugal, April 18, 2023.

Luísa Lopes, The role of adenosine A2A receptor in cognitive dysfunction. French Purine Club 2023, France, Online, June 7, 2023.

Luísa Lopes, Synaptic proteins implicated in cognitive vulnerability. IBRO2023, Spain, September 12, 2023.

Cátia Reis, Investigação em medicina do sono e o papel das novas tecnologias. XLII Congresso Anual Sociedade Portuguesa de Medicina Dentária, Portugal, October 10, 2023.

Luísa Lopes, A diversidade geracional na perspetiva da longevidade e envelhecimento saudável. Católica Business School, Portugal, October 17, 2023.

Luísa Lopes, Unlocking the secrets of the aged synapse. FRM, Portugal, November 16, 2023.

Luísa Lopes, The NMDA receptor in aged diseased synapses. Mexico, November 17, 2023.

Luísa Lopes, The role of NMDA receptors in the aged glutamatergic synapses. CIBB, Portugal, December 20, 2023.



Cátia Reis, Sessão Hot Topics Sono – Ritmos circadianos. Congresso Nacional de Neurologia, Portugal.

Cátia Reis, Science communication in an Era of “alternative facts”. eSleep – European Sleep Research Society, Portugal, Online, Portugal.

Miguel Remondes, It’s Really All About Timing - Functional characterization of neural circuits responsible for goal-directed behaviors in the healthy and Autistic brain. CBIOS ULHT Research Seminars, Portugal.

Miguel Remondes, The Use of AI in Scientific Research. IMM’s Master's Day, Portugal.

Miguel Remondes. 15th Workshop of Biomedical Engineering WBME.

Miguel Remondes, Labcoats and Laptops: Neuroscience through different lenses. ENCODS MEETING 2023 - Federation of European Neuroscience Societies, Portugal.

### **Communications**

#### Communications in International Conferences:

Pedro Batista, Directional Leads for Deep Brain Stimulation: A Comprehensive Survey and Literature Review. EANS Webinars, Online. (Oral Presentation)

Luísa Lopes, Age-Dependent NMDA Receptor Function is Regulated by the Amyloid Precursor Protein. SFN 2023, USA. (Poster Presentation)

Cátia Reis, Subjective sleep quality and sleepiness dynamics on a group of military submariners: before, during and after a mission. World Congress on Sleep Medicine, Brazil. (Oral Presentation)

Cátia Reis, Phenotypic differences in sleep and circadian rhythms in delayed sleep wake-phase disorder patients with and without comorbid depression, Advances in Sleep and Circadian Science. (ASCS) Congress, USA. (Oral Presentation)

#### Communications in National Conferences:

Pedro Batista, Four-eyed Neurosurgeon: Experiência da utilização de smartglasses em Neurocirurgia com assistência remota. 38º Congresso da Sociedade Portuguesa de Neurocirurgia, Portugal, May 25, 2023. (Oral Presentation)

Pedro Batista, ChatGPT: inovação ou risco na educação do doente com Doença de Parkinson submetido a cirurgia de Estimulação Cerebral Profunda? 38º Congresso da Sociedade Portuguesa de Neurocirurgia, Portugal, May 25, 2023. (Oral Presentation)

Pedro Batista, Malformações arteriovenosas da fossa posterior tratadas cirurgicamente e fatores preditores dos resultados. 38º Congresso da Sociedade Portuguesa de Neurocirurgia, Portugal, May 25, 2023. (Oral Presentation)

### **Prizes and Honours**

Luísa Lopes and Pedro Batista, “la Caixa” Impulse Innovation Award 2023.

### **Advanced Teaching**

Luísa Lopes, Coordination of Master Curricular Unit, Master in Biomedical Sciences, Portugal.

Luísa Lopes, Lecture, MSc/PhD Neurosciences, Portugal.

Luísa Lopes, Lecture, PhD Programme in Experimental Biology and Biomedicine, Portugal.

Luísa Lopes, Lecture, PhD Mental Health, Portugal.

Luísa Lopes, Lecture, Course in Neurodegenerative Diseases, NMS Lisbon Portugal.

Luísa Lopes, Lecture, Neurophysiology Course, France.

### **MSc Theses**

Estefanía García Luna, Sleeping habits and job performance, a study in agrotechnology companies in Colombia, Supervisor: Cátia Reis, Master in Psychology in Business and Economics – Universidade Católica Portuguesa, Portugal, August 7, 2023.

Catarina Ferreira, Direct Conversion of Human Skin Fibroblasts into induced Neurons: A Model to Study Age-Related Synaptic Dysfunctions, Supervisor: Joana Coelho, Faculdade de Ciências da Universidade de Lisboa, Portugal, September 26, 2023.

Luís M, Behavioral and Cognitive Defects in the VPA-ASD rodent model of Autism, Supervisor: Miguel Remondes, Faculdade de Ciências da Universidade de Lisboa, Portugal.

### **PhD Theses**

Joana Rajão-Saraiva, Mechanisms underlying the physiological role of Amyloid Precursor Protein in glutamatergic synapses, Supervisor: Luísa Lopes, Co-Supervisor: Paula Pousinha, Faculdade de Medicina da Universidade de Lisboa, Portugal.

## Valorization of Knowledge / Social and Economic Impact

### Partnerships with Industry in 2023

Bial, Research Project, Contract Research.

Ionis, Research Project, Collaborative Research.

### Science and Society in 2023

Luísa Lopes - Monthly opinion article to Público: <https://www.publico.pt/autor/luisa-lobes>

Luísa Lopes - Bimonthly opinion article to Líder in the Futuristas project:  
<https://lidermagazine.sapo.pt/os-futuristas-o-futuro-do-futuro-a-nova-rubrica-editorial-da-lider-e-apresentada-hoje/>

Luísa Lopes - Several interviews and participations in podcasts:  
<https://www.engenhariaradio.pt/2024/01/erro-de-pandora-9/>

The whole group participated in the Brain Awareness Week 2023 with visits and lectures to schools.

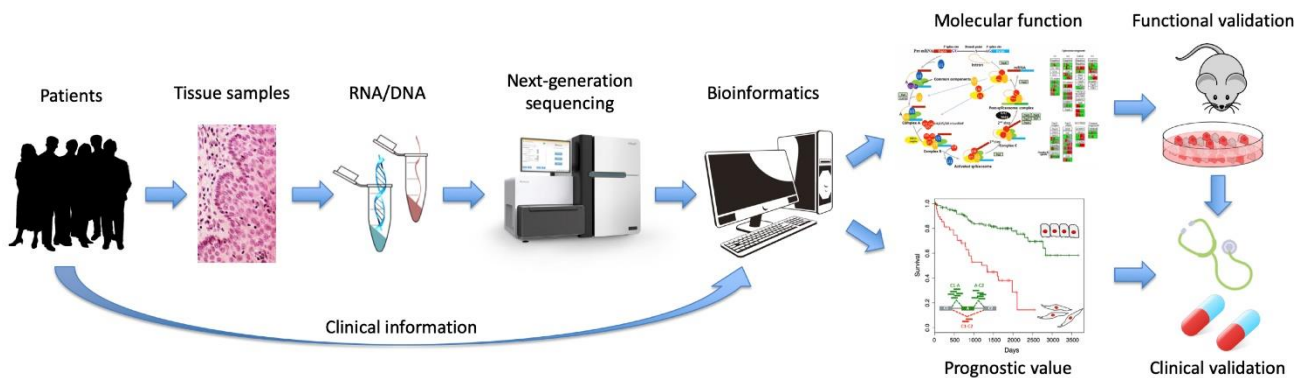
## Nuno Morais Lab

**Head of Laboratory:** Nuno Luís Barbosa Morais, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Guest Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Alexandre Miguel Kaizeler Guedes da Silva Afonso	Master Degree	PhD Student
Ana Marta Fernandes Bica	Master Degree	PhD Student
Joel Amaque da Silva Indi	Master Degree	PhD Student
José Cândido de Oliveira Alves Ferrão	Master Degree	MSc Student
Maria Francisca Telles de Freitas Xara-Brasil	Master Degree	PhD Student (Started January)
Mariana da Ascensão Ferreira	Master Degree	PhD Student
Miguel Casanova Vieira Parente	PhD	MSc Student
Nuno Daniel Saraiva Agostinho	Master Degree	PhD Student (Left May)
Rita Martins Tereso Borges da Silva	Master Degree	PhD Student

### Graphical Abstract



### Lab Interests

We have a long-term interest in the systems-level transcriptional regulation underlying mammalian cell specification, often perturbed in disease. We aim to understand how RNA-level (transcription initiation, splicing, etc.) changes in (mostly) human tissues increase proneness to diseases, namely cancer, neurodegenerative disorders and other ageing-related pathologies. We thereby aim to identify molecular targets for functional exploration *in vitro* and *in vivo*.

We also combine molecular and clinical information for the unveiling of novel candidate prognostic factors and therapeutic targets. Along the way, we develop some tools for assisting non-computational scientists in their analyses of transcriptomic data.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

We released a stable version of scStudio, a web app for interactive and flexible analysis of single-cell RNA-seq data, that has been instrumental to our collaborations with the teams of Karine Serre (on the role of myeloid cells in the breast tumour microenvironment) and Joana Neves (on immune modulation in tissue repair) at IMM. We also introduced significant improvements to two other bioinformatics web apps, betAS (intuitive analysis and visualisation of differential alternative splicing using beta distributions) and voyAGER (web interface for the analysis of age-related gene expression alterations in human tissues).

Nuno Morais co-organised (with Claus Azzalin, Vanessa Morais and Marc Veldhoen, and help from the Lab), the EMBO Young Scientists' Forum at Instituto de Medicina Molecular João Lobo Antunes.

Nuno Saraiva-Agostinho successfully defended his PhD thesis.

### **Ongoing Projects**

2020/2023: Protocolo Limm. Coordinator: Nuno Morais. Funding Agency: Limm Therapeutics. Reference: Protocolo Limm. Amount: 79 896,00€. Total Amount: 79 896,00€.

2019/2023: Inovação de GWAS em cancro da mama através da integração de genómica funcional. Coordinator: Joana Xavier. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: Intergen. Amount: 500,00€. Total Amount: 500,00€.

## Scientific Impact

### Academic Collaborations

- Claus Azzalin Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Leonor Saúde Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Jesús Gil Lab, MRC LIMS, United Kingdom.
- Neves & Sousa-Victor Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Karine Serre's team (Ribot & Silva-Santos Lab/iMM-Laço Hub), Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Mónica Bettencourt-Dias Lab, Instituto Gulbenkian de Ciência, Portugal.
- Manuel Irimia, CRG Barcelona, Spain.
- Luísa Lopes Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Luís Costa Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### Selected Publications

Ascensão-Ferreira M\*, Martins-Silva R\*, Saraiva-Agostinho N, Barbosa-Morais NL (2023). [betAS: intuitive analysis and visualisation of differential alternative splicing using beta distributions](#). *bioRxiv* 2022.12.26.521935.

**Relevance of the publication:** betAS is a web app and an R package for visual and intuitive analysis of differential alternative splicing from RNA-seq read count data, exploiting Beta distributions for a compromise between modelling the estimation uncertainty in individual samples and accounting for variability among replicates, overlooked or made unintelligible by most other available tools.

Rathore OS, Silva RD, Ascensão-Ferreira M, Matos R, Carvalho C, Marques B, Tiago MN, Prudêncio P, Andrade RP, Roignant JY, Barbosa-Morais NL\*, Martinho RG\* (2020). [NineTeen Complex-subunit Salsa is required for efficient splicing of a subset of introns and dorsal-ventral patterning](#). *RNA*, 26(12):1935-1956.

**Relevance of the publication:** We herein showed that the Prp19 complex subunit Salsa is required for efficient splicing of small first introns and dorsal-ventral patterning in *Drosophila* oogenesis. This study highlights the importance of profiling intron retention and of using Beta distributions in analyses of differential alternative splicing.

Munkley J, Li L, Krishnan SRG, Hysenaj G, Scott E, Dalgliesh C, Oo HZ, Maia TM, Cheung K, Ehrmann I, Livermore KE, Zielinska H, Thompson O, Knight B, McCullagh P, McGrath J, Crundwell M, Harries LW, Daugaard M, Cockell S, Barbosa-Morais NL\*, Oltean S\*, Elliott DJ\*. (2019). [Androgen-regulated transcription of ESRP2 drives alternative splicing patterns in prostate cancer](#). *eLife* 8:e47678.

**Relevance of the publication:** This article describes a regulatory circuit involving ESRP-regulated epithelial splicing switches in prostate cancer. We found that these switches can be triggered by changes in expression of ESRP2 induced by androgens, thus linking hormonal/transcription control to isoform changes. Our group led the alternative splicing analyses, including its integration with clinical information.

de Almeida BP, Vieira AF, Paredes J, Bettencourt-Dias M, Barbosa-Morais NL (2019). [Pan-cancer association of a centrosome amplification gene expression signature with genomic alterations and clinical outcome](#). *PLoS Computational Biology* 15(3):e1006832.

**Relevance of the publication:** We herein showed the pan-cancer association of a centrosome amplification gene expression signature with genomic alterations and clinical outcome and combined data on chemical perturbations and drug sensitivity to identify candidate compounds for selectively targeting cancer cells exhibiting transcriptomic evidence for centrosome amplification.

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

**Relevance of the publication:** We developed a new software for the analysis of large databases with clinical and splicing information for thousands of tumours that allows the detection of patterns of similarities between different cases and the identification of molecular alterations associated with prognosis and resistance to therapy of different types of cancer. In practice, the interactive program allows to quickly convert a lot of genome-wide data into biological information with clinical potential.

### 2023 Publications in Peer-Reviewed Journals

Martins, I., Neves-Silva, D., Ascensão-Ferreira, M., Dias, A. F., Ribeiro, D., Isidro, A. F., Quitéria, R., Paramos-de-Carvalho, D., Barbosa-Morais, N. L., & Saúde, L (2023). Mouse Spinal Cord Vascular Transcriptome Analysis Identifies CD9 and MYLIP as Injury-Induced Players. *International journal of molecular sciences*, 24(7):6433.

### Pre-Prints

Ascensão-Ferreira M\*, Martins-Silva R\*, Saraiva-Agostinho N, Barbosa-Morais NL (2023). betAS: intuitive analysis and visualisation of differential alternative splicing using beta distributions. *bioRxiv* 2022.12.26.521935.

Schneider AL\*, Martins-Silva R\*, Kaizeler A\*, Saraiva-Agostinho N, Barbosa-Morais NL (2023). voyAGER: free web interface for the analysis of age-related gene expression alterations in human tissues. *bioRxiv* 2022.12.22.521681.

Sousa NS, Bica M, Brás MF, Antunes IB, Encarnação IA, Costa T, Martins IB, Barbosa-Morais NL, Sousa-Victor P, Neves J (2023). The immune landscape of murine skeletal muscle regeneration and aging. *bioRxiv* 2023.11.07.565995.

Moreno-Marin N, Marteil G, Fresmann NC, de Almeida BP, Dores K, Fragoso R, Cardoso J, Pereira-Leal JB, Barata JT, Godinho S, Barbosa-Morais NL, Bettencourt-Dias M (2023). High prevalence and dependence of centrosome clustering in mesenchymal tumors and leucemia. *bioRxiv* 2023.03.13.532472.

### **Invited Lectures and Seminars**

Nuno Morais, Biologia computacional no estudo do que os transcritomas nos dizem sobre doenças. O que há de novo no Centro Académico de Medicina de Lisboa, Lisbon, Portugal, March 30, 2023.

Nuno Morais, What makes a good computational biologist? InSlicoClub@UCIBIO, Online, Portugal, June 27, 2023.

Nuno Morais, What transcriptomes tell us about ageing and associated diseases? Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, September 22, 2023.

Nuno Morais, Disease transcriptomes and cognitive biases. NeuroSeS, Lisbon, Portugal, November 7, 2023.

### **Communications**

#### Communications in International Conferences:

Rita Martins-Silva, p16 as a transcriptomic marker of cell senescence regulation. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Alexandre Kaizeler, Does Size Matter? The Role of RNA Length in the Stress Granule Transcriptome. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Francisca Xara-Brasil, Alternative transcript expression in colorectal cancer. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Marta Bica, scStudio: A web portal for intuitive and flexible analysis of public scRNA-seq data. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Marta Bica, scStudio: A web portal for intuitive and flexible analysis of public scRNA-seq data. CICON23 — International Cancer Immunotherapy Conference, Milan, Italy, September 21, 2023. (Poster Presentation)

#### Communications in National Conferences:

Alexandre Kaizeler, A Computational Approach to Define a Stress Granule Signature and its Implication in Cancer. RNA in Disease - RiboMed and IX ptRNA joint meeting, Lisbon, Portugal, January 27, 2023. (Poster Presentation)



Rita Martins-Silva, p16 as a transcriptomic marker of cell senescence regulation. RNA in Disease - RiboMed and IX ptRNA joint meeting, Lisbon, Portugal, January 27, 2023. (Poster Presentation)

Marta Bica, Single-cell transcriptomics in unravelling the therapeutic potential of myeloid cells in breast cancer. RNA in Disease - RiboMed and IX ptRNA joint meeting, Lisbon, Portugal, January 27, 2023. (Oral Presentation)

Mariana Ascensão-Ferreira, Intuitive analysis and visualisation of the alternative splicing landscape of senescent cells. RNA in Disease - RiboMed and IX ptRNA joint meeting, Lisbon, Portugal, January 27, 2023. (Poster Presentation)

Marta Bica, A web portal for intuitive and flexible analysis of public scRNA-seq data. 10X Genomics User Group Meeting (Bonsai Lab), Lisbon, Portugal, May 25, 2023. (Poster Presentation)

Francisca Xara-Brasil, Alternative transcription in colorectal cancer: from (dys)regulation to prognosis and therapeutics. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 10, 2023. (Oral Presentation)

Rita Martins-Silva, p16 as a transcriptomic marker of cell senescence regulation. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 11, 2023. (Poster Presentation)

Alexandre Kaizeler, A Computational Approach to Define a Stress Granule Signature and its Implication in Cancer. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 11, 2023. (Poster Presentation)

Marta Bica, scStudio: A web portal for intuitive and flexible analysis of public scRNA-seq data. XVI CAML PhD Students Meeting, Lisbon, Portugal, May 11, 2023. (Poster Presentation)

### **Organization of Conferences**

Rita Martins-Silva, Alexandre Kaizeler and Marta Bica, Co-Organizer, XVI CAML PhD Students Meeting, Lisbon, Portugal, May 9-12, 2023.

Nuno Morais (& Lab), Co-Organizer, 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12-13, 2023.

### **Networks and Research Infrastructures**

Marta Bica, Mye-InfoBank - Converting molecular profiles of myeloid cells into biomarkers for inflammation and cancer, Member of data mining Working Group.

Nuno Morais, GenomePT - Portuguese distributed genome sequencing and analysis infrastructure, Member of Executive Committee, Work Package leader, local PI.

Nuno Morais, BioData.pt - Portuguese distributed infrastructure for biological data, Instituto de Medicina Molecular João Lobo Antunes representative.

Nuno Morais, Horizon 2020 Twinning: "RiboMed: RNA in disease", Co-PI and work package leader (PI: Maria Carmo-Fonseca).

### **Prizes and Honours**

Nuno Morais, Scientific Merit and Professional Ethics recognition, Rotary Club of Viana do Castelo, Portugal, February 19, 2023.

Rita Martins-Silva, Best Graphical Poster, XVI CAML PhD Students Meeting, Portugal, May 9-12, 2023.

Marta Bica, Best Poster, XVI CAML PhD Students Meeting, Portugal, May 9-12, 2023.

Nuno Morais, Invited referee for Nature Communications and Molecular Oncology.

### **Advanced Teaching**

Nuno Morais, Coordination of Master Curricular Unit, Bioinformatics, Masters in Biomedical Research and in Oncobiology, Instituto de Medicina Molecular João Lobo Antunes/Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 2, 2023.

Nuno Morais, Lecture, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 10, 2023.

Nuno Morais, Lecture, Systems Biology, PhD Programs Plants for Life and Molecular Biosciences, ITQB, Oeiras, Portugal, February 7, 2023.

Nuno Morais, Lecture, Applied Computational Multi-Omics, Masters in Computational Biology & Bioinformatics, NOVA School of Science and Technology, Caparica, Portugal, April 3, 2023.

Nuno Morais, Lecture, Bioinformatics, Masters in Biomedical Research, NOVA Medical School, Lisbon, Portugal, October 10, 2023.

Nuno Morais, Coordination of Master Curricular Unit, Computational Biology, Masters in Biomedical Engineering, Instituto Superior Técnico, Lisbon, Portugal, October 16, 2023.

Nuno Morais, Lecture, Neuroethics, Masters in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 19, 2023.

Nuno Morais, Coordination of Master Curricular Unit, Bioinformatics, Masters in Biomedical Research, Instituto de Medicina Molecular João Lobo Antunes/Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 19, 2023.

### **PhD Theses**

Nuno Saraiva-Agostinho, Developing Web Apps for Analyses of Transcriptomes, Supervisor: Nuno Morais, Co-Supervisor: Sérgio de Almeida, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 5, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Nuno Morais was interviewed by José Maria Pimentel for 45 Graus, the most listened to podcast devoted to Critical Thinking in Portugal (March 2023).

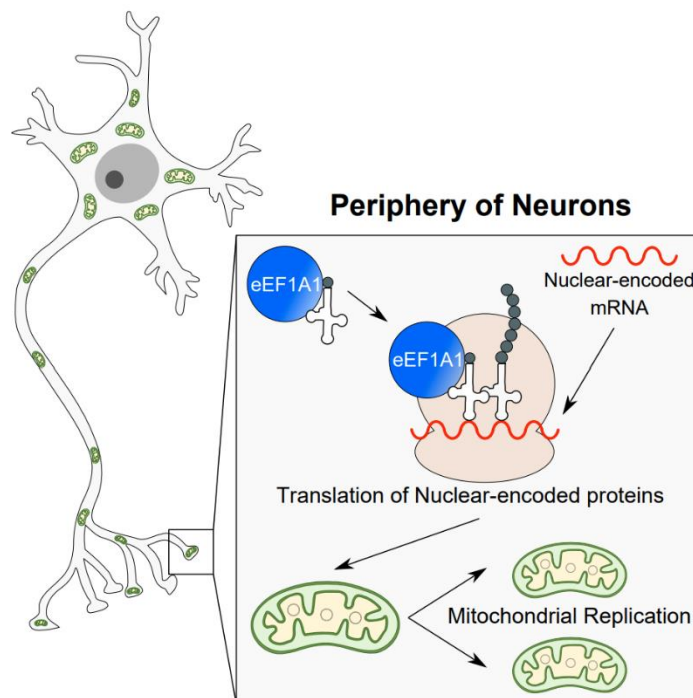
## Vanessa Morais Lab

**Head of Laboratory:** Vanessa A. Morais, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Beatriz Marta Ferreira Madeira Ramos	Master Degree	PhD Student
Andreia Sofia Faria Pereira	PhD	Postdoctoral Researcher
Bernardo Cetra Antunes	Master Degree	PhD Student
Carlos Eduardo Cardanho dos Ramos	Master Degree	PhD Student (Left December)
Elvira Pequeno Leites	Master Degree	PhD Student
Filipa Alexandra Barroso Gonçalves	Master Degree	PhD Student (Left September)
Renata Lopes Familiar Couto	PhD	Postdoctoral Researcher
Rita Abrunhosa Soares	PhD	Postdoctoral Researcher
Tomás Martins Lopes Parra Mateus	University Degree	MSc Student (Left December)

### Graphical Abstract



*Mitochondrial replication occurs in distal regions of neurons: Up until recently, it was thought that mitochondria were only able to replicate at the soma side of neurons. Our recent work has unveiled that mitochondria can replicate at distal regions of the neuron. In neurons, this mitochondrial replication processes requires nuclear-encoded protein translation and mitochondrial-encoded translation is not required for mitochondrial DNA to replication in neurons. Moreover, we have identified that the nuclear-encoded elongation factor eEF1A1 is upregulated at the synapse and is required for mitochondrial replication.*

### **Lab Interests**

Our overarching goal is to clarify the intimate crosstalk between the host cell – the neuron – and the powerhouse organelle – the mitochondria. Synaptic mitochondria compared to mitochondria in other cells, need to cope with increased calcium loads and high energy demands during synaptic activity and neurotransmitter release. However, the evoked mechanisms that enable mitochondria to adapt to this neuronal environment remain elusive. My lab aims to decipher the intrinsic properties of synaptic mitochondria and to scrutinize their relevance for the diseased brain, and to unravel the mitochondrial signature of other brain cells, namely astrocytes and microglia. For this, we focus on mitochondrial morpho-distribution, preferential metabolic fuel source, and the mitochondrial-mediated crosstalk between neurons-astrocytes-microglia.

To achieve this we combine state-of-the-art cell biology, biochemistry and imaging approaches with advanced microfluidic and magnetic separation techniques.

### **Research Fields**

- Molecules of Life: Biological Mechanisms, Structures and Functions
- Neuroscience and Disorders of the Nervous System

### **Major Scientific Achievements in 2023**

A proper mitochondrial function is of utmost importance in neurons. However, little is known about mitochondrial biology and brain homeostasis.

At present, we have:

- Confirmed that standard culture conditions of primary neurons are not being performed in adequate physiological conditions, and that these conditions have a major impact on the mitochondrial bioenergetic profile of these cell types.
- Developed a strategy to isolate different neural cell types from the same mouse brain, thus significantly reducing variability between experiments.
- Unraveled metabolic fuel preference of mitochondria at synapse.
- Deciphered that mitochondrial replication can occur in distal parts of the neuron.
- Observed that modulating mitochondrial dynamics can be a powerful approach to regulate neural stem cell fate.

Our research findings are yielding promising molecular targets that will enable us to unravel the importance of mitochondrial function for synapse biology, and overall brain homeostasis.

## Ongoing Projects

2021/2024: Função mitocôndrial em Esclerose Múltipla: abordagens para prever progressão da doença e promover remielinização. Coordinator: Vanessa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: MITOCHONDRIALMS - PTDC/MED-NEU/7976/2020. Amount: 249 987,50€. Total Amount: 249 987,50€.

2018/2023: EMBO. Coordinator: Vanessa Morais. Funding Agency: European Molecular Biology Organization. Reference: EMBO. Amount: 250 000,00€. Total Amount: 250 000,00€.

2016/2023: SynapticMitochondria: Quality Control and Maintenance of Synaptic Mitochondria. Coordinator: Vanessa Morais. Funding Agency: European Commission. Reference: ERC StG 679178. Amount: 1 300 000,00€. Total Amount: 1 300 000,00€.

## Scientific Impact

### Academic Collaborations

- VIB - Leuven, Belgium.
- North Western University, USA.
- Charité / MDKZ, Germany.
- University Luebeck, Germany.
- University of Exeter, United Kingdom.

### Selected Publications

Faria-Pereira, A; Temido-Ferreira, M; Morais, V A (2022). [BrainPhys neuronal media supports physiological function of mitochondria in mouse primary neuronal cultures](#). **Frontiers in Molecular Neuroscience**, 15: 1-12. DOI: 10.3389/fnmol.2022.837448.

**Relevance of the publication:** Work reveals that standardized culture conditions of primary neuron cultures has a major impact on the mitochondrial bioenergetic profile of these neural cell types.

Soares R, Ribeiro FF, Lourenço DM, Rodrigues RS, Moreira JB, Sebastião AM, Morais VA, Xapelli S (2020) [Isolation and expansion of neurospheres from postnatal \(P1–3\) mouse neurogenic niches](#). **Journal of Visualized Experiments**, 159: e60822.

**Relevance of the publication:** A methods paper with visual-aid that clearly shows how mouse neurosphere cultures from neural stem cell niches can be obtained and maintained and enabling cell-based assays and neural differentiation.

Morais VA\*, Haddad D, Craessaerts K, De Bock P, Swerts J, Vilain S, Aerts L, Overbergh L, Grünewald A, Seibler P, Klein C, Gevaert K, Verstreken P, De Strooper B\* (2014). [PINK1 loss of function mutations affect mitochondrial complex I activity via NdufA10 ubiquinone uncoupling.](#)

**Science** 344:203-7. \*shared corresponding authors.

**Relevance of the publication:** Here we show that PINK1 mediates the phosphorylation of an electro-transport chain Complex I subunit, thereby regulating the coupling of Complex I to ubiquinone.

Haddad D, Vilain S, Vos M, Esposito G, Matta S, Kalscheuer V, Craessaerts K, Leyssen M, Morais VA\*, Verstreken P\* (2013). [Mutations in the intellectual disability gene Ube2a cause neuronal dysfunction and impair parkin-dependent mitophagy.](#) **Molecular Cell** 50:831-41. \*shared

corresponding authors.

**Relevance of the publication:** In intellectual disability patients we found mutations in the E2 conjugase Ube2a and showed that it acts with the E3 ligase Parkin to mediate mitophagy.

Morais VA, Verstreken P, Roethig A, Smet J, Snellinx A, Vanbrabant M, Haddad D, Frezza C, Mandemakers W, Vogt-Weisenhorn D, Van Coster R, Wurst W, Scorrano L, De Strooper B (2009).

[Parkinson's disease mutations in PINK1 result in decreased Complex I activity and deficient synaptic function.](#) **EMBO Molecular Medicine** 1:99-111.

**Relevance of the publication:** A landmark paper that has changed the PINK1 field: PINK1 loss-of-functions causes reduced mitochondrial Complex I activity.

### 2023 Publications in Peer-Reviewed Journals

Nóbrega-Pereira S, Santos F, Oliveira Santos M, Serafim TL, Lopes AP, Coutinho D, Carvalho FS, Domingues RM, Domingues P, Bernardes de Jesus B, Morais VA, Dias S (2023). Mitochondrial Metabolism Drives Low-density Lipoprotein-induced Breast Cancer Cell Migration. *Cancer Res Commun.* 3(4):709-724. doi: 10.1158/2767-9764.CRC-22-0394

Rodrigues JS, Faria-Pereira A, Camões SP, Serras AS, Morais VA, Ruas JL, Miranda JP (2023). Improving human mesenchymal stem cell-derived hepatic cell energy metabolism by manipulating glucose homeostasis and glucocorticoid signaling. *Front Endocrinol.* 13:1043543. doi: 10.3389/fendo.2022.1043543

### Pre-Prints

Cortes-Figueiredo F, Asseger S, Chien C, Zimmermann HG, Ruprecht K, Schmitz-Hübsch T, Bellmann-Strobl J, Paul F, Morais VA (2023). CD4+ T cell mitochondrial genotype in Multiple Sclerosis: a cross-sectional and longitudinal analysis. *medRxiv* 2023.03.22.23287580; doi: <https://doi.org/10.1101/2023.03.22.23287580>

### **Invited Lectures and Seminars**

Vanessa A. Morais, The double-faceted role of PINK1 in Parkinson's disease. University of Coimbra - PDBEB Courses, Portugal, January 30, 2023.

Vanessa A. Morais, Impact of Mitochondrial Function in Neurodegenerative Disorders and Metabolic Diseases. CAML Sessões Clínicas, Portugal, April 27, 2023.

Vanessa A. Morais, Importance of Mitochondria in Parkinson's Disease. XXX Aniversário da Licenciatura Bioquímica, Portugal, April 28, 2023.

Vanessa A. Morais, Mitochondrial Quality Control and Neurodegeneration. MITOporto International Meeting, Portugal, May 12, 2023.

Vanessa A. Morais, Mitochondrial Quality Control and Neurodegeneration. 13th EMBO Young Scientists' Forum, Portugal, October 13, 2023.

### **Communications**

#### Communications in International Conferences:

Bernardo Antunes, Unveiling the metabolic signature of synaptic mitochondria. MITOporto International Meeting, Portugal, May 12, 2023. (Poster Presentation)

Ana B. Ramos, Parkinson's disease: impact of the PINK1-ACAD9 axis on the mitochondrial lipid metabolism and bioenergetics. MITOporto International Meeting, Portugal, May 12, 2023. (Poster Presentation)

Elvira P. Leites, PINK1 and its relevance in different neural cells. MITOporto International Meeting, Portugal, May 12, 2023. (Poster Presentation)

Rita Soares, The role of mitochondrial dynamics in neural stem cell fate. MITOporto International Meeting, Portugal, May 12, 2023. (Poster Presentation)

Carlos Cardanho-Ramos, Mitochondrial replication at the periphery of neurons requires eEF1A1 and local translation of nuclear-encoded proteins. MITOporto International Meeting, Portugal, May 12, 2023. (Oral Presentation)

Andreia Faria-Pereira, The unique bioenergetic fingerprint of synaptic mitochondria. MITOporto International Meeting, Portugal, May 12, 2023. (Oral Presentation)



Renata Couto, Imaging of mitochondrial properties of a living mouse brain using in vivo two-photon microscopy. MITOporto International Meeting, Portugal, May 12, 2023. (Poster Presentation)

Bernardo Antunes, Unveiling the metabolic signature of synaptic mitochondria. EuroMit2023, Italy. (Poster Presentation)

Renata Couto, An experimental protocol for in vivo imaging of brain mitochondrial properties with multiphoton microscopy. EuroMit2023, Italy. (Poster Presentation)

Rita Soares, Uncovering Mitochondrial properties as novel targets for neural stem cell differentiation in the Subventricular Zone. ISN-ESN Meeting 2023, Portugal. (Oral Presentation)

Rita Soares, Mitochondrial properties alter along postnatal neural stem cell differentiation in the Subventricular Zone. FENS Regional Meeting 2023, Portugal. (Poster Presentation)

Ana B. Ramos, Impact of the PINK1-ACAD9 axis on the mitochondrial lipid metabolism and bioenergetics in Parkinson's Disease. EMBO Workshop Inter-organelle contacts biology, Italy. (Poster Presentation)

Andreia Faria-Pereira, The unique bioenergetic fingerprint of synaptic mitochondria. Gordon Research Conference 2023 – Mitochondria in Health and Disease, Italy. (Poster Presentation)

Communications in National Conferences:

Bernardo Antunes, Unravelling the metabolic signature of synaptic mitochondria. XVI CAML/NeurULisboa PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Portugal, May 9-12, 2023. (Oral Presentation)

Ana B. Ramos, Parkinson's disease: impact of the PINK1-ACAD9 axis on the mitochondrial lipid metabolism and bioenergetics. XVI CAML/NeurULisboa PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Portugal, May 9-12, 2023. (Oral Presentation)

Elvira P. Leites, Impact of PINK1 function in different neural cells and its relevance for Parkinson's disease. XVI CAML/NeurULisboa PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Portugal, May 9-12, 2023. (Oral Presentation)

Carlos Cardanho-Ramos, eEF1A1 and nuclear-encoded protein translation are required for mitochondria to replicate in distal regions of neurons. XVI CAML/NeurULisboa PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Portugal, May 9-12, 2023. (Oral Presentation)

### **Organization of Conferences**

Vanessa A. Morais, Co-Organizer, 13th EMBO Young Scientists' Forum, Portugal, October 12-13, 2023.

### **Prizes and Honours**

Andreia Faria-Pereira, Awarded an EMBO Scientific Exchange Grant (10137) to fund research visit to Prof. Michael Schrader's lab (University of Exeter, United Kingdom) from February 2023 to April 2023.

Renata Couto, Best poster award in the MitoPorto – International meeting on Mitochondrial Physiology, Redox Biology and Genetics, Portugal, May 2023.

Rita Soares, European Society for Neurochemistry Young Members Symposia Award, August 2023.

Rita Soares, International Society for Neurochemistry travel grant, August 2023.

Ana Ramos, Travel Grant - EMBO Workshop Inter-organelle Contacts Biology, Fiuggi, Italy, October 2023.

### **Advanced Teaching**

Ana Ramos, Coordination of PhD Curricular Unit, LisbonBiomed PhD course 2023, Portugal.

Ana Ramos, Workshop Organization, Workshop on "Statistical Thinking", organized by the iMM Training Hub, Portugal.

Elvira P. Leites, Workshop Organization, Workshop on "Statistical Thinking", Portugal.

Rita Soares, Workshop Organization, Workshop on "Statistical Thinking", Portugal.

Carlos Cardanho-Ramos, Workshop Organization, Workshop on "Statistical Thinking", Portugal.

Renata Couto, Course Organization, Workshop on Introduction to Statistics, Portugal.

Renata Couto, Course Organization, Workshop on Severity Classification and Reporting, Portugal.

### **MSc Theses**

Tomás Mateus, The role of b-hydroxybutyrate on the energetic homeostasis of synapses and neurons, Supervisor: Vanessa Morais, Instituto de Medicina Molecular João Lobo Antunes, Portugal, December 7, 2023.

### **PhD Theses**

Rita Soares, Role of mitochondrial dynamics and metabolism in postnatal neural stem cells differentiation, Supervisor: Vanessa Morais, Co-Supervisor: Sara Xapelli, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Portugal, May 19, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Rita Soares, Article in the newspaper Público – “Como usar as nossas fábricas de energia para potenciar a regeneração do cérebro”, December 2023.

Rita Soares, Participation in the activities of the European Researchers' Night, Lisbon, Portugal, September 2023.

Rita Soares, Lecture at Agrupamento de Escolas de Cister, Alcobaça to promote the Brain Awareness Week, June 2023. Audience: 150 students from 2nd, 4th, 5th, 9th grades and high school students

Rita Soares, Lecture at Salesianos do Estoril to promote the Brain Awareness Week, April 2023. Audience: 10 students from 5th grade.

Carlos Cardanho-Ramos, 3 Minute Thesis – Comunicação em Ciência, Universidade de Lisboa, Lisbon, Portugal, April 26-28, 2023.

Andreia Faria-Pereira, Volunteer at European Researchers' Night 2023, September 29, 2023.

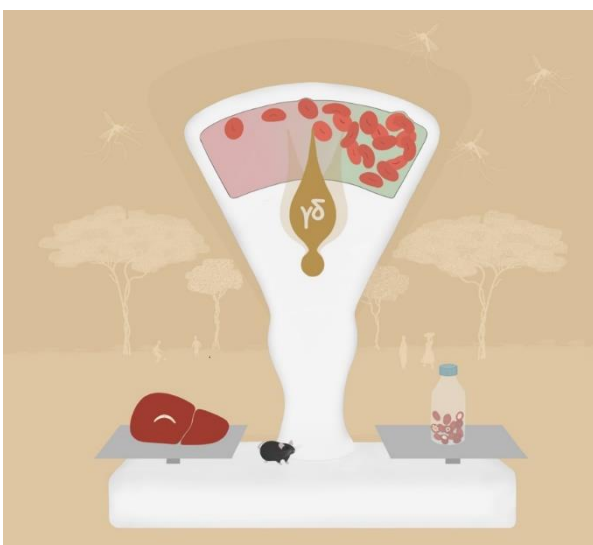
## Maria Mota Lab

**Head of Laboratory:** Maria M. Mota, PhD, Group Leader and Executive Director at Instituto de Medicina Molecular João Lobo Antunes

### Team

Ana Catarina Salgueiro Rodrigues	University Degree	MSc Student
Ana Filipa Caetano Parreira	University Degree	Lab Technician
Ana Margarida Aires Alves Vigário	PhD	Visiting Researcher
André Simões Soares	University Degree	MSc Student (Started May. Left August)
Ângelo António Ferreira Chaves do Rosário Chora	PhD	Senior Postdoctoral Researcher
Bárbara Daniela Araújo Pinheiro Teixeira	Master Degree	PhD Student
Cristina Fernández Arias	PhD	Visiting Researcher (Left November)
Inês Fernandes Bento	PhD	Senior Postdoctoral Researcher
Laura Jantz	University Degree	MSc Student (Left October)
Mariana Vale Amaro de Sousa	University Degree	MSc Student (Started April)
Marta Pires de Miranda	PhD	Senior Postdoctoral Researcher
Nuno Miguel Valente Leal	Master Degree	Lab Technician
Robert Paul Jansen	University Degree	MSc Student (Started January. Left June)
Sara de Jesus Santos Baptista	Master Degree	PhD Student
Sofia Pinto Guia Marques	PhD	Lab Manager
Sónia Maria Leite Pereira	Master Degree	PhD Student (Left September)
Yvonne Azasi	PhD	Postdoctoral Researcher

### Graphical Abstract



*Fine-tuning Malaria Severity. Chora et al. (Immunity) demonstrates the contribution of the liver stage of Plasmodium infection towards the clinical outcome of disease - The liver stage-dependent activation of  $\gamma\delta$  T cells and the integration of host responses during both the liver and the blood stages of infection dictates malaria severity. Drawing by Helena Pinheiro*

### Lab Interests

*Plasmodium* is a fascinating organism that lives a parasitic life style between *Anopheles* mosquitoes and a high variety of vertebrates. In humans, *Plasmodium* is the causative agent of malaria, which still kills a child every minute. *Plasmodium* has co-lived with humans for millennia and we have known it as the cause of malaria for more than 120 years. Still, the goal of malaria eradication remains unfulfilled, partly due to our limited understanding of the biology of *Plasmodium* and of the complex relationship, it maintains with its human host and the environment. Our team aims to generate landmark discoveries that will undoubtedly change the field of parasitology by pursuing two long-lasting questions: (i) What is so special about the liver that allow *Plasmodium* to achieve such an extraordinary rate of replication? & (ii) Why do people die of malaria?

### Research Fields

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

### Major Scientific Achievements in 2023

Our recent work calls into question the long-standing assumption that liver infection does not modulate severity of malaria. Actually, data show that even though severe manifestations of malaria only occur during the BS of infection, signals from the preceding liver stage contribute to disease outcomes, with liver stage and the blood stage interacting towards pathology and disease severity (Chora et al., 2023. Immunity).

Following on previous studies we have now addressed how *Plasmodium* parasites respond to amino acid (AA) availability. The data challenge the paradigm that *Plasmodium* spp. cope with inconsistent AA supply by hibernating until more nutrients are available. In contrast, we showed that *Plasmodium* parasites actively respond to a decrease in methionine and isoleucine by activating, in each life cycle stage, a different protein kinase, ultimately leading to a reprogramming of replication and parasite development (Marreiros et al, 2023. Communications Biology).

## Ongoing Projects

2023/2028: *Plasmodium* liver stage schizogony: high replication and genetic diversity. Coordinator: Maria Mota. Funding Agency: European Commission. Reference: ERC-2022-ADG-PASSAGE. Amount: 2 467 196,25€. Total Amount: 2 467 196,25€.

2023/2026: Genetic variability in *Plasmodium* Liver Stage Schizogony. Coordinator: Maria Mota. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - HR23-00499 – GENEPLISS. Amount: 499 999,50€. Total Amount: 499 999,50€.

2023/2024: Genetic variability in *Plasmodium* liver stage schizogony. Coordinator: Inês Bento. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.04143.PTDC. Amount: 49 772,50€. Total Amount: 49 772,50€.

2022/2023: The enemy within: The unexpected Role of red blood cell Homeostasis in Malarial Anemia. Coordinator: Cristina Arias. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/BIA-BIO/0644/2021. Amount: 49 921,25€. Total Amount: 49 921,25€.

2022/2023: *Plasmodium* exploitation of host immune complement system in malaria. Coordinator: Yvonne Azasi. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/SAU-PAR/1426/2021. Amount: 49 750,00€. Total Amount: 49 750,00€.

2018/2023: 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€.

## Scientific Impact

### Academic Collaborations

- Ann T. Tate, Department of Biological Sciences, Vanderbilt University, USA.
- Catherine Merrick, Department of Pathology, University of Cambridge, United Kingdom.
- Hernando A. Del Portillo. Instituto de Salub Global Bacelona (ISGlobal) & Germans Trias i Pujol Research Institute (IGTP), Spain.
- Ian Cheeseman, Host-Pathogen interactions program at Texas Biomedical Research Institute, USA.
- Katarzyna Modrzynska, School of Infection & Immunity, United Kingdom.
- Mara K N Lawniczak, Parasites and Microbes Programme, Wellcome Sanger Institute, United Kingdom.

- Sabrina Absalon, Indiana University, USA.
- Shalev Itzkovitz, Weizmann Institute of Science, Israel.
- William R. Heath, Peter Doherty Institute for Infection and Immunity, University of Melbourne, Australia.

### Selected Publications

Chora ÂF, Marques S, Gonçalves JL, Lima P, Gomes da Costa D, Fernandez-Ruiz D, Marreiros MI, Ruivo P, Carvalho T, Ribeiro RM, Serre K, Heath WR, Silva-Santos B, Tate AT, Mota MM (2023).

[Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  \$\gamma\delta\$  T cells and IL-17-promoted stress erythropoiesis](#). *Immunity* 56(3):592-605.e8.

**Relevance of the publication:** This work shows that, in the experimental cerebral malaria (ECM) model, infection of the liver by *Plasmodium* modulates severity of disease by generating gamma delta ( $\gamma\delta$ ) T cells that produce IL-17. Data reveals that IL-17 produced by the  $\gamma\delta$  T cells promotes splenic reticulocytosis and that the resulting increase in reticulocyte availability curtails the development of ECM. Overall, these findings challenge the long-standing assumption that liver infection does not modulate severity of malaria.

Afriat, A., Zuzarte-Luís, V., Bahar Halpern, K., ...Mota, M.M., Itzkovitz, S. (2022). [A spatiotemporally resolved single-cell atlas of the Plasmodium liver stage](#). *Nature*, 611(7936), pp. 563–569.

**Relevance of the publication:** The first comprehensive study of *in vivo* gene expression during the liver stage of *Plasmodium berghei*. Gene-expression data from infected hepatocytes and parasite cells over time is provided and the data suggest that the parasite randomly infects hepatocytes but preferentially develops in pericentral hepatocytes and fails to develop in a subpopulation of periportal hepatocytes. This publication considerably advances our understanding of parasite–host interactions.

Mukherjee, D., Chora, Â.F., Lone, J.-C., ...Varga-Weisz, P., Mota, M.M. (2022). [Host lung microbiota promotes malaria-associated acute respiratory distress syndrome](#). *Nature*

### Communications

**Relevance of the publication:** This work shows that alterations of the host microbiota colonizing the lung are a contributing factor of host mortality due to MA-ARDS, a severe malaria pathology. Sequestration of *Plasmodium* causes persistent immune activation with production of the anti-inflammatory cytokine IL-10, facilitating the outgrowth of the local microbiota and contributing to the establishment of MA-ARDS. These data may prove useful in the clinical management of patients with respiratory life-threatening complications.

Real E, Rodrigues L, Cabal GG, Enguita FJ, Mancio-Silva L, Mello-Vieira J, Beatty W, Vera IM, Zuzarte-Luís V, Figueira TN, Mair GR, Mota MM (2018). [Plasmodium UIS3 sequesters host LC3 to avoid elimination by autophagy in hepatocytes](#). *Nature Microbiology* 3(1):17-25.

**Relevance of the publication:** Our work shows that *Plasmodium berghei* parasites infecting hepatic cells rely on a parasite protein – UIS3 – that resides at the parasitophorous vacuole membrane to avoid elimination by host-cell-mediated autophagy. UIS3 acts as a bona fide autophagy inhibitor by competing with host LC3-interacting proteins for LC3 binding. We propose that the protein-protein interaction between UIS3 and host LC3 represents a target for antimalarial drug development.

Mancio-Silva L, Slavic K, Grilo Ruivo MT, Grosso AR, Modrzynska KK, Vera IM, Sales-Dias J, Gomes AR, MacPherson CR, Crozet P, Adamo M, Baena-Gonzalez E, Tewari R, Llinás M, Billker O, Mota MM (2017). [Nutrient sensing modulates malaria parasite virulence](#). *Nature* 13:213-216.

**Relevance of the publication:** A kinome analysis combined with chemical and genetic approaches identified Plasmodium kinase – KIN - as a critical regulator that senses nutrients and controls a transcriptional response to the host nutritional status. KIN shares homology with SNF1/AMPK $\alpha$ , and the data suggest that it is part of a functionally conserved cellular energy-sensing pathway. Overall, these findings reveal a key parasite nutrient-sensing mechanism that is critical for modulating parasite replication and virulence.

### 2023 Publications in Peer-Reviewed Journals

Vigário AM and Pamplona A (2023).  $\gamma\delta$  T cells as immunotherapy for malaria: balancing challenges and opportunities. *Front. Immunol.* 14:1242306.

Henriques P, Rosa A, Caldeira-Araújo H, Soares P and Vigário AM (2023). Flying under the radar – impact and factors influencing asymptomatic DENV infections. *Front. Cell. Infect. Microbiol.* 13:1284651.

Lahree A, Mello-Vieira J, Mota MM (2023). The nutrient games - Plasmodium metabolism during hepatic development. *Trends Parasitol.* 39(6):445-460.

Harris CT, Tong X, Campelo R, Marreiros IM, Vanheer LN, Nahiyaan N, Zuzarte-Luís VA, Deitsch KW, Mota MM, Rhee KY, Kafsack BFC (2023). Sexual differentiation in human malaria parasites is regulated by competition between phospholipid metabolism and histone methylation. *Nat Microbiol.* 8(7):1280-1292.

Chora ÂF, Marques S, Gonçalves JL, Lima P, Gomes da Costa D, Fernandez-Ruiz D, Marreiros MI, Ruivo P, Carvalho T, Ribeiro RM, Serre K, Heath WR, Silva-Santos B, Tate AT, Mota MM (2023). Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  $\gamma\delta$  T cells and IL-17-promoted stress erythropoiesis. *Immunity.* 56(3):592-605.e8.



