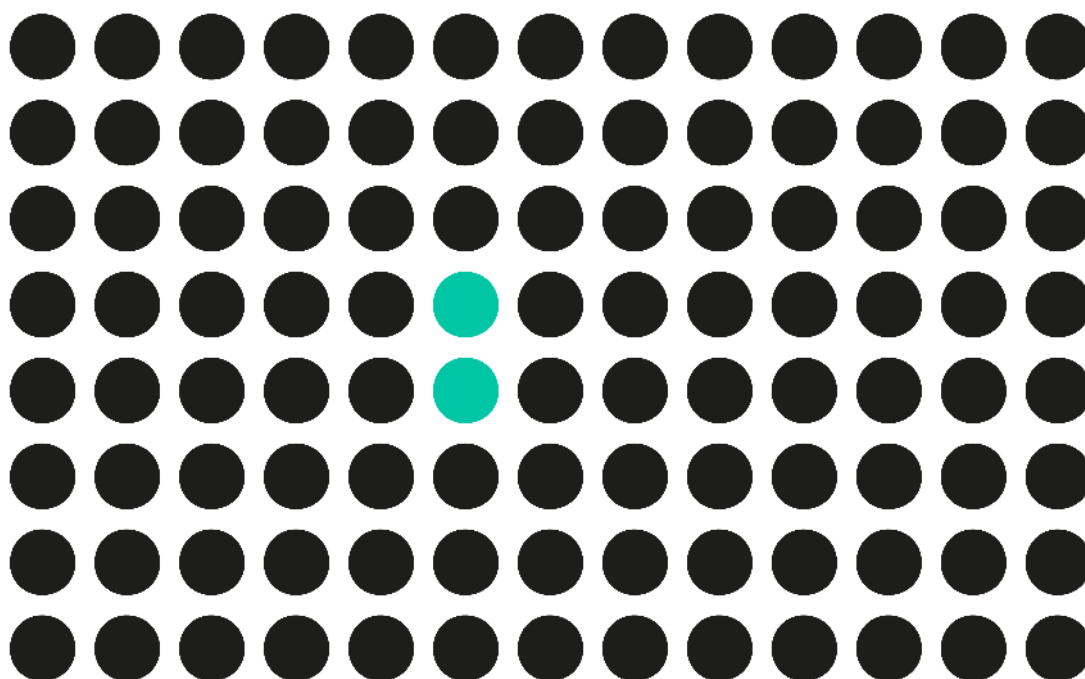




Instituto  
de Medicina  
Molecular

João  
Lobo  
Antunes

## Scientific Report 2017



Lisbon, March 2018

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## Structure & Organization

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 Laboratory Associated to 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 the 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 Associate Members

Universidade de Lisboa;

Faculdade de Medicina da Universidade de Lisboa;

Hospital de Santa Maria;

Associação para a Investigação e o Desenvolvimento da Faculdade de Medicina;

Fundação Oriente.

### Board of Trustees

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

## Board of Directors

**M. Carmo-Fonseca**

MD, PhD – President

**Maria M. Mota**

PhD – Executive Director

**Bruno Silva-Santos**

PhD – Vice-Director

## Administration Board

The Administration Board is composed by the Directors, the Research Program Coordinators, and the Directors of the Faculty of Medicine, University of Lisbon and Santa Maria Hospital. It meets at least twice a year to define scientific strategies and actions, administrative organization plans and budgetary priorities.

## 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 programs and include international experts of scientific fields.

**Caetano Reis e Sousa**

PhD – Francis Crick Institute, London, England

**Carlos Caldas**

MD, PhD – Cambridge Cancer Center, England

**Elaine Mardis**

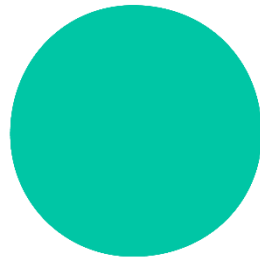
PhD – Institute for Genomic Medicine at NationWide Children’s Hospital, United States of America

**Paul Peter Tak**

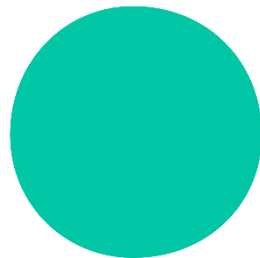
MD, PhD – University of Amsterdam, Netherlands

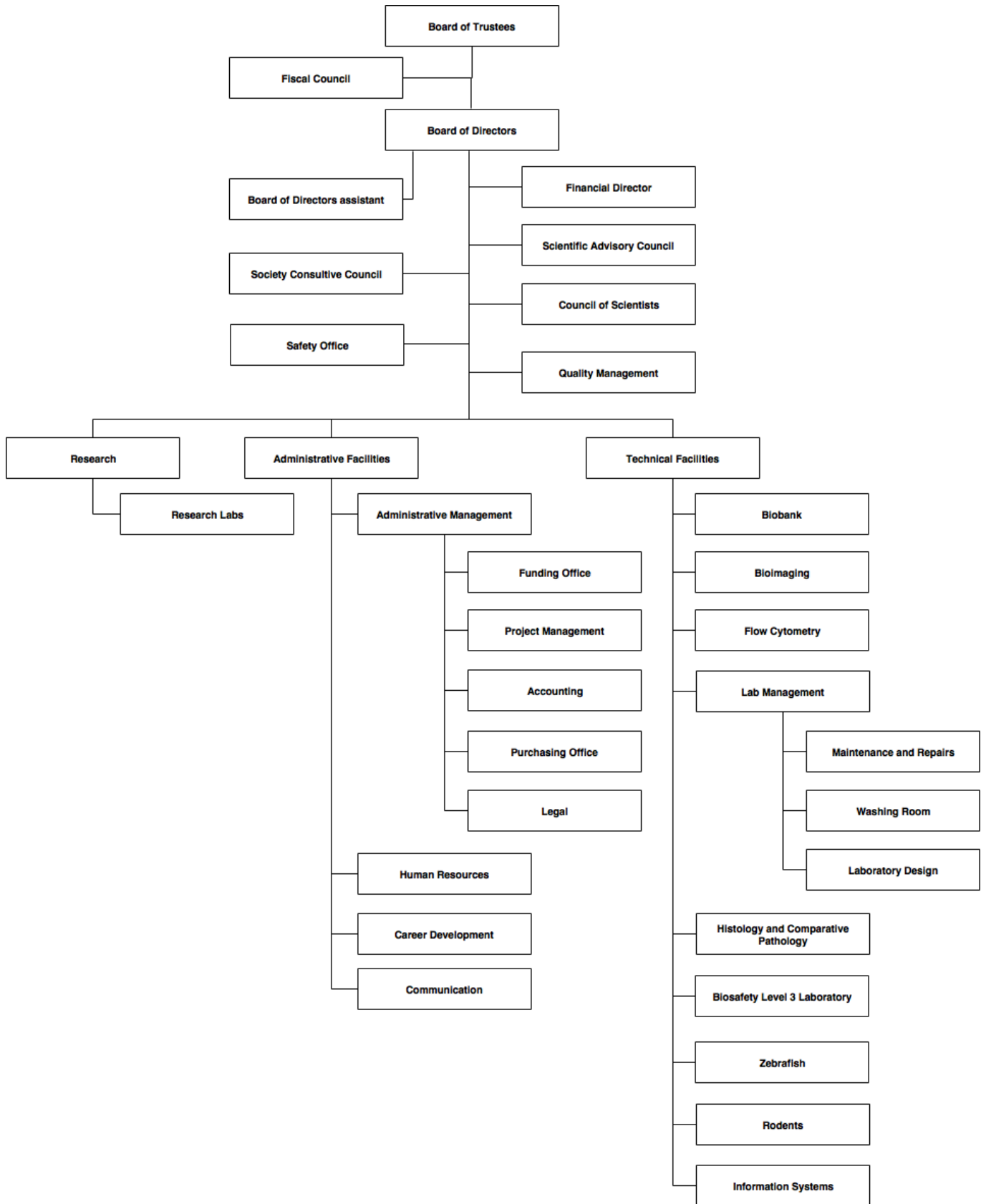
**Philippe Sansonetti**

MD, PhD – Pasteur Institute, France



# Organigram







## Evaluation Reports 2017

### 2013 Evaluation of FCT Research and Development Labs

#### Period of Evaluation:

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

2015 – 2020: Research strategies and planned work for the next six years (2015-2020), consolidated as a strategic programme.

#### Evaluation Panel:

Panel 3: Health and Life Sciences.

**Final Classification:** Excellent.

#### Panel's overall comments (Stage 2):

The site visit confirmed to a large extent the conclusions of the initial assessment that the unit has an excellent overall standing. It pointed out to some insufficiencies in the scientific output of a significant fraction of the integrated members listed in the initial application, and in the intensity of technology transfer that were openly discussed with both the unit leaders and the active group of students and postdocs. The site visit team recommended (i) a redefinition of the role of the less productive integrated members in research, teaching or management tasks that should lead to a reduction in the number of integrated members and independent groups; (ii) increased efforts in securing substantial financial resources through contracts with industry. It was satisfied with the clarification of the novel management and governance processes that have been established and praised Prof Maria Carmo-Fonseca, the Principal Investigator of the proposal and the Executive Director of IMM since 2002, to have promoted Dr. Maria Mota as the unit Director. Prof Maria Carmo-Fonseca now serves as IMM President in an oversight role with veto power on strategic decisions, and a focus on international development. Dra. Maria Mota is supported on her role as Executive Director by two Vice Directors, Dr. Henrique Veiga-Fernandes and Bruno Silva-Santos, and an experienced Finance Director, Mrs. Margarida Pinto-Gago<sup>1</sup>. In order to achieve this in a transition period of reorganization of its staff dedicated to research and a context of potential shortage of public funding, the new IMM Board of Directors will require strong financial and managerial support from the University of Lisbon and the Faculty of Medicine. The Panel considered that the proposed strategic programme provides a solid basis for the future development of the unit in the next period, and that the budget requested was adequate, but recommended that the full executive power should be endowed to the coordinator during her term for its implementation, while the former director and President takes charge of international cooperation.

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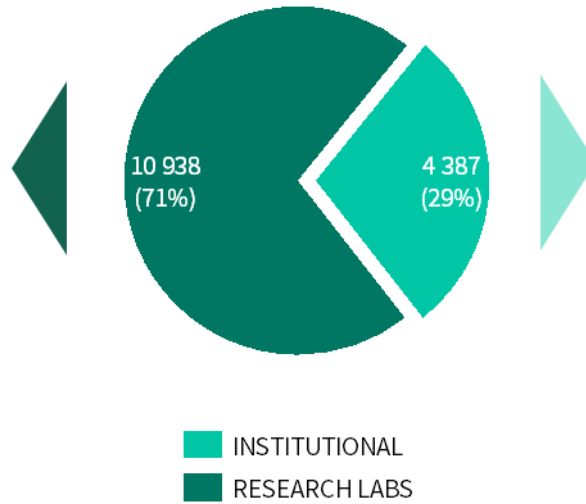
<sup>1</sup> Since 2017, Dra. Maria Mota is supported on her role as Executive Director by one Vice-Director, Dr. Bruno Silva-Santos, and a Finance Director, Fausto Lopo de Carvalho.

## Research Funding

### Expenditure in 2017 by Funding Source

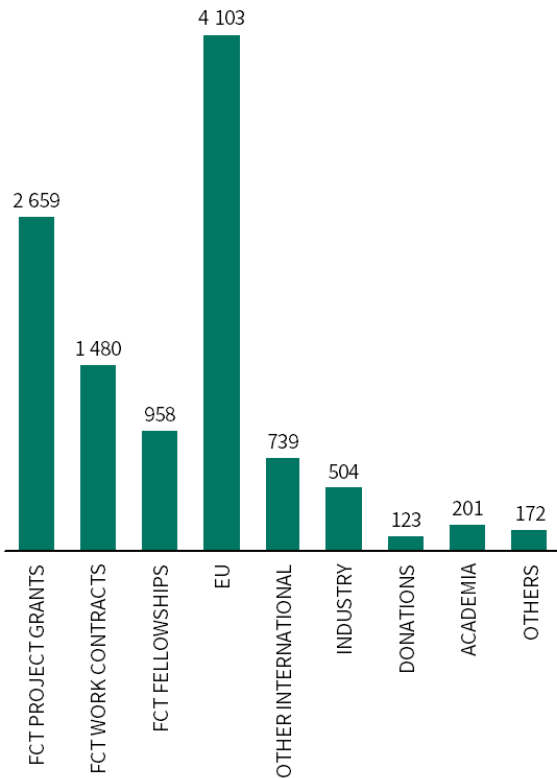
Total Expenditure: € 15 324 835

Total Expenditures 15,3M



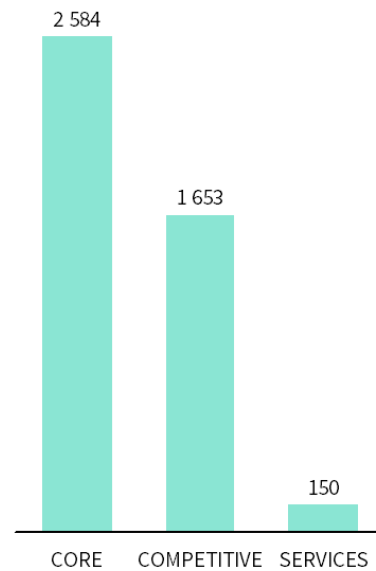
#### Research Labs

All Values in 000 Euros



#### Institutional

All Values in 000 Euros



## 2017 Expenditure

			(EUROS)
<b>INSTITUTIONAL</b>	CORE	2 584 026	
	COMPETITIVE	1 652 742	
	SERVICES	149 806	<b>4 386 575</b>
<b>RESEARCH LABS</b>	FCT PROJECT GRANTS	2 658 940	
	FCT WORK CONTRACTS	1 479 790	
	FCT FELLOWSHIPS	958 354	
	EU	4 102 645	
	OTHER INTERNATIONAL	738 869	
	INDUSTRY	503 819	
	ACADEMIA	122 555	
	DONATIONS	201 497	
	OTHERS	171 791	<b>10 938 261</b>
<b>TOTAL</b>			<b>15 324 835</b>

## Number of Ongoing Research Grants in 2017

### 161 Research Grants:

Public National FCT: 63

Private National: 46

Public Other National: 4

Of which with the industry – 20

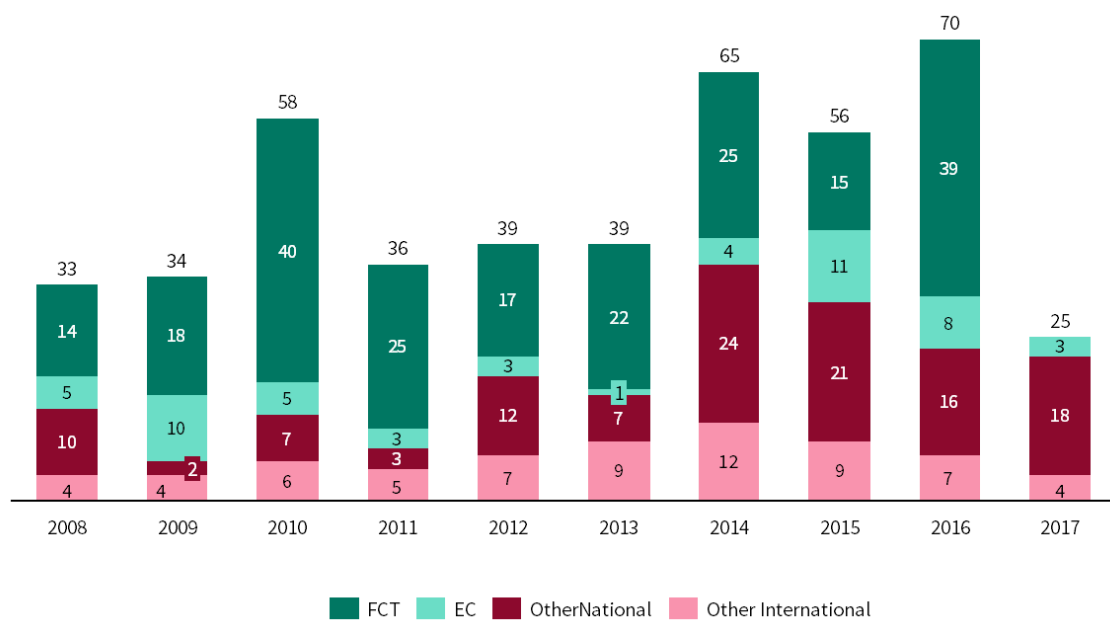
Public Other International: 4

Private International: 19

Public European Commission: 25

Of which with the industry – 3

## Number of Research Grants Initiated at IMM from 2008 to 2017



## Research Funding Initiated in 2017

### Research Grants (25):

National Public: 3

International Public: 3

National Private: 15

International Private: 4

## Projects Initiated in 2017 through Competitive Funds

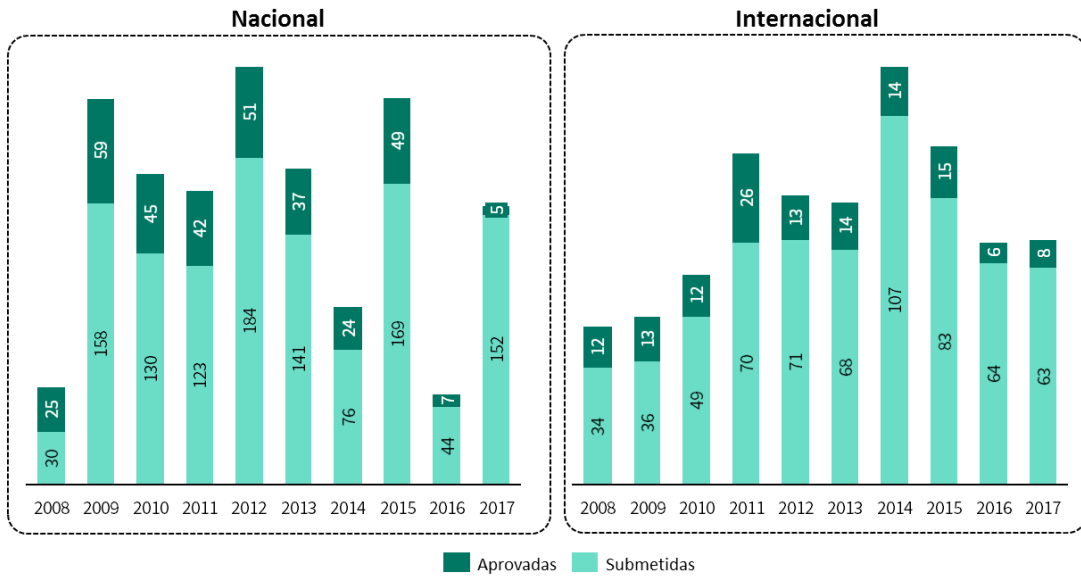
FUNDING AGENCY	RESEARCHER	iMM BUDGET
European Commission	Tiago Rodrigues	€ 160 635,60
	Maria Carmo-Fonseca	€ 279 000,00
	Maria Carmo-Fonseca	€ 1 001 137,50 (Lisbon University)
European Molecular Biology Organisation	Claus Azzalin	€ 150 000,00
Programa Operacional Regional de Lisboa 2020	Nuno Morais	€ 123 711,00
	Pedro Simas	€ 560 085,00
	José Henriques	€ 306 178,00
Malaria Vaccine Initiative	Miguel Prudêncio	€ 49 457,00
L'Association Française du Syndrome de Rett	Maria José Diógenes	€ 30 000,00
CHDI Foundation	Joaquim Ferreira	€ 63 572,00
Bial Foundation	Diana Prata	€ 50 000,00
José de Mello Saúde	Cláudia Faria	€ 12 500,00
Fundo iMM-Laço	Sérgio Dias	€ 38 500,00
	Karine Serre	€ 49 500,00
	Sandra Casimiro	€ 31 278,00
Crioestaminal/Associação Viver a Ciência	Luísa Figueiredo	€ 20 000,00

## Protocols, Donations & Awards<sup>2</sup>

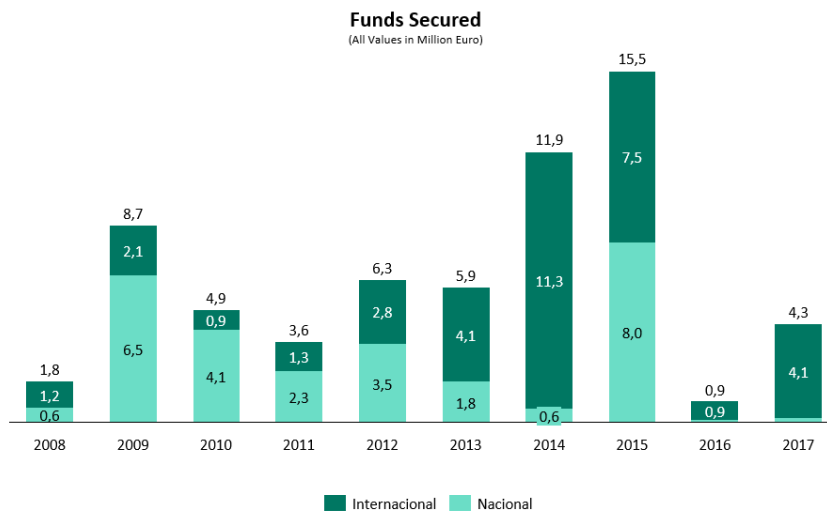
FUNDING AGENCY	RESEARCHER	iMM BUDGET
Cytokinetics, Inc.	Mamede de Carvalho	€ 7 700,00
Merck	Miguel Prudêncio	€ 84 300,00
	Luis Costa	€ 25 000,00
Merck Sharp & Dohme	Luis Costa	€ 7 500,00
Roche Farmacêutica Quimica	Luis Costa	€ 10 000,00
Bristol-Myers Squibb	Luis Costa	€ 10 000,00
Celgene	João Eurico Fonseca	€ 1 000,00
Novartis	João Eurico Fonseca	€ 12 680,00
Sociedade Portuguesa de Reumatologia	João Eurico Fonseca	€ 9 500,00
		€ 5 884,00
		€ 25 000,00
		€ 18 000,00
		€ 8 750,00
		€ 12 500,00
Bial	João Eurico Fonseca	€ 4 831,25
		€ 4 831,25
Sociedade Portuguesa de Dermatologia e Venerologia	Paulo Filipe	€ 2 500,00

<sup>2</sup> Were considered the protocols, donations and awards that fund projects, infrastructures and seminars.

## iMM Applications and Secured Competitive Funding



**Figure 1:** Submitted and approved applications in international and national competitive funding schemes since 2008. The number of submitted applications corresponds to those effectively communicated to the Funding Office. The number of approved applications for 2017 corresponds to those with known results as of February 2018.



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

## Funding Sources of iMM Applications

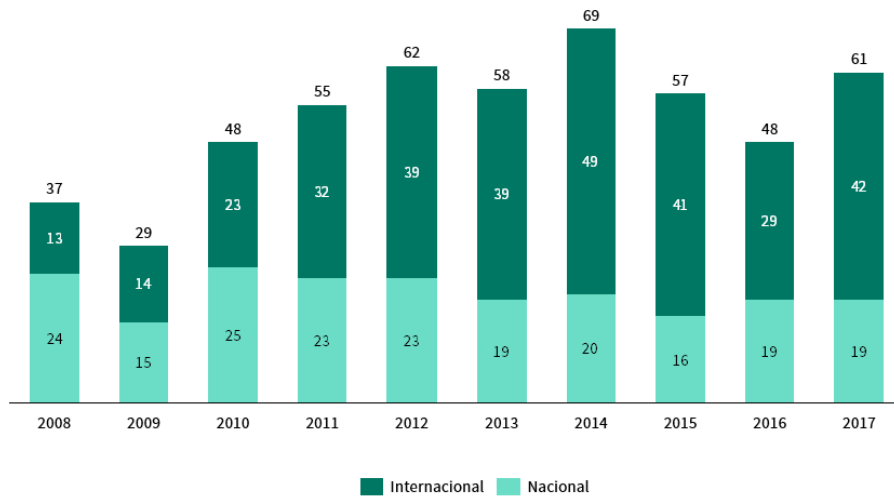
In 2017, iMM researchers and staff have submitted grants to the following funding schemes:

INTERNATIONAL				
PRIVATE FUNDS		PUBLIC FUNDS		
Wellcome Trust	Collaborative Award in Science	European Commission - Horizon 2020	Excellent Science	European Research Council - Starting Grant
European Molecular Biology Organization	Long-Term Fellowships		Excellent Science	European Research Council - Consolidator Grant
	Young Investigator			European Research Council - Advanced Grant
	Installation Grant			European Research Council - Synergy Grant
Merck	Grant for Oncology Innovation		Excellent Science	Marie Skłodowska-Curie Actions - Individual Fellowships
Fondation Leducq	Transatlantic Networks of Excellence Program			Marie Skłodowska-Curie Actions - Innovative Training Networks
Louis-Jeantet Foundation	Louis-Jeantet Prize for Medicine 2018			Future and Emerging Technologies
Brain&Behavior Research Foundation	NARSAD Young Investigator Grant		Societal Challenges	Food security, sustainable agriculture and forestry, marine and maritime and inland water research and the bioeconomy
International OCD Foundation	IOCDF Research Grants			Health, demographic change and well-being
Alzheimer's Association	Research Grants		Spreading excellence and widening participation	Twinning
Thrasher Research Fund	Early Career Award	European & Developing Countries Clinical Trials Partnership		
L'Association Française du Syndrome de Rett	Research Grants	European Regional Development Fund	Interreg Sudoe Programme	
Medicine for Malaria Ventures	Research Grants	Columbian Science Agency	COLCIENCIAS - Columbian Science Agency call for Projects	
Bayer	Grants4Targets			
MPN Research Foundation/Leukemia & Lymphoma Society	MPN Challenge			
National Multiple Sclerosis Society	Pilot Research Grants			
Worldwide Cancer Research	Research Grants			
Crohn's & Colitis Foundation	Senior Research Award			
Swiss Bridge	Swiss Bridge Award			
amfAR	Innovation Grants			
AXA Research Fund	AXA Post-doctoral Fellowships			

Pfizer	Inflammation ASPIRE Research Awards
RettSyndrome.org	Basic Research Grants
Michael J. Fox	Computational Tools for Parkinson's Disease
CIFAR Global Academy	CIFAR Azrieli Global Scholars
AFM Téléthon	Trampoline Grants
	Research Grants
Sanofi - Institut Pasteur	Sanofi - Institut Pasteur Awards
Concern Foundation	Conquer Cancer Now Award

NATIONAL			
PRIVATE FUNDS		PUBLIC FUNDS	
NEDAI	Bolsa de Estudos em Autoimunidade	Fundação para a Ciência e Tecnologia	Projetos de Investigação Exploratória - Programa UTAustin-Portugal
Liga Portuguesa Contra o Cancro	Bolsas Terry Fox		Projetos de IC&DT
	Bolsas LPCC		Projetos Conjuntos - Iniciativa Conhecimento para o Desenvolvimento (FCT-AKDN)
	Prémio Nacional de Oncologia, Manuel Sobrinho Simões		Programa de Cooperação Transnacional entre Portugal e o Brasil (FCT-CAPES)
Fundação Astrazeneca	Innovate Competition		Protocolo com Fundação Professor Francisco Pulido Valente - Prémio Pulido Valente
	Prémio FAZ Ciência		
Sociedade das Ciências Médicas de Lisboa   Laboratórios Pfizer	Prémio Pfizer Investigação Básica		PORLisboa2020 Portugal 2020
Santa Casa da Misericórdia de Lisboa - Neurociências	Prémio Mantero Belard		
	Prémio Castro e Melo		
	Prémio João Lobo Antunes		
Gilead Sciences	Programa Gilead GÉNESE		
Crioestaminal   Associação Viver a Ciência	Prémio Crioestaminal		
L'Oreal Portugal   Comissão Nacional da Unesco   Fundação para a Ciência e Tecnologia	Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência		





**Figure 3:** Evolution of the diversity of international and national funding schemes for which iMM researchers submitted applications from 2008 to 2017.

## 2017 iMM Activities Highlights

### Human Resources 2017

		2016	2017
<b>Researchers</b>	PhD	200	194
	PhD Students	106	117
	MSc Students	63	75
	Master	86	93
	Graduate	51	33
	Other	9	10
		<b>515</b>	<b>522</b>
<b>Technical Staff</b>	PhD Staff	8	8
	Master	29	27
	Graduate	31	29
	Other	20	22
		<b>88</b>	<b>86</b>
<b>Administrative Staff</b>	PhD Staff	7	6
	Master	9	9
	Graduate	15	16
	Other	5	5
		<b>36</b>	<b>36</b>
<b>TOTAL</b>		<b>639</b>	<b>644</b>

### Selection of Prizes and Awards

#### LPCC/Pfizer Grant

Inês Gomes (Luís Costa Lab)

#### Fundo iMM-Laço: A Caminho da Cura

Karine Serre (Bruno Silva-Santos Laboratory)

Sérgio Almeida (Group Leader)

#### CoHiTec 2016 Program

Diana Prata Laboratory

Ana Martins, Ivo Martins e Patrícia Carvalho (Nuno Santos Laboratory)

#### Bial Award 2017: Honorable Mention

Bruno Silva-Santos

#### Executiva Award: "As 25 Mulheres Mais Influentes"

Maria M. Mota

**'Innovation and Entrepreneurship' Category of the Marie Skłodowska-Curie Actions 2017 Prizes**

Diana Prata (3<sup>rd</sup> Place)

**Fundo de Investigação da Sociedade Portuguesa de Reumatologia**

João Eurico da Fonseca Laboratory

**Pfizer Grant: Sociedade Portuguesa de Reumatologia**

João Eurico da Fonseca Laboratory (3<sup>rd</sup> Place)

**JAKIE Sociedade Portuguesa de Reumatologia Grant**

João Eurico da Fonseca Laboratory (1<sup>st</sup> Place)

**Grant Association Française du Syndrome de Rett**

Maria José Diógenes (Ana Sebastião Laboratory)

**Scientific Awards Universidade de Lisboa/Caixa Geral de Depósitos 2017**

Luísa Lopes (Honorable Mention)

Nuno Santos

Joaquim Ferreira

**Welcome Trust Collaborative Grant**

Luísa Figueiredo

**ERC Consolidator Grant**

Luísa Figueiredo

**Pfizer Award: Basic Research**

Maria M. Mota

**Santa Casa da Misericórdia: Mantero Belard Award**

Maria José Diógenes (Ana Sebastião Laboratory)

**Santa Casa da Misericórdia Awards: João Lobo Antunes Award**

Bruno Miranda (José Ferro Laboratory)

**Pulido Valente Science Award 2017**

Ana Filipa Guedes (Nuno Santos Laboratory)

**Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência**

Inês Bento (Maria Mota Laboratory)

**Professor Nicolau van Uden Award 2017 (Sociedade Portuguesa de Microbiologia)**

José Melo Cristino (Mário Ramirez Laboratory)

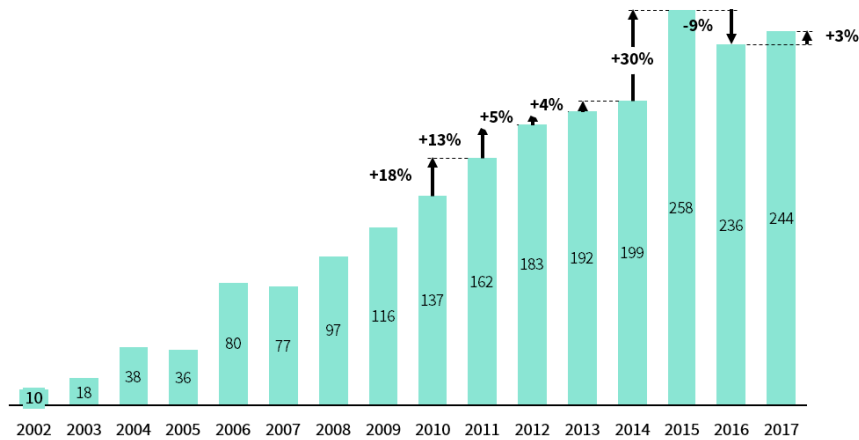
## Productivity at a Glance

	2016	2017
Total Publications International Journals	236	244
Publications in Journals with Impact Factor > 10	33	23
Communications in Conferences – International	332	274
Communications in Conferences – National	226	375
Seminars and Invited Lectures	358	344
Organization of Conferences	74	78
PhD Thesis	16	16
MSc Thesis	57	48
Prizes, Awards and Distinctions	96	75

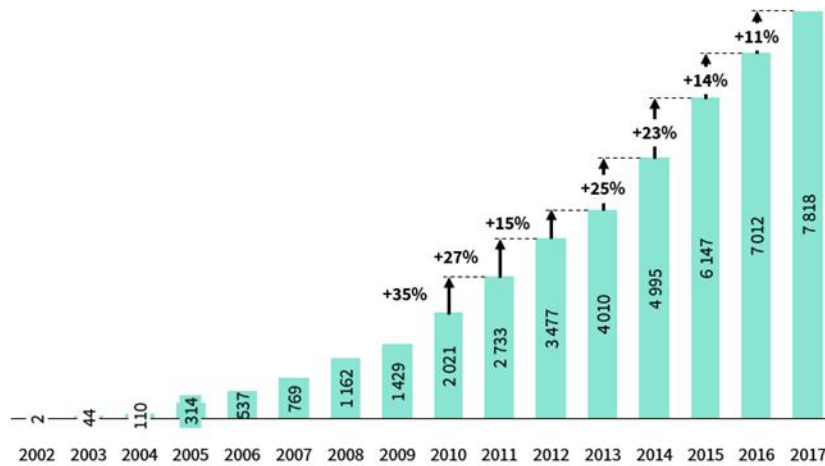
## iMM Publications in International Journals

### Citation Report

(Source: Web of Science™)



Published Items in Each Year: 2002-2017



Citations in Each Year: 2002-2017

**Papers in 2017: 244**

**Papers since 2002: 2.125**

**Sum of the times cited: 43.735**

**Average citations per item: 20.58**

**h-index: 84**

**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:** All years. 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 iMM publications.

## 10 Most Cited Articles 2002-2017

Healy DG, Falchi M, O'Sullivan SeanS et al (2008). Phenotype, genotype, and worldwide genetic penetrance of LRRK2-associated Parkinson's disease: a case-control study. *LANCET NEUROLOGY*. **7** (7) 583-590. (IF: 26.284, Citations: 597).

Ostrowski M, Carmo NB, Krumeich S et al (2010). Rab27a and Rab27b control different steps of the exosome secretion pathway. *NATURE CELL BIOLOGY*. **12** (1) 19-30. (IF: 20.06, Citations: 527).

Henry DH, Costa L, Goldwasser F et al (2011). Randomized, Double-Blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients with Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma. *JOURNAL OF CLINICAL ONCOLOGY*. **29** (9) 1125-1132. (IF: 24.008, Citations: 501).

Ratziu V, Bellentani S, Cortez-Pinto H et al (2010). A position statement on NAFLD/NASH based on the EASL 2009 special conference. *JOURNAL OF HEPATOLOGY*. **53** (2) 372-384. (IF: 12.486, Citations: 432).

Hansen C, Angot E, Bergstrom AL et al (2011). alpha-Synuclein propagates from mouse brain to grafted dopaminergic neurons and seeds aggregation in cultured human cells. *JOURNAL OF CLINICAL INVESTIGATION*. **121** (2) 715-725. (IF: 12.784, Citations: 382).

Lefaucheur J, Andre-Obadia N, Antal A et al (2014). Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *CLINICAL NEUROPHYSIOLOGY*. **125** (11) 2150- 2206. (IF: 3.866, Citations: 372).

Sousa AE, Carneiro J, Meier-Schellersheim M et al (2002). CD4 T cell depletion is linked directly to immune activation in the pathogenesis of HIV-1 and HIV-2 but only indirectly to the viral load. *JOURNAL OF IMMUNOLOGY*. **169** (6) 3400-3406. (IF: 4.856, Citations: 338).

Duarte A, Hirashima M, Benedito R et al (2004). Dosage-sensitive requirement for mouse D114 in artery development. *GENES & DEVELOPMENT*. **18** (20) 2474-2478. (IF: 9.413, Citations: 335).

Zerr I, Kallenberg K, Summers DM et al (2009). Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. *BRAIN*. **132** 2659- 2668. (IF: 10.292, Citations: 323).

Di Fonzo A, Rohe CF, Ferreira RJ et al (2005). A frequent LRRK2 gene mutation associated with autosomal dominant Parkinson's disease. *LANCET*. **365** (9457) 412-415. (IF: 47.831, Citations: 320).

## Selected Publications

Miranda H, Szego EM, Oliveira LMA, Breda C, Darendelioglu E, de Oliveira RM, Ferreira DG, Gomes MA, Rott R, Oliveira M, Munari F, Enquita FJ, Simões T, Rodrigues EF, Heinrich M, Martins IC, Zamolo I, Reiss O, Cordeiro C, Ponces-Ferreira A, Lashuel HA, Santos NC, Lopes LV, Xiang W, Jovin TM, Penque D, Engelder S, Zweckstetter M, Klucken J, Giorgini F, Quintas A, Outeiro TF (2017). Glycation potentiates  $\alpha$ -synuclein-associated neurodegeneration in synucleinopathies. *BRAIN* (IF: [10.292](#)).

Ribeiro ST, Tesio M, Ribot JC, Macintyre E, Barata JT, Silva-Santos B (2017). Casein kinase 2 controls the survival of normal thymic and leukemic  $\gamma\delta$  T cells via promotion of AKT signaling. *LEUKEMIA* (IF: [11.702](#)).

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## Seminars & Workshops

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### Computational Biology and Bioinformatics Seminar

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**05<sup>th</sup> January**

“Alternative splicing during neuronal development”

Mariana Ferreira – Nuno Morais Lab

**19<sup>th</sup> January**

“Specific Betweenness: finding molecular bridges between diseases”

Francisco Pinto – FCUL

**02<sup>nd</sup> February**

“ReMatCh: An efficient pipeline for targeted discovery of allelic variants”

Miguel Machado – Mário Ramirez Lab

**15<sup>th</sup> February**

“Computational models unravel the functioning of regulatory networks”

Claudine Chaouiya – IGC

**02<sup>nd</sup> March**

“Alternative splicing in human (unhealthy) aging”

Ana Carolina Leote – Nuno Morais Lab

**29<sup>th</sup> March**

“Transcriptional profile of follicular T helper (Tfh) cells induced by type1 and type2 adjuvants”

Saumya Kumar – Luís Graça Lab

**07<sup>th</sup> April**

“Discovery of large genomic inversions using long range information”

Can Alkan – Bilkent University, Turkey

**26<sup>th</sup> April**

“Allelic variant finding in bacterial species with chewBBACA”

Mickael Silva – Mário Ramirez Lab

**11<sup>th</sup> May**

“Harmful behavior mediated by parasites and pathogens: a mathematical model and a few experimental examples”

Francisco Dionísio – FCUL

**24<sup>th</sup> May**

“Why do motor neurons die? Lessons from cross-disease transcriptome and pathway analysis in SMA and ALS”

Margarida Gama-Carvalho – FCUL

**07<sup>th</sup> June**

“Plasmid ATLAS - plasmid identification from whole genome sequencing data”

Tiago Jesus – Mário Ramirez Lab

**05<sup>th</sup> July**

"Bioinformatics Services at IGC in the context of BioData.pt and ONEIDA"  
Daniel Sobral – IGC

**13<sup>th</sup> September**

"Better than your eyes: image analysis by morphodynamical modelling"  
Jorge Carneiro – IGC

**27<sup>th</sup> September**

"GNU Parallel: make the most of your CPUs"  
Miguel Machado – Mário Ramirez Lab

**11<sup>th</sup> October**

"Splicing kinetics revealed by nascent transcript sequencing"  
Kenny Rebelo – Carmo-Fonseca Lab

**25<sup>th</sup> October**

"INNUENDO Platform: integrating high-throughput sequencing into bacterial foodborne pathogen surveillance"  
Bruno Gonçalves – Mário Ramirez Lab

**08<sup>th</sup> November**

"Don't keep your research for yourself: interactive web data sharing"  
Nuno Agostinho – Nuno Morais Lab

**06<sup>th</sup> December**

"From Liquid Biopsies to Systems Biomedicine: Tracking networks targeted by circulating microRNAs in metabolic diseases"  
Inês Mollet – CEDOC

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## Immunology Club

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**08<sup>th</sup> February**

"Molecular mechanisms controlling the survival and differentiation of human  $\gamma\delta$  thymocytes"  
Sérgio Ribeiro, PhD Student – Bruno Silva-Santos Lab

**01<sup>st</sup> March**

"Glial-cell-derived neuroregulators control type 3 innate lymphoid cells and gut defence"  
Bethania Garcia Cassani, PhD Student – Henrique Veiga-Fernandes Lab

**20<sup>th</sup> March**

"The Repertoire and Specificity of Follicular Regulatory T Cells" - PhD Thesis  
Ana Raquel Macieiras de Oliveira, PhD – Luís Graça Lab

**12<sup>th</sup> July**

"Once a CD4 T cell, always a CD4 T cell? Not if IL-4 is around!"  
Helena Cabaço, Pos-Doctoral Researcher - Human Immunodeficiency & Immune Reconstitution Laboratory; iMM

**26<sup>th</sup> July**

"Immune reconstitution following Allogeneic Stem Cell Transplantation: Altered naïve and memory Treg and Tcon subset pools in Chronic Graft versus Host Disease"

Maria Soares – João Lacerda Lab

**17<sup>th</sup> October**

"Non-lipid antigen-recognition by NKT cells"

Catarina Almeida, Pos-Doctoral Researcher - Godfrey Lab, Peter Doherty Institute, University of Melbourne

**18<sup>th</sup> October**

"LRBA deficiency: Clinical phenotype, mouse model and biological pathomechanisms"

Laura Gamez Diaz, PhD Student - Center for Chronic Immunodeficiency, CCI, Freiburg

**08<sup>th</sup> November**

"MicroRNA-146a controls IFN-g production and functional plasticity in gd T cells by targeting Nod1"

Anita Gomes, PhD – Bruno Silva-Santos Lab

**06<sup>th</sup> December**

"Study of the impact of IL-7Ra gain of function mutation in vivo leukemogenesis"

Tiago Soares, Master Student – João Barata Lab

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**Internal Seminar**

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**18<sup>th</sup> January**

"Natural killing of tumors"

Bruno Silva-Santos – Group Leader, iMM

**25<sup>th</sup> January**

"Metabolic shifts in cancer"

Sérgio Dias – Group Leader, iMM

**08<sup>th</sup> February**

"Pointing in the right direction: a tale of forces in vascular biology"

Cláudio Franco – Group Leader, iMM

**22<sup>nd</sup> February**

"Notch: There's more than one way to skin a cat"

Domingos Henrique – Group Leader, iMM

**08<sup>th</sup> March**

"Understanding rare diseases: Adenosine Kinase Deficiency, developmental delay and seizures"

Ana Sebastião – Group Leader, iMM

**22<sup>nd</sup> March**

"Mitochondria Quality Control: the role of PINK1"

Vanessa Morais – Group Leader, iMM

**05<sup>th</sup> April**

"T cell homeostasis in graft versus host disease"  
João Lacerda – Group Leader, iMM

**19<sup>th</sup> April**

"Modeling the dynamics of HIV-1 during therapy"  
Rui Ribeiro – Luís Graça Lab

**03<sup>rd</sup> May**

"Parasites have an internal circadian clock"  
Luísa Figueiredo – Group Leader, iMM

**31<sup>st</sup> May**

"Targeting metastatic cells with peptide"  
Miguel Castanho – Group Leader, iMM

**21<sup>st</sup> June**

"'Promance' - PrPc and alpha-synuclein love affair in early synaptic dysfunction"  
Luísa Lopes – Group Leader, iMM

**28<sup>th</sup> June**

"The role of oxytocin in social cognition"  
Diana Prata – Group Leader, iMM

**12<sup>th</sup> June**

"Using Computational Models to Understand Psychiatric Disorders and their Treatment from Molecules to Behavior"  
Tiago Maia – Mamede de Carvalho Lab

**27<sup>th</sup> September**

Edgar Gomes – Group Leader, iMM

**25<sup>th</sup> October**

"Antibiotic consumption and antibiotic resistance - more than meets the eye?"  
Mário Ramirez – Group Leader, iMM

**08<sup>th</sup> November**

"What transcriptomes tell us about disease"  
Nuno Morais – Group Leader, iMM

**22<sup>nd</sup> November**

"Sensory Integration in Memory-driven Choice Behaviors"  
Miguel Remondes – Group Leader, iMM

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## Monday Lectures

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### **09<sup>th</sup> January**

"Regulation of mitochondrial gene expression"

Michal Minczuk – MRC Mitochondrial Biology Unity, Cambridge Biomedical Campus, Hills Road, Cambridge and CB2 0XY

Host: Vanessa Morais

### **16<sup>th</sup> January**

"Novel cell-cell communication networks in organotropic metastasis"

Bruno Costa-Silva – Champalimaud Research

Host: Sérgio Dias

### **23<sup>rd</sup> January**

"The mechanisms controlling the trunk size of vertebrates"

Moisés Mallo – Gulbenkian Institute of Science

Host: Domingos Henrique

### **30<sup>th</sup> January**

"Putting the "Multi" in Multiscale Modeling"

Manuel Melo – ITQB

Host: Miguel Castanho

### **06<sup>th</sup> February**

"CTLA-4 mediated control of T cell dependent autoimmunity"

Lucy Walker – University College

Host: Luís Graça

### **13<sup>th</sup> February**

"Malaria Parasite Epigenetics: A Maze or a Path to new Therapy"

Artur Scherf - Institut Pasteur

Host: Luísa Figueiredo

### **06<sup>th</sup> March**

"Approaching clinical transplantation tolerance"

Giovanna Lombardi – King's College London

Host: João Lacerda Lab

### **13<sup>th</sup> March**

"Probing Entry and Egress of Enveloped Viruses using Atomic Force Microscopy"

Pierre-Emmanuel Milhiet – Centre de Biochimie Structurale (CNRS/INSERM) Montpellier

Host: Nuno Santos

### **20<sup>th</sup> March**

"Molecular regulatory mechanisms from single cell & bulk transcriptomics"

Chris Ponting – University of Edinburgh/MRC

Host: Nuno Morais

**27<sup>th</sup> March**

"Circadian clocks in fibroblast and mouse models of mood disorders"

David K Welsh – Department of Psychiatry, University of California, San Diego

Host: Luísa Lopes

**03<sup>rd</sup> April**

"Proliferation control in Drosophila neural stem cells"

Catarina Homem – CEDOC

Host: Edgar Gomes

**10<sup>th</sup> April**

"A synthetic biology approach to mammalian development"

Alfonso Martinez-Arias – University of Cambridge

Host: Domingos Henrique

**15<sup>th</sup> May**

"Reprogramming the Genetic Code"

Jason Chin – MRC Laboratory of Molecular Biology, Cambridge~

Host: Gonçalo Bernardes

**29<sup>th</sup> May**

"Breaks and Bouts in a Paradigm Shift of the Health-Related Energy Expenditure Continuum"

Luís Bettencourt Sardinha – Faculdade de Motricidade Humana, Universidade de Lisboa

Host: Domingos Henrique

**05<sup>th</sup> June**

"Translating the trypanosome surface"

Michael Ferguson – School of Life Sciences, University of Dundee, Scotland

Host: Luísa Figueiredo

**12<sup>th</sup> June**

"To be or not to be: the hair cell dilemma during ear development"

Fernando Giráldez – DCEXS-Universitat Pompeu Fabra at PRBB, Barcelona

Host: Domingos Henrique

**19<sup>th</sup> June**

"Evolution of Regulatory Landscapes"

José Luiz Gómez-Skarmeta – Spanish Research Council (CSIC), Centro Andaluz de Biología del Desarrollo, CSIC/ Universidad Pablo de Olavide, Seville

Host: Domingos Henrique

**26<sup>th</sup> June**

"Salamander regeneration – regulation and evolution"

András Simon – Karolinska Institute

Host: Edgar Gomes

**03<sup>rd</sup> July**

"DNA repair nucleases: putting chromosomes through the shredder"

João Matos – Department of Biology, ETH Zürich

Host: Claus Azzalin



**10<sup>th</sup> July**

"Antibodies on the Video Screen - Bipedal Antibody Walking on Membranes observed with High-Speed AFM"

Peter Hinterdorfer – Johannes Kepler University Linz

Host: Nuno Santos

**24<sup>th</sup> July**

"Brazilian Initiative on Precision Medicine: Challenges and the Future"

Benilton Carvalho – University of Campinas, São Paulo

Host: Nuno Morais

**11<sup>th</sup> September**

"Cues and barriers for immune cell and tumor extravasation"

Ronen Alon – The Department of Immunology, the Weizmann Institute of Science

Host: Edgar Gomes

**18<sup>th</sup> September**

"Inflammatory mediators trigger pathological new bone formation in experimental spondyloarthritis"

Leonie M van Duivenvoorde – Amsterdam Academic Medical Centre

Host: João Eurico da Fonseca

**25<sup>th</sup> September**

"Hippocampal Adult Neural Stem Cells in Neurological Insults and Neurodegeneration"

Carlos Fitzsimons – University of Amsterdam

Host: Sara Xapelli

**02<sup>nd</sup> October**

"Information coding and plasticity in the whisker somatosensory system of the rodent"

Valerie Ego-Stengel – CNRS

Host: Miguel Remondes

**09<sup>th</sup> October**

"iRhoms: novel physiological roles and trafficking regulators"

Colin Adrian – IGC Oeiras

Host: Sérgio Almeida

**16<sup>th</sup> October**

"The senescence-associated secretory phenotype: linking senescence and inflammation"

Jesús Gil – MRC London Institute of Medical Sciences

Host: Nuno Morais

**23<sup>rd</sup> October**

"A genome-wide screen reveals genes with key roles in pre-erythrocytic development of the malaria parasite Plasmodium"

Volker Heussler – Institute of Cell Biology, University of Bern

Host: Miguel Prudêncio

**30<sup>th</sup> October**

“Nanoscale Regulation of Clot Structure, Implications for Thrombosis”

Robert Ariens – Leeds Institute of Cardiovascular and Metabolic Medicine, Faculty of Medicine and Health, University of Leeds

Host: Nuno Santos

**06<sup>th</sup> November**

“Dyp-FISH: Dynamic Patterned FISH to interrogate mRNA and Protein Subcellular spatial patterning”

Musa Mhlanga – Division of Chemical Systems & Synthetic Biology, University of Cape Town~

Host: Domingos Henrique

**27<sup>th</sup> November**

“Single cell imaging of tumour heterogeneity and response to therapy in human-zebrafish xenografts-towards personalised medicine”

Rita Fior – Fundação Champaulimaud

Host: Domingos Henrique

**04<sup>th</sup> December**

Master Thesis Awards: “Deciphering parasite persistence in adipose tissue”

Tiago Rebelo – Luísa Figueiredo Lab

**04<sup>th</sup> December**

Master Thesis Awards: “Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer”

Bernardo Almeida – Nuno Morais Lab

**04<sup>th</sup> December**

Master Thesis Awards: “Role of PLCy1 in the Resistance Mechanism to Anti-EGFR Therapy in Metastatic Colorectal Cancer”

Raquel Duarte – Luís Costa Lab

**11th December**

“When chromatin and sex come together”

Paulo Navarro-Costa – IGC Oeiras

Host: Domingos Henrique

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## Neurosciences Seminar

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**09<sup>th</sup> January**

“Endovanilloid control of pain modulation by the rostroventromedial medulla in an animal model of diabetic neuropathy”

Daniel Martins, PhD Student – Diana Prata Lab

**16<sup>th</sup> January**

“Guilt and the time of consciousness”

Maria Fernanda Palma – Faculdade de Direito, Instituto de Direito Penal e Ciências Criminais, Centro de Investigação em Direito Penal e Ciências Criminais

**23<sup>rd</sup> January**

"In Search of a Multisensory Neural Coding"

Jorge Cardoso, Master Student – Miguel Remondes Lab

**30<sup>th</sup> January**

"Characterization of cell death in the ex-vivo slice model of epileptogenesis"

Cláudia Cavacas, Master Student – Ana Sebastião Lab

**06<sup>th</sup> February**

"How tissue mechanics influences CNS axon guidance and neural regeneration"

Graham Sheridan, Professor – University of Brighton

**13<sup>th</sup> February**

"LPS-induced inflammation in organotypic slices and its effects upon epileptiform activity"

Leonor Rodrigues, Master Student – Ana Sebastião Lab

**20<sup>th</sup> February**

"Neurogenesis in a rat model of Alzheimer's disease"

Sara Paulo, Master Student – Ana Sebastião Lab

**06<sup>th</sup> March**

"Interference of Adenosinergic System in Endocannabinoid Signalling at the hippocampus"

Joana Freire, Master Student – Ana Sebastião Lab

**13<sup>th</sup> March**

"Mental time travel and intertemporal decision making: a complex relationship"

Fabio Paglieri, PhD - Institute for Cognitive Science and Technologies of the CNR (National Research Council), Rome

**20<sup>th</sup> March**

"gd T cells are the major source of IL-17 in the meninges and control brain cognitive functions"

Miguel Ribeiro, Master – Bruno Silva-Santos Lab and Luísa Lopes Lab

**27<sup>th</sup> March**

"Localizing the epileptogenic focus: a non-invasive approach"

Vânia Tavares, PhD Student – Diana Prata Lab

**03<sup>rd</sup> April**

"Brain cell sorting and Splicing: a binocular way to look at Parkinson's disease"

Maria Bourdone, PhD Student – Nuno Morais Lab

**10<sup>th</sup> April**

"The relationship between loneliness and dementia: a behavioral, cellular and molecular rodent study"

Ann Van der Jeugd, PhD – Laboratory of Biological Psychology, Faculty of Psychology and Educational Sciences, KU Leuven

**24<sup>th</sup> April**

"Unravelling the proteomic identity of synaptic mitochondria"

Andreia Pereira, PhD Student – Vanessa Morais Lab

**08<sup>th</sup> May**

“The limbic system as a target for cannabinoid actions”

Francisco Mouro, PhD Student – Ana Sebastião Lab

**15<sup>th</sup> May**

“Astrosomes: Artificial Astrocytes as a Novel Approach to Regulate Neuronal Communication”

Ana Armada-Moreira, PhD Student – Ana Sebastião Lab and Interdisciplinary Nanoscience Center, Aarhus University

**22<sup>nd</sup> May**

“Oxytocin – not only a “social” neuropeptide. Implications from fMRI studies”

Katja Brodman, PhD – Diana Prata Lab

**29<sup>th</sup> May**

“Evaluation of the receptor-mediated function of lactate in neuronal activity”

Haïssa de Castro, PhD Student – Department of Fundamental Neuroscience, University of Lausanne, Switzerland

**05<sup>th</sup> June**

“Adenosinergic system and BDNF signaling: how they are involved in schizophrenia?”

Sara Tanqueiro, PhD Student – Ana Sebastião Lab

**12<sup>th</sup> June**

“Trans-cranial Magnetic Stimulation in severe anorexia nervosa”

Alessia Avila, PhD Student – Diana Prata Lab

**19<sup>th</sup> June**

"Peptidergic modulation of pain: role of relaxin-3/RXFP3 forebrain networks in the descending control of nociception"

João Covita, PhD Student – University of Bordeaux and Florey Institute of Neuroscience and Mental Health, University of Melbourne

**26<sup>th</sup> June**

"Neuromodulation mediated by VEGF and adenosine in Amyotrophic Lateral Sclerosis (ALS) mice model"

Nádia Rei, PhD Student – Ana Sebastião Lab

**03<sup>rd</sup> July**

"Characterization of ( $\gamma\delta$ ) T cells on a Alzheimer's Disease model"

Helena Brigas, PhD Student – Bruno Silva-Santos Lab and Luísa Lopes Lab

**10<sup>th</sup> July**

"Genetic deletion of adenosine A2A receptor in mice model of Alzheimer's disease: impact on LTP and LTD"

Carolina Peixoto, Master Student – Luísa Lopes Lab

**17<sup>th</sup> July**

"How to increase adenosine levels in a Rett Syndrome mouse model?"

Catarina Lourenço, PhD Student – Ana Sebastião Lab

**24th July**

“On the road of TrkB receptors”

João Gomes, PhD Student – Ana Sebastião Lab

**04th September**

“Unveiling the trophic actions of adenosine A2A receptors in postnatal neurogenesis - Interaction with brain-derived neurotrophic factor”

Filipa Ribeiro, PhD Student – Ana Sebastião Lab

**11th September**

“The mechanisms behind Kyotorphin and Amidated-Kyothorphin action: an exploratory project for Alzheimer’s Disease therapy”

Rita Belo, PhD Student – Ana Sebastião Lab

**25th September**

“Cannabinoid modulation of postnatal neurogenesis”

Rui Rodrigues, PhD Student – Ana Sebastião Lab

**02nd October**

“Enhanced lineage-directed differentiation of Neural Stem Cells via modulation of mitochondria dynamics”

Rita Soares, PhD Student – Ana Sebastião Lab and Vanessa Morais Lab

**09th October**

“From complex microreactor to artificial astrocytes”

Ana Moreira, PhD Student – Ana Sebastião Lab

**16th October**

“Neuronal Adenosine A2A Receptor leads to LTD-to-LTP shift through NMDA Receptor overactivation in the hippocampus”

Mariana Temido, PhD Student – Luísa Lopes Lab

**23th October**

“PINK1: a Gatekeeper for Mitochondrial Quality Control”

Elvira Leites, PhD Student – Vanessa Morais Lab

**30th October**

“Nature of the GABA Transporter GAT1 malfunction in thalamic astrocytes in absence epilepsy: The starting point”

Tatiana Morais, PhD Student – University of Cardiff

**06th November**

“fMRI and EEG depict altered action-valence interactions in alcohol addiction and at-risk populations”

Lena Ernst, PhD Student – Mamede de Carvalho Lab

**13th November**

“Targeting neuroinflammation in multiple sclerosis”

Andreia Barateiro, PhD – Research Institute for Medicine (iMed.Ulisboa), Faculdade de Farmácia, Universidade de Lisboa

**20<sup>th</sup> November**

“Characterization of cell death in the ex vivo slice model of epileptogenesis”  
Cláudia Cavacas, PhD Student – Ana Sebastião Lab

**27<sup>th</sup> November**

“Relevance of astrocytes/microglia communication for NLRP3 signaling in the CNS - proof of concept in an ex-vivo epilepsy model”  
Catarina Almeida, Master Student – Ana Sebastião Lab

**04<sup>th</sup> December**

“Impact of CB1 receptor-mediated calcium signalling upon GABA and glutamate transporters in rat cortical astrocytes”  
Joana Ribeiro, MSc Student – Ana Sebastião Lab

**11<sup>th</sup> December**

“Characterization of the adenosinergic system and the BDNF-mediated signalling in heterozygous females of the Mecp2 KO model”  
Jéssica Rosa, Master Student – Ana Sebastião Lab

**18<sup>th</sup> December**

“Role of A2a receptor activation on adult oligodendrogenesis in a mouse model of Multiple Sclerosis”  
Joana Mateus, Master Student – Ana Sebastião Lab

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## Oncobiology Club

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**04<sup>th</sup> January**

"The role of metabolic reprogramming and mitochondrial respiration in breast cancer aggressive phenotype induced by hypercholesterolemia"  
Maria Beatriz Morgado – Sérgio Dias Lab

**18<sup>th</sup> January**

“Oncology research in Portugal between the 20th and the 21st century. A portrait of its institutional and semantic networks”  
Oriana Brás – SOCIUS-CSG-ISEG-UL; ASPIC

**15<sup>th</sup> February**

"Prognostic value of CELF2 in colorectal cancer and its association to distinct functions in RNA processing"  
Lina M. Gallego-Paez, PhD – Nuno Morais Lab

**22<sup>nd</sup> February**

"Spicy drug conjugates and protein-templated reactions - Novel drug delivery methods for selective cytotoxicity of cancer cells"  
Charlotte Baker, PhD Student – Gonçalo Bernardes Lab

**15<sup>th</sup> March**

“Quantitative dynamics of single-tumor-cell-lineages that underpin relapse of acute myeloid leukemia”  
Francisco Caiado, PhD – Bruno Silva-Santo Lab

**29<sup>th</sup> March**

"Role of PLCy1 in the Resistance Mechanism to Anti-EGFR Therapy in Metastatic Colorectal Cancer"

Raquel Duarte, MsC – Luís Costa Lab

**26<sup>th</sup> April**

"Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer"

Bernardo Almeida – Nuno Morais Lab

**21<sup>st</sup> June**

"Epigenetic drivers of genomic instability and intratumor heterogeneity"

Mafalda Matos, PhD Student – Sérgio Almeida Lab

**03<sup>rd</sup> October**

"A myeloid-centric view of cancer – Anti-tumour myeloid cells: myth or reality?"

Karine Serre, PhD – Bruno Silva-Santos Lab

**31<sup>st</sup> October**

"Intravital microscopy of acute leukemia and bone marrow microenvironments"

Delfim Duarte – Imperial College London, IPO, Universidade do Porto

**29<sup>th</sup> November**

"The role of mitochondrial adaptations in the acquisition of the phenotype induced by LDL in breast cancer"

Susana Monteiro, Master Student – Sérgio Dias Lab

**13<sup>th</sup> December**

"Hybrid capture-based genomic profiling of circulating tumor DNA from patients with estrogen receptor-positive metastatic breast cancer"

Maria Rita Dionísio – Luís Costa Lab and Serviço de Oncologia HSM

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**Other Events**

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**16<sup>th</sup> January**

Gender Balance in Science - Debate: "Inside Research, around researchers"

Reiko Kuroda, Audrey Odom, Georgios Kararigas, Maria Leptin, Lucy Hoareau and Miguel Castanho

**17<sup>th</sup> January**

PostDoc Day

Audrey Odom and Reiko Kuroda

**20<sup>th</sup> January**

LisbonBioMed Seminar: "Dynamic interactions between healthy and malignant haematopoietic cells and the bone marrow microenvironment"

Cristina Lo Celso – Imperial College London

Host: João Barata

**08<sup>th</sup> February**

CoHiTec 2017 Presentation Session

**14<sup>th</sup> February**

CAML Rheumatology Series: “Mesenchymal stem cells applications in rheumatology”

Christian Jorgensen – Montpellier University, France

**09<sup>th</sup> March**

ReTuBi Series: “Light and dark sides of aPKC”

Masanori Nakayama, PhD – Max-Planck Institute for Heart and Lung Research, Germany

**14<sup>th</sup> March**

Lição de Abertura do Tronco de Neurociências: “Ausências Epiléticas: O que são e como se originam”

Prof. Doutor Fernando Lopes da Silva – Centro de Neurociências da Universidade de Amesterdão & Universidade de Lisboa

**15<sup>th</sup> March**

Symposium: Biomarkers for Alzheimer’s Disease

**16<sup>th</sup> March**

iMM ERC Symposium - 10th Anniversary

Bruno Silva-Santos, Cláudio Franco, Edgar Gomes, Henrique Veiga-Fernandes, João Barata, Maria M. Mota and Vanessa Morais – iMM

**24<sup>th</sup> March**

EFIS On Tour

**04<sup>th</sup> May**

Startups Seminar

**08<sup>th</sup> May**

iMM Scientific Retreat: PhD and Post-Doc Short Talks

**18<sup>th</sup> – 19<sup>th</sup> May**

Grants Office Workshop

**24<sup>th</sup> – 26<sup>th</sup> May**

XI iMM/CAML PhD Students Meeting

**30<sup>th</sup> May**

9<sup>th</sup> Edition: Crioestaminal/Viver a Ciência Award

**31<sup>st</sup> May**

“Amnis® ImageStream®X Mark II Technology: benefits of quantitative image analysis of cells in flow”

Clara Cigni, PhD, Flow and Imaging Cytometry Application Specialist – Merck

**06<sup>th</sup> June**

Special ReTuBi Seminar: “The Temporal Basis of Angiogenesis”

Katie Bentley – Harvard Medical School

Host: Cláudio Franco



**21<sup>st</sup> June**

ReTuBi Lecture: “Functional specialization of human dendritic cell subsets”  
Dr. Elodie Segura – Institut Curie, France  
Host: Luís Graça

**22<sup>nd</sup> June**

“Clinical Aspects of the Immunopathogenesis of Ageing and Metabolic Complications in Treated HIV Infection”  
Prof. Suzanne Crowe – Associate Director Burnet Institute, Melbourne, Australia

**25<sup>th</sup> September**

“Sensory integration for memory-dependent choice behaviors”  
Miguel Remondes, Head of Lab – iMM

**17<sup>th</sup> October**

iMM innovators (iMMi) Competition – TwinnToInfect

**19<sup>th</sup> October**

ASPIC: Encontro Sobre Investigação em Cancro da Mama - «Da Investigação Básica à Clínica: análise de uma imagem com a sociedade civil»

**23<sup>rd</sup> October**

ReTuBi Lecture: “Frustrated endocytosis in cell migration and mechanotransduction”  
Guillaume Montagnac – Gustave Roussy Institute

**24<sup>th</sup> October**

ReTuBi Lecture: "Notch signaling in vasculature: angiogenesis and beyond"  
Andreas Fischer – German Cancer Research Center (DKFZ)

**31<sup>st</sup> October**

Master/PhD in Neurosciences Lecture: "Genetic approaches to fight neurodegenerative diseases"  
Luís Pereira de Almeida – FFUC

**03<sup>rd</sup> November**

Conference – Tribute to João Lobo Antunes: "O cérebro do Adolescente"  
Sarah-Jayne Blakemore and Maria Mota – University College London, iMM

**06<sup>th</sup> November**

“Cell Discoverer 7: Your automated platform for live cell imaging”  
Dr. Soren Prag – Carl Zeiss Microscopy GmbH  
Host: José Rino

**08<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: “Neuronal regeneration”  
Mónica Sousa – UP

**08<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: “The ubiquitin/proteasome system and control of neuronal death”  
Carlos Duarte – FCTUC, CNC

**14<sup>th</sup> November**

"Dislipidemia no lupus eritematoso sistémico"

Jozélio Carvalho – Universidade de São Paulo and Universidade Federal da Bahia

**15<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: "Neuroimaging: an overview"

Eduardo Ducla-Soares – FCUL

**15<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: "Optogenetic manipulation of neuronal circuits"

João Peça – CNC

**16<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: "Genetic approaches to fight neurodegenerative diseases"

Fani Neto – FMUP

**23<sup>rd</sup> November**

Master/PhD in Neurosciences Lecture: "Brain Rhythms: networks, cognitive functions and multimodal functional imaging"

Fernando Lopes da Silva – Univ. Amsterdam/FMUL/IST

**29<sup>th</sup> November**

HiTech Information Session

**05<sup>th</sup> November**

Master/PhD in Neurosciences Lecture: "Neuromarketing and Law"

Fernando Araújo – FDUL

**12<sup>th</sup> December**

"The Gulbenkian Training Program in Bioinformatics (since 1999). The building of a sustainable training model and some ways to scale it up"

Pedro Fernandes, Bioinformatics Training Coordinator – IGC Oeiras

**12<sup>th</sup> December**

CAML Rheumatology Series: "The proteasome – victim or culprit in autoimmunity"

Eugene Feist, Rheumatology and Clinical Immunology – Charité - Universitätsmedizin Berlin

**12<sup>th</sup> December**

"The IL-7 pathway in acute lymphoblastic leukemia"

Scott Durum – Center for Cancer Research, National Cancer Institute, USA

**13<sup>th</sup> December**

Master/PhD in Neurosciences Lecture: "Artificial Intelligence: a view on Morality, or artificial agents with qualities"

Hélder Coelho – FCUL

**13<sup>th</sup> December**

Master/PhD in Neurosciences Lecture: "Reciprocal inputs between Neuroscience and Robotics"

José Santos Victor – IST

**13<sup>th</sup> December**

"LARP1: gatekeeper of ribosome production"

Bruno Fonseca – Children's Hospital of Eastern Ontario, Ottawa, Canada

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**Out of Our Box**

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**05<sup>th</sup> January**

"Maps and nautical charts historically: two of a kind or different cartographic paradigms?"

Joaquim Alves Gaspar – Centre for the History of Science and Technology, Faculty of Sciences, University of Lisbon

**20<sup>th</sup> July**

"How To Kill a Scientist (on TV)"

Cosima Herter - Science Writer and Consultant for Orphan Black (Netflix)

Host: Luís Graça

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**Parasitology Club**

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**17<sup>th</sup> January**

"N6-methyladenosine in Trypanosoma brucei RNA: it is functional?"

Idálio Viegas – Luísa Figueiredo Lab

**24<sup>th</sup> January**

"Plasmodium Divalent Metal Transporter: biology, function and peculiarities"

Ksenija Slavic, PhD – Maria Mota Lab

**31<sup>st</sup> January**

"The unEXpected role of a blood stage protein during liver stage development of Plasmodium parasites"

João Vieira, PhD Student – Maria Mota Lab

**07<sup>th</sup> January**

"Host-Plasmodium Energy Dynamics : a PhD thesis proposal"

Aparajita Lahree, PhD Student – Maria Mota Lab

**21<sup>st</sup> February**

"Searching for the UIS4 role during malaria liver stage infection"

Viriato M'Bana, PhD Student – Maria Mota Lab

**07<sup>th</sup> March**

"The role of LncRNAs in Trypanosoma brucei"

Fabien Guegan – Luísa Figueiredo Lab

**14<sup>th</sup> March**

"Liver stage Malaria-, from antigen processing to an immune evasion strategy- PhD Project presentation"

Sara Baptista – Maria Mota Lab

**21<sup>st</sup> March**

“Pb(PfCS@UIS4), an Investigational Medicinal Product”  
António Mendes – Miguel Prudêncio Lab

**28<sup>th</sup> March**

“Why so sweet VSG? Variable surface glycoprotein glycosylation pattern may affect host distribution”  
Miguel Ferreira – Luísa Ferreira Lab

**04<sup>th</sup> April**

“Plasmodium exploitation of host methionine metabolism”  
Vanessa Luís – Maria Mota Lab

**18<sup>th</sup> April**

“Uptake and metabolism of arginine impact Plasmodium development in the liver”  
Patrícia Mendes – Miguel Prudêncio Lab

**02<sup>nd</sup> May**

“Exploring genome databases and cheminformatics tools towards discovery of new drugs and vaccines against tropical parasitic diseases”  
Pedro Cravo – Instituto de Higiene e Medicina Tropical (IHMT), Universidade Nova de Lisboa

**16<sup>th</sup> May**

“Clock parasites: circadian rhythms in malaria parasite”  
Inês Bento – Maria Mota Lab

**23<sup>rd</sup> May**

“Adipose tissue is a reservoir of Trypanosoma brucei parasites throughout infection”  
Sandra Trindade, Post-Doc – Luísa Figueiredo

**06<sup>th</sup> June**

“Bacteria is the only culture we have... What does Plasmodium have to say about it?”  
Debanjan Mukherjee – Maria Mota Lab

**20<sup>th</sup> June**

“Can we add novelty in Trypanosoma brucei biology?”  
Idálio Viegas – Luísa Figueiredo Lab

**04<sup>th</sup> July**

“The promiscuous Plasmodium in host endosomal harem”  
Aparajita Lahree, PhD Student – Maria Mota Lab

**11<sup>th</sup> July**

“The (api)complexity of Plasmodium parasites!”  
João Vieira, PhD Student – Maria Mota Lab

**18<sup>th</sup> July**

“What can Trypanosomes teach us about protection against malaria?”  
Ana Margarida Vaz – Luísa Figueiredo Lab and Miguel Prudêncio Lab

**25<sup>th</sup> July**

"UIS4 role, what the new?"

Viriato M'Bana – Maria Mota Lab

**26<sup>th</sup> September**

"T. brucei glycosylation control and tropism"

Miguel Ferreira – Luísa Figueiredo Lab

**17<sup>th</sup> October**

"The Hitchhiker's Guide to Malaria"

Thomas Hanscheid - Instituto de Microbiologia, FMUL

**23<sup>rd</sup> October**

"Can we understand tuberculosis from host-pathogen alterations?"

Margarida Saraiva – i3s Porto

**07<sup>th</sup> November**

"Bioinformatics: It's not black magic. 5 steps to get you started with data analysis"

Daniel Neves – Luísa Figueiredo Lab

**14<sup>th</sup> November**

"The role of GSK3 as a virulence factor in Plasmodium infection"

Leonardo Rocha – Maria Mota Lab

**14<sup>th</sup> November**

"Using proteomics to understand how parasites adapt to the host environment"

Mariana Sequeira – Luísa Figueiredo Lab

**05<sup>th</sup> December**

"UIS3-LC3 interaction - A novel drug target for malaria therapy?"

Sonali Setua – Maria Mota Lab

**12<sup>th</sup> December**

"Host-parasite coevolution between Toxoplasma gondii and the house mouse"

Jonathan Howard – IGC

**18<sup>th</sup> December**

"Bionanosensors: Nanotechnology for biodetection"

Ricardo Franco – FCT/NOVA and UCIBIO/REQUIMTE

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## Pharmacology Series

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**09<sup>th</sup> January**

"VIH, activação imunitária e terapêutica antirretroviral"

Robert Badura, MD, MSc – Hospital de Santa Maria, CHLN, EPE; Faculdade de Medicina da Universidade de Lisboa

**13<sup>th</sup> February**

"Therapeutic options in Hepatitis C: a review"

José Pedro Rodrigues – Hospital Egas Moniz, Centro Hospitalar Lisboa Oriental e Instituto de Patofisiologia, Faculdade de Medicina, Universidade de Lisboa

**10<sup>th</sup> April**

"Polymedication"

Joana Vaz – Serviço de Medicina Interna do Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental

**08<sup>th</sup> May**

"Brain connectivity changes due to prolonged cannabinoid intake"

Francisco Mouro, PhD Student – Ana Sebastião Lab

**11<sup>th</sup> September**

"Uso clínico de opioides"

Paulo Reis Pina – Casa de Saúde de Idanha, Sintra

**09<sup>th</sup> October**

"Delirium nos cuidados intensivos: Da teoria aos desafios práticos"

Carolina Paulino, MD – UCIP, Hospital de São Francisco Xavier

**18<sup>th</sup> December**

"Paradoxo da obesidade na doença renal - identificação e validação de novos biomarcadores"

Ana Rita Martins – Faculdade de Medicina de Lisboa e Hospital de Santa Cruz, CHLO

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## PhD Dissertation Presentation

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**05<sup>th</sup> January**

"Endothelial Notch Ligands in Bone Marrow Function and in Malignancy"

Dra. Inês Sofia Alvarez Martins

**10<sup>th</sup> January**

"Intervenção Nutricional direccionada aos Estilos de Vida em Indivíduos com Obesidade [Indivíduo]: Elaboração de Protocolo Clínico e Avaliação de Efectividade"

Dr. José Miguel Lopes Camolas

**01<sup>st</sup> February**

"Deciphering the role of aB-crystalline in Huntington's Disease"

Dra. Ana Cristina Oliveira

**08<sup>th</sup> February**

"Molecular mechanisms controlling the survival and differentiation of human gamma delta thymocytes"

Dr. Sérgio Ribeiro

**09<sup>th</sup> February**

"Clinical pharmacology of oral anticoagulants: Pharmacoepidemiology, safety and pharmacoconomics"

Dr. Daniel Caldeira

**24<sup>th</sup> February**

“Microcirculation and Inflammation in a Numerical Simulation Approach”

Dra. Ana Rosa Miranda dos Santos Silva Herdade

**13<sup>th</sup> March**

“Lost in Time. A Neurophilosophical Quest to Understand the Perception of Time in MCI Patients”

Dra. Sara Cunha Leal Rocha Coelho

**14<sup>th</sup> March**

“Neuropsychological contribution to the study of White Matter Changes: a 10-year longitudinal study”

Dra. Sofia Ribeiro Esperança da Silva Madureira

**20<sup>th</sup> March**

“The Repertoire and Specificity of Follicular Regulatory T Cells”

Dra. Ana Raquel de Oliveira

**27<sup>th</sup> March**

“Sinais quantitativos e qualitativos de lesão cerebral na Escala de Inteligência de Wechsler para Adultos 3ª Edição (WAIS-III)”

Dra. Marta de Assunção Gonçalves Montera

**12<sup>th</sup> April**

"The Impact of Rheumatic Diseases on Early Retirement"

Dr. Pedro Almeida Lares

**19<sup>th</sup> April**

"How early inflammatory events affect bone nano properties at rheumatoid arthritis onset"

Dr. Bruno Miguel Costa Vidal

**27<sup>th</sup> April**

"LRRK2 Mutations in Parkinson's Disease"

Dra. Maria Leonor Brito de Arriaga Correia Guedes Moller Miranda

**04<sup>th</sup> May**

“Development of an Innovative Real-Time Assay for Antimalarial Sensitivity Testing”

Dra. Maria Sousa Rebelo

**05<sup>th</sup> May**

“Unraveling the Molecular Mechanisms Underlying Alpha-Synuclein Oligomerization and Cytotoxicity”

Dra. Susana Alexandra de Barros Gonçalves

**11<sup>th</sup> May**

“Trajetórias do Bem-Estar: Efeitos Temporais dos Determinantes Psicossociais da Saúde em Contexto Laboral”

Dra. Mariana Augusta Lopes de Matos Pinheiro Carreira Neto

**15<sup>th</sup> May**

“Emergência da Tuberculose Multirresistente e extensivamente Resistente. Caracterização em Co-Infetados por VIH e em Imunocompetentes”

Dr. Fernando Manuel Tavares Maltez

**29<sup>th</sup> June**

"Neuroexcitability control by adenosine and BDNF at the adult hippocampus"

Dra. Mariana Colino de Oliveira

**05<sup>th</sup> July**

"Avaliação das Capacidades Cognitivas Não-Verbais na Afasia de Etiologia Vascular"

Dr. José Manuel Borges Fonseca

**27<sup>th</sup> July**

"Sleep, Sleep-disordered-breathing, Cognition and Prematurity"

Dra. Yu-Shu Huang

**26<sup>th</sup> September**

“Transcription Dynamics Prevents RNA-mediated Genomic Instability Through SRPK2-dependent DDX23 Phosphorylation”

Dr. S R Chaitanya Sridhara

**07<sup>th</sup> November**

“Contribution for the characterization and performance improvement of primary angioplasty in Portugal”

Dr. Hélder Horta Pereira

**16<sup>th</sup> November**

“Time trends of treatment and outcomes in women with T1 node-negative breast cancer”

Dra. Inês Maria Vaz Duarte Luís

**24<sup>th</sup> November**

“Unveiling the trophic actions of adenosine A2A receptors in neurite outgrowth and postnatal neurogenesis – Interaction with brain-derived neurotrophic factor”

Dra. Ana Filipa Ferreira Cunha Ribeiro

**28<sup>th</sup> November**

“Molecular mechanisms by which low doses of ionizing radiation promote neovascularization in ischemic tissues”

Dra. Paula Alexandra Gomes de Oliveira

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**Pizza Seminar**

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**10<sup>th</sup> January**

“Mechanisms of Regulatory T cell recruitment by Mesenchymal Stem Cells in vitro”

Rita Azevedo – João Lacerda Lab

“Targeting membranes as antiviral strategy”

Bárbara Gomes – Nuno Santos Lab



**24<sup>th</sup> January**

“Epileptogenic focus localization using complexity analysis of BOLD signals”  
Vânia Tavares, PhD Student – Diana Prata Lab

**21<sup>st</sup> January**

“Is endoplasmic reticulum giving a hand in moving the nucleus?”  
Cátia Janota, PhD Student – Edgar Gomes Lab

“Generation and characterization of fully human antibody specific to the Interleukin-7 receptor, a potential target for T-cell Acute Lymphoblastic Leukemia”

Padma Akkapeddi, PhD Student – Gonçalo Bernardes Lab and João Barata Lab

**04<sup>th</sup> April**

“Angiocrine factors as modulators of spinal cord regeneration”  
Isaura Martins, PhD – Leonor Saúde Lab

“Exploring the actions of Kyotorphin and Amidated-Kyotorphin as possible pharmacological therapy for Alzheimer's Disease”

Rita Belo, PhD Student – Ana Sebastião Lab and Miguel Castanho Lab

**18<sup>th</sup> April**

“Molecular Analysis of VEGF and VEGF receptors in SOD1 (G93A) mice at different disease stages”

Nádia Rei, PhD Student – Ana Sebastião Lab

“Behavioral adaptation to partially observable changes in the environment: a reinforcement learning approach”

Vasco Conceição, PhD Student – Mamede de Carvalho Lab

**02<sup>nd</sup> May**

“Network (poly) pharmacology of natural products”

Tiago Correia de Oliveira Rodrigues – Gonçalo Bernardes Lab

“Action-valence interactions explored with fMRI: Basic systems and differences in alcohol dependency”

Lena Ernst, PhD – Mamede de Carvalho Lab

**16<sup>th</sup> May**

“The role EXP2 during the invasion of the hepatocyte by Plasmodium sporozoites”

João Mello-Vieira, PhD Student – Maria Mota Lab

**30<sup>th</sup> May**

“Neutrophil-mediated inhibition of tumour-associated IL-17-producing  $\gamma\delta$  T cells”

Sofia Mensurado – Bruno Silva-Santos Lab

“Positioning nuclei at the periphery of skeletal muscle cells”

William Roman – Edgar Gomes Lab

**20<sup>th</sup> June**

“Understanding the effects of anticancer peptides on cancer cells and their selectivity towards exosomal membranes”

Julia Skalska, PhD Student – Miguel Castanho Lab

**12<sup>th</sup> September**

“ALT cancers in a funk – FANCM is essential for ALT cell viability”  
Richard Pentz, PhD Student – Claus Azzalin Lab

**26<sup>th</sup> September**

“Metabolic Oligosaccharide Engineering - A tool for Malaria?”  
Annabel Kitowski – Gonçalo Bernardes Lab

**07<sup>th</sup> November**

“A dynamic model of behaviour therapy”  
Ana Pôrtelo, PhD Student – Mamede de Carvalho

“Neuronal regulation of type 2 innate lymphoid cells via neuromedin U”  
Vânia Cardoso, PhD Student – Champalimaud Foundation: Veiga-Fernandes Lab

**21<sup>st</sup> November**

“Exploring the impact of noncoding genetic variation on lysosomal function”  
Christian Ramos – Carmo-Fonseca Lab

“Low doses of ionising radiation induce angiogenesis: therapeutic implications”  
Filipa Marques – Susana Constantino

**05<sup>th</sup> December**

“Reinforcement learning in Tourette syndrome and attention deficit hyperactivity disorder”  
Ângelo Dias, PhD Student – Mamede de Carvalho Lab

“TERRA associated functions in maintaining telomeres in telomerase-positive human cancer cells”  
José Nobre – Claus Azzalin Lab

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**Special Seminar**

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**06<sup>th</sup> January**

“From starting a PhD to becoming a scientist”  
António Coutinho, Professor  
Host: Leonor Parreira and Luís Graça

**03<sup>rd</sup> February**

“Mitochondria and Lysosomes – in sickness and in health, till autophagy do us part”  
Nuno Raimundo, PhD – University Medical Center Göttingen  
Host: Vanessa Morais

**24<sup>th</sup> March**

“The cradle of thymopoiesis: embryonic thymus is initially seeded by lympho-myeloid restricted progenitor’s independently of Notch”  
Tiago C. Luís, PhD, Junior Researcher Fellow – University of Oxford

**28<sup>th</sup> March**

Career Opportunities at Hovione  
Sandra Teixeira and Luísa Nunes – Hovione  
Host: iMM

**11<sup>th</sup> April**

"Age-related mutagenesis of driver genes in the male germline"  
Irene Tiemann-Boege – Institute of Biophysics, Johannes Kepler University, Linz, Austria  
Host: Nuno Morais

**17<sup>th</sup> April**

Special Seminar Enable Editing  
Marie Claude Laffitte – Glaslow University

**26<sup>th</sup> May**

"Intellectual Property Protection: Creating Value From Research"  
John Van Amsterdam, Ph.D., J.D. – Wolf Greenfield & Sacks, Intellectual Property Law, USA  
Host: Career Development

**02<sup>nd</sup> June**

"Defined and Scalable Systems for the Production of Human Oligodendrocyte Progenitor Cells from Pluripotent Stem Cells"  
Gonçalo Rodrigues – Instituto Superior Técnico/U.C. Berkeley

**02<sup>nd</sup> June**

Launching Event: iMM innovators (iMMi)

**14<sup>th</sup> June**

Johan Henriksson – Sanger Institute, Cambridge, UK

**26<sup>th</sup> September**

"RNA polymerase II Transcription and co-transcriptional processing across mammalian genomes"  
Nicholas Proudfoot – Oxford University

**12<sup>th</sup> October**

"A DaNGeRous Talk About Dendritic Cells"  
Caetano Reis e Sousa – Francis Crick Institute, London

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## Technological Series

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**04<sup>th</sup> October**

"FIXATION: from hole body to single organism"  
Andreia Pinto – Histology and Comparative Pathology Laboratory, iMM

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## TwinnToInfect // EXCELLtoINNOV Seminar

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### **19<sup>th</sup> January**

“AhRimmunity”

Brigitta Stockinger – The Francis Crick Institute, UK

Host: Marc Veldhoen

### **02<sup>nd</sup> February**

"PI3K in immunity, infection and cancer"

Klaus Okkenhaug

Host: Marc Veldhoen

### **02<sup>nd</sup> March**

“Lymphocyte commitment in fetal hematopoiesis”

Ana Cumano – Institut Pasteur, França

Host: Bruno Silva-Santos

### **06<sup>th</sup> April**

“Microenvironment and Immunity”

G rard Ebrel – Institut Pasteur, Frana

Host: Marc Veldhoen

### **11<sup>th</sup> May**

"Injury and repair: Surprising discoveries at the pathogen-host cell interface”

Norma Andrews – University of Maryland

Host: Lu sa Figueiredo

### **06<sup>th</sup> July**

“Immune Responses and Tumourigenesis”

Tak Mak – University of Toronto

Host: Marc Veldhoen

### **07<sup>th</sup> September**

"Malaria"

Tania de Koning-Ward – Deakin University

Host: Maria Mota

### **02<sup>nd</sup> November**

“Sexually-Transmitted Infections and Pathways leading to Elevated HIV Target Cells in the Foreskin: Implications for the HIV Epidemic in South Africa”

Clive Gray – University of Cape Town

Host: Marc Veldhoen and Bruno Silva-Santos

### **02<sup>nd</sup> November**

“Granuloma development during TB progression”

M. Jackson Marakalala – School of Public Health, USA

Host: Marc Veldhoen and Bruno Silva-Santos

**02<sup>nd</sup> November**

“Genomic regulatory mechanisms for early T-cell lineage commitment“

Ellen Rothenberg – California Institute of Technology

Host: Marc Veldhoen and Bruno Silva-Santos

**09<sup>th</sup> November**

“Novel signals and markers underlying B cell responses to Plasmodium infection“

Damián Eduardo Pérez Mazliah – The Francis Crick Institute, UK

Host: Bruno Silva-Santos

**07<sup>th</sup> December**

“Generation of human T cells with HLA-restricted antigen specificity“

Juan Carlos Zúñiga-Pflücker – Toronto University

## iMM Advanced Training // Career Development

The iMM is strongly committed to providing the best training for success in science to researchers at different stages in their careers.

### Team

**Executive Manager:** Filipa Nunes, PhD.

**Executive Committee:** Leonor Saúde, PhD (Chair); Vanessa Morais, PhD, Edgar Gomes, PhD.

**LisbonBioMed PhD Program Director:** Domingos Henrique, PhD.

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 (Lisbon AMC), a consortium that provides an integrated form of education and training in Biomedicine and Clinical Research, combining multidisciplinary and internationalization.

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

The majority of iMM PhD students belong to the Lisbon AMC PhD Program that runs in the campus since 2010. In addition, iMM also hosts students from other national (e.g. GABBA) and international PhD Programs (e.g. MC-ITN, MIT-PT).

In 2013, iMM was awarded FCT funding to create the Lisbon Biomedical and Clinical Research PhD Program – **LisbonBioMed**, and in January 2017, we welcomed the fourth edition 12 PhD students. Furthermore, iMM is a partner in five other multi-institutional FCT PhD Programs: the Bioengineering - Cell Therapies and Regenerative Medicine (**CTRM**), the Molecular Biosciences - Biology at the Host Microbe Interface (**B@HMI**), the Lisbon University Doctoral Program in Integrative Neuroscience (**NeurULisboa**), the Medicinal Chemistry PhD Programme (**MedChemTrain**) and the Medical Biochemistry and Biophysics (**M2B-PhD**) PhD Programs.

Overall, the integrated management of ongoing and new Master, PhD and Postdoctoral Programs will further enrich our scientific environment promoting multidisciplinary and facilitating the development of individual projects within the areas of Biomedicine and Clinical Medicine.

### Advanced Training in Numbers

	2017
<b>Post-Doctoral Fellows</b>	80
Started in 2017	26
<b>PhD Students</b>	126
Started in 2017	41
<b>MSc Students</b>	109
Started in 2017	74

In 2017, IMM hosted students enrolled in 7 different **FCT PhD Programs**:

- LisbonBioMed: 38
- M2B-PhD: 11
- NeurULisboa: 9
- CTRM: 5
- MedChemTrain: 2
- GABBA: 1
- PGCD: 5
- MIT-Portugal: 3

Besides Lisbon AMC PhD students, IMM hosted **13 PhD students from other Institutions/Universities**: 1 Universidade Federal da Bahia; 1 Università di Bologna; 1 University of Porto; 2 University of Coimbra; 8 Instituto Superior Técnico, University of Lisbon.

**41 PhD Students started at IMM in 2017**, including 12 LisbonBioMed PhD students: Carlos Diogo Labão Alpiarça Sousa de Almeida, Elvira Pequeno Leites, Eunice Ribeiro João Silva Paisana, Helena Alexandra Ribeiro de Carvalho Pinheiro, Henrique Pedro Pereira da Silva Amaral Machado, João Maria Rodrigues Perlico da Cruz Sabino, Luís Pedro Dias Bernardo Maricoto Monteiro, Marcin Makowski, Marco Calvinho Cavaco, Mariana Ascensão Ferreira, Patrícia Alexandra Lona Abreu, Rita Abrunhosa Soares.

In 2017, **16 PhD theses** were concluded, 13 of which were attributed by the *Faculdade de Medicina da Universidade de Lisboa* (FMUL).

## Advanced Courses

### A total of 11 Advanced Courses were organized

#### 8 Courses organized under the CAML PhD Programme in 2017

##### **Towards a Creative and Critical Mind**

Organizer: Domingos Henrique

Date: 9<sup>th</sup> January to 3<sup>rd</sup> March (16 ECTS)

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

##### **Statistics for Beginners**

Organizer: Domingos Henrique

Date: 5<sup>th</sup> January to 16<sup>th</sup> March, every Thursday (1 ECTS)

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

##### **The road map to the scientific job market**

Organizer: Workshop group of the PhD Students Committee

Date: 16<sup>th</sup> March

This workshop aims to provide the necessary tools for PhD students to enter into the scientific job market. The discussion was focused not only on available job opportunities, but also on how to captivate a recruiter from the application to the interview.

##### **Laboratory Animal Science**

Organizer: Joana Marques

Date: 27<sup>th</sup> March to 13<sup>th</sup> April (1.5 ECTS)

The course was targeted to functions A, C and D of rodents and fish, according to Directive 2010/63/EU. Theoretical sessions covered the following topics: Ethics and the 3R's; Biology and husbandry; Animal behavior and welfare; Surgery and pain management; Euthanasia and humane endpoints. Practical sessions focused on procedures and techniques in rodents and fish. This course is a requirement to be able to work with animal models.



### **Laboratory Animal Science**

Organizer: Joana Marques

Date: 04<sup>th</sup> to 22<sup>nd</sup> September (1.5 ECTS)

The course was targeted to functions A, C and D of rodents and fish, according to Directive 2010/63/EU. Theoretical sessions covered the following topics: Ethics and the 3R's; Biology and husbandry; Animal behavior and welfare; Surgery and pain management; Euthanasia and humane endpoints. Practical sessions focused on procedures and techniques in rodents and fish. This course is a requirement to be able to work with animal models.

### **1<sup>st</sup> FLxFlow Course - Principles and Applications of Flow Cytometry**

Organizer: José Rino

Date: 16<sup>th</sup> to 20<sup>th</sup> October (1.5 ECTS)

This course introduced the basic principles and applications of flow cytometry to beginners: from fluorophores and panel design, instruments operation, required controls and statistical analysis to data publication and potential applications. The course consisted of theoretical talks and practical sessions with remote teaching where students learned how to set up an experiment, run a multi-color experiment, perform compensation and analyze data. There were also practical hands-on sessions in immunophenotyping, cell cycle, cell death & apoptosis and imaging flow cytometry.

### **Communication: Turn yourself into a successful speaker!**

Organizer: Workshop group of the PhD Students Committee

Date: 9<sup>th</sup> October

This is an interactive course that gives the students the tools to communicate more effectively with an audience in a scientific congress, making their communication more impactful, persuasive and confident.

### **Advanced Topics in Statistics**

Organizer: Domingos Henrique

Date: 2<sup>nd</sup> November to 28<sup>th</sup> December, every Thursday (2 ECTS)

This is an advanced course that follows the introductory course ("Statistics for beginners"), and aims to teach advanced statistical methods and techniques for data analysis in biomedical sciences. Participants must have previous experience in biostatistics (from the introductory course or from similar courses). Participants are encouraged to bring their data to be discussed. Course is suited for MDs who need to understand medical statistics at an advanced level, and interpret/analyse the results of studies and scientific papers.

2 Courses organized by the iMM Postdoctoral Association (PDA) in 2017

**MasterClass in Fundamentals of Innovation and Technology Transfer**

Organizer: PDA

Date: 8<sup>th</sup> June

A full-day interactive workshop covering the following topics: business manager as an example of career outside academia, basis of intellectual property in healthcare and life sciences, and basis of contracts in innovation and tech transfer.

**Illustration Workshop**

Organizer: PDA

Date: 16<sup>th</sup> November

The course combines an introductory theoretical session with several exercises, using the Illustrator software.

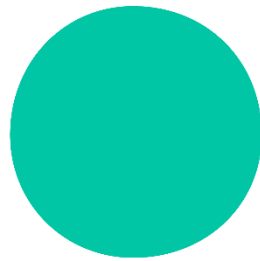
1 Course organized under the “Research in Tumour Biology – ReTuBi” European project

**Career development and soft skills for young scientists – from Lisbon to the World**

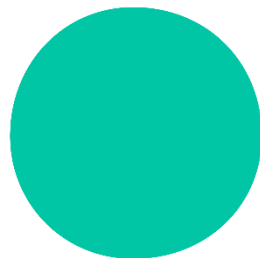
Organizer: ReTuBi project

Date: 22-24<sup>th</sup> February

This 2-day workshop was focused on the 2 main themes: career development in academia and beyond; and research ethics & scientific integrity.



# 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.

Azzalin, Claus M.
Barata, João T.
Bernardes, Gonçalo J. L.
Carmo-Fonseca, Maria
Castanho, Miguel
Costa, Luís
De Almeida, Sérgio
De Carvalho, Mamede
Dias, Sérgio
Ferreira, Joaquim
Ferro, José
Figueiredo, Luísa
Filipe, Paulo
Fonseca, João Eurico
Franco, Cláudio
Gomes, Edgar
Graça, Luís
Henrique, Domingos
Lacerda, João F.
Lopes, Luísa V.
Morais, Nuno
Morais, Vanessa
Mota, Maria M.
Prata, Diana
Prudêncio, Miguel
Ramirez, Mário
Remondes, Miguel
Saldanha, Carlota
Santos, Nuno C.
Saúde, Leonor
Sebastião, Ana
Silva-Santos, Bruno
Simas, Pedro
Sousa, Ana E.
Veiga-Fernandes, Henrique
Veldhoen, Marc

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## Azzalin, Claus M.

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### Major Interests / Objectives

Telomeres are heterochromatic nucleoprotein structures 'capping' ends of linear eukaryotic chromosomes. Dysfunctional telomeres cause severe chromosome instability, thereby unleashing cascades of cellular reactions that are common hallmarks of human diseases such as cancer and premature aging. We employ molecular biology, cell biology and biochemistry to understand how telomeres execute their protective functions and how telomeric dysfunctions are mechanistically linked to pathological conditions. In particular, we study how the telomeric long noncoding RNA TERRA participates in maintaining proper telomere structure and functions in both normal and diseased human cells.

### Head of Laboratory

Claus Maria Azzalin, PhD

### Research Team

Ana Margarida da Silva Figueira	Master	Lab Manager (Started April)
José Carlos Perez Nobre	Master	Investigator
Patrícia Alexandra Lona Abreu	Master	PhD Student (Started March)
Pedro Miguel Torres Mascarenhas Ribeiro Martins	Graduate	MSc Student (Started September)
Rajika Arora	PhD	Post-Doctoral Investigator
Richard Pentz	Master	PhD Student (Started February)
YongWoo Lee	PhD	Post-Doctoral Investigator

### Laboratory Keywords / Research Areas

TERRA, Telomeres, Cancer, Aging, Genome stability, RNA processing.

### Major Scientific Achievements

In 2017 we published a research article where the functions of human Cactin were for the first time revealed. Depletion of human Cactin leads to premature sister chromatid separation and genome instability. Cactin is essential for efficient splicing of thousands of pre-mRNAs, and incomplete splicing of the pre-mRNA of Sororin, a cohesin-associated factor, is responsible for the aberrant chromatid separation in Cactin-depleted cells. Our data point to novel pathways of gene expression regulation dependent on Cactin.

In collaboration with two Swiss laboratories, we published two research articles where we showed that: *i)* the introduction of either MS2 or PP7 stem-loops affects the processing and subcellular localization of mRNA; *ii)* ALT-positive yeasts present both systemic and specific metabolic responses to genetically-induced telomerase dysfunction, and these metabolic changes can be associated with generic stress responses as well as specific responses like accelerated aging.

### **Selected Publications**

Moravec M, Wischnewski H, Bah A, Hu Y, Liu N, Lafranchi L, King MC and Azzalin CM (2016). TERRA promotes telomerase-mediated telomere elongation in *Schizosaccharomyces pombe*. *EMBO Reports* 17, 999-1012. (IF: 8.568, Citations: 11).

Lorenzi LE, Bah A, Wischnewski H, Shchepachev V, Sonesson C, Santagostino M, Azzalin CM (2015). Fission yeast Cactin restricts telomere transcription and elongation by controlling Rap1 levels. *EMBO Journal* 34, 115-129. (IF: 9.792, Citations: 5).

Arora R, Lee YW, Wischnewski H, Brun CM, Schwarz T and Azzalin CM (2014). RNaseH1 regulates TERRA-telomeric DNA hybrids and telomere maintenance in ALT tumor cells. *Nature Communications* 5, e5220. (IF: 12.124, Citations: 55).

Shchepachev V, Wischnewski H, Missiaglia E, Sonesson C and Azzalin CM (2012). Mpn1, Mutated in Poikiloderma with Neutropenia Protein 1, Is a Conserved 3'-to-5' RNA Exonuclease Processing U6 Small Nuclear RNA. *Cell reports* 2, 855-865. (IF: 8.282, Citations: 26).

Chawla R, Redon S, Raftopoulou C, Wischnewski H, Gagos S and Azzalin CM (2011). Human UPF1 interacts with TPP1 and telomerase and sustains telomere leading-strand replication. *EMBO Journal* 30, 4047-4058. (IF: 9.792, Citations: 45).

### **Ongoing Research Projects**

2017/2020: TERRA and telomere transcription: towards therapies for healthy aging. Coordinator: Claus Maria Azzalin. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG 3576. Amount: € 150 000,00. Total Amount: € 150 000,00.

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

2016/2018: The multiple roles of TERRA in telomere length maintenance, telomere integrity, cancer and cellular senescence. Coordinator: Claus Maria Azzalin. Funding Agency: Swiss National Science Foundation. Reference: 31003A\_160338. Amount: € 272 083,00. Total Amount: € 272 083,00.

### **Publications in Peer Review Journals**

Heinrich S, Sidler CL, Azzalin CM, Weis K (2017). Stem-loop RNA labeling can affect nuclear and cytoplasmic mRNA processing. *RNA* 23, 134-141. (IF: 4.94, Citations: 5).

Zanini IM, Sonesson C, Lorenzi LE, Azzalin CM (2017). Human Cactin interacts with DHX8 and SRRM2 to assure efficient pre-mRNA splicing and sister chromatid cohesion. *J Cell Sci* 130, 767-778. (IF: 4.431, Citations: 1).

Buettner F, Jay K, Wischnewski H, Stadelmann T, Saad S, Jefimovs K, Mansurova M, Gerez J, Azzalin CM, Dechant R, Ibáñez AJ (2017). Non-targeted metabolomic approach reveals two distinct types of metabolic responses to telomerase dysfunction in *S. cerevisiae*. *Metabolomics* 13, 53. (IF: 3.692, Citations:--).

### **Communications in International Conferences**

Azzalin CM. Invited speaker and chairman for the EMBO meeting 'Nuclear structure and dynamics', L'isle-sur-la-Source, France, October 2017. (Oral Presentation).

Azzalin CM. Invited speaker for the workshop 'Telomeres in Health, Aging and Disease' UNESP Botucatu, Brazil, December 2017, (Oral Presentation).

### **Communications in National Conferences**

Azzalin CM. Invited speaker for the GABBA Symposium 'Nano 2 Universe', Porto, Portugal, July 21, 2017. (Oral Presentation).

### **Internationalisation**

Our group is directly collaborating with several laboratories in Europe and in the USA. Additionally, members of our laboratory regularly attend and present at international conferences on genomic stability and telomeres.



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## Barata, João T.

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### Major Interests / Objectives

We aim to understand the role of cell-autonomous alterations and microenvironmental cues in the development of cancer, focusing mainly on the dissection of signaling pathways essential for tumor maintenance. To do so, we make use of patient material, as a key source of insights into the disease, and integrate different biochemical, cellular and molecular biology techniques with appropriate *in vitro* and *in vivo* models - enabling an overall appreciation of the molecular, cellular and systemic nuances associated with cancer. The basic and pre-clinical research we perform is translation-oriented and enriched by active collaborations with clinicians. Ultimately, we aim to identify and characterize molecular targets for the development of novel, more selective therapies against cancer.

### Head of Laboratory

João Pedro Taborda Barata, PhD, Associate Professor

### Team

Afonso Rocha Martins de Almeida	PhD	Post-Doctoral Investigator
Alice Sofia dos Santos Melão	Master	PhD Student
Ana Patrícia Cebola Cachucho	Master	Investigator (Started February)
Ana Rita Freitas Martins de Matos Fragoso	PhD	Investigator
Ana Sofia Machado Moreira	Graduate	MSc Student (Started September)
Ana Sofia Navarro Ramalho	Graduate	MSc Student (Started July)
Andreas Noe	Master	Investigator (Started October/Left December)
Andreia de Jesus Amaral Gomes Barbosa Fonseca	PhD	Post-Doctoral Investigator, BioFIG (Left June)
Bruno António Caetano Cardoso	PhD	Post-Doctoral Investigator
Carlos Manuel Tavares da Custodia	Master	Investigator
Claudia Maria Coelho de Faria	MD/PhD	Post-Doctoral Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor, Clinical Specialist
Daniel Ribeiro	PhD	Post-Doctoral Investigator
Eunice Ribeiro João Silva Paisana	Master	PhD Student (Started March)
Gonçalo Lopes Martins e Pereira	Graduate	Trainee (Started October)
Isabel da Conceicao Alves Alcobia Principe Henriques	PhD	Post-Doctoral Investigator, Assistant Professor
Joana Margarida Luís Gonçalves	Graduate	MSc Student (Started September)
Luís Pedro Dias Bernardo Maricoto Monteiro	Master	PhD Student
Mafalda dos Santos Dias Duque	Graduate	Investigator

Mariana Lobato de Oliveira	Master	PhD Student
Mayara Ferreira Euzébio	Graduate	Investigator (Started September)
Padma Akkapeddi	Master	PhD Student
Samuel Luis Sequeira Lemos	Master	Investigator (Started November)
Tatiana Sofia Carneiro Duque	Undergraduate	Trainee (Started January/Left December)
Teresa Laura Mendes Serafim	PhD	Lab Manager
Tiago André Dias Soares	Graduate	MSc Student (Left August)

### Laboratory Keywords / Research Areas

Cancer biology, Leukemia, Signal transduction, Cellular and molecular biology, Rational targeted therapies, Brain tumors.

### Major Scientific Achievements

The lab studies mainly hematological tumors (especially lymphoid leukemias) and brain tumors. Two examples of important collaborative research efforts published in 2017 are the demonstration that CK2 controls the survival of both normal thymic and leukemia  $\gamma\delta$  T-cells via activation of Akt, in collaboration with Silva-Santos Lab (Ribeiro et al, Leukemia 2017) and the characterization of intertumoral heterogeneity within medulloblastoma subgroups, an international study in which C. Faria participated (Cavalli et al, Cancer Cell 2017). Our involvement in the organization of and high-level participation in, international scientific events and networks should also be highlighted (e.g. First YoungEHA Research Meeting, MAGIC Network of Excellence, etc).

### Selected Publications

Martins LR, Lúcio P, Melão A, Antunes I, Cardoso BA, Stansfield R, Bertilaccio MT, Ghia P, Drygin D, Silva MG, Barata JT (2014). Activity of the clinical-stage CK2-specific inhibitor CX-4945 against chronic lymphocytic leukemia. *LEUKEMIA* 28, 179–182. (IF: 11.702, Citations: 37).

Zenatti PP, Ribeiro, Li, Zuurbier L, Silva MC, Paganin M, Tritapoe J, Hixon JA, Silveira AB, Cardoso BA, Sarmiento LM, Correia N, Toribio ML, Kobarg J, Horstmann M, Pieters R, Brandalise SR, Ferrando AA, Meijerink JP, Durum SK, Yunes JA, Barata JT (2011). Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia. *NATURE GENETICS* 43, 932-939. (IF: 27.959, Citations: 161).

Silva A, Laranjeira ABA, Martins LR, Cardoso BA, Demengeot J, Yunes JA, Seddon B, Barata JT (2011). IL-7 contributes to the Progression of Human T-cell Acute Lymphoblastic Leukemias. *CANCER RESEARCH* 71, 4780-4789. (IF: 9.122, Citations: 51).

Henriques CM, Rino J, Nibbs RJ, Graham GG, Barata JT (2010). IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R $\alpha$  in T cells. *BLOOD* 115, 2724-2731. (IF: 13.164, Citations: 56).

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. (IF: 12.784, Citations: 239).

### Ongoing Research Projects

2017/2019: Identificação de novas terapias no tratamento do astrocitoma pilocítico em idade pediátrica. Coordinator: Cláudia Maria Coelho de Faria. Funding Agency: José de Mello Saúde. Reference: Manuel de Mello CFaria. Amount: € 12 500,00. Total Amount: € 12 500,00.

2016/2019: Aberrant IL7R signaling in leukemogenesis: from the basics to potential therapeutics. Coordinator: João Pedro Tabora Barata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FAPESP/20015/2014. Amount: € 199 778,00€. Total Amount: € 400 000,00.

2016/2019: Brain Tumours. Coordinator: Cláudia Maria Coelho de Faria. Funding Agency: Fundação Millennium BCP. Reference: Millenium BTT. Amount: € 90 000,00. Total Amount: € 90 000,00.

2015/2020: IL7SigNeTure: IL-7/IL-7R signaling networks in health and malignancy. Coordinator: João Pedro Tabora Barata. Funding Agency: European Commission. Reference: ERC CoG 648455. Amount: € 1 988 125,00. Total Amount: € 1 988 125,00.

2015/2017: Selective death using a microRNA-detector system in T-cell acute lymphoblastic leukemia. Coordinator: Ana Rita Freitas Martins de Matos Fragoso. Funding Agency: Liga Portuguesa Contra o Cancro – Terry Fox Foundation. Reference: Terry Fox – Ana Rita Fragoso. Amount: € 15 000,00. Total Amount: € 15 000,00.

2014/2018: Development of new therapeutic strategies in Acute Leukemia. Coordinator: Ana Rita Freitas Martins de Matos Fragoso. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00788/2013. Amount: € 50 000,00. Total Amount: € 50 000,00.

2011/2020: Research into brain tumors. Coordinator: Cláudia Maria Coelho de Faria. Funding Agency: Clientes Diversos. Reference: BTT. Amount: € 213 993,00. Total € 213 993,00.

### **Other Projects**

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

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

### **Publications in Peer Review Journals**

Ribeiro ST, Barata JT\*, Silva-Santos B\* (\*co-corresponding authors) (2017). Multifaceted CK2 in malignant and healthy T cells. *Oncotarget* 8 (53): 90622-90623. (Commissioned editorial). (IF: 5.168, Citations:--).

Oliveira ML, Akkapeddi P, Alcobia I, Almeida AR, Cardoso BA, Fragoso R, Serafim TL, Barata JT (2017). From the outside, from within: Biological and therapeutic relevance of signal transduction in T-cell acute lymphoblastic leukemia. *Cellular Signalling* 38: 10-25. (Commissioned review) (IF: 3.937, Citations: 2).

Silva SL, Albuquerque AS, Matoso P, Charmeteau-de-Muylder B, Cheynier R, Ligeiro D, Abecasis M, Anjos R, Barata JT, Victorino RM, Sousa AE (2017). IL-7-Induced Proliferation of Human Naive CD4 T-Cells Relies on Continued Thymic Activity. *Frontiers in Immunology* 8: 20. (IF: 6.429 Citations: 2).

Ribeiro ST, Tesio M, Ribot JC, Macintyre E, Barata JT, Silva-Santos B (2017). Casein Kinase 2 controls the survival of normal thymic and leukemic gamma-delta T-cells via promotion of AKT signaling. *Leukemia* 31 (7): 1603-1610. (IF: 11.702, Citations: 2).

Cavalli FMG, Remke M, Rampasek L, Peacock J, Shih DJH, Luu B, Garzia L, Torchia J, Nor C, Morrissy AS, Agnihotri S, Thompson YY, Kuzan-Fischer CM, Farooq H, Isaev K, Daniels C, Cho BK, Kim SK, Wang KC, Lee JY, Grajkowska WA, Perek-Polnik M, Vasiljevic A, Faure-Conter C, Jouvett A, Giannini C, Nageswara Rao AA, Li KKW, Ng HK, Eberhart CG, Pollack IF, Hamilton RL, Gillespie GY, Olson JM, Leary S, Weiss WA, Lach B, Chambless LB, Thompson RC, Cooper MK, Vibhakar R, Hauser P, van Veelen MC, Kros JM, French PJ, Ra YS, Kumabe T, López-Aguilar E, Zitterbart K, Sterba J, Finocchiaro G, Massimino M, Van Meir EG, Osuka S, Shofuda T, Klekner A, Zollo M, Leonard JR, Rubin JB, Jabado N, Albrecht S, Mora J, Van Meter TE, Jung S, Moore AS, Hallahan AR, Chan JA, Tirapelli DPC, Carlotti CG, Fouladi M, Pimentel J, Faria CC, Saad AG, Massimi L, Liao LM, Wheeler H, Nakamura H, Elbabaa SK, Perezpeña-Diazconti M, Chico Ponce de León F, Robinson S, Zapotocky M, Lassaletta A, Huang A, Hawkins CE, Tabori U, Bouffet E, Bartels U, Dirks PB, Rutka JT, Bader GD, Reimand J, Goldenberg A, Ramaswamy V, Taylor MD (2017). Intertumoral Heterogeneity within Medulloblastoma Subgroups. *Cancer Cell* 31 (6):737-754. (IF: 27.407, Citations: 18).

Ermini L, Morganti E, Post A, Yeganeh B, Caniggia I, Leadley M, Faria CC, Rutka JT, Post M (2017) Imaging mass spectrometry identifies prognostic ganglioside species in rodent intracranial transplants of glioma and medulloblastoma. *PLoS One* 12(5):e0176254. (IF: 2.806, Citations: 1).

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

Barata JT. Twists and turns of IL-7/IL-7R-mediated signaling in T-ALL. T-ALL Workshop, Leuven, Belgium, March 17-19, 2017.

Barata JT. Too much of a good thing: IL-7R-mediated signaling and T-cell leukemia. GABBA Symposium: T lymphocyte activation, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, March 31, 2017.

Fragoso R. Selective death using a microRNA-detector system in T-ALL acute lymphoblastic leukemia. II Jornadas de Investigação em Oncologia em Portugal LPCC-NRS 2017, Lisbon, Portugal, April 6, 2017.

### **Communications in International Conferences**

Ribeiro D, Lopes I, Custódia C, Silva J, Abreu M, Barata JT. IL-7 Flexibly Regulates Autophagy-dependent Viability of T-cell Acute Lymphoblastic Leukemia Cells. T-ALL Workshop, Leuven, Belgium, March 17-19, 2017. (Poster Presentation).

Pinto I, Lobato M, Barata JT, Fragoso R. A Dual Role of NRARP in T-cell Acute Lymphoblastic Leukemia Pathogenesis. T-ALL Workshop, Leuven, Belgium, March 17-19, 2017. (Poster Presentation).

Fragoso R, Gírio A, Cardoso BA, Martins LR, Bortolini A, Correia NC, Grosso AR, Yunes JA, Pflumio F, Barata JT. Involvement of CASZ1 in T-cell acute lymphoblastic leukemia. YoungEHA Research Meeting on Molecular Aspects of Hematological Disorders, Madrid, Spain, June 22, 2017. (Oral Presentation).

Ribeiro D, Lopes I, Custódia C, Silva J, Abreu M, Barata JT. IL-7 Flexibly Regulates Autophagy-dependent Viability of T-cell Acute Lymphoblastic Leukemia Cells. 22<sup>nd</sup> Congress of the European Hematology Association, Madrid, Spain, June 22-25, 2017. (Poster Presentation).

Pinto I, Oliveira ML, Barata JT, Fragoso R. Regulation of NOTCH and WNT signaling pathways by NRARP in T-cell acute lymphoblastic leukemia. 22<sup>nd</sup> Congress of the European Hematology Association, Madrid, Spain, June 22-25, 2017. (Poster Presentation).

Oliveira ML, Garcia EG, Langenau DM, Barata JT. Oncogenic IL-7 receptor cooperates with Myc and activated Notch to accelerate T-cell leukemogenesis in zebrafish. Conferência ZDM10 da Zebrafish Disease Models Society, San Diego, USA, August 5-8, 2017. (Poster Presentation).

Loontjens S, Durinck K, Van de Walle I, Moore FE, Vanhauwaert S, Janssens E, Dewyn G, Depestel L, Oliveira ML, Barata JT, Langenau DM, Van Vlierberghe P, Taghon T, Speleman F. Scrutinizing PHF6 regulatory networks in T-ALL and normal hematopoiesis using zebrafish. ZDM10 Conference of the Zebrafish Disease Models Society, San Diego, USA, Agosto 5-8, 2017. (Poster Presentation).

### **Communications in National Conferences**

Faria C, Custódia C, Barata JT. Patient-derived xenografts of brain metastases – a tool for translational medicine. NEURO 2017, Congresso Nacional das Sociedades Portuguesas de Neurocirurgia e Neurologia, Madeira, Portugal, June 1-3, 2017. (Oral Presentation).

Gírio A, Cardoso BA, Fragoso R, Martins LR, Correia NC, Grosso AR, Bortolini A, Yunes JA, Pflumio F, Barata JT. CASZ1 is overexpressed in T-cell acute lymphoblastic leukemia and promotes cell transformation via MEK/Erk and PI3K signaling. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017. (Oral Presentation).

Oliveira ML, Gomes AM, Martins LR, Duarte J, Barata JT. STAT5 activation associates with high risk and poor prognosis in pediatric B-cell acute lymphoblastic leukemia. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017. (Poster Presentation).

Ribeiro D, Lopes I, Custódia C, Silva J, Abreu M, Barata JT. IL-7 Flexibly Regulates Autophagy-dependent Viability of T-cell Acute Lymphoblastic Leukemia Cells. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017. (Poster Presentation).

Pinto I, Duque M, Oliveira M, Cabrita R, Barata JT, Fragoso R. Regulation of NOTCH and WNT signaling pathways by NRARP in T-cell acute lymphoblastic leukemia. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017. (Oral Presentation).

Custódia C, Paisana E, Cascão R, Barata JT, Faria C. An intracardiac patient-derived xenograft model of brain metástases. X NeuroOncologia, Congresso Nacional da Associação Portuguesa de Neuro-Oncologia, Braga, Portugal, November 10-11, 2017. (Poster Presentation).

Duque T, Linheiro R, Barata JT, Fragoso R. Definition of a T-ALL-specific microRNA expression profile. Research Day for Medical Students/20<sup>th</sup> Workshop “Education through Science”, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 13, 2017. (Poster Presentation).

### **Organisation of Conferences**

Fragoso R. Participation at the speed-meeting event during the Jornadas Tecnológicas (JorTec 2017), Faculty of Sciences and Technology, Nova University of Lisbon, Costa da Caparica, Portugal, February 7, 2017.

Barata JT. Member of the evaluation panel of Oral Sessions VI and VII. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017.

Barata JT. Organizer (with François Radvanyi). ReTuBi Twinning Network 2017 Summer School, Oceanário de Lisboa, Lisbon, Portugal, May 29-31, 2017.

Barata JT. Organizer (with Peter Jordan, Duarte Barral and François Radvanyi) and co-Chair (with Alexandre do Carmo) of Session 2. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017.

Barata JT. Chair, Basic-Science-in-Focus session on: Mouse models of acute leukemia (Sunday, 25 June). 22<sup>nd</sup> Congress of the European Hematology Association, Madrid, Spain, June 22-25, 2017.

Barata JT. Organizer (with Iñaki Martin-Subero and Juan Bueren). YoungEHA Research Meeting on Molecular Aspects of Hematological Disorders, Madrid, Spain, June 22, 2017.

Faria C. Organizer. 10<sup>th</sup> Annual Meeting of the Portuguese Neuro-Oncology Society. Hospital de Braga, Braga, Portugal, November 10-11, 2017.

Fragoso R. Member of the evaluation panels of the Poster Session III and Oral Communication Session. Research Day for Medical Students/20<sup>th</sup> Workshop “Education through Science”, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 13, 2017.

Fragoso R. Moderator of the oral communication session. Research Day for Medical Students/20<sup>th</sup> Workshop “Education through Science”, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 13, 2017.

Faria C. Organizer (with Ana Espada de Sousa, Susana Fernandes and Ricardo Fernandes). Research Day for Medical Students/20<sup>th</sup> Workshop “Education through Science”, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 13, 2017.

### **Internationalisation**

Our projects regularly involve collaborations with international research groups in Europe, USA and Brazil. Current international collaborators in the leukemia projects include: Alberto Martelli (University of Bologna, Italy), Ben Seddon (UCL, England), David Langenau (MGH, Harvard University, USA), Doreen Cantrell (University of Dundee, Scotland), Nigel Pyne (University of Strathclyde, England), Paul Coffey (Utrecht UMC, The Netherlands), Scott Durum (NCI, USA), Silvio Perea (CIGB, Cuba).



Current international collaborators in the brain tumor projects include: Michael D. Taylor (University of Toronto, Canada), James T. Rutka (University of Toronto, Canada) and Marc Remke (University of Dusseldorf, Germany).

In addition, we are executing an FCT-FAPESP collaborative project grant with a Brazilian research group from the state of São Paulo - Andres Yunes (Centro Infantil Boldrini, Brazil).

Barata JT co-organized the YoungEHA Research Meeting on Molecular Aspects of Hematological Disorders for the European Hematology Association.

Barata JT is involved in the international project H2020-TWINN-2015 - ReTuBi “Towards outstanding research and training in tumour biology”, as task leader. This project promotes interactions between different groups working on diverse areas of Cancer Research from IMM, Institut Curie (France) and DKFZ (Germany).

Faria C participates in international consortia for the study of the most common pediatric brain tumors: MAGIC – Medulloblastoma Advanced Genomics International Consortium; GENE – Global Ependymoma Network of Excellence.

Faria C is the Chair of the Young Investigators and Innovators Group of the International Society of Pediatric Oncology – Europe (SIOP-E) Brain Tumor Group (BTG) since September 2017.

### **Prizes, Honours and Awards**

Faria C. Codman Award – Best oral presentation. Congress of the Portuguese Neurosurgical Society (NEURO2017).

Ribeiro D. Travel award. 22<sup>nd</sup> Congress of the European Hematology Association, Madrid, Spain, June 22-25, 2017.

Oliveira ML. Travel award. ZDM10 Conference organized by the Zebrafish Disease Models Society, San Diego, USA, August 5-8, 2017.

### **Patents/Prototypes**

“Identification of alsterpaullone as a novel small molecule inhibitor to target group 3 medulloblastoma– RDLP#994” (Faria C co-inventor with Dr. James Rutka).

### **Advanced Teaching**

Faria C taught at the session “bridging the gap”. LisbonBioMed International FCT PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 12, 2017.

Barata JT coordinated (together with Sérgio Dias and Gonçalo Bernardes) and taught at the “Tissues and Tumors” week. LisbonBioMed International FCT PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 16-20, 2017.

Almeida A taught the topic “T cell Homeostasis” at the GABBA PhD program from University of Porto, Porto, Portugal, March 23, 2017.

Almeida A taught the topics “T Cell immunology” and “Innate Cell immunology” at the PGCD: Programa de Pós-Graduação Ciência para o Desenvolvimento, International Postgraduate course, Cidade da Praia, Cabo Verde, June 5-10, 2017.

Barata JT taught the topic “Signaling in Cancer” at the Advanced Course on “Fundamentals of Genetics, Development and Neoplasia”, International Postgraduate Programme, School of Health Sciences, University of Minho, Braga, Portugal, October 25, 2017.

### **Science and Society**

Faria C presented the seminar “Drug discovery through genomics in medulloblastoma – how a neurosurgeon can treat patients in the lab” in 8<sup>th</sup> Annual International Medical Students Meeting, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 10, 2017.

The lab joined the Brain Tumor Team (BTT) on 7<sup>th</sup> of May to participate in a run/walk event to create awareness for cancer research and, particularly, for brain tumor research.

The BTT gathered health care professionals, scientists, patients and their families aiming to support cancer research and to create hope for the future of patients affected with brain cancer.

The lab participated in the European Researchers’ Night, September 29, presenting the interactive exhibition “Novas Terapêuticas no Tratamento da Leucemia”.

The lab participated in the event “Oncology: Talking with Scientists”, specially dedicated to the Portuguese cancer patient associations and promoted by the ReTuBi project in partnership with Instituto de Medicina Molecular João Lobo Antunes and Fundo IMM-Laço.

Alcobia I and Fragoso R presented "The Biology of Cancer in one hour" ReTuBi School Seminars, for high school students, in Rainha D. Amélia and Dona Leonor schools, respectively.

### **MSc Thesis Completed**

Inês Pinto, 17/04/2017, “The role of NRARP in the pathogenesis of T-cell Acute Lymphoblastic Leukemia”, Faculty of Medicine, University of Lisbon. Supervisor: Rita Fragoso and João T. Barata.

Mafalda Duque, 29/11/2017, “The role of NRARP and its therapeutic potential in T-cell Acute Lymphoblastic Leukemia”, Instituto Superior Técnico, University of Lisbon. Supervisor: Rita Fragoso.

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## Bernardes, Gonçalo J. L.

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### Major Interests / Objectives

At GBernardes Lab, we work at the interface of Chemistry & Biology. At the core of our research program is the development of novel chemoselective methods that are compatible with biological systems, and their use to redesign the structure & function of proteins of biological & therapeutic interest, with the intention of understanding & influencing human disease. In the area of synthetic biology, we are mostly interested in the specific delivery of toxic molecules to cancer cells and in the construction of homogenous glycoproteins as vaccines candidates. We are also investigating the delivery of therapeutic amounts of CO to diseased tissues, using CO-releasing molecules that have the potential to become safe treatments, by controlling CO release in vivo in a spatial and temporal manner.

### Head of Laboratory

Gonçalo José Lopes Bernardes, PhD, Assistant Professor

### Research Team

Ana Maria dos Santos Guerreiro	Master	PhD Student (Started April)
Annabel Katharina Kitowski	Master	PhD Student
Bárbara Beatriz da Costa Botelho Sousa	Graduate	MSc Student (Started September)
Carlos Diogo Labão Alpiarça Sousa de Almeida	Master	PhD Student
Charlotte Louise Baker	Master	PhD Student
Florian Sieglitz	PhD	Post-Doctoral Investigator (Left December)
João Daniel da Silva Seixas	PhD	Post-Doctoral Investigator
João Diogo Osorio de Castro Conde	PhD	Post-Doctoral Investigator (Started October)
Maria Inês Sousa de Albuquerque	Master	Investigator
Marta Franco Coimbra Marques	PhD	Post-Doctoral Investigator
Padma Akkapeddi	Master	PhD Student
Pedro Miguel Saraiva Duarte Cal	PhD	Post-Doctoral Investigator, Faculdade Farmácia da Universidade de Lisboa
Pedro Ricardo Morgado Henriques	Master	PhD Student
Roberto Russo	Master	PhD Student
Rui Traquete	Master	PhD Student
Susana André Lima Lobo	PhD	Post-Doctoral Investigator (Left March)
Tiago Correia de Oliveira Rodrigues	PhD	Investigator, Faculdade Farmácia da Universidade de Lisboa, Assistant Professor

### Laboratory Keywords / Research Areas

Site-selective protein modification, Synthetic biologics, Targeted cancer therapeutics, Carbohydrate-based vaccines.

### Selected Publications

Jiménez-Moreno E, Guo Z, Oliveira BL, Albuquerque IS, Kitowski A, Guerreiro A, Boutureira O, Rodrigues T, Jiménez-Osés G, Bernardes GJL (2017). Vinyl ether–tetrazine pair for the traceless release of alcohols in cells. *Angew Chem*, 56, 243-247. (IF: 11.994, Citations: 7).

Oliveira BL, Guo Z, Boutureira O, Guerreiro A, Jiménez-Osés G, Bernardes GJL (2016). A minimal, unstrained S-allyl handle for pre-targeting Diels–Alder bioorthogonal labelling in live cells. *Angew. Chem. Int. Ed*, 55, 14683–14687. (IF: 11.994, Citations: 3).

Krall N, da Cruz FP, Boutureira O, Bernardes GJL (2016). Site-selective protein-modification chemistry for basic biology and drug development. *Nature Chemistry* 8, 103. (IF: 25.870, Citations: 14). Highlighted in *Nature Chem.* 2016, 8, 91: A little less conjugation, a little more accuracy.

Bernardim B, Cal PMSD, Matos MJ, Oliveira BL, Martínez-Sáez N, Albuquerque IS, Corzana F, Burtoloso ACB, Jiménez-Osés G, Bernardes GJL (2016). Stoichiometric and Irreversible Cysteine-selective Protein Modification using Carbonylacrylic Reagents. *Nature Communications*, 7. (IF: 12.124, Citations: 8).

Rodrigues T, Sieglitz F, Somovilla VJ, Cal PMSD, Galione A, Corzana F, Bernardes GJL (2016). Unveiling (-)-Englerin A as a modulator of L-type calcium channels. *Angew. Chem. Int. Ed.*, 55. (IF: 11.994, Citations: 3).

### Ongoing Research Projects

2017/2019: TRPLigDrugConj: TRPV1-targeted ligand-drug conjugates to treat prostate cancer. Coordinator: Tiago Correia de Oliveira Rodrigues. Funding Agency: European Commission. Reference: MSCA IF 743640. Amount: € 160 635,60. Total Amount: € 160 635,60.

2016/2019: Unravelling Bronic Acids Bioconjugation and Targeted Delivery. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-QOR/1434/2014. Amount: € 20 000,00. Total Amount: € 195 060,00.

2016/2018: LDC4PCaTher: BMX-Targeted Ligand-Drug Conjugates for Prostate Cancer Therapy. Coordinator: João Daniel da Silva Seixas. Funding Agency: European Commission. Reference: MSCA IF 702428. Amount: € 160 635,60. Total Amount: € 160 635,60.

2016/2018: Molecular Imaging Techniques of Liver Fibrosis. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: HMSP-ICT/0012/2013. Amount: € 142 300,00. Total Amount: € 142 300,00.

2015/2019: GLYCOVAX: A training network for the rational design of the next generation of well-defined glycoconjugate vaccines. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: European Commission. Reference: MSCA ITN 675671. Amount: € 238 356,36. Total Amount: € 3 554 499,69.

2015/2019: ProteinConjugates: A training network for the chemical site-selective modification of proteins: Preparation of the next-generation of therapeutic chemically-defined protein conjugates. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: European Commission. Reference: MSCA ITN 675007. Amount: € 741 939,48. Total Amount: € 2 542 771,03.

2014/2018: PerBiolmag: Exploring pericyclic reactions for bioorthogonal imaging of biological. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: European Commission. Reference: MSCA CIG 630731. Amount: € 100 000,00. Total Amount: € 100 000,00.

2014/2018: Modulation and targeting of calcium channels with ligand-drugs conjugates for selective cancer cell killing. Coordinator: Gonçalo José Lopes Bernardes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00014/2012. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

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

### Publications in Peer Review Journals

Freedy AM, Matos MJ, Omar Boutureira O, Corzana F, Guerreiro A, Somovilla VJ, Rodrigues T, Nicholls K, Xie B, Jiménez-Osés G, Brindle KM, Neves AA, Bernardes GJL (2017). Chemoselective Installation of Amine Bonds on Proteins through Aza-Michael Ligation. *J. Am. Chem. Soc.* 2017, 139, 18365–18375. (IF: 13,858, Citations:--).

Bertoldo JB, Rodrigues T, Dunsmore L, Aprile FA, Marques MC, Rosado L, Boutureira O, Steinbrecher TB, Sherman W, Corzana F, Terenzi H, Bernardes GJL (2017). Post-expression regioselective mutagenesis reveals a water-bridged cysteine–cysteine redox regulation mechanism in bacterial protein tyrosine phosphatases. *Chem (Cell Press)* 2017, 3, 665–677. (IF: --, Citations: 1).

Martínez-Sáez N, Shuang S, Oldrini D, Sormanni P, Boutureira O, Carboni F, Compañón I, Deery MJ, Vendruscolo M, Corzana F, Adamo R, Bernardes GJL (2017). Oxetane grafts site-selectively installed on native disulfides enhance protein stability and activity in vivo. *Angew. Chem. Int. Ed.* 2017, 47, 14963–14967. (IF: 11.994; Citations:--).

Kitowski A, Jiménez-Moreno E, Salvadó M, Mestre J, Castellón S, Jiménez-Osés G, Boutureira O, Bernardes GJL (2017). Oxidative Activation of C–S Bonds with an Electropositive Nitrogen Promoter Enables Orthogonal Glycosylation of Alkyl over Phenyl Thioglycosides. *Org. Lett.* 2017, 19, 5490-5493. (IF: 6.579, Citations:--).

Li R, Rajan R, Wong WCV, Reid DG, Duer MJ, Somovilla VJ, Martinez-Saez N, Bernardes GJL, Hayward R, Shanahan M (2017). In situ characterization of advanced glycation end products (AGEs) in collagen and model extracellular matrix by solid state NMR. *Chem. Commun.* 2017, 100, 13275–13380. (IF: 6.319; Citations:--).

Alcock LJ, Farrell KD, Akol MT, Jones GH, Tierney MM, Kramer HB, Pukala TL, Bernardes GJL, Perkins MV, Chalker JM (2017). Norbornene probes for the study of cysteine oxidation. *Tetrahedron.* (IF: 2.651; Citations: 1).

Kim WG, Kang ME, Lee JB, Jeon MH, Lee S, Lee J, Choi B, Cal PMSD, Kang S, Kee Jung-Min, Bernardes GJL, Rohde Jan-Uwe, Choe W, Hong SY (2017). Nickel-Catalyzed Azide–Alkyne Cycloaddition to Access 1,5-Disubstituted 1,2,3-Triazoles in Air and Water. *J. Am. Chem. Soc.* 2017, 139, 12121–12124. (IF: 13.858, Citations: 3).

Worthington MJH, Kucera RL, Albuquerque IS, Gibson CT, Sibley A, Slattery AD, Campbell JA, Alboaiji SFK, Muller KA, Young J, Adamson N, Gascooke JR, Jampaiah D, Sabri YM, Bhargava SK, Ippolito SJ, Lewis DA, Quinton JS, Ellis AV, Johs A, Bernardes GJL, Chalker JM (2017). Laying Waste to Mercury: Inexpensive Sorbents Made from Sulfur and Recycled Cooking Oils. *Chem. Eur. J.* 2017, 23, 16219–16230. (IF: 5.317, Citations: 2).

Oliveira BL, Guo Z, Bernardes GJL (2017). Inverse electron demand Diels–Alder reactions in chemical biology. *Chem. Soc. Rev.* 2017, 46, 4811–5174. (IF: 38.618, Citations: 6).

Boutureira O, Martínez-Sáez N, Brindle KM, Neves AA, Corzana F, Bernardes GJL (2017). Site-selective modification of proteins with oxetanes. *Chem. Eur. J.* 2017, 23, 6483–6489. (IF: 5.317, Citations: 2).

Kwan TT-L, Boutureira O, Frye EC, Gupta MK, Wallace S, Wu Y, Zhang F, Sore HF, Galloway WRJD, Chin JW, Welch M, Bernardes GJL\*, Spring DR (2017). Protein modification via alkyne hydrosilylation using a substoichiometric amount of ruthenium (II) catalyst. *Chem. Sci.* 2017, 8, 3871–3878. (IF: 8.668, Citations 1).

Pereira MMA, Mahú I, Seixas E, Martínéz-Sánchez N, Kubasova N, Pirzgalska RM, Cohen P, López M, Bernardes GJL\*, Domingos AI\* (\*co-senior authors) (2017). A brain-sparing diphtheria toxin for chemical genetic ablation of peripheral cell lineages. *Nature Communications* 2017, 8, 14967. (IF:12.124, Citations: 1).

Cal PMSD, Sieglitz F, Santos FMF, Carvalho CP, Guerreiro A, Bertoldo JB, Pischel U, Gois PMP, Bernardes GJL (2017). Site-selective installation of BASHY fluorescent dyes to Annexin V for targeted detection of apoptotic cells. *Chem. Commun.* 2017, 53, 368-371. (IF:6.319, Citations: 1).

Cal PMSD, Matos MJ, Bernardes GJL (2017). Trends in therapeutic drug conjugates for bacterial diseases: a patent review. *Expert Opin. Ther. Pat.* 2016, 27, 179–189. (IF:3.041, Citations: 2)

### Invited Lectures and Seminars

Bernardes GJL. CICbioGUNE, Bilbao, Spain, January 2017. Host: Prof. Jesús Jiménez-Barbero.

Bernardes GJL. i3S – Instituto de Investigação e Inovação em Saúde, University of Porto, Portugal, January 2017.



Bernardes GJL. RSC Harrison-Meldola Memorial Prize Lecture, School of Chemistry, University College Dublin, Dublin, Ireland, January 2017.

Bernardes GJL. RSC Harrison-Meldola Memorial Prize Lecture, School of Chemistry, University of St. Andrews, St. Andrews, Scotland, January 2017.

Bernardes GJL. Seattle Genetics, Seattle, USA, March 2017. Host: Dr. Peter Senter.

Bernardes GJL. Institute for Protein Design, University of Washington, USA, March 2017. Host: Prof. David Baker.

Bernardes GJL. Champalimaud Foundation, Lisbon, Portugal, March 2017.

Bernardes GJL. Lecture tour in Australia – Flinders University, Adelaide University and The University of Sydney, Australia, April 2017.

Bernardes GJL. 253<sup>rd</sup> ACS National Meeting and Exposition, San Francisco, USA, April 2017.

Bernardes GJL. Genentech Inc., San Francisco, USA, April 2017. Host: Dr. Thomas Pillow.

Bernardes GJL. Department of Biochemistry, University of Oxford, Oxford, England, May 2017.

Bernardes GJL. University of Barcelona's doctoral program Organic Chemistry, Barcelona, Spain, May 2017.

Bernardes GJL. Max-Planck-Institut für Molekulare Physiologie, Dortmund, Germany, June 2017. Host: Prof. Herbert Waldmann.

Bernardes GJL. 6<sup>a</sup> Reunião Anual da SBBq, Águas e Lindóia, Brazil, July 2017.

Bernardes GJL. Weill Cornell Medicine, New York, USA, August 2017. Host: Dean Prof. Augustine Choi.

Bernardes GJL. 18<sup>th</sup> International Conference on Biological Inorganic Chemistry, Florianópolis, Brazil, August 2017.

Bernardes GJL. Max-Planck Institute for Polymer Research, Mainz, Germany, September 2017. Host: Prof. Tanja Weil.

Bernardes GJL. CeMM – Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria, November 2017. Host: Prof. Giulio Superti-Furga.

Bernardes GJL. 2<sup>nd</sup> Joint NSFC-RSC Symposium on Chemical Biology, London, England, December 2017.

Bernardes GJL. MedImmune, Granta Park, Cambridge, England, December 2017. Host: Dr Peter Ravn.

#### **Communications in International Conferences**

Seixas J. Development of BMX-targeted small molecule drug conjugates for prostate cancer therapy. EFMC International Symposium on Advances in Synthetic and Medicinal Chemistry, Vienna, Austria, August 27-31, 2017. (Poster Presentation).

Rodrigues T. Network polypharmacology of anticancer natural products. SBDD2017, Lusanne, Switzerland, September 6, 2017. (Oral Presentation).

#### **Communications in National Conferences**

Russo R. 3HQs as responsive handles for boronic acid bioconjugation. 9<sup>th</sup> iMed.Ulisboa Postgraduate Students Meeting & 2<sup>nd</sup> i3DU Meeting, Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, July 13-14, 2017. (Poster presentation).

Cal P. Chemically Activated Writer – “Click-to-Acetylate” Concept. XXV Encontro Nacional da Sociedade Portuguesa de Química (ENSQP), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, July 16-19, 2017.

Baker C. Selective Cancer Therapy. XXV Encontro Nacional da Sociedade Portuguesa de Química (ENSQP), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, July 16-19, 2017.

Russo R. Development of small molecular cores for boronic acid ligation in peptides. XXV Encontro Nacional da Sociedade Portuguesa de Química (ENSQP), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, July 16-19, 2017. (Poster Presentation).

Marques MC. A water-mediated mechanism of Protein Tyrosine Phosphatase A: how M. tuberculosis copes with oxidative stress. MiniSymposium Looking for new ways to fight tuberculosis, Instituto de Tecnologia Química e Biológica António Xavier, Oeiras, Portugal, November 30, 2017.

Russo R. Bioconjugation of boronic acids via a 3Hydroxy-Quinolinones platform. 2<sup>o</sup> Encontro do Colégio de Química da Ulisboa, University of Lisbon, Lisbon, Portugal, December 4 -5, 2017. (Flash Oral Presentation).

### **Organisation of Conferences**

Bernardes GJL. Organizer and lecturer. Glicovax 2<sup>nd</sup> Workshop and 1<sup>st</sup> Symposium under the theme Novel Approaches for Glycoconjugation, Lisbon, Portugal, March 2017.

### **Prizes, Honours and Awards**

Bernardes GJL. RSC Harrison-Meldola Memorial Prize Lecture.

### **Advanced Teaching**

Bernardes GJL. Supervisor of biological chemistry courses at Trinity Hall College, Cambridge, England.

Bernardes GJL. Responsible for Part III course Internal Examiner, University of Cambridge, England.

Bernardes GJL. Lecturer on Chemical Biology & Drug Discovery - Undergraduate course, University of Cambridge, England.

Bernardes GJL. Supervisor of biological chemistry courses at Peterhouse College, Cambridge, England.

Bernardes GJL. Lecturer on Chemical Biology of Nucleic Acids - Undergraduate course, University of Cambridge, England.

Bernardes GJL. Lecturer on Anti-Cancer Targeted Therapeutics - Graduate course, University of Cambridge, England.

Bernardes GJL. Lecturer on Chemical Biology of cancer- LisbonBioMed PhD Programme, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal.

### **Science and Society**

Bernardes GJL. Lecturer. Chemical Physiology: Towards Precision Medicine. Rotary Club, Torres Vedras and Lisbon, Portugal, 2017.

Bernardes GJL. Organizer. GLICOVAX Training Event II "Novel approaches for glycoconjugation", Lisbon, Portugal, March 2017.

Seixas J, Marques M, Albuquerque I, Kitowski A, Guerreiro A. Demonstration on chemical biology at the European Researchers' Night, Lisbon, Portugal, September 29, 2017.

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## Carmo-Fonseca, Maria

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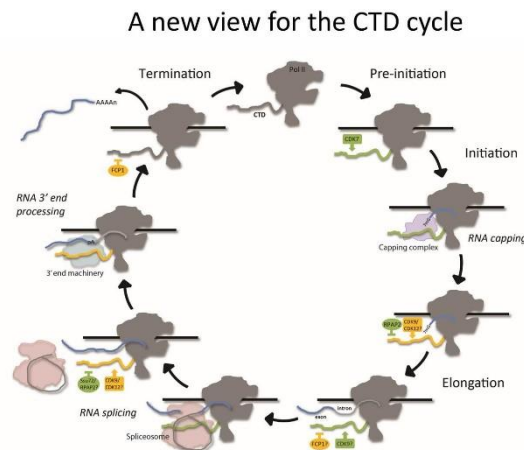
### Major Interests / Objectives

Gene regulation is central to all biology. RNA molecules, with their ability to both encode information and exert catalytic activities, play a key role in the regulation of gene expression. Our group aims to discover molecular pathways and mechanisms implicating RNA in human health and disease. More specifically, we study RNA splicing and its role in the regulation of gene expression in cancer and genetic diseases, and we are exploring new medical applications for RNA.

### Head of Laboratory

Maria do Carmo Salazar Velez Roque da Fonseca, MD/PhD, Full Professor

### Graphical Abstract



### Research Team

Ana Beatriz Domingues Silva	Graduate	MSc Student (Started May)
Ana Cláudia Bernardino Raposo Alves	Master	Technician
Ana Cláudia Dourado Clemente	Master	Consultant
Ana Sofia Temudo Duarte António	Master	Investigator
António Duarte Zapico Bicho de Sousa Franco	Master	MSc Student (Left May)
Bruno Miguel Bernardes de Jesus	PhD	Investigator
Carla Marina Pereira Gomes	Master	Investigator
Catarina Alves do Vale	Graduate	Trainee
Célia Carvalho	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor

Christian Gomes da Silva Ramos	PhD	Post-Doctoral Investigator (Started September)
Cristiano Emanuel Ribeiro Esteves	Undergraduate	Undergraduate (Started February)
Dinora Levy	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa
Domenico Aprile	Graduate	Trainee (Started February/Left July)
Evguenia Pavlovna Bekman	PhD	Investigator, ISCSEM, Assistant Professor
Inês Filipa Banha Godinho	Graduate	MSc Student (Started September)
Joana Desterro	MD/PhD	Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
João Paulo Von Gilsa Lopes	Graduate	MSc Student (Left May)
João Pedro Abreu Pessoa	PhD	Post-Doctoral Investigator (Left November)
José António Branco de Albuquerque	Master	Technician, Faculdade Medicina da Universidade de Lisboa, Technician (Left October)
Kenny Patrick Figueira Rebelo	Graduate	MSc Student
Maria João de Andrade Terras Arez	Graduate	MSc Student (Started August)
Mariana Isabel Lopes Joaquim	Graduate	MSc Student (Left October)
Marta de Jesus Ribeiro	Master	PhD Student (Started September)
Marta Patricia Ribeiro Ferreira	Master	Trainee (Started March/Left October)
Miguel Torres Santana	Graduate	Trainee
Noélia Maria Fernandes Custódio	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Pedro António Pereira Prudêncio	Master	PhD Student
Pedro Santos Barbosa	Master	Investigator (Started September)
Rita Catarina Vaz Drago	Master	PhD Student
Rita Mingot de Almeida Mendes de Almeida	Master	PhD Student
Rodrigo Paiva Gonçalves	Graduate	Trainee
Rui Gonçalo Viegas Russo da Conceição Martinho	PhD	Visiting Researcher
Rui Sérgio de Sousa Luís	Graduate	MSc Student (Started September)
Sandra Martins	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Sérgio Manuel Pires Marinho	Graduate	Technician, Faculdade Medicina da Universidade de Lisboa
Simão José Teixeira da Rocha	PhD	Investigator
Teresa Carvalho	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Teresa Maria Pereira da Silva	Master	PhD Student, Superior Técnico

### Laboratory Keywords / Research Areas

Cell biology, Genomics, RNA splicing, RNA in disease.

## Major Scientific Achievements

Many individual steps in gene expression are kinetically coupled, but how temporal relationships between chemical reactions contribute to the output of the final gene product is still poorly understood. We have investigated the effect of pharmacological splicing inhibitors on mRNA processing and showed that a set of potential anti-cancer drugs affect the stability and transport of mRNAs (Carvalho et al 2017). In collaboration with the Proudfoot lab in Oxford, we have pioneered genome-wide analysis of nascent RNA complexes and we are unraveling unanticipated dynamic links between Pol II and RNA processing during biogenesis of protein coding pre-mRNAs and non-coding RNAs (Schlackow et al 2017). We are also studying how genetic variation affects pre-mRNA splicing and contributes to human disease. In particular, we are interested in the identification of pathogenic variants located deep within introns (Vaz-Drago et al 2017; de Almeida et al 2017).

## Selected Publications

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*. (IF: 30.41, Citations: 131).

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*. (IF: 8.282, Citations: 70).

de Almeida SF, Grosso AR, Koch F, Fenouil R, Carvalho S, Andrade J, Levezinho H, Gut M, Eick D, Gut I, Andrau JC, Ferrier P, Carmo-Fonseca M (2011). Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36. *Nature Struct. Mol. Biol.* (IF: 12.595, Citations: 175).

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 Struct. Mol. Biol.* (IF: 12.595, Citations: 62).

Grosso AR, Gomes AQ, Barbosa-Morais NL, Caldeira S, Thorne NP, Grech G, von Lindern M, Carmo-Fonseca M (2008). Tissue-specific splicing factor gene expression signatures. *Nucleic Acids Research*. (IF: 10.162, Citations: 116).

### Ongoing Research Projects

2017/2024: The Discoveries CTR: Implementation of the discoveries centre for regenerative and precision medicine, a new centre of excellence in Portugal. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Funding Agency: European Commission. Reference: Teaming 739572. Amount: € 1 001 137,50 (Lisbon University). Total Amount: € 14 996 606,25.

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

2016/2019: The non-coding transcriptome in stemness and aging. Coordinator: Bruno Miguel Bernardes de Jesus. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MED/0032/2014. Amount: € 188 175,00. Total Amount: € 188 175,00.

2016/2019: Molecular constraints to pre-mRNA splicing in fast dividing cells. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BID/0395/2014. Amount: € 98 888,00. Total Amount: € 198 831,00.

2016/2019: Making sense of antisense transcription. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BCM/5899/2014. Amount: € 200 000,00. Total Amount: € 200 000,00.

2016/2019: Comprehensive study of the dynamics of epigenetic processes involving lncRNAs during iPSC reprogramming. Coordinator: Simão José Teixeira da Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BEX-BCM/2612/2014. Amount: € 157 880,00. Total Amount: € 157 880,00.

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

2016/2017: Pesquisa de mutações nos genes IDH. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Funding Agency: Celgene Sociedade Unip., Lda. Reference: Celgene MCFonseca. Amount: € 27 750,00. Total Amount: € 27 750,00.



2015/2020: Exploring the role of lncRNAs and chromatin modifying complexes for the establishment of defined chromatin states. Coordinator: Simão José Teixeira da Rocha. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00242/2014/CP1236/CT0009. Amount: € 50 000,00. Total Amount: € 50 000,00.

2015/2020: The non-coding transcriptome in stemness and aging. Coordinator: Bruno Miguel Bernardes de Jesus. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00166/2014/CP1236/CT0001. Amount: € 49 961,00. Total Amount: € 49 961,00.

2014/2017: Epigenetics and alternative splicing: Role in immune T cell differentiation and leukemogenesis. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FCT-ANR/BIM-ONC/0009/2013. Amount: € 200 000,00. Total Amount: € 409 874,00.

#### **Publications in Peer Review Journals**

Carvalho T, Martins S, Rino J, Marinho S, Carmo-Fonseca M (2017). Pharmacological inhibition of the spliceosome subunit SF3b triggers EJC-independent NMD. *J Cell Sci.* 130 (9): 1519-1531. (IF: 4.431, Citations:--).

Schlackow M, Nojima T, Gomes T, Dhir A, Carmo-Fonseca M, Proudfoot NJ (2017). Distinctive patterns of transcription and RNA processing for human lincRNAs. *Mol Cell* 65 (1): 25-38. (IF: 14.714, Citations: 20).

Vaz-Drago R, Custódio N, Carmo-Fonseca M (2017). Deep intronic mutations and human disease. *Hum Genet* May 12 doi: 10.1007/s00439-017-1809-4. (IF: 4.637, Citations: 1).

Mendes de Almeida R, Tavares J, Martins S, Carvalho T, Enguita FJ, Brito D, Carmo-Fonseca M, Lopes LR (2017). Whole gene sequencing identifies deep-intronic variants with potential functional impact in patients with hypertrophic cardiomyopathy. *Plos One* 12(8):e0182946. (IF: 2.806, Citations:--).

Rino J, de Jesus AC, Carmo-Fonseca M (2017). Quantitative image analysis of single-molecule mRNA dynamics in living cells. *Methods in Molecular Biology*, 1563: 229-242. (IF:--, Citations:--).

Pires VB, Simões R, Mamchaoui K, Carvalho C, Carmo-Fonseca M (2017). Short (16-mer) locked nucleic acid splice-switching oligonucleotides restore dystrophin production in Duchenne Muscular Dystrophy myotubes. *Plos One* 12(7):e0181065. (IF: 2.806, Citations:--).

Sridhara SC, Carvalho S, Grosso AR, Gallego-Paez LM, Carmo-Fonseca M, de Almeida SF (2017). Transcription dynamics prevent RNA-mediated genomic instability through SRPK2-dependent DDX23 phosphorylation. *Cell Reports* 18: 334-343. (IF: 8.282, Citations: 10).

da Rocha ST, Heard E (2017). Novel players in X-inactivation – insights into Xist-mediated silencing and chromosome conformation. *Nature Structural and Molecular Biology* 24:197-204. (IF: 12.595, Citations: 10).

### **Invited Lectures and Seminars**

Carmo-Fonseca M. Stem cells in heart failure. Hipertensão arterial e insuficiência cardíaca – estado da arte, University of Lisbon, Lisbon, Portugal, January 6, 2017.

Carmo-Fonseca M. From medical school to basic gene expression research. Annual meeting of the PhD Program in “Mechanisms of disease and regenerative medicine”, University of Faro, Faro, Portugal, January 9, 2017.

Carmo-Fonseca M. Transcription and splicing in close encounter. Seminarios Severo Ochoa-avances en Biología Molecular. Centro de Biología Molecular Severo Ochoa, Universidad Autónoma de Madrid, Madrid, Spain, February 3, 2017.

Carmo-Fonseca M. Hearts-on-a-chip. “Leading the Heart” Meeting, Bayer, Lisbon, Portugal, March 25, 2017.

Carmo-Fonseca M. Combining live cell microscopy and NET-seq to study co-transcriptional splicing. EMBO course on “iCLIP: genomic views of protein-RNA interactions”. Institute of Molecular Biology, Mainz, Germany, March 29, 2017.

Carmo-Fonseca M. Novel molecular technologies for hematological malignancies. “Leaping Forward” International Clinical Congress, Lisbon, Portugal, May 13, 2017.

Carmo-Fonseca M. Uma viagem pela biologia do cancro do pulmão. AstraZeneca Lung Cancer Summit 2017, Lisbon, Portugal, May 20, 2017.

Carmo-Fonseca M. Medicina de precisão em oncologia: desafios futuros. Lição Ducla Soares, Reunião Anual da Sociedade Portuguesa de Hematologia, Vilamoura, Portugal, November 18, 2017.

Bernardes de Jesus B. Aging barriers in tissue fitness and stemness Invited seminar, Center for Neurosciences of Coimbra, Coimbra, Portugal, November 10, 2017.

### **Communications in International Conferences**

da Rocha ST, Pires V, Alves AR, Picard C, Heard E. Genetic dissection of Xist lncRNA reveals conserved functional RNA domains involved in facultative heterochromatin formation during X-inactivation. EMBO meeting on Epigenetics and chromatin, European Molecular Biology Laboratory, Heidelberg, Germany, May 03-06, 2017. (Poster Presentation).

Vaz-Drago R, Jesus AC, Martin RM, Carvalho C, Rino J, Custódio N, Carmo-Fonseca M. Kinetics of pre-mRNA cleavage and termination in living cells. 22<sup>nd</sup> Annual Meeting of the RNA Society, Prague, Czech Republic, May 30-June 3, 2017. (Oral Presentation).

Silva TP, Bekman E, Fernandes TG, Rodrigues CAV, Diogo MM, Cabral JMS, Carmo-Fonseca M. Cerebellar differentiation and maturation from Human Induced Pluripotent Stem Cells. International Society for Stem Cell Research, Annual Meeting, Boston, USA, June 14-17, 2017. (Poster Presentation).

Vaz-Drago R, Jesus AC, Martin RM, Carvalho C, Rino J, Custódio N, Carmo-Fonseca M. Live-cell imaging of RNA 3' end formation. EMBO Workshop on Regulation of RNA 3' end formation across eukaryotic genomes, Oxford, England, September 20-24, 2017. (Poster Presentation).

Brandão DP, da Rocha ST, Joaquim M, Aprile D, Pereira de Almeida L, Duarte ST. Loss of imprinting at the 15q11-q13 region during reprogramming results in a novel iPSC model for Angelman syndrome. CSH meeting on Stem Cell Biology, CSHL, Cold Spring Harbor, USA, September 25-29, 2017. (Poster Presentation).

Bernardes de Jesus B, Marinho SP, Sousa-Franco A, Alves-Vale C, Carvalho T, Carmo-Fonseca M. Silencing the long non-coding RNA antisense to Zeb2 facilitates reprogramming of aged fibroblasts and safeguards stem cell pluripotency. Stem Cell Biology Meeting, CSH, New York, USA, September 25-29, 2017. (Poster Presentation).

Silveira C, Sousa AC, Janeiro A, Felizardo M, Carmo-Fonseca M. ddPCR to detect EGFR T790M. Liquid Biopsies EMBL Course, European Molecular Biology Laboratory, Heidelberg, Germany, October 09-13, 2017. (Poster Presentation).

Vaz-Drago R, Custódio N, Carmo-Fonseca M. The impact of deep-intronic mutations on human disease. Forty Years of mRNA Splicing: From Discovery to Therapeutics. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, USA. October 22-25, 2017. (Poster Presentation).

### **Communications in National Conferences**

Silva TP, Bekman E, Fernandes TG, Rodrigues CAV, Diogo MM, Cabral JMS, Carmo-Fonseca M. Cerebellar differentiation and maturation from Human Induced Pluripotent Stem Cells. PhD Open Days, Lisbon, Portugal, April 5-6, 2017.

Matos S, Desterro J, Nunes A, Gomes da Silva M, Chacim S, Mariz M, Esteves G, Raposo J, Botelho A, Ribeiro L, Martins V, Guerreiro H, Carmo-Fonseca M. IDH Mutations in AML patients in Portugal. 4<sup>th</sup> International Conference on Acute Myeloid Leukemia: molecular and translational, advances in biology and treatment, Estoril, Portugal, October 5-7, 2017. (Poster Presentation).

Bernardes de Jesus B, Marinho SP, Sousa-Franco A, Alves-Vale C, Carvalho T, Carmo-Fonseca M. Silencing the long non-coding RNA antisense to Zeb2 facilitates reprogramming of aged fibroblasts and safeguards stem cell pluripotency. Physiology: from development to disease, Champalimaud Research Center, Lisbon, Portugal, October 9-11, 2017. (Poster Presentation).

Lopes JGV, Aprile D, da Rocha ST. Systematic DNA methylation analysis reveals prevalence of imprinting defects in mouse iPSCs. 10<sup>th</sup> International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Covilhã, Portugal, October 12-14, 2017. (Oral Presentation).

Brandão DP, Joaquim ML, Aprile D, Onofre I, Álvaro A, Pereira de Almeida L, Duarte ST, da Rocha ST. Loss of imprinting at the 15q11-q13 region during reprogramming results in a novel iPSC model for Angelman syndrome. 10<sup>th</sup> International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Covilhã, Portugal, October 12-14, 2017. (Poster Presentation).

Silva TP, Bekman E, Fernandes TG, Rodrigues CAV, Diogo MM, Cabral JMS, Carmo-Fonseca M. Cerebellar differentiation and maturation from Human Induced Pluripotent Stem Cells. 10<sup>th</sup> International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Covilhã, Portugal, October 12-14, 2017. (Oral Presentation).

Gonçalves R, Ribeiro M, Martins S, Carvalho T, Carmo-Fonseca M. Analysis of alternative splicing in hiPSC derived cardiomyocytes. 10<sup>th</sup> International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Covilhã, Portugal, October 12-14, 2017. (Poster Presentation).

Ribeiro M, Tavares J, Garcia B, Carmo-Fonseca M. Discriminating power of computational tools for genetic diagnosis of hypertrophic cardiomyopathy. 21<sup>a</sup> Reunião Anual da Sociedade Portuguesa de Genética Humana, Caparica, Portugal, November 16-18, 2017. (Poster Presentation).

Ramos, CG, Klein AD, Futerman AH, Carmo-Fonseca M. Exploring the impact of noncoding genetic variation on lysosomal function. 21<sup>a</sup> Reunião Anual da Sociedade Portuguesa de Genética Humana, Caparica, Portugal, November 16-18, 2017. (Poster Presentation).

Matos S, Desterro J, Nunes A, Gomes da Silva M, Chacim S, Mariz M, Esteves G, Raposo J, Botelho A, Ribeiro L, Martins V, Guerreiro H, Carmo-Fonseca M. Mutações ID em doentes com LMA em Portugal. Reunião Anual da Sociedade Portuguesa de Hematologia, Vilamoura, Portugal, November 16-18, 2017. (Oral Presentation).

### **Organisation of Conferences**

Carmo-Fonseca M. Invited to chair the session "RNA localization and transport", 22<sup>nd</sup> Annual Meeting of the RNA Society, Prague, Czech Republic, May 30-June 3, 2017.

### **Internationalisation**

Carmo-Fonseca M. Coordinates an EU H2020 Research and Innovation Staff Exchange (RISE) program entitled "LysoMod: Genetic and small molecule modifiers of lysosomal function".

Carmo-Fonseca M. Participates in a EUH2020 Teaming Grant with the University College London entitled "Implementation of the Discoveries Centre for Regenerative and Precision Medicine, a new Centre of Excellence in Portugal".

Carmo-Fonseca M. Collaborates with Prof. N. Proudfoot at the University of Oxford on bioinformatics analysis of transcription and co-transcriptional RNA processing.

da Rocha ST collaborates with Prof. Edith Heard at the Curie Institute on RNA-seq and ChIP-seq experiments on inducible Xist non-coding RNA mutants and their effects on X-linked gene inactivation.

### **Prizes, Honours and Awards**

Carmo-Fonseca M. Invited as external expert advisor to review the biomedical science and engineering landscape in the National University of Ireland Galway. Site visit on June 23, 2017.

Alves-Vale C. 1ª Menção Honrosa - Prémio GAPIC David-Ferreira, “Unravelling the role of the long noncoding RNA NORAD in breast cancer”.

### **Advanced Teaching**

Bernardes de Jesus B. Master in Evolution and developmental biology, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, May 2017.

### **Science and Society**

Carmo-Fonseca M. Empreendedorismo: as dinâmicas empresariais e das instituições. Ciclo de Conferências na Ordem dos Engenheiros, Lisbon, Portugal, March 31, 2017.

### **MSc Thesis Completed**

Kenny Patrick Figueira Rebelo, 08/06/2017, “Splicing kinetics revealed by nascent transcript sequencing”, Faculty of Sciences, University of Lisbon. Supervisor: Maria Carmo-Fonseca.

Mariana Joaquim, 13/10/2017, “Direct conversion as a model system to explore the role of a lncRNA as a target for Angelman Syndrome”, Faculty of Sciences and Technology, Nova University of Lisbon. Supervisor: Simão Teixeira da Rocha.

Rodrigo Paiva Gonçalves, 31/10/2017, “Assessment of hiPSC derived cardiomyocytes maturation in extended culture by analysis of alternative splicing expression patterns”, Faculty of Sciences, University of Lisbon. Supervisor: Teresa Carvalho.

Miguel Torres Santana, 17/11/2017, “Enhancing reprogramming and transdifferentiation through long non-coding RNAs”, Faculty of Sciences, University of Lisbon. Supervisor: Bruno Bernardes de Jesus.

Catarina Alves-Vale, 27/07/2017, “Unravelling the role of the long noncoding RNA NORAD in breast cancer”, Faculty of Medicine, University of Lisbon. Supervisor: Bruno Bernardes de Jesus.

## Castanho, Miguel

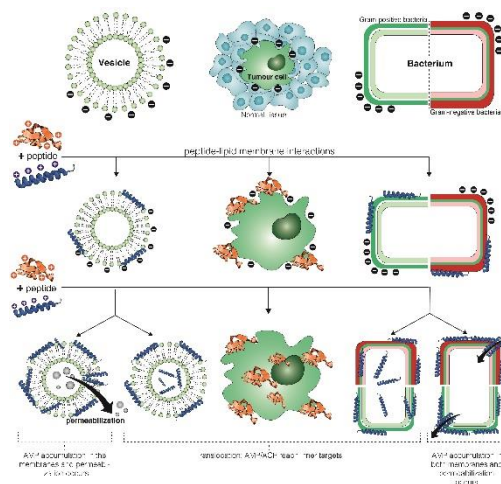
### Major Interests / Objectives

There are many biological processes that depend on the interaction between peptides/proteins and membrane lipids, such as viral fusion, translocation across epithelia or innate immune defence. Some of these may be inspiring to develop innovative therapeutical tools. The goal of the MCastanho Lab is to unravel the physical principles that govern lipid-peptide interactions, with implications in viral fusion (HIV and Dengue virus are of particular interest), analgesia and translocation of the blood-brain barrier, and development of antimicrobial and anticancer drugs. We are interested not only in drug targets and drug discovery itself, but also in the molecular-level mechanism of action of efficient and safe drugs.

### Head of Laboratory

Miguel A. R. B. Castanho, PhD, Full Professor

### Graphical Abstract



### Research Team

Ana Filipa Daniel da Cruz	Graduate	MSc Student
Ana Rosa Miranda dos Santos Silva Herdade	PhD	Investigator (Started October)
Ana Salomé Rocha do Nascimento Veiga	PhD	Assistant Professor
Carla Iris Cadima Couto	PhD	Post-Doctoral Investigator
Diana Maria Diez Gaspar	PhD	Post-Doctoral Investigator
Diogo Alexandre de Mendonça	Graduate	MSc Student
Filipa Dias de Oliveira	Graduate	PhD Student (Started May)
Inês Rego de Figueiredo	Master	Trainee (Left September)



Julia Michalina Skalska	Master	PhD Student
Juliana Rodrigues Perazzo	Master	PhD Student, NA
Marco Calvino Cavaco	Master	PhD Student
Sandra Isabel Rodrigues de Aguiar	PhD	Post-Doctoral Investigator
Sara Raquel Neves Coelho	Master	Investigator (Started March)
Susana Filipa Almeida Dias	Master	PhD Student
Tânia Raquel Martins dos Santos	Master	PhD Student
Tiago Nascimento Figueira	Master	PhD Student
Vera Luísa Santos Neves	PhD	Post-Doctoral Investigator

### Laboratory Keywords / Research Areas

Drug discovery, Peptide, Antimicrobials/anticancer drugs, HIV, Dengue, Blood-brain barrier.

### Major Scientific Achievements

In 2017 we have:

- Found, using Atomic Force Microscopy, that PvD1, a defensin isolated from common bean, has antitumor action and abrogates metastatic breast cancer cells adhesion to brain endothelium.
- Demonstrated that novel peptides derived from Dengue virus capsid protein translocate reversibly the blood-brain barrier through a receptor-free mechanism. The published paper has been chosen to be highlighted in ACS chemical research in toxicology. The technology was patented in agreement with Technophage SA (WO/2016/120843, CA2975059A1) for the development of anti-Alzheimer's Disease therapies.
- Unraveled potent membrane-targeting antibacterial peptides from viral capsid proteins, consolidating a previous finding that viral proteins are largely unexplored sources of antimicrobial peptides.
- Shown that the in vivo efficacy of measles virus fusion protein-derived peptides is modulated by the properties of self-assembly and membrane residence.

### Selected Publications

Neves V, Aires da Silva F, Morais M, Gano L, Ribeiro E, Pinto A, Aguiar S, Gaspar D, Fernandes C, Correia JDG, Castanho MARB (2017). Novel peptides derived from Dengue virus capsid protein translocate reversibly the blood-brain barrier through a receptor-free mechanism. ACS Chem. Biol. 12, 1257. DOI: 10.1021/acschembio.7b00087. (IF: 4.995, Citations: 2).

Figueira T, Dias FO, Almeida I, Mello EO, Gomes VM, Castanho MARB, Gaspar D (2017). Challenging metastatic breast cancer with the natural defensin PvD1. *Nanoscale* 9, 16887. doi: 10.1039/c7nr05872a. (IF: 7.367, Citations:--).

Freire JM, de Figueiredo IR, Valle J, Veiga AS, Andreu D, Enguita FJ, Castanho MARB (2017). siRNA cell-penetrating peptides complexes as a combinatorial therapy against chronic myeloid leukemia using BV173 cell line as model. *J. Control. Release* 245, 127. <https://doi.org/10.1016/j.jconrel.2016.11.027>. (IF: 7.786, Citations: 7).

Figueira TN, Palermo LM, Veiga AS, Huey D, Alabi CA, Santos NC, Welsch JC, Mathieu C, Horvat B, Niewiesk S, Moscona A, Castanho MARB, Porotto M (2017). In vivo efficacy of measles virus fusion protein-derived peptides is modulated by the properties of self-assembly and membrane residence. *Journal of virology* 91, e01554-16. doi: 10.1128/JVI.01554-16. (IF: 4.663, Citations: 7).

Perazzo J, Lima C, Heras M, Bardají E, Lopes-Ferreira M, Castanho MARB (2017). Neuropeptide Kyotorphin Impacts on Lipopolysaccharide-Induced Glucocorticoid-Mediated Inflammatory Response. A Molecular Link to Nociception, Neuroprotection, and Anti-Inflammatory Action. *ACS chemical neuroscience*, 8, 1663-1667. doi: 10.1021/acscemneuro.7b00007. (IF: 3.883, Citations:--).

### Ongoing Research Projects

2016/2019: Peptides for blood-brain barrier transmigration and drug delivery - novel therapies for the central nervous system. Coordinator: Vera Luisa Santos Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-NAN/1578/2014. Amount: € 140 090,00. Total Amount: € 190 090,00.

2016/2019: Towards the development of innovative highly effective dual action anti-HIV peptides. Coordinator: Ana Salomé Rocha do Nascimento Veiga. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/4412/2014. Amount: € 143 133,00. Total Amount: € 193 123,00.

2016/2019: Cell-cell communication in metastatic breast cancer: a control point that can lead to breast cancer treatment. Coordinator: Diana Maria Diez Gaspar. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BQB/1693/2014. Amount: € 187 151,00. Total Amount: € 187 151,00.

2016/2019: Alzheimer3D: Trifunctional Conjugates for the Selective Drug Delivery in Alzheimer's Disease. Coordinator: Vera Luísa Santos Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/5512/2014. Amount: € 12 000,00. Total Amount: € 198 364,00.

2016/2019: Overcoming the Brain Drug Delivery Bottleneck: Development of single domain antibodies for brain targeting and drug delivery across the Blood-Brain Barrier. Coordinator: Vera Luísa Santos Neves. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BIO/0508/2014. Amount: € 19 800,00. Total Amount: € 192 320,00.

2015/2019: INPACT: Innovative peptides against cancer and pathogenic bacteria, with advances in science, biopharmaceutical drug development, product market targeting, training, and communication. Coordinator: Miguel Augusto Rico Botas Castanho. Funding Agency: European Commission. Reference: MSCA RISE 644167. Amount: € 463 500,00. Total Amount: € 1 390 500,00.

#### **Other Projects**

2015/2020: Engineering protease-resistant alpha-beta for broad-spectrum antivirals. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Funding Agency: National Institute of Health. Reference: 5R01AI114736. Amount: € 300 000,00. Total Amount: € 1 225 000,00.

#### **Publications in Peer Review Journals**

Figueira TN, Palermo LM, Veiga AS, Huey D, Alabi CA, Santos NC, Welsch JC, Mathieu C, Horvat B, Niewiesk S, Moscona A, Castanho MARB, Popotto M (2017). In vivo efficacy of measles virus fusion protein-derived peptides is modulated by the properties of self-assembly and membrane residence. *J. Virol.* 91, e01554-16. (IF: 4.663, Citations: 3).

Freire JM, de Figueiredo IR, Valle J, Veiga AS, Andreu D, Enguita FJ, Castanho MARB (2017). siRNA cell-penetrating peptides complexes as a combinatorial therapy against chronic myeloid leukemia using BV173 cell line as model. *J. Control. Release* 245, 127-136. (IF: 7.786, Citations: 4).

Figueira TN, Freire JM, Cunha-Santos C, Heras M, Gonçalves J, Moscona A, Popotto M, Veiga AS, Castanho MARB (2017). Quantitative analysis of molecular partition towards lipid membranes using surface plasmon resonance. *Sci. Rep.* 7, 45647. (IF: 4.259, Citations:--).

Dias SA, Freire JM, Pérez-Peinado C, Domingues MM, Gaspar D, Vale N, Gomes P, Andreu D, Henriques ST, Castanho MARB, Veiga AS (2017). New Potent Membrane-Targeting Antibacterial Peptides from Viral Capsid Proteins. *Front. Microbiol.* 8,775. (IF: 4.076, Citations: 1).

Pérez-Peinado C, Dias SA, Domingues MM, Benfield AH, Freire JM, Radis-Bapsta G, Gaspar D, Castanho MARB, Craik DJ, Henriques ST, Veiga AS, Andreu D (2017). Mechanism of bacterial membrane permeabilization of crotalidicin (Ctn) and its fragment Ctn[15-34], antimicrobial peptides from ralesnake venom. *J. Biol. Chem.* In press. (IF: 4.125, Citations:--).

Figueira TN, Oliveira FD, Almeida I, Mello EO, Gomes, VM, Castanho MARB, Gaspar D (2017). Challenging metastatic breast cancer with the natural defensin PvD1. *Nanoscale* 9(43), 16887-16899. doi: 10.1039/c7nr05872a. (IF: 7.367, Citations:--).

Cavaco M, Castanho MARB, Neves V (2017). Peptibodies: An elegant solution for a long-standing problem. *Biopolymers* (in press) DOI: 10.1002/bip.23095. (Publication has been chosen to be the cover of the journal). (IF: 2.248, Citations:--).

Neves-Coelho S, Eleutério RP, Enguita FE, Neves V, Castanho, MARB (2017). A New Noncanonical Anionic Peptide That Translocates a Cellular Blood–Brain Barrier Model. *Molecules* 22(10), 1753 DOI:10.3390/molecules22101753. (IF: 2.861, Citations:1).

Neves V, Aires da Silva F, Morais M, Gano L, Ribeiro E, Pinto A, Aguiar S, Gaspar D, Fernandes C, Correia JDG, Castanho MARB (2017). Novel peptides derived from Dengue virus capsid protein translocate reversibly the blood-brain barrier through a receptor-free mechanism. *ACS Chem. Biol.* 12 (5), 1257–1268. DOI: 10.1021/acscchembio.7b00087 (Publication has been chosen to be highlighted in ACS chemical research in toxicology). (IF: 4.995, Citations: 2).

Perazzo J, Lima C, Heras, M, Bardaji E, Lopes-Ferreira M, Castanho MARB (2017). Neuropeptide Kyotorphin Impacts on Lipopolysaccharide-Induced Glucocorticoid-Mediated Inflammatory Response. A Molecular Link to Nociception, Neuroprotection, and Anti-Inflammatory Action. *ACS Chemical Neuroscience* 8, 1663-1667. (IF: 3.883, Citations:--).

Cruz-Oliveira C, Almeida AF, Freire JM, Caruso MB, Morando MA, Ferreira VNS, Assunção-Miranda I, Gomes AMO, Castanho MARB, Da Poian AT (2017). Mechanisms of Vesicular Stomatitis Virus Inactivation by Protoporphyrin IX, Zinc-Protoporphyrin IX, and Mesoporphyrin IX. *Antimicrob Agents Chemother* 61(6), e00053-17. doi: 10.1128/AAC.00053-17. (IF: 4.302, Citations: 1).

Perazzo J, Castanho MARB, Santos SS (2017). Pharmacological Potential of the Endogenous Dipeptide Kyotorphin and Selected Derivatives. *Frontiers in Pharmacol* 7, 530 (IF: 4.400, Citations: 2).

Neves V, Aires da Silva F, Morais M, Gano L, Ribeiro E, Pinto A, Aguiar S, Gaspar D, Fernandes C, Correia JDG, Castanho MARB (2017). Dengue virus-derived peptides translocate across the blood-brain barrier. *Chem. Res. Toxicol* 30(5) (Published abstract). (IF: 3.529, Citations:--).

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

Castanho M. Presented invited seminars in UENF - Universidade Estadual do Norte Fluminense and UNESP - Universidade Estadual Paulista, Campus de S. José do Rio Preto, both in Brazil.

Salomé Veiga A. Presented an invited seminar at the Institute for Molecular Bioscience, The University of Queensland, Australia.

#### **Communications in International Conferences**

Pinto SN, Mil-Homens D, Castanho M, Prieto M, Coutinho A, Veiga AS. Optimization of fluorimetric and confocal microscopy techniques to unravel vancomycin activity against *Staphylococcus aureus* biofilms. 27<sup>th</sup> ECCMID, Vienna, Austria, April 2017. (Oral Communication).

Neves V, Aires da Silva F, Correia JDG, Castanho M. Novel peptides derived from Dengue virus capsid protein translocate reversibly the blood-brain barrier through a receptor-free mechanism. 25<sup>th</sup> American Peptide Symposium, Whistler, Canada, June 17-22, 2017. (Poster Presentation).

Freire JM, Dias SA, Pérez-Peinado C, Domingues MM, Gaspar D, Andreu D, Henriques ST, Castanho M, Veiga AS. Exploring viral proteins for membrane-active peptides. 25<sup>th</sup> American Peptide Symposium, Whistler, Canada, June 17-22, 2017. (Poster Presentation).

Dias SA, Freire JM, Pérez-Peinado C, Domingues MM, Gaspar D, Vale N, Gomes P, Andreu D, Henriques ST, Castanho M, Veiga AS. Novel Viral Capsid Protein-Derived Peptides with Potent Antibacterial Activity. 7<sup>th</sup> International Meeting on Antimicrobial Peptides, Copenhagen, Denmark, August 2017. (Poster Presentation).

Neves-Coelho S, Neves V, Castanho M. A new cell-penetrating peptide for drug delivery to the brain. 5<sup>th</sup> Italian Experience in Biomedical Research: Young Minds at Work, Desenzano del Garda, Brescia, Lombardy, Italy, October 20-21, 2017. (Oral Presentation and Chair).

Dias SA, Freire JM, Pérez-Peinado C, Domingues MM, Gaspar D, Vale N, Gomes P, Andreu D, Henriques ST, Castanho M, Veiga AS. New Antibacterial Peptides Derived from Viral Capsid Proteins. 5<sup>th</sup> Italian Experience in Biomedical Research: Young Minds at Work, Desenzano del Garda, Italy, October 20-21, 2017. (Oral Presentation).

Figueira TN, Oliveira FD, Almeida I, Mello EO, Gomes VE, Castanho M, Gaspar D. Challenging breast cancer brain metastases development with the natural peptide PvD1. 12<sup>th</sup> Australian Peptide Conference, Noosa Heads, Australia, October 2017. (Poster Presentation).

#### **Communications in National Conferences**

Cavaco M, Neves V, Gaspar D, Castanho M. Trans-BBB peptides for targeting brain metastases. LisbonBioMed Retreat, Quinta dos Machados, Mafra, Portugal, April 10-12 2017. (Oral Communication).

Cavaco M, Neves V, Gaspar D, Castanho M. Trans-BBB peptides for targeting brain metastases. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Communication).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Kyotorphin and amidated-kyotorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. XI iMM/CAML PhD Student Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Oliveira FD, Freire J, Robalo MP, Piedade MFM, Andreu D, Veiga AS, Garcia MH, Castanho M, Gaspar D, Morais TS. Study of cell penetrating peptides as drug delivery systems for chemotherapeutic drugs and their anticancer properties. 1<sup>o</sup> Encontro do Colégio de Química, University of Lisbon, Lisbon, Portugal, July 21-22, 2017. (Poster Presentation).

Skalska J, Mello EO, López MR, Jiménez-Monzón R, McNaughton-Smith G, Gomes VM, Gaspar D, Castanho M. Understanding the effects of anticancer peptides on cancer cells and their selectivity towards exosomal membranes. 1<sup>o</sup> Encontro do Colégio de Química, University of Lisbon, Lisbon, Portugal, July 21-22, 2017. (Poster Presentation).

Dias SA, Freire JM, Pérez-Peinado C, Domingues MM, Gaspar D, Vale N, Gomes P, Andreu D, Henriques ST, Castanho M, Veiga AS. Viral capsid proteins as a source for new membrane-targeting antibacterial peptides. 1<sup>o</sup> Encontro do Colégio de Química, University of Lisbon, Lisbon, Portugal, July 21-22, 2017. (Poster Presentation).

Aguiar S, Andre A, Neves V, Coelho S, Castanho M, Aires-da-Silva F. Single domain antibodies for brain targeting and drug delivery. MicroBiotec2017: 7<sup>th</sup> Congress of Microbiology and Biotechnology, Porto, Portugal, December 7-9, 2017. (Oral Communication).

Pinto SN, Dias SA, Mil-Homens D, Fernandes F, Andreu D, Castanho M, Prieto M, Coutinho A, Veiga AS. Unravelling the antibiofilm mechanism of action of the antimicrobial peptide pepR. MicroBiotec2017: 7<sup>th</sup> Congress of Microbiology and Biotechnology, Porto, Portugal, December 7-9, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Kyotorphin and amidated-kyotorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. XLVII Reunião Anual da Sociedade Portuguesa de Farmacologia, Fundação Bissaya Barreto Bencanta, Coimbra, Portugal, 2017. (Oral Communication).

Belo R, Perez-Peinado C, Valle J, Andreu D, Sebastião A, Neves V, Castanho M, Diógenes MJ. Neuronal mechanisms behind Kyotorphin and Amidated-Kyotorphin effects. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Communication).

Belo R, Perez-Peinado C, Valle J, Andreu D, Sebastião A, Castanho M, Neves V, Diógenes MJ. On the road of KTP and KTP-NH<sub>2</sub> neuronal mechanisms of action. 3<sup>rd</sup> PhD Students Meeting of the Mind-Brain College, Reitoria da Universidade de Lisboa, Lisbon, Portugal, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Exploring Kyotorphin and Amidated-Kyotorphin actions upon synaptic transmission and plasticity, and on calpains and caspases activation. XV Meeting of the Portuguese Society for Neuroscience, Hotel Meliã Braga, Braga, Portugal, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Exploring Kyotorphin and Amidated-kyotorphin actions: synaptic transmission and calpains and caspases activation. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Lisbon, Portugal, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Kyotorphin and amidated-kyotorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017. (Poster Presentation).

### **Internationalisation**

Our expertise is the development and application of tailored biophysical techniques to dissect the molecular mechanism of action of membrane-active peptides directly in viruses, bacteria or cells so that innovative drugs and therapeutic tools can be devised. Peptides are from three sources: i) Organic synthesis, for which we have long standing collaborations with leading reference labs in Spain, ii) Natural products, for which we have collaborations in Brazil, the country with the most diverse biome on Earth, and iii) Pharma products during development phase. Molecular virology studies are carried out in collaboration with two international reputed researchers in the field in Brazil and USA.

Using a judicious network of complementary collaborations, we streamline our activity from innovative molecules to effective applications.

It is worth highlighting that MCastanho Lab coordinates a H2020 project involving ten teams from five countries in three continents aimed at developing drug leads to fight bacteria and brain-targeted metastatic breast cancer.



### **Advanced Teaching**

Gaspar D. Anticancer Peptides. Lecturer at LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 30, 2017.

Neves V. Overcoming the blood-brain barrier to treat brain diseases. LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 31, 2017.

Gaspar D. Contributed talk. Cell-to-Cell Communication as a Control Point in Metastatic Breast Cancer. Terapia Celular e Génica Course, Instituto Superior Técnico, Lisbon, Portugal, May 19, 2017.

Gaspar D. Contributed talk. Cell-to-Cell Communication as a Control Point in Metastatic Breast Cancer. i3DU PhD Program, Advanced Course on Pharmaceutical Biophysics, Lisbon, Portugal, May 25, 2017.

Neves V. Blood Brain Barrier: Challenges to develop new therapeutic tools to act in the brain. Seminar for Masters Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, November, 2017.

Participation as tutor at the LisbonBioMed (iMM) and M2B PhD (FMUL) PhD Programs 2017. Nanomedicine and Biochemistry.

### **Science and Society**

Veiga AS, Neves V, Gaspar D, Dias SA, Oliveira FD, Neves-Coelho S. Promotion of Science Activities in European Researchers' Night, Lisbon, Portugal, September 29, 2017.

Dias SA. Presentation of Science Experiments to a 5-year class of "Colégio Sagrado Coração de Maria", Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, 2017.

### **MSc Thesis Completed**

Sara Neves-Coelho, 18/01/2017, "Drug delivery to the brain: design of peptides for selective blood-brain barrier transmigration", University of Lisbon. Supervisor: Miguel Castanho. Co-Supervisor: Vera Neves.

Ana Filipa Daniel da Cruz, 30/11/2017, “Study of antimicrobial peptides’ activity against bacterial biofilms”, University of Lisbon. Supervisor: Ana Salomé Veiga. Co-Supervisor: Ana Coutinho.

Diogo Alexandre de Mendonça, 29/11/2017, “Biophysical Characterization of Measles Virus Fusion-Inhibitory Peptides: a Focus on Membrane Interactions and Self-Assembly”, University of Lisbon. Supervisor: Miguel Castanho. Co-Supervisor: Ana Coutinho.

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## Costa, Luís

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### Major Interests / Objectives

Metastases are the hallmark of cancer lethality. They represent a unique and complex phenomenon associated, not only with genomic alterations in cancer cell, but also with a heterotypic signaling between cancer cells and host tissues. Our aim is to better understand the molecular mechanisms involved in tumour 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 tumour and corresponding metastasis (using colorectal cancer (CRC) as a model). Ultimately, we plan to construct and comprehensively analyze an OncoDynamic Biobank that will contribute to interpret the different time points of metastatic cancer progression, including host immune response.

### Head of Laboratory

Luís António Marquês da Costa, MD/PhD

### Research Team

António Manuel Marujo Palma	Graduate	MSc Student (Started September)
Arlindo Júlio Rebelo da Silva Ferreira	Master	Investigator, MD
Catarina Pinheiro Barracha Pinto de Abreu	Graduate	MSc Student (Started October)
Daniela Maria Grou Ramalho	Graduate	MSc Student (Started September)
Inês André Correia	Graduate	MSc Student (Left January)
Inês Fernandes Gomes	Master	Investigator
Irina Margarida Pereira Machado Alho Duarte	PhD	Investigator (Left November)
Isabel Cristina Ferreira Fernandes Borges da Costa	Master	Investigator, CHLN, Clinical Specialist, Assistant Professor
Joana Patrícia Gomes Vieira	Master	Investigator (Started February/Left June)
Marta Sofia Alves Martins	PhD	Investigator
Patrícia Alexandra Pardal Martins	Master	Investigator (Started March)
Patrícia Borges Alves	Graduate	MSc Student (Started September)
Patrícia Isabel Martins Corredeira	Master	Investigator
Pedro Nuno Lopes Mendes Calheiros Andrade	Master	Investigator (Started July)
Raquel Sofia Cruz Duarte	Master	MSc Student
Sandra Cristina Cara de Anjo Casimiro	PhD	Post-Doctoral Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Sandra Sofia Chorão Lavajo Lucas	Graduate	Investigator
Teresa Raquel Duarte Pacheco	PhD	Post-Doctoral Investigator

### **Laboratory Keywords / Research Areas**

Metastasis, Metastatic organotropism, Tumor microenvironment, Leader genes signatures, Therapy resistance, Oncodynamics.

### **Major Scientific Achievements**

In 2017, we have established our Oncodynamics Biobank, which is a prospective collections of liquid biopsies from breast, prostate, colorectal and myeloma cancer patients, designed to characterize both the host immune response and tumor clonal evolution during cancer progression under therapy. We have also initiated the multi-institutional RAMBO-223 trial, a prospective, single-cohort, observational study of patients with metastatic castration resistant prostate cancer treated with radium-223 dichloride. Moreover, we have discovered serum Y-box binding protein 1 as a biomarker of bone disease progression in patients with breast cancer and bone metastases. And we found a novel role of Phospholipase C g1 in resistance to Cetuximab in metastatic colorectal cancer. Finally, in a retrospective multicenter observational cohort study of early breast cancer, we found that ovarian function suppression in premenopausal patients (under 35) confer overall survival benefit at 5 years.

### **Selected Publications**

Ferreira A, Alho I, Vendrell I, Melo M, Brás R, Costa AL, Sousa AR, Mansinho A, Abreu C, Pulido C, Macedo D, Pacheco T, Correia L, Costa L, Casimiro S (2016). The prognostic role of RANK SNP rs34945627 in breast cancer patients with bone metastases. *Oncotarget* 7(27), 41380-9 (IF: 5.168, Citations:--).

Body JJ, Casimiro S, Costa L (2015). Targeting bone metastases in prostate cancer: improving clinical outcome. *Nature Reviews Urology* 12, 340-56. (IF: 7.735, Citations: 21).

Costa L (2014). Which bisphosphonate to treat bone metastases?. *Lancet Oncology* 15(1), 15-16. (IF: 33.900, Citations: 2).

Pakala SB, Rayala SK, Wang RA, Ohshiro K, Mudvari P, Reddy SD, Zheng Y, Pires R, Casimiro S, Pillai MR, Costa L, Kumar R (2013). MTA1 promotes STAT3 transcription and pulmonary metastasis in breast cancer. *Cancer Res* 73, 3761. (IF: 9.122, Citations: 14).

Henry D, Costa L, Goldwasser F, Hirsh V, Hungria V, Prausova J, Scagliotti GV, Sleeboom H, Spencer A, Vadhan-Raj S, von Moos R, Willenbacher W, Woll PJ, Wang J, Jiang Q, Jun S, Dansey R, Yeh H (2011). A Randomized, Double-blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma. *Journal of Clinical Oncology* 9(9), 1125-1132. (IF: 24.008, Citations: 382).

### **Ongoing Research Projects**

2017/2018: ONCODYNAMICS. Coordinator: Luis António Marques da Costa. Funding Agency: Several. Reference: ODB. Amount: € 60 000,00. Total Amount: € 60 000,00.

2017/2017: Valor prognóstico e terapêutico do Receptor Activador do NFkB (RANK) em cancro da mama. Coordinator: Sandra Cristina Cara de Anjo Casimiro. Funding Agency: Fundo iMM-Laço. Reference: Laço SCasimiro. Amount: € 31 278,00. Total Amount: € 31 278,00.

2016/2018: Involvement of PLCY1 in the resistance Mechanism to Anti-EGFR Therapy in Metastatic Colorectal Cancer. Coordinator: Marta Sofia Alves Martins. Funding Agency: Liga Portuguesa Contra o Cancro - Terry Fox Foundation. Reference: Terry Fox - MMartins. Amount: € 15 000,00. Total Amount: € 15 000,00.

2016/2017: Marcadores Moleculares de Metastização Óssea. Coordinator: Luis António Marques da Costa. Funding Agency: Not Applicable. Reference: Marcadores Moleculares de Metastização Óssea2. Amount: € 10 000,00. Total Amount: 10 000,00.

2015/2018: Analysis of RANK protein expression in Cohort 2 using immunohistochemistry (IHC) in 70 matched primary breast cancer tumors and distant metastasis. Coordinator: Luis António Marques da Costa. Funding Agency: Amgen Inc. Reference: Amgen LCosta. Amount: € 29 105,60. Total Amount: € 29 105,60.

2012/2017: Cancro Pâncreas e Caquexia - ADAM17 e TNF. Coordinator: Luis António Marques da Costa. Funding Agency: Private Donation. Reference: Cancro Pâncreas e Caquexia. Amount: € 6 000,00. Total Amount: € 6 000,00.

2009/2019: Cancer Genomics Consortium. Coordinator: Luis António Marques da Costa. Funding Agency: Several. Reference: GCGC. Amount: € 437 174,00. Total Amount: € 437 174,00.

### Other Projects

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

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

### Publications in Peer Review Journals

Ferreira AR, Bettencourt M, Alho I, Costa AL, Sousa AR, Mansinho A, Abreu C, Pulido C, Macedo D, Vendrell I, Pacheco TR, Costa L, Casimiro S (2017). Serum YB-1 (Y-box binding protein 1) as a biomarker of bone disease progression in patients with breast cancer and bone metastases. *J Bone Oncol*. Jan 28;6:16-21. (IF: 1.471, Citations:1).

Lambertini M, Ferreira AR, Di Meglio A, Poggio F, Puglisi F, Sottotetti F, Montemurro F, Poletto E, Bernardo A, Risi E, Dellepiane C, Sini V, Minuti G, Grasso D, Fancelli S, Del Mastro L (2017). Patterns of care and clinical outcomes of HER2-positive metastatic breast cancer patients with newly diagnosed stage IV or recurrent disease undergoing first-line trastuzumab-based therapy: a multicenter retrospective cohort study. *Clinical Breast Cancer Dec;17(8):601-610.e2*. (IF: 2.816, Citations:--).

Von Moos R, Costa L, Ripamonti CI, Niepel D, Santini D (2017). Improving quality of life in patients with advanced cancer: Targeting metastatic bone pain. *European Journal of Cancer* 71, 80-94. (IF: 6.029, Citations: 1).

### Other Publications International

Pulido C, Vendrell I, Ferreira AR, Casimiro S, Mansinho A, Alho I, Costa L (2017). Bone metastasis risk factors in breast cancer. *Ecancermedalscience*. Jan 24;11:715. (IF:--, Citations: 2).

Costa L, Ferreira AR (2017). Adjuvant zoledronic acid to treat breast cancer: not for all. *Lancet Oncol*. Nov;18(11):1437-1439 (IF: 33.900, Citations:--).

Luna Pais H, Alho I, Vendrell I, Mansinho A, Costa L (2017). Radionuclides in oncology clinical practice - review of the literature. Dalton Trans. 42, 14475-14487. (IF: 4.029, Citations:--).

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

Costa L. New drug toxicity. ESMO Update for Practising Oncologists, Lisbon, Portugal, March 2017.

Casimiro S. Preventing bone metastases in ER-positive breast cancer: Identification and clinical validation of putative prognostic biomarkers and therapeutic targets. Jornadas de Investigação em Oncologia em Portugal, NRS-LPCC, April 6, 2017.

Martins M. Role of PLCg1 in the resistance mechanism to anti-EGFR therapy. Jornadas de Investigação em Oncologia em Portugal, NRS-LPCC, April 6, 2017.

Costa L. Cancer Research: A Selection of “Hot Spots”. Instituto Português de Oncologia-Portuguese League Against Cancer, Lisbon, Portugal, April 2017.

Costa L. Bone Health in Curable Breast Cancer. Leaping Forward Meeting, Lisbon, Portugal, May 2017.

Costa L. Liquid Biopsies in Clinical Oncology: How many dimensions and how much dynamics. 24<sup>th</sup> Cancer Porto Meeting, Porto, Portugal, May 2017.

Costa L. Bone-targeted therapies in Prostate cancer: updating the landscape. Multidisciplinary Genitourinary Oncology Course, Lisbon, Portugal, October 13, 2017.

Costa L. Personalized Medicine in Cancer: Aims and Challenges for Portugal. European Commission, Brussels, October 25, 2017.

Casimiro S. RANK – RANKL signaling pathway in the context of breast cancer and bone metastases. Department of Cancer Genetics, Oslo University Hospital, Oslo, Norway, October 26, 2017.

### **Communications in International Conferences**

Ferreira AR, Ribeiro J, Mayer A, Brito M, Miranda A, Fernandes JP, Passos-Coelho JL, Costa L, Vaz-Luís I. Use and effectiveness of adjuvant ovarian function suppression (OFS) in premenopausal women with early breast cancer. European Society of Medical Oncology Annual Meeting 2017. (Poster Presentation).

Ferreira AR, Alho I. Bone biomarkers: from research & clinical practice. CHLN/FMUL/CAML Preceptorship in Bone Metastases 2017. (Oral Presentation).

Cruz-Duarte R, Fernandes A, Borralho P, Pacheco TR, Abreu C, Costa L, Martins M. Role of PLCg1 in the Resistance Mechanism to Anti-EGFR Therapy in Metastatic Colorectal Cancer. XXIV Porto Cancer Meeting, Porto, Portugal, May 2017. (Poster Presentation).

### **Communications in National Conferences**

Ferreira AR, Miranda A, Mayer A, Passos Coelho JL, Fernandes J, Gouveia J, Brito M, Ribeiro J, Costa L, Vaz-Luís I. Auditing program in the multi-institutional prospective ROR-Sul study: clinicopathological characteristics, patterns of care and clinical outcomes of patients with breast cancer. Jornadas do Registo Oncológico Regional do Sul 2017, 2017. (Oral Presentation).

Ferreira A, Ribeiro J, Miranda A, Mayer A, Passos Coelho JL, Fernandes J, Gouveia J, Brito M, Costa L, Vaz-Luís I. The effectiveness of ovarian suppression in the adjuvant treatment of breast cancer: a multi-institutional retrospective cohort study. Jornadas do Registo Oncológico Regional do Sul 2017, 2017. (Oral Presentation).

Gamiro J, Jorge S, Fernandes I, Nobre E, Leitão J, Lopes JÁ, Gomes da Costa A. Desafio diagnóstico em doente com Esclerose Tuberosa: um caso clínico. Encontro Renal 2017, XXXI Congresso Português de Nefrologia, Vilamoura, Portugal, April 2017. (Poster Presentation).

Paiva R, Mansinho A, Alvim Cecília, Pais HL, Macedo D, Fernandes I, Costa L. Pazopanib em Sarcomas de Tecidos Moles: Experiência de um Centro. 14º Congresso Nacional de Oncologia, Aveiro, Portugal, October 26-29, 2017. (Poster Presentation).



Mansinho A, Ferreira AR, Casimiro S, Alho I, Vendrell I, Costa AL, Sousa AR, Abreu C, Pulido C, Macedo D, Pacheco T, Correia L, Fernandes I, Costa L. Rácio neutrófilos-linfócitos (NLR) como factor preditivo de tempo até eventos esqueléticos (TTSRE) e sobrevivência global (SG) em doentes com carcinoma da mama e metastização óssea. 14º Congresso Nacional de Oncologia, Aveiro, Portugal, October 26-29, 2017.

#### **Internationalisation**

Costa L, Casimiro S. Research Collaboration Agreement with Oslo University Hospital - "Analysis of SNP rs34945627 in women with primary breast cancer".

#### **Prizes, Honours and Awards**

Bello R, Gomes J. Best Oral Presentation, Research Day 2017, GAPIC Students, Faculty of Medicine, University of Lisbon, Lisbon, Portugal.

#### **Advanced Teaching**

Costa L. Breast Cancer Diagnosis and Treatment: Still on the Road to improve Results. 3<sup>rd</sup> ESOP-ESO Advanced Master Class in Oncology Pharmacy, Lisbon, Portugal, May 2017.

Casimiro S. Multiple ways of imaging human breast cancer xenografts and metastases in mice. Workshop on Preclinical Small Animal in Vivo Imaging, Instituto de Medicina Molecular João Lobo Antunes, C2TN-IST, October 13, 2017.

#### **Science and Society**

Acção de Sensibilização Cancro, Ciência e Eu, organizada pelo Fundo IMM-Laço, Escola Secundária da Ramada, March 30, 2017.

Investigadora convidada no programa Minuto de Saúde e Inovação – Retratos da Saúde, emitido pela SIC Mulher, May 3, 2017.

Investigadora convidada no artigo “É a nova cruzada científica: por que morrem 30% das mulheres com cancro da mama?”, publicado no Diário de Notícias, July 22, 2017.

Acção de Sensibilização Cancro, Ciência e Eu, organizada pelo Fundo iMM-Laço, CABIFY, October 11, 2017.

Acção de Sensibilização Cancro, Ciência e Eu, organizada pelo Fundo iMM-Laço, Willis Towers Watson, November 10, 2017.

### **MSc Thesis Completed**

Inês Correia, 17/01/2017, “Analysis of the effect of the over-expression of receptor activator of NFκB (RANK) in estrogen receptor-positive breast cancer cells over lymphatic and distant metastasis in an orthotopic mouse model”, Faculty of Medicine, University of Lisbon. Supervisor: Sandra Casimiro.

Raquel Cruz-Duarte, 07/02/2017, “Role of PLCg1 in the Resistance Mechanism to Anti-EGFR Therapy in Metastatic Colorectal Cancer”, Faculty of Medicine, University of Lisbon. Supervisor: Marta Martins.

Inês do Vale Costa Santos, 21/06/2017, “Immunogenicity of Colorectal Cancer with Microsatellite Instability”, Faculty of Medicine, University of Lisbon. Supervisor: Luís Marques da Costa.

José Franco Frazão, 27/07/2017, “Estudo do SNP rs2274223 numa população portuguesa de doentes com CRC”, Faculty of Medicine, University of Lisbon. Supervisor: Marta Martins.

Sara Magno, 06/02/2017, “Tumores do testículo – experiência do CHLN”, Faculty of Medicine, University of Lisbon. Supervisor: Isabel Fernandes.

### **PhD Thesis Completed**

Inês Luís, 16/11/2017, “Time trends of treatment and outcomes in women with T1 node negative breast cancer”, Faculty of Medicine, University of Lisbon. Supervisor: Luís Marques da Costa and Nancy U. Lin.