Marreiros IM, Marques S, Parreira A, Mastrodomenico V, Mounce BC, Harris CT, Kafsack BF, Billker O, Zuzarte-Luís V, Mota MM (2023). A non-canonical sensing pathway mediates *Plasmodium* adaptation to amino acid deficiency. *Commun Biol.* 6(1):205.

### **Invited Lectures and Seminars**

Maria M. Mota, The Host-*Plasmodium* Affair. Cell Biology and Infection Seminar, Pasteur Curie MBOC, Institute Pasteur, France, February 5, 2023.

Maria M. Mota, Host-*plasmodium* interaction: a tale of symbiosis and pathogenesis. Parasitology Seminars, PennVet University of Pennsylvania, Online, April 10, 2023.

Ângelo Ferreira Chora, GD T cells: fine-tuners of malaria pathology. GD T cell club Webinar Series, Online, July 27, 2023.

### **Communications**

#### Communications in International Conferences:

Bárbara Teixeira, Detecting the liver stage of *Plasmodium* infection associated with extracellular vesicles. The Extracellular Vesicles: Friends and Foes II, Israel, March 1, 2023. (Poster Presentation)

Maria M. Mota, Host-*plasmodium* interaction: a tale of symbiosis and pathogenesis. EMBO | EMBL Symposium: The cellular mechanics of symbiosis, Heidelberg, Germany, March 8, 2023. (Oral Presentation)

Maria M. Mota. 2023 British Society for Parasitology Spring Meeting, Edinburgh, United Kingdom, April 11, 2023. (Oral Presentation)

Yvonne Azasi, Parasite exploitation of host immune complement C1s during malaria infection. Malaria Gordon Research Seminar, Barcelona, Spain, May 27, 2023. (Poster Presentation)

Yvonne Azasi, Transcription factors as key regulators of *Plasmodium* nutrient sensing and virulence. Malaria Gordon Research Seminar, Barcelona, Spain, May 28, 2023. (Poster Presentation)

Maria Mota. 21st Awaji International Forum on Infection and Immunity, Japan, September 3, 2023. (Oral Presentation)

Inês Bento, Expanding the Knowledge in Liver Stage *Plasmodium* Replication using Expansion Microscopy. Molecular parasitology Meeting XXXIV, Woods Hole, USA, September 17, 2023. (Poster Presentation)

Ângelo Ferreira Chora, GD T cells: fine-tuners of malaria pathology. 10th gamma delta T cell Conference, Portugal, September 20, 2023. (Poster Presentation)

Bárbara Teixeira, The liver stage of *Plasmodium* infection – written in extracellular vesicles? The 1st MOVE Symposium, Malaga, Spain, October 1, 2023. (Poster Presentation)

#### Communications in National Conferences:

Ana Margarida Vigário, Madeira's dengue outbreak - neutralizing antibodies 8 years after a symptomatic infection. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Ana Margarida Vigário, Dengue virus infection and long-term health status in Madeira Island: a retrospective questionnaire-based study. 6º Congresso Nacional de Medicina Tropical, Lisbon, Portugal, April 20, 2023. (Poster Presentation)

Bárbara Teixeira, The liver stage of *Plasmodium* infection - written in extracellular vesicles? The 2nd meeting of the Portuguese Network on Extracellular Vesicles, Lisbon, Portugal, June 7, 2023. (Oral Presentation)

#### **Prizes and Honours**

Bárbara Teixeira, Best Presentation Award in the 2nd meeting of the Portuguese Network on Extracellular Vesicles.

Inês Bento, Poster Award - Molecular Parasitology Meeting XXXIV, Woods Hole, USA.

#### **Advanced Teaching**

Inês Bento, Lecture, LisbonBioMed, Portugal, February 13, 2023.

Inês Bento, Lecture, JorTec de Biologia Celular e Molecular, Portugal, February 15, 2023.

Sofia Marques and Inês Bento, Lecture, Masters in Microbiology', Portugal, March 29, 2023.

Ana Margarida Vigário, Lecture, Pós-graduação em Avanços em Oncobiologia Molecular Aplicada ao Diagnóstico e Terapêutica, Portugal, May 24, 2023.

## Valorization of Knowledge / Social and Economic Impact

### Science and Society in 2023

Inês Bento, 'Inspiring Stories by Inspiring Girls Portugal', February 8, 2023.

Ana Margarida Vigário, "UMa investiga" RTP Madeira, Dengue: a importância de compreender as infeções assintomáticas e a situação serológica", February 9, 2023.

Sofia Marques, Ana Parreira, Inês Bento and Nuno Leal, Uma viagem pela Malária, Ciência di Noz Manera!, Programa RAISE, February 15, 2023.

Maria Mota, Conferência Juventude RR/SCML "As chaves do futuro", CCB, April 20, 2023.

Maria Mota, Sessão Harari, O Futuro da Humanidade: Desafios do século XXI, May 29, 2023.

Sofia Marques, Animais na Ciência, Speed Dating - Noite Europeia dos Investigadores 2023, Champalimaud Foundation, September 2023.

Sofia Marques and Inês Bento, "Mosquito Lab - Malária" Workshop AIMS Masterclasses for Medical Students, November 6, 2023.

Maria Mota, Fórum de Outono do INESC - Papel das Entidades de Interface na Criação e Dinamização de Ecossistemas de Inovação, November 21, 2023.

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## Joel Perez-Perri Lab

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**Head of Laboratory:** Joel Perez-Perri, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes (Started July)

### Lab Interests

Aging is characterized by a progressive decline in cellular homeostasis and stands as the single most significant risk factor for many prevalent human diseases. At the heart of cellular homeostasis is the cell's ability to control gene expression, which entails the production of the RNAs and proteins required for proper cellular function. This process is exceptionally complex and prone to age-related malfunction.

Crucial steps in gene expression regulation are elicited at the RNA level by RNA-binding proteins (RBPs) and non-coding RNAs. There is mounting evidence suggesting that many of these processes become compromised in our tissues as we get old. However, the origin, extent and functional implications of these changes remain poorly understood. Our primary objective is to decipher how RBP malfunction and disruptions in RNA regulatory processes contribute to the aging process, and to utilize this knowledge to develop novel therapies aimed at promoting healthspan.

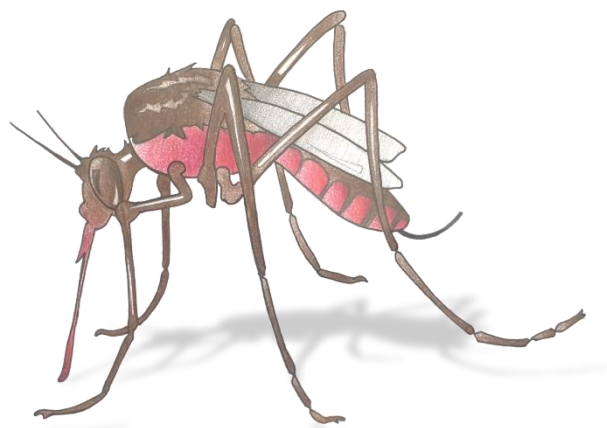
## Miguel Prudêncio Lab

**Head of Laboratory:** Miguel Prudêncio, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Akriti Srivastava	PhD	Postdoctoral Researcher (Started January)
Ana Catarina Freire Fraga	University Degree	MSc Student (Left January)
Ana Sofia Pinto Santana	University Degree	MSc Student
Andreia Filipa Bonecas Mósca	PhD	Postdoctoral Researcher
Bárbara Daniela Araújo Pinheiro Teixeira	Master Degree	PhD Student
Carla Sofia Bastos Oliveira	University Degree	Lab Technician
Catarina Maria Vicente Rôla	University Degree	MSc Student (Left May)
Daniela Cristina de Henriques Brás	Master Degree	PhD Student
Diana Alves Moita	Master Degree	PhD Student
Diana Marisa Pinto Freire Fontinha	PhD	Postdoctoral Researcher
Helena Isabel Marques Nunes Cabaço	PhD	Senior Postdoctoral Researcher
Isabel Margarida Meneses Moules	University Degree	MSc Student (Left January)
Madalena Soares Ferreira de Jesus Carvalho	University Degree	MSc Student (Left April)
Maria Beatriz Valença Rodrigues Maneira Câncio	University Degree	MSc Student (Started September)
Marta Correia Vicente Carvalho de Matos	University Degree	PhD Student (Started September)
Raquel Alves de Azevedo	Master Degree	PhD Student (Left January)
Rita Mateus Lopes	University Degree	MSc Student (Left October)

### Graphical Abstract



*Depiction of Anopheles mosquito, responsible for transmission of malaria parasites. Drawing by Inês Simões.*

### **Lab Interests**

Our research interests span a wide range of topics within the malaria field, with particular emphasis on the hepatic stage of infection by *Plasmodium* parasites.

Our current research focuses on:

- Investigating the reciprocal influence of *Plasmodium* and viral or parasitic co-infections.
- Developing and evaluating the activity of novel antiplasmodial compounds.
- Addressing current bottlenecks and knowledge gaps in whole-sporozoite vaccination against malaria.
- Investigating immunomodulation strategies for enhancement of vaccine efficacy.
- Developing a novel whole-sporozoite vaccination strategy.
- Generating monoclonal antibodies against human *Plasmodium* parasites.
- Developing novel strategies to assess *Plasmodium* hepatic infection.

### **Research Fields**

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

### **Major Scientific Achievements in 2023**

Throughout 2023, we have:

- Established new models of co-infection between *Plasmodium* parasites and different viral infection agents.
- Established a novel setup for culturing of Leishmania parasites.
- Established the proof-of-concept of a novel strategy for drug-based immunomodulation of antimalarial responses.
- Elucidated the impact of infection by SARS-CoV-2 on a subsequent *Plasmodium* infection and on malaria pathology.
- Employed rodent models to carry out the most comprehensive head-to-head comparative analysis to date of different whole-sporozoite formulations for vaccination against malaria.
- Established a new model to investigate the impact of age and pre-exposure to malaria parasites on the efficacy of whole-sporozoite vaccination against malaria.

## Ongoing Projects

2023/2023: Ivermectin hybrids – potential insecticidal and multistage antiplasmodial drugs for malaria control. Coordinator: Diana Fontinha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02624.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2022/2024: *Plasmodium*, herpesvirus and the development of Burkitt's lymphoma. Coordinator: Miguel Prudêncio. Funding Agency: Ares Trading, S.A. Reference: VIRIATO MBANA – MPRUDENCIO. Amount: 15 000,00€. Total Amount: 15 000,00€.

2021/2024: Whole-organism vaccines against *P. falciparum* and *P. vivax* malaria with enhanced efficacy and scope. Coordinator: Miguel Prudêncio. Funding Agency: “la Caixa” Foundation. Reference: LA CAIXA - MALVAX+ - HR21-00848. Amount: 758 082,50€. Total Amount: 758 082,50€.

2020/2023: AMAZING – toxinas de serpentes da AMAZónia: INvestiGação na valorização de biorrecursos. Coordinator: Miguel Prudêncio. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: CIRCNA/BRB/0281/2019. Amount: 74 615,00€. Total Amount: 234 214,63€.

2017/2023: *Plasmodium falciparum*-infected mosquitoes in order to obtain infective sporozoides to be employed in hepatic cell-infection studies. Coordinator: Miguel Prudêncio. Funding Agency: Ares Trading, S.A. Reference: MERCK. Amount: 342 509,53€. Total Amount: 342 509,53€.

2015/2023: *Plasmodium* infection of 3D hepatic cell cultures. Coordinator: Miguel Prudêncio. Funding Agency: IBET. Reference: 3D HEPATIC INFECTIONS. Amount: 251 250,00€. Total Amount: 251 250,00€.

## Scientific Impact

### Academic Collaborations

- Merck KGaA, Germany.
- Guru Nanak Dev University, India.
- University of Washington, USA.
- Sanaria, Inc., USA.
- Leiden University Medical Centre, The Netherlands.
- Oregon Health & Science University, USA.
- Universidade do Porto, Portugal.

- Radboud University Medical Centre, The Netherlands.
- University of Oxford, United Kingdom.

### Selected Publications

D. Moita, C. Rôla, H. Nunes-Cabaço, G. Nogueira, T.G. Maia, A.S. Othman, B. Franke-Fayard, C.J. Janse, A.M. Mendes\*, M. Prudêncio\* (2023). [The effect of dosage on the protective efficacy of whole-sporozoite formulations for immunization against malaria](#). **NPJ Vaccines**, 182, 1-12.

**Relevance of the publication:** This paper provides the most comprehensive head-to-head comparative analysis of different whole-sporozoite vaccines against malaria in a rodent model of *Plasmodium* infection.

D. Moita, T.G. Maia, M. Duarte, C.M. Andrade, I.S. Albuquerque, A. Dwivedi, J.C. Silva, L. González-Céron, C.J. Janse, A.M. Mendes, M. Prudêncio (2022). [A genetically modified \*Plasmodium berghei\* parasite as a surrogate for whole-sporozoite vaccination against \*P. vivax\* malaria](#). **NPJ Vaccines**, in press.

**Relevance of the publication:** This paper describes for the first time the pre-clinical characterization of a novel rodent *Plasmodium*-based candidate for vaccination against *P. vivax* malaria

I.J. Reuling, A.M. Mendes, G.M. de Jong GM, A. Fabra-García, H. Nunes-Cabaço, G.J. van Gemert, W. Graumans, L.E. Coffeng, S.J. de Vlas, A.S.P. Yang, C.K. Lee, Y. Wu, A.J. Birkett, C.F. Ockenhouse, R. Koelewijn, J.J. van Hellemond, P.J.J. van Genderen, R.W. Sauerwein, M. Prudêncio (2020). [Safety and efficacy of a genetically modified rodent malaria parasite against \*Plasmodium falciparum\* malaria: an open-label randomized phase 1/2a trial](#). **Science Transl. Med.**, 12, eaay2578.

**Relevance of the publication:** First-in-humans clinical evaluation of the biological activity of a transgenic *P. berghei* sporozoite immunization platform expressing *P. falciparum* circumsporozoite protein (PbVac) against controlled human malaria infection (CHMI).

M. Sanches-Vaz, A. Temporão, R. Luis, H. Nunes-Cabaço, A.M. Mendes, S. Goellner, T. Carvalho, L.M. Figueiredo\*, M. Prudêncio\* (2019). [Trypanosoma brucei infection protects mice against malaria](#). **PLoS Pathogens**, 15, e1008145.

**Relevance of the publication:** First experimental assessment of the reciprocal impact between *Plasmodium* and *Trypanosoma* parasites in a rodent model of both infections.



A.M. Mendes, M. Machado, N. Gonçalves-Rosa, I.J. Reuling, L. Foquet, C. Marques, A.M. Salman, A.S.P. Yang, K.A. Moser, A. Dwivedi, C.C. Hermsen, B. Jiménez-Díaz, S. Viera, J.M. Santos, I. Albuquerque, S.N. Bhatia, J. Bial, I. Angulo-Barturen, J.C. Silva, G. Leroux-Roels, C.J. Janse, S.M. Khan, M.M. Mota, R.W. Sauerwein, M. Prudêncio (2018). [A Plasmodium berghei Sporozoite-Based Vaccination Platform against Human Malaria](#). *NPJ Vaccines*, 3, 33.

**Relevance of the publication:** Establishment of the proof-of-concept and pre-clinical validation of *P. berghei*-based vaccination against human malaria.

### 2023 Publications in Peer-Reviewed Journals

M. Sulik, D. Fontinha, D. Steverding, S. Sobczak, M. Antoszczak, M. Prudêncio, A. Huczyński (2024). Unexpected rearrangement of ivermectin in the synthesis of new derivatives with trypanocidal and antiplasmodial activities. *Eur. J. Med. Chem.*, 263, 115951.

A. Fraga, A.F. Mósca, D. Moita, J.P. Simas, H. Nunes-Cabaço, M. Prudêncio (2023). SARS-CoV-2 decreases malaria severity in co-infected rodent models. *Front. Cell. Infect. Microbiol.*, 13, 1307553.

D. Moita, H. Nunes-Cabaço, C. Rôla, B. Franke-Fayard, C.J. Janse, A.M. Mendes, M. Prudêncio (2023). Variable long-term protection by radiation-, chemo-, and genetically-attenuated *Plasmodium berghei* sporozoite vaccines. *Vaccine*, 41, 7618-7625.

D. Moita, C. Rôla, H. Nunes-Cabaço, G. Nogueira, T.G. Maia, A.S. Othman, B. Franke-Fayard, C.J. Janse, A.M. Mendes\*, M. Prudêncio\* (2023). The effect of dosage on the protective efficacy of whole-sporozoite formulations for immunization against malaria. *NPJ Vaccines*, 182, 1-12.

M. Marinović, H. Rimac, L.P. de Carvalho, C. Rôla, S. Santana, K. Pavić, J. Held, M. Prudêncio, Z. Rajić (2023). Design, synthesis and antiplasmodial evaluation of new amide-, carbamate-, and ureido-type harmicines. *Bioorg. Med. Chem.*, 94, 117468.

M.J. Oliveira, S. Caetano, A. Dalot, F. Sabino, T.R. Calmeiro, E. Fortunato, R. Martins, E. Pereira, M. Prudêncio, H.J. Byrne, R. Franco, H. Águas (2023). A simple polystyrene microfluidic device for sensitive and accurate SERS-based detection of infection by malaria parasites. *Analyst*, 148, 4053.

G. da Silva, A.F.S. Luz, D. Duarte, D. Fontinha, V.L.M. Silva, F.A.A. Paz, A.M. Madureira, S. Simões, M. Prudêncio, F. Nogueira, A.M.S. Silva, R. Moreira (2023). Facile access to structurally diverse antimalarial indoles using a one-pot A3 coupling and domino cyclization approach. *ChemMedChem*, 18, e2023002.

S.S. Mendes, M. Sorg, C.M. Luís, D. Fontinha, D. Francisco, D. Moita, C.C. Romão, M.G. Pinho, C. Pimentel, M. Prudêncio, L.M. Saraiva (2023). Conjugated Carbon Monoxide Releasing Molecules have broad-spectrum antimicrobial activity. *Fut. Med. Chem.*, 15 (12), 1037-1048.

M. Fonte, D. Fontinha, D. Moita, O. Caño-Prades, Y. Avalos-Padilla, X. Fernàndez-Busquets, M. Prudêncio, P. Gomes, C. Teixeira (2023). New 4-(N-cinnamoylbutyl) aminoacridines as potential multi-stage antiplasmodial leads. *Eur. J. Med. Chem.*, 258, 115575.

K.H. Breiterová, A. Ritomská, D. Fontinha, J. Kroustková, D. Suchánková, A. Hošťálková, M. Šafratová, E. Kohelová, R. Perinová, R. Vrabec, D. Francisco, M. Prudêncio, Lucie Cahlíková (2023). Derivatives of Amaryllidaceae Alkaloid Ambelline as Selective Inhibitors of Hepatic Stage of *Plasmodium berghei* Infection in Vitro. *Pharmaceutics*, 15, 1007.

J.F. Santos, R. Azevedo, M. Prudêncio, F. Marques, Y. Le Gal, D. Lorcy, C. Fernandes (2023). Block Copolymer Micelles Encapsulating Au(III) Bis(Dithiolene) Complexes as Promising Nanostructures with Antiplasmodial Activity. *Pharmaceutics*, 15, 1030.

#### **Invited Lectures and Seminars**

M. Prudêncio. Perspetivas para a vacinação contra a malária. 43º Ciclo de Conferências sobre Doenças Infeciosas, Hospital de Santa Maria, Portugal, February 17, 2023.

M. Prudêncio. Messenger RNA and new vaccines. Basic Sciences for Sustainable Development, Academia das Ciências de Lisboa, Portugal, March 15, 2023.

M. Prudêncio. Da ideia à patente e da patente à validação clínica de um candidato a vacinação contra a malária. PhDoing: Hoje Ciência, Inovação Amanhã!, Coimbra Institute for Clinical and Biomedical Research, Portugal, May 26, 2023.

M. Prudêncio. Recent advances and new strategies for malaria vaccination. 6th Egas Moniz International Scientific Congress, Monte de Caparica, Portugal, July 5, 2023.

M. Prudêncio. Lessons learnt from the first licensed mRNA vaccines for COVID-19. Congresso Saúde Pública 23, Culturgest, Lisboa, Portugal, July 15, 2023.

M. Prudêncio. Lessons learnt from the first licensed mRNA vaccines for COVID-19. 39º Congresso da Sociedade Portuguesa de Pneumologia, Portugal, November 10, 2023.

## **Communications**

### Communication in International Conferences:

Bárbara Teixeira. Detecting the liver stage of Plasmodium infection associated with extracellular vesicles. Extracellular Vesicles: Friends and Foes II, Israel, March 19, 2023. (Poster Presentation)

Andreia Mósca. Impact of a gammaherpesvirus on Plasmodium berghei infection in vivo. EMBO Young Scientists' Forum (EYSF), Portugal, October 12, 2023. (Poster Presentation)

Bárbara Teixeira. The liver stage of Plasmodium infection – written in extracellular vesicles? 1st Mobility for Vesicles Research in Europe (MOVE) Symposium, Spain, October 24, 2023. (Poster Presentation)

### Communications in National Conferences:

Bárbara Teixeira. The liver stage of Plasmodium infection – written in extracellular vesicles? XVI CAML PhD Meeting, Portugal, May 9, 2023. (Poster Presentation)

Diana Moita. The effect of dosage on the protective efficacy of whole-sporozoite formulations against malaria. 7th RedeSaúde Conference, Portugal, November 14, 2023. (Poster Presentation)

## **Organization of Conferences**

Miguel Prudêncio, Co-Organizer. 7th RedeSaúde Conference, Portugal, November 14, 2023.

## **Advanced Teaching**

Miguel Prudêncio, Lecture, LisbonBioMed, Portugal, February 14, 2023.

Miguel Prudêncio, Lecture, Masters in Biochemistry, Portugal, May 24, 2023.

Miguel Prudêncio, Lecture, Masters in Molecular Biology and Genetics, Portugal, September 27, 2023.

Diana Moita, Lecture, Masters in Molecular Biology and Genetics, Portugal, September 29, 2023.

Miguel Prudêncio, Lecture, Masters in Biomedical Research, Portugal, October 26, 2023.

Diana Moita, Lecture, Masters in Biomedical Research, Portugal, October 26, 2023.

Miguel Prudêncio, Lecture, Masters in Evolution and Developmental Biology, Portugal, October 26, 2023.

Miguel Prudêncio, Lecture, Masters in Public Health and Tropical Medicine, Mozambique, November 21, 2023.

Miguel Prudêncio, Lecture, Masters in Public Health and Tropical Medicine, Mozambique, November 27, 2023.

### **Prizes and Honours**

Diana Moita, 1st Prize 7th RedeSaúde Conference.

Miguel Prudêncio, Prémio Universidade de Lisboa / Caixa Geral de Depósitos.

### **MSc Theses**

Madalena Carvalho, Characterization of a novel whole-sporozoite vaccine against malaria, Supervisor: Raquel Azevedo, Co-Supervisor: Miguel Prudêncio, Faculdade de Ciências da Universidade de Lisboa, Portugal, March 15, 2023.

Ana Fraga, Plasmodium berghei/SARS-CoV-2 co-infection phenotype in murine models, Supervisor: Miguel Prudêncio, Co-Supervisor: Andreia Mósca, Faculdade de Ciências da Universidade de Lisboa, Portugal, March 30, 2023.

Rita Lopes, Using a high-throughput genetic screen to identify Plasmodium molecules that interact with the host's innate immune system, Supervisor: António Mendes, Co-Supervisor: Miguel Prudêncio, Faculdade de Ciências da Universidade de Coimbra, Portugal, June 15, 2023.

Sofia Santana, Screening of compounds against malaria parasites, Supervisor: Diana Fontinha, Co-Supervisor: Miguel Prudêncio, Instituto Superior Técnico da Universidade de Lisboa, Portugal, November 17, 2023.

### **PhD Theses**

Américo José dos Santos Alves, Novel spiro-lactams as new antimicrobial agents, Supervisor: Teresa Maia, Co-Supervisor: Miguel Prudêncio, Faculdade de Ciências da Universidade de Coimbra, Portugal, January 5, 2023.

Raquel Azevedo, Targeting the transmission stage of malaria parasites by drug- and vaccine-based approaches, Supervisor: Miguel Prudêncio, Co-Supervisor: Blandine Franke-Fayard, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 26, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Merck KGaA, Understanding immunomodulatory properties of antimalarial agents. Type of partnership: Contract Research.

### **Science and Society in 2023**

Education:

- “Specific defense mechanisms: vaccines”, 10th and 11th grades (16-17 years old), Conversas com Investigadores, Centro Ciência Viva do Alviela – Carsoscópio, February 27, 2023.

Media Appearances:

- Media appearances on TV, radio and printed press in relation to COVID-19, malaria and science policy.

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## Mário Ramirez Lab

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**Head of Laboratory:** Mário Ramirez, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Catarina da Silva e Costa	PhD	Senior Postdoctoral Researcher
Ana Isabel de Aquino Friães	PhD	Senior Postdoctoral Researcher
Ana Margarida Pires Lavado de Sousa Modesto	Master Degree	Trainee (Left June)
Andreia Filipa Guerreiro Nunes	University Degree	MSc Student (Started September)
Beatriz Vicente dos Santos	University Degree	MSc Student (Left July)
Bruno Brandão de Capistrano	University Degree	MSc Student (Left June)
Bruno Filipe Ribeiro Gonçalves	Master Degree	PhD Student
Catarina Inês Marques de Sousa Mendes	PhD	PhD Student (Left April)
Elisabete Raquel Ferreira Martins	PhD	Senior Postdoctoral Researcher
Fábio Alexandre Súbttil Limpo	University Degree	MSc Student (Left December)
Inês Pereira Blum	University Degree	MSc Student (Left December)
Inês Vicente de Almeida	University Degree	MSc Student
Joana Filipa Gomes da Silva	Master Degree	Lab Technician
José Augusto Gamito Melo Cristino	PhD	Clinical Staff Scientist
Marcos Daniel Caetano Borges de Pinho	PhD	Senior Postdoctoral Researcher
Maria Inês Filipe Mendes	University Degree	MSc Student (Started September)
Milani Sibell Rodrigues	High School Diploma	MSc Student (Left June)
Mykyta Forofontov	Bachelor Degree	MSc Student
Rafael Fresca Mamede	Master Degree	PhD Student
Rita Alexandra Marinheiro Melão	University Degree	MSc Student (Left April)
Rita Margarida Nina Cunha	University Degree	MSc Student (Started September)
Sara Mateus Mahomed	MD/Master Degree	Clinical Researcher
Sheila Correia Joosab	University Degree	MSc Student (Left July)
Thomas Hanscheid	PhD with Habilitation	Clinical Staff Scientist
Yara de Sousa Lobo Almeida	University Degree	MSc Student (Left July)
Yenine Telma Santos Martins	University Degree	MSc Student (Left December)

### Lab Interests

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations. By exploring the relationships between commensal and disease-causing populations of the same bacterial pathogen, we hope to identify particularly virulent clones as well as successful colonizers for further characterization. A strong bioinformatics effort in microbial genomics, microbial typing data sharing, data analysis and visualization tools is ongoing.

The development of novel laboratory methodologies for the diagnosis of infectious diseases, with a special interest in malaria, is also an active area of research.

### **Research Fields**

- Integrative Biology: From Genes and Genomes to Systems
- Prevention, Diagnosis and Treatment of Human Diseases

### **Major Scientific Achievements in 2023**

We made new releases and continued to develop chewBBACA, a tool to create and use whole-genome multilocus sequence typing (wgMLST) and core-genome MLST (cgMLST) schemas. We documented an increase of *Streptococcus pyogenes* pediatric invasive infections following the COVID-19 pandemic that was accompanied by the expansion of a highly virulent clone that was already circulating previously, highlighting a potential role for increased host susceptibility due to lack of circulation of *S. pyogenes* during the pandemic. We continued monitoring pneumococcal invasive disease after the introduction of the 13-valent conjugate vaccine into the national immunization program for children and found that the decrease in disease during the pandemic was followed by a rebound that led to more cases being reported in 2022-23, raising the possibility of an important reduction of the benefits of vaccination and reinforcing the importance of molecular diagnostic methods in the surveillance of these infections.

### **Ongoing Projects**

2023/2025: Creating and refining whole-genome and core-genome typing schemas for pathogen surveillance. Coordinator: Mário Ramirez. Funding Agency: European Commission. Reference: CENTAUR - ISID\_JRA\_GUN1. Amount: 121 947,50€. Total Amount: 121 947,50€.

## **Scientific Impact**

### **Academic Collaborations**

- Institut Pasteur, France.
- Instituto Nacional de Saúde Dr. Ricardo Jorge, Portugal.
- Boston Children's Hospital, USA.
- INESC-ID, Portugal.
- Amsterdam UMC, The Netherlands.

### Selected Publications

Gouveia, C., Bajanca-Lavado, M. P., Mamede, R., Araújo Carvalho, A., Rodrigues, F., Melo-Cristino, J., Ramirez, M., Friães, A., Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Pediatric Invasive Streptococcal Disease, & Portuguese Study Group of Paediatric Invasive Streptococcal Disease (2023). [Sustained increase of paediatric invasive \*Streptococcus pyogenes\* infections dominated by M1UK and diverse emm12 isolates, Portugal, September 2022 to May 2023](#). **Euro Surveillance: Bulletin Europeen Sur Les Maladies Transmissibles = European Communicable Disease Bulletin**, 28(36), 2300427.

**Relevance of the publication:** It was the third published description of an increase in GAS invasive infections post-COVID. We found that this increase was not due to a single clone, as found in the UK, but to diverse lineages and that the increase in Portugal was sustained throughout many months, which was also not the case in the UK. These findings highlight the multifactorial causes that may be behind this increase in different regions.

Martins, E. R., Nascimento do Ó, D., Marques Costa, A. L., Melo-Cristino, J., & Ramirez, M (2022). [Characteristics of \*Streptococcus agalactiae\* colonizing nonpregnant adults support the opportunistic nature of invasive infections](#). **Microbiology Spectrum**, 10(3), e0108222. <https://doi.org/10.1128/spectrum.01082-22>

**Relevance of the publication:** This was the largest study of asymptomatic carriage of *Streptococcus agalactiae* (GBS) in non-pregnant adults. We found that the colonization rate among nonpregnant adults was like that of pregnant women and that colonization increased with age, potentially explaining the higher incidence of disease with older age. Asymptomatically carried lineages were indistinguishable from those causing infections, not having identified any GBS lineages having enhanced disease potential.

Silva-Costa C, Gomes-Silva J, Pinho MD, Friães A, Ramirez M, Melo-Cristino J (2022). [Continued vaccine breakthrough cases of serotype 3 complicated pneumonia in vaccinated children, Portugal \(2016-2019\)](#). **Microbiol Spectr** e0107722.

**Relevance of the publication:** This paper continues to document the importance of serotype 3 pneumococcal invasive disease in Portugal. We were pioneers in implementing a molecular diagnostic approach to identify and serotype pneumococci in pleural effusions. Application of these methodologies has the potential to change our view of the morbidity associated with pneumococcal infections and to more accurately measure the impact of vaccination.

Mamede R, Vila-Cerqueira P, Silva M, Carriço JA, Ramirez M (2021). [Chewie Nomenclature Server \(chewie-NS\): a deployable nomenclature server for easy sharing of core and whole genome MLST schemas](#). **Nucleic Acids Res** 49:D660–D666.

**Relevance of the publication:** This paper reports the creation of a website to allow sharing whole-genome multilocus sequence typing (wgMLST) or core-genome MLST (cgMLST) schemas to allow a broader adoption of the proposed schemas facilitating the reproducibility and comparability of data generated by various groups. This website is particularly geared towards the sharing of schemas created by the chewBBACA software but also other allele-calling software.



Adegbite, B. R., Edoa, J. R., Ndzebe Ndoumba, W. F., Dimessa Mbadanga, L. B., Mombo-Ngoma, G., Jacob, S. T., Rylance, J., Hänscheid, T., Adegnika, A. A., & Grobusch, M. P. (2021). [A comparison of different scores for diagnosis and mortality prediction of adults with sepsis in Low-and-Middle-Income Countries: A systematic review and meta-analysis](#). *EClinicalMedicine*, 42, 101184.

**Relevance of the publication:** This paper reports a systematic review and meta-analysis of the utility of scores for diagnosis and prediction of mortality in patients with suspected infection in Low-and-Middle-Income Countries. We found that the performances of current scores ranged from poor to acceptable. This led to the suggestion that future studies should combine selected or modified elements of different scores.

### 2023 Publications in Peer-Reviewed Journals

Silva-Costa, C., Gomes-Silva, J., Santos, A., Ramirez, M., Melo-Cristino, J., & Portuguese Group for the Study of Streptococcal Infections (2023). Adult non-invasive pneumococcal pneumonia in Portugal is dominated by serotype 3 and non-PCV13 serotypes 3-years after near universal PCV13 use in children. *Frontiers in Public Health*, 11, 1279656.

Mendes, G., Santos, M. L., Ramalho, J. F., Bruschy-Fonseca, A., Lito, L., Mendes-Pedro, D., Duarte, A., Melo-Cristino, J., & Caneiras, C (2023). Genomic characterisation of a novel KPC-98-producing clinical *Klebsiella pneumoniae* strain conferring resistance to ceftazidime/avibactam. *International Journal of Antimicrobial Agents*, 62(6), 107013.

Grobusch, M. P., Ruiz Del Portal Luyten, C., Visser, B. J., de Jong, H. K., Goorhuis, A., & Hanscheid, T (2023). Overcoming publication and dissemination bias in infectious diseases clinical trials. *The Lancet. Infectious Diseases*, S1473-3099(23)00455-3.

Gouveia, C., Bajanca-Lavado, M. P., Mamede, R., Araújo Carvalho, A., Rodrigues, F., Melo-Cristino, J., Ramirez, M., Friães, A., Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Pediatric Invasive Streptococcal Disease, & Portuguese Study Group of Paediatric Invasive Streptococcal Disease (2023). Sustained increase of paediatric invasive *Streptococcus pyogenes* infections dominated by M1UK and diverse emm12 isolates, Portugal, September 2022 to May 2023. *Euro Surveillace: Bulletin Europeen Sur Les Maladies Transmissibles = European Communicable Disease Bulletin*, 28(36), 2300427.

Pinto Junior, V. L., Valadas, E., & Hanscheid, T (2023). Combating vaccine hesitancy requires knowledge of misfortunes and controversies. *Acta Medica Portuguesa*, 36(9), 537–540.

Riche, C. V. W., Cassol, R., Falci, D. R., Ramirez, M., & Dias, C. A. G. (2023). Epidemiology and risk factors for mortality among methicillin-resistant *Staphylococcus aureus* bacteremic patients in Southern Brazil. *PloS One*, 18(4), e0283774.

Marinho, P. F., Vieira, S. L., Carvalho, T. G., Peleteiro, M. C., & Hanscheid, T (2023). A novel and simple heat-based method eliminates the highly detrimental effect of xylene deparaffinization on acid-fast stains. *American Journal of Clinical Pathology*, 160(1), 81–88.

Bouchami, O., Machado, M., Carriço, J. A., Melo-Cristino, J., de Lencastre, H., & Miragaia, M (2023). Spontaneous genomic variation as a survival strategy of nosocomial *Staphylococcus haemolyticus*. *Microbiology Spectrum*, 11(2), e0255222. <https://doi.org/10.1128/spectrum.02552-22>

Marinho, P. F., & Hanscheid, T (2023). A simple heat-based alternative method for deparaffinization of histological sections significantly improves acid-fast staining results for *Mycobacteria* in tissue. *MethodsX*, 10, 102079.

Schnyder, J. L., de Jong, H. K., Bache, E. B., van Hest, R. M., Schlagenhauf, P., Borrmann, S., Hanscheid, T., & Grobusch, M. P. (2023). On the potential for discontinuing atovaquone-proguanil (AP) ad-hoc post-exposure and other abbreviated AP-regimens: Pharmacology, pharmacokinetics and perspectives. *Travel Medicine and Infectious Disease*, 52, 102520.

### **Pre-Prints**

Xie, O., Morris, J. M., Hayes, A. J., Towers, R. J., Jespersen, M. G., Lees, J. A., Zakour, N. L. B., Berking, O., Baines, S. L., Carter, G. P., Tonkin-Hill, G., Schrieber, L., McIntyre, L., Lacey, J. A., James, T. B., Sriprakash, K. S., Beatson, S. A., Hasegawa, T., Giffard, P., ... Davies, M. R. (2023). Inter-species gene flow drives ongoing evolution of *Streptococcus pyogenes* and *Streptococcus dysgalactiae* subsp. *Equisimilis* (p. 2023.08.10.552873). *bioRxiv*.

### **Invited Lectures and Seminars**

M Ramirez, *S. pneumoniae*: An architect of genetic plasticity. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Lisbon, May 8, 2023.

## Communications

### Communications in International Conferences:

Martins M, Increase of macrolide resistance among group B streptococcus invasive disease in non-pregnant adults in Portugal (2016-2021) was driven by a single clone. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Denmark, April 15, 2023. (Poster Presentation)

Silva-Costa C, Small decrease of PCV13 serotypes in invasive pneumococcal disease in adults in Portugal 7 years after PCV13 universal use in children. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Denmark, April 15, 2023. (Poster Presentation)

Silva-Costa C, Vaccine serotypes and the post-pandemic rebound of pediatric invasive disease in Portugal (2018-2022) (P1304). 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Denmark, April 15, 2023. (Poster Presentation)

Ramirez M, Etiologic diagnosis from pleural effusion and empyema in pediatrics: is it worth looking beyond *Streptococcus pneumoniae* in the post-pneumococcal vaccine era? 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Denmark, April 15, 2023. (Poster Presentation)

Silva-Costa C, Pediatric non-invasive pneumococcal pneumonia (pNIPP) in Portugal (2017-2022): dominance of serotypes 11A and 23B and the continued importance of vaccine serotypes 3 and 19F. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 8, 2023. (Oral Presentation)

Joana Gomes-Silva, Sustained importance of *Streptococcus pneumoniae* among pediatric complicated pneumonia in Portugal (2019-22). 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 8, 2023. (Poster Presentation)

Friães A, Pediatric invasive infections caused by *Streptococcus pyogenes* in Portugal (2014-2022). 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 8, 2023. (Poster Presentation)

Friães A, Upsurge of pediatric invasive *Streptococcus pyogenes* (Group A *Streptococcus*) infections in Portugal dominated by M1UK and emm12 lineages. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 8, 2023. (Oral Presentation)

Marcos Pinho, *Staphylococcus aureus* causing pediatric invasive infections in Portugal are a diverse population with low representation of MRSA and important virulence genes. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 8, 2023. (Oral Presentation)

Martins M, Changing epidemiology of Group B Streptococcal infections among neonates in Portugal: 2005-2019 surveillance. 41st Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Portugal, May 9, 2023. (Oral Presentation)

Silva-Costa C, Invasive pneumococcal disease in adults in Portugal: small decrease in PCV13 serotypes (2019-2022). 16th European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo), Crete, May 23, 2023. (Poster Presentation)

Silva-Costa C, Serotype 3 dominance in pediatric complicated pneumococcal pneumonia in Portugal during the COVID-19 pandemic (2020-2022). 16th European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo), Crete, May 23, 2023. (Oral Presentation)

Almada-Correia I, Unraveling the mysteries of the connection between gut and the chronic activation of the immune system in Systemic Lupus Erythematosus. European Congress of Rheumatology EULAR 2023, Italy, May 32, 2023. (Poster Presentation)

Martins ER, Changing genetic lineages among *Streptococcus agalactiae* causing invasive disease in non-pregnant adults in Portugal (2016-2021). 3rd International Symposium on *Streptococcus agalactiae* Disease (ISSAD 2023), Brazil, October 16, 2023. (Poster Presentation)

Martins ER, *Streptococcus agalactiae* causing neonatal infections in Portugal (2005–2019): diversification and emergence of a CC17/PI-2b multidrug resistant sublineage. 3rd International Symposium on *Streptococcus agalactiae* Disease (ISSAD 2023), Brazil, October 16, 2023. (Poster Presentation)

Costa-Reis P, Study of the Gut Microbiota and Permeability in Lupus Nephritis. ESPN 55th Annual Meeting, Lithuania, October 28, 2023. (Oral Presentation)

Melo-Cristino J, Pediatric invasive pneumococcal disease: the importance of molecular methods in the diagnosis and serotyping of *Streptococcus pneumoniae* in culture negative samples. 16th International Conference on Molecular Epidemiology and Evolutionary Genetics of Infectious Diseases, Germany, November 14, 2023. (Poster Presentation)

#### Communications in National Conferences:

Costa-Reis P, Microbiota, permeabilidade intestinal e endotoxémia no lúpus eritematoso sistémico. XXVIII Jornadas de Pediatria do Hospital de Santa Maria, Portugal, February 22, 2023. (Oral Presentation)

Almada-Correia I, Gut permeability in lupus nephritis: results from the GUT-LUPUS study. VII Congresso Hispano-Português de Nefrologia Pediátrica 2023 and XLVI Congreso Español de Nefrologia Pediátrica 2023, Portugal, May 28, 2023. (Oral Presentation)

Boto CM, Comparação entre pneumonia por *Streptococcus pneumoniae* versus *Streptococcus pyogenes*. 23º Congresso Nacional de Pediatria, Portugal, October 25, 2023. (Poster Presentation)

Couto C, Infecção profunda dos tecidos moles por *Streptococcus* do grupo A, sem fascíte - a propósito de uma série de casos. 23º Congresso Nacional de Pediatria, Portugal, October 25, 2023. (Poster Presentation)

Forofontov M, Infections in humans in Portugal raise the possibility of food chain transmission of ST283 *Streptococcus agalactiae* from Southeast Asia to Europe. 2nd Microbiome PT Summit, Portugal, October 26, 2023. (Poster Presentation)

#### **Organization of Conferences**

M Ramirez, Co-Organizer, 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Denmark, April 15, 2023.

M Ramirez, Co-Organizer, 16th European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo), Crete, May 23, 2023.

### **Advanced Teaching**

Ramirez M, Coordination of Master Curricular Unit, Medical Microbiology, Portugal, February 1, 2023.

Ramirez M, Lecture, Masters in Biomedical Research, Portugal, December 1, 2023.

### **MSc Theses**

Bruno Brandão de Capistrano, Caracterização de *Streptococcus dysgalactiae* subsp. *equisimilis* responsável por infeção não invasiva no Homem, Supervisor: Pinho M, November 27, 2023.

### **PhD Theses**

Catarina Inês Marques de Sousa Mendes, Towards accreditation in metagenomics for clinical microbiology, Supervisor: Carriço J, Co-Supervisor: Ramirez M, April 17, 2023.

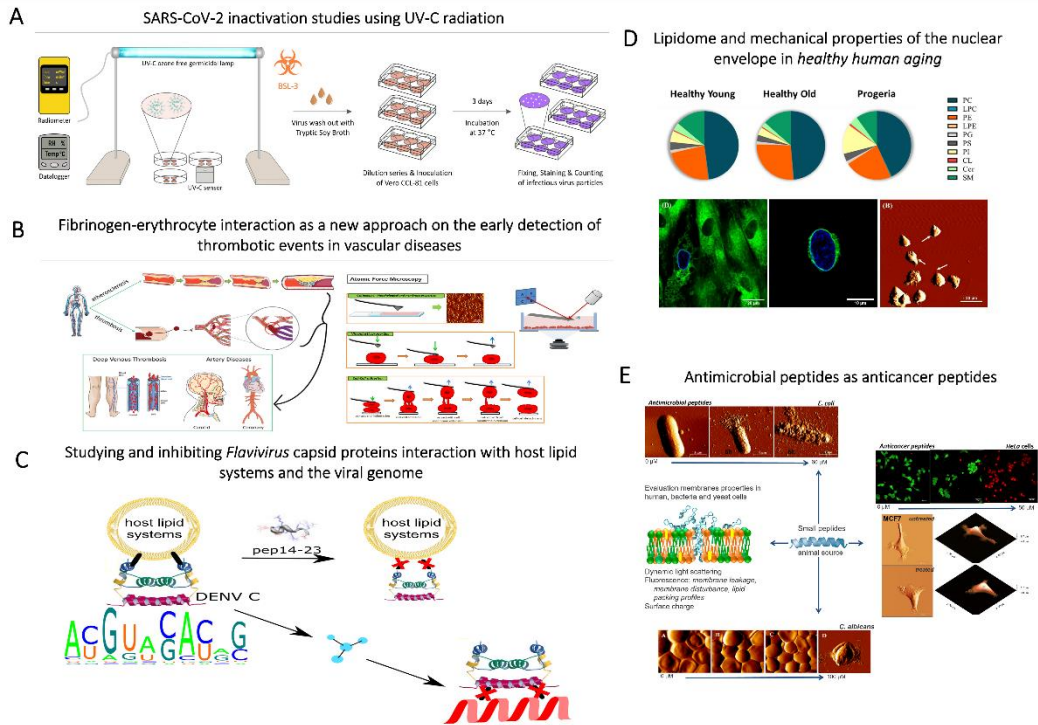
## Nuno Santos Lab

**Head of Laboratory:** Nuno Santos, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Associate Professor with Habilitation at Faculdade de Medicina da Universidade de Lisboa

### Team

Aivaras Vilutis	Master Degree	MSc Student (Started July)
Ana de Souto Martins	PhD	Postdoctoral Researcher (Left November)
Ana Luísa Regatão Tomás	PhD	Postdoctoral Researcher
Ana Paula Morais Condesso	University Degree	MSc Student (Started November)
Ana Rita da Conceição Ferreira da Fonseca	University Degree	MSc Student (Left August)
Andreia Isabel Pereira Cardetas	University Degree	MSc Student (Left September)
Anna Reichel	PhD	Postdoctoral Researcher
Catarina Isabel de Sousa Lopes	Master Degree	PhD Student
Filomena Maria Dias Almeida Carvalho Arede	PhD	Staff Scientist
Francisco Xavier Santos Rocha	University Degree	MSc Student (Started September)
Inês de Andrade Matos Gonçalves Saraiva	Master Degree	PhD Student
Ítala Cristine Silva	Master Degree	PhD Student (Left March)
Ivo Cristiano da Rocha Martins	PhD	Staff Scientist
Joana Catarina Ribeiro Ricardo	PhD	Lab Manager (Started December)
José Maria Ribeiro Coelho	University Degree	MSc Student (Left December)
Maria Constança Gomes Redinha Pais do Amaral	Master Degree	PhD Student (Left March)
Maria João Martins Sarmiento	PhD	Postdoctoral Researcher
Maria Teresa Damásia Freitas Santos	High School Diploma	Lab Technician
Nelly Marine Carreira da Silva	Master Degree	PhD Student
Patrícia Morgado da Silva	Master Degree	PhD Student (Left August)
Pedro Miguel Soares Castro	PhD	Postdoctoral Researcher
Renata Pereira das Neves Baptista Matinhos	University Degree	MSc Student (Started September)
Sónia Gonçalves Abreu	PhD	Staff Scientist
Tomás Luís Guerra Alves Vieira	University Degree	MSc Student (Started September)

## Graphical Abstract



## Lab Interests

Biochemical and biophysical processes occurring in membranes of human cells, and their viral, fungal and bacterial pathogens. Study of the infection cycle and strategies for the inactivation of enveloped viruses, namely SARS-CoV-2, HIV-1, dengue, West Nile, Zika and pediatric respiratory viruses. Collaboration with (inter)national industrial and academic partners, on the development of COVID-19 management and marketable strategies with different applications. Study of fibrinogen-erythrocyte and erythrocyte-erythrocyte binding as a risk determinant in different cardiovascular diseases. Pre-clinical evaluation of membrane activity and mechanism of action of antimicrobial (AMP) and anticancer (ACP) peptides, by themselves or combined with metal nanoparticles. Development of biosensor systems using innovative protein-ligand interactions (e.g. amyloid-based biosensors). Study of cell nucleus biomechanics in human physiological aging and protein-lipid interactions in the nuclear compartment.



### **Research Fields**

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

### **Major Scientific Achievements in 2023**

Among our 2023 achievements, a few are especially worth of notice: i) the promising development of new drug leads to be used and improved as broad-spectrum antivirals and antivirals specifically targeting Zika virus; ii) the translational research results obtained during a follow-up study of carotid artery disease patients, together with clinicians from the Santa Maria Hospital, enabling a better assessment of cardiovascular risk; iii) the identification of the mechanism of action of the antimicrobial peptide EcDBS1R4, which can modulate the activity of ATP synthase upon sequestering cardiolipin at the membrane level; and, iv) the successful completion of two additional PhDs at the Lab.

### **Ongoing Projects**

2023/2025: Res4PrioPath – An Integrated Antiviral Discovery Platform of Broad-Spectrum Small Molecule Inhibitors of Viral Targets from Priority Preparedness Pathogens. Coordinator: Nuno Santos. Funding Agency: European Commission (ISIDORE JRA Programme). Amount: 89 267,06€. Total Amount: 818 063,63€.

2023/2024: AMP-AgNP conjugates: the mutual reinforcement of antibacterial activity. Coordinator: Sónia Gonçalves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.01991.PTDC. Amount: 50 000,00€. Total Amount: 50 000,00€.