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## De Almeida, Sérgio

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### Major Interests / Objectives

Our research focuses on the mechanisms that regulate chromatin dynamics during transcription and DNA damage response and how they coordinate with the processes that safeguard the genome integrity. Our general aims are twofold: first, we aim at investigating the epigenetic regulation of transcription; in addition, we study the molecular mechanisms that sense, signal and repair DNA damage. A major focus of our research is to understand how changes in transcription, chromatin modification and DNA repair are linked to the development of human diseases such as cancer.

### Head of Laboratory

Sérgio Alexandre Fernandes de Almeida, PhD, Assistant Professor

### Research Team

Alexandra Coitos Vítor	Master	PhD Student
Ana Isabel Afonso Duarte	Graduate	Investigator (Started September)
Ana Margarida Esteves Ferreira	Graduate	MSc Student
Ana Rita Fialho Grosso	PhD	Investigator
Cristiana Marisa de Sousa Morgado	Graduate	MSc Student (Started September)
João Maria Rodrigues Perlico da Cruz Sabino	Master	PhD Student (Started March)
João Pedro Agostinho de Sousa	Graduate	MSc Student (Started September)
Mafalda Alexandra Ramos de Matos	Master	PhD Student
Robert M. Martin	PhD	Post-Doctoral Investigator
Silvia Filipa Camoeira Gonçalves de Carvalho	Master	Investigator
Sree Rama Chaitanya	PhD	PhD Student (Left November)

### Laboratory Keywords / Research Areas

Epigenetics, Chromatin biology, Cancer biology, Gene expression, DNA repair.

### Major Scientific Achievements

In 2017 the members of our unit have:

- Published two original manuscripts in international journals (Sridhara et al. Cell Reports 2017 & Bonnet et al. Molecular Cell 2017).
- Presented our research work in 7 national and international conferences.
- Participated in advanced teaching in PhD and MSc programs.

- Completed one PhD and one MSc thesis.

### **Selected Publications**

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* 17. (IF: 8.282, Citations: 9).

Grosso AR, Leite AP, Carvalho S, Matos MR, Martins FB, Vítor AC, Desterro JM, Carmo-Fonseca M, de Almeida AF (2015). Pervasive transcription read-through promotes aberrant expression of oncogenes and RNA chimeras in renal carcinoma. *eLife*. (IF: 7.725, Citations: 24).

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*. (IF: 7.725, Citations: 69).

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*. (IF: 10.162, Citations: 46).

de Almeida SF, Grosso AR, Koch F, Fenouil R, Carvalho S, Levezinho H, Eick D, Gut I, Andrau JC, Ferrier P, Carmo-Fonseca M (2011). Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 lysine 36. *Nature Structural and Molecular Biology*. (IF: 12.595, Citations: 123)

### **Ongoing Research Projects**

2016/2019: Novel tumorigenic mechanisms of aberrant epigenetic regulation in clear cell renal cell carcinoma. Coordinator: Sérgio Alexandre Fernandes de Almeida. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-ONC/0016/2014. Amount: € 199 944,00. Total Amount: € 199 944,00.

2015/2019: Decoding pseudogene transcriptional regulation during cell proliferation. Coordinator: Ana Rita Fialho Grosso. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00510/2014/CP1236/CT0007. Amount: € 50 000,00. Total Amount: € 50 000,00.

### Other Projects

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

### Publications in Peer Review Journals

Bonnet A, Grosso AR, Elkaoutari A, Coleno E, Presle E, Sridhara SC, Janbon G, Géli V, de Almeida SF, Palancade B (2017). Introns protect eukaryotic genomes from transcription-associated genetic instability. *Molecular Cell*, 2017 Aug 17;67(4):608-621.e6. doi: 10.1016/j.molcel.2017.07.002. Recommended by Faculty of 1000. Highlighted in Science (01 Sep 2017: Vol.357, Issue 6354, 883-884 DOI: 10.1126/science.357.6354.883-e). (IF: 14.714. Citations: 1).

Sridhara SC, Carvalho S, Grosso AR, Gallego-Paez LM, Carmo-Fonseca M, de Almeida SF\* (2017). Transcription dynamics prevent RNA-mediated genomic instability through SRPK2-dependent DDX23 phosphorylation. *Cell Reports*; 18(2):334-343 doi: j.celrep.2016.12.050. 2016. (IF: 8.282. Citations: 9).

### Invited Lectures and Seminars

de Almeida SF. Outcome of epigenetic deregulation in cancer. ReTuBi Joint Summer School, Lisboa, May 28, 2017.

### Communications in International Conferences

Matos MR, Posa I, Grosso AR, de Almeida SF. Pan-cancer analysis of intratumor heterogeneity and its epigenetic determinants. 1<sup>st</sup> Crick International Cancer Conference, London, England, September 2017. (Poster Presentation).

Grosso AR. Epigenetic drivers of genomic instability and intratumor heterogeneity. Big Data in Biology and Health Conference, Hixton, England, September 2017. (Poster Presentation).

Vítor AC, Sabino JC, Sridhara SC, Grosso AR, Martin RM, de Almeida, SF. Reciprocal regulatory links between transcription and DNA double strand break repair. 2<sup>nd</sup> EACR Conference on Protecting the Code: Epigenetic Impacts on Genome Stability, Berlin, Germany, October-November 2017. (Poster Presentation).

Grosso AR. Epigenetic drivers of genomic instability and intratumor heterogeneity. Epigenomics of common diseases Conference, Hixton, England, November 2017. (Poster Presentation).

### **Communication in National Conferences**

Matos MR, Posa I, Grosso AR, de Almeida SF. Epigenetic drivers of genomic instability and intratumor heterogeneity. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Vítor AC, Martin RM, Sridhara SC, de Almeida, SF. Reciprocal regulatory links between transcription and DNA double strand break repair. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

### **Internationalisation**

During the last year our team:

- Published two original research papers in international journals.
- Presented our research work in four international conferences.
- Maintained collaborative projects with research labs from the ETH (Switzerland) and the Jacques Monod Institute (France).

### **Prizes, Honours and Awards**

de Almeida SF. Nominated member of the Lisbon Academy of Sciences.

de Almeida SF. Awarded a project grant from Fundo IMM-Laço 2017 (€ 25 000).

### **Advanced Teaching**

Co-organised the module "Molecular & Cell Biology". LisbonBioMed PhD Program, Class of 2017, University of Lisbon, Lisbon, Portugal, January 2017.

### **MSc Thesis Completed**

Ana Margarida Ferreira, 10/10/2017, “Depicting epigenetic mechanisms involved in the regulation of pseudogene expression”, University of Lisbon. Supervisor: Ana Rita Grosso.

### **PhD Thesis Completed**

Sreerama Chaitanya Sridhara, 26/09/2017, “Transcription Dynamics Prevents RNA-mediated Genomic Instability Through SRPK2-dependent DDX23 Phosphorylation”, Faculty of Medicine, University of Lisbon. Supervisor: Sérgio de Almeida.

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## De Carvalho, Mamede

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### Major Interests / Objectives

Our unit investigates the motor neuron function and its degeneration, peripheral nerve function and small fibre neuropathy, modulation of central nervous system function, behaviour and imaging-neurocomputational models of brain dysfunction. We are contributing to a more complete comprehension of the electrophysiological signs in motor neuron degeneration, reliable evaluation of the small fibres, electrical current influence on nervous system activity and on the understanding of brain structures in behaviour disturbances. In the future, we aim to approach new techniques to measure small fibre and anterior horn cells function, plasticity of the spinal cord motor activity, and the interaction between brain imaging, behaviour, motor movement disorders and electrophysiology.

### Head of Laboratory

Mamede de Carvalho, PhD

### Research Team

Ana Catarina de Oliveira da Silva Pronto Laborinho	Graduate	Investigator
Ana Catarina dos Santos Farinha	Master	PhD Student
Ana Isabel Ladeira Portêlo	Master	PhD Student, NA
Ana Rita Mendes Londral Gamboa	PhD	Investigator
Anabela Leuschner Fernandes Cardoso Pinto Noronha Sanches	MD/PhD	Principal Investigator, CHLN , Consultant , Faculdade Medicina da Universidade de Lisboa , Associate Professor
Andreia Leitão Tavares Ribeiro dos Santos	Graduate	PhD Student
Ângelo Rodrigo Neto Dias	Graduate	PhD Student
Anna Caroline Marques dos Anjos Braga	Master	Investigator
Bruno André e Silva Miranda	MD/PhD	Investigator (Started March)
Fernando Manuel Pinto Ferreira Domingos	MD/PhD	Investigator, Assistant Professor
Gabriel Miltenberger Miltényi	MD/PhD	Principal Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Isabel Maria dos Santos Conceição	Graduate	Investigator, Teaching Assistant , Clinical Specialist
Isabel Martins De Castro	Graduate	Technician
João Daniel Galvão Antunes	Graduate	MSc Student (Started September)
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Investigator, Hospital da Luz , Faculdade Medicina da Universidade de Lisboa , Assistant Professor
José Filipe Oliviera Castro	Master	Investigator



Lena Helene Ernst	PhD	Post-Doctoral Investigator, NA
Leonel Almeida Luis	Graduate	Investigator, Hospital de Santa Maria , Clinical Specialist
Maria da Conceição Jonet de Azevedo Coutinho	MD/PhD	Investigator, Associate Professor
Mariana Fernandes Alves Pereira	Graduate	MSc Student
Mário Joao Martins Oliveira	MD/PhD	Investigator
Marta Luísa Gromicho Morgado Silva	PhD	Post-Doctoral Investigator
Michael Swash	MD/PhD	Investigator
Nataniel João Gonçalves Cleto Rosa	Master	PhD Student
Pedro Jorge Filipe Pereira	Master	Investigator
Pedro Miguel Tojais Rodrigues Alves	Graduate	Investigator, Teaching Assistant
Sofia Rita Cardoso	Master	PhD Student, Faculdade Ciências da Universidade de Lisboa, NA
Susana Cristina Da Costa Pinto	MD/PhD	Investigator
Sofia Fernades	Master	PhD Student
Tiago Vaz Maia	PhD	Principal Investigator
Vasco Manuel Aranha da Conceição	Master	PhD Student
Vera Lúcia Poço Galdes	Graduate	PhD Student

### Laboratory Keywords / Research Areas

Amyotrophic lateral sclerosis, Neurophysiology and respiratory involvement, Atrial fibrillation and autonomic nervous system, Neurocomputational modelling of brain disorders, Familial amyloid polyneuropathy and early markers of disease, Attention deficit hyperactivity disorder, Biological signal processing.

### Major Scientific Achievements

Our Unit is involved in neuromuscular disorders, in particular amyotrophic lateral sclerosis (ALS) and familial amyloid polyneuropathy (FAP), and in the nascent field of computational psychiatry. In ALS, we have incorporated a number of international consortiums involved in genetics, reporting of new genes, we are coordinating a European project and kept leading activity in neurophysiology. In FAP, we have proposed new methods for early diagnosis and initiated a large study on epidemiology. In computational psychiatry we published in Nature Neuroscience on this topic (Huys\*, Maia\*, & Frank, 2016; \*equal contributions, cited 40 times) and we co-edited a special issue of Biological Psychiatry: Cognitive Neuroscience and Neuroimaging devoted to the topic. We also published a novel computational account of schizophrenia in Biological Psychiatry (Maia & Frank, in press; IF: 11.212) that has already been recommended twice in Faculty of 1000.

### Selected Publications

Horga\* G, Maia\* TV, Marsh R, Hao X, Xu D, Duan Y, Tau GZ, Graniello B, Wang Z, Kangarlu A, Martinez D, Packard MG, Peterson BS (2015). Changes in corticostriatal connectivity during reinforcement learning in humans. *Human Brain Mapping*, Vol. 36, No. 2, pp. 793-803. 36, 793-803. (IF: 4.530, Citations: 1).

Turner MR, Hardiman O, Benatar M, Brooks BR, Chio A, de Carvalho M, Kiernan MC (2013). Controversies and priorities in amyotrophic lateral sclerosis. *Lancet Neurology* 322, 310. <http://www.sciencedirect.com/science/article/pii/S147444221370036X>. (IF: 26.284, Citations: 174).

Maia TV, Frank MJ (2011). From reinforcement learning models to psychiatric and neurological disorders. *Nature Neuroscience* 162, 154. <http://www.nature.com/neuro/journal/v14/n2/full/nn.2723.html>. (IF: 17.839, Citations: 241).

de Carvalho M, Dengler R, Eisen A, England JD, Kaji R, Kimura J, Swash M (2007). Electrodiagnostic criteria for diagnosis of ALS. *Clinical Neurophysiology* 503, 497. <http://www.sciencedirect.com/science/article/pii/S1388245707006438>. (IF: 3.866, Citations: 374).

Maia TV, McClelland, JL (2004). A reexamination of the evidence for the somatic marker hypothesis: What participants really know in the Iowa-gambling task? *Proceedings of the National Academy of Sciences of the United States of America* 16080, 16075. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC528759/>. (IF: 9.661, Citations: 480).

### Ongoing Research Projects

2016/2019: Unravelling Prognostic markers in NEUROdegenerative diseases through CLINical and OMICS data integration. Coordinator: Mamede Alves de Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EEI-SII/1937/2014. Amount: € 48 791,00. Total Amount: € 197 346,00.

2015/2018: ONTOlogy-based web database for understanding Amyotrophic Lateral Sclerosis. Coordinator: Mamede Alves de Carvalho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: JPND-PS/001/2013. Amount: € 140 000,00. Total Amount: € 140 000,00.

### Other Projects

2016/2018: SynaNet: Neurologic and Psychiatric disorders: from synapses to networks. Coordinator: Ana Maria Ferreira de Sousa Sebastião. Funding Agency: European Commission. Reference: TWINNING 692340. Amount: € 525 437,50. Total Amount: € 999 996,25.

2016/2017: Social and non-social reinforcement learning in humans: a model-based pharmacofMRI approach. Coordinator: Diana Maria Pinto Prata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: BIG 2016 DPrata. Amount: € 97 335,00. Total Amount: € 97 335,00.

2008/2018: THAOS: Transthyretin-associated amyloidoses outcomes survey - A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidoses. Coordinator: Claudio Rapezzi. Funding Agency: Fold Rx Pharmaceuticals. Reference: THAOS. Amount: Not Applicable. Total Amount: Not Applicable.

### Publications in Peer Review Journals

Gonçalves M, de Carvalho M, Peixoto C, Alves P, Barreto C, Oliva A, Pinto S, Laborinho-Pronto A, Gromicho M, Costa J (2017). Phosphoneurofilament heavy chain and vascular endothelial growth factor as cerebrospinal fluid biomarkers for ALS. *Amyotr Lat Scler Frontotemporal Degener* 18:134-136. (IF: 3.054, Citations:--).

Pinto S, Alves P, Swash M, de Carvalho M (2017). Phrenic nerve stimulation is more sensitive than measuring thickness by ultrasound in early ALS progression. *Neurophysiol Clin* 47, 69-73. (IF: 1.593, Citations: 4).

Pinto S, Gromicho M, de Carvalho M (2017). Sialorrhoea and reversals in ALS functional rating scale. *J Neurol Neurosurg Psychiatry* 88:187-188. (IF: 7.349, Citations: 1).

de Carvalho M, Swash M (2017). Physiology of the fasciculation potentials in amyotrophic lateral sclerosis: which motor units fasciculate? *J Physiol Sci*. (IF: 2.075, Citations: 1).

Pinto S, de Carvalho M (2017). Correlation between Forced Vital Capacity and Slow Vital Capacity for the assessment of respiratory involvement in Amyotrophic Lateral Sclerosis: a prospective study. *Amyotr Lat Scler Frontotemporal Degener* 18:86–91. (IF: 3.054, Citations: 3).

Swash M, de Carvalho M, (2017). Risk factors for onset of ALS (editorial). *Eur J Neurol*. (IF: 3.866).

Neuwirth C, Barkhaus PE, Burkhardt C, Castro J, Czell D, de Carvalho M, Nandedkar S, Stålberg E, Weber M (2017). Motor Unit Number Index (MUNIX) detects motor neuron loss in pre-symptomatic muscles in Amyotrophic Lateral Sclerosis. *Clin Neurophysiol* 128:495-500. (IF: 3.054, Citations: 4).

Nordin A, Akimoto C, Wuolikainen A, Alstermark H, Forsberg K, Baumann P, Pinto S, de Carvalho M, Hübers A, Nordin F, Ludolph AC, Meyer T, Grehl T, Schweikert K, Weber M, Holmøy T, Morita M, Tysnes OB, Benatar M, Lange D, Bisgård C, Asgari N, Tarvainen I, Brännström T, Andersen PM (2017). Sequence variation in C9orf72 downstream of the hexanucleotide repeat region and its effect on repeat-prime PCR interpretation: A large multinational screening study. *Amyotr Lat Scler Frontotemporal Degener* 18:256-264. (IF: 3.080, Citations: 1).

Oliveira Santos S, Swash, M, de Carvalho, M (2017). The generator site in acquired autoimmune neuromyotonia. *Clin Neurophysiol* 128; 643–646. (IF: 3.866, Citations: 2).

Gromicho M, Santos M, Pinto A, Pronto-Laborinho A, de Carvalho (2017). Young-onset rapidly progressive ALS associated with heterozygous FUS mutation. *Amyotr Lat Scler Frontotemporal Degener*. (IF: 3.054, Citations:--).

Pinto S, de Carvalho M (2017). Seasons and ALS time of death. *Amyotr Lat Scler Frontotemporal Degener*. 18:291–295. (IF: 3.054, Citations:-).

Kirsten P, Johnsen B, Tankisi H, Johnsen B, Camdessanché JP, de Carvalho M, Fawcett PRW, Labarre-Vila A, Liguori R, Nix W, Schofield I, Fuglsang-Frederiksen A (2017). Added value of electromyography in the diagnosis of myopathy: a consensus exercise. *Clin Neurophysiol* 128; 697-701. (IF: 3.866, Citations:--).

de Carvalho M, Kiernan M, Swash M (2017). Fasciculation in ALS: origin and pathophysiological relevance. *J Neurol Neurosurg Psychiatry* 88:773-779. (IF: 7.349, Citations: 3).

Sant'Anna R, Almeida MR, Varejo N, Gallego P, Esperante S, Ferreira P, Pereira-Henriques A, Palhano FL, de Carvalho M, Foguel D, Reverter D, Saraiva MJ, Ventura S (2017). Cavity filling mutations at the thyroxine-binding site dramatically increase transthyretin stability and prevent its aggregation. *Sci Rep* 24; 7:44709. (IF: 4.259, Citations:--).

McLaughlin RL, Schijven D, van Rheenen W, van Eijk KR, O'Brien M, Kahn RS, Ophoff RA, Goris A, Bradley DG, Al-Chalabi A, van den Berg LH, Luykx JJ, Hardiman O, Veldink J, Project MinE GWAS Consortium, Schizophrenia Working Group of the Psychiatric Genomics Consortium (2017). Genetic correlation between amyotrophic lateral sclerosis and schizophrenia. *Nat. Commun.* (IF: 12.124, Citations: 6).

Oliveira Santos M, Ohana B, de Carvalho (2017). Celiac disease and a novel association with a multifocal acquired motor axonopathy (MAMA) (letter). *Clin Neurophysiol* 128:1596–1598. (IF: 3.866, Citations:--).

Oliveira Santos M, de Carvalho (2017). Brain white matter demyelinating lesions and amyotrophic lateral sclerosis in a patient with C9orf72 hexanucleotide repeat expansion. *Mult Scler Relat Disord.* (IF: 2.349, Citations:--).

de Carvalho, Ryczkowski A, Andersen P, Godinho M, Grosskreutz J, Ku?ma-Kozakiewicz M, Petri S, Piotrkiewicz M, Miltenberger Miltenyi G (2017). International Survey of ALS Experts about Critical Questions for Assessing Patients with ALS. *Amyotr Lat Scler Frontotemporal Degener.* (IF: 3.054, Citations:--).

de Carvalho M, Gooch C (2017). Friend or Foe? The Yin and Yang of Gastrostomy in the Management of ALS (editorial). *Neurology.* (IF: 7.592, Citations:--).

Pinto S, de Carvalho M (2017). Comparison of slow and forced vital capacities on ability to predict survival in ALS. *Amyotr Lat Scler Frontotemporal Degener* 18:291–295. (IF: 3.054, Citations:--).

de Carvalho M (2017). Prolongation of Terminal Latency of the Phrenic Nerve in Amyotrophic Lateral Sclerosis - Is it Clinically Useful, and what are the Mechanisms? (letter). *Clin Neurophysiol* (IF: 3.866, Citations:--).

Pinto S, de Carvalho M (2017). Health status perspectives in Amyotrophic Lateral Sclerosis. *Neurodeg Dis.* (IF: 2.842, Citations:--).

de Carvalho M, Poliakov A, Tavares C, Swash M (2017). Interplay of upper and lower motor neuron degeneration in amyotrophic lateral sclerosis. *Clin Neurophysiol* 128: 2200–2204. (IF: 3.866, Citations:--).

Campos C, de Carvalho M (2017). Riluzole-Induced Recurrent Pancreatitis. *J Clin Neurosc.* (IF: 1.557, Citations:--).

de Carvalho M (2017). Cramps and Vinpocetine in ALS (letter). *Amyotr Lat Scler Frontotemporal Degener.* (IF: 3.054, Citations:--).

Pronto-Laborinho A, Gromicho M, Pereira M, Pinto S, Barros MA, Swash M, de Carvalho M (2017). Plasma Level of Club Cell CC-16 Predicts Outcome in ALS. *Acta Neur Scand.* (IF: 3.087, Citations:--).

Al-Chalabi A, Andersen PM, Chandran S, Chio A, Corcia P, Couratier P, Danielsson O, de Carvalho M, Desnuelle C, Grehl T, Grosskreutz J, Holmøy T, Ingre C, Karlsborg M, Kleveland G, Christoph Koch J, Koritnik B, KuzmaKozakiewicz M, Laaksovirta H, Ludolph A, McDermott C, Meyer T, Mitre Ropero B, Mora Pardina J, Nygren I, Petri S, Povedano Panades M, Salachas F, Shaw P, Silani V, Staaf G, Svenstrup K, Talbot K, Tysnes OB, Van Damme P, van der Kooi A, Weber M, Weydt P, Wolf J, Hardiman O, van den Berg LH (2017). ENCALS statement on edaravone. *Amyotr Lat Scler Frontotemporal Degener.* (IF: 3.054, Citations:--).

Guedes L, Chan RB, Gomes MA, Bouça R, Soares T, Xu Y, Gaspar P, Alcalay RN, Ferreira JJ, Outeiro TF, Miltenberger-Miltenyi G. Serum lipid alterations in GBA-associated Parkinson's disease. *Parkinsonism Relat Disord.* 2017; 44:58-65. (IF: 4.484, Citations:--).

Maia TV, Frank MJ (2017). An integrative perspective on the role of dopamine in schizophrenia. *Biological Psychiatry*, Vol. 81, pp. 52-66 (IF: 11.412, Citations: 19).

Maia TV, Conceição VA (2017). The roles of phasic and tonic dopamine in tic learning and expression. *Biological Psychiatry*, Vol. 82, No. 6, pp. 401-412. (IF: 11.412, Citations: 2).

Maia TV, Huys QJM, Frank MJ (2017). Theory-based computational psychiatry. *Biological Psychiatry*, Vol. 82, No. 6, pp. 382-384 \*Authors contributed equally. (IF: 11.412, Citations:--).

Conceição VA, Dias A, Farinha AC, Maia TV (2017). Premonitory urges and tics in Tourette syndrome: computational mechanisms and neural correlates. *Current Opinion in Neurobiology*, Vol. 46, pp. 187-199. (IF: 6.133, Citations:--).

Hinkelbein J, Lamperti M, Akeson J, Santos J, Costa J, De Robertis E, Longrois D, Novak-Jankovic V, Petrini F, Struys MMRF, Veyckemans F, Fuchs-Buder T, Fitzgerald R (2017). European Society of Anaesthesiology and European Board of Anaesthesiology guidelines for procedural sedation and analgesia in adults. *European Journal of Anaesthesiology*; 34:1-19 (IF: 3.570, Citations:2).

Freitas Castro V, Nascimento Alves P, Franco AC, Martins IP, Conceição I (2017). Cognitive impairment in liver transplanted patients with transthyretin-related hereditary amyloid polyneuropathy. *Amyloid*; 24(2):110-114. doi: 10.1080/13506129.2017.1335639. Epub 2017 Jun 7. (IF:3.373, Citations:--).

Almeida V, Conceição I, Fineza I, Coelho T, Silveira F, Santos M, Valverde A, Geraldo A, Maré R, Aguiar TC, Mendonça C, Martins J, Medeiros L, Barroso C, Vieira JP, Moreno T, Negrão L, Dias MS, Lacerda L, Evangelista T (2017). Screening for Pompe disease in a Portuguese high-risk population. *Neuromuscul Disord*; 27(8):777-781. doi: 10.1016/j.nmd.2017.03.010. (IF: 2.969, Citations: 1).

Azevedo Coutinho MDC, Cortez-Dias N, Cantinho G, Conceição I, Guimarães T, Lima da Silva G, Nobre Menezes M, Francisco AR, Plácido R, Pinto FJ (2017). Progression of myocardial sympathetic denervation assessed by 123I-MIBG imaging in familial amyloid polyneuropathy and the effect of liver transplantation. *Rev Port Cardiol*; 36(5):333-340. doi: 10.1016/j.repc.2016.08.010 (IF: 1.195, Citations:--).

Dyck PJ, Kincaid JC, Dyck PJB, Chaudhry V, Goyal NA, Alves C, Salhi H, Wiesman JF, Labeyrie C, Robinson-Papp J, Cardoso M, Laura M, Ruzhansky K, Cortese A, Brannagan TH 3rd, Khoury J, Khella S, Waddington-Cruz M, Ferreira J, Wang AK, Pinto MV, Ayache SS, Benson MD, Berk JL, Coelho T, Polydefkis M, Gorevic P, Adams DH, Plante-Bordeneuve V, Whelan C, Merlini G, Heitner S, Drachman BM, Conceição I, Klein CJ, Gertz MA, Ackermann EJ, Hughes SG, Mauermann ML, Bergemann R, Lodermeier KA, Davies JL, Carter RE, Litchy WJ (2017). Assessing mNIS+7Ionis and international neurologists' proficiency in a familial amyloidotic polyneuropathy trial. *Muscle Nerve*; 56(5):901-911. doi: 10.1002/mus.25563. (IF: 2.605, Citations:--).

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Teixeira PP, Oliveira MM, Ramos R, Rio P, Cunha PS, Delgado AS, Ferreira RC (2017). Left atrial appendage volume as a new predictor of atrial fibrillation recurrence after catheter ablation. *Journal of Interventional Cardiac Electrophysiology*, 49(2), 165-171. (IF: 1.676, Citations:--).

Aguiar RS, Oliveira M, Valente B, Silva CP, Almeida ML, Cruz FR (2017). Ventricular electrical storm after acute myocardial infarction successfully treated with temporary atrial overdrive pacing. *Medicina intensiva*, 41(4), 252. (IF: 1.231, Citations:--).

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Oliveira M. Autonomic Nervous System Disturbances in Cardiovascular Disorders. *Cardiol Young*, 25(4), 647-654. (IF: 0905, Citations:--).

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### Other Publications International

Laranjo S, Geraldés V, Oliveira M, Rocha I (2017). Insights into the background of autonomic medicine. *Revista Portuguesa de Cardiologia (English Edition)*, 36(10), 757-771. (IF: 1.195, Citations:--).

Abreu A, Oliveira M, Cunha PS, Santa Clara H, Portugal G, Rodrigues IG, Branco L (2017). Does permanent atrial fibrillation modify response to cardiac resynchronization therapy in heart failure patients? *Revista Portuguesa de Cardiologia (English Edition)*, 36(10), 687-694. (IF: 1.195, Citations:--).

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Rio P, Oliveira MM, Cunha PS, da Silva MN, Branco LM, Galrinho A, Ferreira RC (2017). What happens to non-responders in cardiac resynchronization therapy? *Revista Portuguesa de Cardiologia (English Edition)*, 36(12), 885-892. (IF: 1.195, Citations:--).

### Other Publications National

Oliveira M. CPC2017: O coração da Cardiologia em Portugal, *Revista Perspectivas*, March, 2017.

Oliveira M. Terapêutica farmacológica das Doenças Cardiovasculares - ANTIARRÍTMICOS Livro de Prevenção e Reabilitação Cardiovascular – Edição Sociedade Brasileira de Cardiologia/Sociedade Portuguesa de Cardiologia (1<sup>st</sup> Edition Abril/2016) ISBN 978-972-97099-4-4 (pp 243-252). (Book Chapter).

Oliveira M. Carto System. Experiência e casos clínicos do Hospital Santa Marta (CHLC). In “20 Anos de parceria visionária”, Edição Biosense Webster, Johnson & Johnson pp 28-31, 2017. (Book Chapter).

### Invited Lectures and Seminars

Oliveira M. CDI na Miocardiopatia não isquêmica - do entusiasmo a desilusão? Curso de Atualização em Cardiologia e Medicina Cardiovascular, Lisbon, Portugal, January 2017.

Oliveira M. Cardiopatias elétricas e prática desportiva (novos consensos de Bethesda). Arritmias no coração do atleta. Arritmias 2017, Cascais, Portugal, February 2017.

Oliveira M. FA “silenciosa” detectada por dispositivos implantados. Quando e quem anticoagular? Novos anticoagulantes orais – aspectos práticos. Arritmias 2017, Cascais, Portugal, February 2017.

Coelho T, Conceição I, Inês M, Soares M, de Carvalho M, Costa J. Real-world experience: Expert insights from everyday clinical practice. VI Symposium on Advances and Research in Transthyretin Amyloidosis, Vienna, Austria. February 2017. (Invited Presentation).

Conceição I. Doença de Pompe. IV Simpósio Doenças Raras, Sintomas Comuns: Olhares Diferentes, Interesses Similares, Figueira da Foz, Portugal, February 18, 2017.

Conceição I. The asymptomatic gene carrier: how to review (Workshop). ARIA VI – Looking to the Future: Meeting the challenge of early diagnosis and optimal treatment, Vienna, Austria, February 24-25, 2017.

Oliveira M. Fibrilhação Auricular. Doenças Cardiovasculares: Fibrilhação Auricular e Síncope 34º Encontro Nacional da Associação de Medicina Geral e Familiar, Estoril, Portugal, March 2017.

Oliveira M. Olhar o Coração: Conhecimento, Inovação e Arte. Sessão de Abertura do XXXVIII Congresso Português de Cardiologia, Salgados, Portugal, April 2017.

de Carvalho M. Amyotrophic Lateral Sclerosis: overview. 2º Simpósio Esclerose Lateral Amiotrófica: Ciência e Sociedade, Lisbon, Portugal, April 2017.

de Carvalho M. Integração dos Cuidados Paliativos em Doenças Neuromusculares. Congresso de Cuidados Continuados e Paliativos, Lisbon, Portugal, May 2017.

Oliveira M. Como tratar a Fibrilhação Auricular Persistente? Em busca do sucesso... Academia CUF, Porto, Portugal, May 2017.

Conceição I. hTTR-Amyloidosis: How can we reach the right diagnosis? FIP Webinar, June 1, 2017.

de Carvalho M. Clinical Neurophysiology in the Intensive Care. Respiratory Evaluation. European Congress of Clinical Neurophysiology, Budapest, Hungary, September 2017.

de Carvalho M. Atualidade do estudo eletromiográfico no diagnóstico das miopatias. Reunião de Outono da Sociedade Portuguesa de Estudos de Doenças Neuromusculares, Coimbra, Portugal, September 2017.

de Carvalho M. Investigação – um compromisso com a esperança. Conferência Viver o Presente na Esperança da Cura, Lisbon, Portugal, September 2017.

Oliveira M. Prevenção da Morte Súbita no Coração Estruturalmente Normal. XXIII Jornadas de Cardiologia de Santarém, Santarém, Portugal, September 2017.

M I, Coelho T, Conceição I, Soares M, de Carvalho M, Costa J. Surviving transthyretin familial amyloid polyneuropathy. Spanish Hereditary Amyloidosis by TTR (hATTR) National Meeting, Madrid, Spain, September 2017. (Invited Presentation).

Conceição I. TTR\_FAP - Travel of a gene. “Meet the Expert” A jornada do doente com amiloidose hereditária – TTR Course, Lisbon, Portugal, September 28- 29, 2017.

Conceição I. TTR\_FAP - How to follow-up TTR-FAP carriers. “Meet the Expert” A jornada do doente com amiloidose hereditária – TTR Course, Lisbon, Portugal, September 28- 29, 2017.

Conceição I. Management of TTR-FAP. “Meet the Expert” A jornada do doente com amiloidose hereditária – TTR Course, Lisbon, Portugal, September 28- 29, 2017.

de Carvalho M. Phenotypic variation and diagnostic criteria. International Symposium on Amyotrophic Lateral Sclerosis (ALS): state of the art, Bolonha, Italy, October 2017.

Conceição I. Long-term treatment of TTR-FAP: what does this mean for Neurologist in our patients? 1<sup>st</sup> European ATTR Amyloidosis Meeting, Paris, France, November 1-3, 2017.

Conceição I. hATTR amyloidosis - diagnostic and treatment challenges: can we improve the care of patients? Peripheral Nerve Society Meeting, Sitges, Spain, 2017.

Conceição I. A Holistic Approach Towards Cure and Care of ATTR Patients.

Maia TV. Keynote Lecturer. Using computational models to develop rigorous and comprehensive accounts of neuropsychiatric disorders. International College of Neuropsychopharmacology 2017 Thematic Meeting: Treatment-Resistant Depression, Prague, Czech Republic, 2017.

Maia TV. A bottom-up computational approach to psychopathology. Presidential Symposium on Computational Psychiatry and Its Intersection with the NIMH Research Domain Criteria Initiative, 57<sup>th</sup> Annual Meeting of the Society for Psychophysiological Research, Vienna, Austria, 2017.

Maia TV. Participant/Discussant (by invitation from the Director of the National Institute of Mental Health, USA). Workshop on Computational Psychiatry: Opportunities and Challenges for the Future, National Institute of Mental Health, Bethesda, USA, 2017.

Maia TV. A reinforcement-learning account of Tourette syndrome. 25<sup>th</sup> European Congress of Psychiatry, Florence, Italy, 2017.

Maia TV. A reinforcement-learning perspective on the role of dopamine in schizophrenia. 6<sup>th</sup> European Conference on Schizophrenia Research, Berlin, Germany, 2017.

Maia TV. Reinforcement learning and Tourette syndrome. 72<sup>nd</sup> Annual Meeting of the Society of Biological Psychiatry (Satellite Meeting on Computational Psychiatry), San Diego, California, 2017.

Miltenberger-Miltenyi G. Interrelation of genetic variants between lysosomal diseases and other entities. I Reunión del Grupo Español de Enfermedades de Depósito Lisosomal (Geedl) Y Otras Enfermedades Hematológicas Singulares, Zaragoza, Spain, 2017.

Castro J. Como avaliar um doente com neuropatia de pequenas fibras. “Meet the Expert” – A jornada do doente com amiloidose hereditária – TTR, Lisbon, Portugal, 2017. (Invited Presentation).

Domingos F. Fisiologia do equilíbrio ácido-base. IV Curso De Equilíbrio Hidro-Electrolítico e Ácido-Base, Amadora, Portugal, 2017.

### **Communications in International Conferences**

Leote J, Valls-Solé J, Costa J, Casanova-Molla J, Oleaga L, Fonseca J, Nunes RG, Ferreira HA. Vocal accelerometer recording of TMS evoked language disturbances: preliminary study for awake surgery application. 2<sup>nd</sup> International Brain Stimulation Conference, Barcelona, Spain, March 2017. (Poster Presentation).

Heiman-Patterson T, Cudkowicz M, De Carvalho M, Genge A, Hardiman O, Jackson C, Lechtzin N, Mitsumoto H, Silani V, Rudnicki SA, Kulke S, Andrews JA, Van den Berg L. Understanding the Use of Noninvasive Ventilation in the Treatment of Amyotrophic Lateral Sclerosis in the US and Europe: results of an international physician survey. American Academy of Neurology, Boston, USA, April 2017. (Poster Presentation).

Adams D, Coelho T, Conceição I, Waddington Cruz M, Schmidt H, Buades J, Campistol J, Pouget J, Berk J, Ziyadeh N, Partisano A, Chen J, Sweetser M, Gollob J, Suhr O. Phase 2 Open-Label Extension (Ole) Study of Patisiran, an Investigational RNA Interference (RNAi) Therapeutic for The Treatment of Hereditary ATTR Amyloidosis with Polyneuropathy. ISPOR 22<sup>nd</sup> Annual International Meeting, Boston, USA, May 20-24, 2017. (Poster Presentation).

M I, Coelho T, Conceição I, Bago D'Uva T, Carvalho M, Costa J. Life Expectancy and Costs of Transthyretin Familial Amyloid Polyneuropathy. ISPOR 22<sup>nd</sup> Annual International Meeting, Boston, USA, May 20-24, 2017. (Poster Presentation).

van den Berg L, Cudkowicz M, de Carvalho M, Genge A, Hardiman O, Jackson C, Lechtzin N, Mitsumoto H, Silani V, Andrews JA, Kulke S, Rudnicki A, Heiman-Patterson T. Use of Noninvasive Ventilation in the Treatment of ALS in Europe Versus in the US: Results of an International ALS Specialist Survey. ENCALS Meeting 2017, Ljubliana, May 2017. (Poster Presentation).

Pinto S, de Carvalho M. Survival in Amyotrophic Lateral Sclerosis and its Dependency of Slow and Forced Vital Capacity. ENCALS Meeting 2017, Ljubliana, May 2017. (Poster Presentation).

Moreira R, Oliveira M, Morais L, Silva Cunha P, Nogueira da Silva M, Lousinha A, Tereno Valente B, Daniel P, Delgado A, Pimenta R, Braz M, Ferreira RC. Risk of atrial fibrillation after catheter ablation of typical atrial flutter: a long-term outcome study. Europace, Vienna, June 2017.

Cabanelas N, Daniel P, Cunha PS, Silva N, Valente B, Lousinha A, Morais L, Delgado A, Pimenta R, Ferreira RC, Oliveira M. Junctional rhythm induction or increase in atrio-ventricular node refractoriness in typical atrio-ventricular nodal reentry tachycardia ablation: which is the best marker of success? Europace, Vienna, June 2017.

Miranda B, Pinto S, de Carvalho M. The Impact of Spasticity on Diaphragm Contraction: electrophysiological assessment. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Oral Presentation).

Miranda B, Castro J, Conceição I. Transthyretin familial amyloid polyneuropathy: the neuropathy progression on treated patients compared with natural disease progression. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Oral Presentation).

Adams D, Coelho T, Conceição I, Waddington Cruz M, Schmidt H, Buades J, Campistol J, Pouget J, Berk J, Ziyadeh N, Partisano A, Chen J, Sweetser M, Gollob J, Suhr O. Phase 2 open-label extension (OLE) study of patisiran with or without a TTR stabilizer for the treatment of hereditary ATTR (hATTR) amyloidosis with polyneuropathy. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Oral Presentation).

Alces PN, de Carvalho M, Reimão S, Fonseca AC, Canhã P. Voluntary Control of Plegic Limb During Yawning after Stroke. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Campos C, de Carvalho M. Riluzole-Induced Recurrent Pancreatitis. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Campos C, Santos MO, Roque R, Conceição I, de Carvalho M. Mitochondrial Neurogastrointestinal Encephalomyopathy: Novel pathogenic mutation in Thymidine Phosphorilase gene in a patient from Cape Verde Islands. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Oral Presentation).

Oliveira Santos M, Caldeira I, de Carvalho M. Brain White Matter Demyelinating Lesions and Amyotrophic Lateral Sclerosis in a Patient with C9orf72 Hexanucleotide Repeat Expansion. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Dias M, Castro J, Sousa R, de Carvalho M. A Rare Cause of Facial Asymmetry. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Dias M, Castro J, Sousa R, de Carvalho M. Bilateral Carpal Tunnel Syndrome as an Adverse Effect of Pembrolizumab. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Alves PN, Castro V, Franco A, Martins IP, Conceição I. Cognitive impairment in transthyretin related familial amyloid polyneuropathy. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Campos C, Oliveira Santos M, Roque RVFR, Conceição I, de Carvalho M. Mitochondrial neurogastrointestinal encephalomyopathy: Novel pathogenic mutation in thymidine phosphorilase gene in a patient from Cape Verde. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Campos C, Oliveira Santos M, Conceição I. Transthyretin familial amyloid polyneuropathy: A new clinical score for monitoring disease progression. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Broqueira Rodrigues F, Bentes C, Sousa D, Duarte G, Franco A, Marques R, Nzwalo H, Peralta R, Ferro JMMC, Costa J. Frequency of post-stroke epileptiform activity - a systematic review and meta-analysis of observational studies. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017.

Oliveira Santos M, Inês M, Conceição. Transthyretin-related familial amyloid polyneuropathy: Demographic and phenotypical characterization of a patients' cohort (followed) in a Portuguese Cente. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, the Netherlands, June 24-27, 2017. (Poster Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NS, Carvalho FA. Using AFM to Study Red Blood Cells' Morphology and Elasticity on Amyotrophic Lateral Sclerosis. European Biophysical Societies' Association, Edinburgh, Scotland, July 2017. (Oral Presentation).

Polydefkis M, Ebenezer G, Adams D, Coelho T, Conceicao I, Waddington Cruz M, Schmidt H, Buades J, Campistol J, Pouget J, Berk J, Partisano A, Chen J, Gollob J, Suhr O. Effect of Patisiran on Nerve Fiber Density and Amyloid Content in Skin: Results from Phase 2 Open Label Extension (Ole) Study In hATTR Amyloidosis. Peripheral Nerve Society Meeting, Sitges, Spain, July 7-12, 2017. (Oral Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes morphology and elasticity on Amyotrophic Lateral Sclerosis. 19<sup>th</sup> IUPAB Congress and 11<sup>th</sup> EBSA Congress, Edinburgh, Scotland, July 16-20, 2017.

de Carvalho M, Pereira M, Fernandes S, Miranda PC. Neuromodulation of Lower Limbs Motor Circuitry with Transcutaneous Lumbar Spinal Cord Direct Current Stimulation. 16<sup>th</sup> European Congress of Clinical Neurophysiology, Budapest, Hungary, August 30-September 2, 2017. (Oral Presentation).

Johnsen B, Pughahl K, Fuglsang-Frederiksen A, Kollwe K, Paracka L, Dengler R, Camdessanché J-P, Nix N, Liguori R, Schofield I, Maderna L, Czell D, Neuwirth C, Weber M, Drory V, Abraham A, de Carvalho M. Large Inter and Intra-rater Variation on Diagnostic Criteria for Amyotrophic Lateral Sclerosis. 16<sup>th</sup> European Congress of Clinical Neurophysiology, Budapest, Hungary, August 30-September 2, 2017. (Oral Presentation).

Tankisi H, Pughahl K, Johnsen B, Cengiz B, Camdessanché J-P, de Carvalho M. Fuglsang-Frederiksen, Peak Ratio and Motor Unit Potential Analysis in Detection of Chronic Neurogenic Changes in Amyotrophic Lateral Sclerosis. 16<sup>th</sup> European Congress of Clinical Neurophysiology, Budapest, Hungary, August 30-September 2, 2017. (Oral Presentation).

Castro J, Costa J, Castro I, Abreu D, Gonçalves N, Conceição I. Small fiber assessment by sudoscan in transthyretin familial amyloid polyneuropathy treated patients – A longitudinal study. 16<sup>th</sup> European Congress of Clinical Neurophysiology, Budapest, Hungary, August 30-September 2, 2017. (Poster Presentation).

Castro J, Costa J, Castro I, Abreu D, Gonçalves N, Conceição I. Small fiber assessment by Sudoscan in transthyretin familial amyloid polyneuropathy treated patients – a longitudinal study. 16<sup>th</sup> European Congress of Clinical Neurophysiology, Budapest, Hungary, August 30-September 2, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Soares M, de Carvalho M, Costa J. Real-world comparative treatment effectiveness in early-onset transthyretin familial amyloid polyneuropathy patients. 15<sup>o</sup> Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 12-13, 2017. (Oral Presentation).

Inês M, Coelho T, Conceição I, Ferreira L, de Carvalho M, Costa J. Transthyretin familial amyloid polyneuropathy impact on health-related quality of life. 15<sup>o</sup> Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 12-13, 2017. (Oral Presentation).



Inês M, Coelho T, Conceição I, Bago D'Uva T, de Carvalho M, Costa J. Health-related quality of life in patients with transthyretin familial amyloid polyneuropathy in Portugal. 15<sup>o</sup> Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 12-13, 2017. (Oral Presentation).

Inês M, Coelho T, Conceição I, Duarte-Ramos F, de Carvalho M, Costa J. Prevalence of transthyretin familial amyloid polyneuropathy in Portugal during year 2016. 15<sup>o</sup> Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 12-13, 2017. (Poster Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes morphology and elasticity on Amyotrophic Lateral Sclerosis. Advanced School in Biophysical Methods to Study Biomolecular Interactions, São Paulo, Brazil, October 16-27, 2017.

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes morphology and elasticity on Amyotrophic Lateral Sclerosis. Annual Meeting of the Brazilian Biophysics Society, Santos, Brazil, October 27-29, 2017.

Inês M, Coelho T, Conceicao I, Saramago P, Carvalho M, Costa J. Life expectancy and costs of transthyretin familial amyloid polyneuropathy. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Borges M, Carvalho M, Costa J. Costs associated with transthyretin familial amyloid polyneuropathy progression. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Borges M, de Carvalho M, Costa J. Costs Associated with Transthyretin Familial Amyloid Polyneuropathy Progression. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Saramago P, de Carvalho M, Costa J. Life Expectancy and Costs of Transthyretin Familial Amyloid Polyneuropathy. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Borges M, de Carvalho M, Costa J. Costs associated with transthyretin familial amyloid polyneuropathy progression. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Saramago P, de Carvalho M, Costa J. Life expectancy and costs of transthyretin familial amyloid polyneuropathy. ISPOR 20<sup>th</sup> Annual European Congress, Glasgow, Scotland, November 6-10, 2017. (Poster Presentation).

Pinto S, de Carvalho M. Health status perspective in ALS. Amyotroph Lateral Scler Frontotemporal Degeneration 2017. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Oral Presentation).

Pinto A, Braga AC, Guedes S, de Carvalho M. Home telemonitoring for ALS in early and late ventilated patients: a validation study. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Poster Presentation).

Mora JS (on behalf of the AB10015 study group), Hermine O. Masitinib as an add-on therapy to riluzole is safe and effective in the treatment of ALS. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Poster Presentation).

Jackson C, de Carvalho M, Genge A, Heiman-Patterson T, Shefner J. Correlations Between Slow Vital Capacity and Measures of Respiratory Function on the ALSFRS-R. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Poster Presentation).

Pinto S, de Carvalho M. Sniff nasal inspiratory pressure (SNIP) in amyotrophic lateral sclerosis: relevance of the methodology for respiratory function evaluation. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Poster Presentation).

Pinto S, de Carvalho M. Comparison between Slow and Forced Vital Capacities on Survival Prediction in ALS. 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Oral Presentation).

Shefner J, Cudkowicz M, Hardiman O, Meng L, Wolff A, Lee J, Rudnick S, Malik F, Andrews J. Vitality-ALS: results of a phase III trial of tirasemtiv, a fast skeletal muscle troponin activator, as a potential treatment for patients with ALS (Vitality Study Group). 28<sup>th</sup> International Symposium on ALS/MND, Boston, USA, December 2017. (Oral Presentation).

Coutinho MC, Dias NC, Gonçalves S, Cantinho G, Guimarães T, Silva GL, Francisco AR, Santos L, Conceição I, Pinto F. How useful is 99mTc-DPD scintigraphy in diagnosis of cardiac amyloidosis in transthyretin V30M familial amyloid polyneuropathy? American College of Cardiology (ACC) 2017 Congress Washington, USA, 2017. (Poster Presentation).

Rodrigues G, Oliveira M, Cunha PS, Branco L, Galrinho A, Abreu A, Osorio P, Lousinha A, Valente B, Feliciano J, Rio P, Portugal G, Neiva J, Morais L, Cruz Ferreira R. Early time to response in hemodynamic sensor guided cardiac resynchronization therapy. European Congress of Cardiology, Barcelona, Spain, 2017.

Daniel P, Abreu A, Rodrigues I, Oliveira M, Cruz HS, Morais LA, Santos V, Silva Cunha P, Pinheiro T, Napoleao P, Mota Carmo M, Ferreira RC. Is there a correlation between magnitude of response to crt and inflammatory response? European Congress of Cardiology, Barcelona, Spain, 2017.

Morais LA, Goncalves A, Portugal G, Valente B, Lousinha A, Coutinho-Cruz M, Delgado A, Pimenta R, Silva-Cunha P, Oliveira M, Cruz-Ferreira R. Automatic recognition of apnea/hypopnea and relation with atrial tachyarrhythmias burden in pacemakers carriers. Results from an advance algorithm using transthoracic impedance. European Congress of Cardiology, Barcelona, Spain, 2017.

Ilhão R, Abreu A, Rodrigues, Cruz M, Portugal G, Mendonça T, Gonçalves A, Santa Clara H, Oliveira L, Silva-Cunha P, Mota Carmo M, Oliveira M, Ferreira RC. Cardiac sympathetic activity pre and post resynchronization therapy. European Congress of Cardiology, Barcelona, Spain, 2017.

De Carvalho M, Andersen PM, Gromicho M, Grosskreutz J, Kuzma-Kozakiewicz M, Petri S, Piotrkiewicz M, Podsiadtly-Marczykowska T, Stubendorf B, Szacka K, Uysal H. OnWebDuals: the European project funded by national agencies under the patronage of Joint Programme of Neurodegenerative Disease Research (JPND). (Poster Presentation).

Pinto S, de Carvalho M. Relevance of Methology for Analysing Results: the SNIP model in Amyotrophic Lateral Sclerosis. ENCALS Meeting 2017. (Poster Presentation).

### **Communications in National Conferences**

Miltenberger-Miltenyi G. Cerebrospinal fluid biomarkers. Master/PhD in Neuroscience, Cognitive Deterioration in Ageing and Dementia. Symposium: Biomarkers for Alzheimer's disease. Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 15, 2017. (Invited presentations in postgraduate courses).

Francisco JR, Agostinho IG, Conceição I, Almeida A, Pinto FJ, Coutinho CA. Padrão de Deformação Miocárdica não Homogénea do Ventrículo Esquerdo na Polineuropatia Amiloidótica Familiar: será esta a regra? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017. (Oral Presentation).

Santos L, Dias NC, Gonçalves S, Guimarães T, Silva GL, Francisco ARG, Agostinho JR, Gonçalves IS, Conceição I, Almeida AG, Pinto FJ, Coutinho CA. Deformação Pós-Sistólica em Doentes com Polineuropatia Amiloidótica Familiar. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017. (Oral Presentation).

Portugal G, Kosiuk J, Hilbert S, John S, Oliveira M, Hindricks G, Bollman A. In-vivo validation of a novel algorithm for premature ventricular contraction recognition. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017. (Oral Presentation).

Gonçalves-Rosa N, Tavares C, Geraldes V, Montani JP, Rocha I, Oliveira M. Síndrome metabólica e vulnerabilidade para fibrilhação auricular: substrato histopatológico e electrofisiológico num modelo animal. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Monteiro AV, Cunha PS, Oliveira M, Rosa SA, Agapito A, Sousa L, Oliveira JA, Laranjo S, Trigo C, Fragata J, Delgado A, Ferreira RC. Long-term efficacy of implantable cardioverter defibrillator in surgically corrected congenital heart disease – are tetralogy of fallot patients different? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Laranjo S, Loureiro P, Oliveira M, Trigo C, Pinto FF. Genetic and clinical features in inherited long qt syndrome in pediatric age: single center data. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Mesquita DV, Abreu A, Portugal G, Oliveira M, Cunha PS, Aguiar S, Rio P, Santos V, Santa-Clara H, Ferreira R. Redução de taquiarritmias ventriculares na insuficiência cardíaca crónica por modulação do sistema nervoso autónómico cardíaco através de reabilitação cardíaca. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Valente BT, Conceição JM, Silva-Cunha P, Pimenta R, Delgado A, Lousinha A, Osório P, Silva MN, Ramos JS, Oliveira M, Ferreira RC. Experiência de um centro terciário na extração de eléctrodos com a «técnica de pisa». XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Nave-Leal E, Laranjo SM, Alves S, Morais LA, Cunha PS, Ribeiro JP, Oliveira M, Ferreira RC. Sensibilidade à alteração da condição clínica medida pela escala específica de qualidade de vida na síncope - impact of syncope on quality of life. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Pousinho F, Carvalho AF, Sarmiento P, Ferreira MJ, Farias F, Selas M, Oliveira M, Ferreira RC. Consulta de enfermagem de arritmologia - uma realidade. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Portugal G, Cruz MC, Moreira RI, Pimenta R, Delgado A, Brás M, Monteiro A, Valente B, Lousinha A, Silva-Cunha P, Oliveira M, Ferreira RC. Inappropriate therapies in cardioverter-defibrillator recipients lead to late increase in major cardiac adverse events. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Daniel PM, Abreu A, Rodrigues I, Oliveira M, Santa Clara H, Morais L, Santos V, Cunha PS, Pinheiro T, Napoleão P, Carmo MM, Ferreira RC. Is there a correlation between magnitude of response to crt and inflammatory response? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Moreira RI, Abreu A, Rodrigues I, Cruz M, Daniel PM, Portugal G, Clara HS, Oliveira L, Silva-Cunha P, Carmo MM, Oliveira M, Ferreira RC. Effect of cardiac resynchronization therapy on cardiac sympathetic nervous dysfunction and serum high sensitivity c-reactive protein level. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Cabanelas N, Oliveira M, Silva-Cunha P, Silva N, Valente B, Lousinha A, Daniel PM, Morais L, Portugal G, Pimenta R, Delgado A, Ferreira R. Ablation of ventricular tachycardia in patients with severe left ventricular dysfunction and frequent appropriate icd therapy: potential benefits of substrate modification. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Cruz MC, Abreu A, Oliveira M, Delgado A, Oliveira L, Clara HS, Santos V, Portugal G, Rodrigues I, Morais L, Carmo MM, Ferreira RC. Occurrence of sustained ventricular arrhythmias after crt in patients with remote monitoring - can we anticipate the outcome? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Cruz M, Abreu A, Portugal G, Oliveira L, Clara HS, Santos V, Portugal G, Rodrigues I, Morais L, Moreira R, Carmo MM, Ferreira RC. Mibg cardiac scintigraphy as a predictor of adverse events in patients with heart failure with reduced ejection fraction submitted to crt - the particular case of responders. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Portugal G, Portugal G, Silva-Cunha P, Lousinha A, Valente B, Monteiro A, Gonçalves A, Mendonça T, Brás M, Pimenta R, Delgado A, Ferreira RC. What patients benefit the most from remote monitoring? A long-term follow-up study in an icd population. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Silva-Cunha P, Valente B, Delgado A, Pimenta R, Oliveira M. Implantation and clinical performance of a leadless pacemaker in patients with a high-risk profile for complications. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Laranjo S, Oliveira M, Silva-Cunha P, Trigo C, Pimenta R, Delgado A, Pinto F. Catheter ablation of supraventricular tachycardia in children using a limited fluoroscopic approach. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Laranjo S, Alves S, Nave-Leal E, Ribeiro JP, Daniel PM, Lousinha A, Oliveira M, Ferreira RC. Impacto de um programa de tilt training na qualidade de vida de doentes com síncope reflexa recorrente. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Fernandes M, Oliveira M, Primo J, Reis H, Sanfins V, Nicola P. Remote versus in-office monitoring for implantable cardioverter defibrillators: the portlink study (Portuguese research on telemonitoring with carelink). XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Gonçalves A, Morais L, Portugal G, Valente B, Lousinha A, Cruz M, Delgado A, Pimenta R, Nogueira da Silva M, Silva-Cunha P, Oliveira M, Ferreira RC. Automatic recognition of apnea/hypopnea and relation with atrial tachyarrhythmias burden in pacemakers carriers – results from an advance algorithm using transthoracic impedance. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Nogueira da Silva M, Valente B, Silva-Cunha P, Pimenta R, Delgado A, Ramos JS, Gil V, Oliveira M. Crioablação com balão no tratamento da fibrilhação auricular: importância da monitorização do potencial de acção diafragmático na prevenção da lesão do nervo frénico. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Silva-Cunha P, Valente B, Morais LA, Daniel PM, Nogueira da Silva M, Pimenta R, Delgado A, Pereira M, Ferreira RC, Oliveira M. High-resolution 3d voltage mapping with single-puncture approach in atrial fibrillation ablation. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Portugal G, Oliveira M, Silva-Cunha P, Lousinha A, Valente B, Morais LA, Daniel PM, Rodrigues I, Aguiar S, Pimenta R, Delgado A, Ferreira RC. Atrial fibrillation ablation in special populations. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Morais L, Moreira RI, Daniel PM, Portugal G, Lousinha A, Valente B, Cruz M, Pimenta R, Delgado A, Silva-Cunha P, Oliveira M, Ferreira RC. Impact of a septal isthmus line combined with posterior cavotricuspid isthmus ablation based on electroanatomic mapping in the treatment of typical atrial flutter. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Napoleão P, Abreu A, Selas P, Pinheiro T, Oliveira M, Carmo MM. High soluble cd40l associated to cardiopulmonary response of heart failure patients 7 months after cardiac resynchronization therapy. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Daniel PM, Cabanelas N, Silva-Cunha P, Silva N, Valente B, Lousinha A, Morais LA, Delgado A, Pimenta R, Ferreira RC, Oliveira M. Indução de ritmo juncional ou aumento da refratariedade do nódulo aurículo-ventricular na ablação da via lenta da taquicardia de reentrada nodal típica: qual o melhor marcador de sucesso? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Inês M, Coelho T, Conceição I, Soares M, de Carvalho M, Costa J. Real-world comparative treatment effectiveness in early-onset transthyretin familial amyloid polyneuropathy patients. 15ª Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 2017. (Oral Presentation).

Inês M, Coelho T, Conceição I, Ferreira L, de Carvalho M, Costa J. Transthyretin familial amyloid polyneuropathy impact on health-related quality of life. 15ª Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 2017. (Oral Presentation).

Inês M, Coelho T, Conceição I, Bago D'Uva T, de Carvalho M, Costa J. Health-related quality of life in patients with transthyretin familial amyloid polyneuropathy in Portugal. 15ª Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 2017. (Poster Presentation).

Inês M, Coelho T, Conceição I, Duarte-Ramos F, de Carvalho M, Costa J. Prevalence of transthyretin familial amyloid polyneuropathy in Portugal during year 2016. 15ª Conferência Nacional de Economia da Saúde, Coimbra, Portugal, October 2017. (Poster Presentation).

Santos MO, Roque R, Conceição I. Envolvimento respiratório grave num doente da Guiné-Bissau com distrofia muscular das cinturas tipo 2A associada a uma nova mutação patogénica. Congresso de Neurologia, Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 16-18, 2017. (Poster Presentation).

Campos CF, Conceição I. Epidemiologia da neuropatia periférica na área de referência de um centro terciário. Congresso de Neurologia, Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 16-18, 2017. (Oral Presentation).

Silva-Cunha, Valente B, Morais LA, Daniel PM, Silva N, Pimenta R, Delgado A, Pereira M, Ferreira RC, Oliveira M. High-definition 3d voltage mapping with single-puncture approach in atrial fibrillation ablation. Arritmias 2017, Cascais, Portugal, 2017.



Laranjo S, Oliveira M, Silva-Cunha P, Trigo C, Pimenta R, Delgado A, Pinto F. Catheter ablation of supraventricular tachycardia in children using a limited fluoroscopic approach. Arritmias 2017, Cascais, Portugal, 2017.

Portugal G, Valente B, Lousinha A, Cruz M, Delgado A, Pimenta R, Silva N, Silva-Cunha P, Oliveira M, Ferreira RC. Sleep apnea syndrome prevalence and atrial tachyarrhythmias association in pacemaker carriers. Arritmias 2017, Cascais, Portugal, 2017.

Rosa NG, Tavares C, Geraldes V, Montani JP, Rocha I, Oliveira M. Vulnerabilidade para fibrilhação auricular num novo modelo animal de síndrome metabólica. Arritmias 2017, Cascais, Portugal, 2017.

Rodrigues I, Portugal G, Oliveira M, Silva-Cunha P, Lousinha A, Valente B, Morais L, Daniel PM, Aguiar S, Pimenta R, Delgado A, Ferreira RC. Atrial fibrillation ablation in special populations. Arritmias 2017, Cascais, Portugal, 2017.

Rodrigues I, Oliveira M, Silva-Cunha P, Osório P, Lousinha A, Portugal G, Morais L, Daniel PM, Monteiro A, Ferreira RC. Efficacy and safety of internal cardioversion of persistent atrial fibrillation in implantable cardioverter defibrillator patient. Arritmias 2017, Cascais, Portugal, 2017.

Moreira R, Rio P, Silva-Cunha P, Nogueira M, Branco L, Galrinho A, Feliciano J, Pimenta R, Delgado AS, Oliveira M, Ferreira RC. Response and outcomes of cardiac resynchronization therapy in patients with renal dysfunction. Arritmias 2017, Cascais, Portugal, 2017.

### **Organisation of Conferences**

Oliveira M. Organizer and Lecturer. Reunião Nacional de Pacing Cardíaco, Covilhã, Portugal, May 2017.

Oliveira M. Organizer and Lecturer. Summer Meeting 2017, Centro Cultural de Belém, Lisbon, Portugal, July 2017.

Conceição I. "Meet the Expert" A jornada do doente com amiloidose hereditária. TTR Course, Lisbon, Portugal, September 28-29, 2017.

Oliveira M. Organizer and Lecturer. Basic Course on Cardiac Pacing and Implant Skills Builder, Hospital Santa Marta, Lisbon, Portugal, October 2017.

Oliveira M. Organizer and Lecturer. Reunião Nacional de Eletrofisiologia, Guimarães, Portugal, November 2017.

Oliveira M. Organizer and Lecturer. Lead Extraction Management, Hospital Santa Marta, Lisbon, Portugal, December, 2017.

Maia T. Co-Chair. Satellite Meeting on Computational Psychiatry, 72<sup>nd</sup> Annual Meeting of the Society of Biological Psychiatry, San Diego, USA, 2017.

Maia T. Co-Chair. Symposium on Reinforcement Learning Alterations and Dopamine Dysfunction in Psychosis, 6<sup>th</sup> European Conference on Schizophrenia Research, Berlin, Germany, 2017.

Oliveira M. Scientific Committee, Organizer and President. Portuguese Congress of Cardiology – CPC2017: “Olhar o Coração: Conhecimento, Inovação e Arte”.

Oliveira M. National Coordinator and Organizer. European General Registry of Atrial Fibrillation.

Oliveira M. Organizer. Fórum Ciência da Sociedade Portuguesa de Cardiologia – Investigação Clínica, Coimbra, Portugal, 2017.

Domingos F. IV Curso de Equilíbrio Hidro-Electrolítico e Ácido-Base, Amadora, Portugal, 2017.

### **Internationalisation**

This unit encompasses two major scientific branches: Neuromuscular Disorders & Clinical Neurophysiology; and Multimodal study of the neural substrates of Psychiatric and Movement disorders. The former includes amyotrophic lateral sclerosis (ALS) and familial amyloid neuropathy (FAP), disease phenotype and early diagnosis, genotype and disease biomarkers, respiratory and spinal cord physiology, motor unit recruitment and fasciculations, small fiber dysfunction and clinical trials. The latter focuses on the synergistic use of neurocomputational models, functional magnetic resonance imaging (fMRI), behavioral experiments, psychopharmacological interventions, genetics, and psychophysiological techniques to investigate the neural and behavioral substrates of psychiatric disorders that involve disturbances in cortico–basal ganglia circuits—particularly Tourette’s syndrome, obsessive-compulsive disorder, and attention-deficit/hyperactivity disorder. Together, our work links multiple aspects of function, spanning high-level cognition and all levels of motor function: from motor cortical areas to subcortical structures (particularly the basal ganglia), the spinal cord, and the neuromuscular interface.

From this work we intend to develop new methodologies and to increase the understanding of neurological and psychiatry disorders to implement new treatments. We cultivate dynamic interactions with leading international groups with complementary expertise in various areas that benefit from such complementarity.

### **Prizes, Honours and Awards**

Maia T. Grant reviewer for the Medical Research Council, London, 2017.

Maia T. Grant reviewer for the Wellcome Trust, London, 2017.

Pronto Laborinho AC. Boehringer Ingelheim Award – Best Oral Presentation. CPC Investigação do 8º Congresso de Pneumologia do Centro 2017 - Biomarcadores Respiratórios na Abordagem Clínica da Esclerose Lateral Amiotrófica. Pronto-Laborinho, A; Gromicho, M; Pereira, M; Pinto, S; Barros, MA; Swash, M; de Carvalho, M.

Oliveira M. Autonomic Nervous System Disturbances in Cardiovascular Disorders. Jorge Quininha Award 2017.

Inês M, Coelho T, Conceição I, de Carvalho M, Costa J. Financiamento da Amyloidosis Research Consortium para o Projecto “Survival Data for ATTR Amyloidosis”, 2017.

### **Industry Contract Research**

ISIS 420915-CS3. An Open-Label Extension Study to Assess the Long-Term Safety and Efficacy of ISIS 420915 in Patients with Familial Amyloid Polyneuropathy (FAP)s with Familial Amyloid Polyneuropathy. (IONIS Pharmaceuticals, Inc.) - Principal Investigator.

APOLLO: A Phase 3 Multicenter, Multinational, Randomized, Doubleblind, Placebo-controlled Study to Evaluate the Efficacy and Safety of ALN-TTR02 in Transthyretin (TTR)-Mediated Polyneuropathy (Familial Amyloidotic Polyneuropathy-FAP)- Principal Investigator.

“A Multicenter, Open-Label, Extension Study to Evaluate the Long-term Safety and Efficacy of Patisiran in Patients with Familial Amyloidotic Polyneuropathy Who Have Completed a Prior Clinical Study with Patisiran”, Protocol No. ALN-TTR02-006- Principal Investigator.

Scientific Board member of Transthyretin-associated amyloidoses outcomes survey (THAOS) A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidosis.

### **Advanced Teaching**

Conceição I. Seminar and Lessons in Master Degree and Doctoral Program on Neurosciences 2017.

Conceição I. Lessons in Biomechanics - Biomedical Engineering Integrated Master Degree, Neurophysiological Techniques, 2017.

Conceição I. Mestrado Integrado em Medicina.

Conceição I. Mestrado Integrado em Ciências Da Saúde.

Domingos F. Mestrado Integrado em Medicina.

Domingos F. Fisiologia do equilíbrio ácido-base. IV Curso de Equilíbrio Hidro-Electrolítico e Ácido-Base, Amadora, 2017.

Maia T. Regências:

- Mestrado em Neurociências.
- Mestrado Integrado em Engenharia Biomédica.

Maia T. Mestrado Integrado em Medicina.

Costa J.

i. Avaliador - Membro do Painel de Avaliação (Painel de Ciências Médicas e da Saúde) para atribuição de Bolsas de Doutoramento pela Fundação para a Ciência e Tecnologia em 2017.

ii. Avaliador externo do Programa de Estimulo a Projetos de Investigação Interdisciplinar e Translacional – PEPITA, Faculdade de Medicina, Universidade de Coimbra.

iii. Membro do júri do concurso ao 21.º Programa “Educação pela Ciência” financiadas pelo GAPIC/FMUL | Bolsas CHLN (2017).

de Carvalho M.

IIC3 – PROVAS DE MESTRADO

IIC3B – Como Presidente do Juri

- Presidente do Juri na Prova do Mestrado de Neurociências da licenciada Sara Raquel Neves Coelho, com o título Drug Delivery in the Brain: design of peptides for selective blood-brain barrier transmigration. Faculty of Medicine, University of Lisbon, January 2017.
- Presidente do Juri na Prova do Mestrado de Neurociências do licenciado Luís Afonso André, com o título Chronic Cannabinoid Exposure may Produce a Depression Pattern in Adolescence Mice. Faculty of Medicine, University of Lisbon, March 2017.
- Presidente do Juri na Prova do Mestrado Integrado de Medicina do licenciado João Francisco Dionísio, com o título Alterações Vasculares e Novas Abordagens Terapêuticas na Distrofia Muscular de Duchenne. Faculty of Medicine, University of Lisbon, June 2017.
- Presidente do Juri na Prova do Mestrado de Neurociências do licenciado Claudia F M Afonso, com o título New Potential Therapy for Multiple Sclerosis: a role for adenosine A2A receptors. Faculty of Medicine, University of Lisbon, July 2017.
- Presidente do Juri na Prova do Mestrado de Neurociências do licenciado Germano JS Ferreira, com o título Motor and Cognitive Interference on Walking Deficits in People with Parkinsons Disease. Faculty of Medicine, University of Lisbon, July 2017.
- Presidente do Juri na Prova do Mestrado Integrado de Medicina da licenciada Ana Margarida Domingos, com o título Esclerose Lateral Amiotrófica: um caso clínico de insuficiência respiratória inaugural. Faculty of Medicine, University of Lisbon, September 2017.

### **Science and Society**

Oliveira M. Member of the “European Advisory Board” of Medtronic, “International Expert Panel” of Biotronik, “International Strategic Board” of Livanova, International Expert Consultant of Boston Scientific, National Advisory Board for Ensite Precision launch of St Jude Medical and National Expert Panel in Arrhythmology for Rivaroxaban and Apixaban.

Oliveira M. Member of the Advisory Board of the European Project TEMIS/SUDOE - Innovative TEchnologies for personalised Medicine Services.

Oliveira M. Member of the juri for the annual evaluation of cardiology fellows in Santa Marta Hospital, Lisbon, Portugal.

Oliveira M. President of the Juri of the National INFARMED Grant “Fund for Investigation in Diabetes”.

Oliveira M. Tutor for the training of the Cardiology Fellows Pedro Pinto Teixeira and Tiago Mendonça, Santa Marta Hospital and for Junior Allied Professionals in training for Electrophysiology and Implantable Devices (Ana Almeida, Mariana Pereira, Margarida Paulo).

Oliveira M. Coordinator of the Training Programme in Pacing, Electrophysiology and Tilt test/Tilt training for fellows, Santa Marta Hospital (2017 trainees: André Monteiro, Guilherme Portugal, Nuno Cabanelas, Dinis Mesquita, Inês Rodrigues, Madalena Cruz, Rita Ilhão).

Oliveira M. Member of the directive board of the “BATE BATE CORAÇÃO” Association.

Oliveira M. Member of the working group for the “Bolsa de Formação em Eletrofisiologia Cardíaca APAPE/IPRC”.

Pinto FJ, Nobre A, Thomas B, Oliveira M. Moderators. Hipertensão arterial e insuficiência cardíaca - Estado da arte 2017, Aula Magna, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 2017.

Sousa J, Oliveira M. Moderators. One-shot ablation of paroxystic atrial fibrillation: Pulmonary Veins Isolation with crioenergy. VI Congresso Novas Fronteiras em Cardiologia, February 2017.

Sousa J, Oliveira M. Presidents. New advances in ablation of atrial fibrillation, Serge Boveda (França), VI Congresso Novas Fronteiras em Cardiologia, February 2017.

Sousa J, Oliveira M. Moderators. Avanços no Laboratório de Electrofisiologia. VII Congresso Novas Fronteiras em Cardiologia, February 2017.

Glikson M, Oliveira M. Moderators. Hospitalizations in Hf Patients: We Should Care! New Horizons in Heart Failure, Berlim, March 2017.

Oliveira M, Osca J. Moderators. Back To Reality. New Horizons in Heart Failure, Berlim, March 2017.

Calo L (Rome, Italy), Oliveira M (Lisbon, Portugal). Chairpersons. Modulation of Autonomic Nervous System. XIII Congress of the European Cardiac Arrhythmias Society, Rome, Italy, April 2017.

Oliveira M, Sousa J. Discussion Panel. Simpósio – Ablação de Fibrilhação Auricular, XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Oliveira M. Moderator. Melhorando a assistência aos doentes com NOACs – onde estamos hoje? XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Oliveira M, Adragão P. Moderator. Atualizando os meus conhecimentos em Arritmologia Clínica. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Oliveira M. Coordinator and Lecturer. CardioArena – foco nos desafios da inovação. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Morais J, Oliveira M. Moderator. Leading the Heart – Innovation with Rivaroxaban. XXXVIII Congresso Português de Cardiologia, Palácio de Congressos do Algarve, Albufeira, Portugal, April 22-25, 2017.

Oliveira M, Primo J. Moderator. Terapêutica de Ressíncronização Cardíaca: seleção dos doentes. Reunião Nacional de Pacing, Covilhã, Portugal, May 2017.

Bonhorst D, Oliveira M. Moderator. Arritmias. Coração no Centro, Coimbra, Portugal, October 2017.

Costa J. Scientific Grant. Survival data for ATTR amyloidosis. Amyloidosis Research Consortium (ARC), a 501(c)(3) nonprofit organisation based in Boston, USA, April 2017.

### **MSc Thesis Completed**

Artiom V Poliakov, 01/05/2017, “Lesão da Via Corticoespinhal e Variabilidade no Recrutamento de Unidades Motoras”, Master in Neurosciences, Faculty of Medicine, University of Lisbon. Supervisor: Mamede de Carvalho.

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## Dias, Sérgio

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### Major Interests / Objectives

We study cancer as a systemic disease, and our main focus is to understand how cancers communicate with their "host". In detail, we study the role of blood vessels, the involvement of bone marrow-derived cells and of metabolic systemic signals in cancer onset and progression.

### Head of Laboratory

Sérgio Jerónimo Rodrigues Dias, PhD, Associate Professor

### Research Team

Ana Luísa Ferro Espadanal Torres Magalhães	PhD	Post-Doctoral Investigator
Ana Patrícia Quintino Lopes	Graduate	MSc Student (Started September)
Catarina Isabel de Melo Pinheiro	Master	MSc Student (Started September)
Inês Sofia Alvarez Martins	Graduate	PhD Student (Left January)
Neidy Varela Rodrigues	Master	PhD Student
Rita de Sá Martins Pinto Gonçalves	Master	PhD Student (Started September)
Sandrina Nóbrega Pereira	PhD	Post-Doctoral Investigator
Susana Cristina Cachapa Monteiro	Graduate	MSc Student (Left September)

### Laboratory Keywords / Research Areas

Angiogenesis, Tumor spread, Metabolism.

### Major Scientific Achievements

Our main achievements in 2017 were to establish in our Laboratory the necessary tools to address fundamental research questions, such as the metabolic regulation of cancer progression, and the systemic environment as a suppressor of immune cell function during cancer onset and progression. As a result of this effort, we published several papers on these subjects (and have another paper in press, to be published March 2018), presented several Posters at International Meetings, and supervised one Master student (Thesis defense December 2017) and one PhD Student (writing up her Thesis). In addition to our ongoing International and National collaborations, we established fruitful collaborations with several Labs at IMM, including Vanessa Morais, Edgar Gomes, Luis Costa, and Bruno Silva-Santos.



### **Selected Publications**

Nóbrega-Pereira S, Caiado F, Carvalho T, Matias I, Graça G, Gonçalves LG, Silva-Santos B, Norell H, Dias S (2017). VEGFR-2-mediated reprogramming of mitochondrial metabolism regulates the sensitivity of acute myeloid leukemia to chemotherapy. *Cancer Res.*doi: 10.1158/0008-5472.CAN-17-1166. (IF: 9.122, Citations:--).

Costa A, Afonso J, Osório C, Gomes AL, Caiado F, Valente J, Aguiar SI, Pinto F, Ramirez M, Dias S (2013). miR-363-5p regulates endothelial cell properties and their communication with hematopoietic precursor cells. *Journal of Hematology and Oncology* 6(1), 87. (IF: 6.350, Citations: 17).

Caiado F, Carvalho T, Rosa I, Remedio L, Costa A, Matos J, Heissig B, Yagita H, Hattori K, da Silva JP, Fidalgo P, Dias Pereira A and Dias S (2013). Bone marrow-derived CD11b+Jagged2+ cells promote epithelial to mesenchymal transition and metastization in colorectal cancer. *Cancer Research* 73(14), 4233-46. (IF: 9.122, Citations: 17).

Caiado F, Carvalho T, Silva F, Castro C, Clode N, Dye JF and Dias S. (2011) The role of fibrin E on the modulation of endothelial progenitors adhesion, differentiation and angiogenic growth factor production and the promotion of wound healing. *Biomaterials* 32(29), 7096-105. (Journal IF: 8.402, Citations: 38).

Gomes AL, Carvalho T, Torre C, Serpa J and Dias S (2010). Hypercholesterolemia promotes bone marrow cell mobilization by perturbing the SDF1:CXCR4 axis. *Blood* 115(19), 3886-94. (IF: 13.164, Citations: 69).

### **Ongoing Research Projects**

2017/2017: iMM-Laço. Coordinator: Sérgio Jerónimo Rodrigues Dias. Funding Agency: Fundo iMM-Laço. Reference: Laço SDias. Amount: € 38 500,00. Total Amount: € 38 500,00.

### **Other Projects**

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

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

#### **Publications in Peer Review Journals**

Nóbrega-Pereira S, Caiado F, Carvalho T, Matias I, Graça G, Gonçalves LG, Silva-Santos B, Norell H, Dias S (2017). VEGFR-2-mediated reprogramming of mitochondrial metabolism regulates the sensitivity of acute myeloid leukemia to chemotherapy. *Cancer Res*.doi: 10.1158/0008-5472.CAN-17-1166. (IF: 9.122, Citations:--).

Lopes-Coelho F, Nunes C, Gouveia-Fernandes S, Rosas R, Silva F, Gameiro P, Carvalho T, Gomes da Silva M, Cabeçadas J, Dias S, Gonçalves LG, Serpa J (2017). Monocarboxylate transporter 1 (MCT1), a tool to stratify acute myeloid leukemia (AML) patients and a vehicle to kill cancer cells. *Oncotarget*;8(47):82803-82823. (IF: 5.168, Citations:--).

Gregório AC, Lacerda M, Figueiredo P, Simões S, Dias S, Moreira JN (2017). Therapeutic Implications of the Molecular and Immune Landscape of Triple-Negative Breast Cancer. *Pathol Oncol Res*. doi: 10.1007/s12253-017-0307-2. (IF: 1.736, Citations: 1).

Braga S, Cardoso J, Andre S, Brito M, Sanchez P, Orvalho L, Salgado L, Dias S, Pereira-Leal JB, Passos-Coelho JL (2017). Does Hypoxic Response Mediate Primary Resistance to Sunitinib in Untreated Locally Advanced Breast Cancer? *Curr Cancer Drug Targets*;17(1):62-73. (IF: 2.992, Citations:--).

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

Dias S. Invited Speaker. Metabolic Shifts in Cancer. i3S - Instituto de Investigação e Inovação em Saúde, Porto, Portugal, September 29, 2017.

#### **Communication in International Conferences**

Mitochondrial metabolism in breast cancer aggressive phenotype induced by hypercholesterolemia. MitoPorto International Symposium, Porto, Portugal, May 26, 2017. (Poster Presentation).

VEGFR2 signaling regulates the sensitivity of Acute Myeloid Leukemia to chemotherapy by reprogramming mitochondrial metabolism. Champalimaud Research Symposium, Lisbon, Portugal, October 9-11, 2017. (Poster Presentation).

### **Advanced Teaching**

- Coordenador do Módulo “Development and Cancer” do Mestrado de Oncobiologia, Faculty of Medicine, University of Lisbon.
- Coordenador do Módulo “Oncobiology” do Programa Doutoral LisbonBiomed, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon.

Advanced Teaching at other Universities: Lecturer at the following PhD Programs:

- Programa de Doutoramento em Ciências Químicas, Biológicas e Engenharia (ITQB, Nova University of Lisbon).
- Programa Doutoral em Biologia Experimental e Biomedicina (University of Coimbra).
- Programa de Doutoramento em Medicina (FCM, Nova University of Lisbon).
- Programa de Pós-Graduação Ciência para o Desenvolvimento Fundação Gulbenkian/FCT (University of Cape Verde).

And of the following Master Programs:

- Mestrado em Biologia Humana e Ambiente (University of Algarve).
- Mestrado em Biologia Humana e Ambiente (Faculty of Sciences, University of Lisbon).

### **Science and Society**

The biology of Cancer in one hour. Several Lectures at Secondary Schools in the Lisbon Area, including Escola Secundária Odivelas, Escola Secundária D. Dinis, Liceu Passos Manuel, Liceu Camões.

### **MSc Thesis completed**

Susana Monteiro, 11/12/2017, “The role of mitochondrial adaptations in the acquisition of the phenotype induced by LDL in breast cancer”, Faculty of Pharmacy, University of Lisbon. Supervisors: Sérgio Dias and Cecília Rodrigues.

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## Ferreira, Joaquim

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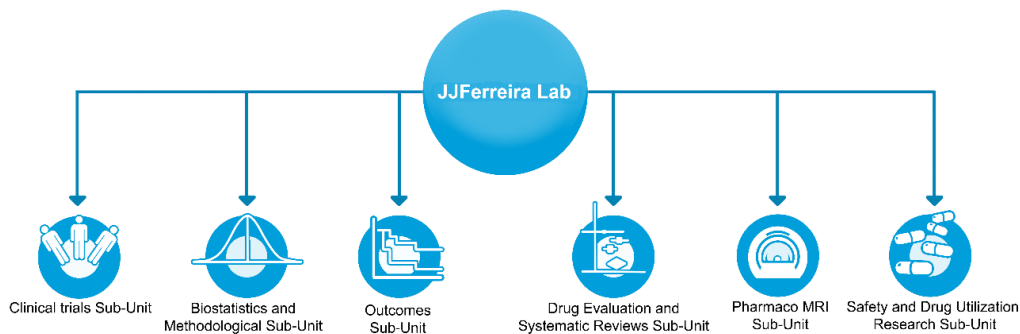
### Major Interests / Objectives

The main mission of the Joaquim Ferreira Lab is to contribute to the development of effective and safe therapeutic interventions through the establishment of optimized methodologies for the design, conduction, analysis and report of clinical trials. The main clinical pharmacology domains of interest are clinical trials methodology, outcomes, systematic reviews, safety, pharmaco MRI and drug utilization. The emphasis is mainly on novel, early phase proof-of-principle clinical studies and new methodological and trial designs but the scope extends throughout the clinical development spectrum. We also envision collaborations with the pharmaceutical industry, facilitating the conduction of clinical trials to a shared role in the early stages of drug and planning of clinical development.

### Head of Laboratory

Joaquim Ferreira, MD/PhD, Clinical Specialist, Associate Professor, Faculty of Medicine, University of Lisbon

### Graphical Abstract



### Research Team

Ana Isabel Santos Augusto	Graduate	Trainee
Ana Marta Teixeira Anes	Master	Investigator, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Ana Patrícia Silva Pita Lobo	Graduate	Investigator, Hospital Fernando da Fonseca, MD
Ana Raquel Duque Gonçalves Fernandes	Master	Investigator (Started June)
Ana Rita Simões Cardoso	Master	Investigator, Campus Neurologico Senior (CNS)

Ana Teresa Martins Sousa Santos	Master	Lab Manager
Anabela Ferreira Valadas	Graduate	Investigator, Hospital São Bernardo, Setúbal, MD
Catarina Afonso Godinho	PhD	Investigator, Campus Neurologico Senior (CNS), Assistant Professor
Claudio Virgilio Antunes David	Graduate	Investigator, CHLN, MD, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Cristina Sampaio	PhD Agregação	Investigator, Faculdade Medicina da Universidade de Lisboa, Full Professor
Daisy Andreína Vieira De Abreu	Master	Investigator
Daniel Gomes Caldeira	Graduate	PhD, Hospital Garcia de Orta, MD, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Daniela Marina Dias Guerreiro	Graduate	Investigator
Ema Roque	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa
Helena Isabel Vicente dos Santos	Graduate	Technician
Isabel Cristina Ramos Peixoto Guimarães	PhD	Investigator, Associate Professor
Joana Margarida do Nascimento Fagundes Carvalho	Graduate	Investigator
João Costa	MD/PhD	Investigator, Hospital da Luz, MD, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
João José Simões Santos	Master	PhD Student (Started May)
Josefa Domingos	Master	Investigator, Campus Neurologico Senior (CNS)
Kelli Destri	Master	Technician
Leonor Correia Guedes	MD/PhD	PhD, CHLN, MD
Luís António Garcez Duarte da Costa Ferreira	Master	Investigator (Started November)
Margarida Borges	Graduate	Investigator, Faculdade Medicina da Universidade de Lisboa, MD, Teaching Assistant
Margherita Fabbri	Graduate	PhD Student, DIBINEM Department of Biomedical and Neuromotor Science, University of Bologna, ALMA MATER STUDIORUM, MD
Maria Isabel Boaventura de Atouguia	Graduate	Investigator, Celgene, MD, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Maria João Bettencourt Pereira Forjaz	PhD	Investigator
Mariana da Cruz Alves	Master	PhD Student (Started December)
Mário Miguel Coelho da Silva Rosa	MD/PhD	Investigator, FML, Invited Assistant, Clinical Specialist
Miguel Coelho	MD/PhD	Investigator, HSM/CHLN, Clinical Specialist
Nilza Karina Cabral Gonçalves	Master	Investigator
Olga Sofia de Oliveira Caetano	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa
Rafaela Alexandra Policarpo Da Rosa	Master	Administrative (Started February)

Raquel de Queirós Bouça Ribeirinho Machado	Master	PhD Student
Raquel José Ladeira Lobo	Master	Investigator
Ricardo Miguel Ribeiro Marques Cunha Fernandes	MD/PhD	Investigator, CHLN, MD, Faculdade Medicina da Universidade de Lisboa, Invited Assistant
Sofia Cristina Pereira Coutinho Reimão	MD/PhD	Investigator, FMUL, Teaching Assistant, Clinical Specialist
Tânia Sofia Santos Silva	Master	Investigator
Tiago Heleno Mendes	Master	Investigator
Tiago Mestre	Master	PhD Student, University of Ottawa, Assistant Professor, MD
Tiago Rodrigues Teodoro	Master	PhD Student, CHLN, MD
Tiago Soares	Master	MSc Student
Vanda Filipa Viseu Cândido Freitas Castro	Master	Investigator, Campus Neurologico Senior (CNS), Clinical Specialist
Verónica Candeias Caniça	Graduate	Investigator

### Laboratory Keywords / Research Areas

Parkinson's disease, Huntington Disease, Movement Disorders, Neuropharmacology, Clinical trials, Systematic reviews.

### Major Scientific Achievements

In 2017:

- Professor Joaquim was awarded with Scientific Award Ulisboa/Caixa Geral de Depósitos – Health 2016/2017;
- Professor Leonor Correia Guedes was awarded with the “Young Investigator Poster Award” during “200 Year Celebration of James Parkinson”, by Royal Academy with the poster “Neuromelanin Magnetic Resonance Imaging of the Substantia Nigra in LRRK2 – related Parkinson’s disease”;
- Our research works were presented on 8 international conferences;
- Our researchers achieved 2 PhD and 2MSc levels;
- 55 original papers were published in peer-review journals.

### Selected Publications

Wenning GK, Geser F, Krismer F, Seppi K, Duerr S, Boesch S, Koellensperger M, Goebel G, Pfeiffer KP, Barone P, Pellecchia MT, Quinn NP, Koukouni V, Fowler CJ, Schrag A, Mathias CJ, Giladi N, Gurevich T, Dupont E, Ostergaard K, Nilsson CF, Widner H, Oertel W, Eggert KM, Albanese A, del Sorbo F, Tolosa E, Cardozo A, Deuschl G, Hellriegel H, Klockgether T, Dodel R, Sampaio C, Coelho M, Djaldetti R, Melamed E, Gasser T, Kamm C, Meco G, Colosimo C, Rascol O, Meissner WG, Tison F, Poewe W (2013). The natural history of multiple system atrophy: a prospective European cohort study. *Lancet Neurology*. (IF: 26.824, Citations: 127).

Seppi K, Weintraub D, Coelho M, Perez-Lloret S, Fox SH, Katzenschlager R, Hametner EM, Poewe W, Rascol O, Goetz CG, Sampaio C (2011). The Movement Disorder Society Evidence-Based Medicine Review Update: Treatments for the Non-Motor Symptoms of Parkinson's Disease. *Movement Disorders*. (IF: 7.072, Citations: 338).

Fox SH, Katzenschlager R, Lim SY, Ravina B, Seppi K, Coelho M, Poewe W, Rascol O, Goetz CG, Sampaio C (2011). The Movement Disorder Society Evidence-Based Medicine Review Update: Treatments for the Motor Symptoms of Parkinson's Disease. *Movement Disorders*. (IF: 7.072, Citations: 227).

Martins, M, Rosa A, Guedes LC, Fonseca BV, Gotovac K, Violante S, Mestre T, Coelho M, Rosa MM, Martin ER, Vance JM, Outeiro TF, Wang L, Borovecki F, Ferreira JJ, Oliveira SA (2011). Convergence of miRNA Expression Profiling, alpha-Synuclein Interacton and GWAS in Parkinson's Disease. *Plos One*. (IF: 2.806, Citations: 96).

Louis ED, Ferreira JJ. (2010). How Common Is the Most Common Adult Movement Disorder? Update on the Worldwide Prevalence of Essential Tremor. *Movement Disorders*. (IF: 7.072, Citations: 233).

### Ongoing Research Projects

2017/2017: Research Design and Data Analysis in Support of Clinical Trial Design and Clinical Research Projects. Coordinator: Joaquim José Coutinho Ferreira. Funding Agency: CHDI Foundation, Inc. Reference: CHDI JFerreira. Amount: € 63 572,00. Total Amount: € 1 368 548,00.

2015/2020: Fair-ParK-II: Conservative iron chelation as a disease-modifying strategy in Parkinson's disease: a multicentric, parallel-group, placebo-controlled, randomized clinical trial of deferiprone. Coordinator: Joaquim José Coutinho Ferreira. Funding Agency: European Commission. Reference: SC3 633190. Amount: € 187 083,00. Total Amount: € 5 998 994,00.

2014/2018: Dysarthria in Parkinson's disease: Lusophony vs. Francophony comparison. Coordinator: Joaquim José Coutinho Ferreira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FCT-ANR/NEU-SCC/0005/2013. Amount: € 151 686,00. Total Amount: € 322 796,00.

2014/2017: Comprehensive unbiased risk factor assessment for genetics and environment in Parkinson's Disease. Coordinator: Joaquim José Coutinho Ferreira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: JPND-RF/0001/2012. Amount: € 130 000,00. Total Amount: € 130 000,00.

2014/2017: Care for Late Stage Parkinsonism. Coordinator: Joaquim José Coutinho Ferreira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: JPND-HC/0002/2012. Amount: € 110 000,00. Total Amount: € 110 000,00.

### **Publications in Peer Review Journals**

Travessa AM, Rodrigues FB, Mestre TA, Ferreira JJ (2017). Fifteen Years of Clinical Trials in Huntington's Disease: A Very Low Clinical Drug Development Success Rate, *Journal of Huntingtons disease*, 6(2): 157-163. (IF:--, Citations: 2).

Matias R, Paixão V, Bouça R, Ferreira JJ (2017). A Perspective on Wearable Sensor Measurements and Data Science for Parkinson's Disease, *Frontiers in Neurology*, 8(677). (IF: 3.552, Citations:--).

Guedes LC, Chan RB, Gomes MA, Conceição VA, Machado RB, Soares T, Xu Y, Gaspar P, Carrico JA, Alcalay RN, *et al* (2017). Serum lipid alterations in GBA-associated Parkinson's disease, *Parkinsonism & Related Disorders*, 44: 58-65. (IF: 4.484; Citations:--).

Rodrigues FB, Ferreira JJ (2017). Overall Survival and Causes of Death in Neurodegeneration-An Overlooked and Underreported Theme, *Jama Neurology*, 74(11): 1379-1379. (IF: 10.029, Citations:--).



Miranda HV, Cassio R, Correia-Guedes L, Gomes MA, Chegao, A, Miranda E, Soares T, Coelho M, Rosa MM, Ferreira JJ, *et al* (2017). Posttranslational modifications of blood-derived alpha-synuclein as biochemical markers for Parkinson's disease, *Scientific Reports* 7(13713). (IF: 4.259, Citations:--).

Brinkman DJ, Tichelaar J, Okorie M, Bissell L, Christiaens T, Likic R, Mañulaitis R, Costa J, Sanz EJ, Tamba BI, Maxwell SR, Richir MC, van Agtmael MA; Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) (2017). Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey among 185 Medical Schools in 27 Countries. *Clinical Pharmacology & Therapeutics*, 102(5):815-822. (IF: 7.266, Citations: 1).

Marques RP, Duarte GS, Sterrantino C, Pais HL, Quintela A, Martins AP, Costa J. Triplet (FOLFOXIRI) versus doublet (FOLFOX or FOLFIRI) backbone chemotherapy as first-line treatment of metastatic colorectal cancer: A systematic review and meta-analysis. *Critical Reviews in Oncology/Hematology*. 118:54-62. (IF: 4.971, Citations:--).

Caldas AC, Levin, J, Djaldetti R, Rascol O, Wenning G, Ferreira JJ. Autor(es) grupo: Movement Disorders Soc MSA Study G. (2017) Critical Appraisal of Clinical Trials in Multiple System Atrophy: Toward Better Quality. *Movement Disorders* 32(10): 1356-1364. (IF: 7.072, Citations:--).

Rodrigues FB, Abreu D, Damásio J, Goncalves N, Correia-Guedes L, Coelho M, Ferreira JJ. Autor(es) grupo: REGISTRY Investigators European (2017). Survival, Mortality, Causes and Places of Death in a European Huntington's Disease Prospective Cohort. *Movement Disorders Clinical Practice*, 4(5): 737-742. (IF: 2.26, Citations: 2).

Guedes, LC, Reimão, S, Paulino, P, Nunes, RG, Bouca-Machado, R, Abreu, D, Goncalves, N, Soares, T, Fabbri, M, Godinho, C, (et al) (2017). Neuromelanin Magnetic Resonance Imaging of the Substantia Nigra in LRRK2-Related Parkinson's Disease, *Movement Disorders*, 32(9): 1331-1333. (IF: 7.072, Citations:--).

Pinto S, Chan A, Guimarães I, Rothe-Neves R, Sadat J (2017). A cross-linguistic perspective to the study of dysarthria in Parkinson'. *Journal of Phonetics*, 64: Páginas: 156-167. (IF: 1.352, Citations: 1).

Pham MH, Elshehabi M, Haertner L, Del Din S, Srulijes K, Heger T, Synofzik M, Hobert MA, Faber GS, Hansen C, Salkovic D, Ferreira JJ, Berg D, Sanchez-Ferro A, van Dieen JH, Becker C, Rochester L, Schmidt G, Maetzler W (2017). Validation of a step detection Algorithm during straight Walking and turning in Patients with Parkinson's disease and older Adults Using an Inertial Measurement Unit at the Lower Back. *Frontiers in Neurology*, 8(457). (IF: 3.552, Citations:--).

Sousa Dc, Leal I, Costa J, Vaz-Carneiro A (2017). Analysis of the Cochrane Review: Anti-vascular Endothelial Growth Factor for Prevention of Postoperative Vitreous Cavity Hemorrhage after Vitrectomy for Proliferative Diabetic Retinopathy. *Cochrane Database Syst Rev*. 2015;8:CD008214. *Acta Médica Portuguesa*, 30(7-8): 513-516. (IF: 0.498, Citations:--).

Rodrigues FB, Duarte G, Costa J, Ferreira JJ, Wild EJ (2017). Tetrabenazine versus Deutetrabenazine for Huntington's Disease: Twins or Distant Cousins? *Movement Disorders Clinical Practice*, 4: 582–585. (IF: 2.26, Citations: 3).

Gouveia M, Fiorentino F, Jesus G, Costa, Borges M (2017). Cost-effectiveness of the 13-valent Pneumococcal Conjugate Vaccine in Children in Portugal. *Pediatric Infectious Disease Journal*; 36(8):782-787. (IF: 2.486, Citations:--).

Fabbri M, Cardoso R, Coelho M, Guedes LC, Rosa MM, Godinho C, Gonçalves N, Antonini A, Ferreira JJ. (2017) Speech and Voice Response to a Levodopa Challenge in Late-Stage Parkinson's Disease. *Frontiers in Neurology* 8:432. (Journal IF: 3.552, Citations:--).

Fabbri M, Coelho M, Guedes LC, Rosa MM, Abreu D, Gonçalves N, Antonini A, Ferreira JJ (2017). Acute response of non-motor symptoms to subthalamic deep brain stimulation in Parkinson's Disease. *Parkinsonism Relat Disord*; 39:37-43 (IF: 4.484, Citations:--).

Caldeira D, Ferreira JJ, Pinto FJ (2017). The era of the novel oral anticoagulants in Portugal. *Revista Portuguesa de Cardiologia*, 36(7-8): 577-578. (IF: 1.195, Citations:--).

Silva MA, Duarte GS, Camara R, Rodrigues FB, Fernandes RM, Abreu D, Mestre T, Costa J, Trenkwalder C, Ferreira JJ (2017). Placebo and nocebo responses in restless legs syndrome A systematic review and meta-analysis, *Neurology*, 88(23): 2216-2224. (IF: 7.592, Citations: 1).

Fabbri M, Coelho M, Guedes LC, Chendo I, Sousa C, Rosa MM, Abreu D, Costa N, Godinho C, Antonini A, Ferreira JJ (2017). Response of non-motor symptoms to levodopa in late-stage Parkinson's disease: Results of a levodopa challenge test, *Parkinsonism & Related Disorders*, 39: 37-43- (IF: 4.484, Citations:--).

Orth M, Bronzova, J, Tritsch C, Dorsey ER, Ferreira JJ, Gemperli A, Autor(es) grupo: EHDN REGISTRY Investigator; HSG COHORT Investigator. Comparison of Huntington's Disease in Europe and North America (2017). *Movement Disorders Clinical Practice*, 4(3): 358-367. (IF: 2.26, Citations:--).

Caldeira D, Rodrigues FB, Pinto, Fausto J, Ferreira JJ, Costa, J (2017). Thromboprophylaxis with Apixaban in Patients Undergoing Major Orthopedic Surgery: Meta-Analysis and Trial-Sequential Analysis. *Clinical Medicine Insights-Blood Disorders*, 10. (IF: 6.857, Citations:--).

Bigotte V, Baptista RB, Costa J, Vaz-Carneiro A (2017). Analysis of the Cochrane Review: Pharmacotherapy for Hyperuricemia in Hypertensive Patients. *Cochrane Database of Systematic Reviews*;4:CD008652. *Acta Medica Portuguesa*, 31;30(5):356-360. (IF: 0.498, citations:--).

Silva MA, Duarte GS, Camara R, Rodrigues FB, Fernandes RM, Abreu D, Mestre T, Costa J, Trenkwalder C, Ferreira JJ (2017). Placebo and nocebo responses in restless legs syndrome: A systematic review and meta-analysis. *Neurology*, 6, 88(23):2216-2224. (IF: 7.592, Citations: 1).

Cristovam E, Almeida D, Caldeira D, Ferreira JJ, Marques T (2017). Accuracy of diagnostic tests for Legionnaires' disease: a systematic review. *Journal of Medical Microbiology*, 66(4): 485-489. (IF: 2.159, citations: 1).

Fabbri M, Abreu L, Santos T, Ferreira JJ (2017). Resting and reemergent tongue tremor as presenting Symptoms of Parkinson's Disease. *Movement Disorders Clinical Practice*, 4(2): 273-274. (IF: 2,26, Citations:--).

Landwehrmeyer, GB, Fitzner-Attas, CJ, Giuliano, JD, Goncalves, N, Anderson, KE, Cardoso, Ferreira JJ, Mestre TA, Stout, JC, Sampaio C (2017). Data Analytics from Enroll-HD, a Global Clinical Research Platform for Huntington's Disease. *Movement Disorders Clinical Practice*, 4(2):212-224. (IF: 2.26, citations: 4).

Wissel J, Bensmail D, Ferreira JJ, Molteni F, Satkunam L, Moraleda S, Rekand T, McGuire J, Scheschonka A, Flatau-Baque B, Simon O, Rochford ETJ, Dressler D, Simpson DM (2017). Safety and efficacy of incobotulinumtoxin a doses up to 800 U in limb spasticity The TOWER study. *Neurology*, 88 (14): 1321-1328. (IF:7.592, Citations: 2).

Pieper D, Pollock M, Fernandes RM, Büchter RB, Hartling L (2017). Epidemiology and reporting characteristics of overviews of reviews of healthcare interventions published 2012–2016: protocol for a systematic review. *Systematic Reviews*;6:73. (IF:--, Citations:--).

Queirós CS, Duarte, G, Costa J, Vaz-Carneiro A (2017). Analysis of the Cochrane Review: Topical Treatments for Scalp Psoriasis. *Cochrane Database Syst Rev*. 2016;2:CD009687. *Acta Médica Portuguesa*, 30(3):163-168. (IF: 0.498, Citations:--).

Mestre TA, Ferreira JJ (2017). Are placebo pills presented as experimental treatment a true placebo? *Pain*, 158(3): 535-535. (IF: 5.445, Citations:--).

Guimarães, I, Cardoso, Pinto S. Ferreira JJ (2017). The Psychometric Properties of the Voice Handicap Index in People With Parkinson's Disease. *Journal of voice: official journal of the Voice Foundation*, 31(2), 258.e13-258.e18. (IF: 1.381, Citations:--).

Rodrigues, FB, Ferreira JJ (2017). Opicapone for the treatment of Parkinson's disease. *Expert Opinion in Pharmacotherapy*, 18(4): 445-453. (IF: 3.894, Citations:--).

Ferreira JJ, Gonçalves N, Valadas A, Januario C, Silva MR, Nogueira L, Vieira JLM, Lima AB (2017). Prevalence of Parkinson's disease: a population-based study in Portugal. *European Journal of Neurology*, 24(5): 748-750. (IF: 3.988, Citations:-).

Contarino MF, Van den Dool J, Balash Y, Bhatia K, Giladi N, Koelman JH, Lokkegaard A, Marti MJ, Postma M, Relja M, Skorvanek M, Speelman JD, Zoons E, Ferreira JJ, Vidailhet M, Albanese A, Tijssen MAJ (2017). Clinical Practice: evidence-Based Recommendations for the Treatment of Cervical Dystonia with Botulinum Toxin. *Frontiers in Neurology*, 8, UNSP 35. (IF: 3.552, Citations: 1).

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### Other Publications International

Lees AJ, Ferreira J, Rascol O, Poewe W, Rocha JF, McCrory M, Soares-da-Silva P, BIPARK-2 Study Investigators (2017). Opicapone as Adjunct to Levodopa Therapy in Patients with Parkinson Disease and Motor Fluctuations: A Randomized Clinical Trial. *JAMA Neurology*;74(2):197-206. (IF: 10.029, Citations: 7).

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Caldeira D, Rodrigues FB, Duarte MM, Sterrantino C, Barra M, Gonçalves N, Pinto FJ, Ferreira JJ, Costa J (2017). Cardiac Harms of Sofosbuvir: Systematic Review and Meta-Analysis. *Drug Safety.* (IF: 3.435, Citations:--).

Thibault L, Rascol O, Corvol JC, Ferreira J, Defebvre L, Deplanque D, Bordet R, Moreau C, Devos D (2017). New perspectives on study designs for evaluating neuroprotection in Parkinson's disease. *Movement Disorders*;32(10):1365-1370. (IF: 7.072, Citations: 2).

Caldeira D (2017). Caffeine does not increase the arrhythmic burden in patients with heart failure and left ventricular systolic dysfunction. *Evid Based Med*. 2017 Oct;22(5). (IF: 0.470, Citations:--).

Caldeira D (2017). Novel Antithrombotic Drugs and Intraocular Bleeding: The Importance of Observational Data and Future Perspectives. *JAMA Ophthalmol*. (IF: 5.625, Citations:--).

Borges J, Rosa MV, Fernandes RM, Nogueira PJ, Bandeira T (2017). National Trends in Hospital Admissions for Bronchiolitis, Asthma and Pneumonia among Pediatric Patients in Portugal, 2002-2012. *Pediatric Pneumology* 52:46. (IF: 2.758, Citations:--).

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

Fernandes R. Alergia medicamentosa. Mesa Redonda - Alergia e não só. XXIII Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 9, 2017.

Ferreira JJ. Opicapone: latest clinical trial data and applications. A Step Forward. Manchester, England, February 10, 2017.

Fernandes R. Discussão da norma de orientação clínica da D.G.S. 4ª Reunião Temática da Sociedade Portuguesa de Alergologia Pediátrica - Alergia Medicamentosa, Sociedade Portuguesa de Alergologia Pediátrica, Batalha, Portugal, February 18, 2017.

Ferreira JJ. Qual o verdadeiro efeito os medicamentos para a memória? Ciclo de tertúlias... 3 meses 3 encontros. Hospital Soerad, Torres Vedras, Portugal, March 7, 2017.

Ferreira JJ. BIAL SYMPOSIUM: Optimized treatment for Parkinson's Disease: does this exist? Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.



Ferreira JJ. Medtronic Round Table DBS and Parkinson's disease: are we doing enough? Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Ferreira JJ. What is the best design for a neuroprotection trial in Multiple System Atrophy? Sympath Symposium in Targeting Synocleinopathies, Vienna, Austria, March 28, 2017.

Costa J. Farmacologia Clínica. Jornadas do Internato Médico SR Sul/2017, Lisbon, Portugal, April 2017.

Guimarães I. Voice use: We do care. University of Macau, Macau, April 5, 2017.

Guimarães I. Demonstrative & practical techniques of warm up and cool down. University of Macau, Macau, April 6, 2017.

Ferreira JJ. Qual o papel dos doentes no seu próprio tratamento? Dia Mundial da Doença de Parkinson, Lisbon School of Economics and Management, Lisbon, Portugal, April 11, 2017.

Ferreira JJ. Os seniores do futuro. V Congresso Nacional de Envelhecimento ativo: Olhares sobre o envelhecimento, Torres Vedras, Portugal, April 12, 2017.

Fernandes R. Biomarcadores inflamométricos no diagnóstico e seguimento da asma. 6º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica, Almancil, Portugal, May 12, 2017.

Fernandes R. Abordagem do doente poli-sensibilizado. 6º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica, Almancil, Portugal, May 12, 2017.

Ferreira JJ. Chair of Round-table: Is drug repositioning possible in dystonia and levodopa-induced dyskinesia? 6<sup>th</sup> Biennial Workshop on Dystonia - Dystonia: the link between hypo-and hyperkinetic movement disorders, Nobile Collegio Farmaceutico, Rome, Italy, May 12-13, 2017.

Guimarães, I. Voice technique for lecturing. Agrupamento Vertical de Almeida Garret, Alfragide, Portugal, May 17-18, 2017.

Fernandes RM. Ultra-LABA, LAMA, Combination Products, Selective Glucocorticoid Receptor Agonists in Pediatric Asthma. XVI CIPP Meeting, International Congress on Pediatric Pulmonology, Lisbon, Portugal, June 22-25, 2017.

Ferreira JJ. The Best years videos. 9<sup>th</sup> Swiss Movement Disorders Symposium, Lucerne, Switzerland, August 31-September 1, 2017.

Ferreira JJ. Moderator of Video session with sit down dinner. 9<sup>th</sup> Swiss Movement Disorders Symposium, Lucerne, Switzerland, August 31-September 1, 2017.

Guedes LC. Implicações genéticas para o diagnóstico, aconselhamento e tratamento da Doença de Parkinson. O progresso no conhecimento da doença, Monte Real, Portugal, September 23, 2017.

Simões R. A Doença de Parkinson é uma doença não motora? O progresso no conhecimento da doença, Monte Real, Portugal, September 23, 2017.

Reimão S. Contributo da imagem para a prática clínica e a investigação na Doença de Parkinson. O progresso no conhecimento da doença, Monte Real, Portugal, September 23, 2017.

Coelho M. Sabemos como progride a Doença de Parkinson? O progresso no conhecimento da doença, Monte Real, Portugal, September 23, 2017.

Ferreira JJ. Prioridades na investigação clínica. O progresso no conhecimento da doença, Monte Real, Portugal, September 23, 2017.

Ferreira JJ. O que aprendemos em 60 anos de tratamento farmacológico da DP? 200 anos desde a descrição da Doença de Parkinson. O progresso no conhecimento da doença. Monte Real, Portugal, September 23, 2017.

Ferreira JJ. PD-COMT inhibition: recent advances. International Conference on the new therapies for Parkinson's disease and dementia, Pisa, Italy, September 25, 2017.

Ferreira JJ. O que aprendemos sobre o tratamento da Doença 200 anos depois de James Parkinson? Fármacos e cirurgia. Comemoração dos 200 anos de James Parkinson. 1<sup>o</sup> Congresso Ibérico de Doenças Neurológicas, Centro de Negócios Transfronteiriço, Elvas, Portugal, October 12, 2017.

Ferreira JJ. What's new in Parkinson's management and research? 2<sup>o</sup> Congresso do conceito Bobath em Portugal, Centro de Cultura e Congressos, Seccção Regional do Norte da Ordem dos Médicos, Porto, Portugal, October 14, 2017.

Fernandes R. Cochrane Portugal: da síntese à disseminação da evidência científica. X Jornadas de Investigação, Escola Superior de Saúde da Cruz Vermelha Portuguesa, Carnaxide, Portugal, October 18, 2017.

Ferreira JJ. Um olhar tridimensional sobre as Doenças Neurodegenerativas. I Encontro Nacional Alzheimer, Parkinson e Esclerose Múltipla, Torres-Novas, Portugal, October 20, 2017.

Ferreira JJ. Steering group meeting, Ongentys, Porto, Portugal, October 24, 2017.

Ferreira JJ. Mesa redonda: Informação preciosa – para o doente, para os cuidados de saúde, para a investigação? C-Health Congress, Lagoas Park Hotel, Oeiras, Portugal, October 25, 2017.

Ferreira JJ. A importância da investigação clínica na formação médica. 10º Fórum Bial de Neurologia, Porto, Portugal, October 28, 2017.

Ferreira JJ. The effectiveness of exercise interventions for people with Parkinson's Disease. Swedish Movement Disorder Society, SWEMODIS, Aronsborg, Sweden, November 9-10, 2017.

Ferreira JJ. Diagnóstico e tratamento médico e a relação com a Fisioterapia, nas disfunções do movimento. Movimento e equilíbrio, X Congresso Nacional de Fisioterapeutas, University of Aveiro, Aveiro, Portugal, November 12, 2017.

Ferreira JJ. Membro do júri. Views in Medical Education. Beyond Med, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, November 15, 2017.

Rosa MM. Diferentes populações com DP ou diferentes decisores? Prescrição de antiparkinsonianos na Europa. Congresso Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 15-18, 2017.

Ferreira JJ. Moderator. O que aprendemos após quase dois anos de utilização de Safinamida na prática clínica espanhola? Simpósio Zambon-Group. Congresso Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 15-18, 2017.

Ferreira JJ. Radiofármacos em saúde mental. XVI Congresso Nacional de Medicina Nuclear, Fundação do Oriente, Lisbon, Portugal, November 24, 2017.

### Communications in International Conferences

Ferreira JJ. Opicapone: latest clinical trial data and applications. A Step Forward, Manchester, England, February 10, 2017. (Oral Presentation).

Rodrigues FB, Duarte G, Costa J, Ferreira JJ, Wild EJ. Tetrabenazine versus deutetrabenazine for Huntington's disease: Twins or distant cousins? CHDI - 12<sup>th</sup> Annual HD Therapeutics Conference, Malta, April 24-27, 2017. (Poster Presentation).

Rodrigues FB, Mestre T, Duarte G, Barra M, Costa J, Sampso C, Ferreira JJ. Therapeutic interventions for symptomatic treatment in Huntington's disease – a Cochrane review. CHDI - 12<sup>th</sup> Annual HD Therapeutics Conference, Malta, April 24-27, 2017. (Poster Presentation).

Fabbri M, Reimão S, Carvalho M, Nunes RG, Abreu D, Guedes LC, Bouça R, Lobo PP, Godinho C, Coelho M, Gonçalves NC, Rosa MM, Antonini A, Ferreira JJ. Substantia nigra area evaluated by neuromelanin-sensitive MRI as an imaging biomarker of disease progression in Parkinson's disease. 3<sup>rd</sup> European Academy of Neurology Congress, Amsterdam, The Netherlands, June 24-27, 2017. (Oral Presentation).

Rodrigues FB, Duarte G, Prescott D, Ferreira JJ, Costa J. Deep brain stimulation for dystonia – Cochrane review. 3<sup>rd</sup> European Academy of Neurology Congress, Amsterdam, The Netherlands, June 24-27, 2017.

Rodrigues FB, Duarte GS, Costa J, Ferreira JJ, Wild EJ. Tetrabenazine Versus Deutetrabenazine for Huntington's Disease: Twins or Distant Cousins? 3<sup>rd</sup> European Academy of Neurology Congress, Amsterdam, The Netherlands, June 24-27, 2017. (Poster Presentation).

Fabbri M, Guimarães I, Coelho M, Correia Guedes L, Rosa MM, Godinho C, Antonini A, Ferreira JJ. Speech and voice response to levodopa in late-stage Parkinson's Disease patients: report from an acute levodopa challenge. 3<sup>rd</sup> European Academy of Neurology Congress, Amsterdam, The Netherlands, June 24-27, 2017. (Poster Presentation).

Freixo C, Anes AM, Augusto A, Rosa MM, Ferreira JJ, Santos MJ, Canhã H, Fonseca JE. Adverse drug reactions in the pediatric population with rheumatological disease. The 3<sup>rd</sup> Congress of the European Association for Clinical Pharmacology and Therapeutics (EAPCT), Prague, Czech Republic, June 24-27, 2017. (Poster Presentation).

### **Communications in National Conferences**

Barbosa R, Castro-Cadas A, Mendonça M, Ferreira JJ, Coelho M. Doença de Parkinson de início súbito: pode um evento de vida major desencadear a Doença de Parkinson? Sinapse 2017, Meeting abstract P0120. (Poster Presentation).

Castro-Caldas A, Ferreira JJ. Distonia acial do OFF isolada em doente com Doença de Parkinson de início precoce. Sinapse 2017, Meeting abstract P0123. (Poster Presentation).

Guimarães I. Research applied to Speech and Language Therapy (SLT). First Symposium of SLT, Associação Portuguesa de Terapeutas da Fala, Funchal, Portugal, September 29-30, 2017. (Oral Presentation).

### **Organisation of Conferences**

Ferreira JJ. Co-organizer. Congresso SPDMov, Esposende, Portugal, March 17-18, 2017.

Ferreira JJ. Organizer and Lecturer. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Rosa MM. Organizer and Lecturer. Curso de Actualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson. Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 -20, 2017.

Costa J. Organizer and Lecturer. Introduction to Systematic Reviews and Meta-analysis, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 26-27, 2017.

Costa J. Member of the International Organizing Committee. 16<sup>th</sup> European Congress of Clinical Neurophysiology (ECCN2017), Budapeste, Hungary, August 30-September 2, 2017.

Costa J. Member of Comissão Organizadora do Curso de Publicação Científica e Medicina Baseada na Evidência? Curso de Pós-Graduação, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, September-December 2017.

Ferreira JJ. Co-organizer. Speech therapy in Parkinson's disease and Parkinsonism, Autumn School, Campus Neurológico Sénior, Torres Vedras, Portugal, October 28-30, 2017.

Ferreira JJ. Organizer and lecturer. 1<sup>st</sup> MDS-ES Summer School for Nurses, Torres-Vedras, Portugal, September 29-October 1, 2017.

Ferreira JJ. European Academy of Neurology Chair Local Organising Committee, Lisbon 2018, CCL Lisboa, Lisbon, Portugal, October 30, 2017.

Fernandes RF. Organizing Committee of Dia da Investigação, as Member of Gabinete de Apoio à Investigação Científica, Tecnológica e Inovação (GAPIC), Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 13, 2017.

### **Prizes, Honours and Awards**

Guedes LC. Poster Award. “Young Investigator Poster Award” - meeting “200 Year Celebration of James Parkinson”, “Neuromelanin Magnetic Resonance Imaging of the Substantia Nigra in LRRK2 – related Parkinson’s disease”, Royal Academy, March 10-11, 2017.

Ferreira JJ. “Membre d’Excellence”. Société Française de Neurologie, 2017.

Ferreira JJ. Scientific Award Ulisboa/Caixa Geral de Depósitos (Scientific Area of Health), 2016/2017.

### **Industry Contract Research**

Medtronic “Acompanhamento de Doentes”.

### **Advanced Teaching**

Fernandes R. Sibilância pré-escolar. Curso de Pediatria – Do Básico à Diferenciação, Módulo V – Pneumologia. Núcleo de Formação e Investigação do Departamento de Pediatria, Associação para as Crianças de Santa Maria, Hospital Santa Maria, Centro Hospitalar Lisboa Norte, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, January 6, 2017.

Fernandes R. Instrumentos de avaliação e outcomes. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 20, 2017.

Rosa MM. Desenvolvimento clínico. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 20, 2017.

Ferreira JJ. Desenho e avaliação da qualidade de ensaios clínicos. Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 20, 2017.

Ferreira JJ. Porque precisamos de ensaios clínicos? Curso de Especialização de Introdução à Investigação Clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 20, 2017.

Fernandes R. Anafilaxia: guidelines diagnósticas e terapêutica. Curso de Alergologia Pediátrica. XXIII Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 8, 2017.

Fernandes R. Asma na criança - Das normas à prática clínica. Curso de Alergologia Pediátrica. XXIII Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 8, 2017.

Ferreira JJ. Pharmacological treatment of Parkinson's disease. MDS-ES Winter School for Young Neurologists, Catania, Italy, February 2-4, 2017.

Ferreira JJ. Is there a role for cohort studies in PD? Total Managements of Parkinson's Disease (II): 16<sup>th</sup> Japan International PD & MD Symposium in Takamatsu, Japan, February 17-19, 2017.

Ferreira JJ. Management of Parkinson's Disease in EU; what can we learn. Total Managements of Parkinson's Disease (I): 16<sup>th</sup> Japan International PD & MD Symposium in Takamatsu, Japan, February 17-19, 2017.

Fernandes R. Novos desenhos de RCTs. Módulo de ensaios clínicos, Curso de Mestrado em Oncobiologia, Faculty of Medicine, University of Lisbon, Lisbon, February 23, 2017.

Costa J. Ensaios Clínicos. Módulo de ensaios clínicos, Curso de Mestrado em Oncobiologia, Faculty of Medicine, University of Lisbon, Lisbon, February 23, 2017.

Simões R. Atypical Parkinsonism. Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Coelho M. Late stage of PD. Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Lobo PP. Dystonia and Botulinium Toxin. Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Mestre T. Chorea & Huntigton' Disease. Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Domingos J. Motor rehabilitation. Congresso SPDMov, New Challenges in the Diagnosis and Treatment of Movement Disorders, Esposende, Portugal, March 17-18, 2017.

Costa J. Neurofisiologia de los trastornos del movimiento. Máster Universitario en Electrodiagnóstico Neurológico. University of Barcelona, Barcelona, Spain, March 20-22, 2017.

Ferreira JJ. Huntington's Disease: why such a low clinical drug development success rate? 12<sup>th</sup> National Parkinson Disease and Movement Disorders Congress, Ercan, Cyprus, April 5-8, 2017.

Ferreira JJ. Pain in Non-Parkinson Disorders, Pathogenesis and Management of Pain in Parkinson's Disease, Padua, Italy, April 18-19, 2017.

Ferreira JJ. Optimizing interventional trial designs for MSA. 5<sup>th</sup> International MSA Congress, Salerno, Italy, April 23, 2017.

Fernandes R. Assessing risk of bias. Curso de Introdução às Revisões Sistemáticas e Meta-análises, Cochrane Portugal, Lisbon, Portugal, April 26-27, 2017.

Ferreira JJ. Tratamento nas Doenças do Movimento – Ensaio Clínicos que há de novo? Fórum de Neurologia, Palace Hotel – Monte Real, Leiria, Portugal, May 19-21, 2017.

Ferreira JJ. Ensaio Clínicos. Programa de Formação em Investigação, Direcção do Internato Médico, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 9, 2017.

Anes AM. Segurança e relato de eventos adversos. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Ferreira JJ. Aspectos práticos da condução de estudos clínicos. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Ferreira JJ. Responsabilidade do investigador. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.



Borges M. Documentos essenciais. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Rosa MM. Introdução e princípios de Boas Práticas Clínicas. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Costa J. Protocolo e estudo clínico. IV Curso de Boas Práticas Clínicas, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 10, 2017.

Ferreira JJ. Movement Disorders for the non-neurologist. Centro di Formazione del Personale Azienda Ospedaliera, Terni, Italy, May 11, 2017.

Ferreira JJ. Is drug repositioning possible in dystonia and levodopa induced dyskinesia? 6<sup>th</sup> Biennial Workshop on Dystonia and Parkinsonism, Rome, Italy, May 12-14, 2017.

Ferreira JJ. Redes de investigação e Tips & Tricks da Investigação clínica. Programa de Formação em Investigação, Direcção do Internato Médico, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 16, 2017.

Anes AM. Qualidade dos cuidados na doença de Parkinson e medição de resultados. Curso de actualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Rosa MM. Gestão da terapêutica – Casos práticos I. Curso de actualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Rosa MM. Gestão da terapêutica – Casos práticos I. Curso de actualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Rosa MM. Terapêutica farmacológica e não farmacológica na doença de Parkinson I. Curso de actualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

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Coelho M. Diagnóstico diferencial dos síndromes parkinsonianas. Curso de atualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Guedes LC. Semiologia e evolução da doença de Parkinson. Curso de atualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Coelho M. Epidemiologia e critérios de diagnóstico da doença de Parkinson. Curso de atualização em Farmacologia Clínica e Farmacoterapia, Doença de Parkinson, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 17 and 20, 2017.

Ferreira JJ. Cognition and motor control – clinical. Movement Disorders: bridging basic science with clinical medicine, Verona, Italy, May 19-20, 2017.

Freixo C, Anes AM, Augusto A, Rosa MM, Ferreira JJ, Santos MJ, Canhão H, Fonseca JE. Adverse drug reactions in the pediatric population with rheumatological disease. The 3<sup>th</sup> Congress of the European Association for Clinical Pharmacology and Therapeutics (EAPCT), Prague, Czech Republic, June 24-27, 2017.

Costa J. Econometria Aplicada à Avaliação Económica em Saúde. 10<sup>a</sup> Edição da Pós-Graduação em Avaliação Económica dos Medicamentos, Lisbon School of Economics and Management, Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, June 2017.

Costa J. Health Research using STATA – Summer School. CEMAPRE, Lisbon School of Economics and Management, June 19-23, 2017.

Ferreira JJ. Drug-induced Movement Disorders. MDS-ES Summer School for Young Neurologists, Marburg, Germany, July 21-23, 2017.

Costa J. Revisão Sistemática. I Congresso Internacional de Saúde Baseada em Evidência – CISBE 2017, Associação Médica Brasileira – AMB, Fortaleza, Brazil, August 17, 2017.

Costa J. Pharmacoepidemiology and Pharmacovigilance in Drug Lifecycle. FCT PhD Programme in Medicines and Pharmaceutical Innovation (i3DU), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal, September 2017.

Coelho M. Atypical Parkinsonism. MDS-ES Summer School for Nurses, Torres-Vedras, Portugal, September 29, 2017.

Ferreira JJ. An approach to patients with Movement Disorders. MDS-ES Summer School for Nurses, Torres-Vedras, Portugal, September 29, 2017.

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Coelho M. Parkinson's Disease: epidemiology, diagnosis, clinical features and progression. MDS-ES Summer School for Nurses, Torres-Vedras, Portugal, September 29, 2017.

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Ferreira JJ. How to design studies for SLT in PD. Speech therapy in Parkinson's Disease and Parkinsonism Autumn School, CNS, Torres Vedras, Portugal, October 28-30, 2017.

Ferreira JJ. Medical management of PD and atypical parkinsonism. Speech therapy in Parkinson's Disease and Parkinsonism Autumn School. CNS, Torres Vedras, Portugal, October 28-30, 2017.

Ferreira JJ. Parkinson's disease phenomenology and progression. Speech therapy in Parkinson's Disease and Parkinsonism Autumn School, CNS, Torres Vedras, Portugal, October 28-30, 2017.

Ferreira JJ. Desenho de ensaios e elaboração do protocolo. Curso de Especialização de Introdução à Investigação clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 15, 2017.

Rosa MM. Desenvolvimento clínico. Curso de Especialização de Introdução à Investigação clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 15, 2017.

Ferreira JJ. Desenvolvimento pré-clínico. Curso de Especialização de Introdução à Investigação clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 15, 2017.

Ferreira JJ. Instrumentos de avaliação e outcomes. Curso de Especialização de Introdução à Investigação clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 16, 2017.

Caldeira D. Avaliação da qualidade de ensaios clínicos. Curso de Especialização de Introdução à Investigação clínica, Programa Doutoral do Centro Académico de Medicina da Universidade de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, December 16, 2017.

Ferreira JJ. Ensaios Clínicos. Mestrado em Cuidados Paliativos, Instituto de Ciências da Saúde, Universidade Católica Portuguesa, Lisbon, Portugal, December 16, 2017.

### **Science and Society**

Guedes LC. A tarde é Sua, November 27, 2017.

Ferreira JJ. EAN interview, 2017.

Guedes LC. A tarde é Sua, June 28, 2017.

Ferreira JJ. Palestra nas comemorações do Dia Mundial da Doença de Parkinson, April 11, 2017.

Ferreira JJ. Tremores são o sintoma mais reconhecível da Doença de Parkinson, SAPO Vídeos, April 15, 2017.

### **MSc Thesis Completed**

Germano Silva Ferreira, 04/07/2017, “Motor and cognitive interference on multitasking walking deficit in people with Parkinson Disease”, Faculty of Medicine, University of Lisbon. Supervisor: Joaquim Ferreira.

Joana Margarida do Nascimento Fagundes Carvalho, 22/11/2017, “Audio perceptive analysis of the parkinsonism associated dysarthria by different health professionals, patimest, relatives and from general population”, Faculty of Medicine, University of Lisbon. Supervisor: Joaquim Ferreira.

### **PhD Thesis Completed**

Daniel Gomes Caldeira, 09/02/2017, “Safety of oral antitrombotic drugs: resource consumption of iatrogenic bleeding in Portugal”, Faculty of Medicine, University of Lisbon. Supervisor: Joaquim Ferreira.

Leonor Correia Guedes, 27/04/2017, “LRRK2 mutations in Parkinson’s disease”, Faculty of Medicine, University of Lisbon. Supervisor: Joaquim Ferreira.

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## Ferro, José

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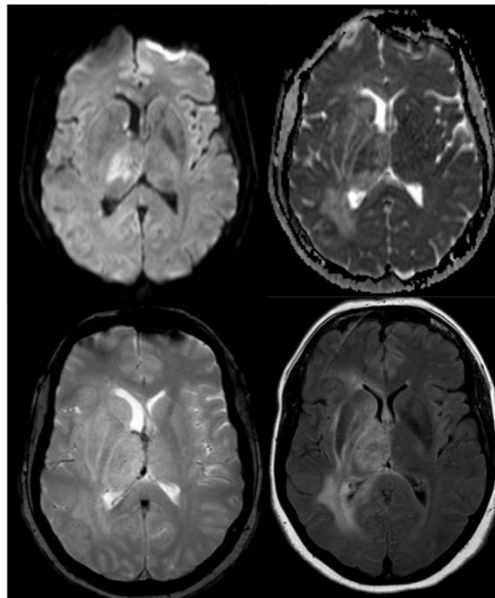
### Major Interests / Objectives

General objective is to increase the knowledge and foster the prevention and treatment of major prevalent and disabling disorders involving the brain, such as cerebrovascular diseases and Alzheimer’s disease. The main advantage is the strong collaboration among the experienced PIs, based on common clinical investigation methodologies and particular features of research expertise, expanded by multiple national and international collaborations in the areas of basic neurosciences, clinical genetics, advanced statistical methods, biological engineering, and neuroimaging. The researchers conducted clinical trials and assessed the clinical impact of different interventions in multinational efforts to get new targeted and personalized treatments for these prevalent and disabling brain disorders.

### Head of Laboratory

José Manuel Morão Cabral Ferro, MD/PhD

### Graphical Abstract



### Research Team

Alexandre Valério de Mendonça	PhD	Principal Investigator
Ana Catarina Gaspar Fonseca	MD/PhD	Investigator
Ana Isabel Figueira Verdelho	MD/PhD	Investigator
Ana Mafalda Lopes Carinha Gonçalves	Master	Investigator (Left June)

Bruno André e Silva Miranda	MD/PhD	Investigator (Started March)
Carla Cristina Paulo Gabriel Bentes	MD	PhD Student/MD
Carolina Pires Maruta	PhD	Investigator
Catarina Beatriz Silva Ferreira	Master	PhD Student (Started March)
Diana de Aguiar Dias de Sousa	Master	PhD Student, MD
Frederico Simões do Couto	MD/PhD	Investigator, MD
Gislaine Castilho de Oliveira	Master	Investigator
Isabel Pavão Martins	MD/PhD	Investigator
José Manuel Borges Fonseca	PhD	Investigator
Lara Isabel Pires Melo Caeiro	PhD	Post-Doctoral Student
Maria Gabriela Mariano Leal	Graduate	Investigator
Maria Luisa Albuquerque	MD	Investigator
Maria Luisa Mendonça Correia Pires	Undergraduate	Administrative
Maria Manuela Gil Guerreiro	PhD	Investigator
Mariana Durão Borges	Master	Investigator (Started October)
Mário Rui Jesus Santos Rodrigues	Master	Investigator
Marisa Marina Fatuda Costa	Undergraduate	Administrative
Patrícia Canhão	MD/PhD	Investigator
Patrícia Raquel dos Anjos Eugénio	Master	Investigator
Pedro Miguel Nascimento Alves	Master	Investigator
Sandra Maria Dias Cardoso	Master	Investigator
Teresa Pinho e Melo	MD	Investigator

### Laboratory Keywords / Research Areas

Cryptogenic stroke, Aphasia, Cognitive decline, Cerebral venous thrombosis.

### Major Scientific Achievements

- Cerebral venous thrombosis (CVT). A) Development of an App for free use in Android and I-Phones (CVT risk score) to calculate the prognosis of individual patients, B) CVT patients with infections and with infratentorial lesions can be safely anticoagulated, C) Pregnancy after CVT is safe.
- We determined NT-proBNP cut-off points for the identification of a cardioembolic aetiology related to undiagnosed atrial fibrillation, its time course in the first 72 hours after an ischemic stroke and validated them in a different cohort.
- We found that motor slowing was correlated with cognitive slowing and that physical activity was associated with a slower progression of vascular cognitive impairment.

- The prevalence of cerebral amyloid pathology, ascertained by positron emission tomography or cerebrospinal fluid biomarkers, has been determined, indicating an approximate 25-year interval between first development of amyloid positivity and onset of dementia.

### Selected Publications

Aguiar de Sousa D, Canhão P, Crassard I, Coutinho J, Arauz A, Conforto A, Béjot Y, Giroud M, Ferro JM, ISCVT-2-PREGNANCY Investigators (2017). Safety of Pregnancy After Cerebral Venous Thrombosis: Results of the ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis)-2 PREGNANCY Study. *Stroke* 48, 3130-3133. (IF: 6.032, Citations: 1).

Premi E, Grassi M, van Swieten J, Galimberti D, Graff C, Masellis M, Tartaglia C, Tagliavini F, Rowe JB, Laforce R Jr, Finger E, Frisoni GB, de Mendonça A, Sorbi S, Gazzina S, Cosseddu M, Archetti S, Gasparotti R, Manes M, Alberici A, Cardoso MJ, Bocchetta M, Cash DM, Ourselin S, Padovani A, Rohrer JD, Borroni B, Genetic FTD Initiative (GENFI) (2017). Cognitive reserve and TMEM106B genotype modulate brain damage in presymptomatic frontotemporal dementia: a GENFI study. *Brain* 140, 1784-1791. (IF: 10.292, Citations: 2).

Amarenco P, Lavallée PC, Labreuche J, Albers GW, Bornstein NM, Canhão P, Caplan LR, Donnan GA, Ferro JM, Hennerici MG, Molina C, Rothwell PM, Sissani L, Školoudík D, Steg PG, Touboul PJ, Uchiyama S, Vicaut É, Wong LK, TIA registry.org Investigators (2016). One-year risk of stroke after transient ischemic attack or minor stroke. *N Engl J Med* 374, 1533. (IF: 72.406, Citations:--).

Dávalos A, Alvarez-Sabín J, Castillo J, Díez-Tejedor E, Ferro J, Martínez-Vila E, Serena J, Segura T, Cruz VT, Masjuan J, Cobo E, Secades JJ, International Citicoline Trial on acUte Stroke (ICTUS) trial investigators (2012). Citicoline in the treatment of acute ischaemic stroke: an international, randomised, multicentre, placebo-controlled study (ICTUS trial). *Lancet* 380, 349. (IF: 47.831, Citations: 74).

Traylor M, Farrall M, Holliday EG, Sudlow C, Hopewell JC, Cheng YC, Fornage M, Ikram MA, Malik R, Bevan S, Thorsteinsdottir U, Nalls MA, Longstreth W, Wiggins KL, Yadav S, Parati EA, Destefano AL, Worrall BB, Kittner SJ, Khan MS, Reiner AP, Helgadottir A, Achterberg S, Fernandez-Cadenas I, Abboud S, Schmidt R, Walters M, Chen WM, Ringelstein EB, O'Donnell M, Ho WK, Pera J, Lemmens R, Norrving B, Higgins P, Benn M, Sale M, Kuhlenbäumer G, Doney AS, Vicente AM, Delavaran H, Algra A, Davies G, Oliveira SA, Palmer CN, Deary I, Schmidt H, Pandolfo M,



Montaner J, Carty C, de Bakker PI, Kostulas K, Ferro JM, van Zuydam NR, Valdimarsson E, Nordestgaard BG, Lindgren A, Thijs V, Slowik A, Saleheen D, Paré G, Berger K, Thorleifsson G, Australian Stroke Genetics Collaborative, Wellcome Trust Case Control Consortium 2 (WTCCC2), Hofman A, Mosley TH, Mitchell BD, Furie K, Clarke R, Levi C, Seshadri S, Gschwendtner A, Boncoraglio GB, Sharma P, Bis JC, Gretarsdottir S, Psaty BM, Rothwell PM, Rosand J, Meschia JF, Stefansson K, Dichgans M, Markus HS, International Stroke Genetics Consortium (2012). Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE collaboration): a meta-analysis of genome-wide association studies. *Lancet Neurol* 951. (IF: 26.284, Citations: 123).

### **Ongoing Research Projects**

2016/2019: Randomized interventional prospective study of the effect of physical activity in vascular cognitive impairment. Coordinator: Ana Isabel Figueira Verdelho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-DES/3706/2014. Amount: € 199 588,00. Total Amount: € 199 588,00.

2016/2018: Fundo de Investigação para a Saúde. Coordinator: Ana Catarina Gaspar Fonseca. Funding Agency: Infarmed. Reference: FPJ001028. Amount: € 80 000,00. Total Amount: € 80 000,00.

2014/2018: Technology, Entrepreneurship and Innovation Policy Lab. Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: CMUP-ERI/TPE/0028/2013. Amount: € 89 300,00. Total Amount: € 350 000,00.

2014/2018: Project Bayer. Coordinator: José Manuel Morão Cabral Ferro. Funding Agency: Bayer. Reference: Bayer JM Ferro. Amount: € 16 000,00. Total Amount: € 16 000,00.

2014/2017: Research to assess policies and strategies for dementia in the young. Coordinator: Alexandre Valério de Mendonça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: JPND-HC/0003/2012. Amount: € 125 000,00. Total Amount: € 125 000,00.

2014/2017: Setting the stage for prevention trials in Genetic Frontotemporal Lobar Degeneration. Coordinator: Alexandre Valério de Mendonça. Funding Agency: Ana Paula dos Santos Marques da Costa. Reference: GenFi. Amount: € 10 000,00. Total Amount: € 10 000,00.

2013/2018: Bolsa AVC. Coordinator: Carla Cristina Paulo Gabriel Bentes. Funding Agency: Tecnifar. Reference: AVC. Amount: € 5 000,00. Total Amount: € 5 000,00.

2013/2017: International study on dural sinus and cerebral vein thrombosis 2. Coordinator: José Manuel Morão Cabral Ferro. Funding Agency: Congrex Schweiz AG. Reference: ISCVT-2. Amount: € 155 000,00 Total Amount: € 155 000,00.

2010/2018: Transient ischaemic attack. Coordinator: Patrícia Martins Canhão Rodrigues. Funding Agency: SOS Attaque Cérébrale. Reference: TIA JM Ferro. Amount: € 14 520,00. Total Amount: € 14 520,00.

### **Other Projects**

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

### **Publications in Peer Review Journals**

Aguiar de Sousa D, Canhão P, Crassard I, Coutinho J, Arauz A, Conforto A, Béjot Y, Giroud M, Ferro JM, ISCVT-2-PREGNANCY Investigators (2017). Safety of Pregnancy After Cerebral Venous Thrombosis: Results of the ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis)-2 PREGNANCY Study. *Stroke* 48, 3130-3133. (IF: 6.032, Citations: 1).

Alves PN, Maruta C, Albuquerque L, Martins IP (2017). Dissociation findings between short-term and long-term memory in autoimmune limbic encephalitis. *J Neurol Sci* 381, 126-127. (IF: 2.295, Citations:-).

Amorim I, Antunes P, Nunes G, Martins IP (2017). Reversible cortical thickening in Hemiplegic Migraine. *Cephalalgia* 1, 333102417690128. (IF: 3.609, Citations:-).

Bentes C, Franco AC, Peralta AR, Viana P, Martins H, Morgado C, Casimiro C, Fonseca C, Geraldês R, Canhão P, Pinho E Melo T, Paiva T, Ferro JM (2017). Epilepsia partialis continua after an anterior circulation ischaemic stroke. *Eur J Neurol* 24, 929–934. (IF: 3.988, Citations:-).

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Bos I, Vos SJ, Frölich L, Kornhuber J, Wiltfang J, Maier W, Peters O, Rüter E, Engelborghs S, Niemantsverdriet E, De Roeck EE, Tsolaki M, Freund-Levi Y, Johannsen P, Vandenberghe R, Lleó A, Alcolea D, Frisoni GB, Galluzzi S, Nobili F, Morbelli S, Drzezga A, Didic M, van Berckel BN, Salmon E, Bastin C, Dauby S, Santana I, Baldeiras I, de Mendonça A, Silva D, Wallin A, Nordlund A, Coloma PM, Wientzek A, Alexander M, Novak GP, Gordon MF, Alzheimer's Disease Neuroimaging Initiative, Wallin ÅK, Hampel H, Soininen H, Herukka SK, Scheltens P, Verhey FR, Visser PJ (2017). The frequency and influence of dementia risk factors in prodromal Alzheimer's disease. *Neurobiol Aging* 56, 33-40. (IF: 5.117, Citations: 1).

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Rohan Z, De Deyn P, Engelborghs S, Cras P, Van Broeckhoven C, Sleegers K, European Early-Onset Dementia (EU EOD) consortium (2017). Deleterious ABCA7 mutations and transcript rescue mechanisms in early onset Alzheimer's disease. *Acta Neuropathol* 134:475-487. (IF: 12.213, Citations:--).

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Nascimento Alves P, Silva C, Baptista J, Lima B, Jacinto M, Trigueiros F, Martins A, Pinho E Melo T, Fonseca AC (2017). Laterality of Pneumonia in Acute Stroke. *Eur Neurol* 77,75-79. (IF: 1.697, Citations:--).

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Silva C, Peralta AR, Bentes C (2017). The urge to move and breath – the impact of obstructive sleep apnea syndrome treatment in patients with previously diagnosed clinically significant restless syndrome. *Sleep Med* 38, 17-20. (IF: 3.391, Citations: 2).

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Vargas M, Costa M, Pinho E Melo T, Ferro JM, Fonseca AC (2017). Increase in the Admission of Stroke Mimics after Change in Emergency Shifts. *Cerebrovasc Dis* 44,68-74. (IF: 2.974, Citations:-).

### **Other Publications International**

Ferro JM, Aguiar de Sousa D, Oliveira S (2017). Cerebral Venous Thrombosis: genetic aspects, In: Sharma P, Meschia J. Stroke Genetics, Springer:295- 326. (IF:--, Citations:--)

Hilkens NA, Algra A, Diener HC, Reitsma JB, Bath PM, Csiba L, Hacke W, Kappelle LJ, Koudstaal PJ, Leys D, Mas JL, Sacco RL, Amarenco P, Sissani L, Greving JP, Cerebrovascular Antiplatelet Trialists' Collaborative Group (2017) Predicting major bleeding in patients with noncardioembolic stroke on antiplatelets: S2TOP-BLEED. Neurology 89:936-943. (IF: 8.320, Citations: 1).

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### **Other Publications National**

Fonseca J (2017) Afasia e a Sociedade. Criap – Terapia da Fala. Nº 4, 49-51.

### **Invited Lectures and Seminars**

Fonseca AC. Alterações do sono como consequência do AVC agudo. 11º Congresso Português do AVC, Porto, Portugal, February 2, 2017.

Ferro JM. AVC e fibrilhação auricular: o que sabemos, o que podemos fazer. 11º Congresso Português do AVC, Porto, Portugal, February 3, 2017.



Fonseca C. Blood pressure variability in stroke – sessão conjunta SPH/SPN/WGESH. 11º Congresso Português de Hipertensão e Risco Cardiovascular Global, Vilamoura, Portugal, February 11, 2017.

Martins IP. Vertigem Posicional e Migraine. Reunião de Inverno Vertigem Posicional, APO – Associação Portuguesa de Otoneurologia, Centro de Ciência do Café, Campo Maior, Portugal, February 18, 2017.

Ferro JM. Drug-induced stroke. 9<sup>th</sup> International Congress of Internal Medicine, Athens, Greece, March 9, 2017.

Martins IP. Manifestações visuais da enxaqueca. Reuniões Clínicas de Oftalmologia, Centro Hospitalar Lisboa Norte, Serviço de Oftalmologia, Lisbon, Portugal, March 31, 2017.

Canhão P. Pros & cons session: to treat or not to treat “Can we treat unclear onset stroke? PROS”. Lisbon Stroke Summit, Lisbon, Portugal, April 8, 2017.

Aguiar de Sousa D. Update in Cerebral Venous Thrombosis. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 16, 2017.

Ferro JM. Acute Treatment of Cerebral Venous Sinus Thrombosis. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 16, 2017.

Fonseca C. Transient ischemic attack – Teaching course: Transient Neurological Syndromes: Clinical and radiological features. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 16, 2017.

Martins IP. Vertigem Posicional. Reunião Anual da Associação Portuguesa de Otoneurologia - APO, Montargil, Portugal, May 19, 2017.

Ferro JM. The new European guidelines for cerebral venous thrombosis. 26<sup>th</sup> European Stroke Conference, Berlim, Germany, May 24, 2017.

Ferro JM. Hemicraniectomia: evidência e ética. Neuro 2017, Funchal, Portugal, June 2, 2017.

Ferro JM. Tromboses venosas cerebrais: novas recomendações da ESO. XIII Congresso de Neurorradiologia, Estarreja, Portugal, June 3, 2017.

Ferro JM. ESO-EAN Guidelines on cerebral venous thrombosis. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 26, 2017.

Ferro JM. Stroke as first presentation of systemic malignancies (including autoimmune encephalitis). 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 26, 2017.

Canhão P. Symposium ESO/EAN - Causes and clinical course of cerebral venous infarction. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 27, 2017.

Aguiar de Sousa. Pathogenesis of venous infarcts. International workshop on cerebral venous thrombosis (ISCVT), 20 years later, what next? Paris, France, October 17, 2017.

Ferro JM. ISCVT 20 years. International workshop on cerebral venous thrombosis (ISCVT), 20 years later, what next? Paris, France, October 17, 2017.

Ferro JM. Decompressive surgery. When? How? International workshop on cerebral venous thrombosis (ISCVT), 20 years later, what next? Paris, France, October 18, 2017.

Fonseca AC. Critérios de qualidade das UAVC. Marcadores de qualidade – art consenso. 8<sup>a</sup> Reunião Nacional de Unidades de AVC, Lisbon, Portugal, October 27, 2017.

Aguiar de Sousa D. AVC – As minhas selecções. As revisões sistemáticas/meta-análises do ano. 15<sup>a</sup> Reunião da Sociedade Portuguesa do Acidente Vascular, Lisbon, Portugal, October 28, 2017.

Fonseca AC. AVC e doenças raras – pistas para diagnostic no AVC isquémico. Embolia cardiogénica. 8<sup>a</sup> Reunião Nacional de Unidades de AVC, Lisbon, Portugal, October 28, 2017.

Ferro JM. Depression and cerebrovascular diseases. 8<sup>th</sup> International Meeting of Psychogeriatrics 2017, Vilamoura, Portugal, November 4, 2017.

Ferro JM. State of the art in diagnostic work-up and therapeutic management. 9<sup>th</sup> Regional Teaching Course in Su-Saharan Africa, Ouagadougou, Burkina Faso, November 8, 2017.

Bentes C. Crises epiléticas na Unidade de AVC. Congresso de Neurologia 2017, Lisbon, Portugal, November 17, 2017.

Ferro JM. Formação em AVC na era da globalização. Congresso de Neurologia 2017, Lisbon, Portugal, November 17, 2017.

Fonseca J. Alterações da Comunicação após Lesão Hemisférica Direita. Perturbação da Comunicação no Adulto por Lesão Neurológica Adquirida. Ciclo de Conferências do Centro de Medicina de Reabilitação - Alcoitão, Alcoitão, Portugal, November 27, 2017.

Maruta C. Especificidades e complementaridade do diagnóstico na Afasia Progressiva Primária. Perturbação da Comunicação no Adulto por Lesão Neurológica Adquirida. Ciclo de Conferências do Centro de Medicina de Reabilitação - Alcoitão, Alcoitão, Portugal, November 27, 2017.

Martins IP. Estou em profunda cogitação...! Serviço de Neurologia, Hospital de Santa Maria, Lisbon, Portugal, November 30, 2017.

Miranda B. The role of prefrontal cortex and striatum in model-free and model-based reinforcement learning. Institute of Neurology, Lisbon, Portugal, December 4, 2017.

#### **Communications in International Conferences**

Williams LR, Ali M, VandenBerg K, Godwin J, Elders A, Abel S, Abo M, Becker F, Bowen A, Brandenburg C, Breitenstein C, Copland D, Cranfill T, di Pietro-Bachmann M, Fillingham J, Gandolfi M, Glize B, Godecke E, Hilari K, Hinckley J, Horton S, Howard D, Jaecks P, Jesus LMT, Jungblut M, Kambanaros M, Khedr E, Kukkonen T, Kang EK, Lambon Ralph MA, Laganaro M, Laska A-C, Leeman B, Lima RR, Lorenz A, MacWhinney B, Martins IP, Mattioli F, Mavi? I, Meinzer M, Noé Sebastián E, Nilipour R, Palmer R, Patricio B, Price C, Prizl Jakovic T, Rose M, Rosso C, Ruitter M, Shisler Marshall R, Smania N, Snell C, Szaflarski JP, Thomas S, van de Meulen I, van de Sandt-Koenderman M, Visch-Brink E, Worrall L, Wright Harris H, Brady MC. REhabilitation and recovery of peopLE with Aphasia after StrokeE (RELEASE): The creation of a multidisciplinary, International Aphasia Database of Individual Patient Data. CATs, Rotterdam, The Netherlands, February 2017. (Poster Presentation).

Bentes C, Peralta AR, Martins H, Casimiro C, Morgado C, Franco A, Viana P, Fonseca AC, Galdes R, Canhão P, Melo TP, Paiva T, Ferro JM. Epileptic manifestations in stroke patients treated with intravenous alteplase. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Ferro JM, Canhão P, Coutinho J, Stam J, Bousser MG. DECOMPRESS – 2 Steering Committee. Prospective registry of decompressive surgery for CVT patients– DECOMPRESS – 2. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Fonseca AC, Alves PN, Inácio N, Melo TP, Canhão P, Ferro JM, Almeida A. Cardiac Magnetic resonance study of the left atrium of ischemic stroke patients with undetermined etiology (CAIUS study). 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Fragata I, Canto-Moreira N, Canhão P. Cerebral perfusion and diffusion in acute and subacute perimesencephalic subarachnoid hemorrhage. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Martinez-Majander N, Yesilot N, Palm F, Tsivgoulis G, Numminen H, von Sarnowski B, Waje-Andreassen U, Ylikotila P, ZeddeM, Huhtakangas J, Fonseca C, Redfors P, de Leeuw FE, Pezzini A, Korv J, Schneider S, Tanislav C, Jatuzis D, Martinez-Sanchez P, Jakala P. Searching for explanations for cryptogenic stroke in the young: revealing the triggers, causes and outcome. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Miranda B, Ferro JM, Canhão P, Stam J, Bousser MG, Crassard I, Barinagarrementeria F, Massaro AR, on behalf of the EXCOA-CVT investigators, The benefit of EXtending oral antiCOAgulant treatment after acute Cerebral Vein Thrombosis (EXCOA-CVT): a cluster observational study. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Vargas M, Costa MR, Pinho e Melo T, Canhão P, Ferro JM, Fonseca AC. Validation of the FABS score to identify stroke mimics in a Portuguese population. 3<sup>rd</sup> European Stroke Organisation Conference, Prague, Czech Republic, May 2017. (Poster Presentation).

Aguiar de Sousa D, Abilleira S, Gattringer T, von Martial R, Kobayashi A, Caso V, Gallofré M, Fazekas F, Szikora I, Fischer U. ESO EAN ESMINT SAFE Survey on Acute Stroke Care in Europe. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Oral Presentation).

Alves PN, Fonseca A, Canhão P. Voluntary control of plegic limb during yawning after stroke. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Poster Presentation).

Amorim I, Antunes A, Leal G, Nunes G, Pavão Martins I. Aphasic aura and reversible MRI image in Hemiplegic Migraine. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Poster Presentation).

Miranda B, Castro J, Conceicao I. Transthyretin familial amyloid polyneuropathy: the neuropathy progression on treated patients compared with natural disease progression. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Oral Presentation).

Miranda B, Pinto S, de Carvalho M. The impact of spasticity on diaphragm contraction: electrophysiological assessment. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Oral Presentation).

Parreira S, Pinho e Melo T, Fonseca ACG. Lumbar puncture in the aetiological investigation of ischaemic stroke of undetermined aetiology. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Poster Presentation).

Rodrigues FB, Bentes C, Sousa A, Duarte GS, Franco A, Marques R, Nzwalo H, Peralta AR, Ferro JM, Costa J. The frequency of post-stroke epileptiform activity - A systematic review and meta-analysis of observational studies. 3<sup>rd</sup> Congress of the European Academy of Neurology, Amsterdam, The Netherlands, June 2017. (Poster Presentation).

Alves PN, Fonseca AC, Martins IP. Reduplicative paramnesia after stroke – lesion overlap and disconnection study. 6<sup>th</sup> Scientific Meeting of the Federation of the European Societies of Neuropsychology. Maastricht, The Netherlands, September 2017. (Poster Presentation).

Fonseca AC, Alves PN, Melo TP, Canhã P, Ferro JM, Almeida AG. Patients with undetermined ischemic stroke etiology show a high percentage of atrial tissue fibrosis. XXIII World Congress of Neurology, Kyoto, Japan, September 2017. (Poster Presentation).

Godinho F, Maruta C, Martins IP. The effect of education on neuropsychological evaluation in patients with mild cognitive impairment. 6<sup>th</sup> Scientific Meeting of the Federation of the European Societies of Neuropsychology, Maastricht, The Netherlands, September 2017. (Poster Presentation).

### Communications in National Conferences

Alves P, Reimão S, Fonseca AC, Canhão P. Controlo voluntário de membro plégico durante o bocejo em doente com AVC isquémico. 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Bentes C, Canhão P, Peralta AR, Viana P, Fonseca AC, Geraldés R, Melo TP, Paiva T, Ferro JM. É o EEG útil no diagnóstico diferencial dos acidentes isquémicos transitórios possíveis? 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Bentes C, Martins H, Peralta AR, Morgado C, Casimiro C, Franco AC, Fonseca AC, Geraldés R, Canhão P, Melo TP, Paiva T, Ferro JM. Manifestações epilépticas em doentes submetidos a trombólise endovenosa com alteplase. 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Bentes C, Patrícia Canhão, Ana Rita Peralta, Pedro Viana, Ana Catarina Fonseca, Ruth Geraldés, Teresa Pinho e Melo, Teresa Paiva, José Manuel Ferro. É o EEG útil no diagnóstico diferencial dos acidentes isquémicos transitórios possíveis? 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Fonseca AC, Alves PN, Inácio N, Melo TP, Canhão P, Ferro JM, Almeida AG. Estudo por Imagem de Ressonância Magnética cardíaca da aurícula esquerda no AVC isquémico de etiologia indeterminada (Estudo CAIUS). 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Parreira S, Alves P, Fonseca AC, Canhão P. Apraxia do vestir – não apenas no vestir. 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Santos M, Canhão P. Prognóstico Vascular dos Acidentes Neurológicos Transitórios Focais e Mistos. 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Vargas M, Costa MR, Melo TP, Canhão P, Ferro JM, Fonseca AC. Validação da escala FABS como instrumento de diagnóstico de “Falsos AVCs” numa coorte de doentes portugueses. 11º Congresso Português do AVC, Porto, Portugal, February 2-4, 2017. (Oral Presentation).

Maruta C, Fonseca J, Campos AR, Farias JP, Santos H, Martins IP. Avaliação neuropsicológica em doentes submetidos a mapeamento funcional intraoperatório de áreas eloquentes para a linguagem. II Congresso Ibérico de Psicologia Clínica e da Saúde, Instituto Superior de Psicologia Aplicada, Lisbon, Portugal, March 23-25, 2017. (Poster Presentation).

Maruta C, Guedes L, Martins IP. Alterações neuropsiquiátricas como sintoma inicial num caso de Demência Fronto-Temporal de causa genética. II Congresso Ibérico de Psicologia Clínica e da Saúde, Instituto Superior de Psicologia Aplicada, Lisbon, Portugal, March 23-25, 2017. (Poster Presentation).

Fonseca AC. Cardiac Magnetic resonance study of the left atrium of ischemic stroke patients with undetermined etiology. 4<sup>o</sup> Annual Conference Health@Lisbon, Lisbon, Portugal, May 4, 2017. (Oral Presentation).

Fonseca J. Separar o trigo do joio. VII Conferencia Práticas Clínicas em Terapia da Fala, Lisbon, Portugal, May 6, 2017. (Oral Presentation).

Fonseca J. Tecnologia na Reabilitação da Linguagem. Empreendedorismo, Inovação e Tecnologia na Saúde. Congresso de Cuidados Continuados e Paliativos do Instituto S. João de Deus, Inovação e Desenvolvimento, Lisbon, Portugal, May 25-26, 2017. (Oral Presentation).

Godinho F, Maruta C, Martins IP. Influência da Escolaridade na Avaliação neuropsicológica do Defeito Cognitivo. NEURO 2017, Funchal, Portugal, June 1-3, 2017. (Oral Presentation).

Maruta C, Fonseca J, Campos AR, Farias JP, Santos H, Martins IP. Avaliação neuropsicológica em doentes submetidos a mapeamento funcional intraoperatório de áreas eloquentes para a linguagem. NEURO 2017, Funchal, Portugal, June 1-3, 2017. (Oral Presentation).

Caeiro L, Carvalho-Dias M, Martins TG, Ferro JM, Verdelho A. Está a apatia após o AVC relacionada com a cefaleia? 31<sup>a</sup> Reunião Grupo de Estudos de Envelhecimento Cerebral e Demências, Lisbon, Portugal, June 30-July 1, 2017. (Oral Presentation).

Caeiro L, Rodrigues MJ, Ferro JM, Verdelho A. Diferenças entre a WMS e a WMS-III: subtestes de Memória Lógica e Pares de Palavras. 31<sup>a</sup> Reunião Grupo de Estudos de Envelhecimento Cerebral e Demências, Lisbon, Portugal, June 30- July 1, 2017. (Oral Presentation).

Fonseca J. Afasia: Mais que uma Perturbação da Comunicação. I Simpósio da Delegação Madeira da APTF. Delegação da Madeira da Associação Portuguesa de Terapeutas da Fala, Funchal, Portugal, September 29, 2017. (Oral Presentation).

Fonseca J. A Afasia é só uma Alteração da Linguagem? I Encontro de Terapeutas ASFE Saúde, Mafra, Portugal, October 14, 2017. (Oral Presentation).

Maruta C, Ferreira C, Ferreira CB, Guerreiro M, Verdelho A, Almeida M, Pereira M, Miltenyi G, Castelo-Branco M, Santiago B, Santana I, Taipa A, De Mendonça. Understanding the initial phases of genetic frontotemporal lobar degeneration - Setting the stage for prevention trials. 8<sup>th</sup> International Meeting of Psychogeriatrics, Vilamoura, Portugal, November 2-4, 2017. (Oral Presentation).

Dias M, Maruta C, Verdelho A. O homem que confundiu a mulher com...uma amante. Congresso de Neurologia 2017, Lisbon, Portugal, November 16-18, 2017. (Poster Presentation).

Pimentel B, Ferro JM, Willeit J, Toll T. Investigação diagnóstica e etiologia do AVC isquémico no adulto jovem: uma comparação retrospectiva entre dois centros. Congresso de Neurologia 2017, Lisbon, Portugal, November 16-18, 2017. (Oral Presentation).

Rosário M, Aguiar de Sousa D, Canhão P. Tetraparésia de instalação aguda em doente com lesão estratégica da área cortical motora bilateral associada a trombose venosa cerebral. Congresso de Neurologia 2017, Lisbon, Portugal, November 16-18, 2017. (Poster Presentation).

Rosário M, Franco C, Fonseca AC. Hematomas parotídeos bilaterais após trombólise com alteplase no AVC isquémico agudo. Congresso de Neurologia 2017, Lisbon, Portugal, November 16-18, 2017. (Poster Presentation).

Fonseca J. Cognição e Linguagem. Que Relação? I Encontro Científico da Obra Social do Pousal, Envelhecimento e Deficiência, Mafra, Portugal, November 17, 2017. (Oral Presentation).

### **Organisation of Conferences**

Canhão P. Scientific Committee. 11<sup>o</sup> Congresso Português do AVC, Porto, Portugal, February 2-4, 2017.

Canhão P. Scientific Committee. Lisbon Stroke Summit, Lisboa, Portugal, April 7-8, 2017.



Fonseca AC. Organizer. Neuro 2017, Sociedade Portuguesa de Neurologia e Sociedade Portuguesa de Neurocirurgia, Funchal, Portugal, May 1-3 June, 2017.

Martins IP, Fonseca J, Miranda F. Organisers. II Curso de Actualização em Avaliação da Afasia com a BAAL, Laboratório de Estudos de Linguagem, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 21-28, 2017.

Fonseca AC. Organizer. Congresso de Neurologia 2017, Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 16-18, 2017.

### **Internationalisation**

- Bentes C (member): Epi-Care (European Reference Network on rare and complex epilepsies).
- Bentes C (co-investigator): MORE – Medtronic Registry on Epilepsy – international registry of refractory epilepsy patients submitted DBS surgery.
- Bentes C (co-investigator): EURAP – European Registry for Pregnancy and safety of anti-epileptic drugs.
- Fonseca C: Secretary of the stroke group in the value of treatment project of the European Brain Council.
- Fonseca C: Member of the Education Committee and of the Membership Committee of the European Stroke Organization.
- Fonseca C: Member of the domain 1 of the “Action plan for stroke 2018” endorsed by the European Stroke Organization and SAFE.
- Fonseca C: Fellow of the European Stroke Society.
- Ferro JM: Member Steering Executive and Adjudication Committee of Industry clinical trials.
- Ferro JM: Member Editorial Board “Stroke” and “European Journal of Stroke”, and of the Advisory Board of “Cerebrovascular Disease” and “Journal of Neurology”.
- Ferro JM: Member Executive Board of the International Stroke Society.
- Ferro JM: Member Scientific Panel for Health, Directorate-General for Research and Innovation (Directorate E – Health) European Commission.

### **Prizes, Honours and Awards**

Ferro J. Outstanding Reviewer. American Heart Association/American Stroke Association, 2017.

Miranda B. João Lobo Antunes Award 2017.

Fonseca J, Raposo A, Martins IP. SPAVC 2017 Award in 11<sup>o</sup> Congresso da Sociedade Portuguesa do Acidente Vascular Cerebral to Recuperação da afasia e cognição, Porto, Portugal, February 2-4, 2017.

Alves P, Reimão S, Fonseca AC, Canhão P. Best Oral Presentation. Caso Clinico do 11<sup>o</sup> Congresso da Sociedade Portuguesa do Acidente Vascular Cerebral, Apoio Controlado voluntário de membro plégico durante o bocejo em doente com AVC isquémico, Porto, Portugal, February 2-4, 2017.

Kaupila LA, Amorim I, Bentes C, Peralta AR. Best Clinical Case. Diálogos em Epilepsia Meeting to. Trazodona: novo anti-epiléptico na síndrome de Dravet? Lisbon, Portugal, November 2017.

### **Industry Contract Research**

2016/2017: RESPECT-CVT: Randomised, Open-label, Exploratory Trial with Blinded Endpoint Adjudication (PROBE), Comparing Efficacy and Safety of Oral Dabigatran Etexilate Versus Oral Warfarin in Patients with Cerebral Venous and Dural Sinus Thrombosis Over a 24-week Period. Coordinator: José Ferro - Global Principal Investigator.

2015-2017: A Phase 3 multicenter randomized double blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of Aducanumab (BIIB037) in subjects with early Alzheimer's disease. Maruta C, in collaboration with Grupo de demênicas (Biogen Idec BIIB037-221AD301 ENGAGE & 221AD302 EMERGE, 2015).

RESPECT-ESUS: Randomized, double-blind evaluation in secondary stroke prevention comparing the efficacy and safety of the thrombin inhibitor dabigatran etexilate 110 or 150 mg (twice daily) versus acetylsalicylic acid (100 mg once daily) in patients with controlled clinical trial Embolic Stroke of Undetermined Source.

GLORIA: Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation.

### **Government/Organisation Contract Research**

European Brain Council. The Value of treatment for brain disorders – policy white paper towards optimizing research and care for brain disorders. Brussels, Belgium 2017.

### **Advanced Teaching**

Aguiar de Sousa D. Seminar: “Multivariable Analysis”. Introduction to Clinical Research: a practical course, Centro Académico Médico de Lisboa Advanced Course, University of Lisbon, January 2017.

Canhão P. Coordinator and Lecturer. “Prognostic Studies” Course, within the Specialized Course “introduction to clinical research: a practical course”, Centro Académico Médico de Lisboa Advanced Course, University of Lisbon, Lisbon, Portugal, March 3-4, 2017.

Ferro JM. Causations Studies. “Curso de especialização em introdução à Investigação Clínica”. Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 17-18, 2017.

Canhão P. Module Coordinator. “Research in Clinical Neurosciences”. Master in Neurosciences, Centro Académico Médico de Lisboa Advanced Course, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, April 4-21, 2017.

Caeiro L. Metodologia da descrição de um caso neuropsicológico. Master in Neurosciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, April 5, 2017.

Ferro JM. Consciência e conceito de pessoa: problemas do estado vegetativo persistente. “VIII Curso Pós-Graduado de actualização. Decisões éticas em fim de vida”, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, April 27, 2017.

Fonseca AC. Diagnostic tests. Lecturer. Master in Neurosciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, April 27, 2017.

Martins IP. Functional organization of the mind, Methods in Cognitive assessment. Master in Neurosciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 2, 2017.

Fonseca AC. Scientific Coordinator. Curso de Atualização em Neurologia, Associação Portuguesa de Medicina Geral e Familiar, Peniche, Portugal, May 3-6, 2017.

Maruta C. Executive functions and the frontal lobes. Master in Neurosciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 9, 2017.

Canhão P. Organizer and lecturer. Prognostic Studies. Programa de Formação em Investigação Clínica do Centro Hospitalar Lisboa Norte, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, May 11, 2017.

Aguiar de Sousa D. Seminar: “Introduction to Systematic Review”. Doctoral program in Neurosciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 2017.

Canhão P. Organizer and Lecturer. “Curso Preparação de Casos Clínicos para Publicação” within “Cursos de Apoio à Investigação do GAPIC”. Centro Académico Médico de Lisboa, University of Lisbon, Lisbon, Portugal, September 28, 2017.

Caeiro L. Diagnostic traps in post-stroke dementia, depression, apathy, etc. European Master in Stroke Medicine. Krems/Viena, Áustria, October 2017.

Caeiro L. How to evaluate cognition in the follow-up of stroke patients? European Master in Stroke Medicine. Krems/Viena, Austria, October, 2017.

Caeiro L. Presentation of a neuropsychological case. European Master in Stroke Medicine. Krems/Viena, Austria, October 2017.

Bentes C. Hipersónias: diagnóstico, aspetos clínicos e terapêuticos. Unidade curricular de Perturbações do Sono e Psicopatologia, Mestrado de Psicopatologia 2016/2017, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017.

### **Science and Society**

Aguiar de Sousa D. First author of the “ESO ESMINT EAN SAFE survey on Stroke care in Europe”, which assessed best available data on access and delivery of acute SU care, IVT and EVT throughout Europe. These data will assist national and European decision makers responsible for implementing better-tailored programmes for care of patients with acute stroke.

Aguiar de Sousa D. Member of the Young Stroke Physicians Committee – European Stroke Organization.

Aguiar de Sousa D. Member of the guideline panel for the “European Stroke Organization Guideline on Cerebral Venous Thrombosis”.

Aguiar de Sousa D. Member of the Scientific Panel on Stroke of the “European Academy of Neurology” as Resident and Research Fellow Section (RRFS) representative.

Aguiar de Sousa D. Member of the WISE group (Women Initiative for Stroke in Europe) – European Stroke Organization.

Canhão P. Coordinator of the activities of the “National Day of the Stroke Day”, Hospital Santa Maria, Lisbon, Portugal, March 31, 2017.

Canhão P. Collaboration in the activities of the “World Stroke Day”, October 29, 2017.

### **MSc Thesis Completed**

Joana Sequeira, 01/03/2017, “Enxaqueca após Acidente Vascular do Tronco Cerebral”, Faculty of Medicine, University of Lisbon. Supervisor: Isabel Pavão Martins.

Catarina Melita, 25/06/2017, “Physical activity for the prevention of vascular cognitive impairment”, Faculty of Medicine, University of Lisbon. Supervisor: Ana Verdelho.

Cláudia Ribeiro, 07/07/2017, “Papel da Fibrilhação Auricular no Jovem com Acidente Vascular Cerebral”, Faculty of Medicine, University of Lisbon. Supervisor: Ana Catarina Fonseca.

Bernardo Pimentel, 07/07/2017, “Diagnostic workup and etiologic diagnosis of ischemic stroke in young adults. A retrospective two-center comparison”, Faculty of Medicine, University of Lisbon. Supervisor: José M. Ferro.

Diogo Antão, 07/07/2017, “Acidente isquémico transitório no doente jovem: factores de risco, etiologia e prognóstico”, Faculty of Medicine, University of Lisbon. Supervisor: Patricia Canhão.

### **PhD Thesis Completed**

Sofia Madureira, 14/03/2017, “Alterações da Substância Branca, evolução neuropsicológica e impacto nos cuidadores: 10 anos de seguimento”, Faculty of Medicine, University of Lisbon. Supervisor: José M. Ferro.

Marta Gonçalves, 27/03/2017, “Sinais quantitativos e qualitativos sugestivos de lesão cerebral na Escala de Inteligência de Weschsler para Adultos 3ª Edição (WAIS-III)”, Faculty of Medicine, University of Lisbon. Supervisor: Isabel Pavão Martins.

José Fonseca, 05/07/2017, “Avaliação das capacidades cognitivas não-verbais na afasia de etiologia vascular”, Faculty of Medicine, University of Lisbon. Supervisor: Isabel Pavão Martins.

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## Figueiredo, Luísa

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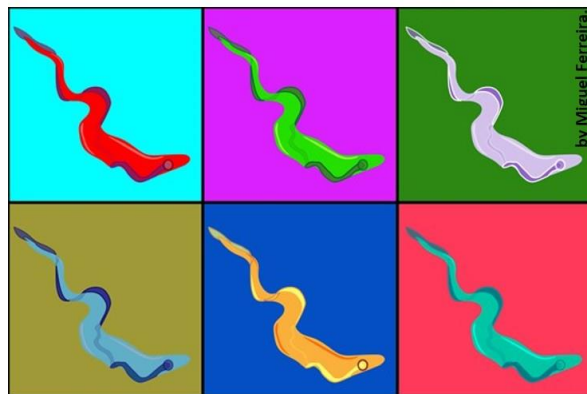
### Major Interests / Objectives

Parasitism relies on the ability of an organism to exploit its host. *Trypanosoma brucei* is a unicellular parasite responsible for a fatal disease in humans (sleeping sickness), and for a chronic disease in cattle (nagana) in Sub-Saharan Africa. We are interested in understanding the cellular and molecular mechanisms employed by trypanosomes to maintain a chronic disease in the host. Our group studies how parasites sense and adapt to the surrounding environment and how they evade the host immune system.

### Head of Laboratory

Luisa Miranda Figueiredo, PhD

### Graphic Abstract



### Research Team

Alexandra Isabel Vidigal Teixeira	Graduate	MSc Student (Started September)
Ana Catarina Dias Pena	PhD	Post-Doctoral Investigator
Ana Filipa de Almeida Rijo Ferreira	PhD	Post-Doctoral Investigator, UTSW
Ana Margarida Roque Sanches Vaz	Master	PhD Student
Daniel Pinto de Oliveira Gonçalves Neves	Master	Investigator (Left November)
Eleonora Aquilini	PhD	Post-Doctoral Investigator (Left May)
Fabien Marc Guegan	PhD	Post-Doctoral Investigator
Francisco Maria dos Santos e Silva Aresta Branco	Master	PhD Student (Left February)
Henrique Pedro Pereira da Silva Amaral Machado	Master	PhD Student (Started March)
Idálio de Jesus Contreiras Viegas	Graduate	PhD Student
Jessica Grace Morgan Bevan	Master	PhD Student (Left November)
João Alexandre Guarita da Silva Rodrigues	PhD	Principal Investigator

Leonor Duarte Pinho	Master	Lab Manager
Mariana Costa Sequeira	Graduate	Defended Masters and Became Investigator (Started November)
Miguel Correia Botelho Chaves Ferreira	PhD	Manager (Left November)
Sandra Isabel Gonçalves Trindade	PhD	Post-Doctoral Investigator
Tiago Bizarra Rebelo	Graduate	Defended Masters and Became Investigator (Started November)

### Laboratory Keywords / Research Areas

Parasite, Adipose tissue, Metabolism, Circadian rhythm, Antigenic variation, Gene expression.

### Major Scientific Achievements

- Award of ERC Consolidator grant (FatTryp).
- Award of collaborative grant of Wellcome Trust, jointly with Universities of Edinburgh and Glasgow.
- Award of national collaborative grant of FCT (Oneida), jointly with ITQB and IGC.
- Master student selected for best thesis of iMM.

### Selected Publications

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais NL, Takahashi J & Figueiredo LM (2017). *Trypanosoma brucei* metabolism is under circadian control. *Nature Microbiology*. 2:17032, doi: 10.1038/nmicrobiol.2017.32. (IF:--, Citations: 9).

*Recommended by Faculty of 1000. Wendy Gibson and McConville.*

Tanowitz HB, Scherer PE, Mota MM and Figueiredo LM (2017). Adipose tissue: A safe haven for parasites?. *Trends Parasitology*. 33(4), 276-284. DOI: 10.1016/j.pt.2016.11.008. (IF: 6.333, Citations: 8).

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* 9 (6), 837–848. DOI: 10.1016/j.chom.2016.05.002. (IF: 14.946, Citations: 43).



*Research Highlight in Nat Rev Microbiol 2016 doi:10.1038/nrmicro.2016.86; Preview in Cell Host & Microbe. 2016 (in press); Highlight in HHMI news. May. 2016; Recommended by Faculty of 1000. Ranking: exceptional (<http://f1000.com/prime/726388249>).*

Aresta-Branco F, Pimenta S, Figueiredo LM (2015). A transcription-independent epigenetic mechanism is associated with antigenic switching in *Trypanosoma brucei*. *Nuclei Acids Research* 44(7), 3131-46. doi:10.1093/nar/gkv1459. (IF: 10.162, Citations: 11).

*Recommended by Faculty of 1000. Ranking: exceptional (<http://f1000.com/prime/726019294>).*

Pena AC, Pimentel MR, Manso H, Vaz-Drago R, Pinto-Neves D, Aresta-Branco F, Rijo-Ferreira F, Guegan F, Pedro Coelho L, Carmo-Fonseca M, Barbosa-Morais NL, Figueiredo LM (2014). *Trypanosoma brucei* histone H1 inhibits RNA polymerase I transcription and is important for parasite fitness in vivo. *Molecular Microbiology* 93(4), 645-6. (IF: 3.898, Citations: 18).

### Ongoing Research Projects

2017/2017: Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes. Coordinator: Luisa Miranda Figueiredo. Funding Agency: Crioestaminal/Associação Viver a Ciência. Reference: Crioestaminal LFigueiredo. Amount: € 20 000,00. Total Amount: € 20 000,00.

2016/2019 Long non-coding RNAs as new diagnostic biomarkers for African sleeping sickness. Coordinator: Fabien Marc Guegan. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-EPI/7099/2014. Amount: € 165 079,00. Total Amount: € 165 079,00.

2016/2019: Metabolic consequences of an infection by African trypanosomes. Coordinator: Luisa Miranda Figueiredo. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MET/4471/2014. Amount: € 186 946,00. Total Amount: € 186 946,00.

2016/2019: An integrated systems approach to uncover the key players in complex protein N-glycosylation in *Trypanosoma brucei*. Coordinator: João Alexandre Guarita da Silva Rodrigues. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BSS/0827/2014. Amount: € 96 106,00. Total Amount: € 149 450,00.

2016/2017: EMBO Small Grant, associated to EMBO Installation Grant “The role of chromatin in antigenic variation of African Trypanosomes”. Coordinator: Luisa Miranda Figueiredo. Funding Agency: European Molecular Biology Organisation. Reference: EMBO SG LFigueiredo. Amount: € 9 200,00. Total Amount: € 9 200,00.

2015/2019: Molecular basis for the efficient biology of trypanosome parasitism. Coordinator: Luisa Miranda Figueiredo. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01050/2014/CP1236/CT0008. Amount: € 46 000,00. Total Amount: € 46 000,00.

2013/2017: Glycopar: Parasite glycobiology and anti-parasitic strategies. Coordinator: João Alexandre Guarita da Silva Rodrigues. Funding Agency: European Commission. Reference: MSCA ITN 608295. Amount: € 689 052,63. Total Amount: € 3 450 856,23.

2012/2017: How parasites use epigenetics to evade host defenses. Coordinator: Luisa Miranda Figueiredo. Funding Agency: Howard Hughes Medical Institute. Reference: HHMI 55007419. Amount: € 467 289,34. Total Amount: € 560 000,00.

#### **Other Projects**

2017/2019: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Nuno Ramos d’Almeida Ramirez. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

2016/2018: TwinToInfect: Unleash iMM’s research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

#### **Publications in Peer Review Journals**

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais NL, Takahashi J & Figueiredo LM (2017). *Trypanosoma brucei* metabolism is under circadian control. *Nature Microbiology*, 2:17032. doi: 10.1038/nmicrobiol.2017.32. (IF:--, Citations: 6).

*Recommended by Faculty of 1000. Wendy Gibson and McConville.*

Smith TK, Bringaud F, Nolan DP and Figueiredo LM (2017). Metabolic reprogramming during the *Trypanosoma brucei* life cycle. *F1000 Research* 6, 1-12. (IF:--, Citations: 2).

McCulloch R, Cobbold CA, Figueiredo LM, Jackson A, Morrison LJ, Mugnier MR, Papavasiliou N, Schnauffer A and Matthews K (2017). Emerging challenges in understanding trypanosome antigenic variation. *Emerging Topics Life Sciences*. 1, 585-592. (IF:--, Citations:--).

Rijo-Ferreira F, Takahashi JS & Figueiredo LM (2017). Circadian rhythms in parasites. *PLoS Pathogens* 13, e1006590. (IF: 6.608, Citations:--).

Tanowitz HB, Scherer PE, Mota MM and Figueiredo LM (2017). Adipose tissue: A safe haven for parasites?. *Trends Parasitol*. 33(4), 276-284. DOI: 10.1016/j.pt.2016.11.008. (IF: 6.333, Citations: 8).

#### **Other Publications International**

Pena AC, Aresta-Branco F and Figueiredo LM. (2017). Epigenetic Regulation in *T. brucei*: Changing Coats Is a Chance to Survive. In *Epigenetics in Infectious Diseases*, Doerfler W, and J Casadesús, eds. (Cham: Springer International Publishing), pp. 221-241. (IF:--, Citations:--).

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

Figueiredo LM. Gene expression of *Trypanosoma* parasites is under space and circadian control. EMBO meeting on Hijacking host cell signalling and epigenetic mimicry during Infections, The Pasteur Institute, Paris, France, June 5, 2017.

Figueiredo LM. *T. brucei* gene expression is under circadian control. University of Wuerzburg, Wuerzburg, Germany, June 6, 2017.

Figueiredo LM. Unexpected phenotypic variability of parasites occupying the adipose tissue. The Crick Institute, London, England, June 30, 2017.

Figueiredo LM. Parasites have clocks. Encontro Nacional da Ciência. Centro Congressos de Lisboa, Lisbon, Portugal, July 5, 2017.

Figueiredo LM. Adipose tissue: a safe haven for *Trypanosoma brucei*. USP Symposium, University of São Paulo, Butantã, São Paulo, Brazil, November 11, 2017.

Figueiredo LM. Parasites that cause jet lag in the host. Symposium 10<sup>th</sup> Anniversary Masters in Evolutionary and Developmental Biology, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, December 21, 2007.

Figueiredo LM. Unexpected phenotypic variability of *Trypanosoma brucei* parasites. Center for Neuroscience and Cell Biology seminars, Faculty of Medicine, University of Coimbra, Coimbra, Portugal, December 6, 2017.

#### **GLYCOBIOLOGY GROUP:**

Rodrigues JA. Protein and Lipid Glycosylation in protozoan parasites. i3S - Instituto de Investigação e Inovação em Saúde GABBA Programme, Porto, Portugal, February 23, 2017.

Rodrigues JA. Plasmodium short N-glycans are critical for parasite survival and development. Gordon Glycobiology Research Conference, Ventura, USA, March 19-24, 2017.

#### **Communications in International Conferences**

Trindade S, Pinto-Neves D, Smith TK, Bringaud F and Figueiredo LM. Adipose tissue is a reservoir of *Trypanosoma brucei* parasites throughout infection. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, USA, April 2017. (Oral Presentation).

Guegan F, Bento F, Pinto-Neves D, Manso H and Figueiredo LM. Role of long non-coding RNA in *Trypanosoma brucei* parasite. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, USA, April 2017. (Oral Presentation).

Figueiredo LM. *T. brucei* metabolism is under circadian control. British Society Parasitology, Dundee, Scotland, April 2017. (Oral Presentation).

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais N, Takahashi J, Figueiredo, LM. Circadian rhythm controls metabolism in *Trypanosoma brucei*. Kinetoplastid Molecular Cell Biology Meeting, Marine Biological Laboratory, Woods Hole, USA, April 2017. (Oral Presentation).

Figueiredo LM. How many different *Trypanosoma brucei* parasites are there in the host? Marine Biological Laboratory – Biology of Parasitism, Woods Hole, USA, July 2017. (Oral Presentation).

Sanches-Vaz M, Prudêncio M, Figueiredo LM. African Trypanosomes confer protection against Plasmodium liver infection. 28<sup>th</sup> Molecular Parasitology Meeting, Woods Hole, USA, September 2017. (Oral Presentation).

Figueiredo LM. Unexpected phenotypic variability of *Trypanosoma brucei* parasites. XXXIII Annual Meeting of the Brazilian Society of Protozoology, Caxambu, Brazil, November 2017. (Oral Presentation).

#### **GLYCOBIOLOGY GROUP:**

Bevan J, Lourenço EC, Ferreira M, Rénio M, Rodrigues JR, Ventura MR. Immobilised Affinity Base Probes for selective enrichment of glycosyltransferases in *Trypanosoma brucei*. Gordon Glycobiology Research Conference, Ventura, USA, March 2017. (Oral and Poster Presentation).

#### **Communications in National Conferences**

Bevan J, Lourenço EC, Ferreira M, Rénio M, Rodrigues JR, Ventura MR. Immobilised Affinity Base Probes for selective enrichment of glycosyltransferases in *Trypanosoma brucei*. 2017 GLUPOR 12 Conference, Aveiro, Portugal, September 11-13, 2017. (Poster Presentation).

Pena AC, Aquilini E, Bevan J, Cornillie J, Ghorbal M, Lopez Rubio JJ, Aebi M, Izquierdo L, Rodrigues JA. Plasmodium short N-glycans are critical for parasite survival and development. GLUPOR 12 Conference, Aveiro, Portugal, September 11-13, 2017. (Poster Presentation).

#### **Organisation of Conferences**

Figueiredo LM. Chair at Gordon Conference on the Biology of Host-Parasite interactions, Salve Regina, USA, July 2017.

#### **Internationalisation**

Our research group acts internationally at several levels. First, by presenting our work and acting as discussion group in international meetings including Molecular Parasitology meeting and Caxambu. Second by establishing and maintaining collaborations (Joseph Takahashi, University of Texas Southwestern Medical Center, USA; Terry Smith, University of St Andrews, Scotland; Frederic Bringaud, Université de Bordeaux; Falk Butter, University of Mainz). Third by being a member of editorial board of a *iScience*, a new journal from Cell Press; acting as journal editor in international journals including *PLoS Pathogens*; and finally, as an invited reviewer for *Nature Microbiology*, *Nature Communications*, *Nucleic Acids Research*, *Journal of Cell Science* and *PLoS Pathogens*.

Fourth, being main examiner in a PhD juri in Institut Pasteur and as an examiner in a juri of “Habilitation à diriger des recherches (HDR)”, France. Fifth, by participating in an international collaborative grant by the Wellcome Trust Fund.

Through the FP7 GlycoPar ITN we currently collaborate with Mike Ferguson (Univ. Dundee), Markus Aebi (ETH Zurich), Luis Izquierdo (ISGlobal, Barcelona), Alvaro Acosta-Serrano (Liverpool School of Tropical Medicine), Rita Gerardy-Schwan (Hannover) and three SMEs, SilicoLife (Braga, PT), Ludger (Abingdon, UK) and SOMBiotech (Barcelona) and have access to GlaxoSmithKline Tres Cantos site (Madrid) devoted to neglected tropical diseases.

### **Prizes, Honours and Awards**

Figueiredo LM. ERC Consolidator grant (FatTryp) Award 2017.

Rebelo T. Best Master Thesis of iMM. November 2017.

Pena AC. Best Poster Award. GLUPOR 12 Conference, Aveiro, Portugal, September 2017.

### **Advanced Teaching**

Main examiner in PhD juri of Maria Rebelo, 4<sup>th</sup> May 2017. Thesis title: "Flow Cytometric Detection of Light Depolarization: A Novel Approach to Detect Antimalarial Drug Resistance in Resource-limited Endemic Region". Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon. Supervisor: Thomas Hanscheid.

### **Science and Society**

Participation as an expert on the Agenda for Science and Clinical Research 2020, an initiative sponsored by the FCT.

Participation in the European Researchers' Night, Museu de Historia Natural da Universidade de Lisboa, Lisbon, Portugal September 29, 2017.

Science Communication: <https://www.youtube.com/watch?v=jYziiP2zBZE>

### MSc Thesis Completed

Sílvia Maria de Jesus Pimenta Teixeira da Silva, 31/05/2017, “*Trypanosoma brucei* distribution in the male reproductive system”, Faculty of Medicine, University of Lisbon. Supervisor: Luisa M. Figueiredo.

Tiago Bizarra Rebelo, 24/10/2017, “Deciphering parasite persistence in adipose tissue”, Faculty of Sciences, University of Lisbon. Supervisor: Luisa M. Figueiredo.

Mariana Costa Sequeira, 22/11/2017, “Using proteomics to understand how parasites adapt to the host environment”, Instituto Superior Técnico. Supervisor: Luisa M. Figueiredo.

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## Filipe, Paulo

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### Major Interests / Objectives

- To understand how pathological skin memory is secured in psoriasis and how efficient are biologicals and phototherapies in clearing this type of immune-mediated memory.
- To understand why psoriasis, an immune-mediated disorder, is more severe in immune-deficient HIV patients.
- To understand the cell cycle dynamics in psoriatic skin, namely that of stem and progenitor cells, and how that dynamics is influenced by pro-inflammatory cytokines.
- To understand how host immune responses influence the differential outcome of two distinct types of Non-Melanoma Skin Cancers (NMSCs), namely Basal Cell Carcinomas and Squamous Cell carcinomas. Also, how host immune responses favor tolerance or promote aggressiveness in NMSCs.

### Head of Laboratory

Paulo Manuel Leal Filipe, MD/PhD, Assistant Professor

### Research Team

Ana Isabel da Costa Martins Teixeira	Master	Investigator (Left November)
Daniela Cunha	Graduate	Investigator
João António Augusto Ferreira	MD/PhD	Investigator
João Borges da Costa	PhD	Investigator, Assistant Professor
João Nuno Maia Rodrigues Silva	MD/PhD	Investigator, Assistant Professor
Luís Miguel dos Santos Reis Soares de Almeida	PhD	Principal Investigator
Maria Clara Gomes da Fonseca Pedro Bicho	MD/PhD	Investigator
Maria Marques Adegas Bairrão Henriques	Graduate	MSc Student (Started May/Left November)
Pedro Henrique Dobrões da Fonseca	Master	Trainee

### Laboratory Keywords / Research Areas

Psoriasis, Phototoxicity, Non-melanoma skin cancer, Cell cycle.



### Major Scientific Achievements

- The identification of the photo-degradation product of Vemurafenib (VB) a key drug in the management of advanced melanoma whose major adverse effect is the development of severe phototoxicity. We have additionally shown that VB, which is lipophilic, is incorporated in cell membranes and upon interaction with UVA induces lipid peroxidation via ROS production, with deleterious effects on cell membranes. These findings are relevant to our understanding of the cellular photodamage phenomenon observed in sun-exposed skin areas in patients treated with VB (Photochem Photobiol Sci., 2015; Toxicol Sci., 2016);
- The identification by mass spectrometry of a 133,977 kDa peptide (complement factor H) in the serum of psoriatic patients whose levels strongly predict disease recurrence (submitted);
- The development of a fast, flow-cytometric assay to estimate absolute lengths (in units of time) of all cell cycle stages (Oncotarget, 2017).

### Selected Publications

Pereira PD, Serra-Caetano A, Cabrita M, Bekman E, Braga J, Rino J, Santus R, Filipe PL, Sousa AE, Ferreira JA (2017). Quantification of cell cycle kinetics by EdU (5-ethynyl-2'-deoxyuridine)-coupled-fluorescence-intensity analysis. *Oncotarget* 8, 40514-40532. (IF: 5.168, Citations: 1).

Raposo I, Lobo I, Amaro C, Lobo ML, Melo H, Parente J, Pereira T, Rocha J, Cunha AP, Baptista A, Serrano P, Correia T, Travassos AR, Dias M, Pereira F, Gonçalo M (2017). Allergic contact dermatitis caused by (meth) acrylates in nail cosmetic products in users and nail technicians – a 5-year study. *Contact Dermatitis* 77, 356-359. (IF: 4.335, Citations:-).

Teixeira A, Morlière P, Ferreira J, Conte MA, Galmiche A, Mazière JC, Santus R, Filipe P (2016). Interplay Between Membrane Lipid Peroxidation and Photoproduct Formation in the Ultraviolet A-Induced Phototoxicity of Vemurafenib in Skin Keratinocytes. *Toxicol Sci.* 154, 289-295. (IF: 4.081, Citations: 1).

Morlière P, Hug GL, Patterson LK, Mazière JC, Ausseil J, Dupas JL, Ducroix JP, Santus R, Filipe P (2014). Chemistry of free radicals produced by oxidation of endogenous aminoketones. A study of 5 aminolevulinic acid and aminoacetone by fast kinetics spectroscopy. *Biochim Biophys Acta.* 2014 Oct; 1840 (10): 3190-7. doi: 10.1016/j.bbagen.2014.07.002. 1840, 3190-7. (IF: 4.702, Citations: 1).

Pinheiro T, Silva R, Fleming R, Gonçalves A, Barreiros MA, Silva JN, Morlière P, Santus R, Filipe P (2014). Distribution and quantitation of skin iron in primary haemochromatosis: correlation with total body iron stores in patients undergoing phlebotomy. *Acta Derm Venereol*; 94 (1): 14-9. doi: 10.2340/00015555-1601. 94, 14-9. (IF: 3.653, Citations: 5).

### **Ongoing Research Projects**

2017/2021: Vascular patterns in non-melanoma skin cancer assessed by reflectance confocal microscopy and 3D imaging. Coordinator: Paulo Manuel Leal Filipe. Funding Agency: Sociedade Portuguesa de Dermatologia e Venerologia and Several Laboratories. Reference: Angiogenesis PFilipe. Amount: € 19 850,00. Total Amount: € 19 850,00.

2016/2017: Th9-IL9R axis: a role in tissue memory in plaque-type psoriasis?. Coordinator: Paulo Manuel Leal Filipe. Funding Agency: Novartis. Reference: Novartis PFilipe. Amount: € 30 400,00. Total Amount: € 30 400,00.

### **Other Projects**

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

### **Publications in Peer Review Journals**

Morlière P, Silva AMS, Seixas RSGR, Boscáe F, Mazière JC, Ferreira J, Santus R, Filipe P (2017). Photosensitisation by voriconazole-N-oxide results from a sequence of solvent and pH-dependent photochemical and thermal reactions. *Photochemical & Photobiological Sciences* (in press). (IF: 2.344, Citations:--).

Duarte A, Silva J, Nagore E, Picoto A, Correia O (2017). Sunbed use among Portuguese beach goers – a crave group while waiting sunbeds to be abolished – cross sectional study. *J Eur Acad Dermatol Venereol.*, 31, e273-e306. (IF: 3.528, Citations:--).

Carreira A, Boavida-Ferreira J, Pereira I, Ferreira J, Filipe P, Boavida-Ferreira, R Monteiro S (2017). Blad-containing oligomer: a novel fungicide used in crop protection as an alternative treatment for tinea pedis and tinea versicolor. *J Med. Microbiol.*, DOI 10.1099/jmm.0.000675 (in press). (IF: 2.159, Citation:--).

Ortins-Pina A, Viana I, Filipe P, Soares de Almeida L (2017). Painful Pustules on Hands and Feet with Acute Hepatitis. *Am J Dermatopathol.* PubMed PMID:28452793. (IF: 1.426, Citations:--).

Teixeira AI, Soares de Almeida, Kutzner H (2017). Agminated Clear Cell Tumor: Na Impostor of PEComa and Distinctive Dermal Clear Cell Mesenchymal Neoplasm. *Am J Dermatopathol.* 39: 212-216. PubMed PMID: 27828802. (IF: 1.426, Citations:--).

Ortins-Pina A, Zumdick M, Weiss T, Rutten A (2017). Cutaneous nodules and violaceous patches on the legs. *Am J Dermatopathol* 2017 Jan 11, doi:10.1097/ PMID:29329132. (IF: 1.426, Citations:--).

Uva L, Leal-Filipe P, Soares-de-Almeida L, Ferreira J, Oliveira A (2017). Reflectance confocal microscopy for the diagnosis of tinea nigra. *Clin Exp Dermatol.* doi: 10.1111/ced.13350. PMID: 29283186. (IF: 1.589, Citations:--).

Tan J, Ortins-Pina A, Borges-Costa J (2017). Skin Diseases in the Era of Highly Active Antiretroviral Therapy: A Retrospective Study of 534 Patients. *Journal of the International Association of Providers of AIDS Care (JIAPAC)* -17:1-5. (IF: 0.98, Citations:--).

Da Rocha MC, Travassos AR, Uva L, Sequeira H, Filipe P (2017). Demodicosis Treatment with Systemic Ivermectin. *Skinmed.* 15:293-295. (IF: 0.45, Citations:--).

Roda Â, Mendonça-Sanches M, Travassos AR, Soares de Almeida L, Metze D (2017). Infliximab therapy for Netherton syndrome: A case report. *JAAD case Rep.*, 3: 550-552. Doi:10.1016/j.jdc.2017.07.019. eCollection 2017. (IF: 0.166, Citations:--).

Da Rocha MC, Travassos AR, Uva L, Sequeira H, Filipe P (2017). Demodicosis Treatment with Systemic Ivermectin. *Skinmed.* 15:293-295. (IF: 0.45, Citations:--).

Roda Â, Mendonça-Sanches M, Travassos AR, Soares de Almeida L, Metze D (2017). Infliximab therapy for Netherton syndrome: A case report. *JAAD case Rep.*, 3: 550-552. Doi:10.1016/j.jdc.2017.07.019. eCollection 2017. (IF: 0.166, Citations:--).

Borges-Costa J, Soares-Almeida L, Guerra J (2017). Mycosis fungoides presenting as a pigmented purpuric dermatosis in a renal-transplanted patient. *Journal of Organ Transplantation*, 1: 1-4. (IF:--, Citations:--).

Oliveira JM, Sobreira G, Velosa J, Telles Correia D, Filipe P (2017). Association of Isotretinoin with Depression and Suicide: A Review of Current Literature. *J Cutan Med Surg*;22(1):58-64. doi: 10.1177/120347541771952, PMID:28705050. (IF: 0.38, Citations:--).

### **Invited Lectures and Seminars**

Borges-Costa J. Dermal mucinosis in renal-transplanted cases: report of two patients. XVII Meeting, Skin Cancer in Organ Transplant Patients, Prague, Czech Republic, March 2017.

Borges-Costa J. Eruptive nevi after initiation of therapy for HIV. Session “Communications in Skin Infections and STIs” Meeting, European Academy of Dermatology and Venereology, Brussels, Belgium, May 2017.

Ortins-Pina A, Llamas-Velasco M, Turpin S, Yang S, Soares-de-Almeida L, Kutzner H. FOS-B expression of epithelioid endothelia helps to discriminate benign epithelioid hemangioma from its malignant impostors. XXXVIII Symposium of the International Society of Dermatopathology – ISDP, Glasgow, Scotland, September 2017.

Borges-Costa J. Borreliosis: Where, when and how to treat. Oral Communication, “Review and Updates in Skin Infections”. XXVI Congress, European Academy of Dermatology and Venereology, Geneva, Switzerland, September 2017.

### **Communications in International Conferences**

Borges-Costa J, Seixas J, Soares de Almeida L, Kutzner H, Filipe P. Erythematous skin nodules in a patient living in Southern Africa. Meeting, European Academy of Dermatology and Venereology, Brussels, Belgium, May 2017.

Ortins-Pina A, Weiss T, Rutten A. Cutaneous amyloid elastosis: A rare finding that may be a clue for systemic disease. XXXVIII Symposium of the International Society of Dermatopathology – ISDP Glasgow, Scotland, September 2017.

Catarino A, Soares-Almeida L, Borges-Costa J. Herpes Zoster-associated immune reconstitution inflammatory syndrome. XXVI Congress, European Academy of Dermatology and Venereology, Geneva, Switzerland, September 2017.

### **Organisation of Conferences**

Filipe P. Chairperson and Organizer. Advanced Symposium in Laser Therapy, Lisbon, Portugal, October 7, 2017.

### **Internationalisation**

Participation in International Meetings, Courses and Conferences.

Research Collaborations with Patrice Morlière and René Santus, CNRS, France, and Heinz Kutzner, Laboratory of DermatoPathology, Friedrichshafen, Germany.

Mobility of Researchers of the Unit to Laboratories of European collaborators.

### **Prizes, Honours and Awards**

Pimenta R, Antunes J, Reis M, Filipe P. Uso sequencial de agentes biológicos num doente com psoríase refratária. Janssen Immunology Real World Evidence Award 2017, May 20, 2017.

### **Advanced Teaching**

Borges-Costa J. Infecção HPV e Condilomas ano-genitais e orais e de Infecção HPV e Cancro. Curso de formação contínua sobre infeções sexualmente transmissíveis, Faculty of Medicine, University of Porto, Porto, Portugal, March 2017.

Borges-Costa J. Patologia dermatológica em viajantes. Pós-graduação em Medicina das Viagens do Instituto de Higiene e Medicina Tropical, Nova University of Lisbon, Lisbon, Portugal, April 2017.

Soares Almeida L (Coordinator). V Curso de Dermatopatologia. Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 18 - 19, 2017.

Borges-Costa J. Psoríase em doentes com infeção pelo VIH. Curso de Psoríase. Associação para o Desenvolvimento da Dermatologia and Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 2017.

Borges-Costa J. Curso Avançado sobre Infeções Sexualmente Transmissíveis. Faculty of Medicine, University of Porto, Porto, Portugal, October 2017.

Borges-Costa J. Dermatologia em Medicina Tropical. Curso de Clínica das Doenças Tropicais 2017, Instituto de Higiene e Medicina Tropical, Nova University of Lisbon, Lisbon, Portugal, October 2017.

Filipe P (Chairperson). Advanced Symposium in Laser Therapy, Lisbon, Portugal, October 7, 2017.

Filipe P, Maia-Nuno J, Ferreira J. Psoríase e Micologia Dermatológica. Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 20-21, 2017.

#### **MSc Thesis Completed**

Maria Marques Adegas Bairrão Henriques, 11/12/2017, “Development of Tools to study Human Hair Follicle Biology in vitro-focus on hair follicle stem cells and their potential application in Vitiligo therapy”, Instituto Superior Técnico, University of Lisbon. Supervisor: João Ferreira and Cláudia Lobato da Silva.

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## Fonseca, João Eurico

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### Major Interests / Objectives

The Rheumatology Research Unit (RRU) results from a partnership between the iMM/FML and the Rheumatology Department of the Santa Maria Hospital, CHLN. Basic scientists and clinicians closely work together to promote translational research and clinical excellence in the field of Rheumatology. Our specific research objectives are the study of the impact of inflammatory joint diseases (such as Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Spondyloarthritis (SpA) and Systemic Lupus Erythematosus (SLE)) on bone and vessel in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies. The long-term objective of the RRU is to achieve recognition as an European League Against Rheumatism Centre of Excellence in Rheumatology.