2023/2024: Biophysical studies of flavivirus capsid protein interactions with key biological targets to achieve its future inhibition. Coordinator: Ivo Martins. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02763.PTDC. Amount: 43 750,00€. Total Amount: 43 750,00€.

2023/2024: ImPlat: A single-cell platform to validate material scaffolds and drugs for the enhanced osteointegration of biomedical implants. Coordinator: Nuno Santos. Funding Agency: PRR (Call for Proposals: Human-Based Models as Drug Discovery Tools). Amount: 79 818,41€. Total Amount: 79 818,41€.

2022/2024: COMPLICE: COoperative Mechanical couPLing of adherens junctions and focal adhesions supporting breast CancEr progression. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIA-BFS/0812/2021. Amount: 31 250,00€. Total Amount: 249 833,75€.

2022/2024: Nano-coatings for prosthetics based on microbial phenazines conjugated with silver nanostars. Coordinator: Pedro Castro. Funding Agency: “la Caixa” Foundation. Reference: COLOR2COAT - CI23-10134. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2024: Fibrinogen-erythrocyte interaction as a new approach on the early detection of thrombotic events in vascular diseases. Coordinator: Nuno Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EMD-TLM/7289/2020. Amount: 181 950,00€. Total Amount: 181 950,00€.

2021/2023: Exploring lamin-lipid interactions and the loss of nuclear structural integrity as the molecular determinants of human aging. Coordinator: Nuno Santos. Funding Agency: European Commission. Reference: LIPLAGE - MSCA - ITN - 892321 - H2020. Amount: 148 090,04€. Total Amount: 148 090,04€.

2020/2023: Biocolour. Coordinator: Nuno Santos. Funding Agency: European Commission. Reference: Biocolour. Amount: 248 093,00€. Total Amount: 248 093,00€.

## Scientific Impact

### Academic Collaborations

- International Iberian Nanotechnology Laboratory, Portugal.
- J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, Czech Republic.
- Departamento de Física, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, Portugal.
- Universidade Católica de Brasília / Universidade Católica Dom Bosco, Campo Grande, Brazil.
- Serviço de Cirurgia Vascular, Centro Hospitalar Universitário Lisboa Norte- Hospital de Santa Maria, Portugal.
- Faculdade de Farmácia da Universidade de Lisboa, Portugal.

- Instituto de Engenharia Biomédica (INEB) / Instituto de Investigação e Inovação em Saúde (i3S), Universidade do Porto, Portugal.
- Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Portugal.
- Departamento de Química, Faculdade de Ciências da Universidade do Porto, Portugal.
- Faculdade de Medicina, Universidade de Brasília, Brazil.
- Universidade de Aveiro, Portugal.
- Bioinformatics Institute (BII), Agency for Science, Technology and Research (A\*STAR), Singapore.
- CNC and Faculdade de Medicina da Universidade de Coimbra, Portugal.

### Selected Publications

Tomás, A. L., Reichel, A., Silva, P. M., Silva, P. G., Pinto, J., Calado, I., Machado, V., Laranjeira, R., Abreu, P., Mendes, P., Ben Sedrine, N., Santos, N. C. (2022). [UV-C irradiation-based inactivation of SARS-CoV-2 in contaminated porous and non-porous surfaces](#). **Journal of Photochemistry and Photobiology B: Biology**, 234, 112531.

Domingues, M.M., Carvalho, F.A., Santos, N.C. (2022). [Nanomechanics of Blood Clot and Thrombus Formation](#). **Annu Rev Biophys**. 51, 201-221.

Marques, M.C., Lousa, D., Silva, P.M., Faustino, A.F., Soares, C.M., Santos, N.C. (2022). [The Importance of Lipid Conjugation on Anti-Fusion Peptides against Nipah Virus](#). **Biomedicines**, 10, 703.

Gomes B, Augusto MT, Felício MR, Hollmann A, Franco OL, Gonçalves S, Santos NC (2018). [Designing improved active peptides for therapeutic approaches against infectious diseases](#). **Biotechnology Advances** 36:415-429.

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.

### 2023 Publications in Peer-Reviewed Journals

Carvalho, M., Medeiros, M. M., Morais, I., Lopes, C. S., Balau, A., Santos, N. C., Carvalho, F. A, Arez, A. P. (2023). 2,3-Diphosphoglycerate and the Protective Effect of Pyruvate Kinase Deficiency against Malaria Infection-Exploring the Role of the Red Blood Cell Membrane. *Int J Mol Sci*. 24(2)1336.

Lopes, C. S., Curty, J., Carvalho, F. A., Hernández-Machado, A., Kinoshita, K., Santos, N. C., Travasso, R. D. M. (2023). A mathematical model of fibrinogen-mediated erythrocyte-erythrocyte adhesion. *Commun Biol.* 6(1)192.

Cerqueira, M. A., Leite, A. C. C. O., Tomás, A. L., Reichel, A., Silva, P. M., Santos, N. C., Michelin, M., Fuciños, P., Pastrana, L. M. (2023). Edible alginate-based films with anti-SARS-CoV-2 activity. *Food Microbiology.* 113, 104251.

Gonçalves, S., Santos, N. C. (2023). Membrane–Peptide Interactions: From Basics to Current Applications 2.0. *International Journal of Molecular Sciences.* 24(8)7202.

Boon, P. L. S., Martins, A. S., Lim, X. N., Enguita, F. J., Santos, N. C., Bond, P. J., Wan, Y., Martins, I. C., Huber, R. G. (2023). Dengue Virus Capsid Protein Facilitates Genome Compaction and Packaging. *Int J Mol Sci.* 24(9)8158.

Makowski, M., Almendro-Vedia, V. G., Domingues, M. M., Franco, O. L., López-Montero, I., Melo, M. N., Santos, N. C. (2023). Activity modulation of the Escherichia coli F1FO ATP synthase by a designed antimicrobial peptide via cardiolipin sequestering. *iScience.* 26, 107004.

Angeles-Boza, A.M., Santos, N.C., Cardoso, M. H. (2023). Editorial: Improving antimicrobial peptides translational potential through peptidomimetics. *Front. Microbiol.* 14, 1304997.

Lopes, C.S., Pronto-Laborinho, A.C., Conceição, V.A., Freitas, T., Matias, G.L., Gromicho, M., Santos, N.C., de Carvalho, M., Carvalho, F.A. (2023). Erythrocytes' surface properties and stiffness predict survival and functional decline in ALS patients. *Biofactors.* 2023, 1-14.

Sarmiento, M. J., Llorente, A., Petan, T., Khnykin, D., Popa, I., Perkovic, M. N., Konjevod, M., Jaganjac, M. (2023). The expanding organelle lipidomes: current knowledge and challenges. *Cell. Mol. Life Sci.* 80, 237.

Davidović, D., Kukulka, M., Sarmiento, M. J., Mikhalyov, I., Gretskaya, N., Chmelová, B., Ricardo, J. C., Hof, M., Cwiklik, L., Šachl, R. (2023). Which moiety drives gangliosides to form nanodomains? *J. Phys. Chem. Lett.* 14, 5791–5797.

Sarmiento, M. J., Fernandes, F. (2023). Choosing the right fluorescent probe. In: Šachl, R., Amaro, M. (eds) *Fluorescence Spectroscopy and Microscopy in Biology.* Springer Series on Fluorescence, vol 20. Springer, Cham.

Soares-Castro, P., Soares, F., Reis, F., Lino-Neto, T., Santos, P. M. (2023). Bioprospection of the bacterial  $\beta$ -myrcene-biotransforming trait in the rhizosphere. *Appl Microbiol Biotechnol*, 107(16)5209-5224.

### **Invited Lectures and Seminars**

Rui Travasso, Adhesion modulates cell migration, erythrocyte morphology and endothelial cell dynamics. LI Winter Meeting on Statistical Physics, Guanajuato, Mexico, January 11, 2023.

Rui Travasso, Adhesion modulates cell migration, erythrocyte morphology and endothelial cell dynamics. Programa de Verão 2023, Laboratório Nacional de Computação Científica, Rio de Janeiro, Brazil, January 16, 2023.

Nuno C Santos, Novos dados sobre a relação placa carotídea-sangue. XIII Congresso Novas Fronteiras em Medicina Cardiovascular, Praia D'El Rey, Óbidos, Portugal, February 25, 2023.

Rui Travasso, Adhesion modulates cell migration, erythrocyte morphology and endothelial cell dynamics. Immuno-engineering Workshop, Turku, Finland, March 14, 2023.

Nuno C Santos, AFM-based force spectroscopy for cardiovascular research. Mechanics of Cells, Tissues and Embryos Summer School, Oeiras and Lisbon, Portugal, June 19, 2023.

Nuno C Santos, Nanotechnology-based assessment of Flavivirus assembly and its inhibition. NanoMed (NanoMedicine) 2023 / Sensors 2023 / SMS (Smart Materials and Surfaces) 2023 / EGF (European Graphene Forum) 2023 Joint International Conferences and Exhibition, Albufeira, Portugal, October 26, 2023.

Nuno C Santos, Atomic force microscopy as a nanotool for cardiovascular research. V Jornadas CBIOS (Center for Biosciences & Health Technologies), Lisbon, Portugal, November 10, 2023.

Pedro Soares-Castro, Exploring *Pseudomonas* spp. as biotech tools towards industrial applications. DBio Seminars, Department of Biology, University of Minho, Portugal, November 28, 2023.

### **Communications**

#### Communications in International Conferences:

Catarina S Lopes, Erythrocyte adhesion and biomechanics on carotid artery disease patients. 2nd Scientific MOSBRI Conference, Zaragoza, Spain, June 6, 2023. (Poster Presentation)

Nuno C Santos, Controls for force spectroscopy binding studies. Mechanics of Cells, Tissues and Embryos Summer School, Oeiras and Lisbon, Portugal, June 20, 2023. (Oral Presentation)

Marlon H Cardoso, An N-capping asparagine-lysine-proline (NKP) motif contributes to a hybrid flexible/stable multifunctional peptide scaffold. 28th American Peptide Symposium (APS), Scottsdale, USA, June 25, 2023. (Poster Presentation)

Ana C Pronto-Laborinho, Erythrocyte membrane properties in patients with ALS. 6th Egas Moniz International Scientific Congress, Portugal, July 5, 2023. (Poster Presentation)

Sónia Gonçalves, Conjugation of nanostars with PaMAP1.9 to improve its anticancer activity. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, July 31, 2023. (Poster Presentation)

Ana L Tomás, Multi-surface disinfection based on UV-C irradiation to mitigate SARS-CoV-2 transmission. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, August 1, 2023. (Poster Presentation)

Maria J Sarmiento, Deciphering the role of nuclear envelope lipids in human healthy aging. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, August 1, 2023. (Poster Presentation)

Nelly M Silva, Biophysical characterization of dengue virus capsid protein interaction with nucleic acids. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, August 2, 2023. (Poster Presentation)

Maria J Sarmiento, Deciphering the role of nuclear envelope lipids in human healthy aging. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, August 3, 2023. (Oral Presentation)

Anna Reichel, Edible alginate-based films as natural anti-SARS-CoV-2 barriers. 14th European Biophysical Society's Association (EBSA) Congress, Sweden, August 4, 2023. (Poster Presentation)

Nuno C Santos, Fibrinogen-mediated erythrocyte-erythrocyte adhesion: clinical relevance, experimental assessment and mathematical modeling. ICBP 2023 – 11th International Conference on Biological Physics, Seoul, South Korea, August 15, 2023. (Oral Presentation)

Sara D Reis, Exploring the therapeutic potential of a new design of tetrahedral DNA nanostructures with a framework-integrated anti-microRNA antisense sequence. ESB2023 – 33rd Annual Conference of the European Society for Biomaterials, Davos, Switzerland, September 5, 2023. (Poster Presentation)

Rui D M Travasso, Exploring fibrinogen-mediated erythrocyte adhesion in collisions. Living Systems Symposium, Alan Turing Institute, London, United Kingdom, September 14, 2023. (Oral Presentation)

Maria J Sarmento, Unveiling the role of nuclear envelope lipids in human physiological aging. 13th EMBO Young Scientists' Forum (EYSF), Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Pedro Soares-Castro, Bacterial prodigiosin as natural biocolorant for sustainable textile applications. 13th EMBO Young Scientists' Forum (EYSF), Lisbon, Portugal, October 12, 2023. (Poster Presentation)

André F Gabriel, Into the heart of cardiac diseases: lessons from a cardiac model. 13th EMBO Young Scientists' Forum (EYSF), Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Anna Reichel, Edible alginate-based films as natural anti-SARS-CoV-2 barriers. 13th EMBO Young Scientists' Forum (EYSF), Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Nuno C Santos, Occurrence and evolutionary conservation analysis of  $\alpha$ -helical cationic amphiphilic segments in the human proteome. 47th Annual Meeting of the Brazilian Biophysical Society, Campinas, Brazil, October 20, 2023. (Poster Presentation)

Rui D M Travasso, Adhesion modulates cell migration and endothelial cell dynamics. 20th International Conference on Flow Dynamics (ICFD), Sendai, Japan, November 6, 2023. (Oral Presentation)

José M Coelho, Antibiofilm effect of synthetic antimicrobial peptides on Gram-positive and Gram-negative bacteria. XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 27, 2023. (Poster Presentation)

Catarina S Lopes,  $\alpha v \beta 3$  integrin peptide integrin peptide inhibitors impact on fibrinogen-erythrocyte binding. XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 27, 2023. (Oral Presentation)

Catarina S Lopes, Title:  $\alpha v \beta 3$  integrin peptide inhibitors impact on fibrinogen-erythrocyte binding. XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 28, 2023. (Poster Presentation)

Sónia Gonçalves, Conjugation of nanostars with PaMAP1.9 to improve its anticancer activity. XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 28, 2023. (Oral Presentation)

José M Coelho, Antibiofilm effect of synthetic antimicrobial peptides on Gram-positive and Gram-negative bacteria. XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 29, 2023. (Oral Presentation)

Communications in National Conferences:

Filomena A Carvalho, Characterization of fibrinogen-erythrocyte binding in arterial vascular disease and its relevance for the early detection of vascular thrombotic events. III Egas Moniz Scientific Journeys, Monte da Caparica, Almada, Portugal, February 1, 2023. (Oral Presentation)

Catarina S Lopes, Erythrocytes' area and membrane properties respectively predict survival and functional decline in ALS patients. III Egas Moniz Scientific Journeys, Monte da Caparica, Almada, Portugal, February 1, 2023. (Oral Presentation)

Nelly M Silva, Biophysical characterization of dengue virus capsid protein interaction with nucleic acids. XVI CAML · VI NeurULisboa PhD Students Meeting, Lisbon, Portugal, May 9, 2023. (Oral Presentation)

Catarina S Lopes, Erythrocyte adhesion and biomechanics on carotid artery disease patients. 3rd Portuguese Young Biophysicists' Meeting, Biophysics Festival 2023, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 1, 2023. (Poster Presentation)

Patrícia M Silva, The effect of aquaporin-3 and aquaporin-5 on pancreatic cancer cell biomechanics and cell-cell adhesion. 3rd Portuguese Young Biophysicists' Meeting, Biophysics Festival 2023, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 1, 2023. (Poster Presentation)



Ana C Pronto-Laborinho, Red cell distribution width (RDW) in ALS. Congresso de Neurologia 2023 – Hot Topics 2023, Porto, Portugal, November 9, 2023. (Oral Presentation)

Ana C Pronto-Laborinho, Erythrocyte membrane properties in patients with ALS. Congresso de Neurologia 2023 – Hot Topics 2023, Porto, Portugal, November 9, 2023. (Poster Presentation)

Pedro Soares-Castro, Addressing uncertainties of the species-level taxonomic classification of a *Pseudomonas* sp. 3rd Symposium of the National Research Infrastructure for Genome Sequencing and Analysis, Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisbon, Portugal, November 17, 2023. (Poster Presentation)

### **Organization of Conferences**

Nelly M Silva, Co-Organizer, 3rd Portuguese Young Biophysicists' Meeting, Biophysics Festival 2023, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 1, 2023.

Nuno C Santos, Co-Organizer, Mechanics of Cells, Tissues and Embryos Summer School, Oeiras and Lisbon, Portugal, June 19-23, 2023.

Nuno C Santos, Co-Organizer, XVIII Iberian Peptide Meeting, Sesimbra, Portugal, November 27-29, 2023.

### **Networks and Research Infrastructures**

Maria J Sarmiento, EpiLipidNet COST Action (CA19105 – Pan-European Network in lipidomics and EpiLipidomics), WG4 and WG5 member, YRI Committee Member.

### **Prizes and Honours**

Nuno C Santos, ULisboa / Caixa Geral de Depósitos 2023 Prize (Biology, Biological Engineering, Biochemistry and Biotechnology).

Nuno C Santos, National Representative of Portugal at the European Peptide Society (EPS).

Nuno C Santos, Ambassador of Biophysical Society (United States of America).

Nuno C Santos, Member of the Executive Committee of EBSA (European Biophysical Societies' Association).

Nuno C Santos, Managing Editor of Peptide Science.

Nuno C Santos, Editorial Board of Recent Patents on Anti-Infective Drug Discovery, Canal BQ (Revista da Sociedade Portuguesa de Bioquímica), Frontiers in Microbiology, Frontiers in Pharmacology, International Journal of Molecular Sciences, Biomolecules e Tropical Medicine and Infectious Disease.

Nuno C Santos, Evaluator for the European Union ERC (European Research Council) grants, and for National Funding Agencies from Belgium (FNRS – Fonds de la Recherche Scientifique), France (ANR – Agence Nationale de la Recherche), Hong Kong Special Administrative Region (Health and Medical Research Fund), Italy (PRIN, Ministry of Education, Universities and Research), Portugal (FCT – Fundação para a Ciência e a Tecnologia), Romania (National Council for Research and Development) and Switzerland (Swiss National Science Foundation).

Filomena A Carvalho, Book Editor of Bio-Nano Interfaces: From Biosensors to Nanomedicines. Special Issue of Biomedicines. Santos NC, Carvalho FA (Ed.s) MDPI, Switzerland (ISSN 2227-9059).

Maria J Sarmiento, Review editor at Frontiers in Molecular Biosciences (molecular biophysics).

Maria J Sarmiento, Referee for international journals: Biomolecules, Cells, Membranes.

### **Advanced Teaching**

Filomena A Carvalho, Lecture, Mestrado em Biologia Estrutural, Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal.

Nuno C Santos, Lecture, Programa Doutoral em Molecular Biosciences (MolBioS), ITQB (Instituto de Tecnologia Química e Biológica), Oeiras, Portugal.

Nuno C Santos, Lecture, Programa de Doutoramento em Ciências da Saúde, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal.

Nuno C Santos, Lecture, Mestrado em Bioquímica, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica, Portugal.

Nuno C Santos, Lecture, Mestrado em Biologia Estrutural, Instituto Superior Técnico da Universidade de Lisboa, Lisbon, Portugal.

Nuno C Santos, Director, Programa Doutoral M2B-PhD – Medical Biochemistry and Biophysics, Portugal.

Nuno C Santos, Coordination of Master Curricular Unit, Bioquímica / Curso de Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Nuno C Santos, Coordination of Master Curricular Unit, Nanomedicina / Curso de Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Nuno C Santos, Coordination of Master Curricular Unit, Metabolismo Geral / Curso de Mestrado em Doenças Metabólicas e Comportamento Alimentar, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Nuno C Santos, Coordination of Master Curricular Unit, Bioquímica / Curso de Mestrado em Doenças Metabólicas e Comportamento Alimentar, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Nuno C Santos, Coordination of Master Curricular Unit, Advanced Techniques in Biomedical Research I / Curso de Mestrado em Investigação Biomédica, Faculdade de Medicina da Universidade de Lisboa, Portugal.

### **MSc Theses**

Maria Zita Gonçalves Guerra Guimarães Matias, Applications of Atomic force microscopy in Disease, Supervisor: Filomena A Carvalho, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 25, 2023.

Anita Campos, Coagulation Disorders and the Impact of Anticoagulant Prophylaxis in Patients with COVID-19, Supervisor: Ana L Tomás, Co-Supervisor: Nuno C Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 31, 2023.

Gonçalo da Luz Matias, Evaluation of the morphological and functional properties of erythrocytes in patients with Amyotrophic Lateral Sclerosis, Supervisor: Filomena A Carvalho, Co-Supervisor: Nuno C Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 19, 2023.

Ana Rita da Conceição Ferreira da Fonseca, Harnessing the biomedical potential of bacterial pigments to develop antimicrobial solutions against multidrug resistant pathogens, Supervisor: Pedro Soares-Castro, Co-Supervisor: Sónia Gonçalves, Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa, Lisbon, Portugal, October 25, 2023.

Andreia Isabel Pereira Cardetas, Towards Antimicrobial Solutions Against Human Pathogens By Exploiting The Biotechnological Potential Of Microbial Pigments, Supervisor: Pedro Soares-Castro, Co-Supervisor: Sónia Gonçalves, Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa, Lisbon, Portugal, November 13, 2023.

### **PhD Theses**

Ana S Martins, Flavivirus capsid proteins interaction with host lipid systems and viral RNA, Supervisor: Ivo C Martins, Co-Supervisor: Nuno C Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 10, 2023.

Marcin Makowski, A molecular approach to investigate the antimicrobial activity of a designed membrane-active peptide, Supervisor: Nuno C Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, June 6, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Stryker, Germany, Understand the effect of an ultra-thin nanocoating in bacterial adhesion to orthopedic implants, Collaborative Research.

INOCON Technologie GmbH, Testing the biocidal efficacy of INOCON's products according to ISO 21702:2019(E), Contract Research.

Castros S. A., SARS-CoV-2 Inactivation Studies Based on UV-C Irradiation, Collaborative Research.

MATGLOW, SARS-CoV-2 Inactivation Studies Based on UV-C Irradiation, Collaborative Research.

CeNTI - Centre for Nanotechnology and Smart Materials, SARS-CoV-2 Inactivation Studies Based on UV-C Irradiation, Collaborative Research.

### **Science and Society in 2023**

Participation in different events centered in promoting Science knowledge in non-specialized audiences, including:

- European Researchers' Night, September 29, 2023.
- Visits to our laboratory of undergraduated students, namely from Colégio Internacional de Vilamoura, November 7, 2023.
- Speed Dating in the Day of Research at Faculdade de Medicina da Universidade de Lisboa, December 13, 2023.

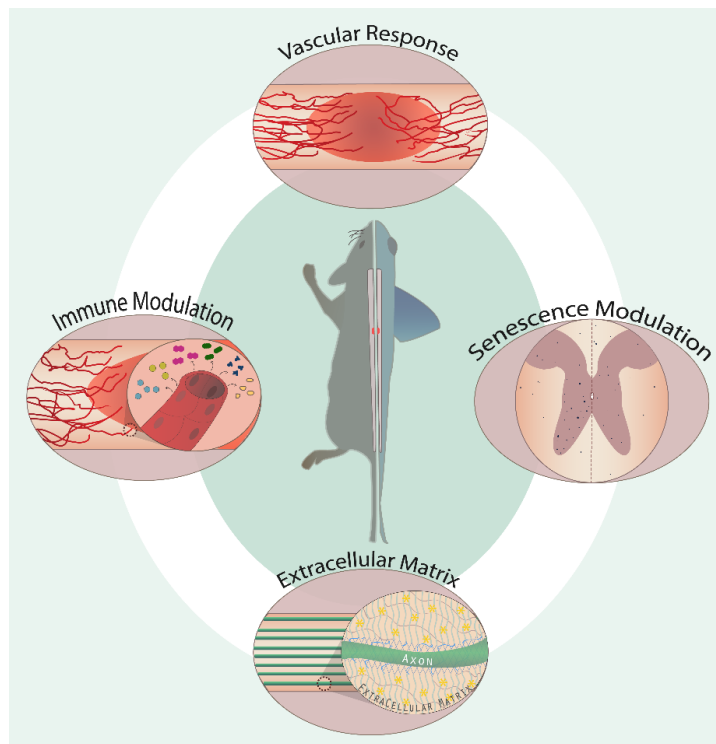
## Leonor Saúde Lab

**Head of Laboratory:** Leonor Saúde, PhD, Group Leader and Director of Zebrafish Unit at Instituto de Medicina Molecular João Lobo Antunes, and Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Catarina Esteves Ribeiro	PhD	Senior Postdoctoral Researcher (Left September)
Ana Filipa Pombinho Isidro	Master Degree	PhD Student
Ana Raquel Dias Quitéria	Master Degree	Lab Technician
Carmen de Sena Tomás	PhD	Visiting Researcher
Dalila Maria Neves Silva	Master Degree	PhD Student
Daniel Filipe Silva Ribeiro	PhD	Postdoctoral Researcher
Gonçalo Mendes Jubilado	Master Degree	MSc Student (Started April)
Inês Ferreira Domingos	Bachelor Degree	MSc Student (Started August)
Isaura Vanessa Antunes Martins	PhD	Postdoctoral Researcher
Madalena Pimentel Marques	Master Degree	PhD Student
Maria Leonor Rebola Lameira	Master Degree	Lab Technician (Left August)
Mariana Antão Ventura Monteiro	University Degree	MSc Student (Left September)
Mariana Antas Rebocho da Costa	Master Degree	PhD Student

### Graphical Abstract



### **Lab Interests**

We want to understand the molecular and cellular mechanisms controlling fundamental repair and regenerative processes activated in the context of a spinal cord injury. Our focus has been on several aspects of the cord microenvironment response after an injury in regenerative versus scarring models.

### **Research Fields**

- Cellular, Developmental and Regenerative Biology
- Neuroscience and Disorders of the Nervous System

### **Major Scientific Achievements in 2023**

We have successfully concluded and published a comprehensive analysis of the vascular distribution and morphology throughout developmental, homeostatic, and regenerative phases of the zebrafish spinal cord – a lacuna that existed in the field. Given the pivotal role that the vasculature assumes in the physiology under normal and injury conditions, this knowledge will certainly be relevant for the spinal cord field.

We were able to assemble the MouseWalker system an inexpensive and open-source method to meticulously delineate the locomotion patterns of rodents with unparalleled spatial and temporal precision. The capability of this system to yield quantitative insights into the locomotor behaviour of animals experiencing spinal injuries bears paramount importance for advancing the field.

### **Ongoing Projects**

2023/2025: CD9/MYLIP\_AGEnts: Targeting pericytes to prevent neuroinflammation and promote barrier integrity after spinal cord injury. Coordinator: Isaura Martins. Funding Agency: Morton Cure Paralysis Fund. Reference: MORTON CURE PARALYSIS FUND - ISAURA MARTINS. Amount: 27 665,08€. Total Amount: 27 665,08€.

2023/2024: Endothelial CD9 as a new anti-inflammatory target to promote spinal cord repair. Coordinator: Isaura Martins. Funding Agency: Fundação para a Ciência e a Tencnologia. Reference: 2022.05669.PTDC. Amount: 49 995,00€. Total Amount: 49 995,00€.

2023/2024: Improving Spinal Cord REgenErAtion by modulating Neutrophil inflammation: lessons from a Zebrafish perspective. Coordinator: Carmen de Sena Tomás. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.02766.PTDC. Amount: 49 901,25€. Total Amount: 1 481 513,00€.

2022/2023: Fundação Astrazeneca Innovate Competition. Coordinator: Leonor Saúde. Funding Agency: Fundação AstraZeneca. Reference: Fundação Astrazeneca Innovate Competition. Amount: 3 000,00€. Total Amount: 3 000,00€.

2021/2023: Células senescentes e o seu fenótipo secretor: novos alvos na reparação da medula espinhal. Coordinator: Leonor Saúde. Funding Agency: Santa Casa da Misericórdia de Lisboa. Reference: Santa Casa da Misericórdia de Lisboa. Amount: 189 941,54€. Total Amount: 189 941,54€.

2019/2023: Targeting induced-senescent cells: a novel approach to promote spinal cord regeneration in mammals. Coordinator: Leonor Saúde. Funding Agency: “la Caixa” Foundation. Reference: SENSE: TARGETING INDUCED-SENESCENT CELLS: A NOVEL. Amount: 444 048,00. Total Amount: 444 048,00.

## Scientific Impact

### Academic Collaborations

- Nova Medical School, Portugal.
- Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- Institute for Research on Cancer and Aging of Nice, France.
- Champalimaud Centre for the Unknown, Portugal.
- Albert Einstein College of Medicine, USA.
- Institute of Child Health, United Kingdom.

### Selected Publications

Ribeiro A, Rebocho da Costa M, de Sena-Tomás C, Rodrigues EC, Quitéria R, Maçarico T, Rosa Santos SC, Saúde L (2023). [Development and repair of blood vessels in the zebrafish spinal cord.](#)

**Open Biol.** 13(8):230103. doi: 10.1098/rsob.230103

**Relevance of the publication:** The main relevance of this study is to provide a comprehensive description of the spinal cord vascular system development, homeostasis and regeneration.

Isidro AF, Medeiros AM, Martins I, Neves-Silva D, Saúde L, Mendes CS. (2023). [Using the MouseWalker to Quantify Locomotor Dysfunction in a Mouse Model of Spinal Cord Injury.](#) **J Vis**

**Exp.** (193). doi: 10.3791/65207

**Relevance of the publication:** The main relevance of this study is to provide a method to quantitatively describe the walking pattern of rodents with high spatial and temporal resolution.

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

**Relevance of the publication:** The main relevance of this study was to show the detrimental effect of induced-senescent cells in the repair outcome in the context of spinal cord injuries in mammals.

Chapela D, Sousa S, Martins I, Cristóvão AM, Pinto P, Corte-Real S, Saúde L (2019). [A zebrafish drug screening platform boosts the discovery of novel therapeutics for spinal cord injury in mammals](#). *Scientific Reports* 9(1):10475.

**Relevance of the publication:** The main relevance of this study was to show that zebrafish larvae can be successfully used as screening platforms for drug repositioning for spinal cord injury indications.

Azevedo AS, Grotek B, Jacinto A, Weidinger G, Saúde L (2011). [The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations](#). *PLoS ONE* 6(7):e22820.

**Relevance of the publication:** In this study, we challenged to the limit the regenerative capacity of the zebrafish and showed that this small vertebrate, through a process of de-differentiation, has an almost unlimited capacity to regenerate its caudal fin.

### 2023 Publications in Peer-Reviewed Journals

Ribeiro A, Rebocho da Costa M, de Sena-Tomás C, Rodrigues EC, Quitéria R, Maçarico T, Rosa Santos SC, Saúde L (2023). Development and repair of blood vessels in the zebrafish spinal cord. *Open Biol.* 13(8):230103. doi: 10.1098/rsob.230103

Martins I, Neves-Silva D, Ascensão-Ferreira M, Dias AF, Ribeiro D, Isidro AF, Quitéria R, Paramos-de-Carvalho D, Barbosa-Morais NL, Saúde L (2023). Mouse Spinal Cord Vascular Transcriptome Analysis Identifies CD9 and MYLIP as Injury-Induced Players. *Int J Mol Sci.* 24(7):6433. doi: 10.3390/ijms24076433

Isidro AF, Medeiros AM, Martins I, Neves-Silva D, Saúde L, Mendes CS (2023). Using the MouseWalker to Quantify Locomotor Dysfunction in a Mouse Model of Spinal Cord Injury. *J Vis Exp.* 193. doi: 10.3791/6520

### Invited Lectures and Seminars

Isaura Martins, Vascular therapeutic approaches to improve spinal cord repair: CD9 and MYLIP as two new vascular injury-induced players. Medical Technologies in Spinal Cord Injury, Portugal.



## Communications

### Communications in International Conferences:

Daniel Ribeiro, A Single-cell Atlas of the Mouse Spinal Cord during the Acute and Chronic Injury Response Phases. Building Bridges in Biology Symposium, Portugal, March 3, 2023. (Oral Presentation)

Isaura Martins, Mouse spinal cord vascular transcriptome analysis identifies CD9 and MYLIP as injury-induced players. Building Bridges in Biology Symposium, Portugal, March 3, 2023. (Oral Presentation)

Leonor Saúde, Senescent cells and their secretory phenotype: novel targets for spinal cord repair. Gordon Research Conference – Spinal cord injury and repair: from mechanisms to translation, Italy, July 9, 2023. (Poster Presentation)

Leonor Saúde, Senescent cells and their secretory phenotype: novel targets for spinal cord repair. International Society Regenerative Biology Inaugural Meeting, Austria, September 4, 2023. (Poster Presentaton)

Isaura Martins, CD9 and MYLIP as two new vascular players in spinal cord injury. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Mariana Rebocho da Costa, Replumbing the Central Nervous System - Macrophages as potential modulators of the vascular response after spinal cord injury in adult zebrafish. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Ana Filipa Isidro, Taking a walk on the acrylic slide: Using the MouseWalker to quantify locomotor dysfunction in a mouse model of spinal cord injury. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Daniel Ribeiro, Single cell analysis of the spinal cord reveals a persistent, injury-induced neuronal cell state. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Madalena Marques, Yoga for Telomeres – can they stretch after a spinal cord injury. 13th EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

#### Communications in National Conferences:

Raquel Quitéria, Histology of the zebrafish injured spinal cord - methods and technical challenges for frozen sections. I Congresso da BioMedLab, Portugal, March 10, 2023. (Poster Presentation)

Raquel Quitéria, Spinal cord embedding using a cryoembedder - a comparative study. I Congresso da BioMedLab, Portugal, March 11, 2023. (Poster Presentation)

Mariana Rebocho da Costa, Replumbing the Central Nervous System - Macrophages as potential modulators of the vascular response after spinal cord injury in adult zebrafish. 3rd International Meeting of the Portuguese Research Network on Spinal Cord Injury, Portugal, June 22, 2023. (Poster Presentation)

Ana Filipa Isidro, Taking a walk on the acrylic slide: Using the MouseWalker to quantify locomotor dysfunction in a mouse model of spinal cord injury. 3rd International Meeting of the Portuguese Research Network on Spinal Cord Injury, Portugal, June 22, 2023. (Poster Presentation)

Daniel Ribeiro, Single cell analysis of the spinal cord reveals a persistent, injury-induced neuronal cell state. 3rd International Meeting of the Portuguese Research Network on Spinal Cord Injury, Portugal, June 22, 2023. (Oral Presentation)

Mariana Rebocho da Costa, Spinal cord vascularization - from development to injury response. DiA Meeting: Inspiring Embryonic Minds, Portugal, October 3, 2023. (Oral Presentation)

#### **Organization of Conferences**

Madalena Marques, Co-Organizer, DiA Meeting: Inspiring Embryonic Minds, Portugal, November 10, 2023.

Dalila Neves Silva, Co-Organizer, DiA Meeting: Inspiring Embryonic Minds, Portugal, November 10, 2023.

#### **Networks and Research Infrastructures**

Madalena Marques, Science Careers PhD Committee, Co-Organizer.

Mariana Rebocho da Costa, Science Careers PhD Committee, Co-Organizer.

Dalila Neves Silva, Science Careers PhD Committee, Co-Organizer.

### **Prizes and Honours**

Isaura Martins, SPBD Outstanding Developmental Biology Paper Award.

Daniel Ribeiro, EMBO Scientific Exchange Grant.

Daniel Ribeiro, Invited referee – Cells.

### **Advanced Teaching**

Leonor Saúde, Lecture, Master in Neurosciences Faculdade de Medicina da Universidade de Lisboa, Portugal, November 8, 2023.

Leonor Saúde, Lecture, Stem Cell Technologies - PhD Advanced Course, Portugal, November 30, 2023.

### **MSc Theses**

Mariana Monteiro, The potential of ABT-263 as a therapeutic agent in spinal cord injury- induced peripheral pathology, Supervisor: Leonor Saúde, Co-Supervisor: Isaura Martins, Faculdade de Medicina da Universidade de Lisboa, Portugal.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Leonor Saúde, Podcast “Aula Prática Lesões da espinhal medula: desafios e oportunidades”, Rádio Observador, October 3, 2023.

<https://observador.pt/programas/mentres-brilhantes/lesoes-da-espinhal-medula-desafios-e-oportunidades/>

Leonor Saúde, "Viver melhor depois dos 60", Visão Saúde nº33, December 2023.

Madalena Marques, "Como usar um peixe para estudar a regeneração do nosso sistema nervoso?" Torres de Ciência em Movimento, November 17, 2023.

Madalena Marques, "Cartas com Ciência", Corresponding Scientist, January 1-June 30, 2023.

## Ana Sebastião Lab

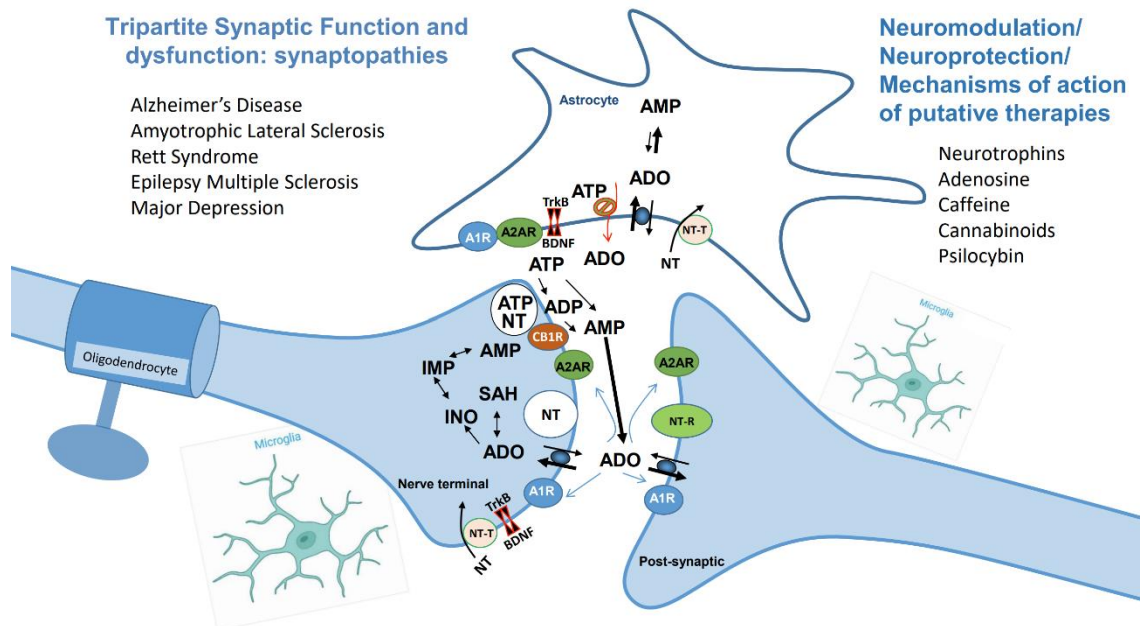
**Head of Laboratory:** Ana M Sebastião, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Full Professor and Director of Instituto de Farmacologia e Neurociências at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Catarina Romão Félix	Bachelor Degree	Lab Manager (Started June)
Ana Laura da Silva Duarte	Bachelor Degree	MSc Student
Ana Paula Morais Condesso	University Degree	MSc Student
Ana Sofia Sousa Pereira	University Degree	MSc Student (Started January)
André Vitorino de Sousa Vares	High School Diploma	MSc Student
Andrei Braniste	University Degree	MSc Student (Left November)
Anwasha Ghosh	Master Degree	PhD Student
Bernardo Pinheiro Luís e Santos Almeida	Bachelor Degree	MSc Student (Started May)
Carolina Maria Vieira Capela	Bachelor Degree	MSc Student (Left August)
Catarina Miranda Lourenço	PhD	Visiting Researcher
Chloé Odette Michèle Galipeau	Bachelor Degree	Trainee
Cláudia Alexandra dos Santos Valente de Castro	PhD	Senior Postdoctoral Researcher
Daniela Cristina Melo Magalhães	Master Degree	PhD Student
Diogo Miguel da Palma Lourenço	Master Degree	PhD Student (Left December)
Elza Quirina Ribeiro Rocha	Bachelor Degree	MSc Student
Fernando Lopez Alvez	Master Degree	PhD Student (Started April)
Galip Yiğit Ünlü	Master Degree	Trainee (Started September)
Gonçalo Valentim André da Costa	Bachelor Degree	Trainee (Started July)
Inês d'Almeida Barroso	High School Diploma	Student (Left May)
Joana Filipa Gonçalves Ribeiro	Master Degree	PhD Student
Joana Moura Mateus	Master Degree	PhD Student
Joana Simão Correia Nunes	High School Diploma	MSc Student
João Baptista Moreira	Master Degree	PhD Student
Joaquim Alexandre Ribeiro	PhD	Staff Scientist
Jorge Miguel Farinha Ferreira	Master Degree	PhD Student
Leandro José Rodrigues Freitas	Bachelor Degree	MSc Student
Leonor Ferreira Correia	Bachelor Degree	Trainee (Started September)
Leonor Pedro Oliveira Ribeiro Rodrigues	Master Degree	PhD Student
Madalena Alves Gualdino	Bachelor Degree	MSc Student
Mafalda Ferreira Manso	Master Degree	PhD Student
Maria Alexandra Pereira Botelho	High School Diploma	Administrative Technician
Maria José de Oliveira Diógenes Nogueira	PhD	Staff Scientist
Mariana de Brito Morais	MD/Master Degree	Clinical Researcher
Mariana Pinto Coelho	Bachelor Degree	MSc Student

Mariana Serra de Sequeira Neuparth Sottomayor	Master Degree	PhD Student
Miguel Leonardo Pereira Marques Mendes Grilo	Bachelor Degree	MSc Student (Started August)
Nuno Alemã Serrano Patriarca Ramalho	High School Diploma	MSc Student
Patrícia Alexandra Branco Fraga	Master Degree	PhD Student (Started February)
Ricardo Silva dos Santos Viais	PhD	Project Manager
Rita Abrunhosa Soares	PhD	Postdoctoral Researcher
Sandra Cristina Henriques Vaz	PhD	Senior Postdoctoral Researcher
Sara Alves Xapelli	PhD	Staff Scientist
Sara Filipa Castro da Costa Pinto	Master Degree	PhD Student
Sara Inteiro de Oliveira	Master Degree	Lab Technician
Sara Raquel Landeira Nabais do Paulo	Master Degree	PhD Student
Tatiana Pinto Morais	PhD	Postdoctoral Researcher
Tiago Miguel Garcia Ferreira	University Degree	MSc Student
Tiago Miguel Reis Gonçalves	High School Diploma	MSc Student (Started September)
Tiago Rodrigo da Costa Coelho	Master Degree	PhD Student

### Graphical Abstract



Outline of the major modulators of synaptic function and of the synaptic dysfunctions that are under focus of the research team

### **Lab Interests**

Fighting against neurologic and psychiatric diseases, a major challenge in Neurosciences, requires the understanding of how synaptic activity is controlled and how to correct its abnormal function. Therefore, our team aims to elucidate how the neuronal and glial components of the tripartite synapse are fine-tuned under normal and dysfunctional situations. How endogenous modulators affect synaptic signaling, neuronal excitability, neuronal and glial maturation, degeneration, renewal and repair, are our current goals of research. We focus on neurotrophic factors, on adenosine and on endocannabinoids, as major endogenous neuromodulators. As exogenous substances we focus on psychoactive drugs (caffeine, cannabinoid receptor ligands, psilocybin and other serotonergic receptor ligands) aiming to know how they influence endogenous neuromodulation at synapses. As disease models we have been interested on those involving neurodegeneration and/or dysregulated excitability, from newborn to aging.

### **Research Fields**

- Neuroscience and Disorders of the Nervous System

### **Major Scientific Achievements in 2023**

We developed a new fully automated, reliable and with high validity tool (SIGAA), to speed up Calcium signaling analysis.

We underscored the pivotal contribution of astrocytes and D-serine to modulate hippocampal plasticity, thus providing essential insights into the intricate interplay between neurons and astrocytes to shape hippocampal synaptic function.

We provided solid evidence of memory deficits in an animal model of absence seizures that do not depend on an anxiety or neophobic phenotype.

We unveiled impairments in Brain Derived Neurotrophic Factor and Adenosine signaling in a female mouse model of Rett Syndrome.

We highlighted major behavioral confounds, as the profound locomotor alterations, and the high susceptibility to stress, in an animal model of depression.

We unveiled a novel neurogenic potential of CBDV via TRPV1 modulation, paving the way to future repair strategies based in non-psychoactive cannabinoids

### Ongoing Projects

2022/2025: TAT-TrkB, a novel neuroprotective compound to fight Alzheimer's disease. Coordinator: Maria José Diógenes. Funding Agency: Santa Casa da Misericórdia de Lisboa. Reference: Prémio Santa Casa Mantero Belard (MB-35-2021). Amount: 99 600,00€. Total Amount: 199 560,00€.

2022/2025: Acção farmacológica é afectada pelo contexto? Dependência contextual das acções neurobiológicas e antidepressivas persistentes da psilocibina. Coordinator: Ana Sebastião. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-FAR/4834/2021. Amount: 250 000,00€. Total Amount: 250 000,00€.

2022/2024: Profilina1 na interface entre microglia, envelhecimento e neurodegeneração. Coordinator: Sandra Vaz. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-NEU/1677/2021. Amount: 12 500,00€. Total Amount: 249 999,10€.

2022/2024: A interação entre a resposta imune inata e adquirida como base do defeito cognitivo presente na Esclerose Múltipla. Coordinator: Sandra Vaz. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-PAT/2582/2021. Amount: 13 750,00€. Total Amount: 249 602,55€.

2022/2023: Early Career Awards. Coordinator: Sara Xapelli. Funding Agency: International Brain Research Organization (IBRO). Reference: International Brain Research Organization (IBRO). Amount: 5 000,00€. Total Amount: 5 000,00€.

2021/2025: Pacto de Inovação "HfPT – Health from Portugal", Novel treatment and early diagnostics of AD. Coordinator: Maria José Diógenes. Funding Agency: Agência Nacional de Inovação, SA. Reference: TTO\_ANE002\_HfPT – MJDígenes. Amount: 395 496,56€. Total Amount: 395 496,56€.

2021/2023: Programa PESSOA - Fundação para a Ciência e a Tecnologia/Campus France - Sara Xapelli. Coordinator: Sara Xapelli. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: Programa PESSOA - Fundação para a Ciência e a Tecnologia/Campus France. Amount: 2 000,00€. Total Amount: 4 000,00€.

2021/2023: ISN CAREER DEVELOPMENT GRANT. Coordinator: Sara Xapelli. Funding Agency: International Society for Neurochemistry. Reference: ISN CAREER DEVELOPMENT GRANT. Amount: 6 607,20€. Total Amount: 6 607,20€.

2021/2023: ISN CAREER DEVELOPMENT GRANT. Coordinator: Sandra Vaz. Funding Agency: International Society for Neurochemistry. Reference: ISN CAREER DEVELOPMENT GRANT. Amount: 7 152,49€. Total Amount: 7 152,49€.

2020/2023: Twinning - EpiEpeNet - Epileptogenesis and Epilepsy Network: from genes, synapses and circuits to pave the way for novel drugs and strategies. Coordinator: Ana Sebastião. Funding Agency: European Commission. Reference: Twinning EpiEpinet - Grant number: 952455. Amount: 587 500,00€. Total Amount: 900 000,00€.

2018/2024: Cronh's & Colitis. Coordinator: Ana Sebastião. Funding Agency: Crohn's & Colitis Foundation. Reference: Cronh's & Colitis. Amount: 32 718,69€. Total Amount: 32 718,69€.

## Scientific Impact

### Academic Collaborations

- University of Cardiff, United Kingdom.
- University of Minesotta, USA.
- Cajal Institute, Spain.
- University of Malta, Malta.
- Univerisdade Federal de Pelotas, Brazil.
- University of Amesterdam, The Netherlands.
- University of the Basque Country EHU/UPV, Spain.
- Maj Institute of Pharmacology, Polish Academy Sciences, Poland.
- Jagiellonian University Medical College, Poland.
- University of Lancaster, United Kingdom.
- Sorbonne Université, France.
- Vilnius University, Lithuania.
- Hugo Arias, USA.
- University of Lund, Sweden.
- Université Paris-Saclay, France.
- AccelBio, Portugal.
- CEDOC, Universidade Nova de Lisboa, Portugal.



- University of Eastern Finland, Finland.
- Faculdade de Engenharia da Universidade do Porto, Portugal.
- University Medical Center Göttingen, Germany.
- Faculdade de Farmácia da Universidade de Lisboa, Portugal.
- CNC, Universidade de Coimbra, Portugal.
- University of Helsinki, Finland.
- Instituto Superior Técnico da Universidade de Lisboa, Portugal.
- Universidade da Beira Interior, Portugal.
- Los Alamos National Laboratory, USA.
- MARE, Universidade de Coimbra, Portugal.
- Centro Hospitalar Universitário Lisboa Norte, Portugal.
- Universidade Federal de São Paulo (UNIFESP), Brazil.
- i3S, Universidade do Porto, Portugal.
- ICBAS, Universidade do Porto, Portugal.
- NIDDKD, NIH, Bethesda, USA.
- Institute of Psychiatry and Neuroscience of Paris, France.
- Prague Psychiatric Center, Czech.
- Sapienza University of Rome, Italy.

### Selected Publications

Armada-Moreira A, Gomes JI, Pina CC, Savchak OK, Joana Gonçalves-Ribeiro J, Rei N, Pinto S, Morais TP, Martins R, Ribeiro FF, Sebastião AM, Crunelli V, Vaz SH (2020). [Going the extra \(synaptic\) mile: excitotoxicity as the road toward neurodegenerative diseases](#). **Frontiers in Cellular Neuroscience**. 14:90.