### Head of Laboratory

João Eurico Fonseca, MD/PhD

### Research Team

Alexandre Figueiredo Brito	Graduate	MSc Student
Ana Filipa Brojo Lopes de Oliveira Ramos Cordeiro	Graduate	Investigator (Started November)
Ana Maria Ferreira Rodrigues	Graduate	PhD Student, Faculdade Medicina da Universidade de Lisboa
Ana Rita Cascão Rodrigues	PhD	Post-Doctoral Investigator
Ângelo Calado	PhD	Principal Investigator (Started October)
Bruno Miguel Costa Vidal	Graduate	Post-Doctoral Investigator
Cláudia Sofia Honrado Marques	Graduate	MSc Student (Started September)
Cristina Dias Botelho da Ponte	Graduate	PhD Student
Diana de Almeida Carmona Fernandes	Master	PhD Student
Elsa Cristina Vieira de Sousa	Graduate	Investigator, Faculdade Medicina da Universidade de Lisboa
Inês Alexandra Pascoal Lopes	Master	Lab Manager
Joana da Silva Marques Coelho Dinis	Master	Investigator (Started September)
Joaquim Miguel Polido Pereira	Graduate	Investigator, CHLN, MD
Maria Helena Regalo da Fonseca	MD/PhD	Principal Investigator, Faculdade Medicina da Universidade de Lisboa, Associate Professor
Maria João Gonçalves	Master	Investigator, CHLN, MD, NA
Maria José Parreira dos Santos	MD/PhD	Senior Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Patricia Godinho Bexiga Martins	Master	Investigator (Started October)

Pedro Nuno Lopes Mendes Calheiros Andrade	Master	Investigator (Left July)
Raquel Patrícia Campanilho Marques Ruivo	Master	Investigator
Rita Alexandra Pedra Aguiar de Moura	PhD	Post-Doctoral Investigator
Rui Pedro Lourenço Teixeira	Master	Investigator
Soraia Patrícia Caetano da Silva	Master	MSc Student (Left February)
Susana Maria da Silva Oliveira	Graduate	MSc Student
Vânia Raquel Gomes Glória	PhD	Investigator
Vasco Madeira Crispim Romão	Master	PhD Student, CHLN, MD

### Laboratory Keywords / Research Areas

Diagnostic, Prognostic and response to treatment markers in rheumatic diseases, Inflammation and bone, Cohorts, Registries and databases, Recommendations and guidelines, Collaboration in clinical trials.

### Major Scientific Achievements

- Characterization of the effect of TNF antagonists on osteoclasts and B cells.
- Pre clinical characterization of Celastrol as an effective treatment for arthritis.
- Impact of early arthritis on bone nanostructure.
- Impact of tofacitinib on bone loss and biomechanics in early arthritis.

### Selected Publications

Carmona-Fernandes D, Santos MJ, Canhão H, Fonseca JE (2013). Anti-ribosomal P protein IgG autoantibodies in patients with systemic lupus erythematosus: diagnostic performance and clinical profile. *BMC Med* 11, R196. (IF: 7.901, Citations: 27).

Moura RA, Cascão R, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2011). Cytokine pattern in early Rheumatoid arthritis favors B cell activation and survival. *Rheumatology*. *Rheumatology* 50(2), 278-82. (IF: 4.818, Citations: 25).

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE (2010). Neutrophils in rheumatoid arthritis: More than simple final effectors. *Autoimmun Rev.* 9, 531-535. (IF: 8.960, Citations: 74).



Cascão R, Moura RA, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graca L, Fonseca JE (2010). Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early rheumatoid arthritis. *Arthritis Res Ther* 12(5), R196. (IF: 4.121, Citations: 39).

Caetano-Lopes J, Nery AM, Canhão H, Duarte J, Cascão R, Rodrigues A, Perpétuo I, Abdulghani S, Amaral PM, Sakaguchi S, Konttinen YT, Graça L, Vaz MF, Fonseca JE (2010). Chronic arthritis leads to disturbances in the bone collagen network. *Arthritis Res Ther* 12(1), R9. (IF: 4.121, Citations: 14).

### **Ongoing Research Projects**

2017/2020: Tapering Biologics in PSA. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: PSA. Amount: € 9 500,00. Total Amount: € 9 500,00.

2017/2020: Systemic Sclerosis Clinical Study. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: SSPECT. Amount: € 8 750,00. Total Amount: € 8 750,00.

2017/2020: The role of lncRNAs in Rheumatoid Arthritis-associated bone degradation. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: lncRNA. Amount: € 12 500,00. Total Amount: € 12 500,00.

2017/2020: Ensaio clínico de mesoterapia. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Bial. Reference: Mesoterapia. Amount: € 4 831,25. Total Amount: € 4 831,25.

2017/2019: B Cells in Juvenile Idiopathic Arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: B cell in AIJ. Amount: € 18 000,00. Total Amount: € 18 000,00.

2017/2018: Autoinflammatory Diseases: analysis based on The Rheumatic Diseases Portuguese Register. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Novartis. Reference: REUMA.PT. Amount: € 12 680,00. Total Amount: € 12 680,00.

2017/2018: Predictors of response to ultrasound-guided sacroiliac joint corticosteroid-injection in patients with active sacroilitis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: US Sacroilitis. Amount: € 5 884,00. Total Amount: € 5 884,00.

2017/2018: Serum sphingolipids as candidate biomarkers in Rheumatoid Arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: Sphingolipids RA. Amount: € 25 000,00. Total Amount: € 25 000,00.

2017/2018: Linking Biomechanics, Inflammation and Bone Formation in Psoriatic Arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: UCB Pharma. Reference: UCB ES. Amount: € 51 350,00. Total Amount: € 51 350,00.

2016/2020: The role of certolizumab in non infectious uveitis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Oftalmologia. Reference: Uveítes. Amount: € 5 000,00. Total Amount: € 5 000,00.

2016/2020: Is ultrasound a good surrogate marker for remission in RA? (Association of ultrasound and histological synovitis in rheumatoid arthritis patients in clinical remission). Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: Ultrasound - SPR JPP. Amount: € 10 000,00. Total Amount: € 10 000,00.

2016/2019: Carbon monoxide guided shuttles (COGSs) to fight Rheumatoid Arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/QEQ-MED/1902/2014. Amount: € 22 000,00. Total Amount: € 199 966,00.

2015/2019: Disease course and adult outcomes of childhood-onset rheumatic diseases. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: Bolsa de Inovação Diagnóstica. Amount: € 14 500,00. Total Amount: € 14 500,00.

2015/2018: Evaluation of celastrol as a candidate for the treatment of rheumatoid arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: CELAR. Amount: € 10 000,00. Total Amount: € 10 000,00.

2014/2019: IL-6 blockade in rheumatoid arthritis patients: impact on Tfh subsets and humoral responses. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Pfizer. Reference: BioTB. Amount: € 2 500,00. Total Amount: € 2 500,00.

2014/2019: Post-transcriptional regulation of response to Etanercept in patients with rheumatoid arthritis. Coordinator: Helena Cristina de Matos Canhão. Funding Agency: Pfizer. Reference: WI187429. Amount: € 40 000,00. Total Amount: € 40 000,00.

2014/2017: How early inflammatory events affect bone nano-properties at the onset rheumatoid arthritis. Coordinator: Bruno Miguel Costa Vidal. Funding Agency: European Calcified Tissue Society/Amgen. Reference: ECTS Bvidal. Amount: € 100 000,00. Total Amount: € 100 000,00.

2013/2019: Inhibition of bone and cartilage degradation in rat induced arthritis treated with tofacitinib. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Pfizer. Reference: WI180320. Amount: € 60 000,00. Total Amount: € 60 000,00.

2013/2018: Synovial pathobiology and clinical differences in elderly and younger-onset of rheumatoid arthritis. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: Sociedade Portuguesa de Reumatologia. Reference: BioTB. Amount: € 3 850,00. Total Amount: € 3 850,00.

2012/2019: Golimumab as first line DMARD therapy in MTX naive psoritic arthritis - a 24 weeks eddicacy and safety study focusing on dactylitis and enthesitis. Coordinator: Elsa Cristina Vieira de Sousa. Funding Agency: Merck Sharp & Dohme. Reference: GO-DACT. Amount: € 36 087,50. Total Amount: € 36 087,50.

2012/2017: How inflammation early affects bone's nano-properties at arthritis onset. Coordinator: João Eurico Cortez Cabral da Fonseca. Funding Agency: UCB Celltech. Reference: UCB\_IIS\_Cimzia. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

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

### Publications in Peer Review Journals

Sousa S, Duarte AC, Cordeiro I, Ferreira J, Gonçalves MJ, Meirinhos T, Rocha TM, Romão VC, Santos MJ (2017). Efficacy and Safety of Vaccination in Pediatric Patients with Systemic Inflammatory Rheumatic Diseases: a systematic review of the literature. *Acta Reumatol Port* 2016; 42: 8-16. (IF: 0.929, Citations:--).

Orr C, Sousa E, Boyle DL, Buch MH, Buckley CD, Cañete JD, Catrina AI, Choy EHS, Emery P, Fearon U, Filer A, Gerlag D, Humby F, Isaacs JD, Just SA, Lauwerys BR, Le Goff B, Manzo A, McGarry T, McInnes IB, Najm A, Pitzalis C, Pratt A, Smith M, Tak PP, Thurlings R, Fonseca JE, Veale DJ (2017). Synovial tissue research: a state-of-the-art review. *Nat Rev Rheumatol* 13:463-475. (IF: 12.188, Citations: 3).

Vieira-Sousa E, Cavaleiro J, Mourão AF, Rodrigues AM, Albino-Teixeira A, Pimentel-Santos FM, Oliveira-Ramos F, Canhão H, Polido-Pereira J, Fonseca JE, Pereira da Silva JA, Romeu JC, Melo Gomes J, Costa L, Graça L, Leandro MJ, Santos MJ, Machado PM, Ramiro S (2017). *Acta Reumatológica Portuguesa: perspectives in 2017*. *Acta Reumatol Port* 42:110-111. (IF: 0.929, Citations:--).

Cascão R, Fonseca JE, Moita LF (2017). Celastrol: A Spectrum of Treatment Opportunities in Chronic Diseases. *Front Med (Lausanne)* 4:69. (IF:--, Citations: 1).

Duarte AC, Santos-Faria D, Gonçalves MJ, Sepriano A, Mourão AF, Duarte C, Neves JS, Águeda AF, Ribeiro PÁ, Daniel A, Neto A, Cordeiro A, Rodrigues A, Barcelos A, Silva C, Ponte C, Vieira-Sousa E, Teixeira F, Oliveira-Ramos F, Araújo F, Barcelos F, Canhão H, Santos H, Ramos J, Pereira J, Costa J, Melo Gomes JA, Cunha-Miranda L, Costa L, Cerqueira M, Cruz M, Santos MJ, Bernardes M, Oliveira P, Abreu P, Figueira R, Barros R, Falcão S, Pinto P, Pimenta S, Capela S, Teixeira V, Fonseca JE (2017). Portuguese recommendations for the use of methotrexate in rheumatic diseases - 2016 update. *Acta Reumatol Port* 42: 127-40. (IF: 0.929, Citations:--).

Duarte C, Sousa-Neves J, Águeda A, Ribeiro P, Daniel A, Eugénio G, Serra S, Araújo F, Barcelos A, Filipe B, Bernardes M, Canhão H, Cerqueira M, Capela S, Cordeiro A, Costa F, Costa L, Cruz M, Cunha Miranda L, Duarte C, Falcão S, Faria D, Figueira R, Freitas JP, Gonçalves MJ, Madruga Dias J, Melo Gomes J, Mourão AF, Neto A, Oliveira Ramos F, Pimenta S, Pinto P, Polido Pereira J, Ponte C, Ramos J, Rodrigues A, Santos H, Santos MJ, Sepriano A, Silva C, Tavares Costa J, Teixeira F, Teixeira V, Valente P, Vieira-Sousa E, Barros R, Abreu P, Fonseca JE, (2017). Portuguese

Recommendations for the use of biological therapies in patients with rheumatoid arthritis- 2016 update. *Acta Reumatol Port* 42: 112-26. (IF: 0.929, Citations:--).

van Steenberg HW, Aletaha D, Beart-van de Voorde LJ, Brouwer E, Codreanu C, Combe B, Fonseca JE, Hetland ML, Humby F, Kvien TK, Niedermann K, Nuño L, Oliver S, Rantapää-Dahlqvist S, Raza K, van Schaardenburg D, Schett G, De Smet L, Szücs G, Vencovský J, Wiland P, de Wit M, Landewé RL, van der Helm-van Mil AH (2017). EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. *Ann Rheum Dis* 76:491-496. (IF: 12.811, Citations: 10).

Costa N, Marques O, Godinho SI, Carvalho C, Leal B, Figueiredo AM, Vasconcelos C, Marinho A, Moraes-Fontes MF, Gomes da Costa A, Ponte C, Campanilho-Marques R, Córias T, Martins AR, Viana JF, Lima M, Martins B, Fesel C (2017). Two separate effects contribute to regulatory T-cell defect in SLE patients and their unaffected relatives. *Clin Exp Immunol* 189: 318-330. (IF: 3.41, Citations: 1).

Germanò G, Monti S, Ponte C, Possemato N, Caporali R, Salvarani C, Macchioni P, Pipitone N (2017). The role of ultrasound in the diagnosis and follow-up of large-vessel vasculitis: an update. *Clin Exp Rheumatol* 35 Suppl 103(1):194-198. (IF: 2.634, Citations: 2).

Azevedo V, Hassett B, Fonseca JE, Atsumi T, Coindreau J, Jacobs I, Mahgoub E, O'Brien J, Singh E, Vicik S, Fitzpatrick B (2017). Differentiating biosimilarity and comparability in biotherapeutics. *Clin Rheumatol* 35:2877-2886. (IF: 2.365, Citations: 1).

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Khmelinskii N, Canhão H, Ainola M, Fonseca JE (2017). Ankylosing Spondylitis Patients Have Impaired Osteoclast Gene Expression in Circulating Osteoclast Precursors. *Front Med* 4:38. (IF:--, Citations: 1).

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### **Other Publications International**

Ponte C, Monti S, Luqmani R. Case report. Pulse Today. Rheumatology clinic - temporal arteritis. 21Apr2017.

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### **Other Publications National**

Ponte C, Fonseca JE (2017). Vasculites. In: Ponce P e Mendes JJ (Eds). Manual de Terapêutica Médica (3a edição). Lisboa: Lidel, 2017: 574-588.

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Capela S, Fonseca JE (2017). Artrite Reumatóide e Espondilartrites. In Ponce P, Mendes JJ (Ed.), Manual de Terapêutica Médica (3a edição). Lisboa: LIDEL.

### **Invited Lectures and Seminars**

Vieira-Sousa E, Fonseca JE. VIII Fórum das Espondilartrites, Monte Real, Portugal, January 13-14, 2017.

Macieira C, Romeu JC, Seixas MI, Fonseca JE. RHEUMA SPACE –a case study. Centro Académico de Medicina de Lisboa, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26, 2017.

Fonseca JE. Biologics, biosimilars and intended copies: what we should know. ASIA Reach Meeting, Hong Kong, China, February 17-18, 2017.

Fonseca JE. Understanding biosimilars and their impact on clinical decision-making. ASIA Reach Meeting, Hong Kong, China, February 17-18, 2017.

Polido-Pereira J. “New therapeutic targets in systemic autoimmune diseases”. 5º Simposio de Enfermedades Autoinmunes Sistémicas de la SER, Corunã, Spain, February 24-25, 2017.

Fonseca JE. Chair. Synovitis Study Group Session, European Workshop on Rheumatology Research, Athens, Greece, March 2-5, 2017.

Vieira-Sousa E, Rodrigues AM. How to write a clinical case. AIMS Meeting – Annual International Medical Students Meeting, Lisbon, Portugal, March 22-23, 2017.

Fonseca JE. Chair. Earlier detection and intervention: implications for long-term outcome. Eight International Immunology Summit, Prague, Czech Republic, March 23-26, 2017.

Fonseca JE. CT-P13 Clinical Trials and Real World data. Biosimilars Expert Meeting, Torres Vedras, Portugal, March 25, 2017.

Vieira-Sousa E. Consulta Partilhada: doentes e patologias partilhadas. Janssen Programa Consulta Partilhada: doentes e patologias partilhadas, March 20, 2017.

Fonseca JE. Rheumatology pathology. How to mislead it?. Update on Dermatology Treatments. 20<sup>th</sup> International Meeting, Porto, Portugal, March 31-April 1, 2017.

Campanilho-Marques R. Principais miosites na criança e adolescente: espectro clínico e terapêutico. Doenças Imunomediadas em Idade Pediátrica, Porto, Portugal, March 2017.

Campanilho-Marques R. Antipalúdicos. XVII Jornadas da ANDAR, Lisbon, Portugal, April 2017.

Santos MJ. Musculoskeletal system – Inflammatory pathology. 9<sup>th</sup> Nuclear Medicine Meeting, Almada, Portugal, April 22, 2017.

Romão VC. Synovial pathobiology and patient stratification in rheumatoid arthritis. 1º Congresso de Investigação em Medicina das Escolas Médicas Portuguesas, Coimbra, Portugal, April 28-29, 2017.

Fonseca JE. Biosimilars: an overview. Biosimilars in Inflammation: the role of manufacturing and the biosimilar environment, Dublin, Ireland, May 3-4, 2017.

Fonseca JE. Interchangeability and Switching: outstanding questions. Biosimilars in Inflammation: the role of manufacturing and the biosimilar environment, Dublin, Ireland, May 3-4, 2017.

Ponte C. Ultrasound in Vasculitis. Recomendações relativas ao uso de ecografia em reumatologia - GoTime meeting 2017, Lisbon, Portugal, May 6, 2017.

Vieira-Sousa E, “Compreender as Espondilartrites”. Dia Mundial da Espondilite Anquilosante, Associação de Doentes com Espondilite Anquilosante (ANEA), São Domingos de Rana, Portugal, May 6, 2017.

Romeu JC. Session Hot Topics em Síndromes de Fragilidade Moderator. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Vieira-Sousa E. Moderator of the session Aspetos Clínicos nas Espondilartrites. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Santos MJ. Necessidades médicas na AR. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Fonseca JE. Chairman. Session Guidelines and Clinical Practice – Aiming at the best care. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Saavedra MJ. A nossa proposta (Reumalinks). Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Oliveira-Ramos F. President. Conference Reumatologia Pediátrica – utilização Off-Label de fármacos biológicos em idade pediátrica. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Santos MJ. Reumatologia Pediátrica – utilização Off-Label de fármacos biológicos em idade pediátrica. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Fonseca JE. Chairman of the Session Signaling the Future in RA management. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Ponte C. O que há de novo no diagnóstico e tratamento nas vasculites de grandes vasos. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Fonseca JE. A brighter future? Biosimilars seen as an additional contribution to better medical outcomes and medical research. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Ponte C. Ultrasound in Giant Cell Arteritis (GCA). Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Vieira-Sousa E. “Mini-artroscopia do joelho” (Curso Pré-Congresso de exames complementares de imagem em Reumatologia). Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Campanilho-Marques R. Moderator of the session “Reumatologia Pediátrica”. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Campanilho-Marques R. Judge of the Images Contest. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Fonseca JE. O melhor do ano em Reumatologia. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Fonseca JE. Fighting with the immune system. Terceiro Forum Imunologia, Aveiro, Portugal, May 19-20, 2017.

Fonseca JE. Osteoarthritis Initiative: a knee Health study. Masters Meeting, Porto Seguro, Brazil, May 27, 2017.

Santos MJ. Utilização de dados reais na reavaliação das tecnologias de saúde – Contributos do Reuma.pt. Reunião Anual RPF “Controvérsias com Medicamentos”, Oeiras, Portugal, May 31, 2017.

Iagnocco A, Romão VC. Chair of the session Interactive cases from the HOT and WIN Sessions. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017.

Fonseca JE. Chair Abstract Session: Cellular drivers of inflammation in rheumatic disease room "N107 / N108". European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017.

Fonseca JE. Chair Session: Highlights of the congress. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017.

Polido-Pereira J. Ultrassonografia do ombro. XXXIV Congresso Brasileiro de Reumatologia, Florianópolis, Brazil, September 13-16, 2017.

Polido-Pereira J. Biomarcadores na biopsia sinovial e sua relevância na personalização do tratamento da artrite reumatoide. XXXIV Congresso Brasileiro de Reumatologia, Florianópolis, Brazil, September 13-16, 2017.

Polido-Pereira J. Oficina: Biopsia sinovial guiada por ultrassonografia. XXXIV Congresso Brasileiro de Reumatologia, Florianópolis, Brazil, September 13-16, 2017.

Fonseca JE. Remission in chronic arthritis: lessons from early arthritis studies and animal models. Pediatric Rheumatology European Congress, Athens, Greece, September 14-17, 2017.

Fonseca JE, Leal I. Fisiopatologia da Uveite não infecciosa e possíveis alvos terapêuticos. Reunião dos Grupos Portugueses de Retina, Vítreo e Inflamação Ocular, Évora, Portugal, September 22-23, 2017.

Fonseca JE, Leal I. O que há de novo na terapêutica da Uveite não infecciosa e revisão da literatura. Reunião dos Grupos Portugueses de Retina, Vítreo e Inflamação Ocular, Évora, Portugal, September 22-23, 2017.

Fonseca JE. Utilização de biológicos na prática clínica. Reunião dos Grupos Portugueses de Retina, Vítreo e Inflamação Ocular, Évora, Portugal, September 22-23, 2017.

Fonseca JE. Registo e monitorização. O exemplo da Reuma.pt. Reunião dos Grupos Portugueses de Retina, Vítreo e Inflamação Ocular, Évora, Portugal, September 22-23, 2017.

Santos MJ. Focus on Rheumatoid arthritis and Psoriatic arthritis. Immunology across borders, Milan, Italy, September 22, 2017.

Ponte C. The value of imaging in Giant Cell Arteritis (GCA). In a decade of Tocilizumab experience, Lisbon, Portugal, September 29, 2017.

Fonseca JE. Update in Rheumatoid Arthritis. In a decade of Tocilizumab experience, Lisbon, Portugal, September 29, 2017.

Fonseca JE. Paradoxical behavior of osteoclasts in axial spondyloarthritis? International Genetics of Ankylosing Spondylitis Consortium, Palermo, Italy, October 12-14, 2017.

Romeu JC, Barreira S. 1ª Reunião de Casos Clínicos Interativos de Reumatologia do Hospital de Sant'Ana, Parede, Portugal, October 12, 2017.

Campanilho-Marques, R. Artrite Idiopática Juvenil: diagnóstico, tratamento, prognóstico. XX Fórum de Apoio ao Doente Reumático. Liga Portuguesa contra as Doenças Reumáticas. Lisbon, Portugal, October 2017.

Grayson PC, Ponte C, Suppiah R. ACR-EULAR Diagnosis and Classification study (DCVAS): an update. American College of Rheumatology annual meeting 2017, San Diego, USA, November 5-8, 2017.

Ponte C, Robson J, Grayson P, Suppiah R, Merkel PA, Watts RA, Luqmani RA. Clinical Symposium - New ACR/EULAR Classification Criteria for ANCA-Associated Vasculitis: Implications for Clinical Practice. New ACR-EULAR Classification Criteria for ANCA-associated Vasculitis: Why and How? American College of Rheumatology annual meeting 2017, San Diego, USA, November 5-8, 2017.

Fonseca JE. Treat to target in imuno-mediated diseases: are we getting closer? Treat to target in pediatric immune mediated diseases, Lisbon, Portugal, November 11, 2017.

Fonseca JE. AS: Beginning of a new era? Reuma Spyx, Estoril, Portugal, November 11, 2017.

Fonseca JE. From immune mediated to Autoinflammatory diseases. Biologics: friends or foes. Lisbon, December 12, 2017.

Fonseca JE. Experiência na utilização- Reumatologia. Medicamentos biosimilares. Ponta Delgada, Portugal, December 14, 2017.

### **Communications in International Conferences**

Vieira-Sousa E, Canhão H, Fonseca JE on behalf of the GO-DACT research team. The GO-DACT Protocol: A Randomized Controlled Trial to Compare The Efficacy Of Golimumab In Combination With Methotrexate (MTX) Versus MTX Monotherapy, In Improving Dactylitis and Enthesitis, In MTX Naïve Psoriatic Arthritis Patients. 37<sup>th</sup> European Workshop for Rheumatology Research (EWRR), Athens, Greece, March 2-4, 2017. (Oral Presentation).

Moura RA, Quaresma C, Vieira AR, Gonçalves MJ, Polido-Pereira J, Romão V, Martins N, Canhão H, Fonseca JE. B-cell phenotype and IgD-CD27- memory B cells are affected by TNF-inhibitors and tocilizumab treatment in rheumatoid arthritis. 37<sup>th</sup> European Workshop for Rheumatology Research (EWRR), Athens, Greece, March 2-4, 2017.

Vieira-Sousa E, Canhão H, Fonseca JE on behalf of the GO-DACT research team. The GO-DACT Protocol: A Randomized Controlled Trial to Compare The Efficacy Of Golimumab In Combination With Methotrexate (MTX) Versus MTX Monotherapy, In Improving Dactylitis and Enthesitis, In MTX Naïve Psoriatic Arthritis Patients. 37<sup>th</sup> European Workshop for Rheumatology Research (EWRR), Athens, Greece, March 2-4, 2017. (Oral Presentation).

Moura RA, Quaresma C, Vieira AR, Gonçalves MJ, Polido-Pereira J, Romão V, Martins N, Canhão H, Fonseca JE. B-cell phenotype and IgD-CD27- memory B cells are affected by TNF-inhibitors and tocilizumab treatment in rheumatoid arthritis. 37<sup>th</sup> European Workshop for Rheumatology Research (EWRR), Athens, Greece, March 2-4, 2017. (Poster Presentation).

Moura RA, Quaresma C, Vieira AR, Gonçalves MJ, Polido-Pereira J, Romão V, Martins N, Canhão H, Fonseca JE. B-cell phenotype and IgD-CD27- memory B cells are affected by TNF-inhibitors and tocilizumab treatment in rheumatoid arthritis. 37<sup>th</sup> European Workshop for Rheumatology Research (EWRR), Athens, Greece, March 2-4, 2017. (Poster Presentation).

Luqmani RA, Craven A, Ponte C, Watts RA. Giant cell arteritis (GCA) and Takayasu arteritis (TAK): a spectrum within the same disease or not? A report from the DCVAS project. 18<sup>th</sup> International Vasculitis and ANCA Workshop, Tokyo, Japan, March 27, 2017. (Oral Presentation).

Ponte C, Monti S, Singh S, Hutchings A, Diamantopoulos AP, Dasgupta B, Schmidt WA, Luqmani RA. Histology findings in giant cell arteritis (GCA) and their relationship with the ultrasound results: analysis of data from the tabul study (temporal artery biopsy vs ultrasound in diagnosis of giant cell arteritis). 18<sup>th</sup> International Vasculitis and ANCA Workshop, Tokyo, Japan, March 27, 2017. (Poster Presentation).

Robson J, Grayson PC, Suppiah R, Ponte C, Khalid S, Judge A, Hutchings A, Watts RA, Merkel PA, Luqmani RA. American College of Rheumatology and European League Against Rheumatism 2017 Provisional Classification Criteria for Granulomatosis with Polyangiitis. BRS Annual Meeting 2017, Birmingham, England, April 2017. (Oral Presentation).



Monti S, Floris A, Ponte C, Vaggers S, Schmidt WA, Diamantopoulos AP, Pereira C, Luqmani RA. The role of ultrasound in the management of Giant Cell Arteritis in routine clinical practice. BRS Annual Meeting 2017, Birmingham, England, April 2017. (Poster Presentation).

Campanilho-Marques R, Deakin C, Simou S, Wedderburn LR, Pilkington C. Efficacy and Safety of Tumour Necrosis Factor Antagonists In A Large Cohort Of Juvenile Dermatomyositis Patients. Global Conference on Myositis, Potomac, Maryland, USA, May 5-8, 2017. (Poster Presentation).

Sanmarti R, Martin Mola E, Fonseca JE, Veale D, Escudero A, González C. Clinical remission in subjects with rheumatoid arthritis treated with subcutaneous tocilizumab as monotherapy or in combination with methotrexate or other non-biologics DMARDs: a real-world clinical trial (ToSpace). XLII Congreso Nacional Sociedad Española de Reumatología, Bilbao, Spain, May 23-26, 2017. (Poster Presentation).

Mourão AF, Eusébio M, Melo-Gomes J, Oliveira-Ramos F, Martins F, Estanqueiro P, Salgado M, Guedes M, Conde M, Carvalho S, Tavares-Costa J, Duarte C, Brito I, Furtado C, Rodrigues A, Sequeira G, Campanilho-Marques R, Branco J, Santos MJ, Eurico-Fonseca J, Canhã H. Reasons for discontinuation of biological agents in patients with juvenile idiopathic arthritis: data from the portuguese register, Reuma.pt (CL). European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Oral Presentation).

Moura RA, Quaresma C, Vieira AR, Gonçalves MJ, Polido-Pereira J, Romão VC, Martins N, Canhã H, Fonseca JE. B-cell phenotype and IgD-CD27- memory B cells are affected by TNF-inhibitors and tocilizumab treatment in rheumatoid arthritis. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Romão VC, Polido-Pereira J, Barros R, Vieira-Sousa E, Luís R, Vitorino E, Saraiva F, Fonseca JE. Ultrasound-guided synovial needle biopsy: single centre experience of an emerging, minimally invasive technique in clinical practice and research. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Duarte AC, Sousa S, Cordeiro A, Santos MJ, Canas da Silva J. Lung involvement in rheumatoid arthritis – a Portuguese reality. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Hetland ML, Østergaard M, Askling J, Gabay C, Nordstrom D, FitzGerald O, Hernández Miguel V, Santos MJ, Rotar Z, Mann H, Iannone F, Nissen MJ, Hauge E, Gomez-Reino J, Díaz-González F, Tomsic M, Pavelka K, O'Shea F, Sullivan C, van de Sande M, van der Horst-Bruinsma IE, Macfarlane GJ, Jones GT, Gudbjörnsson B, Kvien TK on behalf of EuroSpA Study Group. Commonalities and differences in data collection across European spondyloarthritis registries. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Laufer K, Nordström DC, Pavelka K, Hernandez V, Santos MJ, Rotar Z, Iannone F, Codreanu C, Lukina G, Gale SL, Sarsour K, Pethoe-Schramm A, Courvoisier DS, Gabay C. Retention of tocilizumab as monotherapy versus TNF inhibitors with conventional synthetic DMARDs in rheumatoid arthritis patients with inadequate response to TNF inhibitors: a study from the TOCERRA collaboration. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

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Ponte C, Monti S, Singh S, Huchings A, Diamantopoulos AP, Dasgupta B, Schmidt WA, Luqmani RA. Histology findings in giant cell arteritis (GCA) and their relationship with the ultrasound results: analysis of data from the tabul study (temporal artery biopsy vs ultrasound in diagnosis of giant cell arteritis). European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

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Monti S, Ponte C, Carrara G, Rumi F, Hutchings A, Dasgupta B, Luqmani RA. A novel ultrasound scoring system for giant cell arteritis. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Seixas MI, Teixeira V, Ferreira AC, Romeu JC, Macieira C. SLE old aim stays true. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Borges J, Madeira N, Cardoso A, Cunha-Miranda L, Barcelos F, Miguel C, Silva C, Fernandes S, Trinca R, Medeiros D, Campanilho-Marques R, Santos H, Leitão R, Faustino A. Do anxious or depressive rheumatoid arthritis patients on Biotechnologic therapy have worse disease activity, function and quality of life? European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Madeira N, Borges J, Cardoso A, Cunha-Miranda L, Barcelos F, Miguel C, Silva C, Fernandes S, Trinca R, Medeiros D, Campanilho-Marques R, Santos H, Leitão R, Faustino A. Anxiety and depression on disease activity and quality of life of spondyloarthritis patients under biologic therapies. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Cunha-Miranda L, Santos H, Barcelos F, Madeira N, Fernandes S, Borges J, Campanilho-Marques R, Silva C, Miguel C, Cardoso A, Trinca R, Faustino A. Can the use of new technologies improve the use of patient reported outcomes (PROS) and patient participation in a national registry? European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Perpétuo IP, Caetano-Lopes J, Rodrigues AM, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE. Methotrexate and low dose prednisolone downregulate osteoclast function in monocytes from early rheumatoid arthritis patients. European League against Rheumatism (EULAR) Annual European Congress of Rheumatology, Madrid, Spain, June 14-17, 2017. (Poster Presentation).

Ferreira S, Rodrigues F, Afonso Â, Dias S, Polido-Pereira J. Biobanco-iMM Quality Assurance - Factors Involved. Global Biobank Week, Stockholm, Sweden, September 13-15, 2017. (Poster Presentation).

Mourão AF, Eusébio M, Melo Gomes JA, Oliveira Ramos F, Martins FM, Salgado M, Guedes M, Carvalho S, Tavares-Costa JA, Brito I, Duarte C, Furtado C, Rodrigues A, Sequeira G, Campanilho-Marques R, Branco JC, Santos MJ, Fonseca JE, Canhão H. Reasons for discontinuation of biological agents in patients with juvenile idiopathic arthritis: data from the portuguese register, Reuma.pt. 24<sup>th</sup> European Pediatric Rheumatology Congress, Athens, Greece, September, 14-17, 2017. (Poster Presentation).

Santos H, Eusébio M, Borges J, Rosa-Gonçalves D, Ribeiro P, Santos-Faria D, Lopes C, Rovisco J, Agueda AF, Nero P, Valente P, Cravo AR, Santos MJ. Effectiveness of Early Adalimumab Therapy in Psoriatic Arthritis Patients from Reuma.Pt. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Stanevicha V, Terreri MT, Alexeeva E, Katsicas MM, Smith V, Cimaz R, Kostik M, Lehman TJA, Anton J, Sifuentes-Giraldo WA, Sztajnbok F, Avcin T, Janarthanan M, Santos MJ, Nemkova D, Battagliotti C, Eleftheriou D, Harel L, Kallinich T, Minden K, Nielsen SM, Torok KS, Uziel Y, Stevens A, Pilkington C, Helmus N. Patients with Overlap Features Different from Patients without? Results from the Juvenile Systemic Scleroderma Cohort. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Stanevicha V, Terreri MT, Alexeeva E, Katsicas MM, Smith V, Cimaz R, Kostik M, Lehman TJA, Anton J, Sifuentes-Giraldo WA, Sztajnbok F, Avcin T, Janarthanan M, Santos MJ, Nemkova D, Battagliotti C, Eleftheriou D, Harel L, Kallinich T, Minden K, Nielsen SM, Torok KS, Uziel Y, Stevens A, Pilkington C, Helmus N. Male Patients Have a More Severe Course as Female Patients with Diffuse Juvenile Systemic Scleroderma? American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Klotsche J, Foeldvari I, Kasapcopur O, Smith V, Sztajnbok F, Katsicas MM, Cimaz R, Janarthanan M, Anton J, Kostik M, Nemkova D, Sifuentes-Giraldo WA, Stanevicha V, Torok KS, Appenzeller S, Avcin T, Berntson L, Harel L, Kallinich T, Santos MJ, Terreri MT, Uziel Y, Helmus N. Performance of Juvenile Scleroderma Classification Criteria for Juvenile Systemic Sclerosis. Results from the jSSC Inception Cohort. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Dejaco C, Ramiro S, Duftner C, Besson FL, Bley TA, Blockmans D, Brouwer E, Cimmino MA, Clark E, Dasgupta B, Diamantopoulos AP, Direskeneli H, Iagnocco A, Klink T, Neill L, Ponte C, Salvarani C, Slart R, Whitlock M, Schmidt WA. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Schäfer VS, Chrysidis S, Duftner C, Dejaco C, Iagnocco A, Bruyn GA, Carrara G, D'Agostino MA, De Miguel E, Diamantopoulos AP, Fredberg U, Hartung W, Hocevar A, Juche A, Kermani TA, Koster MJ, Lorenzen T, Macchioni P, Milchert M, Døhn UM, Mukhtyar C, Ponte C, Ramiro S, Scirè CA, Terslev L, Warrington KJ, Dasgupta B, Schmidt WA. A Patient Based Reliability Exercise of Omeract Ultrasound Definitions in Giant Cell Arteritis. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Sanmartí R, Fonseca JE, Veale DJ, Escudero-Contreras A, Gonzalez CM. Clinical Remission in Subjects with Rheumatoid Arthritis Treated with Subcutaneous Tocilizumab As Monotherapy or in Combination with Methotrexate or Other Synthetic Dmards: A Real-World Clinical Trial. American College of Rheumatology Annual Meeting 2017, San Diego, USA, November 5-8, 2017. (Poster Presentation).

Khmelinskii N, Teixeira V, Avila-Ribeiro P, Romeu JC. Calcification des ligaments péri-odontoidiens dans l'arthropatie à cristaux de pyrophosphate de calcium: une série de cas unicentrique. 30<sup>e</sup> Congrès Française de Rhumatologie, Porte de Versailles, Paris, France, December 10-12, 2017. (Poster Presentation).

Polido-Pereira J. Biobanking and Cancer. Onconet SUDOE, Montpellier, France, December 14-15, 2017.

### **Communications in National Conferences**

Vieira-Sousa E. The GO-DACT Protocol: A randomized controlled trial to compare the efficacy of golimumab in combination with methotrexate (MTX) versus MTX monotherapy, In improving dactylitis and enthesitis, in MTX naïve psoriatic arthritis patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Oral Presentation).

Campanilho-Marques R, Deakin C, Simou S, Wedderburn LR, Pilkington C. Efficacy and Safety Of Tumour Necrosis Factor Antagonists In A Large Cohort Of Juvenile Dermatomyositis Patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Oral Presentation).

Khmelinskii N, Ponte C, Peixoto D, Rodrigues M, Teixeira L, Sousa S, Aleixo J, Pedrosa T, Serra SS, Castelão W, Cordeiro A, Cordeiro I, Fernandes S, Macieira C, Madureira P, Malcata A, Luz K, Teixeira V, Vieira R, Eusébio M, Martins FM, Sequeira G, Branco JC, Costa L, Canas da Silva J, da Silva JAP, Afonso C, Fonseca JE, Canhão H, Luqmani RA, Santos MJ. Reuma.pt/Vasculitis – two years existence of the Portuguese vasculitis registry. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Oral Presentation).

Lagoas-Gomes J, Sepriano A, Serra S, Eusébio M, Fonseca JE, Saavedra MJ, Cunha-Miranda L, Silva C, Bernardes M, Rosa-Gonçalves D, Costa J, Castelão W, Branco JC, Santos MJ. Drug survival of the first biologic in rheumatoid arthritis and predictors thereof in real world clinical practice. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Oral Presentation).

Mourão AF, Eusébio M, Melo-Gomes J, Estanqueiro P, Salgado M, Conde M, Carvalho S, Costa J, Duarte C, Brito I, Furtado C, Rodrigues AM, Sequeira G, Campanilho-Marques R, Branco JC, Santos MJ, Fonseca JE, Canhão H. Persistence with first biological agente and reasons for discontinuation in patients with juvenile idiopathic arthritis: data from the portuguese register, Reuma.pt. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Oral Presentation).

Cunha-Miranda L, Santos H, Barcelos F, Madeira N, Fernandes S, Borges J, Campanilho-Marques R, Silva C, Miguel C, Cardoso A, Trinca R, Faustino A. Can the use of new technologies improve the use of patient reported outcomes (PROS) and patient participation in a national registry? Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Madeira N, Borges J, Cardoso A, Cunha-Miranda L, Barcelos F, Miguel C, Silva C, Fernandes S, Trinca R, Medeiros D, Campanilho-Marques R, Santos H, Leitão R, Faustino A. Anxiety and depression on disease activity and quality of life of spondyloarthritis patients under biologic therapies. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Borges J, Madeira N, Cardoso A, Cunha-Miranda L, Barcelos F, Miguel C, Silva C, Fernandes S, Trinca R, Medeiros D, Campanilho-Marques R, Santos H, Leitão R, Faustino A. Do anxious or depressive rheumatoid arthritis patients on Biotechnologic therapy have worse disease activity, function and quality of life? Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vieira-Sousa E, Silva S, Vidal B, Lopes I, Canhão H, Fonseca JE. Certolizumab pegol like product mice equivalent reduces paws inflammation in tmTNF transgenic mice. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Perpétuo IP, Caetano-Lopes J, Rodrigues AM, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE. Methotrexate and low dose prednisolone downregulate osteoclast function in monocytes from early rheumatoid arthritis patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vidal B, Cascão R, Finnilä M, Lopes IP, Saarakkala S, Zioupos P, Canhão H, Fonseca JE. Effects of tofacitinib in early arthritis bone loss. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vidal B, Cascão R, Finnilä M, Lopes IP, Saarakkala S, Zioupos P, Canhão H, Fonseca JE. Early arthritis induces disturbances at bone nanostructural level reflected in decreased tissue hardness. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Khmelinskii N, Seixas I, Ponte C, Macieira C. The added value of a vasculitis clinic in a tertiary referral hospital. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Seixas MI, Ávila-Ribero P, Ponte C, Gouveia V, Macieira C. Patients with sensorineural hearing loss: benefits of a collaborative work for systemic evaluation - experience of a single tertiary center. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vieira-Sousa E, Rodrigues AM, Caetano-Lopes J, Fernandes S, Seixas MI, Martins M, Gonçalves MJ, Tenazinha C, Fernandes E, Barros R, Romeu JC. Zoledronate effectiveness and safety in active Paget's disease long-term follow-up and retreatment in clinical practice. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Martins N. Lupus anticoagulant: an antibody possibly associated with sensorineural hearing loss in patients with systemic lupus erythematosus. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Martins N, Seixas MI, Gonçalves MJ, Polido Pereira J, Costa MM, Saavedra MJ, Macieira C, Ramos FO, Canhão H, Fonseca JE. Anti-müllerian hormone and ovarian reserve in systemic lupus erythematosus. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Cascão R, Vidal B, Jalmari Finnilä MA, Lopes IP, Teixeira RL, Saarakkala S, Moita LF, Fonseca JE. Celastrol preserves bone structure and mechanics in arthritic rats. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Cascão R, Carvalho T, Goncalves J, Moita L, Fonseca JE., Efficacy and safety of oral administration of pure celastrol in AIA rats. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Romão VC, Martins AS J, Pinto J, Gonçalves AI, Simão R, Rodrigues W, Salvado F, Macieira C, Fonseca JE. Multidisciplinary sjögren's syndrome clinic: characterization and impact at the clinical and research level. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Rodrigues AM. The burden of spondyloarthritis – PAASPORT a population-based study. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Teixeira V. Clinical outcomes of African patients from Portuguese speaking countries evacuated for medical assessment in Portugal– Rheumatology as a case study. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vieira-Sousa E, Narciso L, Vitorino E, Luís R, Saraiva F, Fonseca JE. Microarthroscopic guided synovial biopsies in rheumatology practice: benefits for the diagnosis and treatment of inflammatory arthritis patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).



Khmelninskii N, Teixeira V, Romeu JC. Calcificação dos ligamentos peri-odontóides na doença por deposição de cristais de pirofosfato de cálcio. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Romão VC, Polido-Pereira J, Barros R, Vieira-Sousa E, Luis R, Vitorino E, Saraiva F, Fonseca JE. Ultrasound-guided synovial needle biopsy: update of experience with an emerging, minimally invasive technique in clinical practice and research. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Dinis JS. Escleromalácia como manifestação rara de Granulomatose com poliangéite. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Teixeira V, Martins N, Saavedra MJ, Romeu JC. Cocaine associated vasculitis – a growing issue. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Dinis JS. Efficacy and safety of imatinib in systemic sclerosis - a curious case report. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Teixeira RL, Luís R, Vitorino E, Polido Pereira J, Saraiva F. Basic crystal phosphate arthropathy diagnosed by ultrasound guided biosy. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Seixas MI. Small vessel involvement in Takayasu arteritis – what is the exact role for biologics? Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Seixas MI. Is there a role for anti-CD20 therapy in spondyloarthritis? Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Romão VC, Barros R, Polido-Pereira J, Vitorino E, Luis R, Marcos-Pinto, Ana, Castro A, Ponte C, Vieira-Sousa E, Saraiva F, Fonseca JE. The importance of repeated ultrasound-guided synovial biopsies and histological analysis in a case of septic/psoriatic arthritis. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Leal I, Cordeiro Sousa D, Miranda Rosa C, Vieira-Sousa E, Romão VC, Quintas AM, Guerra P, Rodrigues W, Marques-Neves C, Fonseca JE. Mycophenolate mofetil as an immunomodulatory for inflammatory eye disease: a case-series from a tertiary centre. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Duarte AC, Sousa S, Cordeiro A, Santos MJ, Canas da Silva J. Lung involvement in rheumatoid arthritis – a Portuguese reality. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Santos H, Eusébio M, Borges J, Rosa-Gonçalves D, Ribeiro P, Santos-Faria D, Lopes C, Rovisco J, Agueda AF, Nero P, Valente P, Cravo AR, Santos MJ. Effectiveness of early adalimumab therapy in psoriatic arthritis patients from Reuma.pt- EARLY PsA. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Vieira-Sousa E, Eusébio M, Ribeiro P, Khmelinskii N, Machado RC, Martins-Rocha T, Bernardes M, Santos-Faria D, Silva JL, Santos H, Miguel C, Carvalho PD, Costa T, Teixeira L, Meirinhos T, Nero P, Santos MJ. Effectiveness and persistence of the first tumor necrosis factor inhibitor in Portuguese psoriatic arthritis patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Duarte AC, Cordeiro I, Ferreira M, Judas T, Loureiro MJ, Carmona S, Santos J, Santos MJ, Cordeiro A. Pulmonary embolism in Systemic Sclerosis – one year follow up. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Teixeira L, Vinagre F, Canas da Silva J, Santos MJS. Redução da dose ou aumento do intervalo de terapêutica biológica – experiência de um serviço. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Cavaleiro J, Mourão AF, Rodrigues AM, Albino Teixeira A, Pimentel-Santos F, Oliveira-Ramos F, Canhão H, Polido-Pereira J, Fonseca JE, Romeu JC, Melo-Gomes J, Costa L, Graça L, Leandro MJ, Santos MJ, Machado P, Ramiro S, Vieira-Sousa E. Acta Reumatológica Portuguesa: the rheumatologists' perspectives in 2017. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Duarte AC, Cordeiro A, Loureiro MJ, Santos MJ. Intravenous Epoprostenol – a promising therapy in scleroderma digital vasculopathy. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Teixeira V, Conde I, Teixeira J, Ponte C. A Deadly Vasculopathy. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Barreira SC, Macieira C. Hook-like Osteophytosis – 2 Clinical Cases. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017. (Poster Presentation).

Viegas I, Campanilho-Marques R, Oliveira Ramos F, Ferreira R, Azevedo S, Asseiceira I, Mirco T, Esteves I, Costa Reis P. Esclerose sistémica juvenil: descrição de um caso clínico. 18º Congresso Nacional de Pediatria, Porto, Portugal, October 25-27, 2017. (Poster Presentation).

da Silva Dinis J, Valido A, Campanilho-Marques R, Oliveira Ramos F. Caso clínico: calcinose cutis como apresentação inicial de uma doença do tecido conjuntivo em idade pediátrica. XXV Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 23-24, 2017. (Poster Presentation).

Madeira N, Cunha Miranda L, Silva C, Miguel C, Medeiros D, Barcelos F, Micaelo M, Campanilho-Marques R, Cardoso A, Trinca R, Santos H. Avaliação clínica centrada no doente: satisfação com a medicação biológica em doentes com Artrite Reumatóide. XXV Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 23-24, 2017. (Poster Presentation).

Madeira N, Cunha Miranda L, Silva C, Miguel C, Medeiros D, Barcelos F, Micaelo M, Campanilho-Marques R, Cardoso A, Trinca R, Santos H. Patient reported outcomes: satisfação na utilização de tablet portátil no Hospital de Dia de Reumatologia. XXV Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 23-24, 2017. (Poster Presentation).

### **Organisation of Conferences**

Fonseca JE, Vieira-Sousa E, Romão V, Ponte C, Teixeira RL, Lopes IP, Calado A. Organizing Committee. IMM Rheumatology Series, in each session we promote site visit and project discussions with the international speakers.

Campanilho-Marques R. Organizer. “Workshop para pais - Doenças Reumáticas da Infância e Adolescência”, Lisbon, Portugal, March 2017.

Campanilho-Marques R, Oliveira-Ramos F, Dinis JS. Organizer. “2º Campo de Atividades em Portugal para crianças e jovens com Doença Reumática Juvenil”, July 2017.

Fonseca JE, Romão V, Lopes I. Organizer. “Formação Artrite Reumatóide: da fisiopatologia à atualidade terapêutica”, Lisbon, Portugal, October 21, 2017.

Fonseca JE, Barreira S, Teixeira RL, Cordeiro I, Teixeira V, Romão V, Lopes I. Organizer. “Formação sobre Doenças Reumáticas “O Melhor dos Dois Mundos”, November 3, 10, 17 and 24, 2017.

Vieira-Sousa E. Organizer. VIII Fórum das Espondilartrites, Monte Real, Portugal, January 13-14 January, 2017.

### **Internationalisation**

Ponte C. Member of the working group responsible for the EULAR recommendations for the use of imaging in the diagnosis and management of large vessel vasculitis in clinical practice.

Ponte C. Member of the working group responsible for the EULAR recommendations for the management of large vessel vasculitis since 2017.

Ponte C. Member of the working groups Emerging Eular Network group (EMEUNET), desde 2014; European Vasculitis Study Group (EUVAS), since 2015, and OMERACT Ultrasound Large-Vessel Vasculitis Subtask Force, also since 2015.

Fonseca JE. Chair of the European Synovitis Study Group of EULAR.

Fonseca JE. Past chair of the EULAR scientific commission.

### **Prizes, Honours and Awards**

Perpétuo IP, Caetano-Lopes J, Rodrigues AM, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE. Best Poster. Methotrexate and low dose prednisolone downregulate osteoclast function in monocytes from early rheumatoid arthritis patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Vieira-Sousa E., Canhão H., Fonseca JE on behalf of the GO-DACT research team. Honorable Mention. The GO-DACT Protocol: A Randomized Controlled Trial to Compare the Efficacy of Golimumab in Combination with Methotrexate (MTX) Versus MTX Monotherapy, In Improving Dactylitis and Enthesitis, In MTX Naïve Psoriatic Arthritis Patients. Congresso Português de Reumatologia, Albufeira, Portugal, May 10-13, 2017.

Kmelinskii N. Fellowship. “Fundo de Apoio à Investigação e Formação em Reumatologia”, Sociedade Portuguesa de Reumatologia, with the project “Predictors of response to ultrasound-guided sacroiliac joint corticosteroid-injection in patients with active sacroiliitis”.

Glória V. Fellowship. “Fundo de Apoio à Investigação e Formação em Reumatologia”, Sociedade Portuguesa de Reumatologia, with the project “Evaluation of lncRNAs role in the control of osteoclastogenesis in rheumatoid arthritis patients.

Fonseca JE. Fellowship. “Fundo de Apoio à Investigação e Formação em Reumatologia”, Sociedade Portuguesa de Reumatologia, with the project “Serum sphingolipids as candidate biomarkers in Rheumatoid Arthritis”.

Moura R. Fellowship. “Fundo de Apoio à Investigação e Formação em Reumatologia”, Sociedade Portuguesa de Reumatologia, with the project “B cells in Juvenile Idiopathic Arthritis: Effect of immunosuppressive treatment”.

Ramos F. Fellowship. “Fundo de Apoio à Investigação e Formação em Reumatologia”, Sociedade Portuguesa de Reumatologia, with the project “Adult outcomes of Juvenile Idiopathic Arthritis”.

Vidal B, Fonseca JE. JAKIE Fellowship. “Long term effect of tofacitinib on bone: friend or foe?”, Sociedade Portuguesa de Reumatologia.

Cordeiro I. 3<sup>th</sup> Place of the Pfizer Fellowship. Systemic Sclerosis Pulmonary Embolism Clinical STUDY (SSPECT), Sociedade Portuguesa de Reumatologia.

Ribeiro PA, Vieira de Sousa E. Celgene Fellowship. Tapering Biologics in PsA, Sociedade Portuguesa de Reumatologia.

### **Advanced Teaching**

Certificação de Investigadores Clínicos segundo o syllabus CLIC da PharmaTrain MJ Santos. Módulo “Introdução à ética de investigação clínica – viés de publicação e registo de ensaios clínicos”.

Vieira-Sousa E. Clinical Trials Unit. LisbonBioMed, Lisbon, Portugal, February 15, 2017.

Fonseca JE. How to get published. LisbonBioMed, Lisbon, Portugal, March 1, 2017.

Fonseca JE. Visit to the Biobank and to the clinical research center. LisbonBioMed, Lisbon, March 1, 2017.

Organization of the translational research week. LisbonBioMed, Lisbon, Portugal. February 27-March 1, 2017

Vieira-Sousa E. O doente com doença Reumática. Mestrado em Enfermagem em Associação Ramo Reabilitação – Processos Fisiopatológicos, Évora, Portugal, March 16, 2017.

Calado A. Respostas metabólicas à hiperglicemia e à hipoglicémia. Mestrado em Doenças Metabólicas e Comportamento Alimentar, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January-March 2017.

Calado A. Metabolismo Glicídico. Mestrado em Doenças Metabólicas e Comportamento Alimentar, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January-March 2017.

Vieira-Sousa E. GO-DACT an example of an investigator initiated trial. Programa de Formação em Investigação Clínica, Centro Hospital Lisboa Norte, Lisbon, Portugal, May 19, 2017.

Fonseca JE. Investigação de translação. Programa de Formação em Investigação Clínica, Centro Hospital Lisboa Norte, Lisbon, Portugal, May 22, 2017.

Polido-Pereira J. Inibidores da JAK na Artrite Reumatoide. Abbvie, Lisbon, Portugal, July 6, 2017.

Fonseca JE. A Fisiopatologia da artrite reumatoide. Formação em Artrite Reumatóide: da Fisiopatologia à Atualidade Terapêutica, Lisbon, Portugal, October 21, 2017.

Romão VC. Manifestações clínicas e prognóstico da artrite reumatóide. Formação em Artrite Reumatóide: da Fisiopatologia à Atualidade Terapêutica, Lisbon, Portugal, October 21, 2017.

Romão VC. Estratégia terapêutica da artrite reumatóide: dos DMARDs clássicos aos DMARDs biológicos. Formação em Artrite Reumatóide: da Fisiopatologia à Atualidade Terapêutica, Lisbon, Portugal, October 21, 2017.

Fonseca JE. Inibição da sinalização intracelular. Fundamentos, evidência e enquadramento na estratégia terapêutica. Formação em Artrite Reumatóide: da Fisiopatologia à Atualidade Terapêutica, Lisbon, Portugal, October 21, 2017.

Ponte C, Germano G, Macchioni P, Possemato N. Large Vessel Vasculitis. Ultrasonography course of vascular involvement in Rheumatological Diseases, Reggio Emilia, Italy, February 6-7, 2017.

Ponte C. Do not overlook giant cell arteritis! More symptoms and new options. 3rd European Summer School, Leipzig, Germany, July 7, 2017.

Campanilho-Marques R. Achados ecográficos patológicos básicos na criança. 1º Curso de Ecografia Musculoesquelética Pediátrica – ESPER, Lisbon, Portugal, November 2017.

### **Science and Society**

Fonseca JE participated in several TV programs and radio programs to talk about rheumatic diseases, clinical trials and translational research.

### **PhD Thesis Completed**

Bruno Miguel Costa Vidal, 17/04/2017, “How early inflammatory events affect bone nano properties at rheumatoid arthritis onset”, Faculty of Medicine, University of Lisbon. Supervisor: João Eurico Fonseca and Helena Canhão.

Luís Santos, “Análise da Qualidade do Osso Osteoporótico”, Doutoramento em Engenharia Biomédica, Universidade Técnica de Lisboa. Supervisor: Paulo Fernandes and João Eurico Fonseca.

Patrícia Reis, “Macrophage Polarization in Pediatric Lupus Nephritis”, Doutoramento em Medicina, University of Medicine. Supervisor: Kathelyn Sullivan (Pennsylvania University Medical School) and João Eurico Fonseca.

Pedro Laires, “The Impact of Rheumatic Diseases on Early Retirement”, Doutoramento em Ciências e Tecnologias da Saúde (Especialidade de Epidemiologia), University of Lisbon. Supervisor: João Eurico Fonseca and Miguel Gouveia (Universidade Católica).

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## Franco, Cláudio

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### Major Interests / Objectives

Appropriate blood supply in multicellular organisms is essential for development, growth and regeneration. Several diseases arise from dysfunction of blood vessels, e.g. diabetic retinopathy, stroke, or tumor angiogenesis. The formation of a functional vascular network requires two distinct processes – SPROUTING ANGIOGENESIS (which expands the network) and VASCULAR REMODELING (which generates a hierarchical network) – both driven by endothelial rearrangements.

Our Lab has the aim to understand the molecular mechanisms regulating coordinated endothelial cell behavior. We want to uncover:

- Novel regulators of endothelial cell migration;
- Molecular regulation of endothelial cell polarity;
- Effects of haemodynamic forces in vascular patterning;
- Novel anti-angiogenic therapies.

### Head of Laboratory

Claudio Areias Franco, PhD

### Research Team

Aida Andreia Pereira Pires Lima	Master	MSc Student (Left March)
Ana Alexandra Baptista Martins Moutinho Russo	Graduate	MSc Student
Ana Sofia Conceição Fernandes	Undergraduate	Lab Manager (Left January)
Catarina Gonçalves Fonseca	Master	PhD Student (Started September)
Dalila Maria Neves Silva	Master	Technician (Started November)
Francisca	PhD	Lab Manager (Started February)
Isabela Corina Santos Fortunato	Undergraduate	Undergraduate
Joana Cristina Reino Carvalho	Master	PhD Student, NA
Maria Angeles Dominguez-Cejudo	PhD	Post-Doctoral Investigator (Started March)
Pedro Miguel Branco Barbacena	Master	PhD Student
Silvia Vaccaro	Master	Investigator (Started March)
Tania Balboni	Master	Visiting Researcher (Started February/Left July)

### Laboratory Keywords / Research Areas

Angiogenesis, Cell migration, Tumor angiogenesis, Endothelial cells, Vascular patterning.



### Major Scientific Achievements

In 2017, our work has uncovered that shear stress and junctional tension compete in the process of establishing network-level collective cell polarity. We established the cellular and molecular principles that define the competitive nature between blood flow and VEGF, the two main organizers of blood vessel formation. We show that these two organizers regulate collective polarity of endothelial cells in a competitive way, and the strength and directionality of each polarity cue defines the transition between vascular sprouting and vascular remodelling events. Currently, using zebrafish, mouse and advanced in vitro models of angiogenesis, we are exploring the mechanisms contributing to blood vessel pattern formation based on the dual and interdependent response to shear stress and chemokines.

#### Publications:

Franco CA & Gerhardt H. *Dev Cell*. 2017 Jun 19;41(6):574-576.

#### Grants:

LeDucq Foundation TransAtlantic Networks of Excellence in Cardiovascular Research (ATTRACT; id:17CVD03).

### Selected Publications

Franco CA, Jones M, Geudens I, Bernabeu MO, Ragab A, Collins RT, Phng LK, Coveney PV, Gerhardt H (2015). Dynamic endothelial cell rearrangements drive developmental vessel regression. *PLoS Biology* 13, e1002163. (IF: 9.797, Citations: 28).

Bentley K, Franco CA, Philippides A, Blanco R, Dierkes M, Gebala V, Stanchi F, Jones J, Cagna G, Kutschera S, Claesson-Welsh L, Vestweber D, Gerhardt H (2014). The role of differential VE-cadherin dynamics in cell rearrangement during angiogenesis. *Nature Cell Biology* 16, 309-21. <http://www.nature.com/ncb/journal/v16/n4/full/ncb2926.html>. (IF: 20.06, Citations: 98).

Guarani V, Deflorian G\*, Franco CA\*, Krüger M, Phng LK, Bentley K, Toussaint L, Dequiedt F, Mostoslavsky R, Schmidt MH, Zimmermann B, Brandes RP, Mione M, Westphal CH, Braun T, Zeiher AM, Gerhardt H, Dimmeler S, Potente M, \*co-second (2011). Acetylation-dependent regulation of endothelial Notch signalling by the SIRT1 deacetylase. *Nature* 473, 234-8. (IF: 40.137, Citations: 199).

Stenzel D\*, Franco CA\*, Estrach S, Mettouchi A, Sauvaget D, Rosewell I, Schertel A, Armer H, Domogatskaya A, Rodin S, Tryggvason K, Collinson L, Sorokin L, Gerhardt H, \* co-first (2011). Endothelial basement membrane limits tip cell formation by inducing Dll4/Notch signalling in vivo. *EMBO reports* 12, 1135-43. (IF: 8.568, Citations: 80).

Jakobsson L, Franco CA, Bentley K, Collins RT, Ponsioen B, Aspalter IM, Rosewell I, Busse M, Thurston G, Medvinsky A, Schulte-Merker S, Gerhardt H (2010). Endothelial cells dynamically compete for the tip cell position during angiogenic sprouting. *Nature Cell Biology* 10, 943-53. (IF: 20.06, Citations: 432).

### **Ongoing Research Projects**

2016/2021: AXIAL.EC: Principles of Axial Polarity-Driven Vascular Patterning. Coordinator: Cláudio Areias Franco. Funding Agency: European Commission. Reference: ERC StG 679368. Amount: € 1 618 750,00. Total Amount: € 1 618 750,00.

2013/2018: Mechanisms of endothelial cell motility and invasion in vascular morphogenesis. Coordinator: Cláudio Areias Franco. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00412/2012. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

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

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

### **Publications in Peer Review Journals**

Franco CA, Gerhardt H (2017). Morph or Move? How Distinct Endothelial Cell Responses to Blood Flow Shape Vascular Networks. *Dev Cell*. 41(6):574-576. review. (Journal IF: 9.174, Citations: 0).

### **Invited Lectures and Seminars**

Franco CA. Pointing in the right direction: a tale of forces in vascular biology. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 2017.

Franco CA. Flow and Chemokines compete to establish the collective polarity. Berlin, Germany, October 2017. Host: Holger Gerhardt.

Franco CA. Principles of blood vessel network organisation. CAML Sessions, Faculty of Medicine, University of Lisbon, Portugal, October 2017. Host: Joao Lacerda.

Franco CA. Cell Dynamics in Vascular Morphogenesis. Curso da Visão, IBILI Institute for Biomedical Imaging and Life Sciences, Coimbra, Portugal, November 2017. Host: Francisco Ambrosio.

Franco CA. Regulating cell behaviour in vascular patterning. Cell therapies and Regenerative Medicine, Instituto Superior Técnico, Lisbon, Portugal, November 2017. Host: Cláudia Lobato.

Franco CA. Regulating collective behaviour in endothelial cells. UC-Biotech, Coimbra, Portugal, December 2017. Host: Lino Ferreira.

### **Communications in International Conferences**

Franco CA. Regulating endothelial collective cell behaviour in vascular morphogenesis. SFB/TR23 Symposium, Germany, 2017.

Franco CA. Cell Migration Under Confinement Workshop, Palmela, Portugal, 2017.

### **Communications in National Conferences**

Franco CA. Dinâmica das células endoteliais na formação da árvore vascular. X ENEBIOQ Congress, Braga, Portugal, 2017.

### **Organisation of Conferences**

Franco CA, Gomes ER. Cell Migration Under Confinement Workshop, Palmela, Portugal, 2017.

### **Internationalisation**

Cell Migration under Confinement Workshop. SFB/TR23 Symposium, Germany (Host: Hellmut Augustin), ENEBIOQ Congress, Portugal, UC-Biotech (Host: Lino Ferreira).

### **Advanced Teaching**

Franco CA. LisbonBioMed PhD Programme. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 2017.

Franco CA. Teaching in IST-INESC Biophysics Course, Lisbon, Portugal, July 2017.

Franco CA. Bioengineering – Cell therapies and Regenerative Medicine PhD Programme, IST, Lisbon, Portugal, November 2017.

Franco CA. Curso da Visao Master Programme, CNC – Center for Neuroscience and Cell Biology, Coimbra, Portugal, November 2017.

Franco CA. Teaching in IST Engineering of Cells and Tissues, Lisbon, Portugal, November 2017.

### **Science and Society**

Franco CA. ReTuBi “Open Afternoon” for cancer patients associations, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 2017.

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## Gomes, Edgar

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### Major Interests / Objectives

Connecting the nucleus to the cytoskeleton is relevant for multiple cellular processes and disruption of these connections result in multiple 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 use different molecular and cellular approaches in combination with time-lapse imaging analysis to address these questions.

### Head of Laboratory

Edgar Rodrigues Almeida Gomes, PhD

### Research Team

Anna Pezzarossa	PhD	Technician
Cátia Alexandra da Silva Janota	Master	PhD Student
Duarte Luis Resende Morais de Ferreira Marques	Undergraduate	Trainee (Started November)
Francisco Javier Calero Cuenca	PhD	Post-Doctoral Investigator
Graciano Silva Leal	PhD	Post-Doctoral Investigator
Helena Alexandra Ribeiro de Carvalho Pinheiro	Master	PhD Student
Joana Marques Pinto Monteiro	Undergraduate	Trainee (Started November)
João Pedro Nunes Paulo da Silva Martins	Master	Investigator
Liliana Leonor Miranda Bento	Master	Project Manager
Mafalda Ramos de Melo Pimentel	Master	PhD Student
Maria Judite Sousa Costa	PhD	Post-Doctoral Investigator
Patrícia Alexandra Brito da Costa	PhD	Post-Doctoral Investigator (Left September)
Sara Raquel Reis de Oliveira Franco Pinheiro	PhD	Investigator
Sara Sofia Gasalho Ferreira	Graduate	Technician
Sree Rama Chaitanya	PhD	Post doctoral Investigator (Started November)
William Roman	PhD	Post-Doctoral Investigator

### Laboratory Keywords / Research Areas

Skeletal muscle, Cell migration, Cell biology, Cytoskeleton.

### Major Scientific Achievements

Our laboratory has been actively working on the identification of mechanisms for nuclear positioning in cells, in particular skeletal muscle myofibers. During 2017, we published two significant manuscripts that address two important questions not yet answered. First, we found how the nucleus is positioned at the periphery of myofibers. Myofibers are multinucleated cells and their nuclei are found at the cell periphery. During development, muscle regeneration and in different muscle disorders, the nuclei are found at the center of the myofiber. We found that nuclei are squeezed to the periphery of the fiber by myofibril contraction and crosslinking, in combination with changes in nuclear stiffness. Our work explains why mutations in apparently diverse proteins leads to a common phenotype of centrally located nuclei in different muscle disorders. Second, we found that nucleation of microtubules from the nuclear envelope is required for proper nuclear positioning in developing myofibers.

### Selected Publications

Gimpel P, Lee YL, Sobota RM, Calvi A, Koullourou V, Patel R, Mamchaoui K, Nédélec F, Shackleton S, Schmoranzler J, Burke B, Cadot B, Gomes ER (2017). Nesprin-1 $\beta$ -Dependent Microtubule Nucleation from the Nuclear Envelope via Akap450 Is Necessary for Nuclear Positioning in Muscle Cells. *Current Biology* 9, 2999. (IF: 8.851, Citations: 2).

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* 19, 1189. (Journal IF: 20.06, Citations: 2).

Falcone S, Roman W, Hnia K, Gache V, Didier N, Lainé J, Aurade F, Marty I, Nishino I, Charlet-Berguerand N, Romero N, Marazzi G, Sassoon D, Laporte J, Gomes ER. (2014) N-WASP is required for Amphiphysin-2/BIN1 dependent nuclear positioning and triad organization in skeletal muscle and is involved in the pathophysiology of centronuclear myopathy. *EMBO Mol Med* 6, 1455-1475. (IF: 9.249, Citations: 21).

Metzger T, Gache V, Xu M, Cadot B, Folker E, Richardson B, Gomes ER\*, Baylies MK\* \*co-corresponding authors (2012). MAP and Kinesin dependent nuclear positioning is required for skeletal muscle function. *Nature* 484, 120. (IF: 40.137, Citations: 83).

Luxton GW\*, Gomes ER\*, Folker ES, Vintinner E, Gundersen GG (2010). Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement. *Science* 329, 5994. (IF: 37.205, Citations: 190).

### **Ongoing Research Projects**

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

2016/2018: Muscleguy: A novel muscle disorders 3D in vitro system for drug screening and validation. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: ERC PoC 713612. Amount: € 150 000,00. Total Amount: € 150 000,00.

2014/2019: Phonics: Positioning the nucleus for cell migration and muscle fiber function. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: ERC CoG 617676. Amount: € 1 968 000,00. Total Amount: € 1 968 000,00.

2014/2019: Positioning the Cell Nucleous. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG EGomes. Amount: € 250 000,00. Total Amount: € 250 000,00.

2014/2019: Positioning the nucleus for cell migration and muscle fiber function. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01477/2013. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

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

### **Publications in Peer Review Journals**

Janota CS, Calero-Cuenca FJ, Costa J, Gomes ER (2017). SnapShot: Nucleo-cytoskeletal Interactions. *Cell* 2017; 169(5):970-970.e1. (IF: 30.41, Citations: 1).

Pimentel MR, Falcone S, Cadot B, Gomes ER (2017). In Vitro Differentiation of Mature Myofibers for Live Imaging. *J Vis Exp*;(119). doi: 10.3791/55141. (IF: 1.232, Citations: 1).

Roman W, Gomes ER (2017). Nuclear positioning in skeletal muscle. *Semin Cell Dev Biol.* 2017 Dec 11. pii: S1084-9521(17)30428-7 doi: 10.1016/j.semcdb.2017.11.005. (IF: 6.614, Citations:--)

### **Invited Lectures and Seminars**

Gomes E. Mechanisms of nuclear positioning in cells. Institute Curie, Paris, France, September 14, 2017. Host: Bruno Goud.

### **Communications in International Conferences**

Gomes E. Myofibril contraction and cross-linking drive nuclear movement to the periphery of skeletal muscle. ASCB/EMBO 2017 Meeting, Philadelphia, USA. (Oral Presentation).

Gomes E. Mechanisms of Triad Formation and Nuclear Positioning in Skeletal Muscle. Gordon Research Conference "Muscle: Excitation-Contraction Coupling", Les Diablerets, Switzerland. (Oral Presentation).

Gomes E. Squeezing the nucleus to the periphery of skeletal myofibers. The Pleiotropic Nuclear Envelope Meeting, Edinburgh, Scotland. (Oral Presentation).

### **Communications in National Conferences**

Gomes E. How to position the nucleus for cell function. Encontro com a Ciência e Tecnologia, Lisbon, Portugal. (Oral Presentation).

### **Organisation of Conferences**

Gomes E. Co-organizer of The Pleiotropic Nuclear Envelope Meeting, The Biochemical Society, Edinburgh, Scotland, August 2017.



### **Advanced Teaching**

Gomes E. PGCD, Cell Biology Course, Cape Verde, February 2017.

Gomes E. Gulbenkian Institute PhD Course, Oeiras, Portugal, October 2017.

Gomes E. Stem Cell Biology course of the Bioengineering – Cell Therapies and Regenerative Medicine PhD Program, Lisbon, Portugal, March 2017.

## Graça, Luís

### Major Interests / Objectives

Our Unit studies mechanisms underlying induction and maintenance of immune tolerance. In other words, we research methods to reprogramme the immune response in situations where the immune system is causing a disease, such as allergy, autoimmunity and transplant rejection.

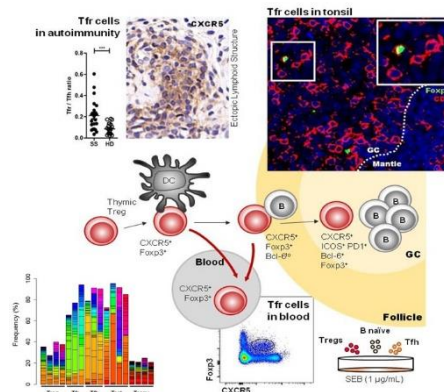
In addition, we are interested in defining the functional properties of lymphocytes that can promote immune tolerance by suppressing pathogenic immune responses. We have been studying how different types of lymphocytes with regulatory function can be induced in the periphery.

We believe that in the foreseeable future antibody therapy, as well as other strategies to modulate the immune system, will have an important repercussion in the quality of life of people suffering from immune mediated diseases.

### Head of Laboratory

Luís Graça, MD/PhD, Associate Professor

### Graphical Abstract



### Research Team

Afonso Silva Pinto Basto	PhD	Post-Doctoral Investigator (Started April)
Ana Água-Doce	PhD	Post-Doctoral Investigator
Ana Catarina Jorge Mendes	Graduate	Lab manager (Started October)
Ana Isabel Neves de Matos	Master	PhD Student (Started April)
Ana Raquel Maceiras Oliveira	Master	PhD Student (Left March)

Carina Sofia Gonçalves Peres	Master	PhD Student, Faculdade de Farmácia da Universidade de Lisboa
Carlos Barata da Silva	Graduate	Investigator (Left September)
Filipa Ramos de Moura Ribeiro	Master	Investigator (Started March)
Raquel Filipa Reis de Freitas	Master	PhD Student
Ricardo Jorge Pires Correia	Graduate	MSc Student (Started August)
Saumya Dileep Kumar	Master	PhD Student
Sílvia Cristina de Paiva e Almeida	PhD	Post-Doctoral Investigator (Left March)
Válter Bruno Ribeiro Fonseca	Master	PhD Student, CHLN - Hospital de Santa Maria, Physician, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Vanessa Alexandra Gonçalves de Oliveira Martins	PhD	Post-Doctoral Investigator
Yaquelin Ortiz Miranda	Graduate	PhD Student

### Laboratory Keywords / Research Areas

Immune tolerance, Regulatory T cell subsets, T follicular helper (Tfh) cells, Allergy, Autoimmunity, Transplantation.

### Major Scientific Achievements

We found Tfh and Tfr cells in the same germinal center differ in their TCR usage: Tfh cells are specific to the immunizing antigen, and Tfr cells retain a TCR specificity similar to Tregs. These results suggest Tfh cells select high-affinity BCRs during affinity maturation, while Tfrs prevent autoimmunity.

We established, using human samples, that human circulating Tfr cells are generated in lymphoid tissues following exposure to antigens, and are not fully mature.

We have shown adoptive transfer of Foxp3+ iNKT cells, due to CXCR6-mediated preferential hepatic homing, leads to liver-specific immune suppression allowing long-term survival of allogeneic islet transplants delivered through intra-portal route in mice.

Finally, we have started a number of clinical studies regarding the impact of Tfh subsets in antibody-mediated human diseases, and how Tfh and Tfr subsets can be used as biomarkers.

### Selected Publications

Fonseca VR, Agua-Doce A, Maceiras AR, Pierson W, Ribeiro F, Romão VC, Pires AR, da Silva SL, Fonseca JE, Sousa AE, Linterman MA, Graca L. (2017) Human blood T(fr)cells are indicators of ongoing humoral activity not fully licensed with suppressive function. *Science Immunology* 2, 11. (Journal IF:--, Citations:--).

Maceiras AR, 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, 21. (Journal IF: 12.124, Citations: 4).

Oliveira VG, Agua-Doce A, Curotto de Lafaille M, Lafaille JJ, Graca L (2013). Adjuvant facilitates anti-CD4 mediated immune tolerance to recombinant factor VIII in hemophilia through a Foxp3-independent mechanism that relies on IL-10. *Blood* 121, 3938. (IF: 13.164, Citations: 10).

Monteiro M, Almeida CF, Agua-Doce A, Graca L (2013). Induced IL-17-producing invariant Natural Killer T cells require activation in presence of TGF-beta. *The Journal of Immunology* 190, 805. (IF: 4.856, Citations: 39).

Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira V, Faro J, Graça L (2011). Regulation of germinal centre reaction by Foxp3+ follicular regulatory T cells. *The Journal of Immunology* 187, 4553. (IF: 4.856, Citations: 188).

### Ongoing Research Projects

2016/2019: Mechanisms used by T follicular helper (Tfh) cells to determine antibody isotype production in Th1 versus Th2 responses. Coordinator: Ana Margarida Tito Martins Água-Doce. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/IMI-IMU/7038/2014. Amount: € 199 971,00. Total Amount: € 199 971,00.

2016/2019: Immunomodulatory effect of CD6-targeting in neuroinflammation. Coordinator: Vanessa Alexandra Gonçalves de Oliveira Martins. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-FTO/3080/2014. Amount: € 162 488,00. Total Amount: € 193 092,00.

2015/2019: Multidisciplinary strategy to develop novel multicomponent nanoscale systems for immune modulation. Coordinator: Luís Ricardo da Silva Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: UTAP-ICDT/DTP-FTO/0016/2014. Amount: € 27 000,00. Total Amount: € 189 274,00.

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

2015/2018: Characterization of T follicular helper (Tfh) cells and B cell isotype switching induced by type 1 and type 2 adjuvants. Coordinator: Luís Ricardo da Silva Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: FAPESP/19906/2014. Amount: € 200 000,00. Total Amount: € 200 000,00.

2015/2017: Targeting Germinal Centre Dysregulation in Allergy. Coordinator: Luís Ricardo da Silva Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: HMSP-ICT/0034/2013. Amount: € 180 672,00. Total Amount: € 300 000,00.

2015/2018: Immune modulatory activity of CD6-targeting monoclonal antibodies. Coordinator: Luís Ricardo da Silva Graça. Funding Agency: Center of Molecular Immunology. Reference: CUBA - CD6. Amount: € 43 700,00. Total Amount: € 43 700,00.

### **Other Projects**

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

### **Publications in Peer Review Journals**

Fonseca VR, Agua-Doce A, Maceiras AR, Pierson W, Ribeiro F, Romão VC, Pires AR, Silva SL, Fonseca JE, Sousa AE, Linterman MA, Graca L (2017). Human Blood CXCR5+Foxp3+ T cells Are Indicators of Ongoing Humoral Activity Not Fully Licensed with Suppressive Function. *Science Immunol.* 2: eaan1487. (IF:--, Citations:--).

Maceiras R, Almeida SCP, Mariotti-Ferrandiz E, Chaara W, Jebbawi F, Six A, Hori S, Klatzmann D, Faro J, Graca L (2017). T follicular helper and T follicular regulatory cells from the same germinal centers have different TCR-specificity. *Nature Commun.* 8: 15067. (IF:12.124, Citations: 4).

Maceiras AR, Fonseca VR, Agua-Doce A, Graca L (2017). T follicular regulatory cells in mice and men. *Immunology.* 152: 25-35. (IF: 3.701, Citations:--).

Almeida SCP, Graca L (2017). IL-9 production by nonconventional T helper cells. *Methods Mol Biol.* 1585:93-109. (IF:1.29, Citations:--).

Bárcia RN, Santos JM, Teixeira M, Filipe M, Pereira ARS, Ministro A, Água-Doce A, Carvalheiro M, Gaspar MM, Miranda JP, Graca L, Simões S, Santos SCR, Cruz P, Cruz H (2017). Umbilical cord tissue-derived mesenchymal stromal cells are able to maintain the immunomodulatory and angiogenic potencies after cryopreservation and subsequent thawing. *Cytotherapy.* 19(3):360-370. (IF:3.203, Citations:--).

Peres C, Matos AI, Coniot J, Sainz V, Zupani E, Silva JM, Graca L, Gaspar RS, Préat V, Florindo H (2017). Poly(lactic acid)-based nanosystems are promising tools for immune modulation. *Acta Biomaterialia.* 48:41-57. (IF:6.319, Citations: 8).

### **Invited Lectures and Seminars**

Graça L. T follicular regulatory cells. European Midwinter Workshop 2017, Angerer Alm, Austria, January 16-18, 2017.

Fonseca V. Clinical reasoning. Annual International Medical Students Meeting, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 10-12, 2017.

Graça L. Regulation of germinal centre responses in mice and humans. European Federation of Immunology Societies on Tour, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 24, 2017.

Graça L. Paradoxes of Immunology. 3<sup>rd</sup> Forum Imunologia Janssen, Aveiro, Portugal, May 20 2017.

Graça L. Tolerance to Factor VIII. Fourth International Therapeutic Tolerance Workshop, Newcastle, England, June 27-30, 2017.

Graça L. Regulation of GC responses with Tfr cells. Institute of Immunology, Medical University of Vienna, Austria, October 3, 2017.

Graça L. Imunopatologia da Psoríase. Serviço de Dermatologia, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, October 20, 2017.

Graça L. Expansion of regulatory T cells to reinstate tolerance. University Department of Surgery, Medical University of Vienna, Austria, October 30, 2017.

Graça L. Regulation of humoral responses by Tfr cells. British Society of Immunology sponsored seminar, Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, England, November 10, 2017.

Fonseca V. Developing the next generation of teachers. Beyond Med, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, November 15, 2017.

Oliveira VG. Tolerance induction to recombinant FVIII in a model of hemophilia. International Society on Thrombosis and Haemostasis (ISTH) Congress, Berlin, Germany, 2017.

### **Communications in International Conferences**

Maceiras AR, Almeida SCP, Mariotti Ferrandiz E, Chacara W, Jebbawi F, Six A, Klatzmann D, Faro J, Graça L. Different TCR specificity requirements in T follicular helper and T follicular regulatory cells from the same germinal centers. Keystone Symposia on B Cells and T Follicular Helper Cells – Controlling Long-Lived Immunity, Whistler, Canada, April 23-27, 2017. (Oral Presentation).

Fonseca VR, Água-Doce A, Maceiras AR, et al. Human circulating CXCR5+Foxp3+ T cells are peripherally-induced Tfr cell precursors. Keystone Symposia Conference: B Cells and T Follicular Helper Cells – Controlling Long-Lived Immunity, Whistler, Canada, April 23-27, 2017. (Poster Presentation).

Kumar S, Almeida SCP, Campos P, Russo M, Carvalho M, Gaca L. Transcriptional profile of follicular and effector T helper cells under type 1 immune responses. Keystone Symposia meeting on B Cells and T Follicular Helper Cells – Controlling Long-Lived Immunity, Whistler, Canada, April 23-27, 2017. (Poster Presentation).

Peres C, Moura L, Matos AI, Sainz V, Viana AS, Gaspar RS, Graça L, Prétat V, Florindo H. Polymeric nanoparticles as breast cancer vaccines and immunomodulators. GRC Cancer Nanotechnology - Multimodal Nano-Therapies against Cancer, Mount Snow, USA, June 18-23, 2017. (Poster Presentation).

Fonseca VR, Romão V, Água-Doce A, et al. Human Blood CXCR5+Foxp3+ T cells Are Indicators of Ongoing Humoral Activity Not Fully Licensed With Suppressive Function. 19<sup>th</sup> Germinal Centre Conference, Venice, Italy, September 14-17, 2017. (Poster Presentation).

Água-Doce A, Romão V, Fonseca V, Fonseca JE, Graca L. IL-6-blockade in rheumatoid arthritis patients: impact on Tfh subsets and humoral responses. 19<sup>th</sup> Germinal Centre Conference, Venice, Italy, September 14-17, 2017. (Poster Presentation).

Kumar S, Almeida SCP, Campos P, Russo M, Carvalho M, Gaca L. Transcriptional profile of T follicular helper (Tfh) cells induced by type 1 and type 2 adjuvants. ENLIGHT-TEN Annual Meeting Vienna, Austria, October 4-6, 2017. (Poster Presentation).

#### **Communications in National Conferences**

Freitas R, Almeida S, Perez S, Padron L, Leon K, Graca L. The effect of CD6 targeting in T cell function and Immunopathology. XI IMM/CAML PhD Meeting, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Freitas R, Almeida S, Leon K, Graca L. Anti-inflammatory effect of CD6 blockade. XLIII Annual Meeting SPI2017, "Breaking the barriers of immunotherapy and vaccination: realities and challenges", i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 14-16, 2017. (Poster Presentation).

Água-Doce A, Romão V, Fonseca V, Fonseca JE, Graca L. IL-6-blockade in rheumatoid arthritis patients: impact on Tfh subsets and humoral responses. XLIII Annual Meeting SPI2017, "Breaking the barriers of immunotherapy and vaccination: realities and challenges", i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 14-16, 2017. (Poster Presentation).

Peres C, Moura L, Matos AI, Sainz V, Viana AS, Gaspar RS, Graça L, Prétat V, Florindo H. Polymeric nanoparticles as cancer vaccines and immunomodulators. 9<sup>th</sup> iMed ULisboa Postgraduate Students Meeting & 2nd i3DU Meeting, Lisbon, Portugal, July 13-14, 2017. (Poster Presentation).



Matos AI, Peres C, Moreiras H, Viana AS, Graça L, Barral D, Conde JP, Florindo HF. Multivalent Polymeric Nanoparticles for Colorectal Cancer Immunotherapy and Immunomodulation. 9<sup>th</sup> iMed ULisboa Postgraduate Students Meeting & 2nd i3DU Meeting, Lisbon, Portugal, July 13-14, 2017. (Poster Presentation).

Fonseca VR. Human circulating CXCR5+Foxp3+ T cells are peripherally-induced Tfr cell precursors. UL Innovation Week, Lisbon, Portugal, 2017. (Oral Communication).

### **Organisation of Conferences**

Graça L, Moretta L. European Federation of Immunology Societies on Tour. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 24, 2017.

### **Internalisation**

During 2017 our group has been involved in several international projects.

We have been leading a collaborative project involving the laboratories of Arlene Sharpe and Laurence Turka (Harvard), Jocelyne Demengeot (IGC), and Ana E. Sousa (iMM). The project is devoted to the study of Tfh subsets in mice and human immune-mediated diseases.

We have a collaboration with a leading expert on adjuvants, Momtchilo Russo, from the University of São Paulo in Brazil. In this project, our groups join resources to investigate how adjuvants influence Tfh subsets during the course of humoral responses.

We have also an ongoing collaborative project with the group of Kalet Leon (Center of Molecular Immunology, Havana, Cuba) for the study of immunomodulatory role of several molecular products.

We participate in a Marie Curie initial training network (ENLIGHT-TEN) that brings together experts in bioinformatics and immunology across Europe.

Finally, we became founders of the European T cell interest group, under the auspices of EFIS (European Federation of Immunology Societies).

### **Prizes, Honours and Awards**

Fonseca V, Romão V, Fonseca JE, Graça L. iMM Innovators Award 2017.

### **Advanced Teaching**

Graça L. Lisbon BioMed PhD Programme, organization of the immunology module, February 2017.

Fonseca V. Lisbon BioMed PhD Programme, lecturer at the immunology module, February 2017.

Graça L. PhD Programme Regenerative Medicine, lecturer in immunology module, IMM/IST, Lisbon, Portugal, March 16, 2017.

Graça L. PhD Viva, Ana Raquel Maceiras, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 20, 2017.

Graça L. PhD Viva, Bruno Vidal, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, April 19, 2017

Graça L. Gabba PhD Programme, lecturer in immunology module, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, April 2017.

Graça L. PhD Viva, Ricardo Miragaia, Universidade do Minho, Guimarães, Portugal, September 26, 2017.

### **Science and Society**

Graça Lab collaborated with visual artist Andrew Carnie, towards the creation of an artwork inspired by the lab research to be exhibited internationally in 2018. The art residency was funded under ENLIGHT-TEN.

Graça Lab collaborated with visual artist Marta de Menezes towards the creation of a new artwork inspired by the lab research to be exhibited internationally in 2018. The art residency was funded under ENLIGHT-TEN.

Polish visual artist Karolina Zyniewicz spent two weeks in GracaLab in order to create new artworks, to be completed in 2018 following a subsequent visit.

Graça Lab collaboration with visual artist Nigel Helyer leading to the development of a new artwork, to be completed in 2018.

Graça L has been invited to the organizing committee of FACTT Festival as scientific consultant. FACTT organized in 2017 visual art exhibitions and seminars, exploring the interface of science and art, in Lisbon (MAAT and MUDE), New York (School of Visual Arts, and NYU), Mexico City (cancelled due to the earthquake), and Berlin. It is coordinated by the ARTE Institute, New York.

Graça L, de Menezes M. Workshop on art and biology. University of Michigan, Ann Arbour, USA, March 29-31, 2017.

Graça L. The intersection of art and biology, summer school (co-organizer), Cultivamos Cultura, Odemira, Portugal, July 2017.

Graça L. 195 anos da Sociedade das Ciências Médicas de Lisboa. Congresso Nacional da Sociedade Portuguesa de Medicina do Trabalho, Culturgest, Lisbon, Portugal, November 2, 2017.

Graça Lab participated in activities to promote the awareness of immunology among young audiences as part of the “International Immunology Day”. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 2017.

#### **MSc Thesis Completed**

Manuel António, 10/05/2017, “Antiphospholipid-associated immune thrombocytopenia”, University of Lisbon, Supervisor: Valter Fonseca.

#### **PhD Thesis Completed**

Ana Raquel Maceiras de Oliveira, 20/03/2017, “The repertoire and specificity of follicular regulatory T cells”, Faculty of Medicine, University of Lisbon. Supervisor: Luis Graça.

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## Henrique, Domingos

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### Major Interests / Objectives

Research in our laboratory has been focused on understanding how cells decide which differentiation paths they follow during embryonic development to generate tissues and organs. Our aim is to elucidate the gene regulatory networks that control cell-fate decision processes in the embryo, using 2 experimental models: i) embryonic stem cells to study the mechanisms underlying their pluripotent state, and ii) neural retina to investigate how neural progenitors generate the variety of neurons that compose the adult eye. The main goal is to understand the molecular mechanisms governing decision processes that stem/progenitor cells employ to differentiate along various fates, thereby generating correctly patterned tissues and organs.

### Head of Laboratory

Domingos Manuel Pinto Henrique, PhD, Assistant Professor

### Research Team

Gonçalo Filipe Ferreira Fernandes	Master	MSc Student
João Manuel Coelho Carreira	Master	PhD Student
Sara Sofia Gasalho Ferreira	Graduate	Technician (Left January)

### Laboratory Keywords / Research Areas

Stem cells, Notch signalling, Pluripotency, Neurogenesis, Gene regulatory networks, Systems biology.

### Major Scientific Achievements

In 2017, activities in our laboratory included:

- Conclusion of 1 MSc thesis (Gonçalo Fernandes, FCUL);
- Organization of a 8-week course for the LisbonBioMed international PhD Program at iMM;
- Organization of a 1-week course on Stem Cell Biology for the international PhD Program in Bioengineering – Cell Therapies and Regenerative Medicine.

### **Other Projects**

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

### **Other Publications National**

Henrique D, Ramos C (2017). "Fases iniciais do Desenvolvimento do Sistema Nervoso", In Rego AC, Duarte CB, Oliveira CR (eds.), "Neurociências", Lisboa, LIDEL, ISBN 978-972-757-693-7.

### **Communications in International Conferences**

Gaspar C, Rosa A, Henrique D. Unique Dll4 function in regulating the Horizontal cell fate in the developing mouse neural retina. The Notch Meeting X, Athene, Greece, October 1-5, 2017.

### **Internationalisation**

Domingos Henrique participated at lab retreat with the labs of Alfonso Martinez-Arias (Cambridge Univ. Dept Genetics), Thomas Lecuit (IBDM; Marseille, France) and Pierre-François Lenne (IBDM; Marseille, France), where he presented results from the lab and gave a keynote talk.

### **Advanced Teaching**

Henrique D. Organized the 8-week course "Towards a Creative and Critical Mind" for the LisbonBioMed International PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 4-February 26, 2017.

Henrique D. Organized the 2-week course on Stem Cell Biology for the International PhD Program in Bioengineering – Cell Therapies and Regenerative Medicine, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 15-26, 2017.

## Lacerda, João F.

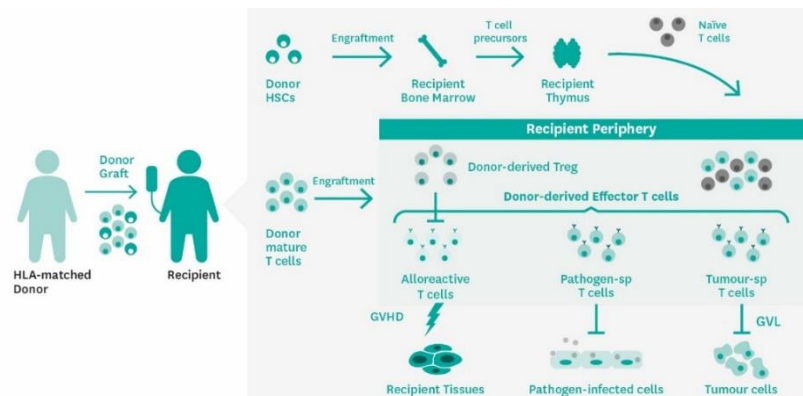
### Major Interests / Objectives

We study immunity after Hematopoietic Stem Cell Transplantation (HSCT), aiming to identify immunological risk factors for complications occurring post-HSCT, such as Graft-versus-Host Disease (GVHD), viral and fungal infections, plus the mechanisms by which these complications emerge. Steroid-resistant GVHD patients are undergoing therapy with donor regulatory T cells (Tregs) while being monitored through immune assays in our lab. We are involved in studies of genetic propensity for invasive fungal infections after HSCT, aiming to identify prognostic markers. We further plan to develop therapies using antigen-specific Tregs to treat GVHD whilst retaining leukemia-specific responses and to use pathogen-specific T cells to treat infections, ultimately aiming to improve HSCT patient survival.

### Head of Laboratory

João Mascarenhas Forjaz de Lacerda, MD/PhD, Associate Professor, Clinical Specialist, Hospital Santa Maria

### Graphical Abstract



### Research Team

Ana Cláudia Batista Jordão Ribeiro	Master	Investigator (Started February)
Ana Cristina Frazão Lopes Alho	MD	PhD Student
Bárbara Coelho da Silva Martins Saraiva	Graduate	Trainee
Ekaterina Minskaia	PhD	Post-Doctoral Investigator
Joana Bianchi Marques Bettencourt Gesta	Master	PhD Student
Laura Ward	PhD	Administrative
Maria Godinho A.V. Duarte Soares	PhD	Principal Investigator

Paulo Nelson Gomes Pereira	PhD	Technician
Rita Isabel Silva de Azevedo	PhD	Post-Doctoral Investigator
Sara Ventura Bucar	Master	Investigator (Left January)

### Laboratory Keywords / Research Areas

Immune reconstitution after hematopoietic stem cell transplantation (HSCT), Graft versus Host Disease (GvHD), Homeostasis of regulatory T cells in patients submitted to HSCT, Adoptive immunotherapy after HSCT, Pathogen-specific immunity after HSCT, Genetic susceptibility for fungal and viral infections.

### Major Scientific Achievements

Completed works:

- Epigenetic control of Foxp3, CAMTA1 and FUT7 genes in human regulatory T cells. (Submitted).
- In vitro recruitment of human regulatory T cells (Treg) in mesenchymal stem cell (MSC) co-cultures (In prep).
- T lymphocyte reconstitution and impact of regulatory T cell (Treg) homeostasis in the maintenance of immune tolerance following allogeneic Hematopoietic Stem Cell Transplantation (In prep).

These contribute significantly to accurate identification of T cell subpopulations, cGVHD pathobiology, immune tolerance and reconstitution post-transplant and mechanisms of MSC-mediated immunomodulation to inform future therapy design.

Since 2015 we have been coordinating a multinational cellular therapy clinical trial. In 2017 we continued to actively recruit patients for the Phase I trial. We are responsible for quality control and deciding the dosage of infused products, plus post-infusion immune monitoring, through FACS and NGS analysis, to track infused clonotypes.

### Selected Publications

Hirakawa M, Matos T, Liu H, Koreth J, Kim HT, Paul NE, Murase K, Whangbo J, Alho AC, Nikiforow S, Cutler C, Ho VT, Armand P, Alyea EP, Antin JH, Blazar BR, Lacerda JF, Soiffer RJ, Ritz J (2016). Low-dose IL-2 selectively activates subsets of CD4+ Tregs and NK cells. *JCI Insight* 1, 18. <https://insight.jci.org/articles/view/89278>. (IF:--, Citations: 10).

Chorny A, Casas-Recasens S, Sintes J, Shan M, Polentarutti N, Garcia-Escudero R, Walland AC, Yeiser JR, Cassis L, Carrillo J, Puga I, Cunha C, Bastos H, Rodrigues F, Lacerda JF, Morais A, Dieguez-Gonzalez R, Heeger PS, Salvatori G, Carvalho A, Garcia-Sastre A, Blander JM, Mantovani A, Garlanda C, Cerutti A (2016). The soluble pattern recognition receptor PTX3 links humoral innate and adaptive immune responses by helping marginal zone B cells. *Journal of Experimental Medicine* 213, 2167. <http://jem.rupress.org/content/213/10/2167.long>. (IF: 11.991, Citations: 6).

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, 646. <http://www.bloodjournal.org/content/bloodjournal/127/5/646.full.pdf>. (IF: 13.164, Citations: 22).

Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Löffler M, Maertens JA, Bell AS, Almeida B, Sousa PS, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano I, Lupi M, Garlanda C, Mantovani A, Velardi A, Romani L, Carvalho A (2014). Genetic deficiency of PTX3 and invasive aspergillosis in stem cell transplantation. *New England Journal of Medicine*, 370(5), 421. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1211161>. (IF: 72.406, Citations: 95).

Azevedo RI, Soares MV, Albuquerque AS, Tendeiro R, Soares RS, Martins M, Ligeiro D, Victorino RM, Lacerda JF, Sousa AE (2013). Long-Term Immune Reconstitution of Naive and Memory T Cell Pools after Haploidentical Hematopoietic Stem Cell Transplantation. *Biology of Blood and Marrow Transplantation* 19, 703. [http://www.bbmt.org/article/S1083-8791\(13\)00053-0/pdf](http://www.bbmt.org/article/S1083-8791(13)00053-0/pdf). (IF: 4.704, Citations: 8).

### Ongoing Research Projects

2015/2019: TREGeneration: Repair of tissue and organ damage in refractory chronic graft versus host disease after hematopoietic stem cell transplantation by infusion of purified allogeneic donor regulatory T lymphocytes. Coordinator: João Mascarenhas Forjaz de Lacerda. Funding Agency: European Commission. Reference: SC3 643776. Amount: € 1 792 894,46. Total Amount: € 5 899 250,00.



### Other Projects

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

### Publications in Peer Review Journals

Cunha C, Gonçalves SM, Duarte-Oliveira C, Leite L, Lagrou K, Marques A, Lupiañez CB, Mesquita I, Gaifem J, Barbosa AM, Pinho Vaz C, Branca R, Campilho F, Freitas F, Ligeiro D, Lass-Flörl C, Löffler J, Jurado M, Saraiva M, Kurzai O, Rodrigues F, Castro AG, Silvestre R, Sainz J, Maertens JA, Torrado E, Jacobsen ID, Lacerda JF, Campos A Jr, Carvalho A (2017). IL-10 overexpression predisposes to invasive aspergillosis by suppressing antifungal immunity. *Journal of allergy and clinical immunology*. 867. (IF:13.081, Citations: 2).

Carvalho A, Duarte-Oliveira C, Gonçalves SM, Campos Jr A, Lacerda JF, Cunha C (2017). Fungal Vaccines and Immunotherapeutics: Current Concepts and Future Challenges. *Curr Fungal Infect Rep*, 11, 16-24. (IF : 0.75, Citations:-).

### Other Publications International

Azevedo R, da Silva CL, Fernandes-Platzgummer A, Minskaia E, Vieira AIS, Cabral JMS, Lacerda JF (2017). Mechanisms of Regulatory T Cell Recruitment by Mesenchymal Stem Cells In Vitro. *Blood*, 130 (Supplement 1), 1161. (IF: 13.164, Citations:--).

Minskaia E, Saraiva B, Soares M, Vieira A, Lacerda JF (2017). Epigenetic control of Foxp3, CAMTA1 and FUT7 genes in human regulatory T cells. *Blood*, 130 (Supplement 1), 1004. (IF: 13.164, Citations:--).

Soares M, Azevedo R, Ferreira I, Bucar S, Ribeiro AC, Ligeiro D, Alho A, Espada E, Junca C, Camacho N, Martins C, Carmo J, Lourenço F, Moreno R, Vaz C, Campos A, Campilho F, Ferreira R, Ritz J, Lacerda F (2017). Increased Naïve and Stem Cell Memory CD8+ T cells in cGVHD. *Blood*, 130 (Supplement 1), 3260. (IF: 13.164, Citations:--).

### **Other Publications National**

Ferrão J, Silva M, Gonçalves L, Gomes S, Loureiro P, Coelho A, Miranda A, Seuanes F, Reis AB, Pina F, Maia R, Kjöllström P, Monteiro E, Lacerda JF6, Lavinha J, Gonçalves J, Faustino P (2017). Widening the spectrum of deletions and molecular mechanisms underlying alpha-thalassemia. *Ann Hematol*, 96, 1921-1929. (IF:3.083, Citations:--).

### **Invited Lectures and Seminars**

Soares MV. Chronic GVHD associates with altered dynamics in T cell reconstitution following Allogeneic Stem Cell Transplantation. XV Congresso de Sociedade Iberica de Citometria, Lisbon, Portugal, May 25-27, 2017.

Lacerda J. T cell homeostasis in chronic graft versus host disease. Faculty of Medicine, University of Porto, Porto, Portugal, April 8, 2017.

Lacerda J. Hematopoietic stem cell transplantation: cell therapies post transplant. APIH, 2º Congresso Hispano-Português de Medicina Transfusional e Terapia Celular, Porto, Portugal, June 3, 2017.

Azevedo R. Células T Reguladoras Naturais, Tregs na doença do enxerto contra o hospedeiro, GVHD, crónico. APIH, 2º Congresso Hispano-Português de Medicina Transfusional e Terapia Celular, Porto, Portugal, June 3, 2017.

Lacerda J. Cellular therapies after hematopoietic stem cell transplantation. 10º Encontro Internacional da SPCE-TC, Covilhã, Portugal, October 13, 2017.

### **Communications in International Conferences**

Azevedo R, Soares M, Ward L, Pinho Vaz C, Edinger M, Baron F, Arpinati M, Warnatz HJ, Yaspo ML, Borodina T, Lehrach H, García-Fiñana M, Koreth J, Ritz J, Lacerda JF. Repair of tissue and organ damage in refractory chronic graft versus host disease after hematopoietic stem cell transplantation by the infusion of purified allogeneic donor regulatory T lymphocytes. European Society for Bone Marrow Transplantation, Marseille, France, March 2017. (Poster Presentation).

Soares M, Azevedo R, Ferreira I, Bucar S, Ribeiro AC, Ligeiro D, Alho A, Espada E, Junca C, Camacho N, Martins C, Carmo J, Lourenço F, Moreno R, Vaz C, Campos A, Campilho F, Ferreira R, Ritz J, Lacerda F. Increased Naïve and Stem Cell Memory CD8+ T cells in cGVHD. American Society of Hematology, Atlanta, USA, December 2017. (Poster Presentation).

Azevedo R, da Silva CL, Fernandes-Platzgummer A, Minskaia E, Vieira AIS, Cabral JMS, Lacerda JF. Mechanisms of Regulatory T Cell Recruitment by Mesenchymal Stem Cells In Vitro. American Society of Hematology, Atlanta, USA, December 2017. (Poster Presentation).

Minskaia E, Saraiva B, Soares M, Vieira A, Lacerda JF. Epigenetic control of Foxp3, CAMTA1 and FUT7 genes in human regulatory T cells. American Society of Hematology, Atlanta, USA, December 2017. (Poster presentation).

Bianchi J, Azevedo R, Ligeiro D, da Silva CL, Lacerda JF. Development of methodologies to recruit and expand regulatory T cells (Tregs) in vitro for subsequent clinical translation. FEBS Immunology Summer School, Hvar, Croatia, December 2017. (Poster Presentation).

#### **Communications in National Conferences**

Saraiva B, Minskaia E, Lacerda J. Focusing on epigenetic control of regulatory T cells. Annual International Medical Students Meeting, Lisbon, Portugal, March 11-13, 2017. (Poster Presentation).

Azevedo R, Soares M, Alho A, Bucar S, Pereira P, Ward L, Pinho Vaz C, Edinger M, Baron F, Arpinati M, Warnatz HJ, Yaspo ML, Borodina T, Lehrach H, García-Fiñana M, Koreth J, Ritz J, Lacerda JF. TREGeneration: Repair of tissue and organ damage in refractory chronic graft versus host disease after hematopoietic stem cell transplantation by the infusion of purified allogenic donor regulatory T lymphocyte. RedeSAÚDE - 3<sup>rd</sup> Innovation Week, Lisbon, Portugal. May 4, 2017. (Oral Presentation).

Soares MV, Azevedo R, Ferreira TI, Bucar S, Alho I, Espada AE, Juncal C, Camacho N, Martins C, Carmo J, Lourenço F, Moreno R, Vaz C, Campos A, Campilho F, Ferreira R, Ritz J, Lacerda JF. Regulatory and conventional T cell dynamics after allogeneic Hematopoietic Stem Cell Transplantation: Chronic Graft versus Host Disease is associated to altered naïve and memory T cell subset pools. RedeSAÚDE - 3<sup>rd</sup> Innovation Week, Lisbon, Portugal. May 4, 2017. (Poster Presentation).

## Organisation of Conferences

Lacerda J. Organizer of TREGeneration General Assembly, Marseille, France, March 24-26, 2017.

## Internationalisation

Our Unit actively collaborated in 2017 with the following investigators:

- Jerome Ritz, Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA, under the sponsorship of the TREGeneration Consortium of the Horizon 2020 Programme.
- Joaquim Cabral, IST-Universidade de Lisboa, also within the framework of Harvard Medical School Portugal Program.
- Matthias Edinger, Universitaetsklinik, Regensburg, under the TREGeneration Consortium of the Horizon 2020 Programme.
- Frederic Baron, Laboratory of Cell and Gene Therapy, CHU Sart-Tilman, Liege, under the TREGeneration Consortium of the Horizon 2020 Programme.
- Mario Arpinati, Department of Hematology “Seragnoli”, University Hospital S. Orsola-Malpighi, Bologna, under the TREGeneration Consortium of the Horizon 2020 Programme.
- John Koreth, Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA, under the auspices of Harvard Medical School Portugal Program and the TREGeneration Consortium of the Horizon 2020 Programme.
- Marie-Laure Yaspo, Max Planck Society, Max Planck Institute for Molecular Genetics, Berlin, under the TREGeneration Consortium of the Horizon 2020 Programme.
- Hans Lehrach, Alacris Theranostics GmbH, Berlin, under the TREGeneration Consortium of the Horizon 2020 Programme and in planning a FET Flagship proposal.
- Marta Garcia-Finana, Department of Biostatistics, Faculty of Health & Life Sciences, University of Liverpool, Liverpool, under the TREGeneration Consortium of the Horizon 2020 Programme.
- Drs. Cristina Cunha and Dr Agostinho Carvalho, Universidade do Minho, for the studies of genetic susceptibility for invasive fungal infections.

- Prof. Britta Eiz-Vesper at the University of Hanover for the generation of third-party pathogen-specific T cells to administer after HSCT.
- Prof. José Antonio Pérez-Simón at the University of Seville in proposing addition to the TREGeneration Consortium of the Horizon 2020 Programme.

### **Advanced Teaching**

Soares M. Lecturer. CD4+ T cell Reconstitution following allogeneic HSCT: Insights into cGVHD development. LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 2, 2017.

## Lopes, Luísa V.

### Major Interests / Objectives

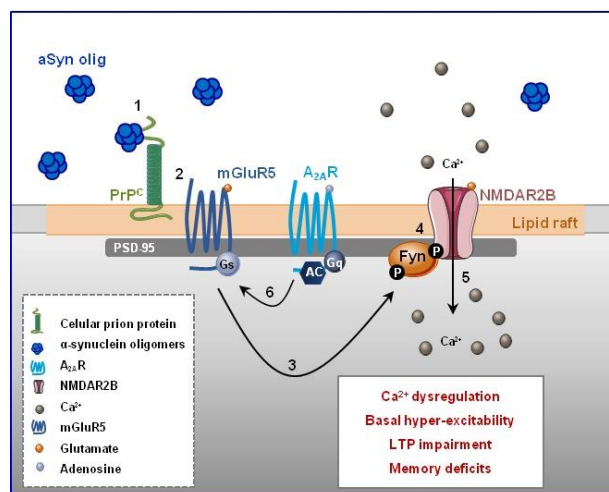
Ageing, stress and neurodegenerative diseases are among the conditions that contribute to the accelerated loss of cognitive function. Our group's work is focused on understanding the mechanisms inducing this "early-ageing", which render the hippocampus - the brain area related to learning and memory – particularly susceptible.

We focus on characterizing the molecular mechanisms associated to hippocampal loss of function and its outcome in behavior performance and synaptic function, using rodent models. We ensure the translation to the human brain, by testing these molecular imprints in healthy and diseased human brain tissue. We are currently focused into exploring the role of adenosine A2A receptors as potential cognitive modulators both in vitro and in vivo.

### Head of Laboratory

Luísa Maria Vaqueiro Lopes, PhD

### Graphical Abstract



### Research Team

Ana Carolina Amaral Peixoto	Master	MSc Student
Ana Inês Marques Morgado	Master	PhD Student
Diana Gabriela Ribeiro Ferreira	Master	PhD Student, University Medical Center Goettingen, Department of NeuroDegeneration and Restorative Research, Faculdade Medicina da Universidade do Porto

Hugo Vicente Miranda	PhD	Post-Doctoral Investigator, Faculdade Medicina da Universidade Nova de Lisboa
Joana Fernandes Esteves Soares Coelho	PhD	Post-Doctoral Investigator
João Pedro da Costa Alvares Viegas Nunes	PhD	Investigator (Started November)
Marcos António dos Santos Rodrigues Gomes	Master	Technician
Mariana Temido Mendes Ferreira	Master	PhD Student, NA
Miguel Alves Rovisco Ribeiro	Master	Trainee
Rui Artur Paiva Loureiro Gomes	PhD	Investigator, Assistant Professor

### Laboratory Keywords / Research Areas

Aging, Neurosciences, Cognition, Hippocampus.

### Major Scientific Achievements

Synucleinopathies such as Parkinson's disease (PD) and dementia with Lewy bodies are characterized by the accumulation of alpha-synuclein (aSyn) in intracellular inclusions. We have been exploring the mechanism by which extracellular aSyn oligomers may affect cognition by damaging the hippocampus, crucial for memory formation in collaboration with Tiago Outeiro (Faculty Medicine Goettingen, Germany), in two former papers (2012 and 2015).

In a paper published in Nature Neuroscience this year, we identified the cellular prion protein (PrPC) as a key mediator in aSyn-induced synaptic impairment, hence suggesting a general role for PrPC beyond prion diseases. We show that extracellular aSyn oligomers form a complex with PrPC inducing the phosphorylation of Fyn kinase via metabotropic glutamate receptors 5 (mGluR5). aSyn engagement of PrPC/Fyn activates NMDA receptor and alters calcium homeostasis. The delineation of a PrPC -mGluR5-Fyn pathway controlled by A2AR in glutamatergic synapses, hints at a common underlying mechanism in early cognitive deficits, which we will further explore.

### Selected Publications

Ferreira DG, Temido-Ferreira M, Miranda HV, Batalha VL, Coelho JE, Szego EM, Marques-Morgado I, Vaz SH, Rhee JS, Schmitz M, Zerr I, Lopes LV\*, Outeiro TF\*. (\*co-senior author) (2017). alpha-Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B. Nature Neuroscience, doi: 10.1038/nn.4648. <https://www.nature.com/articles/nn.4648>. (IF: 17.839, Citations: 2).

Laurent C, Burnouf S, Ferry B, Batalha VL, Coelho JE, Baqi Y, Malik E, Mariciniak E, Parrot S, Van der Jeugd A, Faivre E, Flaten V, Ledent C, D'Hooge R, Sergeant N, Hamdane M, Humez S, Müller CE, Lopes LV, Buée L, Blum D (2014). A2A adenosine receptor deletion is protective in a mouse model of Tauopathy. *Molecular Psychiatry* doi: 10.1038/mp.2014.151. Epub 2014 Dec 2. 21, 97-107. 2016 Jan;21(1):97-107. (IF: 13.204, Citations:--)

Sousa VC, Vital J, Costenla AR, Batalha VL, Sebastiao AM, Ribeiro JA, Lopes LV (2016). Maternal separation impairs long term-potentiation in CA1-CA3 synapses and hippocampal-dependent memory in old rats. *Molecular Psychiatry*, 21, 97. (IF: 13.204, Citations: 28).

Batalha VL, Ferreira DG, Coelho JE, Valadas JS, Gomes R, Temido-Ferreira M, Shmidt T, Baqi Y, Bue L, Muller CE, Hamdane M, Outeiro TF, Bader M, Meijsing SH, Sadri-Vakili G, Blum D, Lopes LV (2016). The caffeine- binding adenosine A2A receptor induces age-like HPA-axis dysfunction by targeting glucocorticoid receptor function. *Scientific Reports*, doi: 10.1038/srep31493. (IF: 4.259, Citations: 5).

Batalha VL, Pego JM, Fontinha BM, Costenla AR, Valadas JS, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV (2013). Adenosine A(2A) receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *MOLECULAR PSYCHIATRY*, 18, 320. <http://www.ncbi.nlm.nih.gov/pubmed/22371048>. (IF: 13.204, Citations: 44).

Diógenes MJ, Dias RB, Rombo DM, Vicente Miranda H, Maiolino F, Guerreiro P, Näsström T, Franquelim HG, Oliveira LM, Castanho MA, Lannfelt L, Bergström J, Ingelsson M, Quintas A, Sebastião AM, Lopes LV, Outeiro TF (2012). Extracellular alpha-synuclein oligomers modulate synaptic transmission and impair LTP via NMDA-receptor activation. *Journal of Neuroscience* 32, 11750. (IF: 5.988, Citations: 73).

### **Ongoing Research Projects**

2016/2019: Targeting the glycation defenses as a protective strategy for Parkinson's disease. Coordinator: Luísa Maria Vaqueiro Lopes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/NEU-OSD/5644/2014. Amount: € 51 000,00. Total Amount: € 199 961,00.



2016/2019: Microglia dysregulation as trigger for chronic brain inflammation. Coordinator: Joana Fernandes Esteves Soares Coelho. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MEC/4778/2014. Amount: € 195 035,00. Total Amount: € 195 035,00.

### Other Projects

2016/2018: SynaNet: Neurologic and Psychiatric disorders: from synapses to networks. Coordinator: Ana Maria Ferreira de Sousa Sebastião. Funding Agency: European Commission. Reference: TWINNING 692340. Amount: € 525 437,50. Total Amount: € 999 996,25.

### Publications in Peer Review Journals

Ferreira DG, Temido-Ferreira M, Miranda HV, Batalha VL, Coelho JE, Szego EM, Marques-Morgado I, Vaz SH, Rhee JS, Schmitz M, Zerr I, Lopes LV\*, Outeiro TF\*. (\*co-senior author) (2017). alpha-Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B. *Nature Neuroscience* doi: 10.1038/nn.4648. (IF: 17.839, Citations: 2).

Rivero-Segura NA, Flores-Soto E, Garcia de la Cadena S, Coronado-Mares I, Gomez-Verjan JC, Ferreira DG, Cabrera-Reyes EA, Lopes LV, Massieu L, Cerbon M (2017). Prolactin-induced neuroprotection against glutamate excitotoxicity is mediated by the reduction of [Ca<sup>2+</sup>]<sub>i</sub> overload and NF- $\kappa$ B activation. *PLoS One*. 2017 May 5;12(5):e0176910. doi: 10.1371/journal.pone.0176910. (IF: 2.806, Citations: 1).

Duroux R, Renault N, Coelho JE, Agouridas L, Blum D, Lopes LV, Melnyk P, Yous S. (2017) Design, synthesis and evaluation of 2-aryl benzoxazoles as promising hit for the A2A receptor. *J Enzyme Inhib Med Chem*. 2017 Dec;32(1):850-864. doi: 10.1080/14756366.2017.1334648. (IF: 4.293, Citations:--).

Miranda HV, Szego EM, Oliveira LM, Breda C, Darendelioglu E, de Oliveira RM, Ferreira DG, Gomes MA, Rott R, Oliveira M, Munari F, Enguita FJ, Simoes T, Rodrigues EF, Heinrich M, Martins IC, Zamolo I, Riess O, Cordeiro C, Ponces-Freire A, Lashuel HA, Santos NC, Lopes LV, Xiang W, Jovin TM, Penque D, Engelender S, Zweckstetter M, Klucken J, Giorgini F, Quintas A, Outeiro TF (2017). Glycation potentiates  $\alpha$ -synuclein-associated neurodegeneration in synucleinopathies. *Brain*. doi: 10.1093/brain/awx056. (IF: 10.292, Citations:--).

Mouro FM, Batalha VL, Ferreira DG, Coelho JE, Baqi Y, Muller CE, Lopes LV, Ribeiro JA, Sebastiao AM (2017). Chronic and acute adenosine A2A receptor blockade prevents long-term episodic memory disruption caused by acute cannabinoid CB1 receptor activation. *Neuropharmacology*; 117:316-327. doi: 10.1016/j.neuropharm.2017.02.021. (IF: 5.012, Citations:--).

de Oliveira RM\*, Miranda HV\*, Outeiro TF (2017). The mechanism of Sirtuin 2-mediated exacerbation of alpha-synuclein toxicity in models of Parkinson's disease. *PLoS Biology*; 15(3):e2000374. (IF: 12.595, Citations: 8).

Miranda HV\*, Outeiro TF\*. Posttranslational modifications of blood-derived alpha-synuclein as biochemical markers for Parkinson's disease. *Scientific Reports*; 7:13713. (IF: 4.259, Citations:--).

#### **Other Publications International**

Blum D, Lopes LV. Editors. (2017) - Adenosine Receptors in Neurodegenerative Diseases, 1<sup>st</sup> Edition eBook ISBN: 978012803745, Elsevier Publishing.

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

Lopes LV. Early synaptic deficits in Parkinson's disease. INSERM Lille, France, June 2017.

Lopes LV. Plenary Speaker. My brain on a 24/7 schedule – impact on memory. XV Meeting of the Portuguese Society for Neurosciences, Braga, Portugal, May 25-26, 2017.

Lopes LV. Plenary Speaker. Early synaptic deficits and caffeine analogues. Universidade Autonoma Mexico, Mexico, March 2017.

#### **Communications in International Conferences**

Ferreira DG, Marques-Morgado I, Lopes LV, Outeiro TF. PrPC mediates synaptic damage triggered by alpha-synuclein oligomers. AD/PD 2017, Vienna, Austria, March 2017.

Melnyk P, Duroux R, Renault N, Coelho JE, Agouridas L, Blum D, Buée L, Furman C, Lopes LV, Yous S. From Virtual Screening to Pharmacological Evaluation of Quinazoline Derivatives as Adenosine A2a Receptor Antagonists for the Potential Treatment of Alzheimer Disease. AD/PD 2017, Vienna, Austria, March 2017.

Melnyk P, Duroux R, Renault N, Coelho JE, Agouridas L, Blum D, Buée L, Furman C, Lopes LV, Yous S. A2A Receptor Antagonists for the Treatment of Alzheimer Diseases: Design, Synthesis and Biological Evaluation of a New Benzoxazole Family. AD/PD 2017, Vienna, Austria, March 2017.

Miranda H, Outeiro TF.  $\alpha$ -synuclein posttranslational modifications as blood biomarkers for Parkinson's disease. AD/PD 2017, Vienna, Austria, March 2017. (Poster Presentation).

Faivre E, Carvalho K, Coelho J, Batalha V, Ferreira DG, Laurent C, Cellai L, Besegher M, Tailieu D, Hamdane M, Buée L, Lopes LV, Blum D. A receptor dysregulation: an instrumental role in Alzheimer's disease? EuroTau meeting, Lille, France, April 2017.

Carvalho K, Faivre E, Coelho JE, Zornbach K, Malik E, Marciniak E, Cellai L, Carvalho K, Flaten V, Demeyer D, Eddarkaoui S, Caillierez R, Schneider M, Humez S, Sergeant N, Chern Y, Muller CE, Buée L, Halle A, Lopes LV, Blum D. Oral administration of a caffeine analog, the A2AR antagonist MSX-3, reduces memory deficits and amyloid levels of APP/PS1dE9 mice. Conférences Jacques Monod, Roscoff, France, June 2017

Faivre E, Carvalho K, Coelho J, Cellai L, Besegher M, Tailieu D, Hamdane M, Buée L, Lopes LV, Blum D. Astrocytic adenosine A2A receptor dysregulation: An instrumental role in the development of Alzheimer's disease. Conférences Jacques Monod, Roscoff, France, June 2017.

Batalha VL, Ferreira DG, Coelho JE, Valadas J, Gomes R, Temido-Ferreira M, Shmidt T, Baqi L, Bue L, Muller CE, Hamdane M, Outeiro TF, Bader M, Meijnsing SH, Sadri-Vakili G, Blum D, Lopes LV. The caffeine-binding adenosine A2A receptor induces age-like HPA-axis dysfunction by targeting glucocorticoid receptor function. 2017 Chronobiology Workshop of the Sleep and Circadian Neuroscience Summer School, University of Oxford, Oxford, England, September 2017. (Poster Presentation).

Marques-Morgado I, Coelho J, Gomes R, Ribeiro M, Bader M, Blum D, Lopes LV. Neuronal Adenosine A2A receptor overexpression induces age-like alterations in microglial and astroglial phenotypes. 2017 Chronobiology Workshop of the Sleep and Circadian Neuroscience Summer School, University of Oxford, Oxford, England, September 2017. (Poster Presentation).

Temido-Ferreira M, Coelho JE, Ferreira DG, Lopes LV. Properties of long-term depression upon aging. 47<sup>th</sup> Annual Meeting of the Society for Neuroscience, Washington, USA, November 2017. (Poster Presentation).

Faivre E, Coelho J, Zornbach K, Malik E, Marciniak E, Cellai L, Carvalho K, Flaten V, Demeyer D, Eddarkaoui S, Caillierez R, Schneider M, Humez S, Sergeant N, Chern Y, Muller CE, Buée L, Halle A, Lopes LV, Blum D. Oral administration of a caffeine analog, the A2AR antagonist MSX-3, reduces memory deficits and amyloid levels of APP/PS1dE9 mice. FHU VasCog Meeting, Lille, France, 2017.

Carvalho K, Faivre E, Coelho J, Cellai L, Humez S, Hamdane M, Buée L, Lopes LV, Blum D. Neuronal and astrocytic upregulation of the caffeine-binding adenosine A2A receptor is detrimental for cognition in a mouse model of Alzheimer's disease like Tau-pathology. FHU VasCog meeting, Lille, France, 2017.

Carvalho K, Faivre E, Coelho J, Zornbach K, Malik E, Marciniak E, Cellai L, Carvalho K, Flaten V, Demeyer D, Eddarkaoui S, Caillierez R, Schneider M, Humez S, Sergeant N, Chern Y, Muller CE, Buée L, Halle A, Lopes LV, Blum D. Chronic treatment with an adenosine A2AR antagonist, ameliorates amyloid pathology and memory deficits in the APP/PS1dE9 model of amyloidogenesis. EURON Meeting, Lille, France, 2017.

#### **Communications in National Conferences**

Temido-Ferreira M, Ferreira DG, Coelho JE, Bader M, Outeiro TF, Marie H, Pousinha PA, Lopes LV. Neuronal adenosine A2A receptor overexpression shifts long-term depression in CA1/CA3 hippocampal synapses. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 2017. (Poster Presentation).

Marques-Morgado I, Coelho JE, Gomes R, Ribeiro M, Bader M, Blum D and Lopes LV. Neuronal Adenosine A2A receptor overexpression induces age-like alterations in microglial and astroglial phenotypes. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 2017. (Poster Presentation).

Marques-Morgado I, Coelho JE, Gomes R, Ribeiro M, Bader M, Blum D and Lopes LV. Overexpression of Adenosine A2A receptor in forebrain neurons induces age-like alterations in microglial and astroglial phenotypes. XLVII Meeting of the Portuguese Society for Pharmacology, Coimbra, Portugal, February 2017. (Oral Communication).

Temido-Ferreira M, Ferreira DG, Coelho JE, Marie H, Pousinha PA, Outeiro TF, Lopes LV. Neuronal adenosine A2A receptor overexpression leads to long-term depression shift caused by NMDAR overexpression in CA1/CA3 hippocampal synapses. XLVII Meeting of the Portuguese Society for Pharmacology, Coimbra, Portugal, February 2017. (Oral communication).

Ribeiro M, Brigas H, Santa C, Valente C, Temido-Ferreira M, Ferreira DG, Coelho J, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. gd T cells are the major source of IL-17 in the meninges and control brain cognitive functions. XVI Portuguese Society for Neuroscience Meeting, Braga, Portugal, May 25-26, 2017.

Marques-Morgado I, Blum D, Coelho JE, Lopes LV. Impact of neuronal adenosine A2A receptor overexpression on glial phenotype of the hippocampus. XVI Portuguese Society for Neuroscience Meeting, Braga, Portugal, May 2017. (Poster Presentation).

Temido-Ferreira M, Ferreira DG, Coelho J, Bader M, Marie H, Pousinha PA, Outeiro TF, Lopes LV. Reversion of age-related changes in long-term depression by adenosine A2A receptor blockade. XVI Portuguese Society for Neuroscience Meeting, Braga, Portugal, May 2017. (Poster Presentation).

Temido-Ferreira M, Ferreira DG, Coelho JE, Bader M, Marie H, Pousinha PA, Outeiro TF, Lopes LV. Properties of long-term depression upon aging. XI IMM/CAML PhD Students Meeting, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Vicente Miranda H, Outeiro TF. Sour side of sugars: Glycation in Huntington's disease. Jornadas Lusófonas de Nutrição, Universidade Lusófona, Lisbon, Portugal. (Oral Presentation).

### **Organisation of Conferences**

Lopes LV. Scientific Committee. XVI Portuguese Society for Neuroscience Meeting, Braga, Portugal, May 2017.

### **Internationalisation**

2 published papers resulting from exchange students (Nadia Rivero, Mexico and Romain Duroux, France) in the lab.

13 communications in international meetings (France, UK, USA).

New collaborations with Mikko Hiltunen (University Eastern Finland) and Neil Dawson (University Lancaster, England) with joint projects and student exchange.

Several joint communications and papers with colleagues from France, Germany and US.

Lopes LV. Invited speaker in Lille, France and in Univ Autonoma Mexico.

### **Prizes, Honours and Awards**

Lopes LV. Honorable Mention Universidade de Lisboa /Caixa Geral de Depósitos Award.

### **Advanced Teaching**

Lopes LV (Since 2017) - STEM mentor for the New York Academy of Sciences Scholar Program.

Lopes LV (Since 2017) - Member of the Parkinson's UK Grant Assessment Panel (GAP2).

Lopes LV. Effects of stress on memory. Faculty the Neurosciences MSc/PhD program at the Faculty of Medicine, University of Lisbon, Lisbon, Portugal.

Lopes LV - Faculty of the IMM Biomed PhD Program (Neuroscience module).

### **Science and Society**

Lopes LV. Resident neuroscientist in the prime-time TV show 'Os Extraordinários' broadcasted by RTP public chain – translating complex brain functions to lay public audience. Collaboration with several media (radio, TV and newspapers) on neuroscience issues.

National and international press coverage on the occasion of the publication of the Nature Neuroscience paper (2017): TV, Newspapers and Radio.

### **MSc Thesis Completed**

Bárbara Gomes, 27/11/2017, "Targeting the glycation defenses as a protective strategy for Parkinson's disease", University of Lisbon. Supervisor: Hugo Miranda.

Ana Carolina Amaral Peixoto, 19/12/2017, "Genetic deletion of adenosine A2A receptor in mice model of Alzheimer's disease: impact on synaptic plasticity", University of Lisbon. Supervisor: Luisa Lopes and Mariana Temido.

### **PhD Thesis Completed**

Diana Ferreira, 30/12/2017, “Unraveling the role of adenosine A2A receptors on alpha-synuclin mediated toxicity”, University of Porto Doctoral Program 2017 (thesis approved in December 2017, defense in February 2018), University of Porto. Supervisor: Tiago Outeiro and Luisa Lopes.

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## Morais, Nuno

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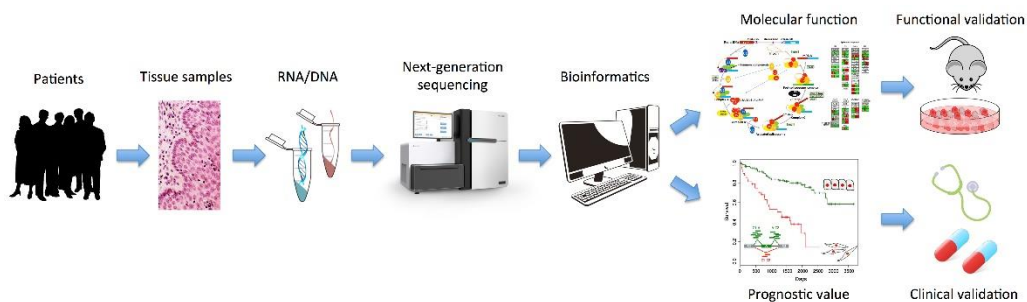
### Major Interests / Objectives

We have a long-term interest in the systems-level transcriptional regulation underlying mammalian cell specification, often perturbed in disease. In particular, we are studying the mechanisms responsible for the association between aberrant transcription and splicing and pathologies like cancer and neurodegenerative disorders. We employ computational biology approaches for the analysis of next-generation sequencing data to find disease-specific transcriptomic signatures, aiming to understand how the regulation of alternative splicing is affected in different pathologies and thereby to identify molecular targets for functional exploration *in vitro* and *in vivo*. We also combine molecular and clinical information for the unveiling of novel candidate prognostic factors and therapeutic targets.

### Head of Laboratory

Nuno Luís Barbosa Morais, PhD

### Graphical Abstract



### Research Team

Ana Carolina de Sousa Leote	Master	Investigator
Bernardo Lucas Carvalho Pereira de Almeida	Graduate	MSc Student
Joel Amaque da Silva Indi	Master	PhD Student (Started June)
Lina Marcela Gallego Páez	PhD	Post Doctoral Investigator
Maria Teresa Proença Mendes Maia	PhD	Post-Doctoral Investigator
Mariana Ascensão Ferreira	Master	PhD Student (Started March)
Marie Catherine Bordone	Master	PhD Student
Nuno Daniel Saraiva Agostinho	Master	PhD Student (Started September)



### **Laboratory Keywords / Research Areas**

Alternative splicing, Transcriptional regulation, Ageing and neurodegenerative disease, Cancer, Transcriptomics, Computational biology.

### **Major Scientific Achievements**

Six lab members wrote a review article, published in *Human Genetics*, on the role of alternative splicing in human biological systems. Nuno Morais was involved in collaborations with the labs of Henrique Veiga-Fernandes and Luisa Figueiredo that yielded publications in *Nature* and *Nature Microbiology*, respectively. Lina Gallego and Nuno Agostinho were also involved in collaborations that yielded publications in *Cell Reports* and *Databases*, respectively.

Lina Gallego was a finalist in the iMM innovators competition and selected for the Biomed X Innovation Center Bootcamp (Heidelberg, Germany), having also received a ReTuBi scholarship conference award.

Nuno Agostinho was awarded an FCT Scholarship to do his PhD in the lab.

Bernardo Almeida completed his Master thesis in Oncobiology with the maximum grade, getting the 2<sup>nd</sup> Prize in the “Best Master Thesis” Awards from iMM and the 2<sup>nd</sup> place in the AstraZeneca Innovate Competition - Translational Research Award.

### **Selected Publications**

Gallego-Paez LM, Bordone MC, Leote AC, Saraiva-Agostinho N, Ascensão-Ferreira M, Barbosa-Morais NL (2017). Alternative splicing: the pledge, the turn, and the prestige: The key role of alternative splicing in human biological systems. *Human Genetics* 136, 1015. (IF: 4.637, Citations: 5).

Cardoso V, Chesné J, Ribeiro H, García-Cassani B, Carvalho T, Bouchery T, Shah K, Barbosa-Morais NL, Harris N, Veiga-Fernandes H (2017). Neuronal regulation of type 2 innate lymphoid cells via neuromedin U. *Nature* 549, 277. (IF: 40.137, Citations: 7).

Braunschweig U, Barbosa-Morais NL, Pan Q, Nachman EN, Alipahani B, Gonatopoulos-Pournatzis T, Frey B, Irimia M, Blencowe BJ (2014). Widespread intron retention in mammals functionally tunes transcriptomes. *Genome Research* 24, 1774. (IF: 11.992, Citations: 127).

Han H, Irimia M, Ross PJ, Sung HK, Alipanahi B, David L, Golipour A, Gabut M, Michael IP, Nachman EN, Wang E, Trcka D, Thompson T, O'Hanlon D, Slobodeniuc V, Barbosa-Morais NL, Burge CB, Moffat J, Frey BJ, Nagy A, Ellis J, Wrana JL, Blencowe BJ (2013). MBNL proteins repress ES-cell-specific alternative splicing and reprogramming. *Nature* 498, 241. (IF: 40.137, Citations: 114).

Barbosa-Morais NL, Irimia M, Pan Q, Xiong HY, Gueroussov S, Lee LJ, Slobodeniuc V, Kutter C, Watt S, Colak R, Kim T, Misquitta-Ali CM, Wilson MD, Kim PM, Odom DT, Frey BJ, Blencowe BJ (2012). The evolutionary landscape of alternative splicing in vertebrate species. *Science* 338, 1587. (IF: 37.205, Citations: 312).

### **Ongoing Research Projects**

2017/2020: GENOME Portugal. Coordinator: Nuno Luís Barbosa Morais. Funding Agency: Portugal 2020. Reference: PINFRA/22134/2016. Amount: € 123 711,00. Total Amount: € 826 226, 00.

2016/2019: PERSEIDS: Personalização de Terapêuticas Oncológicas através de modelação integrada e decisão. Nuno Luís Barbosa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/EMS-SIS/0642/2014. Amount: € 70 408,00. Total Amount: € 199 997,00.

2016/2017: Alternative splicing during neuronal development. Coordinator: Nuno Luís Barbosa Morais. Funding Agency: Fundação AstraZeneca. Reference: FPJ001027. Amount: € 5 000,00. Total Amount: € 5 000,00.

2016/2017: RNA regulation in colorectal cancer: transcriptomic landscapes of metastasis and their clinical implications. Coordinator: Nuno Luís Barbosa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: DEP 2016 NMorais. Amount: € 25 000,00. Total Amount: € 25 000,00.

2015/2019: Transcriptomic landscapes of cancer: studying the transcriptional etiology of metastization and its implications on personalized therapeutics. Coordinator: Nuno Luís Barbosa Morais. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG NMorais. Amount: € 250 000,00. Total Amount: € 250 000,00.

2015/2019: RNA regulation in cancer: defining the transcriptional etiology of metastasis its implications on personalized therapeutics. Coordinator: Nuno Luís Barbosa Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00595/2014/CP1236/CT0002. Amount: € 50 000,00. Total Amount: € 50 000,00.

#### **Other Projects**

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

2015/2018: Angiocrine factors as modulators of spinal cord regeneration. Coordinator: Maria Leonor Tavares Saúde. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MED/3295/2014. Amount: € 186 229,00. Total Amount: € 186 229,00.

#### **Publications in Peer Review Journals**

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais NL, Takahashi JS, Figueiredo LM (2017). Trypanosoma brucei metabolism is under circadian control. *Nat Microbiol* 2, 17032 (IF: Citations: 6).

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 Rep* 18, 334-343 (IF: 8.282, Citations: 9).

Deng M, Brägelmann J, Kryukov I, Saraiva-Agostinho N, Perner S (2017). FirebrowseR: an R client to the Broad Institute's Firehose Pipeline. *Database (Oxford)*; doi: 10.1093/database/baw160 (IF: 3.290, Citations: 1).

#### **Other Publications National**

de Almeida BP, Marteil G, Bettencourt-Dias M, Barbosa-Morais NL (2017). Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer. *Porto Biomedical Journal*, 2(5):182.

### **Invited Lectures and Seminars**

Barbosa-Morais NL. Profiling alternative splicing in evolution and disease. International Institute of Molecular and Cell Biology, Warsaw, Poland, January 19, 2017.

Barbosa-Morais NL. My way into Computational Biology. Career Path Day, International Institute of Molecular and Cell Biology, Warsaw, Poland, January 19, 2017.

Barbosa-Morais NL. Computational Biology: splicing in evolution and disease. X Encontro Nacional dos Estudantes de Engenharia Biomédica, Coimbra, Portugal, March 3, 2017.

Barbosa-Morais NL. Alternative splicing landscapes of ageing and neurodegeneration. CEDOC, Lisbon, Portugal, April 5, 2017.

Barbosa-Morais NL. Computational biology, splicing, evolution and cancer. IHMT PhD Students Retreat, Sesimbra, Portugal, May 28, 2017.

### **Communication in International Conferences**

de Almeida BP, Marteil G, Bettencourt-Dias M, Barbosa-Morais NL. Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer. 3<sup>rd</sup> EACR Conference on Cancer Genomics, Cambridge, England, June 25-28, 2017. (Poster Presentation).

Gallego-Paez L, Martins M, Barbosa-Morais N. CELF2 at the core of a prognostic alternative splicing signature in colorectal cancer. Forty Years of mRNA Splicing, Cold Spring Harbor Laboratory, New York, USA, October 22-25, 2017. (Poster Presentation).

Saraiva-Agostinho N, Barbosa-Morais N. Psychomics - A bioinformatics application for the quantification, analysis and visualisation of alternative splicing from large transcriptomic datasets. Forty Years of mRNA Splicing, Cold Spring Harbor Laboratory, New York, USA, October 22-25, 2017. (Poster Presentation).

Gallego-Paez LM, Martins M, Barbosa-Morais N. CELF2 at the core of a prognostic alternative splicing signature in colorectal cancer. EMBL Conference - Cancer Genomics, European Molecular Biology Laboratory, Heidelberg, Germany, November 5-8, 2017. (Poster Presentation).

### **Communication in National Conferences**

Saraiva-Agostinho, N. Psychomics: Alternative Splicing Quantification, Analysis and Visualisation in Cancer Data. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Oral Presentation).

Leote AC, Barbosa-Morais N. Genomewide profiling of alternative splicing in ageing across human tissues. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Poster Presentation).

de Almeida BP, Marteil G, Bettencourt-Dias M, Barbosa-Morais NL. Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer. 12<sup>th</sup> Young European Scientists Meeting, Porto, Portugal, September 14-17, 2017. (Oral Presentation)

de Almeida BP, Marteil G, Bettencourt-Dias M, Barbosa-Morais NL. Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer. iMed 9.0 Conference, Lisbon, Portugal, October 25-29, 2017. (Oral Presentation).

### **Internationalisation**

Our lab is now mentored by Professor Chris Ponting (University of Edinburgh, Scotland).

Our collaborations with Jesus Gil (Imperial College London, England) on the role of alternative splicing in cell senescence, with Julian Koenig (IMB Mainz, Germany) on the impact of cancer-associated DNA variants on oncogenic splicing deregulation, and with Yogesh Kulathu (University of Dundee, Scotland) on alternative splicing of deubiquitylating enzymes yielded manuscripts under review.

We carried on collaborations with Anna Sablina (VIB-KU Leuven, Belgium) on the impact of hypoxia on alternative splicing and George Garinis (FORTH Crete, Greece) on the impact of TC-NER perturbations on splicing.

We started collaborating with Jernej Ule (Crick Institute London, England) in the context of our project on the prognostic value of alternative splicing deregulation in colorectal cancer. We also started a collaborative effort with a Cancer Research UK team based in Cambridge, led by Professor Sir Bruce Ponder, on the interaction between genetic background and smoking in lung cancer.

Nuno Morais gave two invited talks at the International Institute of Molecular and Cell Biology in Warsaw, Poland (January) and presented two posters at the Meeting on the Forty Years of mRNA Splicing in Cold Spring Harbor Laboratory, New York, USA (October). He also lectured to an international audience at the ReTuBi Joint Summer School in Lisbon (May) and lectured in and organized the Bioinformatics course of the Gulbenkian Graduate Program Science for Development in Praia, Cape Verde (February). Bernardo Almeida presented a poster at the 3<sup>rd</sup> EACR Conference on Cancer Genomics in Cambridge, England (June). Lina Gallego presented a poster at the EMBL Conference on Cancer Genomics in Heidelberg, Germany (November).

### **Prizes, Honours and Awards**

Almeida B. 2<sup>nd</sup> Prize in the “Best Master Thesis” Awards, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal.

Almeida B. 2<sup>nd</sup> place in the AstraZeneca Innovate Competition - Translational Research Award.

Gallego-Paez L. ReTuBi scholarship conference award.

Agostinho N. FCT PhD Scholarship.

### **Advanced Teaching**

Barbosa-Morais N. Lecturer. LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 10, 2017.

Barbosa-Morais N. Lecturer and Organizer. Bioinformatics course of the Gulbenkian Graduate Program Science for Development (PGCD), Praia, Cape Verde, February 6-10, 2017.

Barbosa-Morais N. Lecturer. ReTuBi Joint Summer School, Lisbon, Portugal, May 29, 2017.

### **Science and Society**

Barbosa-Morais N contributed to an article in Visão magazine, aimed at the public, on how to use genetic information against cancer.

Barbosa-Morais N remained a member of the Executive Committee of PAPS (Portuguese-American Post-graduate Society).

### **MSc Thesis Completed**

Bernardo Almeida, 04/12/2017, “Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer”, University of Algarve. Supervisor: Nuno Barbosa Morais and Ana Teresa Maia.

## Morais, Vanessa

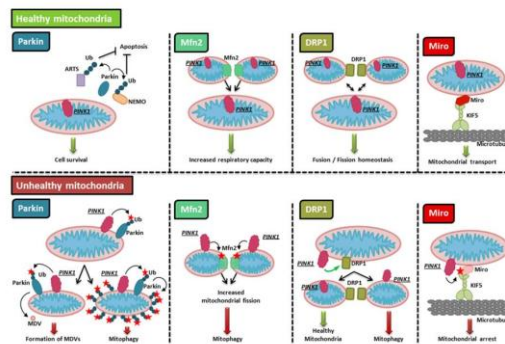
### Major Interests / Objectives

Mitochondria homeostasis is a process involving an intimate crosstalk between energy production and intrinsic quality control. Perturbances of this intricate crosstalk can be fatal for the mitochondria itself or for its host cell. Mitochondria at the synapse have a pivotal role in synapse maintenance and neurotransmitter release. Therefore, mitochondrial function is crucial for the maintenance of a healthy brain. My research focuses on unraveling how synaptic mitochondria have learnt to adapt to their environmental demands, and decipher the mechanisms involved in mitochondrial quality control processes and bioenergetic compensation pathways. Ultimately, the overarching goal is to reveal how the disruption of these acquired mechanisms contributes to neurodegeneration.

### Head of Laboratory

Vanessa Alexandra dos Santos Morais, PhD

### Graphical Abstract



### Research Team

Andreia Sofia Faria Pereira	Master	PhD Student
Carlos Eduardo Cardanho dos Ramos	Master	Investigator (Started December)
Elvira Pequeno Leites	Master	PhD Student (Started March)
Filipa Alexandra Barroso Gonçalves	Master	Investigator
Filipa Sofia Libório Carvalho	PhD	Post-Doctoral Investigator
Filipe Carlos Pereira dos Reis Cortes Figueiredo	MD	PhD Student (Started October)
Rita Abrunhosa Soares	Master	PhD Student (Started March)



### Laboratory Keywords / Research Areas

Mitochondria, Neurodegeneration, Mitophagy, Quality control, Parkinson's disease, mtDNA.

### Major Scientific Achievements

Over the year of 2017, the laboratory had as scientific output 2 peer-reviewed publications (Journal Cell Biol; Biol Psychiatry), 1 review (Biochem Biophys Res Commun) and 1 book chapter (Elsevier publications). Additionally, several lab members attended international and national scientific meetings where their scientific project was presented either as a poster communication or as a selected oral presentation (EMBO/FENS Lecture Course).

### Selected Publications

Aerts L, Craessaerts K, De Strooper B, Morais VA (2015). PINK1 Kinase Catalytic Activity Is Regulated by Phosphorylation on Serines 228 and 402. *J Biol Chem* 290, 2798. (IF: 4.125, Citations: 28).

O'flanagan CH, Morais VA, Wurst W, De Strooper B, O'Neill C (2015). The Parkinson's gene PINK1 regulates cell cycle progression and promotes cancer-associated phenotypes. *Oncogene* 34, 1363. (IF: 7.519, Citations: 25).

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\*, \*shared corresponding authors (2014). PINK1 Loss of Function Mutations Affect Mitochondrial Complex I Activity via NdufA10 Ubiquinone Uncoupling. *Science* 344, 203. (IF: 37.205, Citations: 141).

Haddad D, Vilain S, Vos M, Esposito G, Matta S, Kalscheuer V, Craessaerts K, Leysen M, Nascimento R, Vianna-Morgante A, De Strooper B, Van Esch H, Morais VA\*, Verstreken P\*, \*shared corresponding authors (2013). Mutations in the Intellectual Disability Gene Ube2a Cause Neuronal Dysfunction and Impair Parkin-Dependent Mitophagy. *Molecular Cell* 50, 831. (IF: 14.174, Citations: 48)

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. (IF: 9.249, Citations: 258).

### Ongoing Research Projects

2016/2021: Synaptic Mitochondria: Quality Control and Maintenance of Synaptic Mitochondria. Coordinator: Vanessa Alexandra dos Santos Morais. Funding Agency: European Commission. Reference: ERC StG 679178. Amount: € 1 300 000,00. Total Amount: € 1 300 000,00.

2016/2018: Homeostasis and Maintenance of Synaptic Mitochondria. Coordinator: Vanessa Alexandra dos Santos Morais. Funding Agency: European Molecular Biology Organisation. Reference: EMBO IG VMorais. Amount: € 150 000,00. Total Amount: € 150 000,00.

2015/2020: Maintaining Mitochondria Healthy: The Molecular Checkpoints involved in Mitochondrial Quality Control in Neurons. Coordinator: Vanessa Alexandra dos Santos Morais. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/01693/2014/CP1236/CT0003. Amount: € 50 000,00. Total Amount: € 50 000,00.

### Other Projects

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

### Publications in Peer Review Journals

Leites EP, Morais VA (2017). Mitochondrial quality control pathways: PINK1 acts as a gatekeeper. *Biochem Biophys Res Commun* 291, 31227-5. (IF: 2.466, Citations: 1).

Goiran T, Duplan E, Chami M, Bourgeois A, El Manaa W, Rouland L, Dunys J, Lauritzen I, You H, Stambolic V, Biféri MG, Barkats M, Pimplikar SW, Sergeant N, Colin M, Morais VA, Pardossi-Piquard R, Checler F, Alves da Costa C (2017). beta-Amyloid Precursor Protein Intracellular Domain Controls Mitochondrial Function by Modulating Phosphatase and Tensin Homolog-Induced Kinase 1 Transcription in Cells and in Alzheimer Mice Models. *Biol Psychiatry* 17, 31515-9. (IF: 11.412, Citations: 2).

Vos M, Geens A, Böhm C, Deaulmerie L, Swerts J, Rossi M, Craessaerts K, Leites E, Seibler P, Rakovic A, Lohnau T, De Strooper B, Fendt SM, Morais VA, Klein C, Verstreken P (2017). Cardiolipin promotes electron transport between ubiquinone and Complex-I to rescue PINK1 deficiency. *JCB* 216, 695-708. (IF: 7.955 Citations: 3).

#### **Other Publications International**

Aerts L, Morais VA Chapter 2: Electron Transport Chain. In: Verstreken P, Ed., *Parkinson's Disease: Molecular Mechanisms Underlying Pathology*. San Diego: Academic Press, 2017: 41-75.

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

Morais VA. MitoPorto – Advances in Mitochondrial Research, Porto, Portugal, March 2017.

Morais VA. European Molecular Biology Organisation | European Molecular Biology Laboratory Mechanisms of Neurodegeneration, Heidelberg, Germany, June 2017.

Morais VA. Ciência2017, Lisbon, Portugal, July 2017.

#### **Communications in International Conferences**

Faria-Pereira A, Spinazzi M, Craessaerts K, Savas J, Morais VA. ADPD - 13<sup>th</sup> International Conference on Alzheimer's and Parkinson's Disease, Vienna, Austria, April 2017. (Poster Presentation).

Leites EP, Craessaerts K, De Strooper B, Morais VA. ADPD - 13<sup>th</sup> International Conference on Alzheimer's and Parkinson's Disease, Vienna, Austria, April 2017. (Poster Presentation).

Gonçalves FB, Morais VA. Mitochondria in life, death and disease. European Molecular Biology Organisation | FEBS, Bari, Italy, October 2017. (Poster Presentation).

Faria-Pereira A, Spinazzi M, Craessaerts K, Pinto A, De Strooper B, Savas J, Morais VA. Mitochondria in life, death and disease: Advances in Mitochondrial Research. European Molecular Biology Organisation | FEBS Course, Bari, Italy, October 2017. (Oral Presentation).

### **Communications in National Conferences**

Soares R, Xapelli S, Morais VA. International Symposium MitoPorto – Advances in Mitochondrial Research, Porto, Portugal, May 2017. (Poster Presentation).

Gonçalves FB, Morais VA. MitoPorto – Advances in Mitochondrial Research, Porto, Portugal, May 2017. (Poster Presentation).

Faria-Pereira A, Spinazzi M, Creassarts K, Savas J, Morais VA. MitoPorto - Advances in Mitochondrial Research, Porto, Portugal, May 2017. (Poster Presentation).

Carvalho F, Morais VA. MitoPorto - Advances in Mitochondrial Research, Porto, Portugal, May 2017.

Leites EP, Craessaerts K, Almeida B, Pinto P, Carvalho T, Morais VA. MitoPorto - Advances in Mitochondrial Research, Porto, Portugal, May 2017. (Poster Presentation).

Faria-Pereira A, Spinazzi M, Creassarts K, Savas J, Morais VA. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Soares R, Xapelli S, Morais VA. 3<sup>rd</sup> Meeting of the PhD students from the Mind-Brain College, Lisbon, Portugal, October 2017. (Poster Presentation).

### **Internationalisation**

Our projects involve collaborations with international research groups in Europe and USA. Current international collaborators include:

In Europe - Bart de Strooper (VIB, Belgium); Patrik Verstreken (VIB, Belgium); Christine Klein (University Luebeck, Germany); Frederic Checler (CNRS, France); Cora O’Neil (UCC, Ireland) and Helene Plun-Favreau (UCL, England).

In USA - Jeffrey Savas (NorthWestern University, Chicago); Matthew LaVoie (Harvard University, Boston).

Additionally, I am co-supervisor of the MD/PhD student Filipe Figueiredo, holder of a NeuroULisboa PhD fellowship, together with Friedemann Paul from the Charite University in Berlin.

### **Prizes, Honours and Awards**

Awarded a TeBu-Bio Travelling Grant. 13<sup>th</sup> International Conference on Alzheimer's and Parkinson's Disease, Vienna, Austria, April 2017.

Awarded a TeBu-Bio Travelling Grant. European Molecular Biology Organisation | FEBS | Lecture - Mitochondria in life, death and disease, Bari, Italy, October 2017.

### **Advanced Teaching**

Morais VA. Member of the Scientific Advisory Board of the iMM Career Development Unit.

Morais VA coordinated (together with Sergio Almeida, Claus Azzalin and Nuno Morais) and taught at the "Cell and Molecular Biology" week, LisbonBioMed International FCT PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 2017.

Morais VA taught at the Functional Organization of the Cell Course of the Master in Biochemistry of Health, Instituto de Tecnologia Química e Biológica António Xavier, Nova University of Lisbon, Oeiras, Portugal, October 2017.

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## Mota, Maria M.

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### Major Interests / Objectives

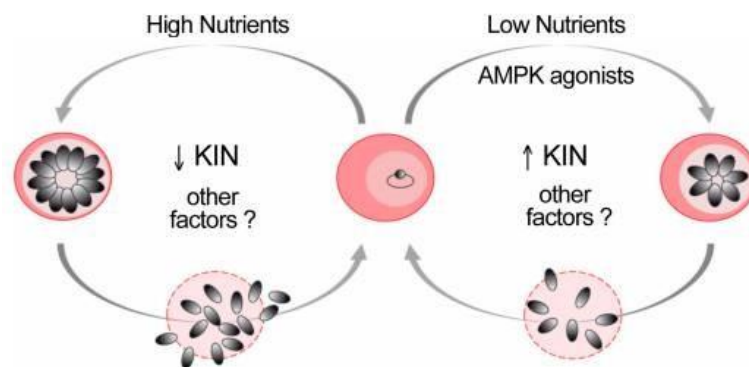
Malaria still exerts an enormous disease burden with half of the planet's population at risk of infection. Malaria control or elimination requires a better understanding of the complex interactions occurring between Plasmodium and its hosts.

In order to provide novel insights into the protean struggle between host and parasite we tackle the most fundamental and conceptually novel questions of host-Plasmodium interactions. We have recently shown that alterations in host metabolism strongly impact both the establishment and the course of a malaria infection by interfering with distinct host and parasite pathways during different stages of infection. Presently we aim to test whether specific host metabolic pathways have shaped and still impact the outcome of a malaria infection.

### Head of Laboratory

Maria Manuel Mota, PhD

### Graphic Abstract



### Research Team

Ana Filipa Caetano Parreira	Graduate	Technician
Ana Margarida Aires Alves Vigário	PhD	Investigator, Assistant Professor - Universidade da Madeira,
Ângelo António Ferreira Chora	PhD	Post-Doctoral Investigator
Aparajita Lahree	Master	PhD Student
Debanjan Mukherjee	PhD	PhD Student
Eliana Real	PhD	Post-Doctoral Investigator (Left September)
Inês Fernandes Bento	PhD	Post-Doctoral Investigator
Iset Medina Vera	PhD	Post-Doctoral Investigator

João Tiago Carvalho Jordão de Mello Vieira	Master	PhD Student
Ksenija Slavic	PhD	Post-Doctoral Investigator
Lénia Marisa Pereira Rodrigues	PhD	Post-Doctoral Investigator (Left September)
Leonardo Filipe Lemos Rocha	Graduate	MSc Student
Maria Inês Moreira Oliveira Leite Marreiros	Master	Investigator
Maria Nogueira de Menezes	Master	External PhD Student (Left April)
Miguel Dinis Monteiro dos Santos	Master	Investigator (Left August)
Sara de Jesus Santos Baptista	Master	PhD Student
Sofia Pinto Guia Marques	PhD	Lab Manager, Investigator
Sonali Setua	PhD	Post-Doctoral Investigator
Tomás Furtado Lemos	Undergraduate	Trainee (Left June)
Vanessa Alexandra Zuzarte Luís	PhD	Post-Doctoral Investigator
Viriato M'Bana	Master	PhD Student

### Laboratory Keywords / Research Areas

Host-Plasmodium interactions, Host response to plasmodium infection, Plasmodium response and adaptation, Nutrient acquisition and nutrient sensing, Cross-talking between liver and blood stages of infection.

### Major Scientific Achievements

2017 was a great year with success in several lines of research. We highlight two major contributions that increased our knowledge on how Plasmodium interacts with its host:

We show for the first time that Plasmodium has the ability to sense and adapt to the host's nutritional status by altering its multiplication rate and virulence. Overall, we have unveiled the master regulator of such nutrient sensing pathway, which is a druggable kinase. Its activation is expected to sustain low parasitemia, which has been previously shown to be protective (Mancio-Silva et al., Nature).

In parallel, our data reveals for the first time that acute and transient dietary alterations markedly impact the establishment of a Plasmodium infection and disease outcome (Zuzarte-Luis et al., Nature Microbiology). Indeed, Plasmodium liver infection is strongly impaired by administration of a high-fat diet for a period as short as 2-4 days. This impairment in infection is mediated by oxidative stress.

### Selected Publications

Zuzarte-Luís V, Mello-Vieira J, Marreiros IM, Liehl P, Chora ÂF, Carret CK, Carvalho T, Mota MM (2017). Dietary alterations modulate susceptibility to Plasmodium infection. *Nat Microbiol.* 2, 1600-1607. (IF: --, Citations: 1).

Mancio-Silva L, Slavic K, Grilo Ruivo MT, Grosso AR, Modrzynska KK, Vera IM, Sales-Dias J, Gomes AR, MacPherson CR, Crozet P, Adamo M, Baena-Gonzalez E, Tewari R, Llinás M, Billker O, Mota MM. (2017) Nutrient sensing modulates malaria parasite virulence. *Nature*, 13, 213-216. (IF: 40.137, Citations: 6).

Slavic K, Krishna S, Lahree A, Bouyer G, Hanson KK, Vera i, Pittman JK, Staines HM, Mota MM (2016). A vacuolar iron-transporter homologue acts as a detoxifier in Plasmodium. *Nat Commun.* 7, 10403. (IF: 12.124, Citations: 12).

Liehl P, Zuzarte-Luís V, Chan J, Zillinger T, Baptista F, Carapau D, Konert M, Hanson KK, Carret C, Lassnig C, Müller M, Kalinke U, Saeed M, Chora AF, Golenbock DT, Strobl B, Prudêncio M, Coelho LP, Kappe SH, Superti-Furga G, Pichlmair A, Vigário AM, Rice CM, Fitzgerald KA, Barchet W, Mota MM (2014). Host-cell sensors for Plasmodium activate innate immunity against liver-stage infection. *Nature Medicine* 20, 47-53. (IF: 29.886, Citations: 79).

### Ongoing Research Projects

2016/2019: Evasão da autofagia da célula hospedeira: mecanismos de sobrevivência do Plasmodium na fase hepática da infecção. Coordinator: Maria Manuel Mota. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MEC/1342/2014. Amount: € 200 000,00. Total Amount: € 200 000,00.

2016/2018: Plasmodium autophagy evasion in the liver-stage: mechanisms and novel therapeutic opportunities. Coordinator: Maria Manuel Mota. Funding Agency: Institut Mérieux. Reference: MRG\_20052016. Amount: € 100 000,00. Total Amount: € 100 000,00

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.



2016/2018: REUSE4MALARIA: Drug Repurposing for malaria chemoprotection. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: ERC PoC 713691. Amount: € 150 000,00. Total Amount: 150 000,00.

2012/2017: ParasiteNutriSensing: Nutrient sensing by parasites. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: ERC StG 311502. Amount: € 1 500 000,00. Total Amount: € 1 500 000,00.

### **Publications in Peer Review Journals**

Zuzarte-Luís V, Mello-Vieira J, Marreiros IM, Liehl P, Chora ÂF, Carret CK, Carvalho T, Mota MM (2017). Dietary alterations modulate susceptibility to Plasmodium infection. *Nat Microbiol.* 2(12):1600-1607. (IF: --, Citations: 1).

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;547(7662):213-216. (IF: 40.137, Citations: 7).

Ng S, March S, Galstian A, Gural N, Stevens KR, Mota MM, Bhatia SN (2017). Towards a Humanized Mouse Model of Liver Stage Malaria Using Ectopic Artificial Livers. *Sci Rep.* 31;7:45424. (IF: 4.259, Citations: 3).

Sá E Cunha C, Nyboer B, Heiss K, Sanches-Vaz M, Fontinha D, Wiedtke E, Grimm D, Przyborski JM, Mota MM, Prudêncio M, Mueller AK (2017). Plasmodium berghei EXP-1 interacts with host Apolipoprotein H during Plasmodium liver-stage development. *Proc Natl Acad Sci U S A.* 14;114(7). (IF: 9.661, Citations: 1).

Meireles P, Sales-Dias J, Andrade CM, Mello-Vieira J, Mancio-Silva L, Simas JP, Staines HM, Prudêncio M. 2017. GLUT1-mediated glucose uptake plays a crucial role during Plasmodium hepatic infection. *Cell Microbiol.* Feb;19(2). (IF: 4.554, Citations: 4).

### **Invited Lectures and Seminars**

Mota MM. Institute Pasteur Molecular Cell Biology, January 7, 2017.

Mota MM. Harvard Business School, Rethinking Malaria Leadership Forum, February 7-8, 2017.

Mota MM. University Padova, Department of Biomedical Sciences, November 15, 2017.

Mota MM. University of Glasgow, Scotland, December 1, 2017.

### **Communications in International Conferences**

Mota MM. BSP- British Society for Parasitology Meeting, University of Dundee, Dundee, Scotland, April 2-5, 2017.

Zuzarte-Luís V. Malaria Gordon Research Seminars, Switzerland, July 2-7, 2017.

Mota MM. 9<sup>th</sup> ÖGMBT Annual Meeting - Austrian Association of Molecular Life Sciences and Biotechnology, Austria, September 26, 2017.

Lahree A. European Molecular Biology Organisation course in Current methods in cell biology at EMBL, Heidelberg, Germany, September 2017. (Poster Presentation).

Mota MM. Mérieux Research Grants Meeting, Annecy, France, October 17, 2017.

### **Communications in National Conferences**

Mota MM. Toxo 14 – Toxoplasma Research Community Biennial Meeting, June 3, 2017.

Mota MM. IMED, Oral Plenary Conference, October 27, 2017.

M'Bana V. Annual PGCD Meeting, Vimeiro, Portugal, November 03-05, 2017.

Baptista S. Annual PGCD Meeting, Vimeiro, Portugal, November 03-05, 2017.

### **Organisation of Conferences**

Zuzarte-Luís V. Instituto de Medicina Molecular João Lobo Antunes Post-Doc Day: Gender Balance in Science, Lisbon, Portugal, January 17, 2017.

Mota MM, Zuzarte-Luís V. Malaria Gordon Research Seminars. Switzerland, July 2-7, 2017.

Bento I. Career opportunities for Postdoctoral researchers in life sciences', Cascais, Portugal, November 22-24, 2017.

## **Internationaliation**

The Mota Lab has developed over the years and strengthen during 2017 a network of international collaborations with multiple laboratories around the world that is allowing us to develop more interdisciplinary projects by bringing together our own interest and expertise on host-Plasmodium with that of others in different areas, such as liver metabolism (J. Mato, CIC, Biogune, Spain), metabolism of microbial pathogens (M. Barrett, Glasgow University, UK), P. falciparum epigenetics (A. Scherf, Institut Pasteur, France), Plasmodium transporters (S. Krishna and H. Staines, St. George's, University of London, UK), Plasmodium genetic technologies (O. Billker, Sanger Institute, UK and G. McFadden, Melbourne University, Australia), human micro livers (S. Bhatia, MIT, USA) and advance research in Plasmodium vivax (J. Prachumsri, Mahidol Vivax Research Unit, Thailand); to ensure the excellence of the science performed in our attempt to answer the most fundamental questions in the field.

Fostered by iMM's TwinnToInfect project and aiming at innovative and technical collaborations the Mota Lab had two researchers doing short-term research missions in the partner institutions namely: Ksenija Slavic that went to Dr. Moritz Treeck Lab at The Francis Crick Institute, UK; and Miguel Santos that went to Prof. Artur Scherf Lab at Institut Pasteur, France.

Also during 2017, Angelo Chora travelled to the lab of Prof. William Heath at the Doherty Institute, University of Melbourne, Australia to perform experiments essential for the success of the research line.

Additionally, in light of her activities as a principal investigator Dr. Maria M. Mota was invited to speak in several international institutions and participated in scientific meetings, either to communicate the data produced by the team or to meet potential collaborators from cross-disciplines. In 2017 we highlight the organization of the Malaria Gordon Research Seminars in Switzerland by Vanessa Zuzarte-Luís and Maria M. Mota.

## **Prizes, Honours and Awards**

Mota MM. Pfizer Award for Basic Research.

Bento I. Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência.

Mukherjee D. 3<sup>rd</sup> year Best Poster Award. XI iMM/CAML PhD Students Meeting Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017.

### **Advanced Teaching**

Zuzarte-Luís V. Aula: Modelos de infecção para doenças transmitidas por vectores. Mestrado em Microbiologia Clínica e Doenças Infecciosas Emergentes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal.

Mota MM, Zuzarte-Luís V. Vector Borne Diseases. Programa de Pós-Graduação Ciência para o Desenvolvimento, Instituto Gulbenkian Ciência/University of Cape Verde.

Vigário M. Tropical Medicine and Clinical Microbiology. Programa de Pós-Graduação Ciência para o Desenvolvimento, University of Cape Verde.

### **Science and Society**

Mota MM. Igualdade de Género na Ciência. Colégio de Nossa Senhora da Graça, Vila Nova de Milfontes, Portugal, March 28, 2017.

Mota MM. Rómulo Ciência Viva, ciclo Ciência às seis, University of Coimbra, Coimbra, Portugal, June 27, 2017.

Mota MM. Oral Plenary Conference. IMED, October 27, 2017.

Mota MM. WPL Round Table Discussion: Ambition - Women in STEM, sponsored by Presidência da República Portuguesa, Palácio de Belém, Lisbon, Portugal, November 8, 2017.

Mota MM. Program “Cientistas no Palácio de Belém” in collaboration with Agência Nacional para a Cultura Científica e Tecnológica (Ciência Viva), Plano Nacional de Leitura and Rede de Bibliotecas Escolares, Portugal, November 28, 2017.

### **MSc Thesis Completed**

Leonardo Rocha, 20/11/2017, “The role of GSK3 as a virulence factor in Plasmodium infection”, Instituto Superior Técnico, University of Lisbon. Supervisor: Iset Vera.

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## Prata, Diana

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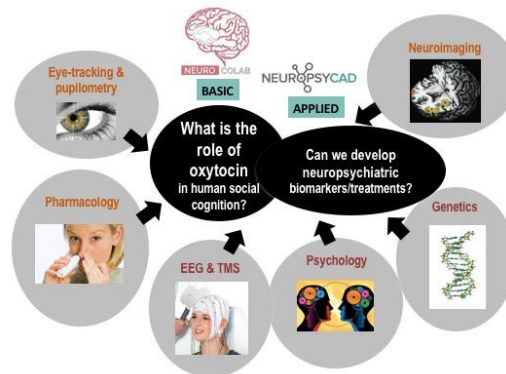
### Major Interests / Objectives

Our interest is the molecular biology of human behaviour, which we aim to translate into improving etiological and therapeutic models of neuropsychiatric disorders. We have reported on the influence of genetic variations on: mental illness risk, brain function/structure and drug treatment response. We are now majorly interested in: 1) the role of oxytocin in social cognition, and its relevance to psychosis, autism and anorexia; and 2) building clinically useful multimodal biomarkers for aiding clinical diagnostic and prognostic predictions. For this, we combine psychological and neuropharmacological experimentation with (epi)genetics, neuroimaging and psychophysiological tools - which is made possible by a diverse team of biomedical engineers, psychologists, biologists and psychiatrists.

### Head of Laboratory

Diana Maria Pinto Prata, PhD, Group Leader (iMM) and Assistant Professor (10% at Superior de Ciências do Trabalho e da Empresa)

### Graphical Abstract



### Research Team

Alessia Avila	Master	PhD Student
Ana Carina Pereira Mendes	Graduate	MSc Student (Left April)
André Raul Araújo de Sousa	Master	MSc Student (Started October)
Beatriz Candeias Simões	Graduate	MSc Student (Started September)
Bernardo Oliveira da Costa Neves	Master	PhD Student, Centro Hospitalar Psiquiátrico de Lisboa, MD (Started April)

Daniel Artur Abreu Martins	Master	Trainee (Left April)
Duarte Manuel Catrola Palma Ferreira	Master	Investigator (Left March)
Gonçalo Aires de Oliveira	MD/PhD	Post-Doctoral Investigator (Started April)
Gonçalo Bairos Cosme	Master	Technician (Started August)
Hugo Alexandre Teixeira Duarte Ferreira	PhD	Visiting Researcher (Started June)
Katja Brodmann	PhD	Post-Doctoral Investigator
Maria Leonor Dinis Neto	Undergraduate	Trainee (Started August)
Mariana Génio Balseiro	Graduate	MSc Student (Started February/Left October)
Marie Zelenina	Graduate	MSc Student (Started October)
Mónica Gonçalves Barbeito Costa	Graduate	MSc Student
Vânia Sofia Santos Tavares	Master	PhD Student
Vasco de Sá Nunes	Undergraduate	Trainee (Started August)

### Laboratory Keywords / Research Areas

Neuroimaging, Genetics, Psychiatry, Social cognition, Machine learning, Neuropharmacology.

### Major Scientific Achievements

In 2017, DPrata Lab has:

- Set up the iMM's first Psychophysiological Facility with €220K-worth of new equipment;
- Received a Marie Curie 3<sup>rd</sup> Prize to the PI as the most promising scientist in 'Innovation and Entrepreneurship';
- Obtained 3 successful national PhD/post-doc fellowships, and the Bial Psychophysiology grant;
- Published 4 international peer-reviewed articles, and 3 national book chapters;
- Orally presented at 3 conferences (all upon invitation to PI) and via poster at 5 conferences (by 5 lab members);
- Been invited (the PI) to present at 5 research seminars;
- Organized 2 symposia in 2 international conferences;
- Performed 32 hours of teaching;
- Participated in a documentary and 2 TV debates, several magazine articles, TV interviews, and in public seminars and workshop activities in schools.

### Selected Publications

Mallas E, Carletti F, Chaddock C, Shergill S, Woolley J, Picchioni M, McDonald C, Toulopoulou T, Kravariti E, Bramon E, Murray R, Barker G, Prata DP (2017). The impact of CACNA1C gene, and its epistasis with ZNF804A, on white matter microstructure in health, schizophrenia and bipolar disorder. *Genes, Brain and Behavior* 16, 479. (IF: 3.743, Citations: 4).

Mallas E, Carletti F, Chaddock C, Woolley J, Picchioni MM, Shergill S, Kane F, Allin M, Barker GJ, Prata DP (2016). Genome-wide discovered psychosis-risk gene ZNF804A impacts on white matter microstructure in health, schizophrenia and bipolar disorder. PeerJ [https://peerj.com/articles/1570/?utm\\_source=TrendMD&utm\\_campaign=PeerJ\\_TrendMD\\_0&utm\\_medium=TrendMD](https://peerj.com/articles/1570/?utm_source=TrendMD&utm_campaign=PeerJ_TrendMD_0&utm_medium=TrendMD). (IF: 2.177, Citations: 10).

R Gurung, Prata DP (2015). What is the impact of genome-wide supported risk variants for schizophrenia and bipolar disorder on brain structure and function? A systematic review. *Psychological Medicine* 45, 2461. (IF: 5.23, Citations: 27).

Prata DP, Mechelli A, Kapur S (2014). Clinically meaningful biomarkers for psychosis: a systematic and quantitative review. *Neuroscience and Biobehavioural Reviews* 45, 134. <http://www.sciencedirect.com/science/article/pii/S0149763414001274>. (IF: 8.299, Citations: 26).

Prata DP, Papagni S, Mechelli A, Fu C, Picchioni M, Kane F, Kalidindi S, McDonald C, Kravariti E, Touloupoulou T, Bramon E, Walshe M, Murray R, Collier DA, McGuire PK (2012). Effect of D-amino acid oxidase activator (DAOA; G72) on brain function during verbal fluency. *Human Brain Mapping*. 33, 143. <http://www.ncbi.nlm.nih.gov/pubmed/21391259>. (IF: 4.53, Citations: 8).

### Ongoing Research Projects

2017/2020: Oxytocin: On the psychophysiology of trust and cooperation. Coordinator: Diana Maria Pinto Prata. Funding Agency: BIAL. Reference: BIAL DPrata. Amount: € 50 000,00. Total Amount: € 50 000,00.

2016/2017: Social and non-social reinforcement learning in humans: a model-based pharmacofMRI approach. Coordinator: Diana Maria Pinto Prata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: BIG 2016 DPrata. Amount: € 97 335,00. Total Amount: € 97 335,00.

2015/2020: Oxytocin and dopamine interplay in humans - on the biological basis of cooperation. Coordinator: Diana Maria Pinto Prata. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00787/2014/CP1236/CT0005. Amount: € 50 000,00. Total Amount: € 50 000,00.

2015/2018: BIOSOCIOCOG: Oxytocin and Dopamine Interplay in Humans – on the Biology of Social Cognition. Coordinator: Diana Maria Pinto Prata. Funding Agency: European Commission. Reference: MSCA CIG 631952. Amount: € 100 000,00. Total Amount: € 100 000,00.

### Other Projects

2016/2018: SynaNet: Neurologic and Psychiatric disorders: from synapses to networks. Coordinator: Ana Maria Ferreira de Sousa Sebastião. Funding Agency: European Commission. Reference: TWINNING 692340. Amount: € 525 437,50. Total Amount: € 999 996,25.

### Publications in Peer Review Journals

Martins D, Mehta M, Prata DP (2017). The “highs and lows” of the brain on dopaminergics: Evidence from neuropharmacology studies in humans. *Neuroscience & Biobehavioral Reviews*. 80:51-371. (IF: 8.299, Citations:--).

Mallas E, Carletti F, Chaddock C, Shergill S, Woolley J, Picchioni M, McDonald C, Touloupoulou T, Kravariti E, Bramon E, Murray R, Barker G Prata DP (2017). The impact of CACNA1C gene, and its epistasis with ZNF804A, on white matter microstructure in health, schizophrenia and bipolar disorder. *Genes, Brain and Behaviour*. (IF: 3.743, Citations: 4).

Tecelao D, Mendes A, Martins D, Bramon E, Touloupoulou T, Kravariti E, Murray R, Prata DP (2017). The impact of psychosis genome-wide associated ZNF804A variation on verbal fluency connectivity. *Journal of Psychiatric Research*. 98:17-21. (IF: 4.183, Citations:--).

Vassos E, Di Forti M, Coleman J, Iyegbe C, Prata DP, Euesden J, O'Reilly P, Curtis C, Kolliakou A Patel H, Newhouse S, Traylor M, Ajnakina O; Mondelli V, Reis-Marques T, Gardner-Sood P, Aitchison K, Powell J, Atakan Z, Greenwood K, Smith S, Ismail K, Pariante C, Gaughran F, Dazzan P, Markus H; David A; Lewis C; Murray R, Breen G (2017). An examination of polygenic score risk prediction in individuals with first episode psychosis. *Biological Psychiatry. Priority Communication*. 8 (6): 470-477. (IF: 11.412, Citations: 11).

Brodmann K, Gruber O, Goya-Maldonado R (2017). Intranasal Oxytocin Selectively Modulates Large-Scale Brain Networks in Humans. *Brain Connect*, 7(7):454-463. (IF: 3.83, Citations: 11).

### Other Publications National

Martins D, Prata DP. A depressão está nos genes? Uma apreciação das bases genéticas e moleculares da depressão major. In A promoção da saúde mental e a prevenção da depressão e suicídio: foco estratégico na integração da saúde mental nos cuidados de saúde primários. EUTIMIA. Lisbon. In press.



Martins D, Prata DP. A suicidalidade está nos genes? Uma visão geral das bases genéticas e moleculares da suicidalidade. In A promoção da saúde mental e a prevenção da depressão e suicídio: foco estratégico na integração da saúde mental nos cuidados de saúde primários. EUTIMIA. Lisbon. In press.

Martins D, Prata DP. Um cérebro deprimido? Alterações neuroimagingológicas na depressão major. In A promoção da saúde mental e a prevenção da depressão e suicídio: foco estratégico na integração da saúde mental nos cuidados de saúde primários. EUTIMIA. Lisbon. In press.

### **Invited Lectures and Seminars**

Tavares V. Epileptogenic focus localization using complexity analysis of BOLD signals. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 24, 2017.

Tavares V. Localizing the epileptogenic focus: a non-invasive approach. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 27, 2017.

Prata DP. Human Neuroscience in Portugal, here we go! TED-like talk upon receipt of the 3<sup>rd</sup> Prize in Innovation and Entrepreneurship in Marie Skłodowska-Curie Actions meeting, Malta, May 2017.

Brodmann K. Oxytocin – not only a social neuropeptide. Implications from social and non-social task-based and task-free neuroimaging studies. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 22, 2017.

Avila A. The Risk at Mental State in Psychosis. 3.<sup>o</sup> Encontro Nacional do Primeiro Episódio Psicótico, Coimbra, Portugal, June 2017.

Prata DP. Elucidating the impact of psychiatric risk genes on cognition with neuroimaging. SynaNet 2017 Summer School, University of Lancaster, Lancaster, England, September 2017.

Prata DP. Neuroscience & Business. Bridging Science and Business event of the Marie Curie Alumni Association, Gdansk, Poland, September 2017.

Prata DP. Elucidating the impact of psychiatric risk genes on cognition with neuroimaging. Cognition, Schizophrenia and Imaging Lab, Psychosis Studies, University of Roehampton, Roehampton, England, October 2017.

Prata DP. Oxytocin in social cognition. Serviço de Imagiologia, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, October 2017.

Prata DP. Using pharmacology, imaging, genetic and psychophysiology at the service of Psychiatry research. Psychiatry Department, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, October 2017.

Prata DP. Artificial Intelligence at the service of psychiatric diagnoses. World Congress of Psychiatry, Berlin, Germany, October 2017.

### **Communications in International Conferences**

Prata DP. Human Neuroscience in Portugal, here we go! TED-like talk upon receipt of the 3<sup>rd</sup> Prize in Innovation and Entrepreneurship in Marie Skłodowska-Curie Actions meeting, Malta, May 2017. (Oral Presentation).

Brodmann K, Richter A, Goya-Maldonado R, Gruber O. Oxytocin receptor gene polymorphisms modulate the reward system in a non-social decision-making task. 23<sup>th</sup> Annual Meeting of the Organization of Human Brain Mapping, Vancouver, Canada, June 2017. (Oral Presentation).

Prata DP. Neuroscience & Business. Bridging Science and Business event of the Marie Curie Alumni Association, Gdansk, Poland, September 2017. (Oral Presentation).

Prata DP. Artificial Intelligence at the service of psychiatric diagnoses. World Congress of Psychiatry, Berlin, Germany, October 2017. (Oral Presentation).

### **Communications in National Conferences**

Tavares V, Vassos E, Stone J, Valli I, Woolley J, Fusar-Poli P, Jones C, Calem M, Chaddock C, Ferreira H, Prata DP. Risk probability of transition to psychosis: a multivariate pattern recognition approach. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Tavares V, Vssos E, Crossley N, Prata DP. Can the genome predict negative symptoms in Schizophrenia?. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Costa M, Tavares V, Brodman K, Lima C, Pinheiro AP, Prata DP. Authenticity recognition in laughter: An EEG study. 3<sup>rd</sup> Meeting of the Mind Brain College, October 19-20, 2017. (Poster Presentation).

### **Organisation of Conferences**

Prata DP. Organizer. 6<sup>th</sup> International Conference on PET/MR and SPECT/MR (PSMR2017), Faculty of Sciences, University of Lisbon, Portugal, May 2017.

Prata DP. Organizer and Speaker. Stratification in Diagnosis and Therapy of Severe Mental Illnesses. Symposium at World Congress of Psychiatry, Berlin, Germany, October 2017.

### **Internationaliation**

The group has several ongoing collaborations, some of which have involved training of lab members abroad or meetings at conferences:

- Within Synanet Twinning consortium, with Lancaster University (England) for a structural and functional neuroimaging genetics study of the Neurexin gene in humans and mice.
- With Emory University (USA) for computational modelling of brain activation and behavioural responses to intranasal oxytocin administration during a social dilemma.
- With University College London (England) for brain imaging, EEG and skin conductance responses during authenticity identification in human emotional vocalizations.
- With King's College London, to study the impact of psychosis polygenic risk scores on brain function and structure.
- With King's College London, for a clinical trial on the impact of TMS in recovery of anorexia nervosa inpatients.

### **Prizes, Honours and Awards**

Prata DP. 3<sup>rd</sup> Prize as Most Promising Scientist in category “Innovation and Entrepreneurship”, Marie Skłodowska-Curie Actions 2017.

Brodmann K. Merit Abstract Award from the Organization of Human Brain Mapping Conference 2017.

Neves B. FCT PhD Fellowship 2017.

Oliveira G. FCT Post-Doc Fellowship.

Ávila A. FCT PhD Fellowship.

### **Advanced Teaching**

Prata DP. Guest Lecturer. LisbonBioMed PhD Programme, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 2017.

Prata DP. Guest Lecture. Imaging Genetics as part of the Psychiatric Research MSc module “Genetics”, Institute of Physics, London, England, February 2017.

Prata DP. Guest Lecturer. When Genetics meets Imaging and Psychiatry. Biomedical Engineering and Biophysics BSc, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, February 2017.

Prata DP. Lecturer. Psychology BSc module “Genetics and Psychophysiology”, ISCTE, Lisbon, Portugal, February-July 2017.

Prata DP. Lecturer. MSc module Biological Basis of Emotions, ISCTE, Lisbon, Portugal, November 2017.

Prata DP. Guest Lecturer. Neuroscience MSc, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, November 2017.

### **Science and Society**

Prata DP. Opening lecture at EASE Business school award ceremony on the Mind of the Entrepreneur, 2017.

Prata DP. Interview for Observador online newspaper on Gender bias in children’s books, 2017.

Prata DP. Newspaper article in Público on “O Ciência 2017 voltou depois à Ciência”, 2017.

Prata DP. Interview in Documentary “Portugal Desconhecido” in History Channel – Portugal, 2017.

Prata DP. TV debate on the theme “Hug” at “Sociedade Civil” in RTP2, 2017.

Prata DP. Interview for magazine of “Diário de notícias”, 2017.

Prata DP. TV debate on the theme “Emotions” at “Sociedade Civil” in RTP2, 2017.

Tavares V. "Técnicas de Visualização dos Cérebro", Lecturer at secondary school meeting European Researchers' Night Escola Secundária de Camões, Lisbon, Portugal, 2017.

Brodmann K. Ich sehe, was du fühlst: Bilder aus den Tiefen unserer Gefühle. Lecturer. 3 Nacht des Wissens, Göttingen, Germany, 2017.

Simões B. O Cérebro e as Emoções. Lecturer at secondary school meeting European Researchers' Night Escola Secundária de Camões, Lisbon, Portugal, 2017.

### **MSc Thesis Completed**

Mariana Génio Balseiro, 15/11/2017, "The effect of a schizophrenia polygenic risk score on brain function during verbal fluency in health, schizophrenia and bipolar disorder", Instituto Superior Técnico, University of Lisbon, Lisbon, Portugal. Supervisor: Diana Prata and Patrícia Figueiredo.

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## Prudêncio, Miguel

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### Major Interests / Objectives

Our interests span a wide range of topics within the malaria field, with particular emphasis on the hepatic stage of infection by the Plasmodium parasite. We are interested in elucidating novel aspects of the biology of Plasmodium infection of liver cells, unveiling novel host-parasite interactions, understanding co-infections between Plasmodium and other parasites, and developing new drug- and vaccine-based anti-malarial strategies.

#### Research Areas:

- Nutrient acquisition and metabolism during Plasmodium development inside hepatic cells;
- Novel Host-Plasmodium molecular interactions;
- The reciprocal influence of Plasmodium and Trypanosoma co-infections;
- Identification of compounds active against Plasmodium liver stages;
- Malaria vaccination.

### Head of Laboratory

Miguel Prudêncio, PhD

### Graphical Abstract



### Research Team

Américo José dos Santos Alves	Master	PhD Student (Started November)
Ana Catarina da Silva Franco	Graduate	Trainee (Left March)
Ana Filipa Gonçalves Teixeira	Master	Investigator
Ana Margarida Roque Sanches Vaz	Master	PhD Student
António Manuel Barbeiro Mendes	PhD	Post-Doctoral Investigator

Daniela Cristina de Henriques Brás	Graduate	MSc Student (Started August)
Denise Rodrigues Francisco	Master	Investigator (Started September)
Diana Alves Moita	Graduate	MSc Student (Started July)
Diana Marisa Pinto Freire Fontinha	PhD	Investigator
Francisca Margarida Van Dunem dos Reis	Master	PhD Student (Started February)
Helena Nunes Cabaço	PhD	Post -Doctoral Investigator (Started September)
Inês Isabel Fernandes Gomes	PhD	Post-Doctoral Investigator
Maria Inês Soares da Costa	Graduate	Trainee (Left May)
Patrícia dos Santos Meireles	PhD	Post-Doctoral Investigator
Pedro Gil Gameiro Eloy Sena Rego	Undergraduate	Trainee
Rafael Alexandre Carvalho Luís	Graduate	MSc Student (Started June)
Rafael Costa de Sousa	Graduate	Trainee (Left November)

### Laboratory Keywords / Research Areas

Malaria, Parasitology, Vaccines, Host-pathogen interactions, Hepatic infection, Plasmodium.

### Major Scientific Achievements

Among other scientific findings, we have (i) demonstrated a crucial role for arginine during hepatic infection by malaria parasites, (ii) identified a novel interaction between Plasmodium EXP-1 and host ApoH proteins, (iii) established a new method for screening of transmission-blocking compounds, and (iv) disclosed the activity of the antiparasitic drug ivermectin and of antiretroviral compounds against Plasmodium liver stages.

Additionally, we have:

- Initiated clinical trials of a new malaria vaccine candidate with the support of PATH-Malaria Vaccine Initiative;
- Been awarded a grant by Merck to establish a new *P. falciparum* facility at IMM and to develop a 3D cell platform for Plasmodium infection;
- Pursued one international patent application (IPA), now granted in several countries, and filed one new IPA;
- Engaged in science outreach activities, dedicated to youngsters and to the general public;
- Had multiple media appearances in relation to our scientific activities.

### Selected Publications

Meireles P, Mendes AM, Aroeira RI, Mounce BC, Vignuzzi M, Staines HM, Prudêncio M (2017). Uptake and metabolism of arginine impact Plasmodium development in the liver. *Scientific Reports* 7, DOI:10.1038/s41598-017-04424-y. (IF: 4.259, Citations: 1).

Machado M, Sanches-Vaz M, Cruz JP, Mendes AM, Prudêncio M (2017). Inhibition of Plasmodium hepatic infection by antiretroviral compounds. *Front. Cell. Infect. Microbiol.* DOI: 10.3389/fcimb.2017.00329. (IF: 4.3, Citations:--).

Azevedo R, Markovic M, Machado M, Franke-Fayard B, Mendes AM, Prudêncio M (2017). A bioluminescence method for in vitro screening of Plasmodium transmission-blocking compounds. *Antimicrob. Agents Chemother.* 61, 202699. (IF: 4.302, Citations: 1).

Cunha CS, Nyboer B, Heiss K, Sanches-Vaz M, Fontinha D, Wiedtke E, Grimm D, Przyborski JM, Mota MM, Prudêncio M\*, Mueller AK\* (\*co-corresponding authors) (2017). P. berghei EXP-1 Interacts with Host Apolipoprotein H during Plasmodium Liver Stage Development. *Proc. Natl. Acad. Sci. USA* 114, E1138. (IF: 9.661, Citations: 2).

Mendes AM, Albuquerque IS, Machado M, Pissarra J, Meireles P, Prudêncio M (2017). Inhibition of Plasmodium liver infection by ivermectin. *Antimicrob. Agents Chemother.* 61, e02005-16. (IF: 4.302, Citations: 6).

### Ongoing Research Projects

2017/2018: A P. berghei-based malaria vaccine. Coordinator: Rui Miguel Prudêncio Cunha Pignatelli. Funding Agency: Malaria Vaccine Initiative. Reference: MVI II. Amount: € 49 457,00. Total Amount: € 49 457,00.

2016/2019: Improving whole-organism vaccines against malaria by genetic modification. Coordinator: António Manuel Barbeiro Mendes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BMD/2695/2014. Amount: € 197 648,00. Total Amount: € 197 648,00.

2015/2017: Plasmodium infection of 3D hepatic cell cultures. Coordinator: Rui Miguel Prudêncio Cunha Pignatelli. Funding Agency: MERCK. Reference: IBET MPrudêncio. Amount: € 75 000,00. Total Amount: 160 000,00.



2013/2017: Prémio BES Inovação. Coordinator: Rui Miguel Prudêncio Cunha Pignatelli. Funding Agency: Banco Espírito Santos. Reference: BES MPrudêncio. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

### **Publications in Peer Review Journals**

Macedo TS, Villarreal W, Couto CC, Moreira DRM, Navarro M, Machado M, Prudêncio M, Batista AA, Soares MBP (2017). Platinum(II)-chloroquine complexes are antimalarial agents against blood and liver stages by impairing mitochondrial function, *Metallomics*, 9, 1548-1561. (IF: 3.975, Citations:--)

Singh K, Okombo J, Brunschwig C, Ndubi F, Barnard L, Wilkinson C, Njogu PM, Njoroge M, Laing L, Machado M, Prudêncio M, Reader J, Botha M, Nondaba S, Birkholtz LM, Lauterbach S, Churchyard A, Coetzer TL, Burrows JN, Yeates C, Denti P, Wiesner L, Egan TJ, Wittlin S, Chibale K (2017). Antimalarial pyrido[1,2-a]benzimidazoles: Lead optimization, parasite life cycle stage profile, mechanistic evaluation, killing kinetics and in vivo oral efficacy in a mouse model. *J. Med. Chem.*, 60, 1432-1448. (IF: 6.259, Citations: 3).

### **Other Publications International**

Mendes AM, Scholzen A, Mueller AK, Khan SM, Sauerwein RW, Prudêncio M (2017). Whole Organism Pre-Erythrocytic Vaccines, In: Rodriguez A. and Mota MM. (Eds) *Malaria: immune response to infection and vaccination*, Springer International Publishing, Cham, Switzerland.

### **Invited Lectures and Seminars**

Prudêncio M. Understanding the Liver Stage of Malaria Parasite to Enable and Accelerate the Development of a Highly Efficacious Vaccine. NIAID, Rockville, USA, August 8-9, 2017. (Oral Presentation).

### **Communications in National Conferences**

Prudêncio M. A New Approach to Malaria Vaccination. BioSAM-Biological Sciences Annual Meeting, Faculty of Science, University of Lisbon, Lisbon, Portugal, April 22, 2017. (Oral Presentation).

Prudêncio M. Challenges in Malaria Vaccination. Salas Dr. Paul Janssen, Lisbon, Portugal, April 28, 2017. (Oral Presentation).

Azevedo R. A bioluminescence method for in vitro screening of Plasmodium transmission-blocking compounds. Workshop Malaria transmission: current challenges and new tools in the elimination context, Instituto de Higiene e Medicina Tropical, Lisbon, Portugal, October 30-31, 2017. (Oral Presentation).

Prudêncio M. Towards a New Vaccine Against Malaria. MICROBIOTEC'17 - Congress of Microbiology and Biotechnology, Universidade Católica, Porto, Portugal, December 7-9, 2017. (Oral Presentation).

### **Organisation of Conferences**

Prudêncio M. Organizer. iMM Innovators Competition (iMMi) - A TwinnToInfect Event, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 16-17, 2017.

### **Internationalisation**

The lab has an extensive network of collaborations with leading International researchers, including:

Kelly Chibale – University of Cape Town;

Peter Eaton - Faculty of Chemistry, Porto;

Thomas Hanscheid - Instituto de Medicina Molecular João Lobo Antunes;

Chris Janse and Shahid Khan - Leiden University;

Clemens Kocken - Biomedical Primate Research Centre, Rijswijk;

Rui Moreira, Francisca Lopes and Ana Ressurreição – Faculty of Pharmacy, Lisbon;

Ann-Kristin Mueller - University of Heidelberg;

Robert Sauerwein - University of Nijmegen;

Bogdan Solaja - Faculty of Chemistry, Belgrade;

Henry Staines and Sanjeev Krishna - St. George's University London;

Branka Zorc – University of Zagreb.

These collaborations involve important scientific exchanges with researchers from these International institutions. Besides, lab members regularly participate in International conferences and meetings. Finally the lab is funded, in part, by two International organizations (the Bill & Melinda Gates Foundation and PATH-MVI) with whom it maintains close interactions.

### **Prizes, Honours and Awards**

Semi-Finalist of the Universal Biotech Innovation Prize 2017, Paris, France.

Luís R. Best Presentation in Basic Science. iMed 9.0 Fundação AstraZeneca Innovate Competition.

Brás D, Alves D, Luís R. Finalists Oral Presentation. iMed 9.0 Fundação AstraZeneca Innovate Competition, October 27, 2017.

Fontinha D. Best Short Presentation Award. 4<sup>th</sup> IMM Post-Doc Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 17, 2017.

### **Patents / Prototypes**

"Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine" (WO 2013156949 A1, also published as CN104302313A, EP2838554A1, US20150071966) Provisional application (Portugal) No. 20121000030819, filed 17.04.2012 PCT international application PCT/IB2013/053050, submitted 17.04.2013, published 24.10.2013. Patent applications filed in Angola, Australia, Brazil, China, India, Japan, Mozambique, South Africa, United States, and European Patent (Euro-PCT), November 2014 Patent granted in India (07.08.2015), Mozambique (17.08.2015), South Africa (23.12.2015), Japan (2015), Australia (03.02.2017) and USA (15.02.2017). "Infected Cell Cultures", European Patent Office application EP 17 160 277.4, filed on 10.03.2017.

### **Advanced Teaching**

Prudêncio M. Concepts, approaches and alternatives in whole-sporozoite malaria vaccination. LisbonBioMed PhD Course, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 14, 2017.

Prudêncio M. Towards a New Malaria Vaccine. GlycoVax, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 23, 2017.

Prudêncio M. Biomolecular methods for malaria research & Development of a new vaccine against malaria. Masters in Clinical Biochemistry, Faculty of Sciences and Technology, Nova University of Lisbon, May 31, 2017.

Prudêncio M. Basic principles of writing a scientific article. Masters in Molecular Biology and Genetics, Faculty of Sciences, University of Lisbon, September 20, 22 and 25, 2017.

Prudêncio M. Animal models in malaria research. Masters in Evolution and Developmental Biology, Faculty of Sciences, University of Lisbon, November 15, 2017.

### **Science and Society**

European Researchers' Night, Lisbon, Portugal, September 29, 2017.

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## Ramirez, Mário

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### Major Interests / Objectives

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations. By exploring the relationships between commensal and disease-causing populations of the same bacterial pathogen, we hope to identify particularly virulent clones as well as successful colonizers for further characterization. A strong bioinformatics effort in bacterial genomics, microbial typing data sharing, data analysis and visualization tools is ongoing. The development of novel laboratory methodologies for the diagnosis of infectious diseases is also an active area of research.

### Head of Laboratory

Mário Nuno Ramos d'Almeida Ramirez, PhD

### Research Team

Ana Isabel Aquino Friães	PhD	Principal Investigator
Ana Teresa Fernandes Alegre Branco	Graduate	Trainee (Started July)
Andreia das Neves Horácio	Master	PhD Student
Bruno Filipe Ribeiro Gonçalves	Graduate	PhD Student
Ana Catarina Silva Costa	PhD	Principal Investigator
Catarina Inês Marques de Sousa Mendes	Graduate	Investigator
Catarina Teresa Condinho Pato	Master	PhD Student
Denise Rodrigues Francisco	Graduate	MSc Student (Left August)
Diogo Nuno Proença Rico Silva	Master	Investigator (Started September)
Elisabete Martins	PhD	Post-Doctoral Investigator
Elísia Graciela da Silva Lopes	Master	Investigator
Gabriela Alexandra Rodrigues Simões	Graduate	MSc Student
Jéssica Fonseca Lisboa	Graduate	Trainee
Joana Filipa Gomes da Silva	Master	Investigator
Joana Rita Sebastião Ferreira da Costa	Graduate	MSc Student (Started September)
João André Nogueira Custódio Carriço	PhD	Principal Investigator
Jorge Miguel Diamantino Miranda	Master	PhD Student
José Augusto Gamito Melo Cristino	MD/PhD	Principal Investigator
Lúcia Marques Prados	Graduate	MSc Student (Started September)
Marcos Daniel Caetano Borges de Pinho	PhD	Principal Investigator
Maria Sousa Rebelo	Master	PhD Student (Left September)
Mariana Isabel Pinto Ferreira	Graduate	MSc Student (Started September)
Mickael Santos da Silva	Master	Investigator
Miguel Alexandre Ferreira Maia Barbosa	Undergraduate	Undergraduate (Left September)
Miguel Paulo Machado	Master	Investigator

Soraia Cristina Lopes Vieira	Graduate	MSc Student
Thomas Hanscheid	MD/PhD	Principal Investigator
Tiago Filipe Salgueiro de Jesus	PhD	Investigator

### Laboratory Keywords / Research Areas

Population biology and genomics, Bioinformatics, Detection of antimalarial drug resistance, Molecular epidemiology, Diagnostic tools, Antibiotic resistance.

### Major Scientific Achievements

Determined that different lineages of serotypes 6 are homogeneously affected by vaccination.

Released an update to our desktop software PHYLOViZ.

Identified diversification among *S. agalactiae* causing neonatal infections in Portugal.

Created lab public repositories of the software currently under development.

Identified a family of polymorphic toxins encoded by temperate prophages.

Development of a novel and easy haemozoin inhibition assay to assess emerging artemisinin resistance.

Evaluation of a novel magneto-optical hemozoin detection method for and sensitivity testing.

### Selected Publications

Friães A, Machado MP, Pato C, Carriço J, Melo-Cristino J, Ramirez M (2015). Emergence of the same successful clade among distinct populations of emm89 *Streptococcus pyogenes* in multiple geographic regions. *MBio* 6, pii:e01780-15. (IF: 6.956, Citations: 9).

Horácio AN, Silva-Costa C, Lopes JP, Ramirez M, Melo-Cristino J, Portuguese Group for the Study of Streptococcal Infections (2016). Serotype 3 remains the leading cause of invasive pneumococcal disease in adults in Portugal (2012-2014) despite continued reductions in other 13-valent conjugate vaccine serotypes. *Front Microbiol* 7, 1616. <http://www.ncbi.nlm.nih.gov/pubmed/27790208>. (IF: 4.076, Citations: 7).

Ribeiro-Gonçalves B, Francisco AP, Vaz C, Ramirez M, Carriço JA (2016). PHYLOViZ Online: web-based tool for visualization, phylogenetic inference, analysis and sharing of minimum spanning trees. *Nucleic Acids Res* 44, W246-251. <http://www.ncbi.nlm.nih.gov/pubmed/27131357>. (IF: 10.162, Citations: 6).

Rebello M, Tempera C, Fernandes JF, Grobusch MP, Hänscheid T (2015). Assessing anti-malarial drug effects ex vivo using the haemozoin detection assay. *Malar J* 14, 140. <http://www.ncbi.nlm.nih.gov/pubmed/25879757>. (IF: 2.715, Citations: 3).