**Relevance of the publication:** In this ‘Highly Cited Paper’ (Web of Knowledge) we explore different causes and consequences of excitotoxicity, discuss the involvement of NMDAR-mediated excitotoxicity and its downstream effects on several neurodegenerative disorders, and identify possible strategies to study new aspects of these diseases that may lead to the discovery of new therapeutic approaches, where the targets are not specific symptoms, but the underlying cellular phenomena of the disease.

Magalhães DM, Pereira N, Rombo DM, Beltrão-Cavacas C, Sebastião AM, Valente CA (2018). [Ex vivo model of epilepsy in organotypic slices-a new tool for drug screening](#). **Journal of Neuroinflammation** 15:203.

**Relevance of the publication:** We developed a new tool, the organotypic slice cultures gradually deprived of serum, to explore the interplay between neuroinflammation and epilepsy and to screen potential drug candidates, within the inflammatory cascades, to reduce/halt Epileptogenesis.

Ribeiro, F. F., Ferreira, F., Rodrigues, R. S., Soares, R., Pedro, D. M., Duarte-Samartinho, M., Aroeira, R. I., Ferreira, E., Valero, J., Solá, S., Mira, H., Sebastião, A. M., Xapelli, S. (2021). [Regulation of hippocampal postnatal and adult neurogenesis by adenosine A2A receptor: Interaction with brain-derived neurotrophic factor](https://doi.org/10.1002/stem.3421). *Stem Cells* (Dayton, Ohio), 39(10):1362–1381. <https://doi.org/10.1002/stem.3421>

**Relevance of the publication:** We show that A2A R activation promotes neural stem cell self-renewal, protects committed neuronal cells from cell death and contributes to a higher density of immature and mature neuronal cells, particularly glutamatergic neurons. Moreover, A2A R endogenous activation was found to be essential for BDNF-mediated increase in cell proliferation and neuronal differentiation. These findings may impact in the development of strategies for brain repair under pathological conditions.

Sandau US\*, Colino-Oliveira M\*, Jones A, Saleumvong B, Coffman SQ, Liu L, Miranda-Lourenço C, Palminha C, Batalha VL, Xu Y, Huo Y, Diógenes MJ, Sebastião AM\*\*, Boison D\*\* (2016). [Adenosine Kinase Deficiency in the Brain Results in Maladaptive Synaptic Plasticity](https://doi.org/10.1523/JNEUROSCI.4511-16.2016). *J Neurosci*. 36:12117-12128 (\*co-first authors; \*\*co-senior authors)

**Relevance of the publication:** We identified maladaptive mechanisms lead to dysregulated synaptic plasticity, cognitive deficits, and increased seizure risk, which result from a mutation in adenosine kinase (ADK). This allowed to disclose an yet unknown disease mechanism (ADK deficiency in humans). Furthermore, we showed that blocking adenosine A2ARs (with a drug already used as therapeutics for other disease), can attenuate the neurological symptoms in mice with ADK deficiency therefore highlighting a putative therapy for ADK deficiency in humans.

Jerónimo-Santos A, Fonseca-Gomes J, Guimarães DA, Tanqueiro SR, Ramalho RM, Ribeiro JA, Sebastião AM, Diógenes MJ (2015). [Brain-derived neurotrophic factor mediates neuroprotection against A \$\beta\$ -induced toxicity through a mechanism independent on adenosine 2A receptor activation](https://doi.org/10.1016/j.gfs.2015.08.001). *Growth Factors*. 2015 Sep 12:1-11.

**Relevance of the publication:** Jerónimo Santos et al (2015) We disclosed a novel mechanism involved in the beta-Amyloid neurodegeneration: Calpain-mediated cleavage of the neurotrophin receptor, TrkB, leading to impairment of BDNF signalling (Citation 71). After this seminal paper we identified the mechanism of activation of calpains: calcium entering through NMDA receptor activation, that the fragment formed from TrkB cleavage is cytotoxic and that it is detected in CSF of Alzheimer's disease patients, therefore likely being a biomarker for this disease.

### 2023 Publications in Peer-Reviewed Journals

Abreu DS, Gomes JI, Ribeiro FF, Diógenes MJ, Sebastião AM, Vaz SH (2023). Astrocytes control hippocampal synaptic plasticity through the vesicular-dependent release of D-serine. *Front Cell Neurosci*. 17:1282841.

Neuparth-Sottomayor M, Pina CC, Morais TP, Farinha-Ferreira M, Abreu DS, Solano F, Mouro F, Good M, Sebastião AM, Di Giovanni G, Crunelli V, Vaz SH (2023). Cognitive comorbidities of experimental absence seizures are independent of anxiety. *Neurobiology of Disease*. 186:106275.

Lopes RF, Gonçalves-Ribeiro J, Sebastião AM, Meneses C, Vaz SH (2023). SIGAA – SIGnaling Automated Analysis: a new tool for Ca<sup>2+</sup> signaling quantification using ratiometric Ca<sup>2+</sup> dyes, Signal, Image and Video Processing, SIViP <https://doi.org/10.1007/s11760-023-02821-7>.

Cunha-Reis D, Vaz SH, Correia-de-Sá P (2023). Editorial: Cellular and molecular targets in epileptogenesis focusing on disease prevention. *Front Cell Neurosci.* 7:1251038.

Carvalho-Rosa JD, Rodrigues NC, Silva-Cruz A, Vaz SH, Cunha-Reis D (2023). Epileptiform activity influences theta-burst induced LTP in the adult hippocampus: a role for synaptic lipid raft disruption in early metaplasticity? *Front Cell Neurosci.*; 17:1117697.

Nunes MJ, Carvalho AN, Reis J, Costa D, Moutinho M, Mateus J, Almeida RM, Brito S, Risso D, Nunes S, Castro-Caldas M, Gama MJ, Rodrigues CMP, Xapelli S, Diógenes MJ, Cartier N, Chali F, Piguet F, Rodrigues E (2023). Cholesterol redistribution triggered by CYP46A1 gene therapy improves major hallmarks of Niemann-Pick type C disease but is not sufficient to halt neurodegeneration. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* Online ahead of print.

Lourenço DM, Soares R, Sá Santos S, Mateus JM, Rodrigues RS, Moreira JB, Vaz SH, Sebastião AM, Solá S, Xapelli S (2023). Unravelling a novel role for cannabidiol in the modulation of subventricular zone postnatal neurogenesis *European Journal of Pharmacology* 959:176079.

Rimbert S, Moreira JB, Xapelli S, Lévi S (2023). Role of purines in brain development, from neuronal proliferation to synaptic refinement. Special Issue: “Purinergic Signaling: 50 years”. *Neuropharmacology* 237:109640. doi: 10.1016/j.neuropharm.2023.109640.

Miranda-Lourenço C, Rosa J, Rei N, Belo RF, Lopes AL, Silva D, Vieira C, Magalhães-Cardoso T, Vais R, Correia-de-Sá P, Sebastião AM, Diógenes MJ (2023). Adenosinergic System and BDNF Signaling Changes as a Cross-Sectional Feature of RTT: Characterization of *Mecp2* Heterozygous Mouse Females. *Int J Mol Sci* Nov 13;24(22):16249.

Farinha-Ferreira, M., Magalhães, D.M., Neuparth-Sottomayor, M., Rafael, H., Miranda-Lourenço, C., Sebastião, A.M. (2023). Unmoving and uninflamed: characterizing neuroinflammatory dysfunction in the Wistar-Kyoto rat model of depression. *Journal of Neurochemistry* (in the press).

Sebastião, A. M., & Ribeiro, J. A. (2023). Adjusting the brakes to adjust neuronal activity: Adenosinergic modulation of GABAergic transmission. *Neuropharmacology*, 236, 109600. <https://doi.org/10.1016/j.neuropharm.2023.109600>

### **Pre-Prints**

RS Rodrigues, JB Moreira, SH Vaz, A Barateiro, SL Paulo, JM Mateus, DM Lourenço, FF Ribeiro, E Loureiro-Campos, P Bielefeld, A Fernandes, AM Sebastião, L Pinto, CP Fitzsimons, S Xapelli (2023). Cannabinoid type 2 receptor inhibition enhances the antidepressant and proneurogenic effects of physical exercise after chronic stress. *bioRxiv* 2023.04.24.538087.

### **Invited Lectures and Seminars**

Maria José Diógenes, How my personal story changed my professional life. ALBA, Online, January 5, 2023.

Ana M Sebastião, Neuromodulation by purines - from neurogenesis towards neuronal signalling and neuroprotection. 1st PRESTO Cost Meeting: P2X receptors as therapeutic targets, Italy, Online, February 9, 2023.

Sara Xapelli, Cannabinoid Actions on Neural Stem Cells: Implications for Pathophysiology. MCC – Medical Cannabis Coimbra - Clearing the smoke on medical cannabis: the importance of the endocannabinoid system in health and disease, Portugal, March 9, 2023.

Tiago Coelho, Art of Neuroscience, The Art of Biological Things, United Kingdom, Online, March 14, 2023.

Ana M Sebastião, On the search of the mechanism involved in the antiseizure action of MRS5474. VIII Semana da Bioengenharia: Exploring the Brain: Bioengineering in Neurosciences, Portugal, March 23, 2023.

Maria José Diógenes, Cleavage of the TrkB-FL receptor in Alzheimer's disease: a new therapeutic target. Turkey, Online, March 30, 2023.

Sara Xapelli, ALBA Mentoring Circles Workshop, Portugal, May 5, 2023.

Sandra Vaz, The insights on role of astrocytes in synaptic function. SPF Seminars, Portugal, Online, July 12, 2023.

Sara Xapelli, From cannabinoids to physical exercise: regulators of postnatal neurogenesis as antidepressant targets. Institut du Fer à Moulin, France, July 13, 2023.

Sara Xapelli, Sharing Career Experience @ISN-ESN 2023. ISN 2023, Portugal, August 11, 2023.

Cláudia Valente, NLRP3 inflammasome inhibition prevents Abeta- and pTau-driven neuroinflammation and neuronal death by pyroptosis in acute hippocampal slices. 2nd PRESTO Cost Meeting: P2X receptors a common route in different diseases: preclinical and clinical aspects, Italy, September 6, 2023.

Ana M Sebastião, Adenosine and seizures: going beyond A1 receptors. 2nd PRESTO Cost Meeting: P2X receptors a common route in different diseases: preclinical and clinical aspects, Italy, September 7, 2023.

Sandra Vaz, Role of astrocytic CB1R in mPFC. XII Reunión de la Red Glial Española, Granada, Spain, September 8, 2023.

Sandra Vaz, Cognitive comorbidities of absence seizures. Mediterranean Neuroscience Society 2023 Meeting, Carthage, Tunisia, October 17, 2023.

Tatiana Pinto Morais, Absence Seizures Comorbidities and Their Pharmacological Modulation. Mediterranean Neuroscience Society 2023 Meeting, Carthage, Tunisia, October 17, 2023.

Sandra Vaz, Role of astrocytic CB1R in mPFC. Instituto de Medicina Molecular João Lobo Antunes Postdoc Day, Lisbon, Portugal, October 19, 2023.

Sandra Vaz, Novel perspectives on the role of astrocytes in synaptic function. CNC Seminars, Coimbra, Portugal, October 27, 2023.

Sara Xapelli, From cannabinoids to physical exercise: regulators of postnatal neurogenesis as antidepressant targets. ESN-ISN Neurochemistry School 2023 - ESN-ISN, Portugal, October 30, 2023.

Tatiana Morais, Tonic GABA inhibition and absence seizures are distinguishably modulated by 5-HT<sub>2A</sub> receptors in normal and epileptic rats. Neuroscience Seminars, Portugal, December 4, 2023.

Cláudia Valente, Targeting Neuroinflammation in Brain Diseases. XXII Congresso do Programa de Pós-Graduação em Biologia Estrutural e Funcional, Brazil, December 5, 2023.

Ana M Sebastião, When minorities take advantage: a new role for adenosine A3Rs? XII Meeting of the Brazilian Purine Club, Brazil.

### **Communications**

#### Communications in International Conferences:

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ. Surveying TrkB-ICD secretion pathways and its presence in cerebrospinal fluid from Alzheimer's disease patients. 2nd Symposium on Alzheimer's Disease: An Update on Pathology and Therapeutics, Portugal, February 10, 2023. (Poster Presentation)

Ferreira-Manso M, Fonseca-Gomes J, F. Belo R, Miranda-Lourenço C, Costa-Coelho T, Sebastião AM, Fernandes A, Diógenes MJ, A novel peptide able to recover cognitive impairments and TrkB-FL levels in an Alzheimer's disease mouse model. 2nd Symposium on Alzheimer's Disease: An Update on Pathology and Therapeutics, Portugal, February 10, 2023. (Poster Presentation)

Lourenço D, Zavalko S, Soares R, Mateus JM, Rodrigues RS, Miranda-Lourenço C, Sebastião AM, Mouro F, Diógenes MJ, Xapelli S, Cannabidiol and neural stem cells, a new hope for Rett syndrome? MCC – Medical Cannabis Coimbra - Clearing the smoke on medical cannabis: the importance of the endocannabinoid system in health and disease, Portugal, March 9, 2023. (Poster Presentation)

Ana Laura Duarte, Characterization of adenosine and BDNF signaling pathways in the pre symptomatic phase of Rett Syndrome. AIMS Annual International (Bio)Medical Students Meeting, Portugal, March 25, 2023. (Poster Presentation)

Rocha E, Meda F, Sebastião AM, Valente CA, Unraveling NLRP3 inflammasome signaling and neuronal death by pyroptosis in Epilepsy. FENS Regional Meeting 2023, Portugal, May 3, 2023. (Poster Presentation)

Ferreira T, Sebastião AM, Valente CA, Pyroptotic deadly curse of neurons in Alzheimer's Disease. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Fonseca E, Moreira JB, Mateus JM, Xapelli S, Oriá R, Fontes-Ribeiro C, Malva J, Effect of methylmercury exposure in svz-derived neural stem/progenitor cell cultures. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Paulo SL, Soares R, Moreira JB, Coelho JE, Lopes LV, Sebastião AM, Valero J, Xapelli S, Physical activity as a potential modulator of adult hypothalamic neurogenesis: from health to Alzheimer's disease. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Lourenço DM, Soares R, Santos SS, Solá S, Mateus JM, Rodrigues RS, Moreira JB, Vaz SH, Sebastião AM, Xapelli S, Cannabidiol and Capsaicin in the modulation of subventricular zone postnatal neurogenesis: a polymodal activity for TRPV1. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Moreira JB, Mateus JM, Vink MA, Vares A, Alves J, Sebastião AM, Lopes LV, Lévi S, Xapelli S, Driving plasticity with caffeine: the effects on adult neurogenesis and synaptogenesis. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Soares R, Lourenço DM, Mota IF, Ana M. Sebastião, Xapelli S, Morais VA, Mitochondrial properties alter along postnatal neural stem cell differentiation in the Subventricular Zone. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Mateus JM, Moreira JB, Lourenço DM, Sebastião AM, Dawson N, Xapelli S, In vitro and in vivo modulation of adult SVZ-derived oligodendrogenesis by BDNF. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Costa-Pinto S, Gonçalves-Ribeiro J., Moreira J., Socodato R., Relvas J.B., Sebastião A.M., Vaz S.H, Early impairments in primary motor cortex transmission and plasticity of SOD1G93A mice. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Gonçalves-Ribeiro J, Magalhães DM, Costa-Pinto S, Sottomayor M, Savchak OK, Lopes RF, Meneses C, Santisteban R, Lillo A, Navarro-Brugal G, Franco R, Sebastião AM, Vaz SH, CB1R activity is dictated by adenosine receptors in the rodent mPFC. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Coelho M, Costa-Pinto S, Sebastião AM, Vaz SH, Impact of cannabinoid receptors modulation in synaptic plasticity during ALS progression. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Rodrigues-Freitas L, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH, Astrocytic CB1R impact on Long-Term Depression in the medial Prefrontal Cortex. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Ribeiro-Rodrigues, L, Paulo, SL, Correia, DS, Fonseca-Gomes, J, Paiva, VH, Sebastião, AM, Diógenes, MJ\*, Xapelli, S\*, The BDNF receptor TrkB-FL is cleaved in a rat model of epilepsy. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Gualdino M, Gonçalves-Ribeiro J, Sebastião AM, Vaz SV, Interaction between CB1 receptors and adenosine A1 receptors on astrocytes: implication on hippocampal synaptic plasticity. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Ana Laura Duarte, Effect of adenosine A<sub>2A</sub> receptor activation on neuronal morphology in a cellular model of Rett Syndrome. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes M, Dysregulation of the BDNF/TrkB system in Alzheimer's disease ramifies in the secretion of a TrkB-derived fragment through extracellular vesicles. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)



Ferreira-Manso M, Costa-Coelho T, Inteiro-Oliveira S, Neuparth-Sottomayor M, Sebastião AM, Diógenes MJ, The in vivo administration of the new compound, TAT-TrkB, prevents hippocampal long-term potentiation deficits in 5xFAD mice. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ, Computational-aided design of small compounds to prevent TrkB-FL cleavage. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Ghosh A, Leonor Ribeiro-Rodrigues, Nádía Rei, Dilip K. Tos, Tatiana P Morais, Sandra H Vaz, Kenneth A Jacobson, Joaquim A Ribeiro, Ana M Sebastião, Adenosine A3 receptor-mediated inhibition of GABA uptake. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Galipeau G, Miguel Farinha-Ferreira, Jean-Charles Mariani, Samuel Diebolt, Louis Barthe, Renata Santos, Zsolt Lenkei, Ana Maria Sebastião, Unravelling the dose-dependence of psilocybin-induced long-lasting behavioral effects. Federation of European Neuroscience Societies Regional Meeting (FENS FRM 2023), Portugal, May 3-5, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, Brain-derived Neurotrophic Factor receptor: cleaved TrkB-FL C-terminal fragment is secreted extracellularly. SNEV Virtual Conference 2023: Everything Everywhere All about Extracellular Vesicles, Online, July 13, 2023. (Poster Presentation)

Mateus JM, Moreira JB, Lourenço DM, Sebastião AM, Dawson N, Xapelli S, Run, brain, run! In vitro and in vivo modulation of adult oligodendrogenesis by Brain-derived neurotrophic factor. 15th Biennial ISN Satellite Meeting on Myelin Biology, Portugal, August 2, 2023. (Oral Presentation)

Rodrigues RS, Moreira JB, Barateiro A, Vaz S, Paulo SL, Mateus JM, Lourenço DM, Ribeiro FF, Loureiro-Campos E, Bielefeld P, Fernandes A, Sebastião AM, Pinto L, Fitzsimons CP, Xapelli S, Countering chronic stress with cannabinoid type 2 receptors and physical exercise: A neurogenic focus. ISN-ESN 2023 Meeting, Portugal, August 8, 2023. (Poster Presentation)

Soares R, Mota IF, Lourenço DM, Sebastião AM, Xapelli S, Morais VA, Uncovering mitochondrial properties as novel targets for neural stem cell differentiation in the subventricular zone. Uncovering mitochondrial properties as novel targets for neural stem cell differentiation in the subventricular zone. ISN-ESN 2023 Meeting, Portugal, August 8, 2023. (Oral Presentation)

Lourenço D, Zavalko S, Sá Santos S, Mateus JM, Rodrigues RS, Miranda- Lourenço C, Sebastião AM, Mouro F, Solá S, Diógenes MJ, Xapelli S, Cannabidivarin and its neurogenic potential as a novel target for Rett syndrome. ISN-ESN 2023 Meeting, Portugal, August 8, 2023. (Oral Presentation)

Farinha-Ferreira, M., Mariani, J-C., Galipeau C., Diebolt S., Barthe, L., Deffieux, T., Tanter, M., Santos, R., Lenkei, Z., Sebastião, A.M, Tripping on dosing: acute and lasting dose-dependent effects of psilocybin on functional connectivity and affective behavior. European Behavioral Pharmacology Society (EBPS) Meeting, Germany, August 17, 2023. (Poster Presentation)

Rocha E, Meda F, Sebastião AM, Valente CA, Targeting NLRP3 Inflammasome: a New Hope for Epilepsy Resistance. 11th IBRO World Congress of Neuroscience 2023, Spain, September 9, 2023. (Poster Presentation)

Pereira A, Rocha E, Sebastião AM, Valente CA, Potential synergy between IL-10 and NLRP3 signaling pathway. 11th IBRO World Congress of Neuroscience 2023, Spain, September 9, 2023. (Poster Presentation)

Ferreira-Moreira JA, Sá-Santos S, Oliveira R, Silva F, Gava MPL, Vaz AR, Brites D, Silva MFB, Simão A, Vaz S, Rodrigues R, Sebastião AM, Castro RE, Xapelli S, Solá S, Bioenergetic reshaping of neural stem cells for a neuroregenerative secretome: clues for exercise-induced Depression relief. 11th IBRO World Congress of Neuroscience 2023, Spain, September 9, 2023. (Poster Presentation)

Farinha-Ferreira, M., Mariani, J-C., Galipeau C., Diebolt S., Barthe, L., Deffieux, T., Tanter, M., Santos, R., Sebastião, A.M, Lenkei, Z, The dose makes the trip: acute and lasting dose-dependent effects of psilocybin on functional connectivity and emotional behavior. 11th IBRO World Congress of Neuroscience 2023, Spain, September 12, 2023. (Poster Presentation)

Galipeau G, Miguel Farinha-Ferreira, Jean-Charles Mariani, Samuel Diebolt, Louis Barthe, Renata Santos, Zsolt Lenkei, Ana Maria Sebastião, Unravelling the role of 5-HT<sub>2A</sub>R activation in the long-lasting behavioral effects of psilocybin. 11th IBRO World Congress of Neuroscience 2023, Spain, September 10, 2023. (Poster Presentation)

Farinha-Ferreira M., Mariani, J.C., Santos, R., Miranda-Lourenço, C., Simões, H., Danylyuk, M.I., Lenkei, Z., Sebastião, A.M, Determining the role of dose and 5-HT<sub>2A</sub>R activation in the lasting affective behavioral effects of psilocybin. Society for Neuroscience (SfN) Meeting, USA, September 14, 2023. (Poster Presentation)

Ferreira-Moreira JA, Sá-Santos S, Oliveira R, Silva F, Gava MPL, Vaz AR, Brites D, Silva MFB, Simão A, Vaz S, Rodrigues R, Sebastião AM, Castro RE, Xapelli S, Solá, Bioenergetic remodeling of neural stem cells for a neuroregenerative secretome: clues for exercise-induced depression relief. ETRS & SPCE-TC 2023 Joint Annual Meeting, Portugal, October 11, 2023. (Oral Presentation)

Farinha-Ferreira, M., Mariani, J-C., Galipeau C., Diebolt S., Barthe, L., Deffieux, T., Tanter, M., Santos, R., Sebastião, A.M., Lenkei, Z, Not too little, not too much: dose-dependent functional connectivity and behavioral effects of psilocybin. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Hiltunen M, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, BDNF receptor dysregulation is mirrored in cerebrospinal fluid and plasma-derived extracellular vesicles from Alzheimer's disease patients. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Ferreira-Manso M, Costa-Coelho T, Inteiro-Oliveira S, Neuparth-Sottomayor M, Sebastião AM, Diógenes MJ, TAT-TrkB administration in vivo prevents hippocampal long-term potentiation deficits in 5xFAD mice. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ, Small Compounds: a promising strategy to prevent TrkB-FL cleavage in Alzheimer's Disease. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Galipeau G, Miguel Farinha-Ferreira, Sandra Marques, João Pedro Silva, Jean-Charles Mariani, Samuel Diebolt, Louis Barthe, Renata Santos, Félix Carvalho, Zsolt Lenkei, Ana Maria Sebastião. EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

Morais TP, Neuparth-Sottomayor M, Pina CC, Sebastião AM, Giovanni G, Vaz SH, Crunelli V, Absence Seizures rescue with BDNF: from seizures to comorbidities. Society for Neuroscience, USA, November 15, 2023. (Poster Presentation)

Rodrigues RS, Moreira JB, Barateiro A, Vaz S, Paulo SL, Mateus JM, Lourenço DM, Ribeiro FF, Loureiro-Campos E, Bielefeld P, Fernandes A, Sebastião AM, Pinto L, Fitzsimons CP, Xapelli S, Cannabinoid type 2 receptor inhibition enhances the antidepressant and proneurogenic effects of physical exercise after chronic stress. ETRS & SPCE-TC 2023 Joint Annual Meeting, Portugal. (Poster Presentation)

Nuno Aleman-Serrano, Costa-Coelho, Tiago; Miranda-Lourenço, Catarina, Diógenes, MJ, Ana Maria Ferreira de Sousa Sebastião, BDNF receptor dysfunction across dementias: evaluating TrkB-ICD in human AD and FTD patient samples. XXV Conference of Young SIF Pharmacologists Urbino, Italy. (Poster Presentation)

Communications in National Conferences:

Gualdino M, Gonçalves-Ribeiro J, Sebastião AM, Vaz SV, Interaction between cannabinoid receptors and adenosine receptors: implication on synaptic plasticity in the hippocampus. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 1, 2023. (Oral Presentation)

Fonseca E, Moreira JB, Mateus JM, Xapelli S, Oriá R, Fontes-Ribeiro C, Malva J, Unravelling the effect of methylmercury exposure in SVZ-derived neural stem/progenitor cell cultures. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 1, 2023. (Oral Presentation)

Rodrigues-Freitas L, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH, Role of astrocytes in the endocannabinoid-mediated long-term depression in the medial prefrontal cortex. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 1, 2023. (Oral Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, Mapping TrkB-ICD extracellularly: Alzheimer's disease cohort validation of BDNF receptor fragment in human cerebrospinal fluid and cargo sorting in extracellular vesicles. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 2, 2023. (Oral Presentation)

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ, TrkB-FL receptor: a virtual-aided design of small compounds to prevent its cleavage. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 2, 2023. (Oral Presentation)

Coelho M, Costa-Pinto S, Sebastião AM, Vaz SH, Characterization of the endocannabinoid system in the SOD1(G93A) mice model throughout disease progression. XVIII Meeting of the Portuguese Society of Pharmacology, Coimbra, Portugal, February 3, 2023. (Oral Presentation)

Ghosh A, Nádia Rei, Dilip K. Tosh, Tatiana P Morais, Sandra H Vaz, Kenneth A Jacobson, Joaquim A Ribeiro, Ana M Sebastião, Adenosine A3 receptor-mediated inhibition of GABA uptake. 53<sup>a</sup> Reunião da Sociedade Portuguesa de Farmacologia (SPF 2023), 41<sup>a</sup> Reunião de Farmacologia Clínica e 22<sup>a</sup> Reunião de Toxicologia, Coimbra, Portugal, February 1-3, 2023. (Oral Presentation)

Galipeau G, Miguel Farinha-Ferreira, Jean-Charles Mariani, Samuel Diebolt, Louis Barthe, Renata Santos, Zsolt Lenkei, Ana Maria Sebastião, Dose-dependent long-lasting behavioral effects of psilocybin. 53<sup>a</sup> Reunião da Sociedade Portuguesa de Farmacologia (SPF 2023), 41<sup>a</sup> Reunião de Farmacologia Clínica e 22<sup>a</sup> Reunião de Toxicologia, Coimbra, Portugal, February 1-3, 2023. (Oral Presentation)

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ, Explore novel compounds to prevent TrkB-FL cleavage. 2nd Symposium on Alzheimer's Disease: An Update on Pathology and Therapeutics, Portugal, February 10, 2023. (Oral Presentation)

Nuno Aleman-Serrano, Costa-Coelho, Tiago, Miranda-Lourenço, Catarina, Diógenes, MJ, Ana Maria Ferreira de Sousa Sebastião, BDNF receptor cleavage across dementias: evaluating TrkB-ICD in human AD and FTD samples. 2nd Symposium on Alzheimer's Disease: An Update on Pathology and Therapeutics, Portugal, February 10, 2023. (Poster Presentation)

Gualdino M, Gonçalves-Ribeiro J, Sebastião AM, Vaz SV, Interaction between CB1 receptors and adenosine A1 receptors on astrocytes: implication on hippocampal synaptic plasticity. Congresso Medical Cannabis Coimbra, Coimbra, Portugal, March 9, 2023. (Poster Presentation)

Coelho M, Costa-Pinto S, Sebastião AM, Vaz SH, Endocannabinoid system in ALS disease progression. Congresso Medical Cannabis Coimbra, Coimbra, Portugal, March 10, 2023. (Poster Presentation)

Morais MB, Morais TP, Sebastião AM, Vaz SH, Modulation of GABA Transporter GAT1 by Adenosine A1 and A2A Receptors in Absence Seizures. 35<sup>o</sup> Encontro Nacional de Epileptologia, Lisboa, Portugal, March 10, 2023.

Costa-Coelho T, Fonseca-Gomes J, Ferreira CB, de Almeida-Borlido C, Hiltunen M, Sebastião AM, Mendonça AD, Diógenes MJ, Novel TAT-TrkB compound in Alzheimer's disease: Rescuing BDNF-mediated synaptic plasticity and cognitive behaviour in 5xFAD mice. Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Portugal, April 11, 2023. (Oral Presentation)

Rodrigues-Freitas L; Gonçalves-Ribeiro J; Sebastião AM; Vaz SH, Unveiling the role of astrocytes in the eCB Long-Term Depression in the rodent mPFC. AIMS Meeting 2023 Research Competition, Lisbon, Portugal, April 13, 2023. (Poster Presentation)

Coelho M, Costa-Pinto S, Sebastião AM, Vaz SH, Modulation of CB1R in synaptic plasticity through ALS progression. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023. (Poster Presentation)

Rodrigues-Freitas L, Gonçalves-Ribeiro J, Sebastião AM, Vaz SH, The Relevance of Astroglial CB1R in the Rodent mPFC Synaptic Plasticity. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023. (Poster Presentation)

Gonçalves-Ribeiro J, Nanclares C, Costa-Pinto S, Neuparth-Sottomayor M, Rodrigues-Freitas L, Gualdino M, Sebastião AM, Araque A, Vaz SH, CB1R downregulates glutamate transporters activity in a astroglial Ca<sup>2+</sup>-manner in the rodent mPFC. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023.

Costa-Pinto S, Gonçalves-Ribeiro J., Moreira J., Socodato R., Relvas J.B., Sebastião A.M., Vaz S.H, Role of astrocytes on the abnormal synaptic transmission and plasticity in the motor cortex and hippocampus of SOD1G93A mice. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023. (Oral Presentation)

Gualdino M, Gonçalves-Ribeiro J, Sebastião AM, Vaz SV, Interaction between CB1 receptors and adenosine A1 receptors on astrocytes: implication on hippocampal synaptic plasticity. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023. (Poster Presentation)

Mateus JM, Moreira JB, Lourenço DM, Sebastião AM, Dawson N, Xapelli, Go the extra mile: in vitro and in vivo modulation of adult oligodendrogenesis by BDNF. VII Symposium of the Portuguese Glial Network, Albufeira, Portugal, May 2, 2023. (Poster Presentation)

Nuno Aleman-Serrano, Costa-Coelho, Tiago, Miranda-Lourenço, Catarina, Diógenes, MJ, Ana Maria Ferreira de Sousa Sebastião, BDNF signaling pathway dysfunction across dementias: TrkB-ICD in human AD and FTD patient samples. FENS Regional Meeting, Algarve, Portugal, Portugal, May 4, 2023. (Poster Presentation)

Ribeiro-Rodrigues, L, Paulo, SL, Paiva, VH, Sebastião, AM, Aronica E, Campos AR, Bentes C, Caeiro, L, Xapelli, S\*, Diógenes, MJ\*, Status epilepticus induces cleavage of TrkB-FL while cleavage prevention reduces seizures. XVI CAML PhD Students Meeting, Portugal, May 10, 2023. (Oral Presentation)

Gonçalves-Ribeiro J, Astrocytic CB1R activity is dictated by adenosine receptors in the rodent mPFC. XVI CAML PhD Students Meeting, Portugal, May 10, 2023. (Oral Presentation)

Costa-Pinto S, Gonçalves-Ribeiro J., Moreira J., Socodato R., Relvas J.B., Sebastião A.M., Vaz S.H, Role of astrocytes on synaptic transmission and plasticity in the motor cortex and hippocampus of SOD1G93A mice. XVI CAML PhD Students Meeting, Portugal, May 11, 2023. (Oral Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, BDNF/TrkB-FL dysregulation is mirrored in extracellular vesicles and in cerebrospinal fluid of an Alzheimer's disease patient series. XVI CAML PhD Students Meeting, Portugal, May 11, 2023. (Oral Presentation)

Nuno Aleman-Serrano; Costa-Coelho, Tiago; Miranda-Lourenço, Catarina; Diógenes, MJ; Ana Maria Ferreira de Sousa Sebastião, BDNF receptor cleavage across dementias: TrkB-ICD in human AD and FTD patient samples. 37<sup>a</sup> Reunião Anual Grupo de Estudos de Envelhecimento Cerebral e Demências, Portugal, June 17, 2023. (Oral Presentation)

Inteiro-Oliveira S, Costa-Coelho T, Ferreira-Manso M, Sebastião AM, Enguita FJ, Diógenes MJ, Small Compounds: a new promising strategy to prevent BDNF receptor cleavage. 37<sup>a</sup> Reunião Anual Grupo de Estudos de Envelhecimento Cerebral e Demências, Portugal, June 17, 2023. (Poster Presentation)

Ferreira-Manso M, Costa-Coelho T, Inteiro-Oliveira S, Neuparth-Sottomayor M, Sebastião AM, Diógenes MJ, TAT-TrkB peptide administration in vivo prevents hippocampal long-term potentiation deficits in 5xFAD mice. 37<sup>a</sup> Reunião Anual Grupo de Estudos de Envelhecimento Cerebral e Demências, Portugal, June 17, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Hiltunen M, Castrén E, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, Dysregulation of the BDNF/TrkB system in Alzheimer's disease ramifies in the secretion of a TrkB-derived fragment through extracellular vesicles. 37<sup>a</sup> Reunião Anual Grupo de Estudos de Envelhecimento Cerebral e Demências, Portugal, June 17, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Umemori J, Castrén E, Sebastião AM, Brites D, Diógenes MJ, Extracellular release of a fragment derived from BDNF receptor cleavage. 2nd Meeting of the Portuguese Network of Extracellular Vesicles, Portugal, June 22, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Umemori J, Castrén E, Sebastião AM, Brites D, Diógenes MJ, Extracellular release of a fragment derived from BDNF receptor cleavage. 2nd Meeting of the Portuguese Network of Extracellular Vesicles, Portugal, June 22, 2023. (Oral Presentation)



Sá-Santos S, Oliveira R, Silva F, Ferreira-Moreira JA, Gava MPL, Vaz AR, Brites D, Silva MFB, Simão A, Vaz S, Rodrigues R, Sebastião AM, Castro RE, Xapelli S, Solá S, Injury and metabolic pulses trigger multiple distinct secretory signals of neural stem cells: clues for exercise-induced Depression relief. 2nd Meeting of the Portuguese Network of Extracellular Vesicles, Portugal, June 22, 2023. (Oral Presentation)

Galipeau G, Miguel Farinha-Ferreira, Jean-Charles Mariani, Samuel Diebolt, Louis Barthe, Renata Santos, Zsolt Lenkei, Ana Maria Sebastião, Long-lasting effects of psilocybin: the role of dose and 5-HT<sub>2A</sub>R activation. Yes Meeting, Porto, Portugal, September 15, 2023. (Oral Presentation)

Silva F, Sá-Santos S, Oliveira R, Ferreira-Moreira JA, Gava MPL, Vaz AR, Brites D, Silva MFB, Simão A, Vaz S, Rodrigues R, Sebastião AM, Castro RE, Xapelli S, Solá S, Neural stem cells use multiple distinct secretory signals to modify their neighbors in response to injury- and metabolic-pulses. iMED Innovate Competition iMED Conference 15.0., Portugal, October 14, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Ferreira CB, de Almeida-Borlido C, Hiltunen M, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, Human Temporal Lobe and Cerebrospinal Fluid Samples Mirror the Dysregulation Signature of the BDNF/TrkB System in Alzheimer's disease. Workshop on Biochemistry of Ageing by Sociedade Portuguesa de Bioquímica, Portugal, Online, November 7, 2023. (Poster Presentation)

Ana Laura Duarte, Exploring Adenosinergic Signaling and Neurite Outgrowth in the Context of Mecp2-. Development in Action Meeting Sociedade Portuguesa de Biologia do Desenvolvimento, Portugal, November 10, 2023. (Poster Presentation)

Costa-Coelho T, Fonseca-Gomes J, Garcia G, Ferreira-Manso M, Ferreira CB, de Almeida-Borlido C, Umemori J, Castrén E, Hiltunen M, Sebastião AM, Mendonça AD, Brites D, Diógenes MJ, BDNF as a beacon of trophic support: Extracellular vesicles mirror BDNF-TrkB dysfunction in Alzheimer's disease. Pizza Seminar, Instituto de Medicina Molecular João Lobo Antunes, Portugal, November 14, 2023. (Oral Presentation)

Nuno Aleman-Serrano; Costa-Coelho, Tiago; Miranda-Lourenço, Catarina; Diógenes, MJ; Ana Maria Ferreira de Sousa Sebastião, BDNF receptor cleavage in Alzheimer's Disease: From mice to humans. 7.ª Conferência Anual da RedeSAÚDE, Portugal. (Oral Presentation)

### **Organization of Conferences**

Sara Xapelli, Organizer, FENS Regional Meeting 2023, Portugal, May 3, 2023.

Sara Xapelli, Organizer, 2023 ISN-ESN Meeting, Portugal, August 8, 2023.

Sandra Vaz, Organizer, Symposium MNS 2023 Meeting, Carthage, Tunisia, October 17, 2023.

Tatiana Pinto Morais, Organizer, Symposium MNS 2023 Meeting, Carthage, Tunisia, October 17, 2023.

### **Networks and Research Infrastructures**

Sara Xapelli, COST Action CA18116: Aniridia: networking to address an unmet medical, scientific, and societal challenge, Management Committee Member.

Sara Xapelli, Portuguese Society for Neuroscience, Vice-President.

Sara Xapelli, Portuguese Society for Stem Cells and Cell Therapies (SPCE-TC), Voter of Fiscal Council.

Sara Xapelli, Mind-Brain College of the University of Lisbon, Member of the Executive Committee.

Sara Xapelli, Maria José Diógenes, Braining, PI.

Sandra Vaz, Cláudia Valente, COST Action CA21130 (PRESTO), Members.

Sandra Vaz, Sara Xapelli, COST Action CA20135 (Teatime), Members.

Tiago Costa-Coelho, Fala-me Neuro, Member/Editor/Designer.

Mafalda Ferreira-Manso, Fala-me Neuro, Member/Editor.

Maria José Diógenes, EPHAR, Member of the Executive Committee.

Maria José Diógenes, Portuguese Society of Pharmacology, President.

Ana Maria Sebastião, EpiEpiNet - Epileptogenesis and Epilepsy Network GA2114690, Coordinator.

Ana Maria Sebastião, COST Action 21130 (PRESTO), Management Committee.

### **Prizes and Honours**

Cláudia Valente, Fellowship (8887.901507/2023-00) as Invited Professor, Program CAPES-PrInt, Brazil.

Mariana Morais, Prémio/Bolsa Científica da Liga Portuguesa Contra a Epilepsia (LPCE).

Tiago Costa-Coelho, Best Poster at 37ª Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demência (GEECD).

Sara Inteiro-Oliveira, Fellowship SPN for FENS Regional Meeting (registration).

Nuno Alemã-Serrano, Fellowship SPN for FENS Regional Meeting (registration).

Nuno Alemã-Serrano, Fellowship SPF for the Italian Conference of Young Pharmacologists.

Nuno Alemã-Serrano, AstraZeneca-FMUL Young Doctor's Research Grant.

Miguel Farinha-Ferreira, FENS travel grant to attend the SFN Conference, Washington.

Miguel Farinha-Ferreira, EBPS travel grant to attend the EBPS Meeting.

Miguel Farinha-Ferreira, SPN travel grant to attend the IBRO Meeting.

### **Advanced Teaching**

Sara Xapelli, Coordination of Master Curricular Unit, Cognitive Science, Portugal, March 1, 2023.

Sandra Vaz and Ana Sebastião, Workshop Organization, Relevance of electrophysiology recordings for glial cells - Workshop of the Portuguese Glia Network, Lisbon, Portugal, March 7, 2023.

Sara Xapelli, Course Organization, Neural stem cells-perspectives for clinical application in brain regeneration, Poland, March 20, 2023.

Maria José Diógenes, Lecture, 3rd Edition of the Neurodegenerative Diseases - Advanced Course, Lisbon, Portugal, March 29, 2023.

Sara Xapelli and Cláudia Valente, Workshop Organization, A jump to a neuropharmacology research Lab - AIMS meeting, Portugal, April 13, 2023.

Sara Xapelli, Course Organization, Neural stem cells for therapies: clinical potential, Poland, June 12, 2023.

Maria José Diógenes, Coordination of Master Curricular Unit, Preclinical research, Master in Clinical Research, Lisbon, Portugal, September 1, 2023.

Sandra Vaz, Workshop Organization, Workshop on EEG - What can we collect from post-mortem tissue?, Lisbon, Portugal, September 28, 2023.

Tatiana Morais, Workshop Organization, Workshop on EEG - What can we collect from post-mortem tissue?, Portugal, September 28, 2023.

Maria José Diógenes, Lecture, The object of pharmacology and basic principles of pharmacokinetics, Master in Clinical Research, Lisbon, Portugal, October 1, 2023.

Cláudia Valente, Lecture, Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lecture "Methodological approaches through antigen-antibody interactions Applications to neuroscience", Portugal, October 4, 2023.

Ricardo Viais, Lecture, Master in Neurosciences, Portugal, October 4, 2023.

Sandra Vaz, Lecture, Glial cells and their ability to control synaptic activity - Master and PhD in Neurosciences, Lisbon, Portugal, October 10, 2023.

Sara Xapelli, Workshop Organization, Neural stem cells and its potential for neuroregeneration - Master and PhD in Neuroscience, Portugal, October 26, 2023.

Sandra Vaz, Workshop Organization, Recordings of synaptic potentials from hippocampal slices - Master and PhD in Neuroscience, Lisbon, Portugal, October 27, 2023.

Cláudia Valente, Lecture, Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lecture "Cell death in healthy and diseased brain", Portugal, October 31, 2023.

Cláudia Valente, Lecture, Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lecture "The role of neuroinflammation in CNS diseases", Portugal, November 2, 2023.

Maria José Diógenes, Lecture, Master in Neurosciences, Lisbon, Portugal, November 7, 2023.

Tiago Costa-Coelho, Workshop Organization, Assessing calpain-mediated TrkB-FL cleavage in mice cortical samples (Neuroscience Master Course Rotation), Portugal, November 8, 2023.

Cláudia Valente, Workshop Organization, Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November 7, 2023.

Sara Xapelli, Lecture, Neural Stem cells and its neuroregenerative potential - Master and PhD in Neuroscience, Portugal, November 9, 2023.

Catarina Miranda-Lourenço, Lecture, Synaptic Dysfunction in Rett Syndrome/Master and PhD in Neurosciences, Portugal, November 15, 2023.

Mafalda Ferreira-Manso, Workshop Organization, Genotyping 5xFAD mice, an animal model of Alzheimer's disease, Portugal, November 22, 2023.

Sara Xapelli, Lecture, Neural Stem cells and its neuroregenerative potential - Master in Biomedical Research, Portugal, November 22, 2023.

Sara Xapelli, Course Organization, PhD Advanced Course: Stem Cell Technologies, Portugal, November 27, 2023.

Sandra Vaz, Lecture, How neurons and glia in neuronal circuits interact with each other? - Master in Biomedical Research, Lisbon, Portugal, November 27, 2023.

Cláudia Valente, Course Organization, Neuroinflammation in Brain Diseases-A double-edged sword, Brazil, November 29, 2023.

Sara Xapelli, Lecture, Animal models of epilepsy - Master and PhD in Neurosciences, Portugal, November 29, 2023.

Sara Xapelli, Lecture, Problem-based Learning and Data Interpretation, Portugal, Date: December 4, 2023.

Sandra Vaz, Lecture, The importance of glia in neurodegenerative disorders - PhD School in "Clinical and Experimental Neuroscience and Psychiatry" of Sapienza University, Rome, Italy, December 11, 2023.

Ana M Sebastião, Course Organization, Master in Neurosciences, Portugal.

Ana M Sebastião, Course Organization, PhD in Neuroscience, Portugal.

Ana M Sebastião, Course Organization, Master in Cognitive Sciences, Portugal.

Ana M Sebastião, Coordination of PhD Curricular Unit, PhD in Cognitive Sciences, Portugal.

### **MSc Theses**

Elina Hiort af Ornäs, The role of TrkB-ICD, a product of brain-derived neurotrophic factor receptor cleavage, in seizure severity using an in vivo model of epilepsy, Supervisor: Sara Xapelli, Linköping University, Sweden, January 11, 2023.

Carolina Capela, Microglia depletion impact in Epileptogenesis - Focusing on NLRP3 inflammasome pathway, Supervisor: Cláudia Valente, Instituto Superior Técnico da Universidade de Lisboa, Portugal, June 23, 2023.

Diana Sousa Correia, Investigating BDNF receptor cleavage in an in vivo model of epilepsy, Supervisor: Sara Xapelli, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 26, 2023.

Nuno Alemã-Serrano, BDNF receptor cleavage in Alzheimer's Disease: From mice to humans, Supervisor: Maria José Diógenes, Co-Supervisor: Alexandre de Mendonça, Instituto de Farmacologia e Neurociências, Instituto de Farmacologia e Neurociências, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 26, 2023.

Catarina Miranda-Lourenço, Study of hippocampal neurotransmitters release and adult neurogenesis in two different phenotypes of a Rett Syndrome mouse model, Supervisor: Maria José Diógenes, Instituto de Farmacologia e Neurociências, Instituto de Farmacologia e Neurociências, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 29, 2023.

Lia Fernandes, Investigation of novel compounds to prevent TrkB-FL cleavage, Supervisor: Maria José Diógenes, Faculdade de Medicina da Universidade de Lisboa, Portugal, July 25, 2023.

Tiago Ferreira, Pyroptotic deadly curse of neurons in Alzheimer's Disease, Supervisor: Cláudia Valente, Faculdade de Medicina da Universidade de Lisboa, Portugal, December 14, 2023.

### **PhD Theses**

Rita Soares, Role of mitochondrial dynamics and metabolism in postnatal neural stem cells differentiation, Supervisor: Vanessa Morais, Co-Supervisor: Sara Xapelli, Faculdade de Medicina da Universidade de Lisboa, Portugal, May 19, 2023.

Diogo Lourenço, Uncovering the neurogenic potential of cannabinoids upon adult neural stem modulation: Cannabidiol as a novel modulator of adult neurogenesis, Supervisor: Sara Xapelli, Faculdade de Medicina da Universidade de Lisboa, Portugal, December 5, 2023.

## Valorization of Knowledge / Social and Economic Impact

### Partnerships with Industry in 2023

AccelBio, Collaborative Research.

### Intellectual Property Rights in 2023

Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, UC, Inventors: Maria José de Oliveira Diógenes Nogueira [PT]; João Filipe Fonseca Gomes [PT]; André Jerónimo Santos [PT]; Ana Maria de Sousa Sebastião [PT]; Carlos Bandeira Duarte [PT], Therapeutic agents, pharmaceutical composition, and associated biomarkers based on TRK-B.

### Science and Society in 2023

#### For the General Public (Adults):

- Maria José Diógenes "Cérebro, medicamentos, pediatria e inclusão", Setúbal, January 20, 2023.
- Maria José Diógenes "Neurociências ao Nível do Organismo", Brain Gain, March 15, 2023.
- Maria José Diógenes, Entrevista sobre doenças neurodegenerativas para a edição de setembro de 2023 da revista "Prevenir".
- Participation in Pint of Science Talk "Neuroinflammation and neurological diseases" Lisboa, May 22, 2023.
- Participation in Episode 2 of the documentary "100 ou Mais" – RTP ([www.rtp.pt/play/p12607/e737496/100-ou-mais](http://www.rtp.pt/play/p12607/e737496/100-ou-mais)).
- Falame Neuro podcast "The plasticity of the brain" (<https://www.falameneuro.pt/cópia-rubricas>).
- iMM InstagramTakeover by Tiago Coelho (July 17-22). Audience: ~5451 people (Instagram followers).
- Tiago Coelho: Compreender Saúde: 1ª Conferência para Professores | Understand health: 1st Conference for Professors as a member of "Fala-me Neuro". Audience: Portuguese school teachers

- Tiago Coelho and Mafalda Manso: Participation in "Fala-me Neuro" dissemination project (January 1-December 31) to disseminate neuroscience content easy and in Portuguese. Audience: All Portuguese native speakers from the world.

- Ana Laura Duarte, Ricardo Viais and Maria José Diógenes: ANPAR webinar "Trofinetide: do laboratório à aplicação clínica" (June 18, 2023). Audience: patients associations, families affected by Rett Syndrome.