Aguiar SI, Brito M, Horácio AN, Lopes J, Ramirez M, Melo-Cristino J, and Portuguese Group for the Study of Streptococcal Infections and the Portuguese Study Group of Invasive Pneumococcal Disease of the Paediatric Infectious Disease Society (2014). Decreasing incidence and changes in serotype distribution of invasive pneumococcal disease in persons aged under 18 years since introduction of 10-valent and 13-valent conjugate vaccines in Portugal, July 2008 to June 2012. *Euro Surveill* 19, pii: 20750. <http://www.ncbi.nlm.nih.gov/pubmed/24698140>. (IF: 7.202, Citations: 20).

### **Ongoing Research Projects**

2017/2019: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Nuno Ramos d'Almeida Ramirez. Funding Agency: Portugal 2020. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

2016/2019: The changing pneumococci: adapting to vaccination and transitioning between colonization and disease. Coordinator: José Augusto Gamito Melo Cristino. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-EPI/1555/2014. Amount: € 179 000,00. Total Amount: €179 000,00.

2016/2019: An integrated system for bacterial genome tracking using high throughput sequencing technology: from identification to visualization. Coordinator: João André Nogueira Custódio Carriço. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: TUBITAK/0004/2014. Amount: € 61 572,00. Total Amount: € 98 721,22.

### **Publications in Peer Review Journals**

Savelkoel J, Binnendijk KH, Spijker R, van Vugt M, Tan K, Hänscheid T, Schlagenhaut P, Grobusch MP (2017). Abbreviated atovaquone-proguanil prophylaxis regimens in travelers after leaving malaria-endemic areas: A systematic review. *Travel Med Infect Dis*. In press. (IF: 3.055, Citations: --).

Hänscheid T, Grobusch MP (2017). Modern hematology analyzers are very useful for diagnosis of malaria and, crucially, may help avoid misdiagnosis. *J Clin Microbiol* 55:3303–3304. ( IF: 3.712, Citations:--).

Guedes LC, Chan RB, Gomes MA, Conceição VA, Machado RB, Soares T, Xu Y, Gaspar P, Carriço JA, Alcalay RN, Ferreira JJ, Outeiro TF, Miltenberger-Miltenyi G (2017). Serum lipid alterations in GBA-associated Parkinson's disease. *Parkinsonism Relat Disord*. pii: S1353-8020(17)30322-X. (IF: 4.484, Citations:--).

Ribeiro TG, Ribeiro-Gonçalves B, da Silva MS, Novais A, Machado E, Carriço JA, Peixe L (2017). *Citrobacter portucalensis* sp. nov., isolated from an aquatic sample. *Int J Syst Evol Microbiol*. 67:3513-3517. (IF: 2.134, Citations:--).

Jamet A, Touchon M, Ribeiro-Gonçalves B, Carriço JA, Charbit A, Nassif X, Ramirez M, Rocha EPC (2017). A widespread family of polymorphic toxins encoded by temperate phages. *BMC Biol* 15:75. (IF: 6.779, Citations:--).

Taboada EN, Graham MR, Carriço JA, Van Domselaar G (2017). Food safety in the age of next generation sequencing, bioinformatics, and open data access. *Front Microbiol* 8:909. (IF: 4.076, Citations: 1).

Gil J, Almeida S, Constant C, Pinto S, Barreto R, Melo-Cristino J, Machado M do C, Bandeira T (2017). Short-term relevance of lower respiratory viral coinfection in inpatients under 2 years of age. *An Pediatr* pii: S1695-4033(17)30189-3. (IF:-- Citations:--).

Visser BJ, de Vries SG, Vingerling R, Gritter M, Kroon D, Aguilar LC, Kraan RBJ, Wieten RW, Danion F, Sjouke B, Adegnika AA, Agnandji ST, Kreamsner PG, Hänscheid T, Mens PF, van Vugt M, Grobusch MP (2017). Serum lipids and lipoproteins during uncomplicated malaria: A cohort study in Lambaréné, Gabon. *Am J Trop Med Hyg* 96:1205–1214. (IF: 2.549, Citations:--).

Martins ER, Pedroso-Roussado C, Melo-Cristino J, Ramirez M, Portuguese Group for the Study of Streptococcal Infections (2017). *Streptococcus agalactiae* causing neonatal infections in Portugal (2005-2015): diversification and emergence of a CC17/PI-2b multidrug resistant sublineage. *Front Microbiol* 8:499. (IF: 4.076, Citations: 1).



Marchaim D, Levit D, Zigron R, Gordon M, Lazarovitch T, Carriço JA, Chalifa-Caspi V, Moran-Gilad J (2017). Clinical and molecular epidemiology of *Acinetobacter baumannii* bloodstream infections in an endemic setting. *Future Microbiol* 12:271–283. (IF: 3.374, Citations:--).

Henriques AR, Melo-Cristino J, Fraqueza MJ (2017). Genetic characterization of *Listeria monocytogenes* isolates from industrial and retail ready-to-eat meat-based foods and their relationship with clinical strains from human listeriosis in Portugal. *J Food Prot* 551–560. (IF: 1.417, Citations: 1).

Diamantino-Miranda J, Aguiar, SI, Carriço JA, Melo-Cristino J, Ramirez M (2017). Clonal and serotype dynamics of serogroup 6 isolates causing invasive pneumococcal disease in Portugal: 1999-2012. *PLoS ONE* 12:e0170354. (IF: 2.806, Citations:--).

Machado MP, Ribeiro-Gonçalves B, Silva M, Ramirez M, Carriço JA (2017). Epidemiological surveillance and typing methods to track antibiotic resistant strains using high throughput sequencing. *Methods Mol Biol* 1520:331–355. (Journal IF:--, Citations: 2).

Nascimento M, Sousa A, Ramirez M, Francisco AP, Carriço JA, Vaz C (2017). PHYLOViZ 2.0: Providing scalable data integration and visualization for multiple phylogenetic inference methods. *Bioinformatics* 33:128–129. (IF: 7.307, Citations: 10).

### Invited Lectures and Seminars

Melo Cristino J. Microbiologia Urinária. Curso de Nefrologia Pediátrica – A Criança com Doença Nefro-Urológica, Sociedade de Nefrologia Pediátrica, Lisbon, Portugal, January 26, 2017.

Melo Cristino J. MALDI-TOF MS. Sociedade de Doenças Infecciosas e Microbiologia Clínica, Porto, Portugal, January 27, 2017.

Melo Cristino J. Pneumococo, a clínica e o laboratório. XXIII Jornada de Pediatria do Hospital de Santa Maria, Lisbon, Portugal, February 9, 2017.

Carriço JA. Genomic Epidemiology: How High Throughput Sequencing changed our view on bacterial strain similarity. *Bioinformatics Open Days*, Braga, Portugal, February 22-24, 2017.

Hanscheid T. As em Doenças Infecciosas: Absurdos e Ameaças da “Medicina Alternativa”. 37º Ciclo de Conferências sobre Doenças Infecciosas, Lisbon, Portugal, March 17, 2017.

Melo Cristino J. Resistência aos antibióticos - Situação em Portugal, Encontros na Luz, Integração de Cuidados de Saúde. Hospital da Luz, Setubal, Portugal, March 22, 2017.

Melo Cristino J. A Ameaça Microbiana. Centro Académico de Medicina de Lisboa Session, Lisbon, Portugal, March 23, 2017.

Melo Cristino J. Retrato da tuberculose na ópera. Conferência de abertura. Simpósio "Tuberculose: A História e o Património". Dia Mundial da tuberculose, Instituto de Higiene e Medicina Tropical, Nova University of Lisbon, Lisbon, Portugal, March 24, 2017.

Hanscheid T. Ciência na cozinha: microbiologia e doenças infecciosas. Infecção e Doenças Infecciosas, Campo Maior, Portugal, May 20, 2017.

Carricho JA. Software Pipelines: The good, the bad and the Ugly. Whole genome sequencing for clinical microbiology: Translation into routine applications. Basel, Switzerland, September 2, 2017.

Carricho JA. Como analisar e Interpretar os dados de WGS no âmbito de vigilância e detecção de surtos? Simpósio: Virar de página na vigilância laboratorial de doenças infecciosas: aplicação da sequenciação total do genoma (WGS), Instituto Nacional de Saúde Ricardo Jorge, Lisbon, Portugal, September 28, 2017.

Melo Cristino J. 9 Antibióticos e Resistências. 12º Curso de Pós-Graduação em Doenças Infecciosas. Serviços de Doenças Infecciosas do CHLC e Instituto de Saúde Ambiental da Faculty of Medicine, University of Lisbon, Algés, Portugal, October, 2017.

Melo Cristino J. Impacto da vacinação na infecção pneumocócica em Portugal. Diferenças na criança e adulto, Sessão de Abertura. 38º Ciclo de Conferências do Serviço de Doenças Infecciosas do Centro Hospitalar Lisboa Norte, Lisbon, Portugal, October 20, 2017.

Melo Cristino J. Como melhorar o diagnóstico microbiológico da Infecção?. Semana do Antibiótico, Conferências São João. Centro Hospitalar de São João, Porto, Portugal, November 22, 2017.

Ramirez M. Global burden of pneumococcal diseases (Invited lecture SP18-1). International Congress of Chemotherapy and Infection (ICC 2017), Taipei, Taiwan, November 24-27, 2017.

### Communications in International Conferences

Silva-Costa C, Aguiar SI, Pinho MD, Friães A, Ramirez M, Melo-Cristino J. The Portuguese Group for the Study of Streptococcal Infections, the Portuguese Study Group of Invasive Pneumococcal Disease of the Paediatric Infectious Disease Society. Serotype distribution among *Streptococcus pneumoniae* isolates causing complicated pneumonia in children in Portugal (2010-2015). 27<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Vienna, Austria, April 22-25, 2017. (Poster Presentation).

Pinho MD, Luebke-Becker A, Wieler LH, Pomba MC, Preziuso S, Melo-Cristino J, Ramirez M. Genotypic characterization of *Streptococcus dysgalactiae* isolates recovered from different hosts. 27<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Vienna, Austria, April 22-25, 2017. (Oral Presentation).

Friães A, Lopes JP, Ramirez M, Melo-Cristino J. Clonal stability among Group A Streptococci causing invasive infections in Portugal. 27<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Vienna, Austria, April 22-25, 2017. (Poster Presentation).

Silva M, Rossi M, Ramirez M, Carriço JA. chewBBACA – a comprehensive and highly efficient workflow for a Blast Score Ratio based allele calling algorithm. Applied Bioinformatics for Public Health Microbiology, Hinxton, England, May 17-19, 2017. (Oral Presentation).

Ribeiro-Goncalves B, Rossi M, Ramirez M, Carrico JA. 2017. Dynamic cgMLST analysis: making the most out of your gene-by-gene data. Applied Bioinformatics for Public Health Microbiology, Hinxton, England, May 17-19, 2017. (Poster Presentation).

Ribeiro-Goncalves B. Whole genome MLST: Phylogenetic inference and metadata visualization. “Genomics in foodborne pathogen surveillance and outbreak investigation” summer course, University of the Basque Country, UPV/EHU, Vitoria- Gasteiz, Spain, July 12, 2017. (Oral Presentation).

Lopes E, Fernandes T, Machado MP, Carriço J, Melo-Cristino J, Ramirez M, Martins E. Portuguese Group for the Study of Streptococcal Infections. Dominance of a macrolide resistant lineage resulting from capsular switching among group B *Streptococcus* invasive disease in non-pregnant adults in Portugal (2009-2015). IDWeek 2017. San Diego, USA, October 4-8, 2017. (Poster Presentation).

Horácio AN, Silva-Costa C, Lopes JP, Ramirez M, Melo-Cristino J. The Portuguese Group for the Study of Streptococcal Infections. Non-invasive pneumococcal pneumonia in adults in Portugal (2012-2015): resilience of vaccine serotypes and emergence of non-vaccine serotypes. IDWeek 2017, San Diego, USA, October 4-8, 2017. (Poster Presentation).

Silva-Costa C, Horácio A, Aguiar SI, Lopes JP, Brito MJ, Ramirez M, Melo-Cristino J. Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society. PCV13 serotypes are still important causes of pediatric invasive pneumococcal disease in Portugal after more than a decade of conjugate vaccine. International Congress of Chemotherapy and Infection (ICC 2017), Taipei, Taiwan, November 24-27, 2017. (Poster Presentation).

Lopes E, Fernandes T, Machado MP, Carriço J, Melo-Cristino J, Ramirez M, Martins E. Portuguese Group for the Study of Streptococcal Infections. Increase of macrolide resistance among group B streptococcus invasive disease in non-pregnant adults in Portugal (2009-2015) was driven by a capsular variant of a single clone. International Congress of Chemotherapy and Infection (ICC 2017), Taipei, Taiwan, November 24-27, 2017. (Poster Presentation).

Horácio AN, Silva-Costa C, Lopes JP, Ramirez M, Melo-Cristino J. Portuguese Group for the Study of Streptococcal Infections. Importance of vaccine serotypes and emergence of non-vaccine serotypes causing non-invasive pneumococcal pneumonia in adults in Portugal (2012-2015). International Congress of Chemotherapy and Infection (ICC 2017), Taipei, Taiwan, November 24-27, 2017. (Oral Presentation).

#### **Communications in National Conferences**

Mendes CI, Pinho M, Melo-Cristino J, Ramirez M, Carriço JA. Pan-genome comparison between *Streptococcus dysgalactiae* subsp. *equisimilis* isolates from human and animal sources. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Oral Presentation).

Silva M, Rossi M, Ramirez M, Carriço JA. chewBBACA – an efficient framework for large-scale prokaryote whole genome/core genome MultiLocus Sequence Typing analyses. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Oral Presentation).

Machado MP, Rossi M, Mendes CI, Nalbantoglu Y, Ramirez M, Borges V, Carriço JA. INNUca, a standardized pipeline for bacteria genome assembly and quality control. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Poster Presentation).

Ribeiro-Gonçalves B, Rossi M, Ramirez M, Carriço JA. Dynamic cgMLST phylogenetic analysis: a tool for exploring large gene-by-gene datasets at different discrimination levels. Bioinformatics Open Days, Braga, Portugal, February 22-24, 2017. (Poster Presentation).

Ribeiro-Gonçalves B. INNUENDO Platform: integrating High-Throughput Sequencing into bacterial foodborne pathogen surveillance. MicroBioTec'17, Porto, Portugal, December 7-9, 2017. (Oral Presentation).

Silva-Costa C, Horácio A, Aguiar SI, Lopes JP, Brito MJ, Ramirez M, Melo-Cristino J. Portuguese Group for the Study of Streptococcal Infections, Portuguese Study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society. Pediatric invasive pneumococcal disease in Portugal: changing epidemiology (2012-2016). MicroBioTec'17, Porto, Portugal, December 7-9, 2017. (Poster Presentation).

Mendes CI, Machado MP, Melo-Cristino J, Ramirez M, Carriço JA. Phase-variable type I restriction-modification systems: A new characterization methodology for high throughput sequencing data. MicroBioTec'17, Porto, Portugal, December 7-9, 2017. (Poster Presentation).

### **Organisation of Conferences**

Hanscheid T. Organizer and Lecturer. Infecção e Doenças Infecciosas, Campo Maior, Portugal, May 20, 2017.

### **Internationalisation**

Working group on malaria cytometry – Howard Shapiro (USA), Brian Grimberg (USA), Grace Chojnowski (Australia), Rui Gardner (Portugal).

Sensitivity testing using flow cytometric principles to detect hemozoin – flow cytometer for measurement in Gabon, in collaboration with Martin Grobusch, head of the Infectious Diseases department, University Hospital Amsterdam, The Netherlands.

Partner in the European Food Safety Authority (EFSA) funded project “INNUENDO: A novel cross-sectorial platform for the integration of genomics in surveillance of foodborne pathogens” (<http://www.innuendoweb.org/>).

Collaboration with Dr. John Rossen in shotgun metagenomics for clinical diagnostics, Head of the Molecular Unit and Principal Investigator Genomics for Infection Prevention, Department of Medical Microbiology, University of Groningen, University Medical Center Groningen.

Participation as experts in the ECDC- EFSA ad hoc working group “Technical support to collect and analyse whole genome sequencing (WGS) data in the joint ECDC-EFSA molecular typing database”.

#### **Prizes, Honours and Awards**

Melo Cristino J. Professor Nicolau van Uden Award 2017, Sociedade Portuguesa de Microbiologia, December 2017.

#### **Advanced Teaching**

Carriço JA. Whole genome MLST: theory. Summer Course “Genomics in foodborne pathogen surveillance and outbreak investigation”. Vitoria-Gasteiz, Basque Country, Spain, July 12-13, 2017.

Carriço JA. From reads to profiles to trees: challenges and solutions in high throughput sequencing data analysis. Summer Course “Genomics in foodborne pathogen surveillance and outbreak investigation”. Vitoria-Gasteiz, Basque Country, Spain, July 12-13, 2017.

Machado MP. QA/QC and automatization of whole genome sequence analysis. Summer Course “Genomics in foodborne pathogen surveillance and outbreak investigation”. Vitoria-Gasteiz, Basque Country, Spain, July 12-13, 2017.

Silva M. Whole genome MLST: implementation. Summer Course “Genomics in foodborne pathogen surveillance and outbreak investigation”. Vitoria-Gasteiz, Basque Country, Spain, July 12-13, 2017.

Ribeiro-Gonçalves B. Whole genome MLST: phylogenetic inference and metadata visualization. Summer Course “Genomics in foodborne pathogen surveillance and outbreak investigation”, Vitoria-Gasteiz, Basque Country, Spain, July 12-13, 2017.

Carricho JA, Machado MP. De novo assembly of bacterial genomes with INNUCA pipeline. Workshop on Genome Assembly and Annotation, Instituto Gulbenkian Ciência, Oeiras, Portugal, October 23-27, 2017.

Carricho JA. Graphical representation of WGS analysis. Regional Capacity-building Workshop for Integration of Next Generation Sequencing in the Clinical Microlab, Herzliya, Israel, October 30-November 1, 2017.

Carricho JA. Interactive Discussion IV – I Have Sequenced a Bacterial Genome – What Is Next? Regional Capacity-building Workshop for Integration of Next Generation Sequencing in the Clinical Microlab, Herzliya, Israel, October 30-November 1, 2017.

Carricho JA. International databases of genomes and genes. Regional Capacity-building Workshop for Integration of Next Generation Sequencing in the Clinical Microlab, Herzliya, Israel, October 30-November 1, 2017.

Carricho JA. Overview of Molecular Typing Approaches for Bacterial Pathogens. Regional Capacity-building Workshop for Integration of Next Generation Sequencing in the Clinical Microlab, Herzliya, Israel, October 30-November 1, 2017.

Carrico JA, Gonçalves-Ribeiro B, Machado MP, Silva M. Faculty on course “From microbial genomics to metagenomics”. Doctoral School in Environmental, Food and Biological Sciences (YEB), University of Helsinki, Helsinki, Finland, December 11-14, 2017.

Carricho JA, Friães A, Hänscheid T, Melo Cristino J, Pinho M, Ramirez M, Silva-Costa C. Organizers and principal faculty of the second cycle course of Clinical Microbiology and Emerging Infectious Diseases, Faculty of Medicine, University of Lisbon, Lisbon, Portugal.

Friães A, Hänscheid T, Melo Cristino J, Pinho M, Ramirez M, Silva-Costa C. Participation on the second cycle course of Microbiology (responsible for the course on Medical Microbiology) of Instituto Superior Técnico, University of Lisbon in collaboration with Faculty of Medicine, Faculty of Sciences and Faculty of Veterinary Medicine, University of Lisbon, Lisbon, Portugal.

Carricho JA. Participation on the second cycle course of Computational Biology/Bioinformatics for Master and PhD programmes (responsible for the module on Molecular Phylogenetics) of Instituto Superior Técnico, University of Lisbon in collaboration with the Faculty of Medicine, University of Lisbon, Lisbon, Portugal.

### **MSc Thesis Completed**

Denise Rodrigues Francisco, 11/05/2017, "Optimization of a flow cytometric assay to measure antimalarial drug effects", Instituto Superior Técnico, University of Lisbon. Supervisor: Hanscheid T.

Jessica Lisboa, 16/11/2017, "Assessment of Anti-parasitic and Antibacterial Effects of Quinoline Drugs", Instituto Superior Técnico, University of Lisbon. Supervisor: Hanscheid T.

### **PhD Thesis Completed**

Maria Rebelo, 04/05/2017, "Development of an innovative Real-Time Assay for Antimalarial Sensitivity testing", Faculty of Medicine, University of Lisbon. Supervisor: Hanscheid T.



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## Remondes, Miguel

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### Major Interests / Objectives

Cognitive deficits present in Alzheimer's Disease, Anhedonia, Depression, and Schizophrenia, have been mapped to neuropathological changes in midline cortical structures, such as the anterior cingulate cortex, necessary for appropriate decision-making, the retrosplenial cortex, critically involved in visual-spatial processing, and the hippocampal formation, critical for episodic memory and any mental function therein dependent. To understand such disorders, it is imperative that we identify the structures and mechanisms underlying the behaviors they affect. We model such behaviors in rodents as goal-directed behaviors of variable complexity, during which we monitor and manipulate the relevant neural circuits, to assess their functions.

### Head of Laboratory

Armando Miguel Caseiro Pires Remondes, PhD

### Research Team

Ana Raquel Pereira	BSc	MSc Student
Ana Sofia Carvalho Cruz	Master	PhD Student
Bárbara Pinto Correia	MSc	PhD Student
Carolina Costa Jorge Marcos Quintino	Graduate	MSc Student
Emanuel Ferreira Fernandes	Master	PhD Student
Gonçalo Aires de Oliveira	PhD	Post-Doctoral Fellow
Gonçalo Correia de Oliveira Ferreira	Graduate	MSc Student (Started September)
Jorge Miguel Claro Cardoso	Graduate	MSc Student
Marcelo Francisco Vieira Dias	Master	PhD Student
Miriam Garrido Marguilho	Undergraduate	Trainee
Thabelo Mmamatseliso Khoboko	Master	PhD Student

### Laboratory Keywords / Research Areas

Cortex-hippocampus, Optogenetics-pharmacogenetics, Electrophysiology during behavior, Spatial maps, Decision, Sensory stimulus.

### Major Scientific Achievements

GDB requires that the SCM is made available to midline cortical regions, ACC through RSC, responsible for decision-making, and dysfunctional in ASD, and Schizophrenia. Besides reporting state-dependent communication between HIPPF and ACC, we have recently identified the synapses connecting the two structures, which we are currently manipulating, in order to assess their role in HIPPF-MC communication during GDB.

To study time processing by HIPPF neurons we recently developed a behavioral task in which success depends on time judgement, and have developed a novel device to record simultaneously from the HIPPF divisions while rats perform this task. We are currently analyzing the results of such neural/behavioral recording while rats process time lapses. We have published the novel recording device in *Frontiers in Neural Circuits*. We have also engaged in public outreach activities, and collaborated with the media.

### Selected Publications

Liang L, Kirk JC, Schmitt LI, Komorowski RW, Remondes M, Halassa MM, Oline SN (2017). Scalable, Lightweight, Integrated and Quick-to-assemble (SLIQ) hyperdrives for functional circuit dissection. *Front. Neural Circuits* <http://journal.frontiersin.org/article/10.3389/fncir.2017.00008>. (IF: 3.005, Citations: 2). 20 article views in 5 days, while in provisional form.

Remondes M \*, Wilson M (2015). Slow-gamma rhythms coordinate cingulate cortical responses to hippocampal sharp-wave ripples during choice behavior. *Cell Reports* <http://dx.doi.org/10.1016/j.celrep.2015.10.005>. (IF: 8.282, Citations: 7).

Wilson M \*, Varela C, Remondes M (2015) Phase organization of network computations. *Curr Opin Neurobiology* 31C, 250-253. doi: 10.1016/j.conb.2014.12.011. (IF: 6.133, Citations: 9).

Remondes M \*, Wilson M (2013). Cingulate-hippocampus Coherence and Trajectory Coding in a Sequential Choice Task. *Neuron* 5, 1277-89. (IF: 14.024, Citations: 22).

### **Ongoing Research Projects**

2016/2017: Neural bases of perception, memory and decision. Coordinator: Armando Miguel Caseiro Pires Remondes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: DEP MRemondes. Amount: € 25 000,00. Total Amount: € 25 000,00.

2014/2019: Cingulate-hippocampal interactions during decision-making. Coordinator: Armando Miguel Caseiro Pires Remondes. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: IF/00201/2013/CP1170/CT0002. Amount: € 50 000,00. Total Amount: € 50 000,00.

### **Other Projects**

2016/2018: SynaNet: Neurologic and Psychiatric disorders: from synapses to networks. Coordinator: Ana Maria Ferreira de Sousa Sebastião. Funding Agency: European Commission. Reference: TWINNING 692340. Amount: € 525 437,50. Total Amount: € 999 996,25.

### **Invited Lectures and Seminars**

Cognitive Maps and Long-range Neural Synchrony During Choice Behavior. IMM 2017 CAML PhD Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 2017.

Brain Maps for Choice Behaviors. VI International Conference in Cognitive Neurodynamics (ICCN), Carmona, Seville, Spain, August 2017.

Sensory integration for memory-dependent choice behaviors. "Mind-Brain Lectures" for the Mind-Brain College of the University of Lisbon, September 2017.

Sensory integration in memory-driven choice behaviors. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, November 2017.

Sensory integration in memory-dependent choice behaviors. FMUL PhD Program in Neuroscience, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017.

Cognitive Maps and Long-range Neural Synchrony During Choice Behaviors. MIT-Portugal PhD Program in Bio-Engineering Neuroscience Course 2017, Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, 2017.

### **Communications in National Conferences**

Cruz AS, Remondes M. Cingulate-hippocampal interactions during memory-guided decisions. Meeting of the Lisbon Mind-Brain College NeurULisboa, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017. (Poster Presentation).

Ferreira-Fernandes E, Remondes M. Why rats turn the way they do?. Meeting of the Lisbon Mind-Brain College NeurULisboa 2017, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017.

Dias M, Remondes M. Time to probe hippocampal function. Meeting of the Lisbon Mind-Brain College NeurULisboa 2017, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017. (Poster Presentation).

Ferreira-Fernandes E, Remondes M. Why rats turn the way they do?. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017.

Dias, M, Remondes M. Time to probe hippocampal function. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017.

Cruz AS, Remondes M. Cingulate-hippocampal interactions during memory-guided decisions. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

### **Internationalisation**

Hosted Valerie Ego-Stengel, PhD, Group Leader at the Unité de Neurosciences Intégratives et Computationnelles. Institut de Neurobiologie Alfred Fessard, France.

Reviewed for the journal Cerebral Cortex.

Reviewer of OPUS Grants for the National Science Center of Poland from 2015 until present.

Reviewer of Grants for ANR France 2016 Program.

Reviewer for FLAD Grants 2017.

"Brain Maps for Choice Behaviors". VI International Conference in Cognitive Neurodynamics (ICCN), Carmona, Seville, Spain, August 2017.

Supervised international medical students: University of Malta Medical Student Tamara Muscat, University of Ljubljana (Slovenia) Medical Student Špela Grilc, University of Malta 2<sup>nd</sup> year Medical student Jessica-Marie Barbara.

Was the main opponent at PhD theses defenses within the Champalimaud International PhD Program Holds collaborations with scientists in the EU and the US.

Lab members have engaged in Summer schools abroad, and graduate students seek international scientists as thesis committee members.

The lab is part of the network "Neurologic and Psychiatric Disorders: from synapses to networks (SynaNet)", which includes labs from the UK, Finland, Italy, and France.

We have recently published in collaboration with two labs at the MIT and NYU.

Our students will present their results in 4 posters submitted to the FENS2018 forum, in Berlin.

### **Prizes, Honours and Awards**

Awarded the Prize of Best Poster of the Lisbon Mind-Brain College NeurULisboa 2017. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, 2017

### **Advanced Teaching**

Member. Doctoral Program in Experimental Biology and Biomedicine, CNC - Center for Neuroscience and Cell Biology, University of Coimbra.

Member and Lecturer. MSc Program Neurasmus ERASMUS Mundus Program and MIT-Portugal PhD Program in Bio-Engineering, to which he lectured.

Member and Lecturer. iMM-FMUL PhD program in Biomedicine – LisbonBioMed. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon.

Member and Lecurer. FMUL PhD Program in Neuroscience – lecture on Neuronal Circuits. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon.

Co-organizer. Neuroscience course for the iMM-FMUL PhD program LisbonBioMed. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon.

Lecturer. MSc program "Microbiologia Clínica e Doenças Infeciosas Emergentes". Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon.

### **Science and Society**

Collaborations with news media (several).

### **MSc Thesis Completed**

Carolina Costa Jorge Marcos Quintino, 15/12/2017, "Oc2M area as a multisensory integrator-anatomical connectivity and synaptic function using in vitro optogenetics", Faculty of Medicine, University of Lisbon. Supervisor: Armando Miguel Caseiro Pires Remondes.

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## Saldanha, Carlota

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### Major Interests / Objectives

We are focused on understanding the cellular and molecular mechanisms underlying acute and recovery of inflammatory responses. Our interest was on deciphering how blood components, blood cells and molecular partners are targeted by fibrinogen, sCD40L and OxLDL. Considering leukocyte recruitment and making use of intravital microscopy, the development of numerical models that simulate the leukocyte-vascular wall interface interactions were also addressed. Under our scope was, as well, the study of biorheological behavior of blood components and fibrinogen-mediated signal transduction of the nitric oxide and its bioavailability on erythrocytes. Consequently, the validation of inflammatory biomarkers in vascular diseases were under questioning. We expect to achieve a better understanding of the inflammatory mechanisms in pathologies, like sepsis and cardiovascular diseases to help in further biomedical management.

### Head of Laboratory

Maria Carlota Saldanha Lopes, PhD Agregação

### Research Team

Ana Rosa Miranda dos Santos Silva Herdade	Master	Investigator (Left September)
Ângelo Calado	PhD	Principal Investigator (Left September)
Beatriz Simões Pinheiro	Undergraduate	Trainee
Mariana Gomes Ferreira	Graduate	MSc Student
Mariana Selas Figueira	Undergraduate	Trainee
Patrícia Alexandra Veloso Napoleão	PhD	Post-Doctoral Investigator (Left June)
Rita Maria Santos Esteves	Graduate	Technician
Tiago Luís Pinto Pereira da Silva	Graduate	PhD Student (Left June)

### Laboratory Keywords / Research Areas

Inflammation, Microcirculation, Neutrophil, Erythrocyte, Leukocyte recruitment, Inflammation, Hemorheology, Microcirculation.

### Major Scientific Achievements

- Forskolin, activator of AC, normalizes the levels of NO efflux from erythrocytes in hyperfibrinogenemia. The same occurs when the inhibitor of the erythrocyte CK2 is present. High [Fibrinogen] induces NO efflux from erythrocytes when band 3 is phosphorylate and [cAMP] low. CHM 2017.
- Therapeutic targets for erythrocytes bioavailability in NO are AChE, AC, Gi, band 3 protein, PTP, PTK, PKC, PI3K and PD3. Molecules 2017.
- In post-capillary venules of mice model of inflammation, increase number of rolling, adherent and crawling neutrophils. Adherent cells deformation slows the motion of others, helping capture. The erythrocyte aggregation contributing to neutrophil approach to the vessel wall. Decrease of erythrocyte deformability during inflammatory response confirms the role of the erythrocyte biorheology in inflammation. Microvasc Res 2017.
- Erythrocytes and neutrophils are enrolled in signal transduction mechanism of inflammatory mediators and disturb the hemorheology. NAPDD 2017.

### Selected Publications

Silva-Herdade AS, Sequeira A, Calado Â, Saldanha C, Kafi O (2017). Hydrodynamics of a free-flowing leukocyte toward the endothelial wall. *Microvascular Research* 112, 7-13. (IF: 2.371, Citations:-).

Napoleão P, Cabral LBP, Selas M, Freixo C, Monteiro MC, Criado MB, Costa MC, Enguita FJ, Viegas-Crespo AM, Saldanha C, Mota Carmo M, Ferreira RC, Pinheiro P (2016). Stratification of ST-elevation myocardial infarction patients based on soluble CD40L longitudinal changes. *Translational Research* 176, 95, DOI 10.1016/j.trsl.2016.04.005. (IF:4.652, Citations:1).

Napoleão P, Ramos C, Cabral LBP, Selas M, Monteiro MC, Criado MB, Viegas-Crespo AM, Saldanha C, Mota Carmo M, Ferreira RC, Pinheiro T. (2015) Changes of sCD40L in the progression of acute myocardial infarction associate to eNOS polymorphisms and VEGF but not to platelet CD62P expression. *Translational Research* 2015, 166:650-659. (IF: 4.652, Citations:--)

de Oliveira S, Reyes-Aldasoro CC, Candel S, Renshaw SA, Mulero V, Calado A (2013). Cxcl8 (Interleukin-8) mediates neutrophil recruitment and behavior in the zebrafish inflammatory response *J.Immunol.* 190, 4349-59. (IF: 4.856, Citations: 3).



de Oliveira S, Vitorino de Almeida V, Calado A, Rosário HS, Saldanha C (2012). Integrin-associated protein (CD47) is a putative mediator for soluble fibrinogen interaction with human red blood cells membrane. *Biochim Biophys Acta* 1818, 481-490. (IF: 3.498, Citations: 2).

#### **Publications in Peer Review Journals**

Silva-Herdade AS, Sequeira A, Calado Â, Saldanha C, Kafi O (2017). Hydrodynamics of a free-flowing leukocyte toward the endothelial wall. *Microvasc Res* 112, 7-13. (IF: 2.371, Citations:--).

Saldanha C (2017). Human erythrocyte acetylcholinesterase in Health and disease. *Molecules* Sep 8;22(9). pii: E1499. doi: 10.3390/molecules22091499. (IF: 2.861, Citations:--).

Saldanha C, Silva-Herdade AS (2017). Physiological properties of erythrocytes in inflammation. *J Cel Biotec* 3, 15-20. (IF:--, Citations:--).

#### **Other Publications International**

Saldanha C, Messias A (2017). Sepsis needs follow-up studies in intensive care units- Another avenue for translational research. *Nov Appro Drug Des Dev*. 1(1): NAPDD.MS.ID. 555555, ISSN: 2575-8942. (IF--, Citations:--).

Saldanha C, Silva-Herdade AS (2017). Erythrocyte as Therapeutic target *Nov Appro Drug Des Dev*. 2(3): NAPDD.MS.ID. 555590 ISSN: 2575-8942. (IF--, Citations:--).

Santini A, Freitas T, Saldanha C, Silva-Herdade A (2017). Lipoproteins effects on erythrocyte nitric oxide metabolism and biorheology. *Clin Med Invest* 2, 1-5. (IF--, Citations:--).

Silva V, Napoleão P, Gerales V, Rocha I (2017). Non-invasive ECG recording for zebrafish. *IEEE 5th Portuguese Meeting on Bioengineering (ENBENG)*. DOI: 10.1109/ENBENG.2017.788948. . (IF--, Citations:--).

Napoleão P, Carmo MM, Pinheiro T (2017). Prognostic evaluation of soluble CD40L in acute myocardial infarction: is not fancy, is science! *Ann Transl Med*. 5, 90. doi: 10.21037/atm.2017.01.58. (IF--, Citations:--).

### **Other Publications National**

Saldanha C (2017). Deformabilidade Eritrocitária Editorial do Boletim da Sociedade Portuguesa de Hemorreologia e microcirculação 32(1); 3-4, (IF 0, Citations 0) Saldanha C. (2017) Micro Instrumentos em Hemorreologia Editorial do Boletim da Sociedade Portuguesa de Hemorreologia e microcirculação 32(12); 3-4. (IF--, Citations:--).

### **Invited Lectures and Seminars**

Saldanha C. Hemorreologia e Exercício Físico. 13<sup>o</sup> Curso de Pós-Graduação em Medicina Desportiva, March 24, 2017.

### **Communication in International Conferences**

Saldanha C, Oliveira I, Napoleão P. Biophysical role of red blood cells in microcirculation. ESM-EVBO 2017 2<sup>nd</sup> joint Meeting of the European Society for Microcirculation (ESM) and Europran Vascular Biology Organization (EVBO), Geneva, Switzerland, May 2017. (Poster Presentation).

Saldanha C, Herdade AS. Changes in Erythrocyte Nitric Oxide Metabolism Induced by Fibrinogen ESM-EVBO 2017 2<sup>nd</sup> joint Meeting of the European Society for Microcirculation (ESM) and Europran Vascular Biology Organization (EVBO), Geneva, Switzerland, May 2017. (Oral Presentation).

Saldanha C, Silva-Herdade AS. Casein Kinase 2 Effects on Nitric Oxide Metabolism and Deformability of Human Erythrocytes. XI International Conference on Hemorheology and Microcirculation Yaroslavl, Russia, July 2017. (Poster Presentation).

### **Communication in National Conferences**

Durão R, Napoleão P. Evaluation of CD40L in heart regeneration after cryoinjury-induced myocardial infarction in Zebrafish. Practical training in Biologia Humana, University of Évora, Évora, Portugal, February 1-April 28, 2017.

Napoleão P, Eugénio P, Calado A. Cardiac repair after induced-myocardial infarct in zebrafish – focus on sCD40L. Congresso Português de Cardiologia, Albufeira, Portugal, April 22-25, 2017.

### **Internationalisation**

Saldanha C. Member of the Strategic Group, European Society of Microcirculation.

Saldanha C. Member of the European Clinical Hemorheology and Microcirculation Coordinating Committee.

Saldanha C. President of the Portuguese Society of Hemorheology and Microcirculation (SPHM).

Saldanha C. Member of Editorial Board of J Cellular Biotechnology.

Saldanha C. Member of Editorial Board of Clinical Hemorheology and Microcirculation.

Saldanha C. Member of Editorial Board of Sciedu Press, Case Reports in Clinical Pathology.

Saldanha C. Member of Editorial Board of J of Eye Diseases.

Saldanha C. Certificate of Excellence Reviewing of Annual Research and Review in Biology.

Saldanha C. Editor in Chief of the Bulletin of the SPHM.

### **Advanced Teaching**

Saldanha C. Organizer. Biochemistry Session of the 13<sup>o</sup> Curso de Pós-Graduação em Medicina Desportiva, March 24, 2017.

Saldanha C. Lecturer. Hemorreologia e Exercício Físico. 13<sup>o</sup> Curso de Pós-Graduação em Medicina Desportiva, March 24, 2017

### **Science and Society**

Saldanha C. Deformabilidade Eritrocitária Editorial do Boletim da Sociedade Portuguesa de Hemorreologia e microcirculação, 2017.

Saldanha C. Microinstrumentos em Hemorreologia Editorial do Boletim da Sociedade Portuguesa de Hemorreologia e microcirculação, 2017.

## Santos, Nuno C.

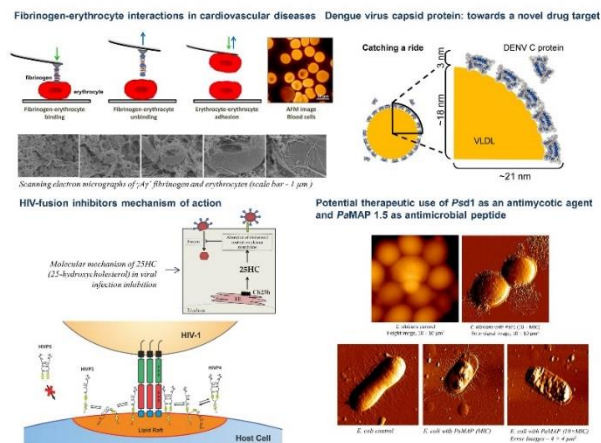
### Major Interests / Objectives

Biochemical and biophysical processes occurring in membranes of human cells, as well as of their viral and bacterial pathogens. Study of the two steps of the enveloped viruses (HIV-1, dengue, West Nile, Zika and pediatric respiratory viruses) life cycle that involve biomembranes – the entrance of the virus or its content into the target cell (including its inhibition) and the assembly of new virions. Study of the binding of fibrinogen to erythrocytes in cardiovascular diseases. Pre-clinical evaluation of the membrane activity and mechanism of action of antimicrobial (AMP) and anticancer (ACP) peptides. On the Nanomedicine area, work on the development of innovative protein-ligand interactions biosensor systems (nanoparticles and amyloid-based biosensors).

### Head of Laboratory

Nuno Fernando Duarte Cordeiro Correia dos Santos, PhD and Habilitation, Associate Professor

### Graphical Abstract



### Research Team

Ana Filipa Barata Duarte Guedes	Master	PhD Student
Ana Souto Martins	Master	PhD Student
André Rodrigues Nascimento	Graduate	MSc Student
Axel Hollmann	PhD	Post-Doctoral Investigator
Bárbara Sofia Lopes Gomes	Master	PhD Student (Left November)
Catarina Isabel de Sousa Lopes	Master	PhD Student (Started May)

Filomena A. Carvalho	PhD	Principal Investigator, Faculdade de Medicina da Universidade de Lisboa, Assistant Professor
Ivo Cristiano da Rocha Martins	PhD	Principal Investigator
Marcelo Alexandre da Costa Tavares Augusto	Master	PhD Student
Marcin Makowski	Master	PhD Student (Started March)
Marco André Manso Rodrigues	PhD	Post-Doctoral Investigator
Maria Teresa Damásia Freitas Santos	Undergraduate	Technician
Mário Romão Felício	Master	PhD Student
Patricia Isabel Duarte Montês Carvalho	Master	PhD Student
Patrícia Morgado da Silva	Master	PhD Student (Started April)
Peter Jonathan Eaton	PhD	Post-Doctoral Investigator (Started December)
Sónia Gonçalves Abreu	PhD	Researcher, Faculdade de Medicina da Universidade de Lisboa

### Laboratory Keywords / Research Areas

Nanomedicine, HIV, Dengue, West Nile, Zika and respiratory viruses, Peptide-based therapies (AMPs, ACPs, pep14-23), Atomic force microscopy (AFM), Biomarkers of cardiovascular diseases

### Major Scientific Achievements

Zika and West Nile virus capsid proteins, like dengue, interact specifically with host lipid systems. These interactions are essential for viral replication, and could lead to new drug leads, as previously done in our lab for dengue virus. The interaction and activity of fusion inhibitor peptides against HIV or paramyxoviruses depends of their biophysical properties, with lipid conjugation or PEG linker inclusion being possible strategies to improve viral inhibition. Synthetic small therapeutic peptides, designed from natural precursors, improve their activity by considering different biophysical properties. PaMAP2/PaMAP 1.9 showed to be active against multiresistant bacteria and cancer cells. EcAMP1R2, a bioinformatics-designed peptide, could also be a promising drug against bacterial infections. Erythrocyte aggregation has a higher probability to occur in arterial hypertension patients, being directly related with the presence of fibrinogen, especially its gamma' variant.

### Selected Publications

Guedes AF, Carvalho FA, Malho I, Lousada N, Sargento L, Santos NC (2016). Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients. *Nature Nanotechnol.* 11, 687-692. (IF: 38.986, Citations: 8).

Vigant F, Santos NC, Lee B (2015). Broad-spectrum antivirals against viral fusion. *Nature Rev. Microbiol.* 13, 426-437. (IF: 26.819, Citations: 27).

Faustino AF, Carvalho FA, Martins IC, Castanho MARB, Mohana-Borges R, Almeida FC, Da Poian AT, Santos NC (2014). Dengue virus capsid protein interacts specifically with very low-density lipoproteins. *Nanomedicine (NBM)* 10, 247-255. (IF: 5.72, Citations: 17).

Hauser CA, Maurer-Stroh S, Martins IC (2014). Amyloid-based nanosensors and nanodevices. *Chem Soc Rev.* 43, 5326-5345. (IF: 38.618, Citations: 58).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC (2010). Atomic force microscopy-based molecular recognition of a fibrinogen receptor on human erythrocytes. *ACS Nano* 4, 4609-4620. (IF: 13.942, Citations: 62).

### **Ongoing Research Projects**

2016/2019: Broad-spectrum antiviral peptides against respiratory viruses. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BQB/3494/2014. Amount: € 197 839,00. Total Amount: € 197 839,00.

2016/2019: Molecular interactions of circulating fibrinogen as a risk factor for cardiovascular and cerebrovascular pathologies. Coordinator: Filomena Maria Dias Almeida Carvalho Arede. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BBB-BMD/6307/2014. Amount: € 184 965,00. Total Amount: € 184 965,00.

2015/2020: Engineering protease-resistant alpha-beta for broad-spectrum antivirals. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Funding Agency: National Institute of Health. Reference: 5R01AI114736. Amount: € 300 000,00. Total Amount: € 1 225 000,00.

2010/2017: The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation. Coordinator: Ivo Cristiano da Rocha Martins. Funding Agency: Fundação Calouste Gulbenkian. Reference: FCG IMartins. Amount: € 50 000,00. Total Amount: € 50 000,00.

### Other Projects

2015/2019: INPACT: Innovative peptides against cancer and pathogenic bacteria, with advances in science, biopharmaceutical drug development, product market targeting, training, and communication. Coordinator: Miguel Augusto Rico Botas Castanho. Funding Agency: European Commission. Reference: MSCA RISE 644167. Amount: € 463 500,00. Total Amount: €1 390 500,00.

### Publications in Peer Review Journals

Augusto MT, Hollmann A, Porotto M, Moscona A, Santos NC (2017). Antiviral lipopeptide-cell membrane interaction is influenced by PEG linker length. *Molecules*, 22, 1190. (IF: 2.861, Citations: 1).

Augusto MT, Hollmann A, Troise F, Veiga AS, Pessi A, Santos NC (2017). Lipophilicity is a key factor to increase the antiviral activity of HIV neutralizing antibodies. *Colloids Surf. B - Biointerfaces*, 152, 311-316. (IF :3.887, Citations:--).

Dias SA, Freire JM, Perez-Peinado C, Domingues MM, Gaspar D, Vale N, Gomes P, Andreu D, Henriques ST, Castanho M, Veiga AS (2017). New Potent Membrane-Targeting Antibacterial Peptides from Viral Capsid Proteins. *Front. Microbiol.* 8, 775. (IF:4.076, Citations:--).

Farias EAD, Nogueira SS, Farias AMD, de Oliveira MS, Soares MDC, da Cunha HN, dos Santos JR, da Silva DA, Eaton P, Eiras C (2017). A thin PANI and Carrageenan-Gold Nanoparticle Film on a Flexible Gold Electrode as a Conductive and Low-Cost Platform for Sensing in a Physiological Environment. *J. Mater. Sci.*, 52, 13365-13377. (IF:2.599, Citations:--).

Felício MR, Silva ON, Gonçalves S, Santos NC, Franco OL (2017). Peptides with dual antimicrobial and anticancer activities. *Front. Chem.*, 5, 5. (IF:3.994, Citations: 5).

Figueira TN, Palermo LM, Veiga AS, Huey D, Alabi CA, Santos NC, Welsch JC, Mathieu C, Horvat B, Niewiesk S, Moscona A, Castanho MA, Porotto M (2017). In vivo efficacy of measles virus fusion protein-derived peptides is modulated by the properties of self-assembly and membrane residence. *J. Virol.*, 91, e01554-16. (IF:4.663, Citations: 3).

Gomes B, Santos NC, Porotto M (2017). Biophysical properties and antiviral activities of measles fusion protein derived peptide conjugated with 25-hydroxycholesterol. *Molecules*, 22, 1869. (IF:2.861, Citations: 1).

Gonçalves S, Silva PM, Felício MR, de Medeiros LN, Kurtenbach E, Santos NC (2017). Psd1 effects on *Candida albicans* planktonic cells and biofilms. *Front. Cell. Infect. Microbiol.*, 7, 249. (IF: 4.300, Citations:--).

Guedes AF, Carvalho FA, Moreira C, Nogueira JB, Santos NC (2017). Essential arterial hypertension patients present higher cell adhesion forces, contributing for fibrinogen-dependent cardiovascular risk. *Nanoscale*, 9, 14897-14906. (IF:7.367, Citations:--).

Hollmann A, Delfederico L, Santos NC, Disalvo EA, Semorile L (2017). Interaction of S-layer proteins of *Lactobacillus kefir* with model membranes and cells. *J. Liposome Res.*, Feb 8, 1-9. (IF:1.971, Citations:--).

Hopp CS, Bennett BL, Mishra S, Lehmann C, Hanson KK, Lin JW, Rousseau K, Carvalho FA, van der Linden WA, Santos NC, Bogyo M, Khan SM, Heussler V, Sinnis P (2017). Deletion of the rodent malaria ortholog for falcipain-1 highlights differences between hepatic and blood stage merozoites. *PLoS Pathog.*, 13, e1006586. (IF:6.608, Citations:--).

Lopes PA, Martins AP, Martins SV, Madeira MS, Santos NC, Moura TF, Prates JA, Soveral G (2017). Higher membrane fluidity mediates the increased subcutaneous fatty acid content in pigs fed reduced protein diets. *Animal*, 11, 713-719. (IF:1.921, Citations:--).

Mathieu C, Augusto MT, Niewiesk S, Horvat B, Palermo LM, Sanna G, Madeddu S, Huey D, Castanho MA, Porotto M, Santos NC, Moscona A (2017). Broad spectrum antiviral activity for paramyxoviruses is modulated by biophysical properties of fusion inhibitory peptides. *Sci. Rep.*, 7, 43610. (IF: 4.259, Citations: 2).

Maturana P, Martinez M, Noguera ME, Santos NC, Disalvo EA, Semorile L, Maffia PC, Hollmann A (2017). Lipid selectivity in novel antimicrobial peptides: implication on antimicrobial and hemolytic activity. *Colloids Surf. B - Biointerfaces*, 153, 152-159. (IF:3.887, Citations: 1).

Pinto ML, Rios E, Silva AC, Neves SC, Caires HR, Pinto AT, Durães C, Carvalho FA, Cardoso AP, Santos NC, Barrias CC, Nascimento DS, Pinto-do-Ó P, Barbosa MA, Carneiro F, Oliveira MJ (2017). Decellularized human colorectal cancer matrices polarize macrophages towards an anti-inflammatory phenotype promoting cancer cell invasion via CCL18. *Biomaterials*, 124, 211-224. (IF: 8.402, Citations: 5).



Roman W, Martins JP, Carvalho FA, Voituriez R, Abella JVG, Santos NC, Cadot B, Way M, Gomes ER (2017). Myofibril contraction and crosslinking drive nuclear movement to the periphery of skeletal muscle. *Nature Cell Biol.*, 19, 1189-1201. (IF:20.060, Citations: 1).

Vicente Miranda H, Szego ÉM, Oliveira LMA, Breda C, Darendelioglu E, de Oliveira RM, Ferreira DG, Gomes MA, Rott R, Oliveira M, Munari F, Enguita FJ, Simões T, Rodrigues EF, Heinrich M, Martins IC, Zamolo I, Riess O, Cordeiro C, Ponces-Freire A, Lashuel HA, Santos NC, Lopes LV, Xiang W, Jovin TM, Penque D, Engelender S, Zweckstetter M, Klucken J, Giorgini F, Quintas A, Outeiro TF (2017) Glycation potentiates alpha-synuclein-associated neurodegeneration in synucleinopathies. *Brain*, 140, 1399-1419. (IF:10.292, Citations:--).

### **Other Publications International**

Lopes CS, Carvalho FA, Santos NC (2017) Atomic Force Microscopy: a tool for imaging, manipulating biomolecules and quantifying single-molecule interactions in biological systems. *Fluorescence Imaging and Biological Quantification*, Raquel Seruca, Jasjit S. Suri, João M. Sanches (eds.), CRC Press – Taylor & Francis Group, Boca Raton, United States of America, pp. 49-64.

### **Invited Lectures and Seminars**

Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Carvalho FA, Santos NC. Atomic force microscopy as a tool to evaluate the risk for cardiovascular diseases in patients. XIX Annual Linz Winter Workshop, Linz, Austria, February 3-6, 2017.

Martins IC. Using peptides & proteins for drug design and nanotechnology. Jornada de Biotecnologia, Universidade Católica Portuguesa, Porto, Portugal, March 15, 2017.

Faustino AF, Guerra GM, Huber RG, Hollmann A, Domingues MM, Barbosa GM, Enguita FJ, Bond PJ, Castanho MA, Da Poian AT, Almeida FC, Martins IC, Santos NC. Conformational changes governing dengue virus capsid protein function and its inhibition by pep14-23. ARBRE-MOBIEU Plenary Meeting – b3 Building Bridges in Biophysics, Porto, Portugal, March 22-24, 2017.

Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Carvalho FA, Santos NC. Atomic force microscopy as a nanotool for cardiovascular risk evaluation. 9<sup>th</sup> Workshop on Biomedical Engineering, Lisbon, Portugal, April 8, 2017.

Carvalho FA. Force Spectroscopy. Biological and Biomedical Applications. BIO-AFM Hands-on Workshop. Faculty of Sciences, University of Porto, Porto, Portugal, April 12, 2017.

Santos NC. Atomic force microscopy as a nanotool for cardiovascular risk evaluation. IMM Scientific Retreat 2017, Évora, Portugal, May 8-10, 2017.

Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Carvalho FA, Santos NC. High fibrinogen levels promote erythrocyte-erythrocyte adhesion: a cardiovascular risk factor in heart failure and arterial hypertension patients. 16<sup>th</sup> Congress of the Spanish Biophysical Society, Seville, Spain, June 6-8, 2017.

Santos NC. AFM as a tool to evaluate the risk for cardiovascular diseases in patients. 2nd International Congress of CiiEM – Translational Research and Innovation in Human and Health Sciences, Monte da Caparica, Portugal, June 11-13, 2017.

Santos NC. AFM imaging and force spectroscopy applications in membrane biophysics. Membrane Biophysics: Impact of Lipids on Health, Disease and Therapy, Porto, Portugal, July 24-28, 2017.

Santos NC. Atomic force microscopy as a nanotool cardiovascular risk evaluation. I Symposium Biomolecular Engineering Lab, Faculty of Sciences and Technology, Nova University of Lisbon, Monte da Caparica, Portugal, July 26, 2017.

Santos NC. AFM-based force spectroscopy. São Paulo School of Advanced Science (ESPCA) on Biophysical Methods to study Biomolecular Interactions, São Paulo, Brazil, October 16-27, 2017.

Santos NC. Biological and biomedical applications of atomic force microscopy. São Paulo School of Advanced Science (ESPCA) on Biophysical Methods to study Biomolecular Interactions, São Paulo, Brazil, October 16-27, 2017.

Santos NC. Dengue virus capsid protein functions and its inhibition by pep14-23. 1<sup>st</sup> FEBS3+ Joint Meeting of the French-Portuguese-Spanish Biochemical and Molecular Biology Societies, Barcelona, Spain, October 23-26, 2017.

Santos NC. Measuring forces at the nanoscale for cardiovascular risk evaluation. University of Seville, Seville, Spain, November 3, 2017.

Santos NC. AFM-based force spectroscopy on the study of cardiovascular and viral infectious diseases. Workshop in Atomic Force Microscopy coupled to Inverted Fluorescence Microscopy, Porto, Portugal, November 15-17, 2017.

#### **Communications in International Conferences**

Guedes AF, Carvalho FA, Lousada N, Sargento L, Santos NC. Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients. Biophysical Society's 61<sup>st</sup> Annual Meeting, New Orleans, USA, February 11-15, 2017. (Poster Presentation).

Felício MR, Fenstersiefer ICM, Porto WF, Franco OL, Santos NC, Gonçalves S. PaMAP1R3: a novel antimicrobial peptide with activity against Gram-negative bacteria. Biophysical Society's 61<sup>st</sup> Annual Meeting, New Orleans, USA, February 11-15, 2017. (Poster Presentation).

Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Carvalho FA, Santos NC. High fibrinogen levels promote erythrocyte-erythrocyte adhesion: A cardiovascular risk factor in heart failure and arterial hypertension patients. Biophysical Society's 61<sup>st</sup> Annual Meeting, Biophysical Society's 61<sup>st</sup> Annual Meeting, New Orleans, USA, February 11-15, 2017. (Poster Presentation).

Gomes B, Hollmann A, Moscona A, Porotto M, Santos NC. Effect of 25-hydroxycholesterol on the interaction of the fusion inhibitor peptide C34 with model membranes and human blood cells. 25<sup>th</sup> American Peptide Symposium, Whistler, Canada, June 17-22, 2017. (Poster Presentation).

Augusto MT, Mathieu C, Porotto M, Moscona A, Santos NC. Broad-spectrum antiviral activity is modulated by biophysical properties of fusion inhibitory peptides. 19<sup>th</sup> IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Carvalho FA, Ribeiro AS, Figueiredo J, Carvalho R, Mestre T, Monteiro J, Guedes AF, Fonseca M, Sanches J, Seruca R, Paredes J, Santos NC. AFM and graph analysis to study P-cadherin/SFK mechanotransduction signalling in breast cancer cells. 19<sup>th</sup> IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Oral Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. Antimicrobial peptides PaMAP 1.9 and 2 are efficient against a clinical multiresistant bacteria. 19th IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Gomes B, Hollmann A, Moscona A, Porotto M, Santos NC. Combining 25-hydroxycholesterol with a fusion inhibitor peptide: interaction with model biomembranes and human blood cells 19th IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Guedes AF, Carvalho FA, Malho I, Lousada N, Sargento L, Santos NC. Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients. 19<sup>th</sup> IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Oral Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study red blood cells' morphology and elasticity on amyotrophic lateral sclerosis. 19th IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Oral and Poster Presentation).

Makowski M, Felício MR, Franco OL, Gonçalves S, Santos NC. EcAMP1R2 is a highly selective designed antimicrobial peptide. 19th IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Martins AS, Nascimento AR, Faustino AF, Santos NC, Martins IC. Understanding Zika virus capsid protein structure and their ability to interact with host lipid systems. 19<sup>th</sup> IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Silva PM, Marques MC, Augusto MT, Porotto M, Moscona A, Santos NC. Cholesterol-conjugated peptide inhibitors of influenza virus: biophysical characterization. 19th IUPAB (International Union of Pure and Applied Biophysics) Congress and 11<sup>th</sup> EBSA (European Biophysical Societies' Association) Congress, Edinburgh, Scotland, July 16-20, 2017. (Poster Presentation).

Martins AS, Faustino AF, Santos NC, Almeida FC, Martins IC. Understanding Flavivirus capsid proteins structure and their ability to interact with host lipid systems. Protein Society 31<sup>st</sup> Annual Symposium, Montreal, Canada, July 24-27, 2017. (Poster Presentation).

Faustino AF, Barbosa GM, Castanho MARB, Piano AT, Santos NC, Almeida FC, Martins IC. New fast probing methodology for studying disordered protein regions using nuclear magnetic resonance spectroscopy. Protein Society 31<sup>st</sup> Annual Symposium, Montreal, Canada, July 24-27, 2017. (Poster Presentation).

Faustino AF, Carvalho FA, Martins AS, Enguita FJ, Almeida FCL, Da Poian AT, Martins IC, Santos NC. Identification of the determinants for dengue virus capsid protein binding to host lipid droplets and plasma lipoproteins. 8<sup>th</sup> AFM BioMed Conference, Krakow, Poland, September 4-8, 2017. (Oral Presentation).

Carvalho AF, Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Santos NC. Role of fibrinogen-erythrocyte and erythrocyte-erythrocyte adhesion on cardiovascular pathologies. 8<sup>th</sup> AFM BioMed Conference, Krakow, Poland, September 4-8, 2017. (Oral Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. PaMAP 1.9 and PaMAP 2: two antimicrobial peptides effective against a clinical isolated multiresistant bacteria. 17<sup>th</sup> FEBS (Federation of European Biochemical Societies) Young Scientists' Forum, Jerusalem, Israel, September 7-10, 2017. (Oral Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. PaMAP 1.9 and PaMAP 2: two antimicrobial peptides effective against a clinical isolated multiresistant bacteria. 42<sup>nd</sup> FEBS (Federation of European Biochemical Societies) Congress – From Molecules to Cells and Back, Jerusalem, Israel, September 10-14, 2017. (Poster Presentation).

Guedes AF, Carvalho FA, Nogueira JB, Moreira C, Santos NC. High fibrinogen levels promote erythrocyte-erythrocyte adhesion in essential arterial hypertension. 42<sup>nd</sup> FEBS (Federation of European Biochemical Societies) Congress – From Molecules to Cells and Back, Jerusalem, Israel, September 10-14, 2017. (Oral Presentation).

Martins AS, Nascimento AR, Faustino AF, Santos NC, Martins IC. Understanding Zika virus capsid protein structure and their ability to interact with host lipid systems. Satellite Meeting of the 42nd FEBS (Federation of European Biochemical Societies) Congress – Integrated Methodologies for Studying Intrinsically Disordered Proteins, Jerusalem, Israel, September 14-15, 2017. (Oral Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes' morphology and elasticity on amyotrophic lateral sclerosis. São Paulo School of Advanced Science (ESPCA) on Biophysical Methods to study Biomolecular Interactions, São Paulo, Brazil, October 16-27, 2017. (Poster Presentation).

Silva PM, Augusto MT, Marques MC, Porotto M, Moscona A, Santos NC. Cholesterol-conjugated peptide inhibitors of influenza virus: biophysical characterization. São Paulo School of Advanced Science (ESPCA) on Biophysical Methods to study Biomolecular Interactions, São Paulo, Brazil, October 16-27, 2017. (Poster Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes' morphology and elasticity on amyotrophic lateral sclerosis. XLII Congresso da Sociedade Brasileira de Biofísica, Santos, Brazil, October 27-29, 2017. (Oral Presentation).

Silva PM, Augusto MT, Marques MC, Porotto M, Moscona A, Santos NC. Cholesterol-conjugated peptide inhibitors of influenza virus: biophysical characterization. XLII Congresso da Sociedade Brasileira de Biofísica, Santos, Brazil, October 27-29, 2017. (Poster Presentation).

Roman W, Martins JP, Carvalho FA, Voituriez R, Abella JV, Santos NC, Cadot B, Way M, Gomes ER. Myofibril contraction and cross-linking drive nuclear movement to the periphery of skeletal muscle. ASCB (American Society for Cell Biology) | EMBO (European Molecular Biology Organization) 2017 Meeting, Philadelphia, USA, December 2-6, 2017. (Oral Presentation).

#### **Communications in National Conferences**

Makowski M, Felício MR, Franco OL, Santos NC, Gonçalves S. Structural and functional characterization of the cationic antimicrobial peptide EcAMP1R2. Chem&BioChem Postgraduate Students Meeting, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, February 9, 2017 (Poster Presentation).

Vasconcelos M, Martins AS, Faustino AF, Santos NC, Martins IC. The predicted structure of Zika virus capsid protein. 8<sup>th</sup> AIMS Meeting (Annual International Medical Students Meeting), Lisbon, Portugal, March 10-12, 2017. (Poster Presentation).

Gomes B, Hollmann A, Moscona A, Porotto M, Santos NC. Combining 25-hydroxycholesterol with a fusion inhibitor peptide: interaction with model biomembranes and human blood cells. ARBRE-MOBIEU Plenary Meeting – b3 Building Bridges in Biophysics, Porto, Portugal, March 22-24, 2017. (Oral Presentation).

Makowski M, Felício MR, Franco OL, Santos NC, Gonçalves S. Studies of the membrane selectivity and activity of EcAMP1R2, a novel antimicrobial peptide. ARBRE-MOBIEU Plenary Meeting – b3 Building Bridges in Biophysics, Porto, Portugal, March 22-24, 2017. (Oral Presentation).

Augusto MT, Hollmann A, Troise F, Veiga AS, Pessi A, Santos NC. Lipophilicity is a key factor to increase the antiviral activity of HIV neutralizing antibodies. ARBRE-MOBIEU Plenary Meeting – b3 Building Bridges in Biophysics, Porto, Portugal, March 22-24, 2017. (Oral Presentation).

Makowski M., Santos NC. Integrative exploration of the biological activity of rationally designed antimicrobial peptides. 1<sup>st</sup> LisbonBioMed Retreat, Mafra, Portugal, April 10-12, 2017. (Oral Presentation).

Carvalho PM, Sequeira D, Santos NC, Domingues MM. Targeted liposome nanoparticle for fibrin blood clot degradation. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Augusto MT, Mathieu C, Porotto M, Moscona A, Santos NC. Broad-spectrum antiviral activity for paramyxoviruses is modulated by biophysical properties of fusion inhibitory peptides. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. Two synthetically designed antimicrobial peptides present high affinity toward bacterial membranes. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Gomes B, Hollmann A, Moscona A, Porotto M, Santos NC. C34-25-HC interacts with model biomembranes and human blood cells: a potential strategy to apply 25-HC in HIV-1 treatment. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira EC, Ariëns RAS, Carvalho FA, Santos NC. Molecular characterization of the fibrinogen-erythrocyte interaction on cardiovascular diseases. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes' biophysical properties on cardiovascular diseases and amyotrophic lateral sclerosis. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Makowski M., Santos NC. Integrative exploration of the therapeutic potential of designed antimicrobial peptides. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).

Martins AS, Nascimento AR, Faustino AF, Carvalho FA, Santos NC, Martins IC. Understanding Flavivirus capsid proteins structure and their ability to interact with host lipid systems. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Pronto-Laborinho AC, Lopes CS, Santos NC, Carvalho FA., de Carvalho M. Molecular Biomarkers Associated with Respiratory Insufficiency in Amyotrophic Lateral Sclerosis. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Silva PM, Augusto MT, Marques MC, Porotto M, Moscona A, Santos NC. Cholesterol-conjugated peptide inhibitors of influenza a virus: biophysical characterization. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017. (Oral Presentation).



Pronto-Laborinho AC, Lopes CS, Santos NC, Carvalho FA, de Carvalho M. Biomarcadores respiratórios na abordagem clínica da esclerose lateral amiotrófica. 8.º Congresso de Pneumologia do Centro, Figueira da Foz, Portugal, June 29-30, 2017. (Oral Presentation).

Guedes AF, Carvalho FA, Santos NC. Fibrinogen-erythrocyte interaction as a new prognosis biomarker in cardiovascular diseases. EIT Health Program, Lisbon, Portugal, July 10, 2017. (Oral Presentation).

Carvalho AF, Guedes AF, Sargento L, Nogueira JB, Lousada N, Moreira C, Santos NC. Role of fibrinogen-erythrocyte and erythrocyte-erythrocyte adhesion on cardiovascular pathologies. 1.º Encontro do Colégio de Química da Universidade de Lisboa – A Química na Investigação da ULisboa, Lisbon, Portugal, July 20-21, 2017. (Oral Presentation).

Carvalho PM, Sequeira D, Santos NC, Domingues MM. Targeted liposome nanoparticles for fibrin blood clot degradation. 1.º Encontro do Colégio de Química da Universidade de Lisboa – A Química na Investigação da ULisboa, Lisbon, Portugal, July 20-21, 2017. (Poster Presentation).

Domingues MM, Carvalho PM, Sequeira D, Santos NC. Liposomes as drug delivery system of fibrinolytic agents to blood clots. 1.º Encontro do Colégio de Química da Universidade de Lisboa – A Química na Investigação da ULisboa, Lisbon, Portugal, July 20-21, 2017. (Oral Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. PaMAP's analogues: antimicrobial peptides with anticancer activities. 1.º Encontro do Colégio de Química da Universidade de Lisboa – A Química na Investigação da ULisboa, Lisbon, Portugal, July 20-21, 2017. (Oral Presentation).

Gomes B. Membrane active peptides as antiviral strategy for enveloped viruses. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Lopes CS. Using AFM to study erythrocytes morphology and elasticity on Amyotrophic Lateral Sclerosis. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Martins AS. Zika virus capsid protein structure interaction with host lipid systems. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes' morphology and elasticity on amyotrophic lateral sclerosis. I Jornadas de Biologia Humana, Universidade de Évora, Évora, Portugal, October 2, 2017. (Oral Presentation).

Pronto-Laborinho AC, Gromicho M, Pereira M, Lopes CS, Santos NC, Carvalho FA, de Carvalho M. Biomarcadores respiratórios na abordagem clínica da esclerose lateral amiotrófica. Congresso de Neurologia 2017, Lisbon, Portugal, November 16-18, 2017. (Oral Presentation).

Augusto MT, Mathieu C, Porotto M, Moscona A, Santos NC. Broad-spectrum antiviral activity is modulated by biophysical properties of fusion inhibitory peptides. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Poster Presentation).

Felício MR, Franco OL, Santos NC, Gonçalves S. Small active peptides: biophysical studies of the peptide-membrane interactions. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Oral and Poster Presentation).

Gomes B, Hollmann A, Moscona A, Porotto M, Santos NC. Combining 25-hydroxycholesterol with a fusion inhibitor peptide: interaction with model biomembranes and human blood cells. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Poster Presentation).

Lopes CS, Pronto-Laborinho AC, de Carvalho M, Santos NC, Carvalho FA. Using AFM to study erythrocytes' morphology and elasticity on amyotrophic lateral sclerosis. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Oral and Poster Presentation).

Makowski M, Felício MR, Franco OL, Gonçalves S, Santos NC. Studying the selectivity and activity of the designed antimicrobial peptide EcAMP1R2. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Oral and Poster Presentation).

Martins AS, Nascimento AR, Faustino AF, Carvalho AF, Santos NC, Martins IC. Understanding Flavivirus capsid protein structure and their ability to interact with host lipid systems. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Poster Presentation).

Silva PM, Augusto MT, Marques MC, Porotto M, Moscona A, Santos NC. Cholesterol-conjugated peptide inhibitors of influenza virus: biophysical characterization. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017. (Oral and Poster Presentation).

Lustosa AKMF, Oliveira ACJ, Quelemes PV, Plácido A, Silva FV, Oliveira IS, Almeida MP, Amorim AGN, Delerue-Matos C, Eaton P, Oliveira RCM, Da Silva DA, Leite JRSA. In situ synthesis of silver nanoparticles in a hydrogel of carboxymethyl cellulose with phthalated-cashew gum as a promising antimicrobial and healing agent. MICRIBIOTEC 17, Congress of Microbiology and Biotechnology 2017, Porto, Portugal, December 7-9, 2017. (Poster Presentation).

### **Organisation of Conferences**

Felício MR, Gomes B, Martins AS. Co-organizers. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017.

Santos NC. Member of the Scientific Committee of the 16<sup>th</sup> Congress of the Spanish Biophysical Society, Seville, Spain, June 6-8, 2017.

Abreu S. Co-organizer. 1.º Encontro do Colégio de Química da Universidade de Lisboa – A Química na Investigação da ULisboa, Lisbon, Portugal, July 20-21, 2017.

Martins IC. Workshop Moderator. Integrated Methodologies for Studying IDPs, COST Satellite Meeting to the 42<sup>nd</sup> FEBS Meeting, Jerusalem, Israel, September 14-15, 2017.

Gomes B, Martins AS. Co-organizers. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017

Domingues MM. Co-organizer. Career Opportunities for PostDoctoral Researchers in Life Sciences, Cascais, Portugal, November 23-24, 2017.

Abreu S. Co-organizer. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017.

### **Internationalisation**

Collaborative publications and/or funded projects with groups from Columbia University (New York, USA), Cornell University (New York, USA), Johns Hopkins Bloomberg School of Public Health (Maryland, USA), New York University School of Medicine (USA), Stanford University School of Medicine (California, USA), The Ohio State University (USA), University of California at Los Angeles (USA), University of California San Francisco (USA), Ecole Normale Supérieure de Lyon (France), International Center for Infectiology Research (Lyon, France), Institut Pasteur (Paris, France), University Claude Bernard Lyon (France), Bernhard Nocht Institute for Tropical Medicine (Hamburg, Germany), CEINGE Biotechnologie Avanzate S.C.R.L. (Napoli, Italy), PeptiPharma (Rome, Italy), University of Cagliari (Italy), Leiden University Medical Center (Netherlands), Pompeu Fabra University (Barcelona, Spain), University of Bern (Switzerland), University of Leeds (England), Catholic University of Brasília (Brazil), Dom Bosco Catholic University (Campo Grande, Brazil), Federal University of Rio de Janeiro (Brazil), University of Brasília (Brazil), CONICET (Buenos Aires, Argentina), University of Buenos Aires (Argentina), University of Quilmes (Argentina), University of Santiago del Estero (Argentina), Agency for Science, Technology and Research (Singapore), National University of Singapore (Singapore) and University of Queensland (Australia).

### **Prizes, Honours and Awards**

Guedes AF. Pulido Valente Ciência Award 2017 (by Fundação Professor Francisco Pulido Valente and Fundação para a Ciência e a Tecnologia), as first author of the article “Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients” (Guedes AF, Carvalho FA, Malho I, Lousada N, Luís Sargento L, Santos NC, 2016, Nature Nanotechnology).

Santos NC. Scientific Award ULisboa / Caixa Geral de Depósitos 2017 (scientific area of Biology, Biology and Biologic Engineering, Biochemistry and Biotechnology).

Guedes AF. Prémio Jovem Biofísico 2017 (by Sociedade Portuguesa de Biofísica), as first author of the article “Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients” (Guedes AF, Carvalho FA, Malho I, Lousada N, Luís Sargento L, Santos NC, 2016, Nature Nanotechnol., 11, 687-692).

Vasconcelos M. Poster Runner-Up Prize. 8<sup>th</sup> AIMS Meeting (by Fundação AstraZeneca), Faculty of Medicine, University of Lisbon, Lisbon, Portugal, March 10-12, 2017.

Gomes B. Best Poster Presentation “Young Investigator Poster Competition”. 25<sup>th</sup> American Peptide Symposium, Whistler, Canada, June 17-22, 2017.

Carvalho AF. Best Oral Presentation. AFM Biomed Conference 2017 (Wiley Young investigator award 2017), Krakow, Poland, September 4-8, 2017.

Martins AS. Best Poster Presentation. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017.

Felício MR. Best Oral Presentation. 2.º Encontro do Colégio de Química da Universidade de Lisboa – UL Chemistry PhD Meeting, Lisbon, Portugal, December 4-5, 2017.

### **Advanced Teaching**

Santos NC. Lecturer. Atomic Force Microscopy. PhD program in Molecular Biosciences (MolBioS) from ITQB (Instituto de Tecnologia Química e Biológica), IBET (Instituto de Biologia Experimental Tecnológica), REQUIMTE (Rede de Química e Tecnologia), CREM (Centro de Recursos Microbiológicos) and IGC (Instituto Gulbenkian de Ciência), Oeiras, Portugal, January 2017.

Santos NC. Coordinator. “Nano & Biochemistry” modules, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 2017.

Carvalho FA. Lecturer. Atomic force microscopy. Mestrado de Biologia Estrutural. Instituto Superior Técnico, Lisbon, Portugal, January 17, 2017.

Carvalho FA. Lecturer. Atomic force microscopy. LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 30, 2017.

Gonçalves S. Lecturer. Drug resistance in bacterial cells: biophysical characterization of peptide-membrane interactions. LisbonBioMed PhD Program Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 30, 2017.

Martins IC. Lecturer. From Dengue to Zika through West-Nile virus: a tale of three proteins and a peptide. LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 30, 2017.

Santos NC. Lecturer. Atomic Force Microscopy: using force at the nanoscale for biological applications. Biochemistry, Healthcare Biochemistry, Biotechnology, Molecular Genetics and Nanomedicine and Micro/Nanotechnologies engineering Master programs, at Faculty of Sciences and Technology, Nova University of Lisbon, Monte da Caparica, March 2017.

Martins IC. Lecturer. Structural biology and drug design meet atomic force microscopy. Formação Graduada em Biologia Estrutural, Instituto Superior Técnico, Lisbon, Portugal, April 21, 2017.

Santos NC. Lecturer. Biological and biomedical applications of light scattering techniques. PhD Program in Medicines and Pharmaceutical Innovation (i3DU), Faculty of Pharmacy, University of Lisbon, Lisbon, May 2017.

Santos NC. Lecturer. Molecular interactions probed by AFM-based force spectroscopy. PhD Program in Medicines and Pharmaceutical Innovation (i3DU), Faculty of Pharmacy, University of Lisbon, Lisbon, July 2017.

Santos NC. Lecturer. Measuring forces at the nanoscale for cardiovascular risk evaluation. Master program on Molecular Genetics and Biotechnology, University of Sevilla, Sevilla, Spain, November 2017.

### **Science and Society**

Santos NC. “As Donas da Casa”, Antena 3, portuguese radio show, Portugal, January 26, 2017.

Santos NC. “Bioquímica”, lecture at “Colégio Sagrado Coração de Maria”, Lisbon, Portugal, March 28, 2017.

The research work of NSantos Lab was featured on mass media news on “Inspira”, Brazil (2017, nº2, pp. 3-5), SIC (Portuguese independent television) and Europeans Researcher’s Night, Portugal (September 29, 2017).

NSantos Lab also participated in different scientific related committees, including iMM/CAML PhD Students Committee (Felício MR, Gomes B, Guedes AF, Martins AS) and iMM Post-Doctoral Association (Domingues MM).



With the aim of promoting the interest in science among young students, the NSantos lab organized visits for undergraduate students via presentations and “speed-dating” style contact with the different components in the Unit’s Research work. Moreover, NSantos lab had visits from students of “Colégio Sagrado Coração de Maria”, and participated in the Science Day (November 24, 2017) of the school (Carvalho FA and Lopes CS).

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## Saúde, Leonor

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### Major Interests / Objectives

We want to understand the cellular and molecular mechanisms controlling fundamental developmental processes and regenerative processes activated upon severe injuries.

### Head of Laboratory

Maria Leonor Tavares Saúde, PhD, Invited Assistant Professor

### Research Team

Ana Catarina Esteves Ribeiro	PhD	Post-Doctoral Investigator
Ana Filipa Canha Pereira	Undergraduate	MSc Student
Ana Margarida Pereira Cristóvão Pinto	Graduate	Technician
Ana Paula Lopes Martins	Undergraduate	MSc Student
Ana Sofia Rocha Batalha	Graduate	MSc Student (Left April)
Dalila Maria Neves Silva	Master	MSc Student (Left April)
Diana Sofia Chapela Duarte Pires	Master	PhD Student
Isaura Vanessa Antunes Martins	PhD	Investigator
José Maria Lage de Sousa Leitão	Graduate	MSc Student
Luís Miguel Beicinha Branco Estronca	PhD	Visiting Researcher (Started February)
Marco António Benjamim Morais	Undergraduate	MSc Student (Started November)
Mariana Antas Rebocho da Costa	Graduate	MSc Student (Started September)
Rita Alexandra Rodrigues Pinto	Master	PhD Student
Sara Maria Ferreira Fernandes	Master	PhD Student
Tiago Filipe Ribeiro Ruas Maçarico	Master	Investigator

### Laboratory Keywords / Research Areas

Early development, Regeneration, Spinal cord, Microenvironment, Zebrafish, Mouse.

### Major Scientific Achievements

We published a paper showing that Foxj1a-positive cells expand in response to injury through a Shh-dependent mechanism and contribute to the restoration of the spinal cord structure in zebrafish (Ribeiro et al, Open Biology 2017).

We produced a collaborative paper in which we show that there are immotile cilia in the zebrafish LR organizer and that Notch signalling through Her12 modulates the motile/immotile cilia ratio downstream of Foxj1a (Tavares et al., Elife 2017).



We established in a spinal cord transection model in zebrafish larvae and using this paradigm, we selected 6 small molecules based on a locomotor improvement assay in collaboration with TechnoPhage, SA.

### **Selected Publications**

Ribeiro A, Monteiro JF, Certal AC, Cristovão AM, Saúde L (2017). Foxj1a is expressed in ependymal precursors, controls central canal position and is activated in new ependymal cells during regeneration in zebrafish. *Open Biology* 7(11), 170139. doi: 10.1098/rsob.170139. (IF: 3.481, Citations:--).

Mendes RV, Martins GG, Martins AM, Saúde L (2014). N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. *Developmental Cell* 30(3), 353-60. (IF: 9.174, Citations: 6).

Fior R, Maxwell AA, Ma TP, Vezaro A, Moens CB, Amacher SL, Lewis J, Saúde L (2012). Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by Mesogenin1. *Development* 139(24), 4656-65. (IF: 5.843, Citations: 26).

Azevedo AS, Grotek B, Jacinto A, Weidinger G, Saúde L (2011). The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. *PloS ONE*, 6(7), e22820. (IF: 2.806, Citations: 28).

Lopes SS, Lourenço R, Pacheco L, Moreno N, Kreiling J, Saúde L (2010). Notch signalling regulates left-right asymmetry through ciliary length control. *Development*, 137(21), 3625-32. (IF: 5.843, Citations: 60).

### **Ongoing Research Projects**

2016/2019: Angiocrine factors as modulators of spinal cord regeneration. Coordinator: Maria Leonor Tavares Saúde. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/BIM-MED/3295/2014. Amount: € 186 229,00. Total Amount: € 186 229,00.

### **Other Projects**

2016/2018: ReTuBi: Towards outstanding research and training in tumour. Coordinator: Edgar Rodrigues Almeida Gomes. Funding Agency: European Commission. Reference: Twinning 692322. Amount: € 788 725,00. Total Amount: € 999 975,00.

### **Other Publications International**

Ribeiro A, Monteiro JF, Certal AC, Cristovão AM, Saúde L (2017). Foxj1a is expressed in ependymal precursors, controls central canal position and is activated in new ependymal cells during regeneration in zebrafish. *Open Biology* 7(11): 170139. doi: 10.1098/rsob.170139. (IF: 3.481, Citations:--).

Tavares B, Jacinto R, Sampaio P, Pestana S, Pinto A, Vaz A, Roxo-Rosa M, Gardner R, Lopes T, Schilling B, Henry I, Saúde L, Lopes SS (2017). Notch/Her12 signalling modulates motile/immotile cilia ratio downstream of Foxj1a in zebrafish left-right organizer. *Elife* e25165. doi: 10.7554/eLife.25165. (IF: 7.725, Citations:--).

Cordeiro M, Carvalho L, Silva J, Saúde L, Fernandes AR, Baptista PV (2017). Gold Nanobeacons for Tracking Gene Silencing in Zebrafish. *Nanomaterials* 7(1), 10; doi:10.3390/nano7010010. (IF: 3.553, Citations: 2).

### **Invited Lectures and Seminars**

Saúde L. Bridging the regeneration gap: insights from the zebrafish. UC Biotech, Parque Tecnológico de Cantanhede, Portugal, July 5, 2017.

### **Communications in International Conferences**

Saúde L, Ribeiro A. Foxj1a cells participate in spinal cord genesis and regeneration in zebrafish. 18<sup>th</sup> International Congress of Developmental Biology, Singapore, June 18-22, 2017. (Poster Presentation).

Paramos-de-Carvalho D. The role of senescent cells in tissue regeneration. 10<sup>th</sup> European Zebrafish Meeting, Budapest, Hungary, July 3-7, 2017. (Poster Presentation).

### **Advanced Teaching**

Saúde L. Lecturer. LisBonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 23, 2017.

Saúde L. Lecturer. ProRegeM - PhD Programme in Mechanisms of Disease and Regenerative Medicine, CEDOC, Lisbon, Portugal, February 7, 2017.

Saúde L. Organizer and lecturer. Genetics & Development Course, Programa de Pós-Graduação Ciência para o Desenvolvimento, Praia, Santiago, Cape Verde, February 20-24, 2017.

Saúde L. Lecturer. PhD Program in Bioengineering – Cell Therapies and Regenerative Medicine, IST/Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 14, 2017.

Saúde L. Lecturer. GABBA PhD Programme, Instituto de Biologia Molecular e Celular, Porto, Portugal, May 15, 2017.

Saúde L. Lecturer. IGC PhD Programme - Integrative Biology and Biomedicine, Instituto Gulbenkian de Ciência, Oeiras, Portugal, May 16, 2017.

Saúde L. Lecturer. IGC PhD Programme - Integrative Biology and Biomedicine, Instituto Gulbenkian de Ciência, Oeiras, Portugal, November 8, 2017.

Ribeiro A. Lecturer. Animal models: zebrafish. IGC PhD programme, Instituto Gulbenkian de Ciência, Oeiras, Portugal, October 16, 2017.

Ribeiro A. Lecturer. Creating diversity and functional integration: the central nervous system. Master in Evolutionary and Developmental Biology, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, March 17, 2017.

### **Science and Society**

Saúde L, Ribeiro A, Martins I, Chapela D, Leitão JM. Participated in European Researchers' Night, Lisbon, Portugal, September 29, 2017.

### **MSc Thesis Completed**

Dalila Silva, 07/03/2017, "The Intermediate Mesoderm, a new player in the establishment of organ laterality?", Faculty of Sciences, University of Lisbon. Supervisor: Leonor Saúde.

## Sebastião, Ana

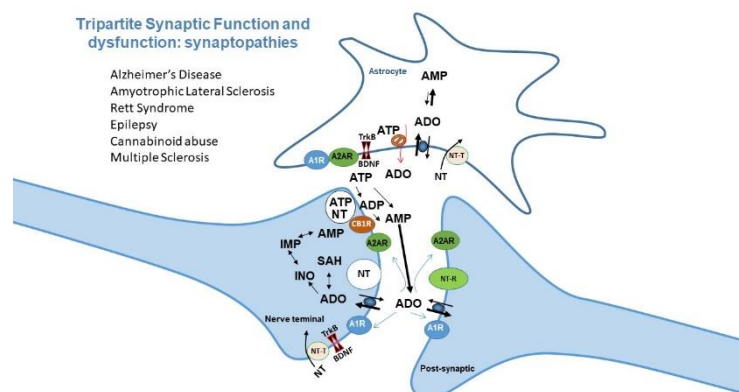
### Major Interests / Objectives

Correct abnormal synaptic function is a main challenge to Neurosciences since it impacts in the possibility to fight neurologic and psychiatric diseases. Our team aims to elucidate how the neuronal and glial components of the tripartite synapse are fine-tuned under normal and dysfunctional situations. How endogenous modulators affect synaptic signalling, neuronal excitability, neuronal and glial maturation, degeneration, renewal and repair, under normal and pathological conditions, are our current goals of research. We focus on neurotrophic factors, on adenosine and on endocannabinoids, as major endogenous modulators. As disease models we have been focusing on those involving neurodegeneration and/or dysregulated excitability.

### Head of Laboratory

Ana M Sebastião, PhD, Full Professor

### Graphical Abstract



### Research Team

Amílcar Silva dos Santos	MD	PhD Student
Ana Filipa Ferreira da Cunha Ribeiro	Master	PhD Student
Ana Iolanda d'Armada Moreira	Master	PhD Student
Ana Sofia Cristóvão Ferreira	MD/PhD	Volunteer Investigator
Ann Van der Jeugd	PhD	Post-Doctoral Investigator (Started March/Left August)
Armando Dulcídio da Silva Cruz	Master	PhD Student
Catarina Isabel Carvalhas de Almeida	Graduate	MSc Student (Started September)
Catarina Miranda Lourenço	Master	PhD Student
Cláudia Alexandra dos Santos Valente de Castro	PhD	Principal Investigator

Cláudia Sofia Beltrão Cavacas	Graduate	MSc Student
Daniela Cristina Melo Magalhães	Master	PhD Student
Diogo Gomes da Cruz	Undergraduate	Trainee (Started October)
Diogo Miguel Rombo	PhD	Investigator
Francisco Melo Albuquerque Saraiva Mouro	Master	PhD Student
Isabel Maria do Amaral Rodeia Rodrigues de Brito	Undergraduate	Trainee
Jéssica Lúcia Albuquerque Rosa	Graduate	MSc Student (Started September)
Joana Amorim Freire	Master	MSc Student
Joana Filipa Gonçalves Ribeiro	Graduate	MSc Student (Started September)
Joana Isabel Ferreira da Graça Gomes	Graduate	MSc Student (Started September)
Joana Moura Mateus	Graduate	MSc Student (Started September)
João Filipe Fonseca Gomes	Master	PhD Student
João Pedro de Almeida Jesus	Graduate	MSc Student (Left April)
Joaquim Alexandre Ribeiro	MD/PhD	Principal Investigator
Jorge Miguel Farinha Ferreira	Graduate	MSc Student (Started October)
Leonor Pedro Oliveira Ribeiro Rodrigues	Graduate	MSc Student
Liana Shvachiy	Graduate	MSc Student (Left August)
Luís Afonso Chambel André	Graduate	MSc Student (Left March)
Margarida Leonor Ferreira Martins	Master	MSc Student (Left November)
Maria Alexandra Pereira Botelho	Undergraduate	Administrative
Maria José Diógenes	PhD	Principal Investigator, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Miranda Mele	PhD	Post-Doctoral Investigator (Started November)
Nádia Raquel Henriques Rei	Master	PhD Student
Nuno Miguel Da Silva Rosa	Graduate	MSc Student (Left April)
Rita Abrunhosa Soares	Master	PhD Student (Left March)
Rita Alexandra Figueira Belo	Master	PhD Student
Rita Cruz Coelho de Mira Ramalho	PhD	Post-Doctoral Investigator
Rita Isabel Pedro Aroeira	PhD	Manager
Rui Miguel Silva Rodrigues	Master	PhD Student
Sandra Cristina Henriques Vaz	PhD	Post-Doctoral Investigator
Sara Alves Xapelli	PhD	Principal Investigator
Sara Luísa Ramalho Tanqueiro	Master	PhD Student
Sara Raquel Landeira Nabais do Paulo	Graduate	MSc Student
Tatiana Pinto Morais	Graduate	PhD Student
Tiago Filipe Martins Rodrigues	MD	Investigator

### Laboratory Keywords / Research Areas

Tripartite synapse mechanisms, Neuronal excitation/inhibition balance, Neurodegenerative mechanisms, Neuroinflammation, Epilepsy, Cannabinoid abuse

## Major Scientific Achievements

We focused upon endogenous and homeostatic control of synaptic activity and plasticity and their implications for learning and memory, and find out:

- Endocannabinoids exert a dual fine-tune homeostatic control of LTP in the hippocampus (Silva-Cruz et al., *Front Pharmacol*).
- Cannabinoid CB1 and CB2 receptors control post-natal neurogenesis (Rodrigues et al, *Front Pharmacol*).
- Cannabinoid-induced memory dysfunction is prevented by adenosine A2A receptor blockade (Mouro et al, *Neuropharmacology*).
- Adenosine kinase deficiency, a rare genetic disease that leads to mental retardation, triggers neuronal adaptation processes, dysregulated synaptic plasticity, cognitive deficits, and increased seizure risk (Sandau et al, *J Neurosci*).
- Enhanced synaptic plasticity in the non-pathological ageing is a compensatory phenomenon, rather than pathological (Pinho et al, *Neuropharmacology*).
- Hippocampal homeostatic plasticity is controlled by erythropoietin (Dias et al, *Cereb Cortex*).

## Selected Publications

Diógenes MJ, Neves-Tomé R, Fucile S, Martinello K, Scianni M, Theofilas P, Lopatár J, Ribeiro JA, Maggi L, Frenguelli BG, Limatola C, Boison D, Sebastião AM (2014). Homeostatic Control of Synaptic Activity by Endogenous Adenosine is mediated by Adenosine Kinase. *Cereb Cortex* 24, 67-80. (IF: 6.559, Citations: 26).

Rocha, MC, Pousinha PA, Correia AM, Sebastião AM, Ribeiro JA (2013). Early changes of neuromuscular transmission in the SOD1 (G93A) mice model of ALS start long before motor symptoms onset. *PLOS ONE* 8, e73846. <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0073846>. (IF: 2.806, Citations: 46).

Dias RB, Rombo DM, Ribeiro JA, Henley JM, Sebastião AM (2013). Adenosine: setting the stage for plasticity. *Trends in Neuroscience* 36, 428-257. (IF: 11.124, Citations: 53).

Diogenes MJ, Costenla AR, Lopes LV, Jerónimo-Santos A, Sousa VC, Fontinha BM, Ribeiro JA, Sebastião AM (2011). Enhancement of LTP in aged rats is dependent on endogenous BDNF. *Neuropsychopharmacology* 36, 1823-1836. (IF: 6.403, Citations: 61).

Sousa VC, Assaife-Lopes N, Ribeiro, JA, Pratt JA, Brett RR, Sebastião AM (2011). Regulation of hippocampal cannabinoid CB1 receptor actions by adenosine A1 receptors and chronic caffeine administration: implications for the effects of 9-tetrahydrocannabinol on spatial memory. *Neuropsychopharmacology* 36, 472-487. (IF: 6.403, Citations: 24).

### **Ongoing Research Projects**

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

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

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

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

2016/2018: SynaNet: Neurologic and Psychiatric disorders: from synapses to networks. Coordinator: Ana Maria Ferreira de Sousa Sebastião. Funding Agency: European Commission. Reference: TWINNING 692340. Amount: € 525 437,50. Total Amount: € 999 996,25.

### **Publications in Peer Review Journals**

Dias RB, Rodrigues TM, Rombo DM, Ribeiro FF, Rodrigues J, McGarvey J, Orcinha C, Jeremy M. Henley JM, Sebastião AM (2017). Erythropoietin Induces Homeostatic Plasticity at Hippocampal Synapses. *Cerebral Cortex*. (IF 6.559, Citations:--).

Silva-Cruz A, Carlström M, Ribeiro JA, Sebastião AM (2017) Dual Influence of Endocannabinoids on Long-Term Potentiation of Synaptic Transmission. *Front Pharmacol.* 8:921.eCollection. (IF: 4.400, Citations:--).

Mouro FM, Batalha VL, Ferreira DG, Coelho JE, Baqi Y, Müller CE, Lopes LV, Ribeiro JA, Sebastião AM (2017). Chronic and acute adenosine A2A receptor blockade prevents long-term episodic memory disruption caused by acute cannabinoid CB1 receptor activation. *Neuropharmacology.* 117:316-327. (IF: 5.012, Citations: 3).

Pinho J, Vale R, Batalha VL, Costenla AR, Dias R, Rombo D, Sebastião AM, de Mendonça A, Diógenes MJ (2017). Enhanced LTP in aged rats: Detrimental or compensatory? *Neuropharmacology.* 114:12-19. (IF: 5.012, Citations:--).

Rodrigues RS, Ribeiro FF, Ferreira F, Vaz SH, Sebastião AM, Xapelli S (2017). Interaction between Cannabinoid Type 1 and Type 2 Receptors in the Modulation of Subventricular Zone and Dentate Gyrus Neurogenesis. *Front Pharmacol.* 8:516. ecollection 2017. (IF: 4.400, Citations:--).

Armada-Moreira A, Taipaleenmäki E, Baekgaard-Laursen M, Schattling PS, Sebastião AM, Vaz SH, Städler B (2017). Platinum Nanoparticle-Based Microreactors as Support for Neuroblastoma Cells. *ACS Appl Mater Interfaces.* (IF: 7.504, Citations:--).

Cunha-Reis D, Ribeiro JA, de Almeida RFM, Sebastião AM (2017). VPAC1 and VPAC2 receptor activation on GABA release from hippocampal nerve terminals involve several different signalling pathways. *Br J Pharmacol.* 174:4725-44737. (IF: 5.491, Citations:--).

Aidil-Carvalho MF, Carmo AJS, Ribeiro JA, Cunha-Reis D (2017). Mismatch novelty exploration training enhances hippocampal synaptic plasticity: A tool for cognitive stimulation *Neurobiol Learn Mem.* 145:240-250. (IF: 3.543, Citations:--).

Cunha C, Santos C, Gomes C, Fernandes, A, Correia AM, Sebastião AM, Vaz AR, Brites D (2017). Downregulated glia interplay and increased miRNA-155 as promising markers to track early ALS stage. *Mol Neurobiol.* (IF: 6.190, Citations:--).

Soares R, Ribeiro FF, Xapelli S, Genebra T, Ribeiro MF, Sebastião AM, Rodrigues CMP, Solá S. (2017). Tauroursodeoxycholic Acid Enhances Mitochondrial Biogenesis, Neural Stem Cell Pool, and Early Neurogenesis in Adult Rats. *Mol Neurobiol.* (IF: 6.190, Citations:--).



Morais T, Coelho D, Vaz SH, Sebastião AM, Valente CA (2017). Glycine receptor activation impairs ATP-induced calcium transients in cortical astrocytes. *Front Mol Neurosci*. (IF: 5.076, Citations:--).

Ferreira DG, Temido-Ferreira M, Miranda HV, Batalha VL, Coelho JE, Szego È, Marques-Morgado I, Vaz SH, Rhee JS, Schmitz M, Zerr I, Lopes LV, Outeiro TF (2017).  $\alpha$ -synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B. *Nature Neuroscience*. 20 (11):1569-1579. (IF: 17.839, Citations: 3).

#### **Other Publications International**

Dale N, Sebastião AM (2017). Dissecting neurovascular-coupling mechanisms: a role for adenosine A2A receptor: An Editorial highlight for 'Correlation of transient adenosine release and oxygen changes in the caudate-putamen. *J Neurochem*. 140:10-12. (IF: 4.083, Citations:--).

#### **Other Publications National**

Cunha RA, Sebastião AM (2017). Sistema Purinérgico. In: *NEUROCIÊNCIAS*, ed: AC Rego, CB Duarte, CR Oliveira, pp 193-212, LIDEL - Edições Técnicas, Lisbon.

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

Valente CA. The potential of organotypic slice cultures. *SynaNet H2020 - First Annual Scientific Meeting*, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017.

Vaz SH. Astrocytes, gliotransmitters and BDNF: working together to shape synaptic plasticity?. *Interdisciplinary Nanoscience Center (iNANO) Seminars*, University of Aarhus, Denmark, February 10, 2017.

Sebastião AM. Understanding rare diseases: Adenosine Kinase Deficiency, developmental delay and seizures. *Instituto de Medicina Molecular João Lobo Antunes*, March 2017.

Diógenes MJ. Rett Syndrome and Alzheimer's disease: different disorders with common features. *RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week*, Lisbon, Portugal, May 4, 2017.

Valente CA. Ex vivo model of epilepsy - a new tool for drug screening RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017.

Diógenes MJ. Investigação em Síndrome de Rett na ULisboa. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017.

Vaz SH, Sebastião AM. On the role of astrocytes in synaptic plasticity. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017.

Xapelli S. Finding modulators of neural stem cells for brain repair. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017.

Sebastião AM. A2AR blockade prevents memory impairment caused by cannabinoids in mice. 7<sup>th</sup> Joint Italian-German Purine Club Meeting: Advances in basic and translational purinergic research, July 20-23, 2017.

Sebastiao AM. Contributo para a compreensão de doenças raras: mecanismos subjacentes à génese de convulsões associadas a deficiência de adenosina cinase. Sessão Clínica Neurologia, Hospital Santa Maria, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, July 2017.

Fonseca-Gomes J. TrkB-FL and TrkB-ICD assessment in Alzheimer's Disease human samples. Lab Meeting, University of Eastern Finland, Kuopio, Finland, November 2017.

Xapelli S. Modulation of postnatal neurogenesis and oligodendrogenesis by adenosine A2A receptors. CNC – Center for Neuroscience and Cell Biology-IBILI seminars, Coimbra, Portugal, 2017.

### **Communications in International Conferences**

Armada-Moreira A, Vaz SH, Städler B. Astrosomes: Artificial astrocytes as a novel approach to regulate neuronal communication. iNANO Day 2017, Aarhus, Denmark, January 11, 2017. (Poster Presentation).

Magalhães D, N Pereira, AM Sebastião, CA Valente. Progression of inflammatory mediators in the organotypic hippocampal slice model of epileptogenesis. XIII European Meeting on Glial Cells in Health and Disease, Edinburgh, Scotland, July 8-11, 2017. (Poster Presentation).