- Maria José Diógenes: "How my personal story changed my professional life". Audience: ALBA community and general public (December 5, 2023). Available at YouTube (<https://www.bing.com/videos/riverview/relatedvideo?&q=Maria+Jos%c3%a9+diogenes+ALBA&&mid=4B7CCD3A9120CB3462B94B7CCD3A9120CB3462B9&&FORM=VRDGAR>).

#### For School Students:

- European Researchers' Night - Who's who in your brain? Take a look at the cells of the nervous system (September 29, 2023). Multiple schools and people of all ages (youngsters, teens, adults and seniors).

- Coordination and participation in 8 visits to schools as part of the Brain Awareness Week organized by SPN and Ciência Viva.

- Coordinator of 1 visit to the laboratories as part of the International Brain Awareness Week (12th grade students). Seminar: Terá o cérebro algum potencial para se regenerar??

- Participation in Ciência di Noz Manera / Science Our Way project (February 2023). Audience: 8th grade students

- Participation in Feira das Profissões, Maria José Diógenes "Percurso de uma cientista e professora universitária", Escola Secundária de Almada.



## Ribot & Silva-Santos Lab

**Head of Laboratory:** Julie Ribot, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes

**Head of Laboratory:** Bruno Silva-Santos, PhD, Group Leader and Vice-Director at Instituto de Medicina Molecular João Lobo Antunes and Full Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Amanda Pires Bonfanti	Master Degree	Trainee (Left February)
Ana Carolina Graís Condeço	Master Degree	Lab Technician
Ana Maria de Amarante Pamplona Dias Santos	PhD	Senior Postdoctoral Researcher
André Luis Bombeiro	PhD	Senior Postdoctoral Researcher
André Miguel Vaz Pinto Santos	University Degree	MSc Student (Left April)
Anita Raquel Quintal Gomes	PhD	Senior Postdoctoral Researcher
Bernardo Nunes Araújo Silva	University Degree	MSc Student (Left July)
Carolina Emanuel Carreira Gomes Jardim	Master Degree	PhD Student
Daniel Pereira Inácio	Master Degree	PhD Student
Deniz Bulgur	Master Degree	Lab Technician
Eller Conti	Master Degree	PhD Student (Left April)
Hugo Marques Caetano	High School Diploma	Trainee (Left December)
Joana Carolina Marinho Cunha	PhD	Postdoctoral Researcher (Left September)
Julie Darrigues	PhD	Postdoctoral Researcher (Left March)
Karine Marie Serre	PhD	Staff Scientist
Leandro Joel Barros Fernandes	Master Degree	PhD Student
Mariana Alexandre Carreira		MSc Student (Started September)
Natacha Maria Gonçalves Silva Sousa	Master Degree	Lab Manager
Rafael Blanco Domínguez	PhD	Postdoctoral Researcher
Raquel Macedo Bento dos Reis e Moura		MSc Student (Started September)
Raven Abrielle Garcia	Master Degree	MSc Student (Started October)
Rodrigo Gaspar Quiaios Fernandes	University Degree	MSc Student
Rúben Gonçalo Rodrigues Pinheiro	PhD	Postdoctoral Researcher (Started March)
Sofia Mensurado Santos	PhD	Postdoctoral Researcher
Vladimir Ghilas	University Degree	MSc Student (Left March)

### Lab Interests

We are interested in the pleiotropic roles of immune cells in tissue (patho)physiology. Within our major research line of Immuno-Oncology, we study T lymphocytes for the identification of molecular mechanisms involved in their differentiation, activation and functions in cancer, with the goal of designing novel immunotherapy strategies.

In a more recent area in our lab – Neuroimmunology – we explore the crosstalk between T cells and the Central and Peripheral Nervous Systems, both in health and disease (neurodegeneration or injury).

Our special focus is the gamma-delta T cell lineage, starting with its thymic development and effector cell differentiation. In the periphery, we investigate their activities in inflamed tissues, sterile inflammation in murine models of tissue degeneration or injury. Overall, our goal is to improve the understanding of how T cells participate in (patho)physiological processes, and how we may manipulate them to promote health and tackle disease.

### **Research Field**

- Physiology in Health, Disease and Aging
- Neuroscience and Disorders of the Nervous System
- Immunity, Infection and Immunotherapy

### **Major Scientific Achievements in 2023**

In 2023 we graduated 3 new Master students in the areas of Biomedical Research - Immunology (Bernardo Silva), Immuno-Oncology (André Vaz Pinto) and Neuroimmunology (Vladimir Ghilas).

We advanced our knowledge on the cellular therapy for cancer developed in our laboratory, Delta One T (DOT) cells, with regard to their mechanisms of recognition of both hematological and solid tumors (unpublished results); and identified a new cross-talk between maternal gamma-delta T cells and the microbiota, which shapes the lung immune system of the offspring (Papotto et al. Cell Rep 2023). The microbiota has also become the focus of one of our Neuro-Immunology projects where we investigate the role of gamma-delta T cells and their key effector cytokine, interleukin-17, in peripheral (sciatic) nerve regeneration (unpublished results).

Finally, we presented our work in various international institutes/ universities in Berlin, Brussels, Frankfurt, Madrid, Vienna, Montpellier and Hamburg.

### **Ongoing Projects**

2023/2025: Deciphering the role of IL-17 on peripheral nerve regeneration. Coordinator: Julie Ribot. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: 2022.01244.PTDC. Amount: 249 982,50€. Total Amount: 249 982,50€.

2023/2025: RESEARCH AGREEMENT - Addendum No. 5. Coordinator: Bruno Silva-Santos. Funding Agency: Lymphact. Reference: RESEARCH AGREEMENT – ADDENDUM. Amount: 611 875,00€. Total Amount: 611 875,00€.

2023/2025: Dissecting the role of breast cancer-resident microbiota: identification of novel biomarkers of clinical outcome and putative therapeutic targets. Coordinator: Karine Serre. Funding Agency: Gilead. Reference: Programa Gilead GÉNESE 2023 - Grant ID number: 21562. Amount: 10 000,00€. Total Amount: 10 000,00€

2021/2024: Regulação da homeostasia das células T nas meninges. Coordinator: Julie Ribot. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/1988/2020. Amount: 250 000,01€. Total Amount: 250 000,01€.

2021/2024: Regulação dos linfócitos T gama-delta no microambiente tumoral e sua manipulação para imunoterapia de cancros sólidos - Regulation of gamma-delta T cells in the tumor microenvironment and their manipulation towards immunotherapy of solid cancers. Coordinator: Bruno Silva-Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-ONC/6829/2020. Amount: 250 000,00€. Total Amount: 250 000,00€.

2020/2024: Cellular and molecular regulators of multifaceted  $\gamma\delta$  T-cells in the tumor microenvironment. Coordinator: Bruno Silva-Santos. Funding Agency: Fundação AstraZeneca. Reference: FAZ\_PremioCiencia\_2020. Amount: 35 000,00€. Total Amount: 35 000,00€.

2018/2024: Tumor-associated neutrophils suppress pro-tumoral IL-17+  $\gamma\delta$  T cells through induction of oxidative stress. Coordinator: Bruno Silva-Santos. Funding Agency: Janssen-Cilag Farmacêutica, Lda. Reference: Prémio Janssen 2018. Amount: 30 000,00€. Total Amount: 30 000,00€.

## Scientific Impact

### Academic Collaborations

- The Francis Crick Institute, United Kingdom.
- Queen Mary University of London, United Kingdom.
- Hamburg Medical School, Germany.
- Toulouse Institute for Infectious and Inflammatory Diseases, France.
- University of Vienna, Austria.

- INSERM, France.
- The University of Giessen (Justus-Liebig-Universität Giessen), Germany.
- University of Torino, Italy.
- Josep Carreras Leukaemia Research Institute, Spain.
- Icahn School of Medicine at Mount Sinai, USA.
- Champalimaud Foundation, Portugal.
- Instituto de Investigação e Inovação em Saúde, Portugal.
- Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### Selected Publications

Lopes N\*, McIntyre C\*, Martin S\*, Raverdeau M\*, Sumaria N, Kohlgruber AC, Fiala GJ, Agudelo LZ, Dyck L, Kane H, Douglas A, Cunningham S, Prendeville H, Loftus R, Carmody C, Pierre P, Kellis M, Brenner M, Argüello RJ, Silva-Santos B\*\*, Pennington DJ\*\*, Lynch L\*\* (2021). [Distinct metabolic programs established in the thymus control effector functions of  \$\gamma\delta\$  T cell subsets in tumor microenvironments](#). *Nature Immunology* 22(2):179-192. (\* and \*\* Equal contributions)

**Relevance of this publication:** This study demonstrated that the two main effector  $\gamma\delta$  T cell subsets, producing either interferon- $\gamma$  (IFN- $\gamma$ ) or interleukin-17 (IL-17), employ different metabolic sources, glucose and lipids, respectively. We showed the importance of this metabolic dichotomy in the tumor microenvironment, since IFN $\gamma$ -producing  $\gamma\delta$  T cells are potent anti-tumor effectors, whereas IL-17-producing  $\gamma\delta$  T cells promote tumor growth, and its impact on tumor progression in pre-clinical models of cancer.

Brigas HC, Ribeiro M, Coelho JE, Gomes R, Gomez-Murcia V, Carvalho K, Faivre E, Costa-Pereira S, Darrigues J, de Almeida AA, Buée L, Dunot J, Marie H, Pousinha PA, Blum D, Silva-Santos B, Lopes LV\*, Ribot JC\* (2021). [IL-17 triggers the onset of cognitive and synaptic deficits in early stages of Alzheimer's disease](#). *Cell Reports*. Aug 31;36(9):109574. (\* Equal contributions)

**Relevance of the publication:** This study reported that the accumulation of IL-17-producing cells in the brain and meninges triggers the early inflammatory events that induce Alzheimer's pathology. Together with our previous study in *Science Immunology* (Ribeiro et al, 2019), we highlight a dual role for IL-17: pro-cognitive at steady state and anti-cognitive upon neurodegeneration, thus implying that a tight control of the homeostasis of meningeal IL-17 producers (mostly  $\gamma\delta$  T cells) is required to maintain brain integrity.

Ribeiro M\*, Brigas HC\*, Temido-Ferreira M, Pousinha PA, Regen T, Santa C, Coelho JE, Marques-Morgado I, Cláudia Valente C, Omenetti S, Stockinger B, Weissman A, Manadas B, Lopes LV, Silva-Santos B\*\* and Ribot JC\*\* (2019). [Meningeal  \$\gamma\delta\$  T cell-derived IL-17 controls synaptic plasticity and short-term memory](#). *Science Immunol*, 4 (40). (\*\*Co-corresponding)

**Relevance of the publication:** We identified a meningeal population of  $\gamma\delta$  T cells that control brain cognitive functions through the production of IL-17. We showed that this cytokine stimulated the production of brain derived neurotrophic factor (BDNF) by glial cells, which promoted neuronal synaptic plasticity required for short-term memory and learning. These findings provided a key missing piece to

the puzzle of immune populations infiltrating the meninges and the regulation of neurophysiology, thus becoming a seminal paper in Neuroimmunology. The study was particularly well received, largely covered by the media (Público, Alzforum, Cosmosmag, Technology Network); highlighted in Nature Immunology and Nature Review Immunology; and awarded a Pfizer Award for Basic Research.

Almeida AA, Correia DV, da Silva CL, da Silva MG, Anjos DR, Silva-Santos B (2016). [Delta One T cells for immunotherapy of chronic lymphocytic leukemia: clinical-grade expansion/ differentiation and preclinical proof-of-concept](#). **Clinical Cancer Research** 22(23):5795-5804.

**Relevance of the publication:** Here we characterized a new method for clinical-grade expansion of human  $\gamma\delta$  T cells for adoptive immunotherapy. We showed that the V $\delta$ 1-enriched product, named “Delta One T” (DOT) cells, upregulated the expression of multiple natural killer receptors, which enhanced their cytotoxic function against tumors. Furthermore, we demonstrated the therapeutic potential of DOT cells in vivo, using a pre-clinical model of chronic lymphocytic leukemia. These data, together with our patented expansion/ differentiation protocol, was critical for the acquisition of our/ iMM’s spin-off company, Lymphact, by the British biotech company, GammaDelta Therapeutics, in 2018.

Ribot JC, deBarros A, Pang DJ, Neves JF, Peperzak V, Girardi M, Borst J, Hayday AC, Pennington DJ and Silva-Santos B (2009). [CD27 is a thymic determinant of the balance between IFN- \$\gamma\$  and IL-17-producing  \$\gamma\delta\$  T cell subsets](#). **Nature Immunol** 10(4): 427-36.

**Relevance of the publication:** Seminal paper, cited over 600 times (Google Scholar), describing two main functional  $\gamma\delta$  T cell subsets, producing either interferon- $\gamma$  (IFN- $\gamma$ ) or interleukin-17 (IL-17), that we distinguished on the basis of CD27 expression levels. We showed that the two subsets diverge early in ontogeny during thymic development, with CD27 signals promoting the IFN- $\gamma$  pathway over the IL-17-producing fate. These findings inspired many subsequent studies, including ours: Schmolka et al. Nat Immunol 2013, Rei et al. PNAS 2014, Muñoz-Ruiz et al. Nat Immunol 2016, Mensurado et al. PLoS Biol 2018 and Lopes et al. Nat Immunol 2021.

### 2023 Publications in Peer-Reviewed Journals

Mensurado S, Blanco-Domínguez R, Silva-Santos B (2023). The emerging roles of  $\gamma\delta$  T cells in cancer immunotherapy. **Nature Reviews Clinical Oncology** 20(3):178-191.

Silva-Santos B, Mensurado S (2023).  $\gamma\delta$  T cells maintain sensitivity to immunotherapy in MHC-I-deficient tumors. **Nature Immunology**. 24(3):387-388.

Papotto PH, Yilmaz B, Pimenta G, Mensurado S, Cunha C, Fiala GJ, Gomes da Costa D, Gonçalves-Sousa N, Chan BHK, Blankenhau B, Domingues RG, Carvalho T, Hepworth MR, Macpherson AJ, Allen JE, Silva-Santos B (2023). Maternal  $\gamma\delta$  T cells shape offspring pulmonary type 2 immunity in a microbiota-dependent manner. **Cell Reports** 42(2):112074.

Chora ÂF, Marques S, Gonçalves JL, Lima P, Gomes da Costa D, Fernandez-Ruiz D, Marreiros MI, Ruivo P, Carvalho T, Ribeiro RM, Serre K, Heath WR, Silva-Santos B, Tate AT, Mota MM (2023). Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  $\gamma\delta$  T cells and IL-17-promoted stress erythropoiesis. *Immunity* 56(3):592-605.

Gonçalo Palrão Costa, Sofia Mensurado, Bruno Silva-Santos (2023). Therapeutic avenues for  $\gamma\delta$  T cells in cancer. *Journal for ImmunoTherapy of Cancer* 11(11): e007955.

Silva-Santos B, Ribot JC, Adams EJ, Willcox BE, Eberl M (2023).  $\gamma\delta$  T cell explorations seek terra firma. *Nature Immunology* 24(10):1606-1609.

Ajendra J, Papotto PH, Parkinson JE, Dodd RJ, Bombeiro AL, Pearson S, Chan BHK, Ribot JC, McSorley HJ, Sutherland TE, Allen JE (2023). The IL-17A-neutrophil axis promotes epithelial cell IL-33 production during nematode lung migration. *Mucosal Immunology* 16(6):767-775.

André L. Bombeiro, Rodrigo G.Q. Fernandes, Julie C. Ribot (2023). New immune regulators of sciatic nerve regeneration? Lessons from the neighbourhood. *Neural Regeneration Research* 19(4):705-706.

Vigário A.M., Pamplona A (2023).  $\gamma\delta$  T cells as immunotherapy for malaria: balancing challenges and opportunities. *Frontiers in Immunology* 14.

### **Invited Lectures and Seminars**

Julie Ribot, gamma-delta T cells in tissue pathophysiology. TissueHome symposium, Vienna, Austria, January 25, 2023.

Bruno Silva-Santos, Delta One T cells: a new immunotherapy for cancer. Building Bridges in Biology, Oeiras, Portugal, March 2, 2023.

Julie Ribot, gamma-delta T cells in tissue pathophysiology. Annual Meeting Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023.

Sofia Mensurado, Cancer Immunotherapies: upgrade your defences. AIMS Meeting 2023, Lisbon, Portugal, April 15, 2023.

Bruno Silva-Santos, Differentiation of gamma-delta T cell subsets implicated in infection and cancer. Charité Seminar Series, Berlin, Germany, April 24, 2023.

Bruno Silva-Santos, Gamma-delta T cells in cancer immunotherapy: my 12 commandments. 4th Gamma-delta Therapies Summit, Boston, USA, July 25, 2023.

Karine Serre, Options and Challenges in multiplexed imaging. Training School Meeting COST-Action Mye-InfoBank, Leuven, Belgium, October 3, 2023.

Karine Serre, Presentation of Instituto de Medicina Molecular João Lobo Antunes. 1st Immuno-Oncology SPO-SPI joint meeting, Conimbriga, Portugal, October 28, 2023.

Bruno Silva-Santos, Delta One T cells: a new  $\gamma\delta$  T cell-based immunotherapy for cancer. 1st Immuno-Oncology SPO-SPI joint meeting, Conimbriga, Portugal, October 28, 2023.

Bruno Silva-Santos, Molecular mechanisms of differentiation and activation of effector gamma-delta T cell subsets. CBMSO-Severo Ochoa seminar series, Madrid, Spain, November 3, 2023.

Julie Ribot, gamma-delta T cells in tissue pathophysiology. French Society for Immunology, Innate T Cell Club Meeting, Montpellier, France, November 9, 2023.

Julie Ribot, gamma-delta T cells in tissue pathophysiology. 1st HCTI/HSII Infection and Immunity Symposium, Hamburg, Germany, November 15, 2023.

Bruno Silva-Santos, Delta One T cells: a new gamma-delta T cell-based cancer immunotherapy. ULB Seminar Series, Brussels, Belgium, November 17, 2023.

Bruno Silva-Santos, Delta One T cells: a new gamma-delta T cell-based cancer immunotherapy. Georg-Speyer Haus Seminar Series, Frankfurt, Germany, November 24, 2023.

## **Communications**

### Communications in International Conferences:

Sofia Mensurado, Molecular determinants of Acute Myeloid Leukemia targeting by Delta One T cells. Keystone Symposia meeting on Cancer Immunotherapy: Mechanisms of Response versus Resistance, Banff, Canada, March 6, 2023. (Oral Presentation)

Rafael Blanco Domínguez, Regulatory T cell depletion unleashes an anti-tumor IFN $\gamma$  gd T cell response in the tumour microenvironment. Keystone Symposia meeting on Cancer Immunotherapy: Mechanisms of Response versus Resistance, Banff, Canada, March 6, 2023. (Poster Presentation)

Rafael Blanco Domínguez, Treg cells are shaped by the tumor microenvironment to target specifically anti-tumor  $\gamma\delta$  T cell subsets. 44 SEI Bi-annual meeting, Bilbao, Spain, May 10, 2023. (Oral Presentation)

Sofia Mensurado, Molecular determinants of Acute Myeloid Leukemia targeting by Delta One T cells. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Oral Presentation)

Carolina Condeço, Molecular determinants of Acute Myeloid Leukemia targeting by Delta One T cells. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Poster Presentation)

Vicente Almeida, Regulation of gd17 T cell homeostasis by stress-derived signals. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Poster Presentation)

André Bombeiro, Investigating the role of IL-17 in Peripheral Nerve Regeneration. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Poster Presentation)

Daniel Inácio, Dissecting the IFN $\gamma$ - versus IL-17-specific mRNAomes of effector gdT lymphocytes. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Oral Presentation)

Anita Q. Gomes, microRNAs are key regulators of the development and functional differentiation of  $\gamma\delta$  T cell subsets. 10th International Gamma-delta T cell conference, Lisbon, Portugal, June 22, 2023. (Poster Presentation)

Rodrigo Fernandes, Investigating the role of IL-17 in Peripheral Nerve Regeneration. IASP International Conference on Neuropathic Pain, Lisbon, Portugal, September 7, 2023. (Poster Presentation)

André Bombeiro, A role for IL-17 in Sciatic Nerve Regeneration. IASP International Conference on Neuropathic Pain, Lisbon, Portugal, September 7, 2023. (Oral Presentation)



Carolina Jardim, Combined TLR3 and CD40 signalling triggers macrophage-dependent antitumour immunity. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Rodrigo Fernandes, Investigating the role of IL-17-microbiota crosstalk in sciatic nerve repair. iMed Conference – Innovate Competition, Lisbon, Portugal, October 18, 2023. (Poster Presentation)

Rodrigo Fernandes, Investigating the role of IL-17 in Peripheral Nerve Regeneration. Vienna BioCentre PhD Symposium, Vienna, Austria, November 9, 2023. (Poster Presentation)

#### Communications in National Conferences:

André Bombeiro, Investigating the role of IL-17 in Peripheral Nerve Regeneration. 48th Annual Meeting of the SPI, Aveiro, Portugal, March 30, 2023. (Poster Presentation)

Carolina Jardim, Combined TLR3 and CD40 signalling triggers macrophage-dependent antitumour immunity. 48th Annual Meeting of the SPI, Aveiro, Portugal, March 30, 2023. (Oral Presentation)

Mafalda Santos, Tissue-resident microbiota: a new player in breast cancer aggressiveness. 48th Annual Meeting of the SPI, Aveiro, Portugal, March 30, 2023. (Poster Presentation)

Rafael Blanco Domínguez, Regulatory T cell depletion unleashes an anti-tumor IFN $\gamma$  gd T cell response in the tumour microenvironment. 48th Annual Meeting of the SPI, Aveiro, Portugal, March 30, 2023. (Oral Presentation)

Anita Q. Gomes, Dissecting the role of microRNAs in effector versus regulatory CD4<sup>+</sup> T cell differentiation during (auto)immune responses in vivo. 27th Annual Meeting of the Portuguese Society of Human Genetics, Instituto Superior Técnico, Lisbon, Portugal, November 25, 2023. (Oral Presentation)

#### **Organization of Conferences**

Bruno Silva-Santos, Julie Ribot, Natacha G. Sousa, Sofia Mensurado, Anita Gomes, Karine Serre, Ana Pamplona and Rafael Dominguez, Organizer, 10th International Gamma-Delta T cell Conference, Lisbon, Portugal, June 20, 2023.

Karine Serre, Co-Organizer, 1st Immuno-Oncology SPO-SPI Joint Meeting, Conimbriga, Portugal, October 28, 2023.

### **Networks and Research Infrastructures**

Ana Pamplona, CYTED - Programa Iberoamericano de Ciencia y Tecnología para el Desarrollo, Member of the Health Committee.

Karine Serre, COST-Action Mye-InfoBank, Member.

Karine Serre, Portuguese Group for Immuno-Oncology, Member.

### **Prizes and Honours**

Sofia Mensurado, Best Oral Communication, 10th International Gamma-delta T cell conference.

### **Advanced Teaching**

Julie Ribot, Lecture, LisbonBioMed PhD Students, Lisbon, Portugal, January 9, 2023.

Karine Serre, Lecture, PhD LisbonBioMed Course, Lisbon, Portugal, January 17, 2023.

Karine Serre, Lecture, Immuno-Oncology, Lisbon, Portugal, February 20, 2023.

Bruno Silva-Santos, Coordination of Master Curricular Unit, Immuno-Oncology, Master in Oncobiology, Lisbon, Portugal, March 13, 2023.

Karine Serre and Sofia Mensurado, Lecture, Immuno-Oncology, Master in Oncobiology, Lisbon, Portugal, March 13, 2023.

Anita Q. Gomes, Lecture, IGC PhD students, Oeiras, Portugal, November 2, 2023.

Rafael Blanco Domínguez, Lecture, Master in Oncobiology, Lisbon, Portugal.

Rafael Blanco Domínguez, Lecture, Master in Biochemistry and Biomedicine, Lisbon, Portugal.

### **MSc Theses**

Vladimir Ghilas, Investigating the role of IL-17 producing  $\gamma\delta$  T cells in peripheral nerve regeneration, Supervisor: Julie Ribot, Co-Supervisor: Bruno Silva-Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, February 28, 2023.

André Miguel Vaz Pinto dos Santos, Regulatory T cell depletion unleashes an IFN $\gamma$ + gd T cell response in the tumour microenvironment, Supervisor: Sofia Mensurado, Co-Supervisor: Bruno Silva-Santos, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 14, 2023.

Gonçalo Palrão Medeiros Costa, Therapeutic avenues for gd T cells in cancer, Supervisor: Bruno Silva-Santos, Co-Supervisor: Sofia Mensurado, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, December 15, 2023.

Bernardo Nunes Araújo Silva, Identification of novel determinants of effector gd T cell differentiation, Supervisor: Anita Q. Gomes, Co-Supervisor: Bruno Silva-Santos, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, December 15, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

LLAT Therapeutics, Study Cell trafficking, tumour infiltration, and tumour control of research grade engineered, blood-derived, expanded Vd1+ T cells; Understand the role of research grade engineered Vd1+ T cells in distinguishing pathology from physiology; characterization of Vd1+ T cell activation through NKR engagement; Functional characterization of trispecific antibodies in vitro and in vivo, Sponsored Research.

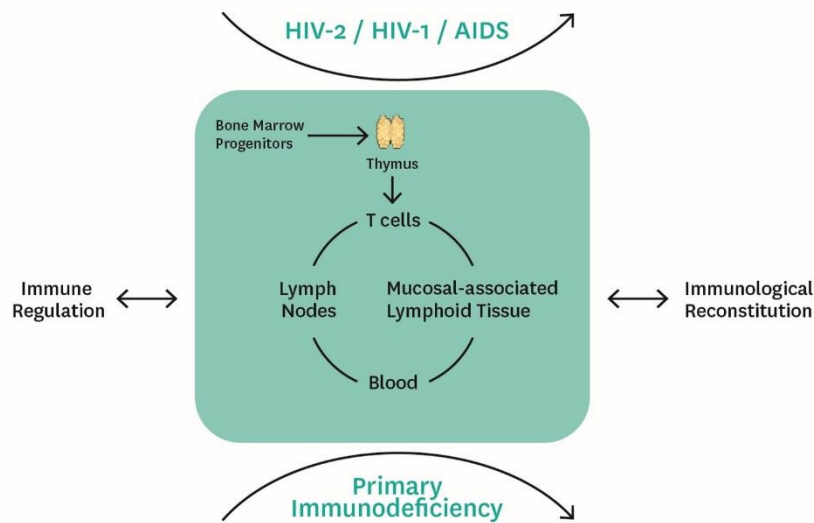
## Ana Espada de Sousa Lab

**Head of Laboratory:** Ana Espada de Sousa, MD, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Investigator Coordinator and Full Professor, Director of the Clinical Immunology Lab at Faculdade de Medicina da Universidade de Lisboa

### Team

Adriana Motta Raymundo	MD/Master Degree	PhD Student
Afonso Rocha Martins de Almeida	PhD	Senior Postdoctoral Researcher
Alexandre Augusto da Silva Figueiredo e Raposo	PhD	Senior Postdoctoral Researcher
Ana Berta da Fonseca Vieira Álvares e Sousa Ferrand de Almeida	MD/PhD	Clinical Researcher
Ana Cláudia Viseu Varandas	MD/Master Degree	Clinical Researcher
Ana Cristina Costa Santos Ferreira de Oliveira Dias	MD/University Degree	Clinical Researcher
Ana Isabel Gouveia Costa da Fonseca Lopes	MD/PhD with Habilitation	Clinical Researcher
André Lopes Reis Gomes Pires	MD/University Degree	Trainee
André Miguel Carapinha Gomes	Master Degree	PhD Student
Beatriz Pedrosa Moleirinho	Master Degree	Lab Technician
Diana Isabel Feliciano dos Santos	University Degree	Lab Manager
Emília de Jesus da Encarnação Valadas	MD/PhD	Clinical Researcher
Emily Jelagat	Master Degree	Lab Technician (Started February. Left September)
Inês Moranguinho Bastardo Moura	Master Degree	PhD Student (Left December)
Isabel Cristina e Castro de Menezes Esteves	MD/University Degree	Clinical Researcher
José Gonçalo Duque Pereira Monteiro Marques	MD/University Degree	Clinical Researcher
Margarida Paulo Pedro	Master Degree	PhD Student (Started November)
Maria Adão Serrano de Sousa Uva	MD/University Degree	Clinical Researcher
Maria Catarina Mota da Silva	MD/PhD	Clinical Researcher
Maria Escórcio Brazão	Highschool	Trainee (Left December)
Maria Margarida Sousa Gonçalves Rei	PhD	Senior Postdoctoral Researcher (Started December)
Nicole de Campos Martins	University Degree	Lab Technician
Patrícia Nicole Guilherme Silva	University Degree	MSc Student (Left September)
Robert Alfred Badura	MD/Master Degree	Clinical Researcher
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 Mendes Fernandes	MD/PhD	Clinical Staff Scientist

## Graphical Abstract



## Lab Interests

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

## Research Fields

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

### **Major Scientific Achievements in 2023**

Computational strategies to extract meaningful biological information from multiomics data are in great demand for effective clinical use. We reported new gene regulatory networks in human thymic regulatory T cells, and demonstrated their significant association to the genome-wide variant landscape of patients with common variable immunodeficiency, in line with their role in the control of inflammatory/autoimmune processes in multigenic diseases. This strategy can be replicated to other cellular/clinical contexts to prioritize variants and to identify putative druggable pathways (filled patent). To further address how human naïve CD4 T cells are maintained throughout life ensuring immune-competence, we generated single-cell data from adults living without a thymus since early infancy, or submitted to allogeneic thymus transplantation. In parallel, the impact of persistent stimulation on the naïve compartment was evaluated through the comparison of HIV-2 and HIV-1 cohorts.

### **Ongoing Projects**

2022/2024: Regeneração pulmonar após lesão pulmonar aguda. Coordinator: Ana Espada de Sousa. Funding Agency: Merck Sharp & Dohme. Reference: PROTOCOLO MSD. Amount: 5 000,00€. Total Amount: 5 000,00€.

2022/2023: RNAscope dos tecidos linfóides de indivíduos infectados pelo HIV-2 ou pelo HIV-1. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences, Lda. Reference: BOLSA NO ÂMBITO DO PROGRAMA GILEAD GÉNESE 2021. Amount: 30 000,00€. Total Amount: 30 000,00€.

2021/2024: Imunodeficiências humanas: papel reparador das células T CD4 naïve - Targeting naïve CD4 T cells to avoid human immunodeficiency. Coordinator: Ana Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/0938/2020. Amount: 249 998,75€. Total Amount: 249 998,75€.

2021/2024: APOIO BOLSA DE INVESTIGAÇÃO. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences, Lda. Reference: APOIO BOLSA DE INVESTIGAÇÃO. Amount: 25 100,00€. Total Amount: 25 100,00€.

2020/2022: CT de Apoio a Bolsas de Investigação Científica. Coordinator: Ana Espada de Sousa. Funding Agency: Janssen-Cilag Farmacêutica. Reference: CT de Apoio a Bolsas de Investigação Científica. Amount: 28 703,36€. Total Amount: 28 703,36€.

2019/2024: Prémio Bolsa Investigação 2019 - Susana Fernandes. Coordinator: Susana Fernandes. Funding Agency: Sociedade Portuguesa de Medicina Interna. Reference: Prémio Bolsa Investigação 2019 - Susana Fernandes. Amount: 10 000,00€. Total Amount: 10 000,00€.

2018/2024: Identification of Common Variable Immunodeficiency genetics. Coordinator: Ana Espada de Sousa. Funding Agency: Vários. Reference: Donativo - Dra. Susana Lopes da Silva. Amount: 15 000,00€. Total Amount: 15 000,00€.

2018/2024: Transmissão VIH-1 na infecção aguda: evolução dos reservatórios em casais com terapêutica precoce. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences, Lda. Reference: Programa Gilead GÉNESE. Amount: 32 000,00€. Total Amount: 20 000,00€.

2015/2024: HIV-2 Infection: Clinical and Biological Repository. Coordinator: Ana Espada de Sousa. Funding Agency: Gilead Sciences, Lda. Reference: Programa Gilead Génese - Ana Sousa. Amount: 20 000,00€. Total Amount: 20 000,00€.

## Scientific Impact

### Academic Collaborations

- Zvi Grossman, MD, PhD – National Institutes of Health (NIH), USA.
- Ruy Ribeiro, PhD – Los Alamos National Laboratory, USA.
- Margarida Gama-Carvalho, PhD – Faculdade de Ciências da Universidade de Lisboa (FCUL), Portugal.
- Ana Abecasis, MD, PhD – Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa (IHMT-NOVA), Portugal.
- Charlotte Cunningham Runddles, MD, PhD – Mount Sinai, USA.
- Fátima Carneiro, MD, PhD and Carla Oliveira, PhD – Instituto de Investigação e Inovação em Saúde, Universidade do Porto (i3S) / Instituto de Patologia e Imunologia Molecular da Universidade do Porto (Ipatimup), Portugal.
- Jacques Van Dongen, MD, PhD and Alberto Orfão, MD, PhD and other members of the Euroflow Consortium, European Consortium.
- Guillaume Monerret, MD – Service d'Immunologie Biologique; Institut des Sciences Pharmaceutiques et Biologiques, EA 7426 Pathophysiology of Injury-Induced Immunosuppression (U. Lyon /Hospices Civils de Lyon / bioMérieux), France.

### 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 FOXP1 deficiency \(nude/SCID\): a report of 2 cases](#). **Blood** 117(2):688-696. Original article.

**Relevance of the publication:** First report of thymus transplantation in FOXP1 deficiency.

Azevedo RI, Soares MV, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE (2009). [IL-7 sustains CD31 expression in human naive CD4+ T cells and preferentially expands the CD31+ subset in a PI3K-dependent manner](#). **Blood** 113(13):2999-3007. Original article.

**Relevance of the publication:** Identification of a role for IL-7 in the maintenance of the CD31 compartment of naïve CD4 T cells considered critical for the preservation of immune competence with ageing.

Pereira-Santos MC, Baptista AP, Melo A, Alves RR, Soares RS, Pedro E, Pereira-Barbosa M, Victorino RMM, Sousa AE (2008). [Expansion of circulating FoxP3+CD25bright CD4+ T cells during specific venom immunotherapy](#). **Clinical & Experimental Allergy** 38(2):291-297. Original article.

**Relevance of the publication:** First report of induction of regulatory CD4 T cells by hymenoptera venom.

Sousa AE, Carneiro J, Meier-Schellersheim M, Grossman Z, Victorino RM (2002). [CD4 T cell depletion is linked directly to immune activation in the pathogenesis of HIV-1 and HIV-2 but only indirectly to the viral load](#). **Journal of Immunology** 169(6):3400-3406. Original article.

**Relevance of the publication:** Reference paper on the role of persistent immune activation in HIV/AIDS immunopathogenesis.

Grossman Z, Meier-Schellersheim M, Sousa AE, Victorino RM, Paul WE (2002). [CD4+ T-cell depletion in HIV infection: are we closer to understanding the cause?](#) **Nature Medicine** 8(4):319-323. Editorial Material.

**Relevance of the publication:** Reference perspective paper on HIV/AIDS immunopathogenesis.

### 2023 Publications in Peer-Reviewed Journals

Manuel M Vicente, Inês Alves, Ângela Fernandes, Ana M Dias, Beatriz Santos-Pereira, Elena Pérez-Anton, Sofia Santos, Tao Yang, Alexandra Correia, Anja Münster-Kühnel, Afonso RM Almeida, Sarina Ravens, Gabriel A Rabinovich, Manuel Vilanova, Ana E Sousa, Salomé S Pinho (2023). Mannosylated glycans impair normal T-cell development by reprogramming commitment and repertoire diversity. *Cellular & Molecular Immunology* volume 20, pages955–968. doi.org/10.1038/s41423-023-01052-7



Ana Rita Presa, Cláudia Varandas, Leonor Esteves Caldeira, Ruben Duarte Ferreira, Tiago Marques, Sara P Silva, José Gonçalo Marques, Susana L Silva (2023). Doença granulomatosa crónica no adulto: Evolução clínica e opções terapêuticas” *Rev Port Imunoalergologia*. 31 (2): pages 103-107.

André M C Gomes, Guilherme B Farias, Amelia C Trombetta, Ana Godinho-Santos, Inês Parreira, Hélder Diogo Gonçalves, Mariana Lessa Simões, Patrício Aguiar, Maria Manuel Deveza, João Inácio, Ana E Sousa, Susana L. Silva (2023). Phenotype of BTK-lacking myeloid cells during prolonged COVID-19 and upon convalescent plasma. *Eur J Haematol*. 110(2):209-212. doi: 10.1111/ejh.13881

Ana Bernardino, Célia Costa, Maria Inês T Silva, Ana Mendes, Amélia S Santos, Susana L. Silva, Marta Neto, Elisa Pedro (2023). Autoadministração de omalizumab na urticária crónica espontânea – Estudo observacional num centro UCARE. *Rev Port Imunoalergologia* 31(2): 123-135

Sofia Couto, Sara Silva, Célia Costa, Susana L Silva (2023). Hiperplasia nodular linfóide no intestino em adultos com Imunodeficiência comum variável. *Rev Port Imunoalergologia*, 31 (2):169-170.

Rita Sousa e Silva, Sara Silva, Rita Luís, Cilénia Baldaia, Susana L Silva (2023). Nodular regenerative hyperplasia in COVID patients: could low-dose oral glucocorticoids be part of the solution? *Eur Ann Allergy Clin Immunol*. 55(6):313-315. doi: 10.23822/EurAnnACI.1764-1489.251

Joana Queiroz Gomes, Sara Silva, Tiago Marques, Susana L Silva (2023). Goods's Syndrome: Immunodeficiency Beyond Thymectomy *Port J Card Thorac Vasc Surg*, 30(2):19-21. doi: 10.48729/pjctvs.313

Alba Torres-Valle, Larraitz Aragon, Susana L Silva, Cristina Serrano, Miguel Marcos, Josefa Melero, Carolien Bonroy, Pedro Pablo Arenas-Caro, David Monzon Casado, Pedro Mikel Requejo Olaizola, Jana Neirinck, Mattias Hofmans, Sonia de Arriba, María Jara, Carlos Prieto, Ana E Sousa, Álvaro Prada, Jacques J M van Dongen, Martín Pérez-Andrés, Alberto Orfao (2023). In-depth blood immune profiling of Good syndrome patients. *Front Immunol*, 14:1285088. doi: 10.3389/fimmu.2023.1285088

### **Pre-Prints**

Raposo AASF, Rosmaninho P, Silva SL, Paço S, Brazão ME, Godinho-Santos A, Tokunaga Y, Nunes-Cabaço H, Serra-Caetano A, Almeida ARM, Sousa AE. Decoding mutational hotspots in human disease through the gene modules governing thymic regulatory T cells, bioRxiv, DOI: 10.1101/2023.12.27.573411

Jan Stuchly, David Novak, Nadezda Brdickova, Petra Hadlova, Ahmad Iksi, Daniela Kuzilkova, Michael Svaton, George Alehandro Saad, Pablo Engel, Herve Luche, Ana E Sousa, Afonso RM Almeida, Tomas Kalina. Deconstructing Complexity: A Computational Topology Approach to Trajectory Inference in the Human Thymus with tviblinDi. bioRxiv, DOI: 10.1101/2023.07.13.547329

### **Invited Lectures and Seminars**

Robert Badura, Persistência e Dinâmica do Reservatório de HIV. 43º Ciclo de Conferências sobre Doenças Infecciosas, Lisbon, Portugal, March 10, 2023.

Ana E Sousa, Dealing with persistent infections: learning with HIV-2. MCBiology 2023 Infection & Immunity, Porto, Portugal, March 16, 2023.

Ana E Sousa, The importance of being naïve. ImmunoHUB, Porto, Portugal, March 17, 2023.

Afonso RM Almeida, Developing strategies to achieve immunocompetence. iMM Internal Seminar, Lisbon, Portugal, April 12, 2023.

Susana Fernandes, Quando o adversário é o sistema imune... XI Congresso Luso-Brasileiro de Medicina Intensiva, Lisbon, Portugal, May 21, 2023.

Susana Fernandes, Is it all in our minds? Cross-talk with the brain. XXVIII Infection and Sepsis Symposium, Porto, Portugal, May 21, 2023.

Susana Lopes da Silva, José Gonçalo Marques, Alexandre Raposo, Afonso RM Almeida and Ana Espada de Sousa, Celebrating 15 years of the Primary Immunodeficiency Center: What is new? Sessões Clínicas do CAML, Lisbon, Portugal, May 25, 2023.

Afonso RM Almeida, Human Thymic Treg Development. iMM-Infinity Immunology Retreat, Lisbon, Portugal, June 7, 2023.

Ana E Sousa, The importance of being naïve. iMM-Infinity Immunology Retreat, Lisbon, Portugal, June 7, 2023.

Susana L Silva, The Expanding Field of Inborn Errors of Immunity. Disentangling the CVID Genetic and Immunological Variability. FOCIS Meeting, Boston, USA, June 20, 2023.

Susana L Silva, Complicações gastroenterológicas na IDCV – importância da multidisciplinaridade. 44<sup>º</sup> Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Tróia, Portugal, October 1, 2023.

Ana E Sousa, HIV-2 RESERVOIRS AND IMMUNE CONTROL. The HIV Reservoirs and Immune Control Conference, Malahide, Ireland, October 4, 2023.

Susana Fernandes, Abordagem inicial da sépsis- Stewardship do diagnóstico (microbiologia, imagiologia, biomarcadores). GIS-ID Webinar, Online, November 23, 2023.

### **Communications**

#### Communications in International Conferences:

Robert Badura (André Pires, Rita Moura, Guilherme B. Farias, Carolina M. Conceição, Ana V. Antão, Bárbara Tavares, Tiago Ferreira, Amelia C. Trombetta, Ana Godinho-Santos, Ana E. Sousa), HIV Infection of Tfh: Interrogating the SAMHD1 contribution through HIV-2. 30th Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, USA, February 19, 2023. (Poster Presentation)

Leonor Esteves Caldeira (Diana F. Santos, Susana Lopes da Silva, Célia Costa), Clinical impact of atopy in patients with chronic spontaneous urticaria. I Congreso Internacional Ibérico SEAIC-SPAIC 2023, Madrid, Spain, March 10, 2023. (Poster Presentation)

Alba Torres-Valle (Jana Neirinck, Sonia de Arriba, Larraitz Aragon, Susana Silva, [...], Ana E. Sousa, Alvaro Prada, Carolien Bonroy, Jacques J.M. van Dongen, Martín Pérez-Andrés, Alberto Orfao), Evaluation of a new age-matched criteria which will improve the identification of Late-onset Combined Immunodeficiency patients. XVIII Congress of The Iberian Society of Cytometry, Madrid, Spain, April 19, 2023. (Oral Presentation)

Alba Torres-Valle (Jana Neirinck, Sonia de Arriba, Larraitz Aragon, Susana Silva, [...], Ana E. Sousa, Alvaro Prada, Carolien Bonroy, Jacques J.M. van Dongen, Martín Pérez-Andrés, Alberto Orfao), Expanded Th1 cells in LOCID and COVID patients are associated with autoimmune cytopenias and interstitial lung disease. XVIII Congress of The Iberian Society of Cytometry, Madrid, Spain, April 19, 2023. (Poster Presentation)

Maria Adão-Serrano (A. M. C. Gomes, J. Santos Silva, A. Almeida, A. Espada de Sousa, J.M. Ribeiro, S. Mendes Fernandes), Lung and serum immune monitoring during acute lung injury supported with VV-ECMO – a malaria-ARDS case supporting feasibility. EuroELSO Congress 2023, Lisbon, Portugal, April 26, 2023. (Poster Presentation)

Alba Torres-Valle (J. Neirinck, S. De Arriba Mendez, L. Aragon, S. Lopes, C. Serrano, D. Subira, M. Ruiz Mercado, L.I. Gonzalez Granados, M. Marcos, S. Ines, C. Martins, M. Hofmans, C. De Vriendt, B. Albarran, G. Hurtado, A. Barez, P.P. Arenas Caro, I. Madruga, A. Martin, J.M. Bastida, I. Davila, T. Contreras, M. Jara, C. Prieto, T. Kerr, F. Haerynck, A. Sousa, A. Prada, C. Bonroy, J.J. Van Dongen, M. Perez Andres, A. Orfao), Validation of conventional and novel laboratory criteria for late onset combined immunodeficiency. 44 Congreso de la Sociedad Española de Inmunología (SEI), Bilbao, Spain, May 11, 2023. (Poster Presentation)

Leonor Esteves Caldeira (Marisa Paulino, Diana F. Santos, Susana Lopes da Silva, Célia Costa), Atopy and response to omalizumab treatment in chronic spontaneous urticaria – A real-life study. Annual Meeting European Academy of Allergy and Clinical Immunology, Hamburg, Germany, June 9, 2023. (Poster Presentation)

Ana Bernardino (Diana F Santos, Elisa Pedro, Anabela Lopes), Perioperative Allergic Reaction to Patent Blue: A Case Series. Annual Meeting European Academy of Allergy and Clinical Immunology, Hamburg, Germany, June 9, 2023. (Poster Presentation)

Sofia Cosme Ferreira (Margarida Gomes, Diana F Santos, Elisa Pedro, Joana Cosme), Clinical and Laboratory profile of Vespula spp allergic patients. Annual Meeting European Academy of Allergy and Clinical Immunology, Hamburg, Germany, June 9, 2023. (Poster Presentation)

Robert Badura (Guilherme B. Farias, Beatriz Moleirinho, Emily Jelagat, Margarida Paulo Pedro, Diana F. Santos, André M.C. Gomes, Rita T. Marques, Zoe Junginger, Carolina M. Conceição, Catarina Godinho-Santos, Afonso R. Almeida, Ana E. Sousa), Early ART initiated during acute HIV infection has a major beneficial impact on naïve CD4+ T-cells. The HIV Reservoirs and Immune Control Conference, Malahide, Ireland, October 1, 2023. (Oral Presentation)

André Gomes (Maria Adão Serrano, Rita Luís, Afonso R.M. Almeida, Ana E. Sousa, Susana M. Fernandes), CCL28 as a possible new player in irreversible lung injury. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Beatriz Moleirinho (Margarida Paulo-Pedro, Diana F. Santos, André M.C. Gomes, Susana L. Silva, Afonso R.M. Almeida, Ana E. Sousa), Living Without Thymus: Impact in the CD4 T-Cell Compartment. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Margarida Paulo-Pedro (Beatriz Moleirinho, Diana F. Santos, André M.C. Gomes, Susana L. Silva, Alexandre A.S.F. Raposo<sup>1</sup> Afonso R.M. Almeida<sup>1</sup> Ana E. Sousa), Once Upon Athymia: The T-Cell Pool of a Patient with Foxn1 Mutation, 17 Years Post-Thymic Transplant. 13th EMBO Young Scientists' Forum, Lisbon, Portugal, October 12, 2023. (Poster Presentation)

Alexandre ASF Raposo (Pedro Rosmaninho, Susana L. Silva, Susana Paço, Maria E. Brazão, Ana Godinho-Santos, Yumie Tokunaga-Mizoro, Helena Nunes-Cabaço, Ana Serra-Caetano, Afonso R.M. Almeida, Ana Espada de Sousa), Decoding mutational hotspots in human disease through the gene modules governing thymic regulatory T cells. 12th ESLHO Symposium on New Developments in Flow Cytometry, Immunogenetics and MRD Assessment, Salamanca, Spain, November 9, 2023. (Poster Presentation)

Beatriz Moleirinho (Margarida Paulo-Pedro, Diana F. Santos, André M.C. Gomes, Susana L. Silva, Afonso R.M. Almeida, Ana E. Sousa), Living Without Thymus: Impact in the CD4 T-Cell Compartment. 12th ESLHO Symposium on New Developments in Flow Cytometry, Immunogenetics and MRD Assessment, Salamanca, Spain, November 9, 2023. (Poster Presentation)

Marta Fernandes (Alice Melão, Tatiana Araújo, Ana Cachucho, David R Adams, Jeongah Oh, Afonso R.M. Almeida, Federico Torta, Vasco Barreto, Susan Pyne, Timothy Hla, Nigel J Pyne, Joao T Barata), Dependence of IL-7R-Mediated Signaling on Sphingosine Kinase Activity in Acute Lymphoblastic Leukemia, but Not Healthy Lymphoid Cells, Is an Exploitable Therapeutic Vulnerability. 65th ASH Annual Meeting & Exposition, San Diego, USA, December 9, 2023. (Poster Presentation)

Communications in National Conferences:

Patrícia Silva (Zoe-Isabella Junginger, Ana E. Sousa and Afonso R.M. Almeida), Investigating CD31 and Wnt signaling modulation in human naïve CD4+ T cell homeostasis. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Patrícia Silva (Zoe-Isabella Junginger, Ana E. Sousa and Afonso R.M. Almeida), Investigating CD31 and Wnt signaling modulation in human naïve CD4+ T cell homeostasis. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Cláudia Estima (Madalena Marques, Gil Oliveira, Guilherme Farias, Ana E Sousa, Margarida Gama-Carvalho), A transcriptomic approach to dissect the role of miR-34c-5p in T cell activation and differentiation. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

André Pires (Rita Moura, Guilherme B. Farias, Carolina M. Conceição, Ana V. Antão, Bárbara Tavares, Tiago Ferreira, Amelia C. Trombetta, Ana Godinho-Santos, Ana E. Sousa), Interrogating the SAMHD1 ability to restrict CD4 T cell infection by HIV-2. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Sofia Cosme Ferreira (Silva MI, Vieira J, Pereira-Silva S, Caiado J, Pedro E, Lopes-Silva S.), Terapêutica Substitutiva com Gamaglobulina – Particularidade da experiência de um coorte Português. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Oral Presentation)

Alexandre ASF Raposo (Pedro Rosmaninho, Susana Paço, Miguel Ângelo-Dias, Ana Godinho-Santos, Yumie Tokunaga, Helena Nunes-Cabaço, Adriana Motta-Raymundo, Susana L. Silva, Afonso R.M. Almeida, Ana Espada de Sousa), Differential Binding in human thymic regulatory T cells refine whole-genome analyses of complex immune diseases. XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

André MC Gomes (Manuel Dias-Silva, Maria Adão-Serrano, Gonçalo Mota, Rita Luís, Afonso R.M. Almeida, Ana E. Sousa, Susana M. Fernandes), CCL28 production throughout the acute respiratory distress syndrome: friend or foe? XLVIII Annual Meeting of the Portuguese Society for Immunology, Aveiro, Portugal, March 29, 2023. (Poster Presentation)

Ana Biscaia (Diana F. Santos), RNAscope™: Tales of Old and New. XXIII Congresso Nacional Técnico de Anatomia Patológica, Santa Maria da Feira, Portugal, May 19, 2023. (Oral Presentation)

Sofia Cosme Ferreira (Elisa Pedro, Sara Silva, Susana Lopes da Silva), Lúpus eritematoso cutâneo secundário a Imunoglobulina G Polivalente endovenosa – a propósito de um caso clínico. 44th Annual Meeting Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Tróia, Portugal, September 28, 2023. (Poster Presentation)

Ana Bernardino (Diana F Santos, Elisa Pedro, Anabela Lopes), Reação alérgica perioperatória ao azul patente: Experiência de um Serviço de Imunoalergologia. 44th Annual Meeting Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Tróia, Portugal, September 28, 2023. (Poster Presentation)

Ruben Duarte Ferreira (Ana Antunes, Fernanda Lucas, Fernanda Rodrigues, Liliana Marques, Sónia Penas, Tânia Mendes, Teresa Almeida, Sara Pereira da Silva, Susana Lopes da Silva, Susana Rodrigues Carvalho), Primeira administração de imunoglobulina humana subcutânea por via facilitada em Portugal. 44th Annual Meeting Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Tróia, Portugal, September 28, 2023. (Poster Presentation)

Alexandre ASF Raposo (Pedro Rosmaninho, Susana L. Silva, Susana Paço, Maria E. Brazão, Ana Godinho-Santos, Yumie Tokunaga, Helena Nunes-Cabaço, Ana Serra-Caetano, Afonso R. M. Almeida, Ana E. Sousa), Decoding mutational hotspots in human disease through the gene modules governing thymic regulatory T cells. 3rd Symposium of the National Research Infrastructure for Genome Sequencing and Analysis (“GenomePT Symposium”), Lisbon, Portugal), November 17, 2023. (Oral Presentation)

Margarida Paulo-Pedro (Beatriz Moleirinho, Diana F. Santos, André M.C. Gomes, Susana L. Silva, Alexandre A.S.F. Raposo, Afonso R.M. Almeida, Ana E. Sousa), Once Upon Athymia: The T-Cell Pool of a Patient with Foxn1 Mutation, 17 Years Post-Thymic Transplant. 3rd Symposium of the National Research Infrastructure for Genome Sequencing and Analysis (“GenomePT Symposium”), Lisbon, Portugal, November 17, 2023. (Poster Presentation)

Beatriz Moleirinho (Margarida Paulo-Pedro, Diana F. Santos, André M.C. Gomes, Susana L. Silva, Afonso R.M. Almeida, Ana E. Sousa), Living Without Thymus: Impact in the CD4 T-Cell Compartment. 3rd Symposium of the National Research Infrastructure for Genome Sequencing and Analysis (“GenomePT Symposium”), Lisbon, Portugal, November 17, 2023. (Poster Presentation)

### **Organization of Conferences**

Susana L Silva, Organizes, GPIP Webinar Series 2023 - Dissecting the variability of CVID by flow cytometry, Online, February 10, 2023.

Susana L Silva, Organizer, Meeting Grupo Português de Imunodeficiências Primárias, Aveiro, Portugal, March 3, 2023.

Susana L Silva, Member of Scientific Committee, Co-Organizer, ID Masterclass. Meet Connect Share, Rotterdam, The Netherlands, November 7, 2023.

Alexandre ASF Raposo, Member of Scientific Committee, Co-Organizer, 3rd Symposium of the National Research Infrastructure for Genome Sequencing and Analysis (“GenomePT Symposium”), Lisbon, Portugal, November 17, 2023.



### **Networks and Research Infrastructures**

Ana E Sousa, Afonso RM Almeida, Susana L Silva, Adriana Raymundo, Diana F. Santos, and Beatriz Moleirinho, EuroFlow – European Consortium for the development and standardization of flow cytometric tests for diagnosis and monitoring of hematological and immunological diseases, Members. Ana E Sousa was a member of the Euroflow Board.

Susana L. Silva, Adriana Raymundo, Diana F. Santos, Alexandre ASF Raposo, Ana E Sousa and José G Marques, ERN RITA – European Reference Network for Immunodeficiency, autoinflammatory and autoimmune diseases, Members. Susana L Silva is the local vice-representative of ERN-RITA Reference Center – Hospital de Santa Maria – Centro Universitário Lisboa Norte.

Ana E Sousa and Alexandre ASF Raposo, Mye-INFOBANK – Converting Molecular Profiles of myeloid cells into biomarkers for inflammation and cancer, Members. Ana E Sousa is MC Member from Portugal.

Ana E Sousa and Alexandre ASF Raposo, Co-Lab AccelBio, Participant.

Ana E Sousa, Alexandre ASF Raposo and Susana L Silva, GenomePT, iMM node for GenomePT

Ana E Sousa, Alexandre ASF Raposo and Susana L Silva, Estratégia Nacional para a Medicina Genómica - PT\_MedGen, iMM node.

Ana E Sousa, Alexandre ASF Raposo and Susana L Silva, 1M Genomes workgroup 6, "Health economics and outcome research", Participant.

Susana M. Fernandes, Comissão Técnica Vacinação para COVID e Gripe da Direção-Geral da Saúde, Participant.

Susana M Fernandes, CAREC, Faculdade de Medicina da Universidade de Lisboa, Member.

Susana L Silva, Grupo de Trabalho Reações de Hipersensibilidade Vacinas COVID-19, Member.

Ana E Sousa, Executive Board of the National Ethical Committee for Clinical Research (CEIC), Member.

Ana E Sousa, National Ethical Committee for Clinical Research (CEIC), Member.

Ana E Sousa, “Comissão de Avaliação de Tecnologias de Saúde (CATS)”, Autoridade Nacional do Medicamento e Produtos de Saúde, I. P. (INFARMED, I.P.), Member.

Ana E Sousa, Scientific Council for Biosciences of the Santa Casa da Misericórdia de Lisboa, Member.

Ana E Sousa and Susana M Fernandes, Scientific Council of the PhD Program of the Centro Académico de Medicina de Lisboa (Faculdade de Medicina da Universidade de Lisboa/Instituto de Medicina Molecular João Lobo Antunes/Hospital de Santa Maria), Members.

Ana E Sousa and Ana Isabel Lopes, Member of the Scientific Council, Scientific Management of the Medical School, Faculdade de Medicina da Universidade de Lisboa, Members.

Robert Badura, Checkpoint LX (projecto comunitário para um diagnóstico precoce), Collaboration.

### **Advanced Teaching**

Afonso RM Almeida, Master Thesis Supervision of student Nicole Martins, Evolutionary and Developmental Biology Masters, Faculdade de Ciências da Universidade de Lisboa, Project: Unveiling the role of CD1a in human regulatory T cell development, January 2023 – Awaiting defense, Portugal.

Afonso RM Almeida, PhD Thesis Co-Supervision of student Ana Cachucho, CAML PhD course, Faculdade de Medicina da Universidade de Lisboa, Project: Characterizing the risk for IL-7R-mediated malignancy in different stages a hematopoietic development, January 2023 – Ongoing, Portugal.

Afonso RM Almeida, PhD Thesis Co-Supervision of student André Gomes, CAML PhD course, Faculdade de Medicina da Universidade de Lisboa, Project: Revealing lung repair after ARDS through the IL-22 path, January 2023 – Ongoing, Portugal.

Susana L Silva, PhD Thesis Co-Supervision of student Sofia Pinto Carvoeiro, Master in Clinical Nutrition, Faculdade de Medicina Universidade de Lisboa (em parceria com Escola Superior de Tecnologia de Saúde de Lisboa), Project: Avaliação do Estado Nutricional em Indivíduos com Imunodeficiência Comum Variável, January 2023 – Ongoing, Portugal.

Afonso RM Almeida, Diana F Santos, Supervision of the Internship of student Fabiana Nascimento, from Escola Superior de Tecnologia do Barreiro, Instituto Politécnico de Setúbal. Project: Introdução à investigação e diagnóstico em Imunologia Clínica, February-June 2023, Portugal.

Afonso RM Almeida, Supervision of the Internship of student Hugo Luiz, from the Biomedical Research Masters, Faculdade de Medicina da Universidade de Lisboa, Investigating the role of CD1a in the development of human regulatory T cells: A comprehensive analysis of CD1a expression, Portugal, May-June 2023.

Susana L Silva, Supervision of the Clinical Immunology Laboratory training period for the final degree/specialty of Josefina Vieira, MD, Interna da Especialidade de Imunoalergologia, Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria, Project: Hipersensibilidade seletiva ao metamizol – reação IgE-mediada?, Portugal, April 1-June 30, 2023.

Susana M. Fernandes and André Gomes, Supervision of the Internship of Melanie Jordan, Erasmus+ Traineeship Program, Portugal, April 10-July 10, 2023.

Robert Badura, Lecture, Infecção por HIV, Mestrado em Nutrição Clínica, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 28, 2023.

Afonso RM Almeida, Diana F Santos, Supervision of the Internship of student Beatriz Silva, from Escola Superior de Tecnologia do Barreiro, Instituto Politécnico de Setúbal, Project: Introdução à investigação e diagnóstico em Imunologia Clínica, Portugal, July-November 2023.

Susana L Silva, Supervision of the Clinical Immunology Laboratory training period for the final degree/specialty of Ana Bernardino, MD, Interna da Especialidade de Imunoalergologia, Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria, Project: Long-Term Clinical and Immunological Efficacy of Sublingual Immunotherapy Pru p 3 in LTP syndrome – Real life study?, Portugal, July 1-September 30, 2023.

Susana L Silva, Lecture, Management of PID complications IG replacement therapies, ID Masterclass, Meet Connect Share, Rotterdam, The Netherlands, November 7, 2023.

Susana L Silva, Lecture, The unmet needs - patient challenges to access care and treatment - The physician perspective, ID Masterclass, Meet Connect Share, Rotterdam, The Netherlands, November 7, 2023.

Robert Badura, Lecture, Epidemiologia da infecção por HIV, Mestrado em Saúde Pública e Medicina Tropical 3ª Ed 2023, Mozambique, November 21, 2023.

Susana M. Fernandes, Lecture, online course of Sepsis - GIS, Portugal, November 23, 2023.

Robert Badura, Lecture, Porque não temos uma vacina contra HIV, Mestrado em Saúde Pública e Medicina Tropical 3ª Ed 2023, Mozambique, November 21, 2023.

Alexandre ASF Raposo, Supervision of curricular internship in Machine Learning of Inês Amado Santos Pinheiro Lucas, Unit: Aplicações de Engenharia e Ciência de Dados, Master Degree: Mestrado em Engenharia e Ciência de Dados, Instituto Superior Técnico (Physics Dept), with the project: Modelling multiomics data for Precision Medicine, Portugal, November 13-December 20, 2023.

Alexandre ASF Raposo, Supervision of the Internship of Maria Escórcio Brazão, from Instituto Superior Técnico (Bioengineering Dept), with the project: Variant calling of Human Genomes in a High-Performance Computer cluster environment, Portugal, December 5-15, 2023.

Afonso RM Almeida, Lecture, Investigating CD4+ T cell homeostasis in extreme settings, Biomedical Research Masters, Instituto de Medicina Molecular João Lobo Antunes-Faculdade de Medicina da Universidade de Lisboa, Portugal.

Afonso RM Almeida and Ana E Sousa, Lecture, LisbonBioMed – PhD Program, Instituto de Medicina Molecular João Lobo Antunes/Faculdade de Medicina da Universidade de Lisboa, Portugal.

Susana M. Fernandes, Coordination of Master Curricular Unit, Annual Regency and Teaching of the Disciplines of Intensive Care Medicine and Internal Medicine of Medicine/Surgery 5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Ana E Sousa, Coordination of Master Curricular Unit, Annual Regency of the Immune System Area of Medicine/Surgery 5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Susana L Silva, Ana E Sousa, Afonso RM Almeida and Susana M Fernandes, Lecture, Annual Teaching of the Immune System Area of Medicine/Surgery 5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Susana L. Silva, Ana E Sousa, Afonso RM Almeida and Susana M Fernandes, Lecture, Annual Teaching of the Optional Discipline of Clinical Immunology to the 3rd-5th year of the Master Degree in Medicine and Master of Clinical Nutrition, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Susana L. Silva and Afonso RM Almeida, Coordination of Master Curricular Unit, Regency of the Optional Discipline of Clinical Immunology to the 3rd-5th year of the Master Degree in Medicine and Master of Clinical Nutrition, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Ana E Sousa, Lecture, Annual collaboration in the teaching of Immunology in the core curriculum for Medical Students, 2nd year, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Robert Badura, Lecture, Annual lectures of the Discipline on Infectious Diseases 5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Robert Badura, Lecture, Annual teaching of the optional Clinical use of Antimicrobials to the 3-5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Robert Badura, Lecture, Annual teaching of the optional discipline of Tropical Neglected Diseases to the 4-5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Robert Badura, Lecture, Annual teaching of the optional Discipline of Tropical Medicine to the 4-5th year of the Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Robert Badura, Lecture, Annual collaboration in the teaching of Infectious Diseases in the core curriculum for Medical Students, 2nd year, Faculdade de Medicina da Universidade de Lisboa, Portugal.

### **MSc Theses**

Tamara Pinto, Endocardite infecciosa e possíveis complicações neurológicas, Supervisor: Robert Badura, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 17, 2023.

Joana Margarida Líbano Amorim Barroso, Sepsis endotypes and phenotypes: Biomarkers and clinical phenotypes upon ICU admission – A systematic review, Supervisor: Susana M. Fernandes, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 7, 2023.

Patricia Silva, Investigating CD31 and Wnt driven signals in naive CD4+ T cell homeostasis, Supervisor: Afonso RM Almeida, Faculdade de Medicina da Universidade de Lisboa, Portugal, September 21, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

AccelBio, Guide and support the transformation of scientific insights into successful drug discovery and development programs that could deliver novel therapeutics, Collaborative Research.

EuroFlow, European Consortium for the development and standardization of flow cytometric tests for diagnosis and monitoring of hematological and immunological diseases, Collaborative Research.

Mye-InfoBank, Converting Molecular Profiles of Myeloid Cells into Biomarkers for Inflammation and Cancer, Collaborative Research.

ERN RITA, European Reference Network that aims at improving the care of patients with Rare Immunological Disorders, Collaborative Research.

ViiV, Robert Badura is Member of the Advisory Board, participating in HIV Xxi optimizing quality of Life for all People Living with HIV (PLHIV), Collaborative Research.

### **Intellectual Property Rights in 2023**

Instituto de Medicina Molecular João Lobo Antunes, Alexandre ASF Raposo, Pedro Rosmaninho and Ana E Sousa, “Genomic Mutations”.

### **Science and Society in 2023**

Susana L. Silva, May 10, 2023 – Participation in Comissão da Saúde – Assembleia da República advocating for Newborn Screening for Primary Immunodeficiencies.

Susana L. Silva, May 14, 2023 – PID Patients and Families Meeting, Aveiro.

Susana L. Silva participation in Global Stakeholder Summit, “Charting a Course for Global Progress in PIDs by 2030”, Cascais, September 7-8, 2023.

Susana L. Silva, Coordinator of Centro de Imunodeficiências Primárias (CIDP), Centro Académico de Medicina de Lisboa.

Susana L. Silva, Medical Advisor –Associação Portuguesa de Doentes com Imunodeficiências Primárias (APDIP).

Ana E Sousa, Member of the Conselho Consultivo do GAT Grupo de Ativistas em Tratamento, Membro da Coligação Internacional SIDA Plus.

Robert Badura, Collaborator of the GAT Grupo de Ativistas em Tratamento, Membro da Coligação Internacional SIDA Plus.

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## Neves & Sousa-Victor Lab

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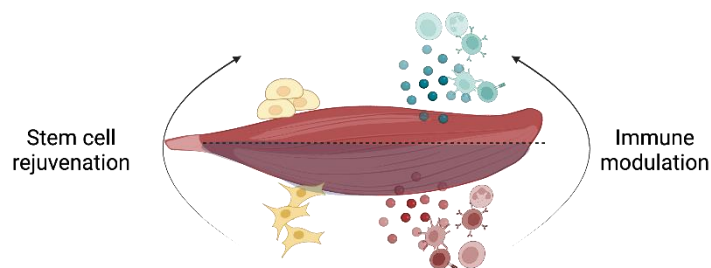
**Head of Laboratory:** Joana Neves, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes

**Head of Laboratory:** Pedro Sousa-Victor, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes

### Team

Ana Cristina Costa Sousa	University Degree	MSc Student (Left October)
Ana Isabel Aguiar Encarnação	University Degree	MSc Student (Started February)
André Jorge Balsinha	University Degree	Trainee (Started October. Left December)
Bárbara de Ferreira Pimenta Mouta e Pereira	High School Diploma	Trainee (Left June)
Beatriz Cardoso Ferreira Dias Jorge	University Degree	MSc Student (Left November)
Débora Alexandra Prata Pinheiro de Castro	University Degree	MSc Student
Filipa Narciso Lagoa	University Degree	MSc Student (Left November)
Inês Curado Batista Antunes	Master Degree	Lab Manager
Inês Isabel Baltazar Belo Martins	Master Degree	PhD Student (Started May)
Júlia Garrido Fernandes	University Degree	Trainee (Left April)
Maria Margarida Ferreira Brás	University Degree	MSc Student (Left December)
Mariana Gonçalves Martins	University Degree	MSc Student (Left September)
Neuza Sofia Simões de Sousa	Master Degree	PhD Student
Tiago Magalhães Nascimento Plácido Costa	University Degree	PhD Student (Started January)

### Graphical Abstract



*Integration of stem cell rejuvenation and immune modulation to restore tissue function in aging*



### **Lab Interests**

The Aging & Tissue Repair is interested in aging and the potential use of regenerative medicine solutions to age-related diseases. Our joint lab includes two independent, complementary, and cooperative research programs led by two group leaders: Joana Neves is focused on inflammatory signaling in aging and immune modulatory strategies to improve regenerative success. Pedro Sousa-Victor aims to understand intrinsic limitations of aged stem cells. The goal is to apply the insights from the study of alterations in the aging immune environment and stem cell aging to develop new stem cell-based therapies to improve the health of old individuals. By studying stem cell function and immune modulatory mechanisms in an integrated manner, rather than as independent problems, we aim to provide a better understanding of the problems and optimized strategies for stem-cell based therapies in aging.

### **Research Fields**

- Cellular, Developmental and Regenerative Biology
- Physiology in Health, Disease and Aging
- Immunity, Infection and Immunotherapy

### **Major Scientific Achievements in 2023**

In 2023, our lab reported a new mechanism of immune modulation operating during regeneration that relies on MANF signaling, is disrupted in aged animals, and is essential for regenerative success. This work demonstrated for the first time how age-related alterations in the immune response to muscle repair compromise regeneration and how immune modulation can be used as an effective strategy to improve muscle repair in aged animals (Sousa et al., *Nature Aging*, 2023). Our group then applied a strategy combining single-cell RNA-sequencing with functional assays to characterize the immune environment in the aged regenerating muscle. We identified previously undescribed immune cell types and a profound remodeling of both myeloid and lymphoid compartments in aging. These discoveries challenged established notions on immune regulation during regeneration, providing a new set of potential targets to improve muscle health and regenerative capacity (Sousa et al., *bioRxiv*, 2023).

### **Ongoing Projects**

2023/2026: Immune regulation of skeletal muscle metabolic health and exercise response in aging. Coordinator: Pedro Sousa-Victor. Funding Agency: “la Caixa” Foundation. Reference: MUSCLEAGEMETAB - HR23-00881. Amount: 499 835,60€. Total Amount: 499 835,60€.

2022/2023: Regulação imune da reparação de tecidos durante o envelhecimento. Coordinator: Joana Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: EXPL/MED-OUT/1601/2021. Amount: 50 000,00€. Total Amount: 50 000,00€.

2021/2023: Estratégias de Rejuvenescimento para Terapias com Células Estaminais no Músculo Esquelético Envelhecido - Rejuvenating Strategies for Stem Cell-Based Therapies in the Aged Skeletal Muscle. Coordinator: Pedro Sousa-Victor. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-OUT/8010/2020. Amount: 249 967,50€. Total Amount: 249 967,50€.

2020/2024: EMBO Young Investigator Network. Coordinator: Pedro Sousa-Victor. Funding Agency: European Molecular Biology Organization. Reference: EMBO - Pedro Victor. Amount: 250 000,00€. Total Amount: 250 000,00€.

## Scientific Impact

### Academic Collaborations

- Instituto de Medicina Molecular João Lobo Antunes, Portugal.
- University of Helsinki, Finland.
- Genentech, USA.
- Aarhus University, Denmark.
- University of Copenhagen, Denmark.
- Centro de Biología Molecular Severo Ochoa, Spain.
- Altos Labs, United States of America.

### Selected Publications

Sousa, N.S., Bica, M., Brás, M.F., Antunes, I.B., Encarnação, I.A., Costa, T., Martins, I.B., Barbosa-Morais, N.L., Sousa-Victor, P.\*\*, and Neves, J.\*\* (2023). [The immune landscape of murine skeletal muscle regeneration and aging](#). **bioRxiv**, DOI: 10.1101/2023.11.07.565995

**Relevance of the publication:** We applied a strategy combining single-cell RNA-sequencing with functional assays to characterize the immune environment in the aged regenerating muscle. We identified previously undescribed immune cell types and a profound remodeling of both myeloid and lymphoid compartments in aging. These discoveries challenged established notions on immune regulation during regeneration, providing a new set of potential targets to improve muscle health and regenerative capacity.

Sousa N.S., Brás M.F., Antunes I.B., Lindholm P., Neves J.\*\*\*, Sousa-Victor, P.\*\* (2023). [Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration](#). **Nature Aging** 3, 585–599

**Relevance of the publication:** We uncovered a new mechanism of immune modulation operating during skeletal muscle regeneration that is disrupted in aged animals. We demonstrate that restoring the myeloid response through immune modulation is a promising therapeutic strategy to improve regenerative capacity of aged muscles.

Neves, J.\*\*\*, and Sousa-Victor, P. \*\* (2020). [Regulation of inflammation as an anti-aging intervention](#). **The FEBS Journal** 287, 43-52

**Relevance of the publication:** In this perspective we discuss the rejuvenation potential of interventions that target chronic inflammation highlighting research strategies that could be used to identify new targets for interventions in aging based on the modulation of inflammatory pathways.

Sousa-Victor P\*, Neves J\*, Cedron-Craft W, Ventura PB, Liao CY, Riley RR, Soife I, van Bruggen N, Kolumam GA, Villeda SA, Lamba DA, Jasper H (2019). [MANF regulates metabolic and immune homeostasis in ageing and protects against liver damage](#). **Nature Metabolism** 1(2):276–290.

**Relevance of the publication:** This work showed that an immune modulator, MANF, is a systemic regulator of organismal immune homeostasis that declines during aging and can be used to reduce chronic inflammation and delay age-related diseases, particularly liver disease.

Neves, J., Zhu, J., Sousa-Victor, P., Konjikusic, M., Riley, R., Chew, S., Qi, Y., Jasper, H., and Lamba, D.A. (2016). [Immune modulation by MANF promotes tissue repair and regenerative success in the retina](#). **Science** 353, aaf3646.

**Relevance of the publication:** This work identified an immune modulatory mechanism and a molecule, MANF, that governs the interaction between damaged retinal and immune cells to promote tissue repair. Our findings provided proof of principle for the use of immune modulators in improving the success of regenerative therapies.

### 2023 Publications in Peer-Reviewed Journal

Sousa N.S., Brás M.F., Antunes I.B., Lindholm P., Neves J.\*\*\*, Sousa-Victor, P.\*\* (2023). Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration. **Nature Aging** 3, 585–599.

### Pre-Prints

Sousa, N.S., Bica, M., Brás, M.F., Antunes, I.B., Encarnação, I.A., Costa, T., Martins, I.B., Barbosa-Morais, N.L., Sousa-Victor, P.\*\*\*, and Neves, J.\*\* (2023). The immune landscape of murine skeletal muscle regeneration and aging. bioRxiv, DOI: 10.1101/2023.11.07.565995

### **Invited Lectures and Seminars**

Pedro Sousa-Victor, Rejuvenating Strategies for stem cell-based therapies in aging. iBiMED Seminars University of Aveiro, Portugal, June 21, 2023.

Pedro Sousa-Victor, The Interplay of Aging, Immune Signaling and Stem Cell Function. EMBO Young Scientists' Forum, Portugal, October 13, 2023.

Joana Neves, Immune modulatory strategies to restore regenerative capacity in the aged muscle. Frontiers in Myogenesis, Brazil, November 10, 2023.

### **Communications**

#### Communications in International Conferences:

Neuza Sousa, Single-cell analysis reveals age-related remodeling of the immune environment of homeostatic and regenerating skeletal muscle. EMBO Young Scientists' Forum, Portugal, October 12, 2023.

### **Prizes and Honours**

Joana Neves, Grant Reviewer Agence Nationale de la Recherche.

Pedro Sousa-Victor, Ad Hoc Reviewer iScience.

Pedro Sousa-Victor, Ad Hoc Reviewer Nature Aging.

### **Advanced Teaching**

Joana Neves, Lecture, Animal Models in Biomedical Research, Master in Biomedical Research, Portugal, January 19, 2023.

Joana Neves, Lecture, 2023 LisbonBioMed PhD Program - Towards a Creative and Critical Mind, Portugal, January 24, 2023.

Pedro Sousa-Victor, Lecture, 2023 LisbonBioMed PhD Program - Towards a Creative and Critical Mind, Portugal, January 24, 2023.

Joana Neves, Lecture, Histology Seminar, Medicine Master Course, Portugal, October 25, 2023.

Joana Neves, Lecture, Advanced Course "Cell and Molecular Mechanisms of Aging and Associated Diseases", Portugal, November 15, 2023.

Pedro Sousa-Victor, Lecture, Stem Cell Technologies PhD Advanced Course, Portugal, November 28, 2023.

### **MSc Theses**

Débora Castro, Peroxisomal modulation of the immune response in aging and tissue repair, Supervisor: Joana Neves, Faculdade de Ciências da Universidade de Lisboa, Portugal, April 4, 2023.

Bárbara Pereira, Comparative characterization of skeletal muscle phenotype in mice during aging and in MANF loss of function conditions, Supervisor: Joana Neves, Co-Supervisor: Pedro Sousa-Victor, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 6, 2023.

Ana Sousa, The role of inflammation in age-related stem cell dysfunction, Supervisor: Joana Neves, Faculdade de Medicina da Universidade de Lisboa, Portugal, October 24, 2023.

Beatriz Jorge, Mechanisms of MANF-mediated immune modulation in tissue repair, Supervisor: Joana Neves, NOVA School of Science and Technology, Portugal, November 22, 2023.

Mariana Martins, Epigenetic regulation of intestinal stem cell aging in drosophila melanogaster, Supervisor: Pedro Sousa-Victor, Escola Superior de Tecnologia da Saúde de Lisboa, Portugal, November 27, 2023.

Ana Isabel Encarnação, Immune Modulation of Skeletal Muscle Regeneration, Supervisor: Joana Neves, Instituto Superior Técnico, Portugal, December 6, 2023.

Filipa Lagoa, The role of the immune system in muscle stem cell aging during regeneration, Supervisor: Pedro Sousa-Victor, Co-Supervisor: Joana Neves, NOVA Medical School, Portugal, December 7, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Instituto de Medicina Molecular João Lobo Antunes, Inventors: Sousa N.S., Neves, J., Sousa-Victor, P, Methods for Increasing Muscle Regeneration.

### **Science and Society in 2023**

Participation in the TV show in RTP2 "Sociedade civil - Músculos", Joana Neves, May 2023.

Participation in the radio show in Observador "Mentes brilhantes - Envelhecimento: Aula prática", Pedro Sousa-Victor, November 2023.

Collaboration in magazine article in Prevenir "Como ser jovem sempre: as repostas da ciência da longevidade", Pedro Sousa-Victor, December 2023.

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## Marc Veldhoen Lab

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**Head of Laboratory:** Marc Veldhoen, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Assistant Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Alea Radcke		MSc Student (Started April. Left October)
Ana Margarida Santos Almeida	PhD	Senior Postdoctoral Researcher (Left February)
Beatriz Frutuoso Vicente	Master Degree	Lab Manager (Left May)
Cristina da Conceição Varandas Ferreira	PhD	Senior Postdoctoral Researcher
Germano Teixeira Vicente		MSc Student (Started April)
Gonçalo André Barata Malpica	Master Degree	PhD Student
Himadri Mukhopadhyay	PhD	Postdoctoral Researcher
Jean-Christophe Lone	Master Degree	PhD Student
João Carlos Martins Fernandes	PhD	Postdoctoral Researcher (Started October)
Leandro Joel Barros Fernandes	Master Degree	PhD Student
Margarida Ferreira Pereira Bobela Kirkby		MSc Student (Started September)
Patrícia Isabel Figueiredo Campos	PhD	PhD Student (Left May)
Silvia Ariotti	PhD	Senior Postdoctoral Researcher (Left May)

### Lab Interests

The Veldhoen-lab has its main interest in T cell biology. This is wide-ranging, from T cell development, activation, memory formation, tissue-resident memory, T cell function, differentiation, and T cell metabolism.

### Research Fields

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

### Major Scientific Achievements in 2023

The main achievement in 2023 was the publication (Barros et al., Nature Communication) of our continued work on how Tissue-resident memory T cells are established. Here we show these cells are not established under type 2 infection of the lungs, but under both type 1 and type 3 infections. The project was a collaborative effort with the IGC and ITQB.

In 2023, the first PhD student of the Lisbon lab successfully defended her thesis.

## Ongoing Projects

2021/2024: Um novo interveniente na ativação de células T - Role of a Novel Player in T cell Activation. Coordinator: Marc Veldhoen. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/MED-IMU/2295/2020. Amount: 249 995,00€. Total Amount: 249 995,00€.

2019/2023: Enhancing Tissue Resident Immunity. Coordinator: Marc Veldhoen. Funding Agency: “la Caixa” Foundation. Reference: HR18-00104, “ETERNITY” - “ENHANCING TISSUE RESIDENT. Amount: 497 158,00€. Total Amount: 497 158,00€.

## Scientific Impact

### Selected Publications

Ferreira C, Barros L, Baptista M, Blankenhaus B, Barros A, Figueiredo-Campos P, Konjar S, Laine A, Kamenjarin N, Stojanovic A, Cerwenka A, Probst HC, Marie JC, Veldhoen M (2020). [Type 1 Treg cells promote the generation of CD8\(+\) tissue-resident memory T cells](#). **Nature Immunology** 21:766-776.

**Relevance of the publication:** A senior author publication from the lab at iMM. This publication is setting the foundations of more projects and investigated the establishment of tissue resident memory T cells. The preliminary data formed the foundation for the successful La Caixa application. The paper describes how the establishment of Tissue Resident Memory T cells ( $T_{RM}$ ) is enhanced by regulatory T cells ( $T_{REG}$ ); a surprising finding since the later are associated with blunting responses. The system setup gave additional insights in the molecular mechanism and may become important to better understand how  $T_{RM}$  cells may be generated for vaccination strategies or tumourtherapies.

Konjar S, Frising UC, Ferreira C, Hinterleitner R, Mayassi T, Zhang Q, Blankenhaus B, Haberman N, Loo Y, Guedes J, Baptista M, Innocentin S, Stange J, Strathdee D, Jabri B, Veldhoen M (2018). [Mitochondria maintain controlled activation state of epithelial-resident T lymphocytes](#). **Science Immunology** 3:eaan2543.

**Relevance of the publication:** A senior author publication from the lab at iMM. The origin of the publication is our interest in the arylhydrocarbon receptor (AhR), the activation of which is required to maintain intestinal T cells. However, we discovered that multiple metabolic pathways are altered in tissue T cells, including the lipid membranes of their mitochondria. These alterations are in part responsible to maintain the semi-activated status of the intestinal T cells. This spurred on more detailed investigations of tissue resident T cells.



Li Y, Innocentin S, Withers DR, Roberts NA, Gallagher AR, Grigorieva EF, Wilhelm C, Veldhoen M (2011). [Exogenous stimuli maintain intraepithelial lymphocytes via aryl hydrocarbon receptor activation](#). *Cell* 147:629-640.

**Relevance of the publication:** One of the first senior author publications at the start of the setup of my own lab. The paper describes how the arylhydrocarbon receptor (AhR), is highly expressed in tissue resident T cells such as found in the skin and intestine. There it plays a fundamental role to maintain this particular cell population. Of note, we showed that ligands able to stimulate the AhR pathway can be derived from food; the brassica family of vegetables. The paper publication coincided with the ERC consolidator grant application and EMBO YIP election.

Veldhoen M, Hirota K, Westendorf AM, Buer J, Dumoutier L, Renauld JC, Stockinger B (2008). [The aryl hydrocarbon receptor links TH17-cell-mediated autoimmunity to environmental toxins](#). *Nature* 453:106-109.

**Relevance of the publication:** First author publication showing how a to that point not appreciated factor, the arylhydrocarbon receptor (AhR), links T cell immune response, via Th17 cells, to external and metabolic influences. AhR has an impact on how well Th17 cells differentiate, which in turn effects severity of autoimmunity. This paper stood at the basis of much subsequent work and the labs interest in T cells residing in tissues and their metabolism, which remain very relevant.

Veldhoen M, Hocking RJ, Atkins CJ, Locksley RM, Stockinger B (2006). [TGFbeta in the context of an inflammatory cytokine milieu supports de novo differentiation of IL-17-producing T cells](#). *Immunity* 24:179-189.

**Relevance of the publication:** First author publication showing the differentiation of a novel helper T cell subset; Th17. This paper stood at the basis of a paradigm shift in immunology, moving away from a fixed dichotomy of helper subsets providing protection to intracellular pathogens and helminths to include a third effector subset against extracellular pathogens, which shows high flexibility and ability to convert into other subsets. In addition, the resulting Th17 subset has been shown to be highly relevant in autoimmune diseases, with subsequent successful clinical applications deriving from the work, especially successful against psoriasis.

### 2023 Publications in Peer-Reviewed Journals

Barros, L., Piontkivska, D., Figueiredo-Campos, P., Fanczal, J., Ribeiro, S. P., Baptista, M., Ariotti, S., Santos, N., Amorim, M. J., Pereira, C. S., Veldhoen, M. and Ferreira, C (2023). CD8(+) tissue-resident memory T-cell development depends on infection-matching regulatory T-cell types. *Nat Commun* 14:5579.

Hasan, Z., Masood, K. I., Qaiser, S., Khan, E., Hussain, A., Ghous, Z., Khan, U., Yameen, M., Hassan, I., Nasir, M. I., Qazi, M. F., Memon, H. A., Ali, S., Baloch, S., Bhutta, Z. A., Veldhoen, M., Pedro Simas, J., Mahmood, S. F., Ghas, K. and Hussain, R (2023). Investigating the impact of prior COVID-19 on IgG antibody and interferon gamma responses after BBIBP-CorV vaccination in a disease endemic population: A prospective observational study. *Health Sci Rep* 6:e1521.

Masood, K. I., Qaiser, S., Abidi, S. H., Khan, E., Mahmood, S. F., Hussain, A., Ghous, Z., Imtiaz, K., Ali, N., Hasan, M., Memon, H. A., Yameen, M., Ali, S., Baloch, S., Lakhani, G., Alves, P. M., Iqbal, N. T., Ahmed, K., Iqbal, J., Bhutta, Z. A., Hussain, R., Rottenberg, M., Simas, J. P., Veldhoen, M., Ghias, K. and Hasan, Z (2023). Humoral and T cell responses to SARS-CoV-2 reveal insights into immunity during the early pandemic period in Pakistan. *BMC Infect Dis* 23:846.

Rebelo, M., Tang, C., Coelho, A. R., Labao-Almeida, C., Schneider, M. M., Tatalick, L., Ruivo, P., de Miranda, M. P., Gomes, A., Carvalho, T., Walker, M. J., Ausserwoeger, H., Pedro Simas, J., Veldhoen, M., Knowles, T. P. J., Silva, D. A., Shoultz, D. and Bernardes, G. J. L (2023). De Novo Human Angiotensin-Converting Enzyme 2 Decoy NL-CVX1 Protects Mice From Severe Disease After Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *J Infect Dis* 228:723-733.

Veldhoen, M. and Bertoletti, A (2023). SARS-CoV-2 clearance after breakthrough infection correlates with fit and happy T cells. *Immunol Cell Biol* 101:587-589.

### **Invited Lectures and Seminars**

Marc Veldhoen, Coimbra University, Coimbra, January 12, 2023.

Marc Veldhoen, Maastricht University, The Netherlands, January 26, 2023.

Marc Veldhoen, Universidade Católica, Portugal, May 25, 2023.

### **Communications**

#### Communications in International Conferences:

Marc Veldhoen. Angeren Alm, EMBO meeting, St Johann, Austria, February 9, 2023. (Oral Presentation)

Marc Veldhoen. EU Horizon Europe Science fair, Brussels, Belgium, March 15-16, 2023. (Oral Presentation)

Marc Veldhoen. Instituto de Medicina Molecular João Lobo Antunes - Infinity Meeting (Lisbon and Tolouse), Arrábida, Portugal, July 5-7, 2023. (Oral Presentation)

Marc Veldhoen. "la Caixa" Health (2019) Meeting, Spain, September 21-22, 2023.

Jean-Christophe Lone. 13<sup>th</sup> EMBO Young Scientists' Forum, Portugal, October 12, 2023. (Poster Presentation)

#### Communications in National Conferences:

Marc Veldhoen. Instituto de Medicina Molecular João Lobo Antunes Scientific Retreat, Portugal, September 18-19, 2023. (Oral Presentation)

#### **Organization of Conferences**

Marc Veldhoen, Co-Organizer, Angeren Alm, EMBO meeting, St Johann, Austria, February 9, 2023.

Marc Veldhoen, Co-Organizer, 13<sup>th</sup> EMBO Young Scientists' Forum, Portugal, October 12-13, 2023.

#### **MSc Theses**

Íris da Mota Lima Correia Ramos, KLRG1 as a putative marker for tissue-resident memory T cell precursors: understanding from its ontogeny to reactivation, Supervisor: Marc Veldhoen, Faculdade de Medicina da Universidade de Lisboa, February 12, 2023.

Alea Radcke, A novel factor in T cell activation and metabolism, Faculdade de Medicina da Universidade de Lisboa, October 17, 2023.

#### **PhD Theses**

Patrícia Campos, Immune-microbe crosstalk: the modulation of the adaptive immune system by the microbiota and SARS-CoV-2, Supervisor: Marc Veldhoen, Faculdade de Medicina da Universidade de Lisboa, May 4, 2023.

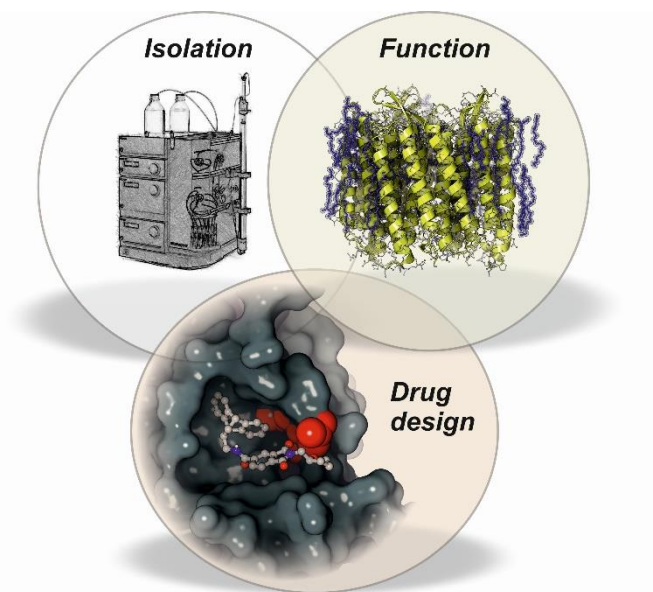
## Analytical and Structural Biochemistry Unit

**Director:** Francisco J. Enguita, PhD, Assistant Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

André Filipe Gonçalves Gabriel	Master Degree	PhD Student
Marina Célia Nunes Ferreira da Costa Henriques da Silva	PhD	Senior Postdoctoral Researcher

### Graphical Abstract



*Portfolio of techniques and methods available at the ASB facility for the isolation and functional characterization of biomolecules*

### Description of the Facility

The Analytical and Structural Biochemistry (ASB) unit is devoted to the production, analysis and functional characterization of biological macromolecules including recombinant proteins, antibodies and nucleic acids. We also offer our expertise in bioinformatics and structural biology to the iMM community for the study of structure-function relationships in biological macromolecules and in-silico drug design by computer-aided methods.

## Major Achievements in 2023

During 2023, the Analytical and Structural Biochemistry (ASB) unit has continued its implementation in the scientific community of the IMM and Faculdade de Medicina da Universidade de Lisboa, establishing a solid portfolio of chromatographic techniques, a complete functional wet-lab hardware, and expanding the different in silico methods offered for biomolecular characterization, namely those related with structure prediction by AI and molecular dynamics.

## Scientific Impact

### Academic Collaborations

- Ana Lúcia Leitão, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal.
- Afshin Beheshti, Broad Institute and NASA, USA.
- Nuno Santos, Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Portugal.
- Stan Watowich, Texas Advanced Computer Center, USA.
- Maria José Diógenes, Instituto de Medicina Molecular João Lobo Antunes, Instituto de Neurociências, Faculdade de Medicina da Universidade de Lisboa, Portugal.
- Ana Sebastião, Instituto de Medicina Molecular João Lobo Antunes, Instituto de Neurociências, Faculdade de Medicina da Universidade de Lisboa, Portugal.
- Rocio Toro, Facultad de Medicina, Universidad de Cadiz, Spain.
- Douglas C. Wallace, Children's Hospital of Philadelphia, USA.

### 2023 Publications in Peer-Reviewed Journals

Shiu PKT, DiStefano JK, Alahari SK, Enguita FJ, Feinberg MW, Sideris N, Bayraktar S, Castellano L, Buitrago DL, Caporali A, Mannucci A, Goel A (2023). The Non-Coding RNA Journal Club: Highlights on Recent Papers-13. *Noncoding RNA*. 9(6):76. doi: 10.3390/ncrna9060076.

Narayanan SA, Jamison DA Jr, Guarnieri JW, Zaksas V, Topper M, Koutnik AP, Park J, Clark KB, Enguita FJ, Leitão AL, Das S, Moraes-Vieira PM, Galeano D, Mason CE, Trovão NS, Schwartz RE, Schisler JC, Coelho-Dos-Reis JGA, Wurtele ES, Beheshti A (2023). A comprehensive SARS-CoV-2 and COVID-19 review, Part 2: host extracellular to systemic effects of SARS-CoV-2 infection. *Eur J Hum Genet*. doi: 10.1038/s41431-023-01462-1.

Guarnieri JW, Dybas JM, Fazelinia H, Kim MS, Frere J, Zhang Y, Soto Albrecht Y, Murdock DG, Angelin A, Singh LN, Weiss SL, Best SM, Lott MT, Zhang S, Cope H, Zaksas V, Saravia-Butler A, Meydan C, Foox J, Mozsary C, Bram Y, Kidane Y, Priebe W, Emmett MR, Meller R, Demharter S, Stentoft-Hansen V, Salvatore M, Galeano D, Enguita FJ, Grabham P, Trovao NS, Singh U, Haltom J, Heise MT, Moorman NJ, Baxter VK, Madden EA, Taft-Benz SA, Anderson EJ, Sanders WA, Dickmander RJ, Baylin SB, Wurtele ES, Moraes-Vieira PM, Taylor D, Mason CE, Schisler JC, Schwartz RE, Beheshti A, Wallace DC (2023). Core mitochondrial genes are down-regulated during SARS-CoV-2 infection of rodent and human hosts. *Sci Transl Med.* 15(708):eabq1533. doi: 10.1126/scitranslmed.abq1533.

Leitão AL, Enguita FJ (2023). Editorial: Secondary metabolism: an unlimited foundation for synthetic biology, volume II. *Front Microbiol.* 14:1200928. doi: 10.3389/fmicb.2023.1200928.

Enguita FJ, Leitão AL, Mattick JS (2023). RNA Regulatory Networks 2.0. *Int J Mol Sci.* 24(10):9001. doi: 10.3390/ijms24109001.

Boon PLS, Martins AS, Lim XN, Enguita FJ, Santos NC, Bond PJ, Wan Y, Martins IC, Huber RG (2023). Dengue Virus Capsid Protein Facilitates Genome Compaction and Packaging. *Int J Mol Sci.* 24(9):8158. doi: 10.3390/ijms24098158.

Yazdani B, Sirous H, Enguita FJ, Brogi S, Wing PAC, Fassihi A (2023). Discovery of novel direct small-molecule inhibitors targeting HIF-2 $\alpha$  using structure-based virtual screening, molecular dynamics simulation, and MM-GBSA calculations. *Mol Divers.* doi: 10.1007/s11030-023-10650-6.

Enguita FJ, Pereira S, Leitão AL (2023). Transcriptomic Analysis of Acetaminophen Biodegradation by *Penicillium chrysogenum* var. *halophenicum* and Insights into Energy and Stress Response Pathways. *J Fungi (Basel).* 9(4):408. doi: 10.3390/jof9040408.

Rajão-Saraiva J, Dunot J, Ribera A, Temido-Ferreira M, Coelho JE, König S, Moreno S, Enguita FJ, Willem M, Kins S, Marie H, Lopes LV, Pousinha PA (2023). Age-dependent NMDA receptor function is regulated by the amyloid precursor protein. *Aging Cell.* 22(3):e13778. doi: 10.1111/accel.13778.

### **Pre-Prints**

Haltom J, Trovao NS, Guarnieri J, Vincent P, Singh U, Tsoy S, O'Leary CA, Bram Y, Widjaja GA, Cen Z, Meller R, Baylin SB, Moss WN, Nikolau BJ, Enguita FJ, Wallace DC, Beheshti A, Schwartz R, Wurtele ES (2023). SARS-CoV-2 Orphan Gene ORF10 Contributes to More Severe COVID-19 Disease. medRxiv. 27:2023.11.27.23298847. doi: 10.1101/2023.11.27.23298847.

Pathmendra P, Park Y, Enguita FJ, Byrne JA (2023). Verification of nucleotide sequence reagent identities in original publications in high impact factor cancer research journals. bioRxiv. doi: <https://doi.org/10.1101/2023.02.03.526922>.

### **Invited Lectures and Seminars**

Enguita FJ. Principles and practice of computer-aided drug design(CADD). Computational Biology and Bioinformatics Seminar, Instituto de Medicina Molecular João Lobo Antunes, Portugal, April 19, 2023.

### **Communications**

#### Communications in International Conferences:

Gabriel AF. The Battle for the Heartbeat: How circRNA-RBP Interactions Impact Atrial Fibrillation. 28th Annual RNA Society Meeting, June 2, 2023. (Poster Presentation)

#### Communications in National Conferences:

Gabriel AF. Predicting circRNA-RBP interactions in Atrial Fibrillation. IX ptRNA meeting – RNA in Disease, Lisbon, Portugal, January 27, 2023. (Poster Presentation)

Gabriel AF. Sailing through the Surface to Unveil the Inner Workings of AC16 Cells: A Biophysical and Transcriptomic Expedition towards an Atrial Fibrillation cell model. XVI CAML & VI NeurULisboa PhD Students Meeting, Lisbon, Portugal, May 9, 2023. (Poster Presentation)

### **Prizes and Honours**

Enguita FJ, Handling editor of Briefings in Bioinformatics, Oxford University Press, UK.

Enguita FJ, Editorial Board Member, non-coding RNA, MDPI, Switzerland.

Enguita FJ, Editorial Board Member, International Journal of Molecular Sciences, MDPI, Switzerland.

Enguita FJ, Member of evaluation panel, National Science Foundation (NCN, Narodowe Centrum Nauki), Grant programs OPUS, PRELUDIUM and SONATA.

Enguita FJ, Member of evaluation panel, European Innovation Council, EISMEA program.

Enguita FJ, Member of evaluation panel, PhD and Post-doctoral fellowships, FWO ((Fonds Wetenschappelijk Onderzoek - Vlaanderen, FWO), Belgium.

### **Advanced Teaching**

Enguita FJ, Lecture, Cardiovascular Science, PhD program, Faculdade de Medicina da Universidade de Coimbra, Portugal, February 21, 2023.

Enguita FJ, Lecture, Food Quality Master program, FCT, Universidade Nova de Lisboa, Portugal, May 19, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Enguita FJ, was invited as participating artist to the Scientific Art Exhibition "explore la beauté des couleurs dans la nature, à travers les yeux d'œuvres d'art scientifiques", Centre Otium, Geneva, Switzerland (January-April 2023). This exhibition integrated graphical art of scientific facts, including digital designs, photographs and models.

Enguita FJ, participated as artistic collaborator and designer in the exhibition "A rare sight", organized by the I3S institute in Oporto, Portugal, within the PHASage collaborative project (September-October, 2023). This exhibition intended to explain different neurodegenerative diseases to the general public. The exhibition was designed involving patients and scientists, combining human and molecular points of view of the disease mechanisms.



## Biobank Unit

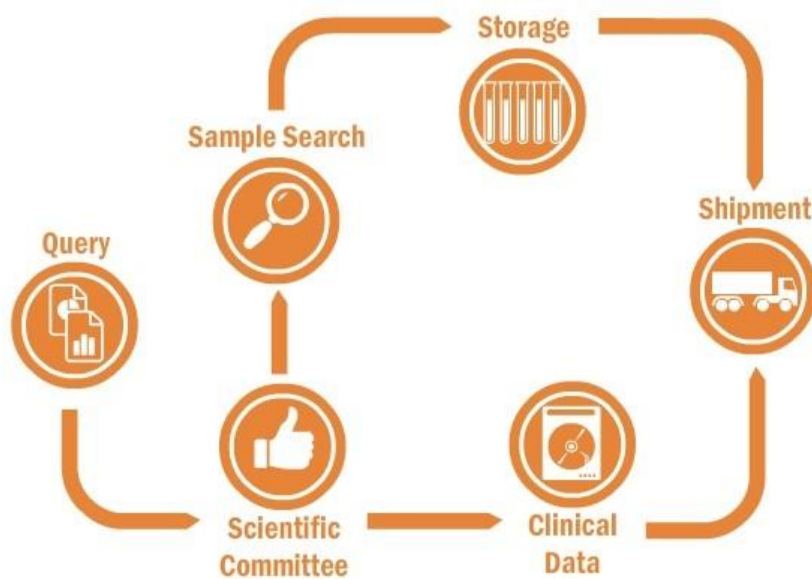
**Director:** Cláudia Faria, MD, PhD, Consultant Neurosurgeon at Centro Hospitalar Universitário Lisboa Norte-Hospital Santa Maria, Invited Assistant Professor of Neurosurgery and Neurology at Faculdade de Medicina da Universidade de Lisboa

**Director:** Sérgio Dias, PhD, Co-Leader of the Advanced Breast Cancer Innovation Translational Laboratory (CARE) at Instituto de Medicina Molecular João Lobo Antunes, Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Andreia Alexandra Farinha Lopes	Master Degree	Lab Technician
Ângela Maria Cerqueira Coelho Afonso	Master Degree	Biobank Unit Area Manager
Ionela Alexandra Filofteia Toader	Master Degree	Lab Technician
José António Cordeiro Torres Maximino	Master Degree	Clinical Data Manager (Started November)
Raquel Sofia Cruz Duarte	PhD	Clinical Researcher (Started April. Left June)

### Graphical Abstract



### Description of the Facility

Biobanks are strategic tools for the development of medicine and translational research. The Biobanco-iMM CAML includes biological samples (from surgery, biopsies, blood samples, ...) which are voluntarily (upon filling an Informed Consent) donated with permission for preservation and future use in biomedical research.

The Biobanco-iMM CAML facilitates the study of the pathogenesis of multiple diseases with enormous impact on human health (such as neurological diseases, rheumatic disorders, and cancer), contributing towards the development and establishment of new prognostic and diagnostic tests and identification of new therapeutic targets.

Our vision is that the Biobanco-iMM CAML will contribute to promoting health and the well-being of society, but will also have the potential to act as a catalyst for new opportunities for cooperation between national and international researchers, institutions, and the pharmaceutical industry.

### **Major Achievements in 2023**

In 2023, Biobanco-iMM CAML collected 27.800 samples. Upon filling out a specific informed consent form, the patients/donors provide blood, urine, tissue, and saliva, as well as detailed clinical information. We established 3 new collections (Ascites, Myositis, and TASTY).

Healthy donors are the engine of the population biobanks and are represented by all the people who accept the invitation to participate in a research/epidemiological project. Since we are mostly disease-oriented biobanks we collect data and samples from patients and their involvement is becoming more and more valuable. Biobanco-iMM CAML works very closely with patient organizations. During 2023, we promote 38 “open days” for blood donations.

Biobanco-iMM CAML achieved a sample turnover of 37%. On the training field, in 2023, we organized 2 training courses with a total of 50 participants.

## **Scientific Impact**

### **Academic Collaborations**

- José Cabeçadas, Instituto Português de Oncologia de Lisboa Francisco Gentil EPE, Portugal.
- Manuel Valiente, Centro Nacional de Investigaciones Oncológicas, CNIO, Spain.
- Rafael Roque, Neuropathology Department, Centro Hospitalar Universitário Lisboa Norte, Portugal.
- Teresa Pacheco, Oncology Department, Centro Hospitalar Universitário Lisboa Norte, Portugal.
- Isidro Cortes-Ciriano, EMBL-EBI, Cambridge, United Kingdom.

- Marc Remke, Department of Pediatric Oncology, Hematology and Clinical Immunology German Cancer Consortium (DKTK), University Hospital Düsseldorf, Düsseldorf, Germany.
- Nuno Verdasca, Instituto Nacional Ricardo Jorge, Portugal.
- Prof. Dr. Marc Peeters, Universiteit Antwerpen, Belgium.

### 2023 Publications in Peer-Reviewed Journals

Ana Teresa Melo, Eduardo Dourado, Raquel Campanilho-Marques, Matilde Bandeira, Sofia C Barreira, José Costa, Rita Pimenta, Sofia Antunes-Duarte, Inês Cordeiro, João E Fonseca (2023). Myositis Multidisciplinary Clinic in a Tertiary Referral Center. *J Multidiscip Healthc.* 16:1127–1139.

Daniel Picard, Jörg Felsberg, Maïke Langini, Paweł Stachura, Nan Qin, Jadranka Macas, Yvonne Reiss, Jasmin Bartl, Florian Selt, Romain Sigaud, Frauke-D. Meyer, Anja Stefanski, Kai Stühler, Lucia Roque, Rafael Roque, Aleksandra A. Pandrya, Triantafyllia Brozou, Christiane Knobbe-Thomsen, Karl H. Plate, Alexander Roesch, Till Milde, Guido Reifenberger, Gabriel Leprivier, Claudia C. Faria, Marc Remke (2023). Integrative multi-omics reveals two biologically distinct groups of pilocytic astrocytoma. *Acta Neuropathol* (146):551-564.

Joana Rajão-Saraiva, Jade Dunot, Aurore Ribera, Mariana Temido-Ferreira, Joana E. Coelho, Svenja König, Sébastien Moreno, Francisco J. Enguita, Michael Willem, Stefan Kins, Hélène Marie, Luísa V. Lopes, Paula A. Pousinha (2023). Age-dependent NMDA receptor function is regulated by the amyloid precursor protein. *Aging Cell* 22(3)e13778.

Neuza Domingues, Joana Gaifem, Rune Matthiesen, Diana P. Saraiva, Luís Bento, André R.A. Marques, Maria I.L. Soares, Julio Sampaio, Christian Klose, Michal A. Surma, Manuel S. Almeida, Gustavo Rodrigues, Pedro Araújo Gonçalves, Jorge Ferreira, Ryan Gouveia e Melo, Luís Mendes Pedro, Kai Simons, Teresa M.V.D. Pinho e Melo, M. Guadalupe Cabral, Antonio Jacinto, Ricardo Silvestre, Winchil Vaz, Otília V. Vieira (2023). Cholesteryl hemiazelate identified in CVD patients causes in vitro and in vivo inflammation. *J Lipid Res.* 64(9):100419.

Eunice Paisana, Rita Cascão, Carlos Custódia, Nan Qin, Daniel Picard, David Pauck, Tânia Carvalho, Pedro Ruivo, Clara Barreto, Delfim Doutel, José Cabeçadas, Rafael Roque, José Pimentel, José Miguéns, Marc Remke, João T Barata, Claudia C Faria (2023). UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease. *Neurooncol* 5(1).

### **Invited Lectures and Seminars**

Ângela Afonso, Biobancos. Universidade Lusófona, Portugal, February 10, 2023.

Ângela Afonso, Biobancos. Mestrado em Investigação Clínica, Portugal, May 3, 2023.

### **Communications**

#### Communications in International Conferences:

Sérgio Dias, Cancer Research Initiatives at IMM. 2023 USA-Portugal Leaders in Cancer Research, Portugal, July 20, 2023. (Oral Presentation)

Sérgio Dias, Systemic signals modulate breast cancer metastatic behavior. ASPIC-ASEICA International Meeting, Portugal, October 27, 2023. (Oral Presentation)

### **Organization of Conferences**

Cláudia Faria, Co-Organizer, Internal Seminars NeuroSeS, Portugal.

### **Networks and Research Infrastructures**

Cláudia Faria, EATRIS-ERIC, Chair of Board of National Directors.

Sérgio Dias, Biobanco.PT, Coordinator of the National Biobanks Network.

### **Advanced Teaching**

Sérgio Dias, Coordination of Master Curricular Unit, Oncobiology Module, Master Program in Biomedical Science, Portugal, January 2, 2023.

Sérgio Dias, Coordination of Master Curricular Unit, Developmental Biology and Cancer Module, Master Program in Oncobiology, Portugal, January 2, 2023.

Sérgio Dias, Coordination of Master Curricular Unit, Angiogenesis and Cancer Class, Master Program in Molecular and Cell Biology of Cancer, Faculdade de Ciências da Universidade de Lisboa, Portugal, January 2, 2023.

Sérgio Dias, Coordination of PhD Curricular Unit, The Biology of Cancer Module, LisbonBioMed PhD Program (Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa), Portugal, January 2, 2023.

Sérgio Dias, Lecture, Class on Metabolism and Cancer, ITQB (PhD Program), Portugal, January 2, 2023.

Biobanco, Course Organization, Curso Avançado em Biobancos, Portugal, September 13, 2023.

Biobanco, Course Organization, Curso Avançado em Biobanco-PALOP, Portugal, December 4, 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Mursla, Develop a blood test that can detect early-stage hepatocellular carcinoma (HCC), Collaborative Research.

Exscientia, Systematically investigate if malignant pleural effusion and ascites are a viable model system to study the activity and mode of action of apoptosis inducing and immunomodulatory drugs using the Pharmacoscopy high content imaging platform, Contract Research.

Ono Pharma, Evaluation of different compounds for the immune response using PBMC derived from the peripheral blood of C9-ALS/FTD patients, Collaborative Research.

Sanofi, Economic and epidemiological impact of RSV in the Iberian Peninsula (RHEDI), Collaborative Research.

Alchemab, ALS Patients Study, Collaborative Research.

iLoF, OptStab iLoF, Collaborative Research.

Ophiomics, EsoPredict/ EsoDetect – V1, Collaborative Research.

### **Science and Society in 2023**

Cláudia Faria promoted the creation of the iMM Science Club in the Pediatrics Department at Hospital de Santa Maria, Lisbon.

Sérgio Dias writes a monthly opinion article published (online) in “Visão”, a generalist magazine. In October 2023 a book authored by Sérgio Dias and illustrated by Helena Pinheiro, containing the first 12 Articles published in Visão, was published by Instituto de Medicina Molecular João Lobo Antunes.

Sérgio Dias coordinates visits (and gives lectures) of members of the general public to the Instituto de Medicina Molecular within the framework of “Laço Association-sponsored research activities”. A total of 8 visits were organized during 2023.

## Bioimaging Unit

**Director:** José Rino, PhD

### Team

Aida Andreia Pereira Pires Lima dos Santos	Master Degree	Technician
Ana Beatriz Rodrigues Barbosa	University Degree	Technician (Started January)
Ana Margarida Santos do Nascimento	Master Degree	Senior Technician
António Francisco Pinção Loução Homem Temudo	Master Degree	Senior Technician
Diogo da Silva Coutinho	University Degree	Technician (Started February)

### Graphical Abstract



*The Bioimaging Unit provides support in all steps of research done with Light Microscopy at IMM, from discussing the very first ideas sparked by a question in Consulting services to the Publication of scientific results, which triggers more questions.*

### Description of the Facility

The Bioimaging Unit acts as a support structure to help and nurture research done with Light Microscopy inside the institute. Besides managing high-end resources that include multiphoton, point-scanning confocal, spinning disk confocal, light-sheet and widefield systems, we sit with researchers to teach, train, and create software tools focusing on people and their questions.

We provide iMM scientists and visitors with excellence in scientific know-how and expertise in using light microscopy methods for their research, in a personalized approach.

We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. We develop image analysis and processing tools for microscopy data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques.

### **Major Achievements in 2023**

In 2023, the Bioimaging Unit services were used by 199 users from 34 research labs, 5 of which from outside the iMM. During the year, we trained 78 users in at least one microscopy system, with a total of 125 training sessions and 1396 assistances. We improved our user training and support workflow by combining a new user management system with a tailored approach focused on user needs and usage profile, optimizing both microscope usage efficiency and answering time. We also implemented a new management system for tracking and troubleshooting equipment issues.

The iMM Bioimaging Unit is a ZEISS labs@location Partner, integrating a community of advanced microscopy facilities providing in-depth knowledge, dedicated services across a wide range of applications and instrumentation, and scientific support to ZEISS customers. We are also a node of the Portuguese Platform of Bioimaging (PPBI), a nationwide consortium of imaging facilities which is a Node of the Euro-Bioimaging ERIC.

## **Scientific Impact**

### **Academic Collaborations**

- Centro de Neurociências e Biologia Celular, Universidade de Coimbra, Portugal.
- Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Oeiras, Portugal.

### Selected Publications

Machado H, Temudo A, De Niz M (2023). [The lymphatic system favours survival of a unique \*T. brucei\* population](#). **Biol Open** 12(11):bio059992.

De Niz M, Brás D, Ouarné M, Pedro M, Nascimento AM, Misikova LH, Franco CA, Figueiredo LM (2021). [Organotypic endothelial adhesion molecules are key for \*Trypanosoma brucei\* tropism and virulence](#). **Cell Reports** 36(12):109741.

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.

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.

Martins SB, Rino J, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M (2011). [Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes](#). **Nature Structural Molecular Biology** 18:1115.

### 2023 Publications in Peer-Reviewed Journals

Machado H, Temudo A, De Niz M (2023). The lymphatic system favours survival of a unique *T. brucei* population. **Biol Open** 12(11):bio059992

Silva Pereira S, Brás D, Porqueddu T, Nascimento AM, De Niz M (2023). Investigation of *Trypanosoma*-induced vascular damage sheds insights into *Trypanosoma vivax* sequestration. **Cell Surf** 10:100113

Magalhães F, Andrade C, Simões B, Brigham F, Valente R, Martinez P, Rino J, Sugni M, Coelho AV (2023). Regeneration of starfish radial nerve cord restores animal mobility and unveils a new coelomocyte population. **Cell Tissue Res** 394(2):293-308.

Nóbrega-Pereira S, Santos F, Oliveira Santos M, Serafim TL, Lopes AP, Coutinho D, Carvalho FS, Domingues RM, Domingues P, Bernardes de Jesus B, Morais VA, Dias S (2023). Mitochondrial Metabolism Drives Low-density Lipoprotein-induced Breast Cancer Cell Migration. **Cancer Res Commun** 3(4):709-724.



Martin RM, de Almeida MR, Gameiro E, de Almeida SF (2023). Live-cell imaging unveils distinct R-loop populations with heterogeneous dynamics. *Nucleic Acids Research* 51(20):11010–11023.

Souza NS, Brás MF, Antunes IB, Lindholm P, Neves J, Sousa-Victor P (2023). Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration. *Nature Aging* 3:585-599.

Abreu DS, Gomes JI, Ribeiro FF, Diógenes MJ, Sebastião AM, Vaz SH (2023). Astrocytes control hippocampal synaptic plasticity through the vesicular-dependent release of D-serine. *Front Cell Neurosci* 17:1282841.

Faleiro I, Afonso AI, Balsinha A, Lucas B, Martin RM, Gomes ER, de Almeida SF (2023). Adaptive changes in the DNA damage response during skeletal muscle cell differentiation. *Front Cell Dev Biol* 11:1239138.

Hennig K, Hardman D, Barata DMB, Martins IBB, Bernabeu MO, Gomes ER, Roman W (2023). Generating fast-twitch myotubes in vitro with an optogenetic-based, quantitative contractility assay. *Life Sci Alliance* 6(10):e202302227.

Martins I, Neves-Silva D, Ascensão-Ferreira M, Dias AF, Ribeiro D, Isidro AF, Quitéria R, Paramos-de-Carvalho D, Barbosa-Morais NL, Saúde L (2023). Mouse Spinal Cord Vascular Transcriptome Analysis Identifies CD9 and MYLIP as Injury-Induced Players. *Int J Mol Sci* 24(7):6433.

Dias SA, Pinto SN, Silva-Herdade AS, Cavaco M, Neves V, Tavares L, Oliveira M, Andreu D, Coutinho A, Castanho MARB, Veiga AS (2023). Quantitative Imaging of the Action of vCPP2319, an Antimicrobial Peptide from a Viral Scaffold, against *Staphylococcus aureus* Biofilms of a Clinical Isolate. *ACS Infect Dis* 9(10):1889-1900.

Lourenço DM, Soares R, Sá-Santos S, Mateus JM, Rodrigues RS, Moreira JB, Vaz SH, Sebastião AM, Solá S, Xapelli S (2023). Unravelling a novel role for cannabidivarin in the modulation of subventricular zone postnatal neurogenesis. *Eur J Pharmacol* 959:176079.

Rajão-Saraiva J, Dunot J, Ribera A, Temido-Ferreira M, Coelho JE, König S, Moreno S, Enguita FJ, Willem M, Kins S, Marie H, Lopes LV, Pousinha PA (2023). Age-dependent NMDA receptor function is regulated by the amyloid precursor protein. *Aging Cell* 22(3):e13778.

Ribeiro A, Rebocho da Costa M, de Sena-Tomás C, Rodrigues EC, Quitéria R, Maçarico T, Rosa Santos SC, Saúde L (2023). Development and repair of blood vessels in the zebrafish spinal cord. *Open Biol* 13(8):230103.

Marreiros IM, Marques S, Parreira A, Mastrodomenico V, Mounce BC, Harris CT, Kafsack BF, Billker O, Zuzarte-Luís V, Mota MM (2023). A non-canonical sensing pathway mediates *Plasmodium* adaptation to amino acid deficiency. *Commun Biol* 6(1):205.

Paisana E, Cascão R, Custódia C, Qin N, Picard D, Pauck D, Carvalho T, Ruivo P, Barreto C, Doutel D, Cabeçadas J, Roque R, Pimentel J, Miguéns J, Remke M, Barata JT, Faria CC (2023). UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease. *Neurooncol Adv* 5(1):vdad048.

Alves-Vale C, Capela AM, Tavares-Marcos C, Domingues-Silva B, Pereira B, Santos F, Gomes CP, Espadas G, Vitorino R, Sabidó E, Borralho P, Nóbrega-Pereira S, Bernardes de Jesus B (2023). Expression of NORAD correlates with breast cancer aggressiveness and protects breast cancer cells from chemotherapy. *Mol Ther Nucleic Acids* 33:910-924.

#### **Invited Lectures and Seminars**

José Rino, *Inteligência Artificial em Análise de Imagem Biomédica*. Ciclo de Conferências do Centro de Investigação do Centro Hospitalar de Leiria, Centro Hospitalar de Leiria, Leiria, Portugal, November 16, 2023.

#### **Organization of Conferences**

José Rino, Co-Organizer, SPAOM 2023 – Spanish and Portuguese Advanced Optical Microscopy Meeting, Universidade do Algarve, Faro, Portugal, October 25-27, 2023.

#### **Networks and Research Infrastructures**

José Rino, PPBI – Portuguese Platform of Bioimaging, Node Manager.

#### **Advanced Teaching**

José Rino, Coordination of Master Curricular Unit, *Advanced Techniques in Biomedical Research I – Master's in Biomedical Research*, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 30-February 24, 2023.

José Rino, Lecture, Introduction to Optical Microscopy, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 31, 2023.

José Rino, Lecture, Fluorescence Microscopy, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 31, 2023.

José Rino, Lecture, Optical Sectioning Methods, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 1, 2023.

José Rino, Lecture, FRAP and FRET, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 1, 2023.

José Rino, Lecture, Super Resolution Microscopy, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 2, 2023.

José Rino, Lecture, Digital Image Acquisition and Processing, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 2, 2023.

José Rino, Lecture, Imaging Flow Cytometry, Advanced Techniques in Biomedical Research I – Master’s in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 3, 2023.

José Rino, Lecture, Live cell imaging and F techniques – 2nd Advanced Course on Fluorescence Microscopy and Image Analysis, CICS-UBI, Universidade da Beira Interior, Covilhã, Portugal, February 24-March 24, 2023.

José Rino, Lecture, Super-resolution Microscopy – 2nd Advanced Course on Fluorescence Microscopy and Image Analysis, CICS-UBI, Universidade da Beira Interior, Covilhã, Portugal, February 24-March 24, 2023.

José Rino, Workshop Organization, Zooming In: Advanced Microscopy Workshop – AIMS Meeting, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 13-16, 2023.

Beatriz Barbosa, Workshop Organization, Zooming In: Advanced Microscopy Workshop – AIMS Meeting, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 13-16, 2023.

Diogo Coutinho, Workshop Organization, Zooming In: Advanced Microscopy Workshop – AIMS Meeting, Faculdade de Medicina da Universidade de Lisboa, Portugal, April 13-16, 2023.

José Rino, Lecture, Principles of Flow Cytometry – FLxFlow 4th Course Principles and Applications of Flow Cytometry, Fundação Champalimaud, Lisbon, Portugal, May 8-12, 2023.

José Rino, Lecture, Optical Microscopy – Introduction to Instrumental Analysis in Master's in Biomedical Engineering, Faculdade de Medicina da Universidade de Lisboa, Portugal, June 2, 2023.

José Rino, Lecture, Basic Principles of Confocal Microscopy – Course on Fundamentals of light microscopy and image processing, ITQB-NOVA, Oeiras, Portugal, September 22, 2023.

José Rino, Lecture, The F techniques: FRAP, FRET and FLIM – Course on Fundamentals of light microscopy and image processing, ITQB-NOVA, Oeiras, Portugal, September 22, 2023.

José Rino, Lecture, Live cell imaging of pre-mRNA splicing with single-molecule sensitivity – ESN- ISN Neurochemistry School, Algarve Biomedical Center Research Institute, Faro, Portugal, October 30, 2023.

José Rino, Lecture, Confocal Microscopy Bases – 3rd RESETEageing Training School, Centro de Neurociências e Biologia Celular, Coimbra, Portugal, December 4-5, 2023.

José Rino, Lecture, Live Imaging with Airyscan – 3rd RESETEageing Training School, Centro de Neurociências e Biologia Celular, Coimbra, Portugal, December 4-5, 2023.

José Rino, Course Organization, Introduction to Image Analysis Course, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, December 11-13, 2023.

José Rino, Lecture, Introduction to Automation - Introduction to Image Analysis Course, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, December 11-13, 2023.

## Valorization of Knowledge / Social and Economic Impact

### Partnerships with Industry in 2023

Carl Zeiss Microscopy GmbH, Zeiss Labs@Location, Microscope system presentations, institute excursions within the scope of sales tours or outside of sales tours, performance of customer courses and customer training, production of defined samples and cooperation in the production of application notes (so called "White Papers"), Collaborative Research.

### Science and Society in 2023

Beatriz Barbosa, Diogo Coutinho and José Rino participated in the “Ciência di Noz Manera” school program for 120 students of the “Escola Marquesa de Alorna” on the 15th of February 2023 at Instituto de Medicina Molecular João Lobo Antunes, with the hands-on activity “O micro-mundo: células e peixes-zebra ao microscópio”.

Beatriz Barbosa, Diogo Coutinho and José Rino participated in the “Feira do Livro - Lisboa” with the hands-on activity at the Gradiva stand “The micro-world: cells, fish and other living things under the microscope” on the 4th of June 2023 at Parque Eduardo VII, Lisboa, where visitors could explore different biological samples with an optical microscope.

Beatriz Barbosa and Diogo Coutinho participated in the “European Researchers’ Night” on the 23rd of September 2023 at Fundação Champalimaud, Lisboa, in a microscopy hands-on station where visitors could explore optical microscopes from research grade level to origami and cell phone instruments.

During 2023, we received 24 visits to the microscopy rooms of the Bioimaging Unit from a wide range of audience (industry, academia, policy makers, private sponsors, arts, patient’s associations, and others) and students from different educational stages (middle and high-school, university, post-graduate).

## Comparative Pathology Unit

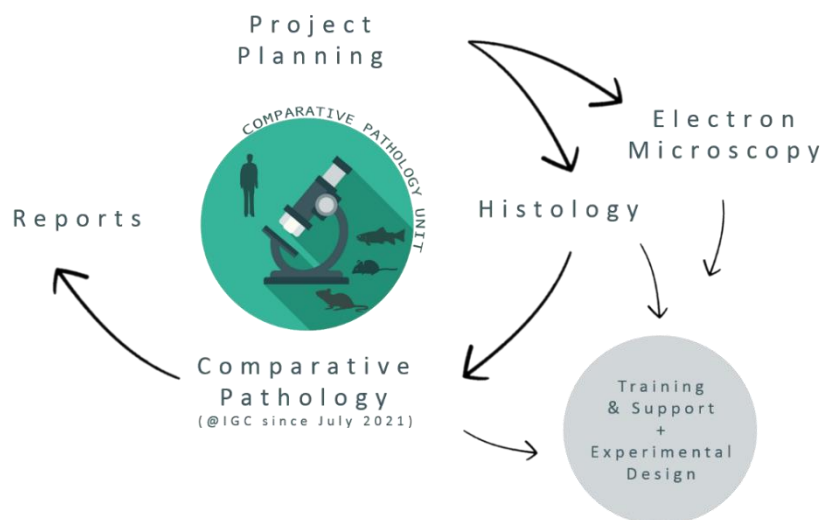
### Team

Luísa Figueiredo, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes – *Commissary*

Ana M. Biscaia Santos, Master Degree, Histology and Comparative Pathology Area Manager and Histology Specialist at Instituto de Medicina Molecular João Lobo Antunes

Ana Margarida Pereira Cristóvão Pinto	University Degree	Senior Technician
Ana Rita Correia Pires	Master Degree	Senior Technician
Joana Gomes Pereira Antunes	University Degree	Lab Technician (Started January)
Moara Lemos	PhD	Senior Technician

### Graphical Abstract



*From Experimental Design & Project Planning to Reporting, Comparative Pathology Unit is a multidisciplinary team, combining Pathology, Histology and Electron Microscopy*

### Description of the Facility

With almost 55 years of combined experience, we are experts in transforming fresh and fixed biological samples (from human, mouse, rat, fish, mosquitoes *et al.*) into thin and ultra-thin sections to be viewed under a Light or an Electron microscope.

In our unit, we have available all Histological standard techniques and provide consultation and optimization of more specialized techniques. We have well established protocols with the IGC EM and Histopathology Unit so we can provide state of the art Pathology and Electron Microscopy to our users, combining technical expertise with scientific background.

Our mission is to achieve the highest level of quality in supporting researchers and to create meaningful data. We focus our work on a continuous improvement policy to provide efficient, high quality flexible services with responsive turn-around time to researchers.

In summary: maintaining the highest level of technical proficiency and ethical principles is our motto.

### **Major Achievements in 2023**

Quality and performance of our Unit improved during 2023 and all main goals were successfully completed. Our methodology during this year allowed us to build-up on several important key performance indicators (KPI), such as the average rate on annual “Facilities Satisfaction Survey” – an astonishing 4.5/5 rate!

Outreach has been a constant during 2023, with several opportunities to represent Comparative Pathology Unit and iMM nationally – 2 team members were accepted for an oral presentation during the annual APTAP Congress, but also internationally, with the invite to co-organize an online workshop with Universidade de Cabo Verde.

We achieved another milestone by organizing the 1st Histo Crash Course – a 3 days hands-on course – that all participants evaluated as Excellent and considered the contents very useful for iMM’s Community.

Following our outreach activities, we had the opportunity to host 6 internship students (~ 1200hours) and 132 students during study visits to the iMM.

## **Scientific Impact**

### **Academic Collaborations**

- Escola Superior de Tecnologia da Saúde de Lisboa, Portugal.
- Escola Superior de Tecnologia da Saúde de Coimbra, Portugal.
- Universidade de Cabo Verde, Cape Verde.
- Universidade Lusófona, Portugal.

### **2023 Publications in Peer-Reviewed Journals**

Fraga, A., Mosca, A. F., Moita, D., Simas, J. P., Nunes-Cabaco, H., & Prudêncio, M. (2023). SARS-CoV-2 decreases malaria severity in co-infected rodent models. *Frontiers in Cellular and Infection Microbiology*.

Marinho, P. F., Vieira, S. L., Carvalho, T. G., Peleteiro, M. C., & Hanscheid, T. (2022). A novel and simple heat-based method eliminates the highly detrimental effect of xylene deparaffinization on acid-fast stains. *bioRxiv*.

Sousa, N. S., Brás, M. F., Antunes, I. B., Lindholm, P., Neves, J., & Sousa-Victor, P. (2023). Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration. *Nature Aging*, 3(5), 585-599.

Tang, C., Coelho, A. R., Rebelo, M., Kiely-Collins, H., Carvalho, T., & Bernardes, G. J. (2023). A Selective SARS-CoV-2 Host-Directed Antiviral Targeting Stress Response to Reactive Oxygen Species. *ACS Central Science*, 9(1), 109-121.

Nóbrega-Pereira, S., Santos, F., Oliveira Santos, M., Serafim, T. L., Lopes, A. P., Coutinho, D., ... & Dias, S. (2023). Mitochondrial metabolism drives low-density lipoprotein-induced breast cancer cell migration. *Cancer Research Communications*, 3(4), 709-724.

Rebelo, M., Tang, C., Coelho, A. R., Labão-Almeida, C., Schneider, M. M., Tatalick, L., ... & Bernardes, G. J. (2023). De Novo Human Angiotensin-Converting Enzyme 2 Decoy NL-CVX1 Protects Mice From Severe Disease After Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *The Journal of Infectious Diseases*, jiad135.

Machado, H., Hofer, P., Zechner, R., Smith, T. K., & Figueiredo, L. M. (2023). Adipocyte lipolysis protects mice against *Trypanosoma brucei* infection. *Nature Microbiology*, 8(11), 2020-2032.

Marinho, P. F., & Hanscheid, T. (2023). A simple heat-based alternative method for deparaffinization of histological sections significantly improves acid-fast staining results for *Mycobacteria* in tissue. *MethodsX*, 10, 102079.

Moita, D., Rôla, C., Nunes-Cabaço, H., Nogueira, G., Maia, T. G., Othman, A. S., ... & Prudêncio, M. (2023). The effect of dosage on the protective efficacy of whole-sporozoite formulations for immunization against malaria. *NPJ Vaccines*, 8(1), 182.

Ribeiro, A., Rebocho da Costa, M., de Sena-Tomás, C., Rodrigues, E. C., Quitéria, R., Maçarico, T., ... & Saúde, L. (2023). Development and repair of blood vessels in the zebrafish spinal cord. *Open Biology*, 13(8), 230103.



Chora, Â. F., Marques, S., Gonçalves, J. L., Lima, P., da Costa, D. G., Fernandez-Ruiz, D., ... & Mota, M. M. (2023). Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  $\gamma\delta$  T cells and IL-17-promoted stress erythropoiesis. *Immunity*, 56(3), 592-605.

Paisana, E., Cascão, R., Custódia, C., Qin, N., Picard, D., Pauck, D., ... & Faria, C. C. (2023). UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease. *Neuro-Oncology Advances*, 5(1), vdad048.

Matos, A. I., Peres, C., Carreira, B., Moura, L. I., Acúrcio, R. C., Vogel, T., ... & Florindo, H. F. (2023). Polyoxazoline-Based Nanovaccine Synergizes with Tumor-Associated Macrophage Targeting and Anti-PD-1 Immunotherapy against Solid Tumors. *Advanced Science*, 10(25), 2300299.

Godinho-Pereira, J., Vaz, D., Figueira, I., Aniceto-Romão, J., Krizbai, I., Malhó, R., ... & Brito, M. A. (2023). Breast Cancer Brain Metastases: Implementation and Characterization of a Mouse Model Relying on Malignant Cells Inoculation in the Carotid Artery. *Cells*, 12(16), 2076.

Carmona-Fernandes, D., Casimiro, R. I., Silva, A., Koskela, A., Finnilä, M. A., Santos, M. J., ... & Fonseca, J. E. (2023). Bone disturbances and progression of atherosclerosis in ApoE knockout mice. *Clinical and Experimental Rheumatology*.

Matos, A. I., Peres, C., Carreira, B., Moura, L. I., Acúrcio, R. C., Vogel, T., ... & Florindo, H. F. (2023). Polyoxazoline-Based Nanovaccine Synergizes with Tumor-Associated Macrophage Targeting and Anti-PD-1 Immunotherapy against Solid Tumors. *Advanced Science*, 10(25), 2300299.

Papotto, P. H., Yilmaz, B., Pimenta, G., Mensurado, S., Cunha, C., Fiala, G. J., ... & Silva-Santos, B. (2023). Maternal  $\gamma\delta$  T cells shape offspring pulmonary type 2 immunity in a microbiota-dependent manner. *Cell Reports*, 42(2).

Gomes, I., Gallego-Paez, L. M., Jiménez, M., Santamaria, P. G., Mansinho, A., Sousa, R., ... & Casimiro, S. (2023). Co-targeting RANK pathway treats and prevents acquired resistance to CDK4/6 inhibitors in luminal breast cancer. *Cell Reports Medicine*, 4(8).

### **Invited Lectures and Seminars**

Ana M Biscaia Santos. Workshop sobre dissecação de aortas de ratinho. Technical Workshops - Champalimaud Centre for the Unknown, Oeiras, Portugal, February 13, 2023.

Ana M Biscaia Santos. Histologia e Citologia - Fase Pré-analítica. Technical Workshops - Universidade Lusófona - Technical Workshops, Lisbon, Portugal, October 12, 2023.

Ana M Biscaia Santos. O impacto da fase pré-analítica na qualidade dos resultados. Technical Workshops - Universidade de Cabo Verde, Online, November 23, 2023.

### **Communications**

#### Communications in National Conferences:

Ana M Biscaia Santos. RNAScope: Tales of Old and New. XXIII Congresso de Anatomia Patológica - APTAP, Santa Maria da Feira, Portugal, May 20, 2023. (Oral Presentation)

Ana Rita Pires. Anatomia Patológica em Investigação - Criopreservação por inclusão em gelatina. XXIII Congresso de Anatomia Patológica - APTAP, Santa Maria da Feira, Portugal, May 20, 2023. (Oral Presentation)

### **Organization of Conferences**

Ana M Biscaia Santos, Organizer, CPU Annual Meeting, Lisbon, Portugal, November 24, 2023.

Ana M Biscaia Santos, Organizer, 1st Histology Crash-Course, Lisbon, Portugal, December 4, 2023.

### **Networks and Research Infrastructures**

Comparative Pathology Unit Staff, COLife's Histology and Pathology Platforms, Member of the network.

Ana Cristóvão Pinto, iMM Get2gether, Member of the network.

Ana M Biscaia Santos, iMM Green Team, Member of the Steering Committee.

Ana M Biscaia Santos, GreenLabs Portugal, Member of the network.

Ana M Biscaia Santos, CTLS, Member of the network.

### **Prizes and Honours**

Ana M Biscaia Santos, Elected for the Green Team Steering Committee.

### **Advanced Teaching**

Ana M Biscaia Santos, Coordination of Bachelor Curricular Unit, Internship coordination – Histopatologia e a Investigação em Ciências Biomédicas Laboratoriais, Lisbon, Portugal.

Ana Rita Pires, Coordination of Bachelor Curricular Unit, Internship coordination – Histopatologia e a Investigação em Ciências Biomédicas Laboratoriais, Lisbon, Portugal.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Science outreach was achieved by hosting 130 students in our facility during study visits to the iMM, with ages between 16 to 21 years old from schools (11<sup>º</sup> and 12<sup>º</sup> Ano) and faculties.

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## Flow Cytometry Unit

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**Director:** Mariana Fernandes, MSc

### Team

Andreia Sofia Ramalho dos Santos	Master Degree	Technician
Margarida Nóbrega Campos de Freitas Araújo	Master Degree	Technician
Rute Regina Ferreira Gonçalves	Master Degree	Technician

### Graphical Abstract



*Services provided by the Flow Cytometry Unit*

### Description of the Facility

The Flow Cytometry Unit provides a state-of-the-art flow cytometry service to iMM researchers and external groups from other research institutes. We aim to aid researchers in obtaining the highest quality samples and data, as well as provide training in adequate use of instruments and flow cytometry principles, experiment planning, data analysis and interpretation.

The unit is equipped with four conventional cell analyzers (one BD LSRFortessa X-20, two BD LSRFortessa - one of which equipped with a HTS - and one BD Accuri C6 Plus), two spectral cell analyzers (one BD FACSymphony A5 SE and one Cytex Aurora - equipped with an ASL), three High Speed Cell Sorters (BD FACSAria III, FACSAria Fusion and FACSymphony S6 SE) and one imaging flow cytometer (Cytex Amnis ImageStream X Mk II). In addition to providing a cell sorting service, we ensure quality control and maintenance procedures for all instruments, along with the implementation of a Quality Management System, according to ISO 9001.

## Major Achievements in 2023

In 2023, we had a total of 168 users from 34 research labs using the Flow Cytometry Unit, 9 of which from external groups. During the past year, we trained 67 new users in at least one flow cytometry analyzer. The Unit introduced spectral cytometry with the installation of: two analyzers, BD FACSymphony A5 SE and a Cytex Aurora; and one cell sorter, BD FACSymphony S6 SE. The new instruments include special features such as: capacity for high-parameter spectral flow cytometry, flexibility and number of simultaneous fluorescent parameters, and autofluorescence extraction, which enables the resolution of difficult cells and populations. In addition, the cell sorter is also fully integrated in a biosafety cabinet for BSL-2 samples (including human samples), and up to 6-way sorting.

The Unit is one of the founders of FLxFlow – a regional network for Flow Cytometry, which aims at bringing together the know-how of flow cytometry facilities in the Lisbon area, enabling advanced training.

## Scientific Impact

### Academic Collaborations

- Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### 2023 Publications in Peer-Reviewed Journals

Barros L, Piontkivska D, Figueiredo-Campos P, Fanczal J, Ribeiro SP, Baptista M, Ariotti S, Santos N, Amorim MJ, Pereira CS Veldhoen M, Ferreira C (2023). CD8+ tissue-resident memory T-cell development depends on infection-matching regulatory T-cell types. *Nat Commun* 14, 5579.

Cardoso BA, Duque M, Gírio A, Fragoso R, Oliveira ML, Allen JR, Martins LR, Correia NC, Silveira AB, Veloso A, Kimura S, Demoen L, Matthijssens F, Jeha S, Cheng C, Pui CH, Grosso AR, Neto JL, De Almeida SF, Van Vlieberghe P, Mullighan CG, Yunes JA, Langenau DM, Pflumio F, Barata JT (2023). CASZ1 upregulates PI3K-AKT-mTOR signaling and promotes T-cell acute lymphoblastic leukemia. *Haematologica*.

Chora ÂF, Marques S, Gonçalves JL, Lima P, Gomes da Costa D, Fernandez-Ruiz D, Marreiros MI, Ruivo P, Carvalho T, Ribeiro RM, Serre K, Heath WR, Silva-Santos B, Tate AT, Mota MM (2023). Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  $\gamma\delta$  T cells and IL-17-promoted stress erythropoiesis. *Immunity* 56(3):592-605.e8.

Faleiro I, Afonso AI, Balsinha A, Lucas B, Martin RM, Gomes ER, de Almeida SF (2023). Adaptive changes in the DNA damage response during skeletal muscle cell differentiation. *Front Cell Dev Biol.* 11:1239138.

Fraga A, Mósca AF, Moita D, Simas JP, Nunes-Cabaço H, Prudêncio M (2023). SARS-CoV-2 decreases malaria severity in co-infected rodent models. *Front Cell Infect Microbiol* 13:1307553.

Gomes AMC, Farias GB, Trombetta AC, Godinho-Santos A, Parreira I, Gonçalves HD, Simões ML, Aguiar P, Deveza MM, Inácio J, Sousa AE, da Silva SL (2023). Phenotype of BTK-lacking myeloid cells during prolonged COVID-19 and upon convalescent plasma. *Eur J Haematol.* 110(2):209-212.

Gomes I, Gallego-Paez LM, Jiménez M, Santamaria PG, Mansinho A, Sousa R, Abreu C, Suárez EG, Costa L, Casimiro S (2023). Co-targeting RANK pathway treats and prevents acquired resistance to CDK4/6 inhibitors in luminal breast cancer. *Cell Rep Med.* 15;4(8):101120.

Magalhães F, Andrade C, Simões B, Brigham F, Valente R, Martinez P, Rino J, Sugni M, Coelho AV (2023). Regeneration of starfish radial nerve cord restores animal mobility and unveils a new coelomocyte population. *Cell Tissue Res.* 394(2):293-308.

Marreiros IM, Marques S, Parreira A, Mastrodomenico V, Mounce BC, Harris CT, Kafsack BF, Billker O, Zuzarte-Luís V, Mota MM (2023). A non-canonical sensing pathway mediates Plasmodium adaptation to amino acid deficiency. *Commun Biol* 6(1):205.

Machado H, Hofer P, Zechner R, Smith TK, Figueiredo LM. Adipocyte lipolysis protects mice against *Trypanosoma brucei* infection (2023). *Nat Microbiol.* 8(11):2020-2032.

Martins I, Neves-Silva D, Ascensão-Ferreira M, Dias AF, Ribeiro D, Isidro AF, Quitéria R, Paramos-de-Carvalho D, Barbosa-Morais NL, Saúde L (2023). Mouse Spinal Cord Vascular Transcriptome Analysis Identifies CD9 and MYLIP as Injury-Induced Players. *Int J Mol Sci.* 24(7):6433.

Moita D, Nunes-Cabaço H, Rôla C, Franke-Fayard B, Janse CJ, Mendes AM, Prudêncio M (2023). Variable long-term protection by radiation-, chemo-, and genetically-attenuated *Plasmodium berghei* sporozoite vaccines. *Vaccine* 12;41(51):7618-7625.

Moita D, Rôla C, Nunes-Cabaço H, Nogueira G, Maia TG, Othman AS, Franke- Fayard B, Janse CJ, Mendes AM, Prudêncio M (2023). The effect of dosage on the protective efficacy of whole-sporozoite formulations for immunization against malaria. *NPJ Vaccines* 24;8(1):182.

Nóbrega-Pereira S, Santos F, Oliveira Santos M, Serafim TL, Lopes AP, Coutinho D, Carvalho FS, Domingues RM, Domingues P, Bernardes de Jesus B, Morais VA, Dias S (2023). Mitochondrial Metabolism Drives Low-density Lipoprotein-induced Breast Cancer Cell Migration. *Cancer Res Commun* 3(4):709-724.

Papotto PH, Yilmaz B, Pimenta G, Mensurado S, Cunha C, Fiala GJ, Gomes da Costa D, Gonçalves-Sousa N, Chan BHK, Blankenhaus B, Domingues RG, Carvalho T, Hepworth MR, Macpherson AJ, Allen JE, Silva-Santos B (2023). Maternal  $\gamma\delta$  T cells shape offspring pulmonary type 2 immunity in a microbiota-dependent manner. *Cell Rep.* 42(2):112074.

Rebelo M, Tang C, Coelho AR, Labão-Almeida C, Schneider MM, Tatalick L, Ruivo P, de Miranda MP, Gomes A, Carvalho T, Walker MJ, Ausserwoeger H, Pedro Simas J, Veldhoen M, Knowles TPJ, Silva DA, Shoultz D, Bernardes GJL (2023). De Novo Human Angiotensin-Converting Enzyme 2 Decoy NL-CVX1 Protects Mice from Severe Disease After Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *J Infect Dis.* 228(6):723-733.

Sousa NS, Brás MF, Antunes IB, Lindholm P, Neves J\*\*, Sousa-Victor, P\*\* (2023). Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration. *Nature Aging* 3: 585–599.

Tomé C, Oliveira-Ramos F, Campanilho-Marques R, Mourão AF, Sousa S, Marques C, Melo AT, Teixeira RL, Martins AP, Moeda S, Costa-Reis P, Torres RP, Bandeira M, Fonseca H, Gonçalves M, Santos MJ, Graca L, Fonseca JE, Moura RA (2023). Children with extended oligoarticular and polyarticular juvenile idiopathic arthritis have alterations in B and T follicular cell subsets in peripheral blood and a cytokine profile sustaining B cell activation. *RMD Open.* 9(3):e002901.

### **Pre-Prints**

Sousa NS, Bica M, Brás MF, Antunes IB, Encarnação IA, Costa T, Martins IB, Barbosa-Morais NL, Sousa-Victor P\*\*, and Neves J\*\* (2023). The immune landscape of murine skeletal muscle regeneration and aging. *bioRxiv*, DOI: 10.1101/2023.11.07.565995

Raposo AASF, Rosmaninho P, Silva SL, Paço S, Brazão ME, Godinho-Santos A, Tokunaga Y, Nunes-Cabaço H, Serra-Caetano A, Almeida ARM, Sousa AE (2023) Decoding mutational hotspots in human disease through the gene modules governing thymic regulatory T cells. bioRxiv, DOI: 10.1101/2023.12.27.573411.

### **Invited Lectures and Seminars**

Mariana Fernandes, Flow Cytometry: a world in constant evolution. IMM Scientific Retreat 2023, Portugal, September 18, 2023.

### **Communications**

#### Communications in International Conferences:

Monteiro M, Dela Cruz G, Fossum A, Mozes A, Bispo C, Rafael-Fernandes M, Andrade C, Workshop: Intelligent Training in Flow Cytometry. Congress of the International Society of Advancement of Cytometry, Canada, May 22, 2023. (Oral Presentation)

Mozes A, Andrade C, Rafael-Fernandes M, Monteiro M, Advantages of establishing a local flow cytometry network within your region. Congress of the International Society of Advancement of Cytometry, Canada, May 22, 2023. (Poster Presentation)

Monteiro M, Rafael-Fernandes M, Mozes A, Andrade C, Establishing a Local Flow Cytometry Network in Lisbon – a Case Study. EU-LIFE 10th Anniversary Conference, Portugal, June 6, 2023. (Poster Presentation)

### **Organization of Conferences**

Rafael-Fernandes M, Co-Organizer, FLxFlow Tech's Café: The Bigfoot Cell sorter – Flexibility and Performance, a legend come true!, Portugal, March 10, 2023.

Rafael-Fernandes M, Co-Organizer, FLxFlow Tech's Café: Multiomics and TotalSeq Reagents, Portugal, November 8, 2023.

Rafael-Fernandes M, Organizer, Synchronized Microscopy and Flow Cytometry: The exclusive advantages of the Imaging Flow Cytometer Amnis® Imagestream®x MK II for Multidisciplinary Research, Portugal.

### **Networks and Research Infrastructures**

Rafael-Fernandes M, Lisbon Flow Cytometry Network (FlxFlow), Member.

Rafael-Fernandes M, Portuguese Flow Cytometry Network (PT-FlowCyt), South Region Coordinator.



Rafael-Fernandes M, International Society of Advancement of Cytometry (ISAC) Biosafety Committee, Member.

Rafael-Fernandes M, International Society of Advancement of Cytometry (ISAC) SOP Repository Task Force, Member.

### **Advanced Teaching**

Rafael-Fernandes M, Lecture, Introduction to the Flow Cytometry Unit. LisbonBiomed – iMM International PhD Programme, Faculdade de Medicina da Universidade de Lisboa, Portugal, January 24, 2023.

Rafael-Fernandes M, Lecture, Principles of Flow Cytometry. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 1, 2023.

Rafael-Fernandes M, Lecture, Data analysis and Reporting. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 2, 2023.

Rafael-Fernandes M, Lecture, Cell Sorting - Basic Notions. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal, February 3, 2023.

Rafael-Fernandes M, Workshop Organization, Intro to FlowJo & Advanced tools & Plugins, Instituto de Medicina Molecular João Lobo Antunes, Portugal, March 10, 2023.

Rafael-Fernandes M, Workshop Organization, How to run a flow cytometry experiment. FLxFlow Course: Principles and Applications of Flow Cytometry, Champalimaud Foundation, Portugal, May 8, 2023.

Rafael-Fernandes M, Lecture, Considerations for planning a flow cytometry experiment and sample preparation. FLxFlow Course: Principles and Applications of Flow Cytometry, Champalimaud Foundation, Portugal, May 9, 2023.

Rafael-Fernandes M, Workshop Organization, Panel Design. FLxFlow Course: Principles and Applications of Flow Cytometry, Champalimaud Foundation, Portugal, May 9, 2023.

Rafael-Fernandes M, Lecture, An Introduction to Flow Cytometry. Introduction to Instrumental Analysis in Master in Biomedical Engineering, Instituto Superior Técnico da Universidade de Lisboa, Portugal, June 6, 2023.

Rafael-Fernandes M, Lecture, Introduction to Flow Cytometry. Bachelor in Medicinal Biotechnology, Instituto Politécnico da Guarda, Portugal, November 20, 2023.

Rafael-Fernandes M, Course Organization, FLxFlow Course: Principles and applications of Flow Cytometry, Champalimaud Foundation, Portugal.

Rafael-Fernandes M, Lecture, Experimental methodologies that use Flow Cytometry: practical sessions. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Rafael-Fernandes M, Lecture, Fluorochromes Spill-over and Compensation. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Rafael-Fernandes M, Lecture, Panel Design and Experimental Planning. Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal.

Rafael-Fernandes M, Coordination of Master Curricular Unit, Advanced Techniques in Biomedical Research I in Master in Biomedical Research, Faculdade de Medicina da Universidade de Lisboa, Portugal.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Silva-Santos B & Rafael-Fernandes M, Video “Citometria de Fluxo” – Técnicas de Laboratório, Manual escolar de Biologia 12ºano, Porto Editora.

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## Information Systems Unit

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**Director:** Daniel Silva, PhD

### Team

Maria da Conceição Correia de Sá Guedes Ferreira	University Degree	Information Systems Technician (Started November)
Miguel Ângelo Conceição Narciso	High School Diploma	Information Systems Technician (Started June)
Pedro André Lozano Luiz de Castro	High School Diploma	Information Systems Senior Technician (Left May)
Pedro Miguel Alves Cordeiro	High School Diploma	Information Systems Technician (Started May)
Rúben Miguel Nunes Antunes	University Degree	Information Systems Technician (Started October)
Telmo Gonçalo dos Reis Marques	High School Diploma	Information Systems Senior Technician (Left May)

### Description of the Facility

The information Systems Unit (USI) is responsible for managing all Information technology topics at iMM. USI is responsible for: 1) managing iMM IT infrastructure and cybersecurity; 2) administrating user privileges and software configuration; 3) maintaining iMM's High Performance Cluster (LOBO) and aid LOBO's users in advanced computation; 4) provide guidelines and curate open data policies and data management; 5) project manage IT projects on any implementation; 6) purchase management IT equipment and software for the whole institute; 7) Provide Helpdesk support for all users.

### Major Achievements in 2023

The year 2023 finished with some major achievements, namely: 1) implementation of Mission Labs' CRC Platform with full compliance with project timelines; 2) implementation of LIMS platform to support Mission Labs' operation; 3) delivering milestones 1, 2 and 3 from the EHDEN project with Biobank; 4) began datacenter upscaling project that will upgrade 3x its storage capacity, remove infrastructure dependencies and reduce energy consumption; 5) helped implement the new purchase portal; 6) optimized network and server performance that resulted in faster access to support applications; 7) began its involvement in the FEAGA (Federated European Genome Archive); 8) improved helpdesk response time

### Communications

#### Communications in National Conferences:

Daniel Felício-Silva. iMM-BioData Pitch. 3rd All Hands da BioData.pt e ELIXIR Portugal, Portugal, November 13, 2023. (Oral Presentation)



## **Networks and Research Infrastructures**

Daniel Felício-Silva, Elixir, Stakeholder.

Daniel Felício-Silva, EHDEN, Stakeholder.

Daniel Felício-Silva, FEGA, Stakeholder.

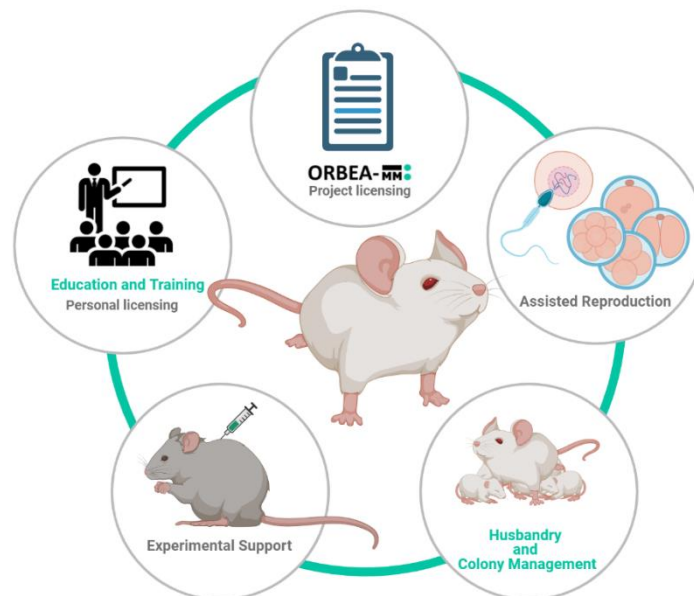
## Rodents Unit

**Director:** Iolanda Moreira, University Degree

### Team

Ana Filipa Peixoto da Cunha	University Degree	Caretaker
Ana Patrícia da Silva Almeida	Master Degree	Caretaker
Cecília Gonçalves Simão	University Degree	Caretaker
Daniel Corte Real Gomes da Costa	Master Degree	Veterinarian
Emílio Jurandir do Carmo	High School Diploma	Caretaker
Felícia Maria Augusto Ramos	University Degree	Caretaker
Leandro Fiorenzo da Cruz Testolina	University Degree	Caretaker
Luciana Vilar Falleiro	Master Degree	Caretaker
Márcia Pereira da Silva	University Degree	Animal Welfare Officer
Mihaela Elena Morari	High School Diploma	Caretaker
Pedro Manuel Nogueira Santos	High School Diploma	Senior Technician
Pedro Manuel Ribeiro de Araújo	Other	Caretaker
Sandra Cuinhane Nascimento	University Degree	Caretaker
Sara Ghirelli	High School Diploma	Caretaker
Silvia Maria Mouta Vivas	University Degree	Caretaker (Started September)
Sónia Maria Leite Pereira	Master Degree	Caretaker (Started September)
Tiago Amaral Panasco	Other	Caretaker (Started October)

### Graphical Abstract



## Description of the Facility

Translating scientific discoveries to clinical applications and to public health improvements is the main goal of biomedical research. Because animal models are necessary to achieve physiologically relevant results, the Rodent Facility is a valuable resource that advances our scientists' understanding of several human diseases and contributes to the development of novel treatments.

To this end, the Rodent Facility provides animal housing and care, colony management, assisted reproduction techniques, surgical and experimental support, advising scientists, and working towards state-of-the-art animal-based research, while maintaining the highest standards of animal welfare. The Rodent Facility follows Portuguese and international laws and recommendations governing good practices, being highly committed to continuous training and education of researchers and staff. All projects are reviewed by the Animal Welfare Body and licensed by the local competent authority.

## Major Achievements in 2023

The Rodent Facility promoted the signing of a Transparency Agreement on Animal Research, an initiative of the European Animal Research Association that promotes the availability of information on the use of animals in biomedical research. A new monitoring system for biological samples was created, in a continuous effort to improve surveillance and maintain the health status of the Facility. A library of experimental protocols and techniques pre-approved by the Animal Welfare Body was made available, assisting applicants in project licensing application processes. To work in an increasingly rigorous manner, the Rodent Facility applied for the licensing regarding the use of animals in its routine operations and support of the activities of the research units.

## Scientific Impact

### 2023 Publications in Peer-Reviewed Journals

Martins I, Neves-Silva D, Ascensão-Ferreira M, Dias AF, Ribeiro D, Isidro AF, Quitéria R, Paramos-de-Carvalho D, Barbosa-Morais NL, Saúde L (2023). Mouse Spinal Cord Vascular Transcriptome Analysis Identifies CD9 and MYLIP as Injury-Induced Players. *International Journal of Molecular Sciences*. doi: 10.3390/ijms24076433.

Isidro AF, Medeiros AM, Martins I, Neves-Silva D, Saúde L, Mendes CS (2023). Using the MouseWalker to Quantify Locomotor Dysfunction in a Mouse Model of Spinal Cord Injury. *JoVE* doi: 10.3791/65207.

Rajão-Saraiva J, Dunot J, Ribera A, Temido-Ferreira M, Coelho JE, König S, Moreno S, Enguita FJ, Willem M, Kins S, Marie H, Lopes LV, Pousinha PA (2023). Age-dependent NMDA receptor function is regulated by the amyloid precursor protein. *Aging Cell*. 22(3):e13778. doi: 10.1111/accel.13778.

Inês Gomes, Lina M Gallego-Páez, Maria Jiménez, Patricia G Santamaria, André Mansinho, Rita Sousa, Catarina Abreu, Eva González Suárez, Luis Costa and Sandra Casimiro (2023). Co-targeting RANK pathway treats and prevents acquired resistance to CDK4/6 inhibitors in luminal breast cancer. *Cell Reports Medicine* 4(8):101120. <https://doi.org/10.1016/j.xcrm.2023.101120>.

Chora ÂF, Marques S, Gonçalves JL, Lima P, Gomes da Costa D, Fernandez-Ruiz D, Marreiros MI, Ruivo P, Carvalho T, Ribeiro RM, Serre K, Heath WR, Silva-Santos B, Tate AT, Mota MM (2023). Interplay between liver and blood stages of Plasmodium infection dictates malaria severity via  $\gamma\delta$  T cells and IL-17-promoted stress erythropoiesis. *Immunity*. 56(3):592-605.e8. doi: 10.1016/j.immuni.2023.01.031. Epub 2023 Feb 17. PMID: 36804959.

RS Rodrigues, JB Moreira, SH Vaz, A Barateiro, SL Paulo, JM Mateus, DM Lourenço, FF Ribeiro, E Loureiro-Campos, P Bielefeld, A Fernandes, AM Sebastião, L Pinto, CP Fitzsimons, S Xapelli (2023). Cannabinoid type 2 receptor inhibition enhances the antidepressant and proneurogenic effects of physical exercise after chronic stress. *bioRxiv* 2023.04.24.538087; doi: <https://doi.org/10.1101/2023.04.24.538087>.

Sousa NS, Brás MF, Antunes IB, Lindholm P, Neves J, Sousa-Victor P (2023). Aging disrupts MANF-mediated immune modulation during skeletal muscle regeneration. *Nat Aging*. 3(5):585-599. doi: 10.1038/s43587-023-00382-5. Epub 2023 Mar 23. PMID: 37118549.

Papotto PH, Yilmaz B, Pimenta G, Mensurado S, Cunha C, Fiala GJ, Gomes da Costa D, Gonçalves-Sousa N, Chan BHK, Blankenhaus B, Domingues RG, Carvalho T, Hepworth MR, Macpherson AJ, Allen JE, Silva-Santos B (2023). Maternal  $\gamma\delta$  T cells shape offspring pulmonary type 2 immunity in a microbiota-dependent manner. *Cell Rep*. 42(2):112074. doi: 10.1016/j.celrep.2023.112074. Epub 2023 Feb 13. PMID: 36787741.

Machado H, Hofer P, Zechner R, Smith TK, Figueiredo LM (2023). Adipocyte lipolysis protects mice against *Trypanosoma brucei* infection. *Nat Microbiol*. 8(11):2020-2032. doi: 10.1038/s41564-023-01496-7. Epub 2023 Oct 12. PMID: 37828246.

Fraga A, Mósca AF, Moita D, Simas JP, Nunes-Cabaço H, Prudêncio M (2023). SARS-CoV-2 decreases malaria severity in co-infected rodent models. *Front Cell Infect Microbiol.* 13:1307553. doi: 10.3389/fcimb.2023.1307553. PMID: 38156320; PMCID: PMC10753813.

Moita D, Nunes-Cabaço H, Rôla C, Franke-Fayard B, Janse CJ, Mendes AM, Prudêncio M (2023). Variable long-term protection by radiation-, chemo-, and genetically-attenuated *Plasmodium berghei* sporozoite vaccines. *Vaccine.* 41(51):7618-7625. doi: 10.1016/j.vaccine.2023.11.023. Epub 2023 Nov 25. PMID: 38007342.

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Paisana E, Cascão R, Custódia C, Qin N, Picard D, Pauck D, Carvalho T, Ruivo P, Barreto C, Doutel D, Cabeçadas J, Roque R, Pimentel J, Miguéns J, Remke M, Barata JT, Faria CC (2023). UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease. *Neurooncol Adv.* 5(1):vdad048. doi: 10.1093/noajnl/vdad048. PMID: 37215954; PMCID: PMC10195208.

Marreiros IM, Marques S, Parreira A, Mastrodomenico V, Mounce BC, Harris CT, Kafsack BF, Billker O, Zuzarte-Luís V, Mota MM (2023). A non-canonical sensing pathway mediates *Plasmodium* adaptation to amino acid deficiency. *Commun Biol.* 6(1):205.

Moita D, Rôla C, Nunes-Cabaço H, Nogueira G, Maia TG, Othman AS, Franke-Fayard B, Janse CJ, Mendes AM, Prudêncio M. (2023) The effect of dosage on the protective efficacy of whole-sporozoite formulations for immunization against malaria. *NPJ Vaccines.* 8(1):182.



### **Pre-Prints**

Joana Gomes-Ribeiro, João Martins, José Sereno, Samuel Deslauriers-Gauthier, Teresa Summavielle, Joana E. Coelho, Miguel Remondes, Miguel Castelo Branco, Luísa V. Lopes (2023). Mapping functional traces of opioid memories in the rat brain. doi: <https://doi.org/10.1101/2023.08.07.552221>

Sousa, N.S., Bica, M., Brás, M.F., Antunes, I.B., Encarnação, I.A., Costa, T., Martins, I.B., Barbosa-Morais, N.L., Sousa-Victor, P.\*\*\*, and Neves, J.\*\* (2023). The immune landscape of murine skeletal muscle regeneration and aging. bioRxiv, DOI: 10.1101/2023.11.07.565995.

### **Networks and Research Infrastructures**

Iolanda Moreira, Laboratory Animal Science Education and Training Working Group, Coordinator.

Iolanda Moreira, ORBEA Working Group, Institutional representative.

Iolanda Moreira, EARA, Representative to the EARA General Assembly.

Daniel Costa, ORBEA Working Group, Institutional representative.

Márcia Silva, ORBEA Working Group, Institutional representative.

### **Advanced Teaching**

Iolanda Moreira, Course organization, 1st Edition Laboratory Animal Science Course for Function A and D, Portugal, April 21, 2023.

Daniel Costa, Lecture, 1st Edition Laboratory Animal Science Course for Function A and D (former FELASA Category B) CONGENTO-harmonized program, Portugal, April 21, 2023.

Daniel Costa, Lecture, 2nd Edition Laboratory Animal Science Course for Function A and D (former FELASA Category B) CONGENTO-harmonized program, Portugal, October 19, 2023.

Iolanda Moreira, Course organization, 2nd Edition Laboratory Animal Science Course for Function A and D, Portugal, October 19, 2023.

Daniel Costa, Course organization, Animal Models in Biomedical Research, Portugal.

Márcia Silva, Lecture, CONGENTO Course on Modules 9, 10 and 11 ("Upgrade Course for Functions B"), Portugal.

Márcia Silva, Lecture, Animal Models in Biomedical Research, Portugal.

Iolanda Moreira, Lecture, Animal Models in Biomedical Research, Portugal.

## **Valorization of Knowledge / Social and Economic Impact**

### **Science and Society in 2023**

Noite Europeia dos Investigadores – Fale com técnicos sobre o uso de animais para fins científicos, Fundação Champalimaud, September 29, 2023.

Iolanda Moreira, Daniel Costa and Márcia Silva, Entrevista no âmbito de um trabalho da unidade curricular de Jornalismo de Ciência, Mestrado de Comunicação e Ciência da Faculdade de Ciências Sociais e Humanas da Universidade Nova de Lisboa, November 28, 2023.

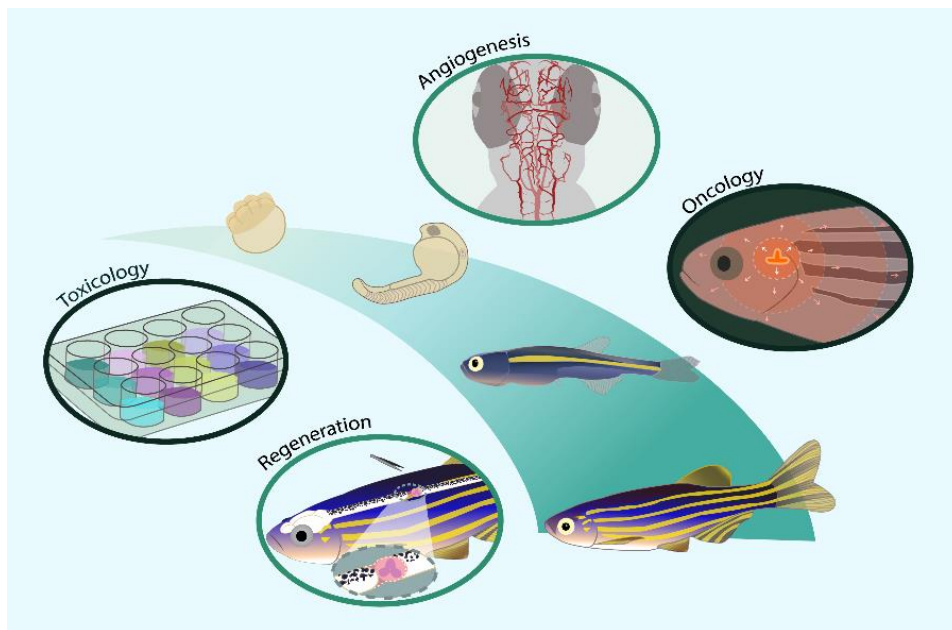
## Zebrafish Unit

**Director:** Leonor Saúde, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes, Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Aida Gonçalves Lino Barros	High School Diploma	Senior Technician
Lara Margarida Marques Saraiva de Carvalho	Master Degree	Zebrafish Unit Area Manager

### Graphical Abstract



### Description of the Facility

The Facility is dedicated to support internal and external research units. It offers comprehensive technical assistance for the use of zebrafish across a diverse array of biomedical research projects.

### Major Achievements in 2023

We have implemented a new database (PyRat Aquatic) to improve the organisation and management of the zebrafish lines and enhance the implementation of 3R policies within the facility.

### Scientific Impact

#### Academic Collaborations

- Miguel Castanho Lab, Instituto de Medicina Molecular João Lobo Antunes, Portugal.

### **2023 Publications in Peer-reviewed Journals**

Ribeiro, A., Rebocho da Costa, M., de Sena-Tomás, C., Rodrigues, E. C., Quitéria, R., Maçarico, T., Rosa Santos, S. C., & Saúde, L (2023). Development and repair of blood vessels in the zebrafish spinal cord. *Open biology*, 13(8):230103. <https://doi.org/10.1098/rsob.230103>.

Cardoso, B. A., Duque, M., Gírio, A., Fragoso, R., Oliveira, M. L., Allen, J. R., Martins, L. R., Correia, N. C., Silveira, A. B., Veloso, A., Kimura, S., Demoen, L., Matthijssens, F., Jeha, S., Cheng, C., Pui, C. H., Grosso, A. R., Neto, J. L., De Almeida, S. F., Van Vlieberghe, P., ... Barata, J. T. (2023). CASZ1 upregulates PI3K-AKT-mTOR signaling and promotes T-cell acute lymphoblastic leukemia. *Haematologica*, 10.3324/haematol.2023.282854. Advance online publication. <https://doi.org/10.3324/haematol.2023.282854>.

### **Networks and Research Infrastructures**

Lara Carvalho, Congento, Education and Training Group.

#### **Advanced Teaching**

Lara Carvalho, Course organization, Laboratory Animal Science Course, Portugal, May 2023.

Leonor Saúde, Workshop organization, AIMS - Zebrafish in Biomedical Research Masterclass, Portugal, November 6, 2023.

Lara Carvalho, Course organization, Laboratory Animal Science Course, Portugal, November 2023.

## **Valorization of Knowledge / Social and Economic Impact**

### **Partnerships with Industry in 2023**

Sparos, Feed Tests, Collaborative Research.

### **Science and Society in 2023**

We conducted numerous visits and actively participated in various activities to raise awareness about our work and our commitment to working with the zebrafish as a biomedical research animal model:

- Visit by Director of Bayer invited by L. Costa's Lab, January 16, 2023.
- Visit by 28 students from 12th grade Escola Básica e Secundária Henrique Sommer, Leiria, January 19, 2023.
- Visit by LisbonBioMed students, January 31, 2023.

- Collaboration with Professor Noélia Custódio (FMUL) in the activity carried out for 120 8th grade students within the scope of the RAISE program, February 15, 2023.
- Visit by 14 agents from insurance companies, May 29, 2023.
- Visit by 18 students from the Master's degree course in Pharmaceutical Sciences from Universidade Lusófona, June 16, 2023.
- Participation in European Researchers' Night (ERN) - Animals in research, Champalimaud Foundation, September 29, 2023.

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## Communication Office

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**Director:** Inês Domingues, PhD

### Team

Ana Cláudia Marques da Silva	University Degree	Senior Communication Officer
Andrés Azzolina	University Degree	Multimedia Officer (Left September)
Helena Alexandra Ribeiro de Carvalho Pinheiro	PhD	Senior Communication Officer

### Description of the facility

The Communication is iMM's first line of interaction with society providing updated, reliable and relevant information on all of iMM's thematic areas, as well as promoting the very best scientific successes made by its research teams. Its mission is to support the internal and external communication, 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, schools, academia, industry, media, 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 office is responsible for the overall image of iMM, our day-to-day activities encompass Media Relations, Science and Society Outreach, Conferences and Events, Institutional Visits, Awareness Campaigns, Social Media, Internal Communication and Public Affairs Training.

### Major Achievements in 2023

In 2023, our communication strategies resulted in an extensive media presence, with estimated values of 681 media clippings. Within the context of the RAISE project, we co-organized the European Researcher's Night. Around 1700 people visited the ERN, over the course of 9 hours, and explored a program of 50 free activities, such as concerts, workshops, hands-on stations, lab visits, and stand-up comedy.

Within the context of iMM-Laço Hub, we co-organized the first Semana da Mama, a 7-days event to raise awareness of breast cancer. We launched the book "Afinal, o que é o cancro?", a collection of 12 opinion articles written by Sérgio Dias, and illustrated by Helena Pinheiro. The podcast C4ncr0 was created with conversations about cancer between scientists, doctors, and patients.

iMM participated in the Lisbon Book Fair with talks and hands-on activities, and we launched Science in the Making, an awarded new science outreach initiative consisting of short animation videos on ongoing projects.

### **Ongoing Projects**

2022/2024: Researchers in Action for Inclusion in Science and Education. Coordinator: Inês Domingues. Funding Agency: European Commission. Reference: RAISE - HORIZON-MSCA-2022-CITIZENS-01-01. Amount: 16 120,00€. Total Amount: 299 607,50€.

### **Invited Lectures and Seminars**

Helena Pinheiro, Workshop on Graphical Design for Scientific Figures. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, June 22, 2023.

### **Organization of Conferences**

Co-Organizer, RNA in Disease – IX ptRNA joint meeting, Portugal, January 26-27, 2023.

Co-Organizer, Feira do Livro de Lisboa, Portugal, May 28, June 3, 4, 8 and 10, 2023.

Co-Organizer, European Researchers' Night (RAISE Project), Portugal, September 29, 2023.

Co-Organizer, 13th EMBO Young Scientists' Forum, Portugal, October 12-13, 2023.

Co-Organizer, Semana da Mama 2023 (iMM-Laço Hub), Portugal, October 24-30, 2023.

### **Prizes and Honours**

The Science in the Making video project was awarded with the 1st prize in the science short video category of Ciencia en Acción 2023 competition.

## Finance and Operations Office

**Director:** Fausto da Costa Santos Lopo de Carvalho, Master/MBA

### Team

**Assistant to the Board of Directors:**

Ana Clara Pereira Faria Artur	Assistant to the Board of Directors
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**Project Management:**

Madalena Gil Martins Reis	Project Management Area Manager
Andreia Sofia Gonçalves Almeida Vaz Veiga	Senior Project Manager
Jorge Miguel Pereira da Silva	Senior Project Manager
Laura Chloe Ward	Senior Project Manager (Started July)
Maria José Flores Marques Antunes	Senior Project Manager
Mariana Advirta da Silva Matos Pereira	Project Manager
Rita Santinho Grenho	Project Manager

**Accounting:**

Sandra Paula da Silva Duarte	Accounting Area Manager
António Guilherme Ramalho Gomes de Almendra	Accounting Administrative Technician
Maria Elisabete Santos Liberato	Senior Accounting Administrative Technician
Maria Fernanda Gonçalves da Veiga Vila-Chã	Administrative Technician
Pedro Miguel da Rosa Santos	Senior Accounting Administrative Technician
Vera Cristina Felício da Conceição Rêgo	Senior Accounting Administrative Technician

**Purchasing and Procurement:**

Alexandre Manuel Raposo de Jesus	Purchasing and Procurement Area Manager
Ana Filipa de Almeida Pereira	Purchasing Administrative Technician
Ana Rita Fonseca Vicente	Senior Purchasing Administrative Technician
Bruno Fernando Costa Baptista	Administrative (Started February. Left November)
Joana de Mello Seixas	Purchasing Administrative Technician (Started September. Left December)
Laura da Silva Alves Dias	Technician (Started December)
Sandra Isabel Francisco Lopes	Senior Purchasing Administrative Technician
Vânia Isabel Estevens Polido Marques Paula	Senior Purchasing Administrative Technician

**Legal and Human Resources:**

Inês Bilé da Silva Plácido	Legal Counsel and Area Manager
Cláudia Aurora Mira Soeiro	Senior HR Administrative Technician
Daniela Sofia Zacarias Urbano	HR Administrative Technician
Joana Rita Correia Relvas	HR Administrative Technician (Started March)
Pedro Humberto Fernandes Monteiro Leite	HR Administrative Technician (Left April)
Rita do Carmo Costa Risco Pífano	HR Administrative Technician
Sara Duarte Pifano da Costa Eiras	Senior HR Administrative Technician
Manuel Vicente Sacadura Zagallo Pacheco Garcia	Lawyer (Started August)



**Safety and Compliance:**

Sara Diana Pinheiro dos Santos	Safety and Compliance Area Manager
Ana Francisca Barroca Lemos	Senior Technician
Bruno Alexandre Dias Martins	Technician (Started April)
Cláudia Sofia Palmeiro Alves da Costa	Senior Technician
Hugo Alexandre Filipe Silva	Technician
Maria Jardim Caramelo Dias Cabral	Senior Technician (Left March)
Rita Catarina Fernandes Brito	Technician

**Washing Room:**

Bashir Shamshudin Habib Alibhai	Senior Technician
Monique Maira Melo Madureira	Senior Technician
Naira Sibila Casimiro Correia	Technician
Paulo Henrique Soares Ferreira	Technician

**Mission Lab:**

Patrícia Napoleão	Mission Lab Area Manager
Daniela Maria Teixeira Leal da Silva	Lab Technician (Left January)
Margarida Xavier Fonseca e Costa	Technician (Left October)
Sandra Filipa Coutinho Protásio	Lab Operations & Technology Manager
Yash Girish Pandya	Postdoctoral Researcher (Left October)
Yulia Carvalho	Senior Technician

**Front Office:**

Ana Catarina Ramalheira	Administrative
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**Major Interest/Objectives**

The Finance and Operations Office operates under an agile organizational model with six departments, Project Management, Purchases and Procurement, Accounting, Legal & HR, Safety and Compliance and Mission Lab each with a dedicated Area Manager empowered to design and implement the strategy for each department, aligned with iMM overall priorities.

The Finance and Operations Office main purpose is to maintain an extremely agile structure to give the best possible support to the scientific community, viewed as internal clients. The six areas working collaboratively, allow for a unified 360° 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.

**Accounting** – iMM statutory accounts and tax returns; Cost and revenue accounting; Reporting and compliance with funding bodies accounting practices; Dedicated report building on cash flow and HR costs.

The goal is to maintain reliable financial information, always in compliance with deadlines, highlighting its benefits for iMM, in general, and for research projects, in particular.

**Core Services:**

Accounting is divided in three major areas:

- Invoicing – iMM Invoicing, supplier invoices and invoice archive management.
- Payments and refunds – Accounts Payable, Refunds and Advance Payments.
- Tax/Fiscal – Human Resources (social security and withholding tax), Suppliers (VAT; withholding tax), annual income statements (IRC, IES).

**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 & Procurement** – Help purchasing decisions; Negotiation; Tendering according to Portuguese and European legislation; Verification of the validity of expenses associated with a research project; Placing the order to the supplier; Tracking delivery times and updating the researcher on lead times.

**Core Services:**

- Procurement - to help make informed, best-value (money, quality and time) purchasing decisions by establishing transversal contracts and agreements with a wide supplier network.
- Purchasing - to maintain, interpret, and enforce the purchasing policy (according to funding bodies) while ensuring that all expenses are eligible, by approving purchases with the help of all departments and handling the dispatching of all Purchase Orders to vendors.
- Logistics - to manage incoming products from suppliers by handling importation procedures and customs clearance while also checking-in and register in our internal system.

**Legal & Human Resources** – As a joint department, Legal & HR works to promote the best support and guidance for scientists and managers in accordance with policies, procedures, and legal requirements to meet the needs of the Institute.

**Legal**

Institutional and Researcher's support

**Core Services:**

- Preparation and revision of agreements and other acts and ensure the legal adequacy of processes, providing the optimum balance between the management promptness and efficiency with the legal utmost clarity and safety.
- Furnishing legal advice to the Board of Directors.

**Human Resources**

Develop, implement and support policies, programs processes and services that add value to iMM and its employees through an agile articulation with all iMM internal stakeholders (several areas and departments of iMM) and external stakeholders (partners and funding agencies).

**Core Services:**

- Employment/ fellowships/ volunteer/ internships contract management from the opening of the competitive procedure/contract signing to the termination of the relationship.
- Payroll processing.
- Facilitating access to occupational medicine.
- Management, monitoring, and organization of the onboarding processes for collaborators (regardless of the type of employment contract).

- Ensuring general information of labour, tax, and organizational nature, including supporting employees regarding their tax status, assignment of Tax Identification Number, social security number, and other tax-related matters.
- Management, monitoring and organization of the expense submission process to funders and update of information regarding the teams to the national funding agency.

**Safety & Compliance** – Our goal is to ensure that all infrastructure, equipment and material requirements for high-quality research are met, while working in a safe and healthy environment, with minimum environmental impact and complying with all legal requirements.

**Core Services:**

- Equipment/Infrastructure management – manage of common equipment, preventive and corrective maintenance, equipment calibration and validation and lab design.
- Washing Room – labware washing and disinfection.
- Safety and Health – comply with legal requirements, in order to minimize the health and safety risks of workers.
- Environment - comply with legal requirements, to minimize the organization environmental impacts.

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.

**Mission Lab** – Our goal is to establish fast-tracking translational research to provide solutions for specific health problems and to deliver new preventive, diagnostic and/or personalized medicine solutions. This will translate into a contribute to the sustainability of iMM-CARE.

**Core Services:**

- Planning and defining Missions scalable workflows.
- Provide support to the of Mission Ethics documentation to be submitted to the Competent Ethics Committee.
- Support logistics, laboratory, and operations of Missions:
  - establish laboratory Standard Operating Procedures (SOPs).

- establish logistic and operations SOPs.
- ensure compliance with Quality according to the legal requirements.
- establish and manage collaborations with clinical and logistic partners.
- establish contracts with external providers to ensure logistics and operations.

### Keywords

- **Project Management** – Facility Cost Management; Consolidation of PM team.
- **Purchases & Procurement** – Simplification; Procurement.
- **Accounting** – Digital Archive; Compliance.
- **Safety & Compliance** – Occupational Medicine; IGAMAOT inspection; Maintenance software to iMM Facilities, Adaptation to RH changes.
- **Legal & HR** – Compliance and Operational Excellence.
- **Mission Lab** – Consolidate R&D setup; Colorectal Cancer Flagship Project.

### Major Achievements

During 2023 two major developments took place at iMM. **The start of the Teaming Project iMM-CARE and the preparatory actions to establish the MoU and bylaws of the new GIMM foundation.** As stated in its vision (more details in [gimm.pt](http://gimm.pt)) – “The Gulbenkian Institute of Molecular Medicine (hereafter GIMM) was created by a consortium of private and public institutions as a private foundation, aiming to become an international, world leading multi- and cross-disciplinary research institute. It seeks to actively encourage individuals in the pursuit of disruptive ideas to advance our fundamental understanding of life, and to meet current and future challenges to global health and well-being. GIMM aims to pursue and leverage the legacy of two outstanding research institutions – Instituto Gulbenkian de Ciência and Instituto de Medicina Molecular - which have merged to create a unique research institute where fundamental and applied science coexist. With campuses in Lisbon and Oeiras, GIMM hosts more than 500 scientists from various nationalities. It fosters a stimulating, curiosity-driven and inclusive scientific culture where multidisciplinary research is pursued in an open and collaborative manner, towards the discovery of fundamental concepts in the life-sciences and the advance of biomedical knowledge.” In December 2023 the Portuguese Government approved the constitution of the foundation, opening the way for the operational procedures regarding merging the two institutions under a common organization in 2024.

iMM-CARE will develop and promote excellence in clinical and translational research, profoundly transforming how clinical and translational research is conceptualized, planned, and implemented to deliver effective solutions to the most pressing health needs.

The CoE will have at its core a mission-driven, human-centered, data-driven research and innovation (R&I) model as a new way to engage all stakeholders – citizens, patients, healthcare professionals, scientists, entrepreneurs, industry, health authorities and government – in interdisciplinary, cross-sectoral collaborations to solve health challenges. In 2023 the project started at fast pace with the implementation of several initiatives according to what was planned under each work packages. The Colorectal Cancer project is the most advanced initiative of iMM-CARE and its operational set-up involved a complex interplay between tech companies, impact consultancy project management and healthcare consultancy to access the burden of disease for the national health system. In 2023 the technology platform that will give support to the sample collection was developed and was considered a major asset and allowed the dry run to start in November 2023 in collaboration with a private hospital. In the end of 2023, a meeting was held with the CEO of the National Health System – Fernando Araújo in coordination with the board of directors of the Hospital de Santa Maria to showcase the investment done so far in addressing a major public health issue in Portugal to explore avenues of collaboration between iMM and the SNS as was done during COVID-19 period. The goal is always to leverage on the experience acquired to maximize the efficiency of each investment decision.

The two above-mentioned major events that took place in 2023 forced the operations team to be ever more responsive while keeping up with the “Business As Usual Tasks”. The **Accounting** team continued its work of rigorously recording documents on projects, always seeking to improve processes and procedures. During 2023, monthly closing and reporting dates were complied, as well as the preparation of dashboards of Cash Flow, HR, and financial reporting of quarterly analyses. **Purchasing & Procurement** was more present in the negotiation phase with all facilities, including the new equipment for Flow Cytometry and Bioimaging, and laboratories. The new purchasing system entered its pilot stage and is live for the beginning of all iMM purchases in 2024. **Project Management** team continued to support researchers and the team was strengthened with new hires that complement the existing set of capabilities in the team. One member of the team was selected by the European Union to be part of an expert team for the widening program. The Teaming project financial planning and dashboard already reveals an above average level of proficiency both in the tools and systems and in the management process. Communication between financial project management and the dedicated teaming project manager was always very fluid giving very good signs for future actions in similar areas. **Legal & HR** continued to work together to enable and support managers and scientists and to prepare the ground for additional HR transformation priorities to be set for the future.

Considering the development of the scientific activity of the Institute, and the challenges brought by the iMM-CARE Teaming project and the future GIMM Foundation, the focus remained on ensuring full compliance and ensure that all processes are developed in a legal and appropriate manner.

As for the **Safety & Compliance**, 2023 saw the arrival of two new group leaders – Zita Santos and Joel Perri as well as a farewell to one group leader that moved to the Católica Biomedical Research Center. Further remodeling took place in Gonçalo Bernardes Lab and Ribot-Santos Lab. Regarding equipment management, new monitoring system was purchased to improve the quality and safety control of several parameters in equipment and rooms and new common equipment was acquired. Finally, the Mission Lab as part of the new CARE structure implemented the Lab information management system (LIMs) as well as the SOPs for the laboratory including licensing and certification. **Mission Lab** team worked closely the science and operations team to successfully plan the roll out of the CRC project dry run as they are responsible for the operational flow of all science operations regarding to the necessary support to be given to the sample collection, fit testing within mission lab premises and all the logistics associated with the several actions of the project.

#### **Accounting:**

During 2023 the accounting team improved processes and procedures in its relationship with external organizations and researchers:

- In February the Navision ERP was changed regarding invoicing for courses and congresses that take place at iMM. The invoicing process has become easier with the creation of a final consumer, in which the taxpayer number is changed when each invoice is issued.
- Cross-referencing the AT portal with suppliers' current accounts, to detect any invoices that haven't reached the accounts and requesting them, so that they are all recorded in the respective month.
- Analyzing invoices with outstanding issues before the close of the months and resolving them so that they are not carried over to the following month.

The team remains focused on meeting the deadlines for closing the months, always seeking to improve its performance, and preparing to respond to new requests for tasks related to the transition from iMM to GIMM.

**Purchasing & Procurement:**

The continuation of the price disruption and inflation felt in 2022 continued affecting 2023, thus continuing the price fluctuations along the whole supply-chain. The Purchasing System was remodeled due to the impact it was having on the routine regarding files for the AT, but even so entered the pilot stage and it will be used by the whole institute with the opening of purchasing in 2024.

The departments continues to be regarded as a key piece on the work of labs and facilities and have been contacted by several people to initiate negotiations on their behalf. We also used the data already in system to see patterns of acquisition and thus create programmed orders for facilities, reducing administrative overhead from multiple to one order, and benefits on buying in bulk regarding time and money spent.

**Project Management:**

The project management team is committed to continuously improving the support given to laboratories and IMM, liaising with financial bodies in all reporting and administrative tasks related to project implementation.

In 2023, we focused on two main areas:

- Implementation of control dashboards, allowing not only a more efficient project management, meeting deadlines and ensure total budget execution but also increasing redundancy in the team, diminishing the impact of holiday season or sick leaves;
- IMM-CARE – Teaming project - Due to its importance in all IMM areas, the Project management team dedicated an increased effort to creating the framework to guide the 6-year project implementation with the consequent strategic impact;

In 2023, the broader scope of project manager's action continues to take place with the participation in Colon Rectal Cancer Mission and Semana da Mama being some examples.

**Legal & HR:**

During 2023 the Legal & HR department was consolidated and the goal of optimizing the human resources operations was reinforced.

The Legal department maintained its support to all the activity of the IMM providing the best counselling for all main legal questions and allowing the institute to operate in a compliant level. The legal team was strengthened with a new legal advisor specialized in labour law and an expert in personal data regulations.



HR procedures were strengthened and some documents, aimed at help iMMers regarding HR matters, were produced, namely a contractual overview of each lab that was sent to each Group Leader to help them to better plan the contractual management of their HR and an information brochure - the Welcome New Parents to inform about new parents rights.

### **Safety & Compliance:**

The year 2023 was marked by significant achievements and an ongoing commitment to excellence.

Regarding Occupational Health and Safety, the joint work with the Occupational Medicine team during the past year has been very successful, especially the joint regular visits to work stations, which made it possible to identify, prevent and correct several situations of musculoskeletal disorders.

The Legal Compliance Audit for the safety and environment areas was also completed, as well as the Annual Compliance Check to iMM radioactive activities. In addition, a GMM/GMO environmental inspection was performed at iMM by a government agency (IGAMAOT), whose results we are still awaiting.

The team responsible for the equipment management and maintenance demonstrated efficiency, ensuring the continuous operation of equipment and facilities, which is especially significant considering the changes in human resources during the past year. The maintenance software (used by S&C) was made available to all iMM facilities to allow a more robust and efficient management of equipment and data. A new monitoring system was purchased to improve the quality and safety control of several parameters in equipment and rooms and new common equipment was acquired: ultrafreezer, fridge/freezer, plate reader, spectrophotometer, centrifuge, biosafety cabinets, and euthanasia systems.

Space renovations were carried out in the 3rd floor bar, in the Zita Santos Lab and Gonçalo Bernardes Lab, in the Brain CDT Lab and in several offices: TTO, Pre-Award, Projects, Legal and HR, Julie Ribot and Bruno Silva Santos, providing safe and functional environments for their activities.

The Washing room continued to improve the services provided to the labs and facilities in a commitment to quality and to make their everyday life easier. There has been a stabilization of the human resources at the washing room, increasing the expertise and operational efficiency.



Collectively, these accomplishments reflect the department's dedication to contribute to the ongoing success of IMM.

**Mission Lab:**

The key significant results from the mission lab team, in 2023, were:

- Lab information management system (LIMs) implemented and almost fully operational.
- Mission Lab SOPs for the laboratory, logistics and operation work initiated.
- Report on the audits and the market research performed regarding the needs of interventions on the facility to obtain Licensing and Certification.
- Launch of the first flagship project in a pilot version.

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## Pre-Award Office

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**Director:** Joana Costa, PhD

### Team

Ana Catarina Henriques Oliveira	PhD	Grants Officer
Francisca Ferreira de Vasconcelos	PhD	Grants Officer

### Description of the Facility

The Pre-Award team proactively supports the iMM community in securing competitive funds for research and institutional activities, in compliance with the terms and conditions of the funding agencies, by offering individualized professional support on the preparation and submission of proposals and on the negotiation of successfully funded applications. We further provide advice to the Board of Directors on trends in national/international science policy and competitive funding landscape.

### Major Achievements in 2023

Dissemination of 300+ funding opportunities; Support to 177 applications to 54 different International and 17 different National Funding Programmes, namely regarding eligibility, legal, budget, technical and administrative aspects, as well as ethics and Open Science requirements; Preparation of material of support, both general and tailored for specific calls - FCT projects, FCT Individual Scientific Employment, CaixaResearch Health and NIH; Restructure and improvement of available resources in intranet; Increased compliance of iMM researchers with the Pre-Award regulations; Support to institutional proposals, namely the FCT LA-CEEC; Capacitation of team members through specific training namely in proposal writing for the European MSCA-Postdoctoral Fellowships and in relevant topics in research management such as Impact, Internationalisation; Open Science; RRI; Policy, Strategy, Evaluation and Foresight; and Proposal Development.

### Invited Lectures and Seminars

Catarina Oliveira & Francisca Vasconcelos. Funding Scientific Research. MSc in Oncobiology, FMUL/iMM, Portugal, May 31, 2023.

Joana Costa. Biobancos-Oportunidades de Financiamento. Biobancos: Potenciar a Investigação em Saúde, Portugal, September 13, 2023.

Joana Costa. Pathways for Research & Innovation. Infoday Horizon Europe: Exploring The Upcoming Opportunities, Portugal, October 27, 2023.

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## Technology Transfer Office

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**Director:** Pedro Silva, University Degree, President of the Board of Directors at Accelbio Association

### Team

Bárbara Sofia Lopes Gomes	PhD	Senior Technology Transfer Officer
Beatriz Paisana Ferreira Bouza da Costa	Master Degree	Technology Transfer Officer (Left October)
Joana Carolina Marinho Cunha	PhD	Technology Transfer Officer (Started September)
Miguel Filipe Duarte	Master Degree	Technology Transfer Officer
Nadine Vasconcelos Conchinha	PhD	Technology Transfer Officer (Started March)

### Description of the Facility

We stimulate the valorization of knowledge produced at iMM through:

- The creation of a favorable internal environment to foster innovation and speed up the translation of promising ideas and results into new medical solutions;
- The protection and licensing of intellectual property;
- The promotion of entrepreneurship and the creation of start-ups;
- A closer interaction with industry (at national and international level) leading to new collaborations;
- The participation, and representation of iMM, to relevant National and European networks and initiatives related with translational research, open innovation and business acceleration.

### Major Achievements in 2023

- Consolidation of iMM's technology transfer activity with 22 new inventions and 17 patent applications in different territories; 10 license agreements (including license option agreements); 10 start-up companies supported; 249 new collaborations with industry supported and 69 new collaborations established (1.3M€); 69 agreements formalized (e.g.: MTA, NDA, IIA); 54 applications to competitive funding schemes supported and 11 applications approved (1.5M€).
- iMM start-up companies secured 16.5M€ in fundraising activities supporting development of new business ideas and/or growth of existing start-ups.
- iMM for the first time in the ranking of top Portuguese organizations for patent applications.

- Internal Call for Proposals: "Human-Based Models as Drug Discovery Tools", in the context of the project "CTI", with a total budget of 456k€. 5 projects awarded out of 13 applications.

### **Invited Lectures and Seminars**

Pedro Silva, How to start a new company with novel drug targets. TT workshop promoted by the Weizmann Institute (Bina), Israel, February 23, 2023.

Pedro Silva, The role of CTIs in fostering innovation in Portugal. Tour des Capitales, Portugal, November 15, 2023.

### **Ongoing Projects**

2023/2026: CTI – Centro de Tecnologia e Inovação do iMM. Coordinator: Pedro Silva. Funding Agency: Agência Nacional da Inovação (ANI). Amount: 6 412 000,00€

2023/2026: HfPt – Health from Portugal. Coordinator: Miguel Duarte. Funding Agency: ANI/IAPMEI (PRR). Amount: 490 558,21€. Total Amount: 118 060 443,28€.

2023/2025: Integrated Services for Infectious Disease Outbreak Research. Coordinator: Pedro Silva. Funding Agency: European Commission. Reference: ISIDORE - GA 101046133. Amount: 750 339,50€. Total Amount: 750 339,50€.

2023/2025: canSERV: Providing cutting-edge cancer research services across Europe. Coordinator: Pedro Silva. Funding Agency: European Commission. Reference: 101058620.

2022/2023: Data River. Coordinator: Beatriz Costa. Funding Agency: Private. Reference: Data River (Business Support Services). Amount: 6 400,00€. Total Amount: 6 400,00€.

2022/2023: EHDEN – Biobanco. Coordinator: Beatriz Costa. Funding Agency: EHDEN. Reference: EHDEN – Biobanco. Amount: 100 000,00€. Total Amount: 100 000,00€.

2021/2023: Leap-Bio. Coordinator: Miguel Duarte. Funding Agency: European Commission. Reference: Leap-Bio. Amount: 151 378, 50€. Total Amount: 151 378, 50€.

2019/2023: SAFE-N-MEDTECH – Safety Testing in the life cycle of nanotechnology-enabled medical technologies for health. Coordinator: Pedro Silva. Funding Agency: European Commission. Reference: GA 814607 – SAFE-N-MEDTECH. Amount: 714 815,00€. Total Amount: 18 466 649,10€.

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## Training Hub

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**Director:** Claus Maria Azzalin, PhD, Group Leader at Instituto de Medicina Molecular João Lobo Antunes and Invited Associate Professor at Faculdade de Medicina da Universidade de Lisboa

### Team

Ana Filipa Duarte Nunes Almeida	PhD	Training Hub Area Manager
Domingos Manuel Pinto Henrique	PhD	Director of Studies
Mafalda de Carvalho Lourenço Morais da Silva	University Degree	Administrative (Left December)
Leonor Saúde	PhD	Coordinator of MSc Studies
Vanessa Morais	PhD	Coordinator of Postdoctoral Training

### Description of the Facility

The Training Hub ensures the proper integration of overall training activities at iMM that are tailored for researchers at different stages of their careers, aiming for an internationally competitive career in academia, industry or clinical medicine environments.

We work closely with MSc students, PhD students, and Postdoctoral researchers to maximize their career prospects through specific programs and activities. These include:

- A MSc Training Program that supports students developing their Master thesis at iMM every year, and a Master Course in Biomedical Research, which started in 2020 within the framework of the CAML consortium.
- An international PhD Program – LisbonBioMed – which offers all PhD students at iMM a flexible and tailored curricular structure at the interplay between laboratory and clinical practice.
- A Post-Doctoral Training Program, structured around specific actions that promote scientific discussion and sharing of experiences, in academia and beyond.

### Major Achievements in 2023

- Organized the first edition of the 2-day Course for Supervisors, targeted to 16 iMM PIs;
- Organized the 8-week LisbonBioMed course “Towards a Creative and Critical Mind” for the 14 new PhD students (LisbonBioMed 2023 Class), including 4 workshops on Biostatistics, Research Ethics and Scientific Integrity, Technology Transfer, Scientific Writing, and Equality, Diversity and Inclusion (EDI).
- Managed to increase by 15% the number of applications from foreign candidates to the LisbonBioMed, and to increase by 27% the number of selected foreign candidates;
- Met with 2nd- and 4th-year PhD students in the context of the PhD Tracker program - 21 PhD students in total;

- Expanded the iMM Alumni network to more than 470 people and organized the first Alumni Meeting, in collaboration with the Communication Office;
- Launched the Best Master Thesis Award, the “Merit Award João Lobo Antunes” for the best PhD Thesis, and the Lídia Silva Santos Postdoctoral Achievement Award.