Morais T, Coelho D, Vaz SH, Sebastião AM, Valente CA. Glycine receptor in astrocytes- effect upon astrocytic communication. XIII European Meeting on Glial Cells in Health and Disease, Edinburgh, Scotland, July 8-11, 2017. (Poster Presentation).

Valente CA, D Magalhães, N Pereira, DM Rombo, AM Sebastião. Incidence of inflammatory features in epileptic-like organotypic slices – a tool for drug screening. XIII European Meeting on Glial Cells in Health and Disease, Edinburgh, Scotland, July 8-11, 2017. (Poster Presentation).

Vaz SH, Jesus J, Sebastião AM. BDNF-mediated facilitation of LTP at the hippocampus is dependent of gliotransmitters release by astrocytes. XIII European Meeting on Glial Cells in Health and Disease, Edinburgh, Scotland, July 8-11, 2017. (Poster Presentation).

Miranda-Lourenço C, Palminha C, Duarte ST, Gaspar C, Colino-Oliveira M, Gomes R, Ferreira S, Rodrigues TM, Lopes LV, Sebastião AM, Diógenes MJ. Adenosinergic system as a new central player in Rett Syndrome. 5<sup>th</sup> European Rett Syndrome Congress 2017, Berlin, Germany, 2017. (Poster Presentation).

#### **Communications in National Conferences**

Armada-Moreira A, Vaz SH, Städler B. Astrosomes: Artificial astrocytes as a novel approach to regulate neuronal communication. I NeurULisboa PhD Meeting, Lisbon, Portugal, January 5-6, 2017. (Oral Presentation).

Belo R, Neves V, Sebastião A, Diógenes MJ. Kytorphin and amidated-kytorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente C, Sebastião AM. Expression of VEGF, Adenosine and VEGF receptors in Amyotrophic Lateral Sclerosis (ALS) mice model at different disease stages. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Sebastião AM, Diógenes MJ. Prevention of BDNF receptor cleavage: future perspectives about its possible application as therapeutic tool. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Rett Syndrome: BDNF signalling and Adenosinergic system changes. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Ribeiro FF, Rodrigues R, Armada-Moreira A, Ferreira F, Sebastião AM, Xapelli S. Finding modulators of neural stem cells for brain repair. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Rodrigues R, Ribeiro FF, Ferreira F, Sebastião AM, Xapelli S. CB1R-CB2R: a cannabinoid two-level interaction controlling subventricular and hippocampal neurogenesis. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Soares R, Genebra T, Ribeiro MF, Ribeiro FF, Xapelli S, Sebastião AM, Rodrigues CMP, Solá S. Tauroursodeoxycholic acid increases mitochondrial biogenesis, neural stem cell pool and early neurogenesis in adult rats. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Tanqueiro SR, Ramalho RM, Sebastião AM, Diógenes MJ. Amyloid- $\beta$ -peptide induces BDNF loss of function by a mechanism dependent on Extrasynaptic NMDA receptors activation. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Rett Syndrome: BDNF signalling and Adenosinergic system changes. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Morais T, Coelho D, Vaz S, Sebastião AM, Valente CA. Expression and function of Glycine receptor in rat cortical astrocytes. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017. (Poster Presentation).

Afonso C, Ribeiro F, Sebastião AM, Xapelli S. Exploring the modulatory role of adenosine A2A receptors in rat in vivo oligodendrogenesis. XLVII Annual Meeting of The Portuguese Pharmacological Society, Coimbra, Portugal, February 2-4, 2017. (Oral Presentation).

Rodrigues RS, Ribeiro FF, Ferreira F, Sebastião AM, Xapelli S. Crosstalk between cannabinoid type 1 and type 2 receptors modulates subventricular and hippocampal neurogenesis. XLVII Annual Meeting of The Portuguese Pharmacological Society, Coimbra, Portugal, February 2-4, 2017. (Oral Presentation).

Brito I, Rosa N, Sebastião AM, Valente CA. Inhibition of inflammatory pathways and its protective effect on epilepsy. Annual International Medical Students Meeting, Lisbon, Portugal, March 10-12, 2017. (Oral Presentation).

Macau R, Cabrita J, Sebastião AM, Vaz SH. Calcium signalling impairment in astrocytes influences BDNF effect upon hippocampal long-term potentiation in mice. Annual International Medical Students Meeting, Lisbon, Portugal, March 10-12, 2017. (Poster Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente CA, Sebastião AM. Molecular analysis of VEGF and VEGF receptors in *sod1(g93a)* mice at different disease stages. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 18, 2017. (Oral Presentation).

Afonso C, Ribeiro FF, Sebastião AM, Xapelli S. Rat in vivo oligodendrogenesis is modulated by adenosine A2A receptors Disease. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Sebastião AM, Diógenes MJ. Relevance of BDNF receptor cleavage on Alzheimer's Disease pathophysiology. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Exploring Kyotorphin and Amidated-kyotorphin actions: synaptic transmission and calpains and caspases activation. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Brain-derived neurotrophic factor signalling and adenosinergic system in Mecp2 knockout mouse model. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Paulo S L, Rodrigues RS, Shvachiy L, Solá S, Sebastião AM, Xapelli S. Neurogenesis in a Rat Model of Sporadic Alzheimer's Disease. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Ribeiro FF, Rodrigues RS, Afonso C, Nabais-Paulo S, Armada-Moreira A, Ferreira F, Sebastião AM, Xapelli S. Finding modulators of neural stem cells for brain repair. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Oral Presentation).

Rodrigues RS, Ribeiro FF, Ferreira F, Sebastião AM, Xapelli S. Modulation of neurogenesis by cannabinoids. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Solá S, Ribeiro MF, Genebra T, Soares R, Fernandes M, Xapelli S, Ribeiro FF, Martins J, Varela A, Gomes AR, Fernandes TG, Diogo MM, Cabral JM, Sebastião AM and Cecília MP Rodrigues. Driving Mitochondrial Bioenergetics To Improve Adult Neurogenesis. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Oral Presentation).

Tanqueiro SR, Ramalho RM, Sebastião AM, Diógenes MJ. Extrasynaptic NMDA receptors play a key role in Amyloid  $\beta$ -mediated BDNF loss of function. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Armada-Moreira A, Schattling P, Taipaleenmäki E, Sebastião AM, Vaz SH, Städler B. Astrosomes: Artificial astrocytes as a novel approach to regulate neuronal communication. 6<sup>th</sup> China-Europe Symposium on Biomaterials for Regenerative Medicine, Porto, Portugal, May 22, 2017. (Oral Presentation).

Afonso C, Ribeiro FF, Sebastião AM, Xapelli S. Adenosine A2A receptors modulate rat in vivo oligodendrogenesis. II Symposium Glial Network, Braga, Portugal, May 24, 2017. (Oral Presentation).

Vaz SH, de Castro-Abrantes H, Cruz-Silva A, Jesus J, Gomes J, Sebastião AM. On the role of astrocytes in synaptic plasticity. II Symposium Glial Network, Braga, Portugal, May 24, 2017. (Oral Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Kyotorphin and amidated-kyotorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Sebastião AM, Diógenes MJ. Prevention of BDNF receptor cleavage on Alzheimer's disease pathophysiology. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Changes in Brain-derived neurotrophic factor and adenosinergic system in Mecp2 knockout mouse model. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente CA, Sebastião AM. Expression of VEGF and VEGF receptors in amyotrophic lateral sclerosis (als) mice model at different disease stages. XI iMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, May 24-26, 2017. (Poster Presentation).

Afonso C, Ribeiro FF, Sebastião AM, Xapelli S. Adenosine A2A receptors modulate rat in vivo oligodendrogenesis. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Oral Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente CA, Sebastião AM. Expression of VEGF and VEGF receptors in Amyotrophic Lateral Sclerosis (ALS) mice model at different disease stages. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Ribeiro FF, Ferreira FF, Soares R, Rodrigues R, Solá S, Mira H, Sebastião AM, Xapelli S. Postnatal hippocampal neurogenesis is regulated by adenosine A2A receptor. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Armada-Moreira A, Schattling P, Taipaleenmäki E, Sebastião AM, Vaz SH, Städler Ba. Astrosomes: Artificial astrocytes as a novel approach to regulate neuronal communication. XV Meeting of the Portuguese Neuroscience Society, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Vaz SH, Jesus J, Gomes J, Sebastião AM. Astrocytes, gliotransmitters and BDNF: working together to shape synaptic plasticity?. XV Meeting of the Portuguese Neuroscience Society, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Exploring Kyotorphin and Amidated-Kyotorphin actions upon synaptic transmission and plasticity and on calpains and caspases activation. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Sebastião AM, Diógenes MJ. Impact of BDNF receptor cleavage on Alzheimer's Disease pathophysiology. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Characterization of BDNF signalling and adenosinergic system in Rett Syndrome. XV Meeting of the Portuguese Society for Neuroscience, Braga, Portugal, May 25-26, 2017. (Poster Presentation).

Soares R, Ribeiro FF, Xapelli S, Genebra T, Ribeiro MF, Sebastião AM, Rodrigues CMP, Solá S. Can a bile acid impact on proliferation and differentiation of adult neural stem cells. MitoPorto – Advances in Mitochondrial Research, Porto, Portugal, May 26, 2017. (Poster Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente CA, Sebastião AM. Neuromodulation mediated by VEGF and adenosine in Amyotrophic Lateral Sclerosis mice model. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, June 26, 2017. (Oral Presentation).

Ribeiro-Rodrigues L, Rombo DM, Sebastião AM, Valente CA. NLRP3 inflammasome as a potential target to reduce epileptic-like activity. Young European Scientist Meeting, Faculty of Medicine, University of Porto, Porto, Portugal, September 14-17 2017. (Oral Presentation).



Paulo SL, Rodrigues RS, Ribeiro FF, Fonseca-Gomes J, Shvachiy L, Solá S, Sebastião AM, Xapelli S. Neurogenesis in a Rat Model of Sporadic Alzheimer's Disease. Young European Scientist Meeting, Faculty of Medicine, University of Porto, Porto, Portugal, September 14-17, 2017. (Poster Presentation).

Rei N, Ribeiro JA, Vaz SH, Valente CA, Sebastião AM. Neuromodulation mediated by VEGF and adenosine in Amyotrophic Lateral Sclerosis mice model. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Belo R, Perez-Peinado C, Valle J, Andreu D, Sebastião A, Neves V, Castanho M, Diógenes MJ. Neuronal mechanisms behind Kyotorphin and Amidated-Kyotorphin effects. 3<sup>rd</sup> M2B PhD Students Meeting, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, September 27-29, 2017. (Oral Presentation).

Rodrigues RS, Ribeiro FF, Ferreira F, Vaz SH, Sebastião AM, Xapelli S. Interaction between cannabinoid type 1 and type 2 receptors in the modulation of subventricular zone and dentate gyrus neurogenesis. 10<sup>th</sup> International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, Covilhã, Portugal, October 12-14, 2017. (Oral Presentation).

Armada-Moreira A, Taipaleenmäki E, Baekgaard-Laursen M, Schattling P, Sebastião AM, Vaz SH, Städler B. Platinum nanoparticle-based microreactors as support for neuroblastoma cells. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Belo R, Perez-Peinado C, Valle J, Andreu D, Sebastião A, Castanho M, Neves V, Diógenes MJ. On the road of KTP and KTP-NH<sub>2</sub> neuronal mechanisms of action. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Cavacas C, Magalhães DM, Sebastião AM, Valente CA. Characterization of cell death in the ex vivo slice model of epileptogenesis. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Rodrigues TM, Vaz SH, Manso N, Belo R, Sebastião AM, Diógenes MJ. Protection of BDNF receptor cleavage: a possible new therapeutic strategy for Alzheimer's disease. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Gomes J, Jesus J, Sebastião AM, Vaz SH. The role of astrocytes on the modulation of synaptic plasticity by Brain-derived neurotrophic factor (BDNF). 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Magalhães DM, Mampay M, Sheridan G, Valente CA. Can modulating of crosstalk between the systemic immune system and CNS ameliorate the depressive and anxiety-like behavior induced by Social Isolated mice?. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Miranda-Lourenço C, Sebastião AM, Diógenes MJ. BDNF signalling and Adenosinergic system in Rett Syndrome. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Oral Presentation).

Mouro FM, Ribeiro, JA, Sebastião AM, Dawson N. Chronic intermittent treatment with WIN 55,212-2 impairs cognition and thalamo-hippocampal-prefrontal functional connectivity. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Oral Presentation).

Paulo SL, Rodrigues RS, Ribeiro FF, Fonseca-Gomes J, Shvachiy L, Solá S, Sebastião AM, Xapelli S. Adult Hippocampal Neurogenesis in a Sporadic Alzheimer 's disease Model. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Rei N, Vaz S, Ribeiro JA, Valente CA, Sebastião AM. Dysregulation of VEGF signaling in Amyotrophic Lateral Sclerosis (ALS) mice model through disease progression. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Ribeiro FF, Ferreira F, Rodrigues RS, Soares R, Neves-Tomé R, Assaife-Lopes N, Santos TE, Armada-Moreira A, Solá S, Mira H, Sousa MM, Sebastião AM, Xapelli S. Trophic actions of adenosine A2A receptors in postnatal neurogenesis and neuronal maturation. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Oral Presentation).

Ribeiro-Rodrigues L, Rombo DM, Loppi S, Sebastião AM, Malm T, Valente CA. Can LPS/ATP-mediated NLRP3 inflammasome activation promote epileptic like activity in organotypic slices?. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Rodrigues R, Ribeiro F, Ferreira F, Vaz S, Sebastião AM, Xapelli S. Cannabinoid CB1R and CB2R cross-modulatory actions on neurogenesis. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Soares R, Xapelli S, Morais VA. Enhanced lineage-directed differentiation of Neural Stem Cells via modulation of mitochondria dynamics. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Tanqueiro SR, Dawson N, Sebastião AM, Diógenes MJ. Deregulation of BDNF signaling in a mice model of schizophrenia. 3<sup>rd</sup> Meeting of the PhD Students from the Mind-Brain College of the University of Lisbon, Lisbon, Portugal, October 19-20, 2017. (Poster Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Rodrigues TM, Vaz SH, Sebastião AM, Diógenes MJ. Protection of BDNF receptor cleavage as a possible therapeutic strategy for Alzheimer's Disease. Alzheimer's Global Summit, Champalimaud Foundation, Lisbon, Portugal, 2017. (Oral Presentation).

Belo R, Neves V, Castanho M, Sebastião A, Diógenes MJ. Exploring the actions of Kyotorphin and Amidated-Kyotorphin as possible pharmacological therapy for Alzheimer's Disease. Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, 2017. (Oral Presentation).

Belo R, Neves V, Sebastião A, Diógenes MJ. Kyotorphin and amidated-kyotorphin effects on hippocampal synaptic transmission and on calpains and caspases activation. XLVII Reunião da Sociedade Portuguesa de Farmacologia, Fundação Bissaya Barreto Bencanta, Faculty of Medicine, University of Coimbra, Coimbra, Portugal, 2017. (Oral Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Alterations in BDNF signalling and adenosinergic system: from presymptomatic to symptomatic stage of Rett Syndrome. XLVII Reunião da Sociedade Portuguesa de Farmacologia, Fundação Bissaya Barreto Bencanta, Faculty of Medicine, University of Coimbra, Coimbra, Portugal, 2017. (Oral Presentation).

Fonseca-Gomes J, Jerónimo-Santos A, Sebastião AM, Diógenes MJ. BDNF receptor cleavage: relevance for Alzheimer's Disease pathophysiology – The 1<sup>st</sup> Year. I Meeting of NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, 2017. (Oral Presentation).

Tanqueiro SR, Dawson N, Sebastião AM, Diógenes MJ. Modulation of BDNF effects by adenosine: a good strategy in schizophrenia?. I Meeting of NeurULisboa Doctoral Programme, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, 2017. (Oral Presentation).

Miranda-Lourenço C, Ferreira S, Sebastião AM, Diógenes MJ. Characterization of BDNF signalling and adenosinergic system in Rett Syndrome. XV Meeting Sociedade Portuguesa de Neurologia, Braga, Portugal, 2017. (Poster Presentation).

Tanqueiro SR, Ramalho RM, Sebastião AM, Diógenes MJ. Amyloid induces BDNF loss of function by a mechanism dependent on Extrasynaptic NMDA receptors activation. XV Portuguese Society for Neuroscience Meeting, Lisbon, Portugal, 2017. (Poster Presentation).

### **Organisations of Conferences**

Sebastião AM, Ribeiro F. Organizer. SynaNet H2020 - First Annual Scientific Meeting, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, January 26-27, 2017.

Valente CA, Xapelli S. Organizers. Training Course on Cell Cultures. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 16-21, 2017.

Diógenes MJ, Aroeira R, Sebastião AM. Organizer. Opening session of the Brain Awareness Week 2017 – Actividade Física e Desporto.

Sebastião AM. Organizer. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week Lisbon, Portugal, May 4, 2017.

Sebastião AM, Aroeira R. Organizer. Annual Meeting of the Mind-Brain College, University of Lisbon, Lisbon, Portugal, October 2017.

### Internationalisation

- Participation in European Research Networks

Twinning H2020 action – SynaNet – Collaboration between several unit members with researchers of the University of Rome, University of Eastern Finland, University of Lancaster.  
Coordinator: Ana Sebastião.

COST Action BM1302 - Joining Forces in Corneal Regeneration Research - Management Committee member: Sara Xapelli.

COST Action BM1402 - Development Of A European Network For Preclinical Testing Of Interventions In Mouse Models Of Age And Age-Related Diseases (MouseAGE). Management Committee Substitute Member: Sara Xapelli.

- Collaborations in scientific projects

On the action of cannabinoids and adenosine on synaptic excitability and cognition (Ana Sebastião projects).

Cristha E Muller (Bonn, Germany).

Karl Jacobson (NIH, Bethesda, USA).

Neil Dawson (Lancaster, England).

Serge Ferré (Baltimore, USA).

On the influence of astrocytes in neuronal function (Sandra Vaz projects)

Brigitte Städler - (Aarhus, Denmark).

Jérôme Baufreton (Bordeaux, France).

Vincent Crunelli (Cardiff, England) (co-supervision of a PhD Student).

On the role of neurogenesis and oligodendrogenesis in neurologic and psychiatric dysfunctions (Sara Xapelli projects)

Carlos Fitzsimons (University of Amsterdam) (co-supervision of a PhD Student).

Helena Mira (Valencia, Spain).

Jussi Paananen (Kuopio, Finland).

On pathophysiological mechanisms in Alzheimers' disease, Rett Syndrome and schizophrenia (Maria José Diógenes projects)

Annakaisa Haapasalo (Kuopio, Finland).

Christopher Parsons (Frankfurt, Germany).

David Blum (Université Lille-Nord de France).

Detlev Boison (Portland, USA).

Eero Castren (Helsinki, Finland).

Mikko Hiltunen (Kuopio, Finland) (co-supervision of a PhD Student).

Neil Dawson (Lancaster, England) (co-supervision of a PhD Student).

Tiago Outeiro, PhD - Department of Experimental Neurodegeneration, Center for Nanoscale Microscopy and Molecular Physiology of the Brain, Center for Biostructural Imaging of Neurodegeneration, University Medical Center Göttingen, Göttingen, Germany.

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

### **Prizes, Honours and Awards**

Diógenes MJ. Novel therapeutic strategy and new biomarker for Alzheimer's Disease based on BDNF receptor cleavage. Mantero Belard 2017 Award, Santa Casa da Misericórdia de Lisboa, Lisbon, Portugal, 2017.

### **Advanced Teaching**

- International training

Courses organized

Valente CA, Xapelli S. Organizer. Training Course on Cell Cultures. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 16-21, 2017.

Supervision of International Internships

Fernández M. Research Exchange Program for Medical Students (supervisors: Claudia Valente, Sara Xapelli, Sandra Vaz). University of Barcelona, Barcelona, Spain.

Martins K. Programa SiPN Experimental Learning da Fundação Luso-Americana para o Desenvolvimento (FLAD). Supervisor: Cláudia Valente. University of Binghamton, New York, USA.

Roman AM. Research Exchange Program for Medical Students (supervisors: Claudia Valente, Sara Xapelli, Sandra Vaz). Lucian Blaga University of Sibiu, Romania.

Fokina T. Research Exchange Program for Medical Students (supervisors: Claudia Valente, Sara Xapelli, Sandra Vaz). UGR Granada, Granada, Spain.

Korte E. Research Exchange Program for Medical Students (supervisors: Claudia Valente, Sara Xapelli, Sandra Vaz). University of Groningen, Netherlands.

- Directive Roles

Sebastião AM – Director of the Doctoral Mind-Brain College ‘Mind and Brain’, University of Lisbon, which integrates 7 Schools (Faculdade de Ciências (FCUL), Faculdade de Farmácia (FFUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL), Instituto Superior Técnico (IST) e Instituto de Ciências Sociais (ICS), and their corresponding research centers, to promote the interaction between scientific, technical and formative valences to further understand brain and cognition as well as to communicate with and for the main achievements to the society.

Sebastião AM – Director of the Integrated Neurosciences PhD Programme (Supported by FCT) which involves 6 Schools (Faculdade de Ciências (FCUL), Faculdade de Farmácia (FFUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL), Instituto Superior Técnico (IST).

Sebastião AM - Member of the Scientific Board of the MScs/PhD in Neurosciences, Faculty of Medicine, University of Lisbon.

Sebastião AM - Member of the Scientific Board MSc/PhD Programme in Cognitive Sciences, University of Lisbon, which involves 4 Schools (Faculdade de Ciências (FCUL), Faculdade de Letras (FLUL), Faculdade de Medicina (FMUL), Faculdade de Psicologia (FPUL).

Sebastião AM – Member of the Coordination Board of the Master in Biomedical Engineering, IST/FMUL.

Ribeiro JA - Coordinator of the Module on Neuroethics, Ms/PhD in Neurosciences.

Sebastião AM – Coordinator of the following modules of the MSc/PhD in Neurosciences: ‘Cellular and Molecular Neurosciences’, ‘Neuronal Networks’, ‘Neuronal Degeneration and Regeneration’.

- ‘Neuroscience Seminars’ run once per week on Mondays, constituting a forum for discussion of scientific achievements, projects to start or running, as well as to invite members from other institutions to share their ideas on different topics. These seminars are open to the iMM community, but are particularly designed for training of Master and PhD students at the Unit.

The seminars are also open to Medical students as well as to members of the Mind-Brain College of the University of Lisbon. Seminar scheduling and organization is in charge of Sandra Vaz, a post-doc at the Unit.

- Seminars at the PhD and Master Courses in Neuroscience. The list below refers to the seminars presented by Unit members or, whenever indicated, by those invited from outside iMM. Again, and as in 3) above, seminars given by members of other iMM Units (1 from Miguel Castanho Lab, 1 from Miguel Remondes Lab, 1 from Diana Prata Lab, 2 from José Ferro Lab) are not listed to avoid repetition with other Unit reports:

September, 27

Diogo Rombo. Evaluation of synaptic activity through electrophysiological recording Techniques

October, 4

Ana Luisa Carvalho (FCTUC, CNC). Modulation of AMPA receptor recycling molecular aspects.

October, 10

Sérgio Gulbenkian (FG/FMUL). Peptidergic innervation of the mammalian vascular system.

October, 18

Nadia Rei, Rita Belo. Receptor quantification assays: relevance for the study of neurodegenerative diseases.

Margarida Gama-Carvalho (FCUL). Genetic dysfunction in motor neuron diseases. João Gomes. BDNF receptor cleavage: relevance for Alzheimer's Disease pathophysiology.

November, 8

Ana Filipa Ribeiro. Modulation of neuronal maturation and differentiation.

Cláudia Valente. Neuroinflammation in epilepsy.

Adelaide Fernandes (FFUL). Molecular dysfunctions in multiple sclerosis.

Carlos Duarte (FCTUC; CNC). The ubiquitin/proteasome system and control of neuronal death.

Susana Solá (FFUL). Driving Cell Death Machinery towards Neural Differentiation.

November, 15

Eduardo Ducla-Soares (FCUL). Neuroimaging: an overview.

João Peça (CNC). Optogenetic manipulation of neuronal circuits.



November, 22

Francisco Mouro. Cannabinoid receptors influence upon memory.

J. Alexandre Ribeiro. Ethics of Neurosciences and Neurosciences of Ethics.

Alexandre de Mendonça. The ethics in neurological research.

Luisa Figueira. Role of an Ethics Committee in a University Hospital.

António Barbosa. Advanced Directives.

December, 6

Fernando Araújo (FDUL). Neuromarketing and Law.

Isabel Rocha. Ethics and legislation in animal research.

December, 13

Luis Madeira. Conscious States.

Hélder Coelho (FCUL). Artificial Intelligence: a view on Morality, or artificial agents with qualities.

José Santos Victor (IST). Reciprocal inputs between Neuroscience and Robotics.

### **Science and Society**

- Brain Awareness Week 2017, 11-18 March, 2017

Opening Session "Cérebro e atividade física". Organizer: Maria José Diógenes in collaboration with many members of the Unit. March 12, 2017.

- Activities with Schools and for Schools

Activities organized by:

Ana Filipa Ribeiro, Maria José Diógenes, Sara Xapelli e Rita Aroeira in collaboration with Mind-Brain College, University of Lisbon. Most unit members actively participated in these activities.

Main activities were:

- "Neurocientistas na Escola"

Several talks were organized crossing different themes:

- Brain structure and function;
- Brain development through age;
- Brain and drugs;
- Neurodegenerative diseases;
- How to study the brain.

The activities involved a total of six visits to schools, between the end of the 2nd period and the beginning of the 3<sup>rd</sup>.

Participating Schools – Number of Students:

Colégio St Peters School, Palmela, Setúbal – 50;

Escola Básica Ferreira de Castro, Mem Martins, Sintra – 45;

Colégio Marista de Carcavelos, Parede, Cascais – 160;

Escola Salesianos do Estoril, Estoril, Cascais – 145;

Escola Secundária Eça de Queirós, Lisbon – 45;

Agrupamento de Escolas da Boa Água, Quinta do Conde, Sesimbra, Setúbal – 150.

Total: 595 Students

- “Laboratórios Abertos”

Neurosciences’ laboratories organized visits for undergraduate students to promote their contact with the different components of the laboratories as well as with the researchers.

Participating Schools – Number of Students:

Colégio de São Filipe, Setúbal (Lower Secondary Education) – 7;

Escola Secundária de Carcavelos (Secondary Education) – 37.

Total: 44 Students

- Other activities:

Sebastião AM - Participation upon invitation on the debate organized by Students at the School of Medicine, opened to the public: Onde Começa a Doença Mental.

Aroeira R. Organizer. Round Table “O impacto da ciência na sociedade – contributos das neurociências” on the grounds of the Annual Meeting of the Mind-Brain College.

Aroeira R. Organizer. Round Table “Academia, empreendedorismo e indústria” on the grounds of the Annual Meeting of the Mind-Brain College.

### **MSc Thesis Completed**

Filipe Huberto Rodrigues Carralves, 17/02/2017, “Alzheimer's disease biomarkers: Knowing the present to understand the future Master in Biopharmaceutical Sciences”, Faculty of Pharmacy, University of Lisbon. Supervisor: Maria José Diógenes

João Pedro de Almeida Jesus, 29/05/2017, “Role of SNARE-dependant gliotransmitter release by astrocytes in the modulation of synaptic plasticity by BDNF”, Master in Neurosciences, Faculty of Medicine, University of Lisbon. Supervisor: Sandra H Vaz.

Nuno Miguel da Silva Rosa, 16/06/2017, “Exploring the effect of NLRP3 inflammasome inhibition in the ex vivo model of epileptogenesis”, Master in Medical Biochemistry, Faculty of Sciences, University of Lisbon. Supervisor: Cláudia Valente.

Joana Isabel Gomes, 21/06/2017, “Role of astrocytes on the modulation of synaptic transmission by Brain-derived neurotrophic factor”, Bachelor Thesis, Faculty of Sciences, University of Algarve. Supervisor: Sandra Vaz.

Cláudia Afonso, 05/07/2017, “New potential therapy for multiple sclerosis: a role for adenosine A2A receptors”, Master in Neurosciences, Faculty of Medicine, University of Lisbon. Supervisor: Sara Xapelli.

Cláudia Sofia Beltrão Cavacas, 17/11/2017, “Characterization of cell death in the ex vivo slice model of epileptogenesis”, Master in Human and Environmental Biology, Faculty of Medicine, University of Lisbon. Supervisor: Cláudia Valente.

#### **PhD Thesis Completed**

Mariana Colino de Oliveira, 29/06/2017, “Neuroexcitability control by adenosine and BDNF at the adult hippocampus”, Faculty of Medicine, University of Lisbon. Supervisor: Ana M. Sebastião.

Ana Filipa Ferreira da Cunha Ribeiro, 24/11/2017, “Unveiling the trophic actions of adenosine A2A receptors in neurite outgrowth and postnatal neurogenesis – Interaction with brain-derived neurotrophic factor”, Faculty of Medicine, University of Lisbon. Supervisor: Ana M. Sebastião.

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## Silva-Santos, Bruno

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### Major Interests / Objectives

We study the biology of T lymphocytes and their key roles in immunity to infection, inflammatory diseases, and cancer. Our projects focus on the development of these cells in the vertebrate thymus and their functions upon export to peripheral tissues. We investigate differentiation and activation signals for T cells using in vivo models for infectious (such as malaria) or autoimmune diseases (such as multiple sclerosis), or cancer (namely breast cancer). We also study human peripheral blood T cells, their recognition and elimination of hematological or solid tumors. Overall, we envisage the identification of molecular mechanisms involved in the differentiation, activation, and function of T cells, aiming towards the design of new treatments for cancer and (auto)immune disorders.

### Head of Laboratory

Bruno Silva Santos, PhD, Associate Professor

### Research Team

Ana Maria de Amarante Pamplona Dias dos Santos	PhD	Post-Doctoral Investigator
Ana Raquel Vicente Lopes	Graduate	MSc Student (Started August)
André Gonçalo do Espírito Santo Simões	PhD	Post-Doctoral Investigator
Anita Raquel Quintal Gomes	PhD	Investigator, Escola Superior de Tecnologia da Saúde de Lisboa, Assistant Professor
Biagio Di Lorenzo	Master	PhD Student
Branka Kolundzija	PhD	Investigator (Left February)
Carolina Emanuel Carreira Gomes Jardim	Master	Investigator (Started February)
Daniel Pereira Inácio	Graduate	MSc Student (Started July)
Daniel Vargas Correia	PhD	Post-Doctoral Investigator
Francisco Landeck Moreira Franco Caiado	PhD	Post-Doctoral Investigator
Gisela Silva Gordino	Master	Investigator
Haakan Rolf Norell	PhD	Investigator (Left December)
Hiroshi Kubo	PhD	Post-Doctoral Investigator (Left March)
Julie Cecile Caroline Ribot	PhD	Principal Investigator
Karine Serre	PhD	Post-Doctoral Investigator
Maria Helena Cristiano Brigas	Master	PhD Student
Miguel Alexandre Ferreira Pinto	Graduate	MSc Student (Left December)
Miguel Alves Rovisco Ribeiro	Master	Trainee
Natacha Maria Gonçalves Silva Sousa	Master	Lab Manager
Nina Alexandra Schmolka	PhD	Post-Doctoral Investigator (Left April)
Paula Estefania Vargas Romero	PhD	Post-Doctoral Investigator (Left December)

Pedro Henrique Papotto Rosa	Master	PhD Student
Sara Alexandra da Costa Pereira	Undergraduate	Trainee (Started February)
Sofia Mensurado Santos	Master	PhD Student
Tiago Maria de Carvalho da Costa Amado	Master	PhD Student
Tiago Roberto Gomes Pestana	Graduate	MSc Student (Started August)

### Laboratory Keywords / Research Areas

T cell development/differentiation, T cell activation, Tumour immunology, Leukemia clonal evolution, Immunopathogenesis of severe malaria, Neuroimmunology.

### Major Scientific Achievements

In 2017, we published 12 papers in international peer-reviewed journals. Some of our major findings were the identification of a primary tumor-induced crosstalk between patrolling monocytes and Natural Killer cells that protects against metastasis formation (Kubo et al. *Cancer Immunol Res* 2017); and the demonstration that IL-17-producing  $\gamma\delta$  T cells can differentiate in response to IL-23 signals in peripheral lymph nodes draining inflammatory sites in a mouse model of multiple sclerosis (Papotto et al. *EMBO Rep* 2017). We were also invited to write reviews for top journals on the development (Muñoz-Ruiz et al. *Trends Immunol* 2017) and inflammatory functions (Papotto et al. *Nature Immunol* 2017) of IL-17-producing  $\gamma\delta$  T cells, which further strengthened our position as one of the leading laboratories in  $\gamma\delta$  T cell research worldwide.

### Selected Publications

Muñoz-Ruiz M, Ribot JC, Grosso AR, Gonçalves-Sousa N, Pamplona A, Pennington DJ, Regueiro JR, Fernandez-Malavé E, Silva-Santos B (2016). TCR signal strength controls thymic differentiation of discrete proinflammatory  $\gamma\delta$  T cell subsets. *Nature Immunology*, 17, 721. <https://www.nature.com/articles/ni.3424>. (IF: 21.506, Citations: 14).

Silva-Santos B, Serre K, Norell H. (2015).  $\gamma\delta$  T cells in cancer. *Nature Reviews Immunology*, 15, 683. <https://www.nature.com/articles/nri3904>. (IF: 39.932, Citations: 73).

Schmolka N\*, Serre K\*, Grosso AR, Rei M, Pennington DJ, Silva-Santos B (2013). Epigenetic and transcriptional signatures of stable versus plastic differentiation of pro-inflammatory  $\gamma\delta$  T cell subsets. *Nature Immunology*, 14 (10), 1093. <https://www.nature.com/articles/ni.2702>. (IF: 21.506, Citations: 24).

Coquet J\*, Ribot JC\*, Babala N, Middendorp S, Xiao Y, Neves JF, Fonseca-Pereira D, Jacobs H, Pennington DJ, Silva-Santos B\*\*, Borst J\*\* (\*Co-first Authors; \*\*Co-senior Authors) (2013). Epithelial and dendritic cells in the thymic medulla promote CD4<sup>+</sup> Foxp3<sup>+</sup> regulatory T cell development via the CD27-CD70 pathway. *Journal of Experimental Medicine*, 210(4), 715. <http://jem.rupress.org/content/210/4/715.long>. (IF: 11.991, Citations: 40).

Correia DV, Fogli M, Hudspeth K, da Silva MG, Mavilio D, Silva-Santos B (2011). Differentiation of human peripheral blood Vdelta1<sup>+</sup> T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells. *Blood*, 118, 992-1001. <http://www.bloodjournal.org/content/118/4/992.long?sso-checked=true>. (IF: 13.164, Citations: 46).

### Ongoing Research Projects

2017/2018: Transcriptional (re)programming of antitumour myeloid cells in breast cancer. Coordinator: Karine Marie Serre. Funding Agency: Fundo IMM-Laço. Reference: Laço KSerre. Amount: € 49 500,00. Total Amount: € 49 500,00.

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

2016/2018: Cancer immunotherapy based on the adoptive transfer of Delta 1 T cells. Coordinator: Bruno Miguel Silva-Santos. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/DTP-PIC/4931/2014. Amount: € 166 389,00. Total Amount: € 180 000,00.

2016/2018: Targeting microRNAs to modulate the differentiation of anti-tumour human gamma-delta T cells. Coordinator: Julie Cecile Caroline Ribot. Funding Agency: INFARMED. Reference: FIS-FIS-2015-01\_ONC\_20150630-162. Amount: € 90 000,00. Total Amount: € 90 000,00.

2015/2020: DevoTed\_miR: MicroRNA determinants of the balance between effector and regulatory T cells in vivo. Coordinator: Bruno Miguel Silva-Santos. Funding Agency: European Commission. Reference: ERC CoG 646701. Amount: € 2 000 000,00. Total Amount: € 2 000 000,00.

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

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

### **Other Projects**

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

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

### **Publications in Peer Review Journals**

Nóbrega-Pereira S, Caiado F, Carvalho T, Matias I, Graça G, Gonçalves LG, Silva-Santos B, Norell H, Dias S (2017). VEGFR-2-mediated reprogramming of mitochondrial metabolism regulates the sensitivity of acute myeloid leukemia to chemotherapy. *Cancer Res.* doi: 10.1158/0008-5472.CAN-17-1166. (IF: 9.122, Citations:--).

Ribeiro ST, Barata JT, Silva-Santos B (2017). Multifaceted CK2 in malignant and healthy T cells. *Oncotarget.* 8(53):90622-90623. (IF: 5.168, Citations:--).

Papotto PH, Reinhardt A, Prinz I, Silva-Santos B (2017). Innately versatile:  $\gamma\delta$ 17 T cells in inflammatory and autoimmune diseases. *J Autoimmun.* doi: 10.1016/j.jaut.2017.11.006. Review. (IF: 7.641, Citations:--).

Papotto PH, Gonçalves-Sousa N, Schmolka N, Iseppon A, Mensurado S, Stockinger B, Ribot JC, Silva-Santos B (2017). IL-23 drives differentiation of peripheral  $\gamma\delta 17$  T cells from adult bone marrow-derived precursors. *EMBO Rep.* 18(11):1957-1967. (IF: 8.568, Citations:--).

Kubo H, Mensurado S, Gonçalves-Sousa N, Serre K, Silva-Santos B (2017). Primary Tumors Limit Metastasis Formation through Induction of IL15-Mediated Cross-Talk between Patrolling Monocytes and NK Cells. *Cancer Immunol Res.* 5(9):812-820. (IF: 8.284, Citations:--).

Di Lorenzo B, Déchanet-Merville J, Silva-Santos B (2017). Peripheral clonal selection shapes the human  $\gamma\delta$  T-cell repertoire. *Cell Mol Immunol.* 14(9):733-735. (IF: 5.897, Citations:--).

Sumaria N, Grandjean CL, Silva-Santos B, Pennington DJ (2017). Strong TCR $\gamma\delta$  Signaling Prohibits Thymic Development of IL-17A-Secreting  $\gamma\delta$  T Cells. *Cell Rep.* 19(12):2469-2476. (IF: 8.282, Citations: 2).

Papotto PH, Ribot JC, Silva-Santos B (2017). IL-17+  $\gamma\delta$  T cells as kick-starters of inflammation. *Nat Immunol.* 18(6):604-611. Review. (IF: 21.506, Citations: 10).

Ministro A, de Oliveira P, Nunes RJ, Dos Santos Rocha A, Correia A, Carvalho T, Rino J, Faísca P, Becker JD, Goyri-O'Neill J, Pina F, Poli E, Silva-Santos B, Pinto F, Mareel M, Serre K, Constantino Rosa Santos S (2017). Low-dose ionizing radiation induces therapeutic neovascularization in a pre-clinical model of hindlimb ischemia. *Cardiovasc Res.* 113(7):783-794. (IF: 5.878, Citations: 1).

Silva-Santos B, Strid J (2017).  $\gamma\delta$  T cells get adaptive. *Nat Immunol.* 18(4):370-372. (IF: 21.506, Citations:--).

Muñoz-Ruiz M, Sumaria N, Pennington DJ, Silva-Santos B (2017) Thymic Determinants of  $\gamma\delta$  T Cell Differentiation. *Trends Immunol.* 38(5):336-344. Review. (IF: 13.287, Citations: 2).

Ribeiro ST, Tesio M, Ribot JC, Macintyre E, Barata JT, Silva-Santos B (2017). Casein kinase 2 controls the survival of normal thymic and leukemic  $\gamma\delta$  T cells via promotion of AKT signaling. *Leukemia* 31(7):1603-1610. (IF: 11.702, Citations: 2).

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

Silva-Santos B. Innate killers in cancer surveillance and immunotherapy. 4<sup>th</sup> International Conference of Translational Medicine on Immune-Mediated Diseases, Palermo, Italy, March 27-29, 2017.



Silva-Santos B. Differentiation and functions of pro-inflammatory gamma-delta T cells. University of Toronto, Toronto, Canada, April 13, 2017.

Ribot J. Analysing T cell subsets within the Central Nervous System in health and disease. XV Congress of Sociedade Ibérica de Citometria, Lisbon, Portugal, May 27, 2017.

Silva-Santos B. Introduction to cancer immunotherapy. XV Congress of Sociedade Ibérica de Citometria, Lisbon, Portugal, May 27, 2017.

Silva-Santos B. Kinase-mediated signalling in thymic gamma-delta T cell development. SINAL 2017 – 8<sup>th</sup> Meeting on Signal Transduction, Pavilhão do Conhecimento, Lisbon, Portugal, June 1-2, 2017.

Silva-Santos B. Fundamentos de Imuno-Oncologia. Semana Digestiva 2017, Albufeira, Portugal, June 9, 2017.

Silva-Santos B. Innate determinants of cancer surveillance and immunotherapy. 43<sup>rd</sup> Annual Meeting of Sociedade Portuguesa de Imunologia, Porto, Portugal, June 15, 2017.

Silva-Santos B. Regulating and manipulating gamma-delta T cells in cancer immunotherapy. King's College London, London, England, June 27, 2017.

Silva-Santos B. Atypical roles for IL-17+ gamma-delta T cells in peripheral tissues. Francis Crick Institute, London, England, July 7, 2017.

Simões A. Delta One T cells: Towards a new cellular immunotherapy for cancer. 1<sup>st</sup> Precision Medicine in Imuno-Oncology Meeting, Instituto Português de Oncologia, Lisbon, Portugal, July 6-7, 2017.

Silva-Santos B. IL-17+ gamma-delta T cells in health and disease. 5<sup>th</sup> BIFS – Basel Immunology Focus Symposium, Basel, Switzerland, August 29, 2017.

Silva-Santos B. The Lymphact story. Conferências RUMO 2017, Lisbon, Portugal, September 23, 2017.

Serre K. Host: Harnessing the power of the immune system is key. International Meeting on Cancer Innovation, CUF, Porto, Portugal, November 10, 2017.

Serre K. Host: Harnessing the power of the immune system is key. International Meeting on Cancer Innovation, CUF, Porto, Portugal, November 11, 2017.

Silva-Santos B. Atypical functions and regulation of IL-17+ gamma-delta T cells in tissues. IL-17 Summit, Munich, Germany, November 25, 2017.

### **Communications in National Conferences**

Ribeiro M, Brigas H, Temido-Ferreira M, Santa C, Coelho J, Marques-Morgado I, Valente C, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. gd T cells are the major source of IL-17 in the meninges and control brain cognitive functions. IMM Post-Doc Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 17, 2017. (Oral Presentation).

Ribeiro M, Brigas H, Temido-Ferreira M, Santa C, Coelho J, Marques-Morgado I, Valente C, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. gd T cells are the major source of IL-17 in the meninges and control brain cognitive functions. XV Annual Meeting of the Sociedade Portuguesa de Neurociências, Braga, Portugal, May 25, 2017. (Oral Presentation).

Brigas H, Wilharm A, Ribeiro M, Sandrock I, Reinhardt A, Oberdorfer L, Silva-Santos B, Prinz I, Ribot JC. Characterization of gd T cell subsets in the male reproductive tract. XLIII Annual Meeting of the Portuguese Society for Immunology, Porto, Portugal, June 14-16, 2017. (Poster Presentation).

Papotto PH, Gonçalves-Sousa N, Schmolka N, Iseppon A, Mensurado S, Stockinger B, Ribot JC, Silva-Santos B. IL-23 drives differentiation of peripheral gd17 T cells from adult bone marrow-derived precursors. XLIII Annual Meeting of the Portuguese Society for Immunology, Porto, Portugal, June 14-16, 2017. (Oral Presentation).

Mensurado S, Rei M, Lança T, Ioannou I, Gonçalves-Sousa N, Kubo H, Malissen M, Papayannopoulos V, Serre K, Silva-Santos B. Neutrophil-mediated inhibition of pro-tumor IL-17-producing gd T cells. XLIII Annual Meeting of the Portuguese Society for Immunology, Porto, Portugal, June 14-16, 2017. (Poster Presentation and Speed Communication).

Ribeiro M, Brigas H, Temido-Ferreira M, Santa C, Coelho J, Marques-Morgado I, Valente C, Omenetti S, Stockinger B, Manadas B, Lopes LV, Silva-Santos B, Ribot JC. gd T cells are the major source of IL-17 in the meninges and control brain cognitive functions. Champalimaud Research Symposium, Lisbon, Portugal, October 9-11, 2017. (Poster Presentation).

Brigas H, Wilharm A, Ribeiro M, Sandrock I, Reinhardt A, Oberdorfer L, Silva-Santos B, Prinz I, Ribot JC. Physiological roles of T cell subsets in the murine male reproductive tract. Champalimaud Research Symposium, Lisbon, Portugal, October 9-11, 2017. (Poster Presentation).

Papotto PH, Gonçalves-Sousa N, Schmolka N, Iseppon A, Mensurado S, Stockinger B, Ribot JC, Silva-Santos B. IL-23 drives differentiation of peripheral gd17 T cells from adult bone marrow-derived precursors. Champalimaud Research Symposium, Lisbon, Portugal, October 9-11, 2017.

### **Organisation of Conferences**

Gonçalves-Sousa N. Co-organizer. XV Congress of Sociedade Ibérica de Citometria, Lisbon, Portugal, May 25-27, 2017.

Gonçalves-Sousa N. Co-organizer. XLIII Annual Meeting of the Portuguese Society for Immunology, Porto, Portugal, June 14-16, 2017.

Silva-Santos B, Norell H. Co-organizers. Immunotherapy Workshop of the Annual Meeting of the Sociedade Portuguesa de Hematologia, Vilamoura, Portugal, November 16, 2017.

### **Internationalisation**

Collaborative work with Drs. Daniel J. Pennington (Blizard Institute, Queen Mary College, London, England), Adrian Hayday (Francis Crick Institute, London, England), Brigitta Stockinger (Francis Crick Institute, London, England), Ton Schumacher (The Netherlands Cancer Institute, Amsterdam, The Netherlands), Domenico Mavilio (Istituto Clinico Humanitas, Milan, Italy), Immo Prinz (University of Hannover, Germany), Julie Déchanet-Merville (CIRID, University of Bordeaux, France), Venizelos Papayannopoulos (Francis Crick Institute, London, England), José Ramon Regueiro (Universidad Complutense, Madrid, Spain).

### **Prizes, Honours and Awards**

Serre K. Sulfur-containing amino acid dietary modulation of breast cancer immunity. Awarded a project grant from Fundo IMM-Laço 2017 (€ 25 000).

Ribot JC. 3<sup>rd</sup> Best Oral Presentation Prize. IMM Post-Doc Day, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal.

Ribot JC. Awarded fee waiver. Champalimaud Research Symposium, Lisbon, Portugal.

Brigas H. Best 2<sup>nd</sup> Year Poster. XI IMM/CAML PhD Students Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, May 24-26, 2017.

Papotto PH. Travel Grant from BioTechne.

Mensurado S. Travel grant. The Beatson Institute, Glasgow, Scotland. Sponsored by Roche, and a travel grant from the European Union's Horizon 2020 research and innovation programme under grant agreement No 692022.

### **Advanced Teaching**

Serre K. Lecturer. Leukocyte subsets in the tumour microenvironment. Oncoimmunology Course, CAML Oncobiology MSc Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 11, 2017.

Silva-Santos B. Co-organizer and lecturer. Checkpoint inhibitors. Oncoimmunology Course, CAML Oncobiology MSc Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 11-14, 2017.

Serre K. Lecturer. Immune cells in the tumour microenvironment. Oncoimmunology Course, CAML Oncobiology MSc Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 11-14, 2017.

Silva-Santos B. Lecturer. Immunology and immunotherapy of cancer. Oncobiology Course, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, January 18, 2017.

Silva-Santos B. Co-organizer and lecturer. Gamma-delta T cell responses to tumors. Immunology Course, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 6-10, 2017.

Serre K. Lecturer. Diversification of T helper cell responses. Immunology Course, LisbonBioMed PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, February 6, 2017.

Silva-Santos B. Lecturer. Effector T cell differentiation. Immunology Course, Gulbenkian PhD Program, Instituto Gulbenkian de Ciência, Lisbon, Portugal, March 7, 2017.

Simões A. Lecturer. Delta One T cells: towards a new cellular immunotherapy for cancer. Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal, March 8, 2017.

Silva-Santos B. Lecturer. T cell differentiation. GABBA PhD Program Course, Instituto de Biologia Molecular e Celular, University of Porto, Porto, Portugal, March 22, 2017.

Silva-Santos B. Lecturer. Translating tumor immunology into cancer immunotherapy. Leaping Forward – International Clinical Congress 2017, Lisbon, Portugal, May 12, 2017.

Simões A. Co-organizer and lecturer. Delta One T cells: development of a novel immunotherapy for cancer. Fronteiras da Investigação em Biologia, Class within Genetic a Molecular Biology Master's Course, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, May 19, 2017.

Silva-Santos B. Talk. Reflections on my career. PhD Student's Retreat, CEDOC, University of Lisbon, Lisbon, Portugal, September 22, 2017.

Silva-Santos B. Lecturer. Why so much hope in cancer immunotherapy?. Preceptorship in Cancer Immunology, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 12 2017.

Ribot J. Lecturer. Future trends in basic research. Preceptorship in Cancer Immunology, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 12 2017.

Ribot J. Lecturer. Impact of murine T cell subsets on physiological aspects of brain functions: LEARNING/MEMORY. NeurULisboa PhD Program, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 25, 2017.

Serre K. Lecturer. Diversification of T helper cell functions. Master of Infectious Diseases, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 6, 2017.

Silva-Santos B. Lecturer. Principles of cancer immunotherapy. Immunotherapy Workshop, Annual Meeting of the Sociedade Portuguesa de Hematologia, Vilamoura, Portugal, November 16, 2017.

Norell H. Lecturer. CAR T-cells for leukemia treatment. Immunotherapy Workshop of the Annual Meeting of the Sociedade Portuguesa de Hematologia, Vilamoura, Portugal, November 16, 2017.

### **Science and Society**

Silva-Santos B. Cancer Immunotherapy. Conferência Cancro, Antena 2, Lisbon, Portugal, January 28, 2017.

Silva-Santos B. Molecular mechanisms of T cell differentiation. IMM ERC Symposium - 10 Years of ERC, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 16, 2017.

Serre K. Interview for “Grande Reportagem cancro da mama: a nova cruzada dos cientistas Portugueses”, Diário de Notícias, July 22, 2017.

Silva-Santos B. Targeting PD-L1 in the new era of Immuno-Oncology. Roche’s “Lançamento Tecentriq”, Lisbon, Portugal, October 20, 2017.

Mensurado S. Cancro, Ciência e Eu. Fundo IMM-Laço Workshop, Escola Secundária da Ramada, Lisbon, Portugal, November 2, 2017.

Silva-Santos. DOT-cells: a caminho de uma nova imunoterapia para o cancro. ReTuBi – Oncologia: Conversa com Cientistas, Instituto de Medicina Molecular João Lobo Antunes, November 13, 2017.

Mensurado S. Ciência a Brincar. Escolinha da Tia Ló, Cascais, Portugal, May 22, 2017.

Mensurado S. Ciência a Brincar. Colégio da Fonte, Oeiras, Portugal, November 24, 2017.

### **MSc Thesis Completed**

Cláudia Reforço, 29/06/2017, “Disseção quantitativa da dinâmica subclonal subjacente à recidiva de Leucemia Mielóide Aguda”, University of Lisbon. Supervisor: Haakan Norell.

Miguel Pinto, 29/11/2017, “Characterization of anti-tumour myeloid cells in an orthotopic mouse model of mammary adenocarcinoma”, University of Porto. Supervisor: Karine Serre.

### **PhD Thesis Completed**

Sérgio Ribeiro, 08/02/2017, “Molecular mechanisms controlling the survival and differentiation of human  $\gamma\delta$  thymocytes”, Faculty of Medicine, University of Lisbon. Supervisor: Bruno Silva-Santos.

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## Simas, Pedro

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### Major Interests / Objectives

We utilize murid herpesvirus 4, which causes persistent infection in B-lymphocytes in laboratory mice, as a model to study human gammaherpesvirus pathogenesis, namely Kaposi's sarcoma associated herpesvirus (KSHV). KSHV is the etiologic agent of KS and primary effusion lymphoma. KSHV infection of tumor cells is primarily latent and KSHV drives cells to proliferate. KSHV persists in latently infected tumor cells as an extrachromosomal, multi-copy episome (plasmid). KSHV latency-associated nuclear antigen (kLANA) mediates KSHV episome persistence, thus tumor cell viability. Since there is no tractable animal model for KSHV, the MuHV-4 model provides a unique opportunity to study gammaherpesviruses in vivo.

### Head of Laboratory

João Pedro Monteiro e Louro Machado de Simas, PhD

### Research Team

André Filipe Coimbra e Seixas	Graduate	MSc Student
Aura Daniela Gonçalves Franco	Graduate	MSc Student (Left October)
Inês Cordeiro Filipe	Master	Trainee (Left May)
Kateryna Kholod	Graduate	MSc Student
Maria Leonor dos Santos Diniz Orge	PhD	Investigator
Marta Pires de Miranda	PhD	Post-Doctoral Investigator
Nelly Marine Carreira da Silva	Graduate	MSc Student (Started September)
Tânia Alexandra da Cruz Rodrigues	Graduate	Trainee (Started October)

### Laboratory Keywords / Research Areas

Herpes virus, B-lymphocytes, Chronic infection, Kaposi sarcoma herpesvirus (KSHV), B cell and lymphomas, MuHV-4 and animal model of infection.

### Major Scientific Achievements

We found that despite 60 million years of evolutionary divergence, kLANA and mLANA act reciprocally on TR DNA and kLANA can rescue mLANA deficient virus to enable chimeric virus to establish latent infection in mice. This system will for the first time allow in vivo investigation of kLANA in a well-established small animal model of infection.



This work is of broad interest as it successfully tests the concept of functional substitution of a human pathogen gene into a model pathogen to allow in vivo investigation. Previously, such chimeric viruses were felt to be non-viable due to evolutionary divergence, and have not been attempted. Importantly, these findings have the potential to be applied to other human pathogens, which lack small animal models.

### **Selected Publications**

Habison AC, de Miranda MP, Beauchemin C, Tan M, Cerqueira SA, Correia B, Ponnusamy R, Usherwood EJ, McVey CE, Simas JP, Kaye KM (2017). Cross-species conservation of episome maintenance provides a basis for in vivo investigation of Kaposi's sarcoma herpesvirus LANA. *PLoS Pathogens* 14;13(9), e1006555. (IF: 6.608, Citations:--).

Decalf J, Godinho-Silva C, Fontinha D, Marques S, Simas JP (2014). Establishment of Murine Gammaherpesvirus Latency in B Cells Is Not a Stochastic Event. *PLoS Pathogens* 10(7), e1004269. (IF: 6.608, Citations: 4).

Godinho-Silva C, Marques S, Fontinha D, Stevenson PG, Simas JP (2014) Defining Immune Engagement Thresholds for in vivo Control of virus-driven Lymphoproliferation. *PLoS Pathogens* 10(6), e1004220. (IF: 6.608, Citations: 1).

Correia B, Cerqueira SA, Beauchemin C, Pires de Miranda M, Li S, Ponnusamy R, Rodrigues L, Schneider TR, Carrondo MA, Kaye KM, Simas JP, McVey CE (2013). Crystal structure of the gamma-2 herpesvirus LANA DNA binding domain identifies charged surface residues which impact viral latency. *PLoS Pathogens* 9(10), e1003673. (IF: 6.608, Citations: 12).

Rodrigues L, Popov N, Kaye KM and Simas JP (2013). Stabilization of Myc Through Heterotypic Poly-Ubiquitination by mLANA is Critical for  $\gamma$ -Herpesvirus Lymphoproliferation. *PLoS Pathogens* 9(8), e1003554. (IF: 6.608, Citations: 5).

### **Ongoing Research Projects**

2016/2019: Chimera virus model to investigate the pathogenesis of Kaposi's sarcoma herpesvirus in laboratory mice. Coordinator: João Pedro Monteiro e Louro Machado de Simas. Fundind Agency: Fundação para a Ciência e a Tecnologia. Reference: PTDC/IMI-MIC/0980/2014. Amount: € 199 998,00. Total Amount: € 199 998,00.

### Other Projects

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

### Publications in Peer Review Journals

Habison AC, de Miranda MP, Beauchemin C, Tan M, Cerqueira SA, Correia B, Ponnusamy R, Usherwood EJ, McVey CE, Simas JP, Kaye KM (2017). Cross-species conservation of episome maintenance provides a basis for in vivo investigation of Kaposi's sarcoma herpesvirus LANA. *PLoS Pathog.* 13(9):e1006555. doi: 10.1371/journal.ppat.1006555. (IF: 6.608, Citations:--).

Meireles P, Sales-Dias J, Andrade CM, Mello-Vieira J, Mancio-Silva L, Simas JP, Staines HM, Prudêncio M (2017). GLUT1-mediated glucose uptake plays a crucial role during Plasmodium hepatic infection. *Cell Microbiol.* 19(2). doi: 10.1111/cmi.12646. (IF: 4.554, Citations: 4).

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## Sousa, Ana E.

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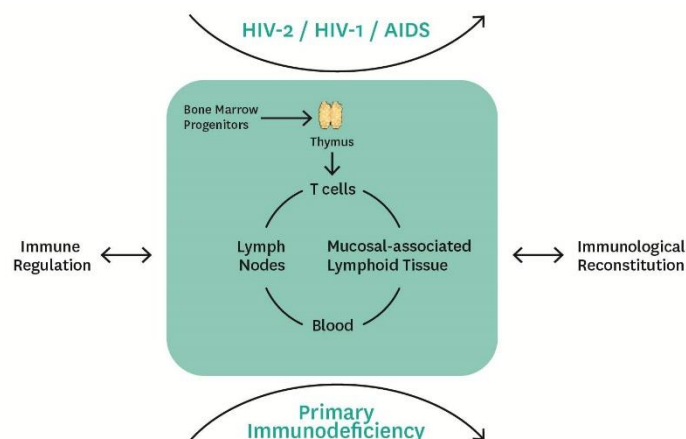
### Major Interests / Objectives

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

### Head of Laboratory

Ana Espada de Sousa, MD, PhD Agregação, Coordinating Investigator and Associate Professor, FMUL

### Graphical Abstract



### Research Team

Alexandre Augusto da Silva Figueiredo e Raposo	MD/PhD	Investigator (Started March)
Ana Berta da Fonseca Vieira Álvares e Sousa Ferrand de Almeida	MD/PhD	Investigator, HSM - CHLN, Clinical Specialist, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Ana Catarina Taborda Godinho dos Santos	PhD	Post-Doctoral Investigator
Ana Isabel Gouveia Costa da Fonseca Lopes	MD/PhD	Investigator, HSM/CHLN, Clinical Specialist, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Ana Isabel Vieira Antão	Graduate	Technician
Ana Luísa Caetano	Graduate	Technician, Faculdade Medicina da Universidade de Lisboa
Ana Rita Varanda Correia Pires	Graduate	Lab Manager (Left October)
Andreia Sofia Ramalho dos Santos	Master	Trainee (Left August)
Bárbara Estefânia da Silva Pereira Nogueira Tavares	Master	MSc Student (Left July)
Helena Nunes Cabaço	PhD	Post-Doctoral Investigator (Left August)
Inês Filipa dos Santos Martins	Master	Consultant
Isabel Cristina e Castro de Menezes Esteves	Master	Investigator, HSM/CHLN, Clinical Specialist, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
João Nuno Marques Vitorino	Undergraduate	Trainee (Left August)
José Gonçalo Duque Pereira Monteiro Marques	Master	Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Maria Catarina Mota da Silva	MD/PhD	Investigator, HSM/CHLN, Clinical Specialist
Maria da Conceição Galvão Barata Pinto Pereira dos Santos	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa
Mariana Gaspar Fonseca	MD/PhD	Post-Doctoral Investigator (Left July)
Miguel Ângelo Simão Dias	Graduate	MSc Student (Started May)
Robert Alfred Badura	Master	Investigator
Ruben Daniel Duarte Ferreira	Master	Investigator
Rui Manuel Martins Victorino	MD/PhD	Principal Investigator, Faculdade Medicina da Universidade de Lisboa, Full Professor, Clinical Service Director
Sara Branco Pereira da Silva	Master	Investigator, HSM/CHLN, MD
Susana Clara Barão Lopes da Silva dos Anjos	MD/PhD	Investigator, HSM/CHLN, Clinical Specialist, Faculdade Medicina da Universidade de Lisboa, Teaching Assistant
Susana Mendes Fernandes	MD/PhD	Investigator, HSM/CHLN, Clinical Specialist, Faculdade Medicina da Universidade de Lisboa, Assistant Professor
Tiago André da Silva Ferreira	Master	Trainee (Left July)
Vitória Rafaela Costa Curto	Master	PhD Student (Started September)
Weronika Anna Samon	Undergraduate	Undergraduate (Started September)
Yumie Tokunaga	Master	PhD Student (Left May)

### **Laboratory Keywords / Research Areas**

Human T Cell homeostasis, Immune regulation, HIV/AIDS immunopathogenesis, HIV-2 infection, Primary immunodeficiencies, Immunological reconstitution.

### **Major Scientific Achievements**

Mucosal CD4 T-cell loss and gut disruption are currently considered main determinants of the inflammatory state that characterizes HIV/AIDS, and a main cause of morbidity in treated HIV-1+ individuals. We generated the first data of gut mucosa of HIV-2+ individuals and found conserved mucosal CD4 T-cells and innate-lymphoid cells, in parallel with tight-junction preservation despite evidence of local HIV-2 replication. We discovered that HIV-2, contrarily to HIV-1, features a reduced ability to directly perturb tight junction structure. We proposed that epithelial integrity preservation allows the local response with sustained production of chemokines implicated in mucosal Th17/Th22 recruitment observed in HIV-2+ patients, which likely counteracts CD4 depletion and maintains mucosal homeostasis. These data provide a possible explanation for the benign course of HIV-2 infection, and have implications for the design of therapies targeting gut recovery in treated HIV-1 infection.

### **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, 688. (IF: 13.164, Citations: 33).

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, 2999. (IF: 13.164, Citations: 44).

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+CD25<sup>bright</sup> CD4+ T cells during specific venom immunotherapy. *Clinical & Experimental Allergy* 38, 291. (IF: 5.264, Citations: 45).

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. *J Immunol* 169, 3400. (IF: 4.856, Citations: 336).

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, 319. (IF: 29.886, Citations: 337).

### **Ongoing Research Projects**

2016/2018: Preservation of human thymic T cell production mediated by hist restriction factors during HIV infection. Coordinator: Helena Isabel Marques Nunes Cabaço. Funding Agency: Gilead Sciences. Reference: PGG/009/2015. Amount: € 30 000,00. Total Amount: € 30 000,00.

2016/2017: Harnessing T Follicular helper cells to control HIV. Coordinator: Ana Cristina Gomes Espada de Sousa. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: DEP 2016 AESousa. Amount: € 50 000,00. Total Amount: € 50 000,00.

2015/2018: HIV-2 Infection: Clinical and Biological Repository. Coordinator: Ana Cristina Gomes Espada de Sousa. Funding Agency: Gilead Sciences. Reference: PGG/054/2014. Amount: € 20 000,00. Total Amount: € 20 000,00.

2015/2018: HIV-2 impact on Lymph Nodes. Coordinator: Susana Mendes Fernandes. Funding Agency: Gilead Sciences. Reference: PGG/059/2014. Amount: € 20 000,00. Total Amount: € 20 000,00.

2014/2018: Mye-EUNITER: European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells. Coordinator: Ana Cristina Gomes Espada de Sousa. Funding Agency: European Commission. Reference: COST BM1404. Amount: Not Applicable. Total Amount: € 645 550,00.

2014/---: Euroflow International Consortium on Primary Immunodeficiency. Coordinator: Ana Cristina Gomes Espada de Sousa. Funding Agency: Not Applicable. Reference: Euroflow. Amount: Not Applicable. Total Amount: Not Applicable.

### Other Projects

2017/2019: ONEIDA: Plataforma Ómica para prevenção e controlo de infeções e de resistência aos antimicrobianos. Coordinator: Mário Nuno Ramos d'Almeida Ramirez. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: LISBOA-01-0145-FEDER-016417. Amount: € 696 698,00. Total Amount: € 2 459 635,55.

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

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

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

2015/2017: Targeting Germinal Centre Dysregulation in Allergy. Coordinator: Luís Ricardo da Silva Graça. Funding Agency: Fundação para a Ciência e a Tecnologia. Reference: HMSP-ICT/0034/2013. Amount: € 180 672,00. Total Amount: € 300 000,00.

### Publications in Peer Review Journals

Fernandes SM, Pires AR, Matoso P, Ferreira C, Nunes-Cabaço H, Correia L, Valadas E, Poças J, Pacheco P, Veiga-Fernandes H, Foxall RB, Sousa AE (2017). HIV-2 infection is associated with preserved GALT homeostasis and epithelial integrity despite ongoing mucosal viral replication. *Mucosal Immunol.*11:236-248. doi: 10.1038/mi.2017.44. (IF: 7.478, Citations:--).

Rocha C, Duarte J, Borrego P, Calado R, Marcelino JM, Tendeiro R, Valadas E, Sousa AE, Taveira N (2017). Potency of HIV-2-specific antibodies increase in direct association with loss of memory B cells. *AIDS* 31:2431-3. doi: 10.1097/QAD.000000000000166. (IF: 5.019, Citations:--).

Fonseca VR, Agua-Doce A, Maceiras AR, Pierson W, Ribeiro F, Romão VC, Pires AR, da Silva SL, Fonseca JE, Sousa AE, Linterman MA, Graca L (2017). Human blood Tfr cells are indicators of ongoing humoral activity not fully licensed with suppressive function. *Sci Immunol.* 2(14). pii: ean1487. doi: 10.1126/sciimmunol.aan1487. (IF:--, Citations:--).

Amaral AJ, Andrade J, Foxall RB, Matoso P, Matos AM, Soares RS, Rocha C, Ramos CG, Tendeiro R, Serra-Caetano A, Guerra-Assunção JA, Santa-Marta M, Gonçalves J, Gama-Carvalho M, Sousa AE (2017). miRNA profiling of human naive CD4 T cells links miR-34c-5p to cell activation and HIV replication. *EMBO J.* 36:346-360. (IF: 9.792, Citations: 1).

Albuquerque AS, Fernandes SM, Tendeiro RT, Cheynier R, Lucas M, Silva SL, Victorino RM, Sousa AE (2017). Major CD4 T-Cell Depletion and Immune Senescence in a Patient with Chronic Granulomatous Disease. *Front Immunol* 8:543. doi: 10.3389/fimmu.2017.00543. (IF: 6.429, Citations:--).

Pereira PD, Serra-Caetano A, Cabrita M, Bekman E, Braga J, Rino J, Santus R, Filipe PL, Sousa AE, Ferreira JA (2017). Quantification of cell cycle kinetics by EdU (5-ethynyl-2'-deoxyuridine)-coupled-fluorescence-intensity analysis. *Oncotarget* 8(25):40514-32. doi: 10.18632/oncotarget.17121. (IF: 5.168, Citations: 1).

Silva SL, Albuquerque AS, Matoso P, Charmeteau-de-Muylder B, Cheynier R, Ligeiro D, Abecasis M, Anjos R, Barata JT, Victorino RM, Sousa AE (2017) IL-7-Induced Proliferation of Human Naive CD4 T-Cells Relies on Continued Thymic Activity. *Front Immunol* 8:20. doi: 10.3389/fimmu.2017.00020. (IF: 6.429, Citations: 2).

Silva SL, Albuquerque A, Amaral AJ, Li QZ, Mota C, Cheynier R, Victorino RMM, Pereira-Santos MC, Sousa AE (2017). Autoimmunity and allergy control in adults submitted to complete thymectomy early in infancy. *PLoS One* 12(7):e0180385. doi: 10.1371/journal.pone.0180385. eCollection 2017. (IF: 2.806, Citations:--).

Almeida JP, Lopes A, Melo A, Pereira-Santos MC, Barbosa M (2017). Selective hypersensitivity to cefazolin and contribution of the basophil activation test. *Eur Ann Allergy Clin Immunol*;49(2):84-87. (IF:--, Citations:--).

Mota C, Carvalho AM, Fonseca V, Silva MT, Victorino RMM (2017). Exuberant liver adenomatosis presenting with iron deficiency anemia. *Clin Case Rep.*16;5(5):574-577. (IF:--, Citations:--).



Mota C, Ferreira C, Oliveira ME, Santos JM, Victorino RMM (2017). Multisystemic Sarcoidosis with Early Gastrointestinal Symptoms. *GE Port J Gastroenterol.* 24(3):137-141. (IF:--, Citations:--).

#### **Other Publications National**

Aguiar R, Lopes A, Ornelas C, Duarte Ferreira R, Caiado J, Mendes A, Pereira Barbosa – (2017) Terapêutica inalatória: técnicas de inalação e dispositivos inalatórios.” *M. Rev Port Imunoalergologia*; 25 (I):9-26. (IF:--, Citations:--).

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

Sousa AE. Controlo da infeção HIV: papel do sistema imunitário. Ciclo de Conferências de Doenças Infecciosas, Lisbon, Portugal, April 7, 2017.

Sousa AE. The immune system perspective: lessons from HIV-2 infection. 4º Congresso Nacional de Medicina Tropical, 1º Encontro Lusófono de SIDA, Tuberculose e Infecções Oportunistas, Lisbon, Portugal, April 20, 2017.

Sousa AE. Importância da investigação na formação pré-graduada MIM – Moderadora. 1º Congresso de Investigação em Medicina das Escolas Médicas Portuguesas, Coimbra, Portugal, April 28, 2017.

Sousa AE. Inflammation and Immune Activation in People Living with HIV. Fórum Janssen de Virologia, Cascais, Portugal, May 6, 2017.

Esteves I. Infections and Vaccines. What’s new? European Academy of Pediatrics Spring Meeting 2017, Vilamoura, Algarve, Portugal, May 13, 2017.

Silva SL. Imunodeficiências no Adulto não - VIH: O tratamento de hoje e o que vem aí. 23º Congresso Anual de Medicina Interna, Porto, Portugal, May 26, 2017.

Sousa AE. The unique HIV-2 equilibrium. Disease Mechanisms in Chronic and Emerging Infections. Max Planck Institute for Infection Biology (MPIIB), Berlin, Germany, June 8, 2017.

Silva SP. Novas perspectivas terapêuticas nas IDPs do Adulto. 38ª Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Figueira da Foz, Portugal, October 6, 2017.

### Communications in International Conferences

Tokunaga Y, Nunes-Cabaço H, Serra-Caetano A, Machado H, Godinho-Santos C, Sousa AE. Regulatory T cell, in the human thymus: A comprehensive approach combining genome-wide analysis and single-cell protein expression by computational flow cytometry. 8<sup>th</sup> International Conference on Bioinformatics Models, Methods and Algorithm, Porto, Portugal, January 2017. (Oral Presentation).

Tokunaga Y, Nunes-Cabaço H, Sousa AE. Differentiation of FOXP3+ regulatory T cells in the human thymus: unbiased approaches circumventing sequential-gating strategy. 7<sup>th</sup> International Workshop of Kyoto T Cell Conference, a Global Thymus Network Meeting KTCC2017, Kyoto, Japan, March 2017. (Poster Presentation).

Ramalho-dos-Santos A, Martins L, Barata J, Sousa AE, Nunes-Cabaço H. IL-4 induces coreceptor reversal in CD4-committed human thymocytes. 7<sup>th</sup> International Workshop of Kyoto T Cell Conference, a Global Thymus Network Meeting KTCC2017, Kyoto, Japan, March 2017. (Poster Presentation).

Ferreira R, Silva SP, Silva SL. A case of portal hypertension in Common Variable Immunodeficiency. European Society for Immunodeficiencies Summer School 2017, Calambrone, Pisa, Italy, May 2017. (Oral Presentation).

Guimarães C, Castro A, Martins M, Correia P, Ferrão A, Franco J, Ferreira T, Fraga S, Morais A, Dias A, Marques JG. Invasive bacterial disease in children with functional or anatomic asplenia. 35<sup>th</sup> Annual Meeting of the ESPID, Madrid, Spain, May 23-27, 2017. (Poster Presentation).

Baptista C, Ferreira F, Ataíde R, Prata F, Mouzinho A, Marques JG. Human Immunodeficiency Virus (HIV) Infection in Children on the 21st Century: a Portuguese Study. 35<sup>th</sup> Annual Meeting of the ESPID, Madrid, Spain, May 23-27, 2017. (Poster Presentation).

Ornelas J, Caiado J, Campos Melo A, Pereira Barbosa M, Pereira Santos MC. Contribution of Basophil Activation Test in Diagnosis of Hypersensitivity Reactions to Oxaliplatin. XXXVI Congress of the European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Oral Presentation).

Carvalho S, Marcelino J, Duarte F, Costa AC, Pereira Santos MC, Pereira Barbosa M. Patients allergic to fish: clinical and immunological characterization of sensitization profile in the last decade. XXXVI Congress of the European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Poster Presentation).

Marcelino J, Carvalho S, Costa AC, Duarte FC, Pereira Santos MC, Pedro E, Barbosa M. Recombinant fish parvalbumin Gad c 1 as a marker of fish Allergy. XXXVI Congress of the European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Oral Presentation).

Ornelas C, Duarte FC, Pereira Santos MC, Pereira Barbosa M. Multiple Food Allergy – Unexpected Culprits. XXXVI Congress of the European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Poster Presentation).

Carvalho S, Marcelino J, Duarte F, Costa AC, Pereira Santos MC, Pereira Barbosa M. Contribution of Recombinant Parvalbumin Gad c 1 in diagnosis and prognosis of fish allergy. XXXVI Congress of the European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Poster Presentation).

Ferreira R, Ornelas C, Joana C, Sínola A, Ferreira MC, Barbosa MB. Sensitization to the pollen of different olive tree cultivars in a group of Portuguese patients. XXXVI Congress of European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017 (Poster Presentation).

Cosme J, Fernandes M, Ornelas C, Ferreira RD, Spínola A, Ferreira MB, Barbosa MB. Can plane tree be considered a marker of polysensitization to pollens? XXXVI Congress of European Academy of Allergy and Clinical Immunology, Helsinki, Finland, June 2017. (Poster Presentation).

Fonseca M, Serra-Caetano A, Barbosa RR, Hammarstrom L, Cascalho M, Silva SL, Sousa AE. Novel TACI variant in Common Variable Immunodeficiency. 8<sup>th</sup> Meeting of the European Society for Immunodeficiencies (ESID 2017), Edinburgh, Scotland, September 2017. (Poster Presentation).

Bessa F, Rodrigues M, Leite L, Silva MT, Mota C, Victorino RMM. Renal cell carcinoma as malabsorption syndrome due to intestinal amyloidosis. European Congress of Internal Medicine, Milan, Italy, September 2017. (Poster Presentation).

Godinho-Santos A, Tavares B, Ferreira T, Antão A, Serra-Caetano A, Matoso P, Rocha C, Nunes-Cabaço H, Foxall RB, Sousa AE. TFH targeting in HIV/AIDS: insights from the attenuated HIV-2 infection. 19<sup>th</sup> Germinal Centre Conference, Venice, Italy, September 2017. (Poster Presentation).

Oliveira I, Fraga AB, Prata F, Tavares M, Virtuoso MJ, Campos T, Mouzinho A, Stone R, Marques JG. Prevalence of Renal Abnormalities in HIV-infected Children and Adolescents - A Multicentric Study. 10<sup>th</sup> World Congress of the World Society for Pediatric Infectious Diseases, Shenzhen, China, December 2 -5, 2017. (Oral Presentation).

Viegas IF, Fraga B, Prata F, Pinto S, Marques JG. Secondary Hemophagocytic Lymphohistiocytosis Syndrome in an African Child. 10<sup>th</sup> World Congress of the World Society for Pediatric Infectious Diseases, Shenzhen, China, December 2-5, 2017. (Poster Presentation).

#### **Communications in National Conferences**

Cunha M, Palha F, Esteves I, Ramos FO, Marques JG. Síndrome PFAPA: casuística de 10 anos. XXIII Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 2017. (Oral Presentation).

Cunha M, Palha F, Esteves I, Ramos FO, Marques JG. Síndrome PFAPA: casuística de 10 anos. XXIII Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 2017. (Oral Presentation).

Pinto PL, Esteves I, Marques JG. Eczema, trombocitopénia e imunodeficiência. XXIII Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 2017. (Poster Presentation).

Miranda M, Martins A, Carvalho S, Serra-Caetano A, Esteves I, Marques JG. Vacinas vivas em crianças com Síndrome de DiGeorge /Deleção do Cromossoma 22q11.2 – Serão seguras?. XV Jornadas Nacionais de Infeciologia Pediátrica, Lisbon, Portugal, May 2017. (Oral Presentation).

Paulino M, Almorós C, Pinto S, Marques JG. Gastreenterite grave por *Cystoisospora belli* em adolescente com infeção por VIH. XV Jornadas Nacionais de Infeciologia Pediátrica, Lisbon, Portugal, May 2017. (Poster Presentation).

Serra-Caetano A, Silva SL, Albuquerque A, Marques JG, Cheynier R, Ligeiro D, Pignata C, Markert ML, Sousa AE. Long-term persistence of aberrant double-negative? T-cells in a patient with FOXP1-null phenotype despite successful thymic transplantation. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Fernandes SM, Pires AR, Matoso P, Ferreira C, Correia L, Valadas E, Poças P, Pacheco P, Sousa AE, Foxall RB. HIV-1 and HIV-2 differentially impact gut epithelial tight junction integrity. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Oral Presentation).

Antão A, Foxall RB, Matoso P, Pires AR, Serra-Caetano A, Sousa AE, Nunes-Cabaço H, Rocha C. HIV-2 infection of lymphoid tissues. RedeSAÚDE – 4<sup>th</sup> Annual Conference, Innovation Week, Lisbon, Portugal, May 4, 2017. (Poster Presentation).

Leite IM, Rodrigues M, Silva MT, Mota C, Victorino RMM. Clozapine-induced pneumonitis- a clinical case report. 23<sup>rd</sup> National Congress of Internal Medicine, Porto, Portugal, May 2017. (Poster Presentation).

Leite IM, Bessa F, Mota CM, Victorino RMM. Heyde's Syndrome: the importance of early recognition. 23<sup>rd</sup> National Congress of Internal Medicine, Porto, Portugal, May 2017. (Poster Presentation).

Marcelino J, Carvalho S, Costa A.C., Duarte FC, Pereira Santos MC, Pereira Barbosa MA. Contributo da parvalbumina recombinante rGad c 1 como marcador de aquisição de tolerância na alergia ao peixe. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Oral Presentation).

Carvalho S, Marcelino J, Duarte FC, Costa AC, Pereira Santos MC, Pereira Barbosa MA. Alergia ao peixe: contribuição da parvalbumina rGad c 1 no diagnóstico e prognóstico. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Oral Presentation).

Ferreira R, Ornelas C, Pereira da Silva S, Morgado R, Pereira D, Escaleira D, Moreira S, Valença J, Pedro E, Branco Ferreira M, Pereira Santos MC, Pereira Barbosa M. Rinite alérgica local- Contributo dos testes “in vivo” e “in vitro” para o diagnóstico. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Oral Presentation).

Paulino M, Marcelino J, Costa AC, Duarte F, Cosme J, Ferreira R, Neto M, Spinola Santos A, Pereira Barbosa M, Pereira Santos MC. Sensibilização a componentes moleculares de aeroalergénios e risco de asma. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Poster Presentation).

Cosme J, Spinola Santos A, Branco Ferreira M, Lopes da Silva S, Pereira Santos MC, Pereira Barbosa M. O contributo dos alergénios moleculares na escolha de imunoterapia a gramíneas e oliveira. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Oral Presentation).

Ferreira R, Carvalho S, Duarte FC, Pereira Santos MC, Pereira Barbosa M. Um caso simples de síndrome pólen-alimentos- importância do diagnóstico molecular. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017. (Poster Presentation).

Cosme J, Spinola Santos A, Bartolomé B, Branco Ferreira M, Pereira Santos MC, Pereira Barbosa M. Ovas de salmão: alergénio emergente do oriente para o ocidente. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Outubro 2017. (Oral Presentation).

Vilardouro AS, Ferreira J, Filipe P, Marques JG. Micetoma e osteomielite da calote craniana por *Nocardia nova*. 18º Congresso Nacional de Pediatria. Porto, Portugal, November 25-27, 2017. (Poster Presentation).

Marques MIN, Vilardouro A, Pinto S, Marques JG. Toxoplasmose cerebral como manifestação clínica de infeção VIH na criança. 18º Congresso Nacional de Pediatria, Porto, Portugal, November 2017. (Poster Presentation).

### **Organisation of Conferences**

Marques JG. XXIII Jornadas de Pediatria, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 8-10, 2017.

Silva SL. XLIII Anual Meeting Sociedade Portuguesa de Imunologia, Porto, Portugal, June 14-16 2017.

Lopes AI. Annual Meeting of the Latin-American Society of Pediatric Gastroenterology, Hepatology and Nutrition (LASPGHAN), Porto, Portugal, June de 2017.

### Internationalisation

- Sousa AE. Part of the EuroFlow International Consortium on Primary Immunodeficiency. <http://euroflow.org/>.
- Sousa AE. National Coordinator and Member of the Management Committee of the COST Action BM1404 “European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells (Mye-EUNITER)”. 2014/2017. Agency: Comissão Europeia. Reference: COST BM1404. <http://www.mye-euniter.eu/>.
- Sousa AE. Member of ENLIGHT-TEN - European Network Linking Informatics and Genomics of Helper T cells comprising TEN beneficiaries. 2015/2019 – ETN funded by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No.: 675395. <http://www.enlight-ten.eu/>.
- Sousa AE. Member of the EFIS-Immunology Letters (IL) Study Group titled “T\_CELL\_CONNECT\_EUROPE”, European Federation of Immunology Societies (EFIS). <https://www.efis.org/efis-support/efis-il-study-groups/index.html>.

### Prizes, Honours and Awards

Pereira Santos MC, Santos AS, Postigo I, Martinez J. SPAIC-ROXALL 2017 Award. Quantificação de alérgenos major de *Dermatophagoides pteronyssinus* em extractos para imunoterapia com alérgenos por via sublingual.

Fernandes SM. ESICM NEXT Fellowship Award in Management of Infection, Utrecht, the Netherlands.

Ferreira R, Ornelas C, Pereira da Silva S, Morgado R, Pereira D, Escaleira D, Moreira S, Valença J, Pedro E, Branco Ferreira M, Pereira Santos MC, Pereira Barbosa M. Prémio SPAIC. Rinite alérgica local- Contributo dos testes “in vivo” e “in vitro” para o diagnóstico. XXXVIII Reunião Anual da SPAIC, Figueira da Foz, Portugal, October 2017.

Vilardouro AS, Ferreira J, Filipe P, Marques JG. Infeciologia-Pfizer Award. Micetoma e osteomielite da calote craniana por *Nocardia nova*. 18º Congresso Nacional de Pediatria. Porto, Portugal. November 25-27, 2017.

### **Industry Contract Research**

Multicentric Clinical trial entitled: “A phase 3 Randomized double blinded Study Comparing TR-701 FA and Linezolid in Ventilated Gram-positive Nosocomial Pneumonia”. Funded by Cubic. PI at Centro Hospitalar Lisboa Norte: Susana M. Fernandes.

### **Government/Organisation Contract Research**

Sousa AE. Member of the National Ethics Committee for Clinical Research (CEIC). Member of the Executive Committee of the National Ethics Committee for Clinical Research (CEIC).

Sousa AE. Member of the “Comissão de Avaliação de Tecnologias de Saúde (CATS)”. INFARMED — Autoridade Nacional do Medicamento e Produtos de Saúde, I. P. (INFARMED, I. P.).

Sousa AE. Coordinator of the GAPIC - Department for promotion of scientific research for medical students and MDs. Faculty of Medicine, University of Lisbon. Fernandes SM. Member of the GAPIC.

Sousa AE. Member of the Board of the FCT PhD program LisbonBioMed, IMM/FM/UL.

Sousa AE. Member of the Executive Board of the FCT PhD program “Biology at the Host Microbe Interface” (INTERFACE for short), ITQB/IGC/IMM. Victorino RMM and Sousa AE, Members of the Scientific Board of the PhD Program of the CAML.

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

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

Victorino RMM, Sousa AE. Members of the Scientific Council, Faculty of Medicine, University of Lisbon.

Lopes AI. Member of the Pedagogic Council, Faculty of Medicine, University of Lisbon.

Lopes AI. Member of the Working Group for Clinical Curriculum Review, Faculty of Medicine, University of Lisbon.

Victorino RMM, Member of the Directive Board of the Sociedade de Ciências Médicas de Lisboa.

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



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

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

Marques JG. Member of the Comissão Nacional de Verificação da Eliminação do Sarampo e da Rubéola.

Marques JG. Representative of the Direção Geral de Saúde (DGS) in the procedure for the acquisition of the intravenous formulation of zanamivir by the hospitals of the health system.

Marques JG. Member of the Centro Hospitalar Lisboa Norte Local Coordination Group of the Program for the Prevention and Control of Infections and Resistance to Antimicrobials.

Marques JG. Coordination of the Haemophilus influenzae Invasive Disease Study Group in the Child.

Marques JG Collaboration in the elaboration of the Guidance of the Direção Geral da Saúde nº 018/2017 of 09/26/2017 "Vaccination against influenza. 2017/2018".

Marques JG. Co-author of the "National Vaccination Program 2017".

Lopes AI. Member of the Ethical Committee of Hospital Santa Maria and CAML.

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

### **Advanced Teaching**

Sousa AE, Pereira-Santos MC, Victorino RMM, Silva SL, Fernandes SM, Serra-Caetano A. Clinical Immunology teaching in the core curriculum for Medical Students. Faculty of Medicine, University of Lisbon.

Sousa AE, Pereira-Santos MC, Victorino RMM, Silva SL, Fernandes SM, Mota C, Serra-Caetano A, A Godinho-Santos. Teaching of the optional discipline of Clinical Immunology. Faculty of Medicine, University of Lisbon.

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

- Joana Cosme from February to May 2017;
- João Marcelino from May to July 2017;
- Tatiana Lourenço from October to January 2018.

Sousa AB, Sousa AE: Collaboration in the teaching of Immunology in the core curriculum for Medical Students. Faculty of Medicine, University of Lisbon.

Lopes AI. Regency and Teaching of the Discipline of Pediatrics (Module VI II), core curriculum. Faculty of Medicine, University of Lisbon.

Lopes AI. Regency of the Elective Discipline Clinical Procedures in Pediatrics. Faculty of Medicine, University of Lisbon.

Lopes AI. Coordination of the Pediatric Module of the Master Program in Clinical Nutrition, Faculty of Medicine, University of Lisbon.

Fernandes SM. Teaching of the Discipline of Intensive Care Medicine. Faculty of Medicine, University of Lisbon.

Marques JG. Teaching of the Discipline of Pediatrics (Module VI II), core curriculum. Faculty of Medicine, University of Lisbon.

Marques JG. Coordination of the Seminar on Vaccination of the Discipline of Pediatrics (Module VI II, core curriculum). Faculty of Medicine, University of Lisbon.

Esteves I. Teaching of the Discipline of Pediatrics (Module VI I), core curriculum. Faculty of Medicine, University of Lisbon.

Marques JG. Vacinas – mitos e preconceitos. XXIII Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, Fevereiro 8-10, 2017.

Marques JG. Infecção VIH - Desafios em populações particulares – Adolescente. Sessão interativa, Virology meeting Point' 2017, Óbidos, Portugal, March 10-11, 2017.

Marques JG. O novo PNV. 9<sup>as</sup> Jornadas de Pediatria do Hospital da Luz, Lisbon, Portugal, June 2, 2017.

Marques JG. Mitos e preconceitos na vacinação. 9<sup>as</sup> Jornadas de Pediatria do Hospital da Luz, Lisbon, Portugal, June 2, 2017.

Marques JG. O papel dos Inibidores da Integrase. Reunião Anual do Grupo de Trabalho sobre Infecção VIH na Criança, Porto, Portugal, September 29, 2017.

Marques JG. Uso Racional de Antibióticos em Pediatria. Sessão Clínica do Centro Materno Infantil do Norte, Porto, Portugal, October 19, 2017.

Marques JG. Vacinas Extra PNV. VII Colóquio do Serviço de Pediatria, Centro Hospitalar Universitário do Algarve, Faro, Portugal, November 24, 2017.

Marques JG. 30 anos de infeção por VIH. 12<sup>o</sup> Curso de Infeciologia Pediátrica, Coimbra, Portugal, January 26-27, 2017.

Marques JG. Visita guiada ao PNV 2017. Curso “Vacinas” incluído nas XXIII Jornadas de Pediatria, Departamento de Pediatria do Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 8-10, 2017.

Marques JG. Amigdalite e Otite Média Aguda. Curso Pediatria na Urgência. Centro de Formação do Centro Hospitalar Lisboa Norte, Lisbon, Portugal, March 17, 2017.

Marques JG. Exantemas Infecciosos. 12<sup>o</sup> Curso de Pós-graduação em Doenças Infecciosas. Algés, Portugal, November 6, 2017.

Marques JG. Hesitação em Vacinar. 1<sup>o</sup> Curso de Vacinas do Hospital Pediátrico. Coimbra, Portugal, November 15, 2017.

Marques JG. Antibioterapia em Pediatria. 9<sup>o</sup> Curso de Antibioterapia. Hospital da Luz, Lisbon, Portugal, November 27, 2017.

Esteves I. Vacina da Varicela. Curso satélite Vacinas - XXIII Jornadas de Pediatria do Hospital Santa Maria, Faculty of Medicine, University of Lisbon, Portugal, February 8, 2017.

Esteves I. Vacinas em circunstâncias especiais. Curso satélite Vacinas - XXIII Jornadas de Pediatria do Hospital Santa Maria, Faculty of Medicine, University of Lisbon, Portugal, February 8, 2017.

Esteves I. Quando investigar Imunodeficiência? XXIII Jornadas de Pediatria do Hospital Santa Maria, Faculty of Medicine, University of Lisbon, Portugal, February 10, 2017.

Esteves I. Hot Topics - Hepatite A. XV Jornadas Nacionais de Infecciologia Pediátrica, Hotel Tivoli Oriente, Lisbon, Portugal, May 5, 2017.

#### **Science and Society**

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

#### **MSc Thesis Completed**

Bárbara Estefânia Tavares, 24/07/2017, “HIV-2 ability to infect human follicular T helper cells”, Masters in Biologia Molecular e Celular, University of Coimbra. Supervisor: Ana E Sousa.

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## Veiga-Fernandes, Henrique

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### Head of Laboratory

José Henrique Veiga Fernandes, PhD (Left May)

### Research Team

Ana Filipa Ribeiro Cardoso	Master	PhD Student (Left May)
Bethania García Cassani	Master	PhD Student (Left May)
Bruno Miguel Belchior Raposo	Master	Technician (Left May)
Chesne Julie Michelle Evelyne	PhD	Post-Doctoral Investigator (Left May)
Cristina Sofia Godinho da Silva	No degree	Post-Doctoral Investigator (Left May)
Hélder Manuel Piedade Ribeiro	Master	Technician (Left May)
Manuela Cristina Fernandes Ferreira	PhD	Post-Doctoral Investigator (Left May)
Rita Gomes Domingues	Master	PhD Student (Left May)
Sales Ibiza	PhD	Post-Doctoral Investigator (Left May)
Silvia Moura Arroz Nobre Madeira	Master	PhD Student (Left May)
Telmo Filipe Araújo Catarino	Master	PhD Student (Left May)
Valdir Avelino Rocha Semedo	Master	PhD Student (Left May)
Vânia Rita de Faria Cardoso	Master	PhD Student (Left May)

### Laboratory Keywords / Research Areas

Lymphoid organogenesis, Haematopoiesis, Innate lymphoid cells, Lymphocyte function.

### Selected Publications

Cardoso V, Chesne J, Ribeiro H, Garcia-Cassani B, Carvalho T, Bouchery T, Shah K, Barbosa-Morais NL, Harris N, Veiga-Fernandes H (2017). Neuronal regulation of type 2 innate lymphoid cells via neuromedin U. *Nature* 549, 277-+. (IF: 40.137, Citations: 7).

Veiga-Fernandes H, Pachnis V (2017). Neuroimmune regulation during intestinal development and homeostasis. *Nature Immunology* 18, 116-122. (IF: 21.506, Citations: 9).

### Ongoing Research Projects

2015/2020: GliaInnateSensing: Glia-derived factors in innate lymphoid cell sensing and intestinal defence. Coordinator: José Henrique Veiga Fernandes. Agency: European Commission. Reference: ERC CoG 647274. Amount: € 2 270 000,00. Total Amount: € 2 270 000,00.

2014/2017: Regulation of Innate Lymphoid Cell function and intestinal defense by neuroregulatory factors. Coordinator: José Henrique Veiga Fernandes. Funding Agency: Cronh's & Colitis. Reference: CCFA HVFernandes. Amount: € 280 258,06. Total Amount: € 254 277,00.

#### **Other Projects**

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

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## Veldhoen, Marc

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### Major Interests / Objectives

Mucosal Immunology; the maintenance, activation and differentiation of T cells at epithelial sites.

We are interested in how innate-like T cells are maintained and activated at the intestinal barrier. We try to understand the cellular and molecular cues, which can result in epithelial T cell activation. Furthermore, we assess how the biology of these cells effect tissue homeostasis and immunity.

### Head of Laboratory

Marc Veldhoen, PhD

### Research Team

Birte Blankenhaus	PhD	Post-Doctoral Investigator (Started April)
Cristina da Conceição Varandas Ferreira	PhD	Investigator
Daniel Villalba Lopez	Master	Investigator (Started November)
Marta Sofia Serra Baptista	Master	Technician
Spela Konjar	PhD	Post-Doctoral Investigator (Started February)

### Laboratory Keywords / Research Areas

Immune regulation, Mucosal Immunity, Th17 cells, T cell differentiation, Intra-epithelial lymphocytes, Auto-immunity.

### Major Scientific Achievements

In 2017, we successfully established our lab and recruited two post-doctoral scientists and one PhD-student.

We finalised a Th17 cell focussed project, which was accepted in Cell Reports (Brucklacher-Waldert, Ferreira et al, 2017). We contributed to the scientific literature with highlights (Immunity, Translational Cancer Research) and a review on Th17 cells (Nature Immunology) and a review on intestinal T cells leading up to our current work and next publications (Frontiers in Immunology).

We completed experiments and contributed to the resubmission of a project accepted in Nature Communications (Fellows et al., 2018). The latter identifies a new histone mark in intestinal epithelial cells, which is modulated by diet and the microbiota.

We contributed to a large international project to highlight the use and reporting of flow cytometry data and the most current protocols, background information and troubleshooting, organised by European Federation of Immunological Societies (EFIS).

### **Selected Publications**

Brucklacher-Waldert V, Ferreira C, Stebegg M, Fesneau O, Innocentin S, Marie JC, Veldhoen M (2017). Cellular Stress in the Context of an Inflammatory Environment Supports TGF-beta-Independent T Helper-17 Differentiation. *Cell Reports* 19, 2357-2370. (IF: 8.282, Citations: 3).

Brucklacher-Waldert V, Ferreira C, Innocentin S, Kamdar S, Withers DR, Kullberg MC, Veldhoen M (2016). Tbet or Continued RORyt Expression Is Not Required for Th17-Associated Immunopathology. *J Immunology* 196(12), 4893-904. (IF: 4.92, Citations: 8).

Withers DR, Hepworth MR, Wang X, Mackley EC, Halford EE, Dutton EE, Marriott CL, Brucklacher-Waldert V, Veldhoen M, Kelsen J, Baldassano RN, Sonnenberg GF (2016) Transient inhibition of RORyt therapeutically limits intestinal inflammation by reducing TH17 cells and preserving group 3 innate lymphoid cells. *Nature Medicine* 22(3), 319-23. (IF: 30.357, Citations: 50).

Zaid A, Mackay LK, Rahimpour A, Braun A, Veldhoen M, Carbone FR, Manton JH, Heath WR, Mueller SN (2014). Persistence of skin-resident memory T cells within an epidermal niche. *PNAS* 111(14), 5307-12. (IF: 9.423, Citations: 83).

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(3), 629-40. (IF: 28.710, Citations: 374).



### Ongoing Research Projects

2015/2020: EXCELLtoINNOV: Leverage research EXCELLENce and INNOVation potencial of Instituto de Medicina Molecular (iMM) through translational biomedical research in Immunity and Infection. Coordinator: Marc Veldhoen. Funding Agency: European Commission. Reference: ERA Chair 667824. Amount: € 2 499 465,00. Total Amount: € 2 499 465,00.

### Other Projects

2016/2018: TwinToInfect: Unleash iMM's research excellence in immunity and infection through twinning to infect Lisbon and Portugal with its increase in competitiveness and innovation. Coordinator: Maria Manuel Mota. Funding Agency: European Commission. Reference: TWINNING 692022. Amount: € 893 500,00. Total Amount: € 999 996,25.

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

### Publications in Peer Review Journals

Brucklacher-Waldert V, Ferreira C, Stebegg M, Fesneau O, Innocentin S, Marie JC, Veldhoen M (2017). Cellular Stress in the Context of an Inflammatory Environment Supports TGF-beta-Independent T Helper-17 Differentiation. *Cell Reports* 19, 2357-2370. (IF: 8.282, Citations: 3).

Konjar S, Ferreira C, Blankenhaus B, Veldhoen M (2017). Intestinal barrier interactions with specialised CD8 T cells. *Frontiers in Immunology* 8, 1281. (IF: 5.695, Citations:--).

Veldhoen M (2017). Interleukin 17 is a chief orchestrator of immunity. *Nature Immunology* 18, 612-621. (IF: 21.506, Citations: 24).

Stubbs TM, Bonder MJ, Stark AK, Krueger F, Team BIAC, von Meyenn F, Stegle O, Reik W (2017). Multi-tissue DNA methylation age predictor in mouse. *Genome Biology* 18, 68. (IF: 11.908, Citations: 23).

Goverse G, Molenaar R, Macia L, Tan J, Erkelens MN, Konijn T, Knippenberg M, Cook EC, Hanekamp D, Veldhoen M, et al. (2017). Diet-Derived Short Chain Fatty Acids Stimulate Intestinal Epithelial Cells To Induce Mucosal Tolerogenic Dendritic Cells. *Journal of Immunology* 198, 2172-2181. (IF: 4.92, Citations 13).

### **Other Publications International**

Veldhoen M (2017). Guidelines for the use of flow cytometry. *Immunity, Inflammation and disease*. 5, 384-385.

Cossarizza A, Veldhoen M, et al. (2017). Guidelines for the use of flow cytometry and cell sorting in immunological studies. *European Journal of Immunology* 47,1584-1797. (IF: 5.179, Citations: 7).

Veldhoen M (2017). Th17 Cells Require You to Chew before You Swallow. *Immunity* 46, 8-10. (IF: 22.845, Citations: 1).

### **Invited Lectures and Seminars**

Epithelial barriers: Maintaining and activating resident lymphocytes. Veterinary School, University of Cambridge, Cambridge, England, February 2017.

### **Communications in International Conferences**

Veldhoen M. TGF $\beta$  and Th17 cell differentiation. Keystone Meeting: TGF- $\beta$  in Immunity, Inflammation and Cancer, Taos, New Mexico, USA, January 2017.

Presence at "Alm retreat" Meeting of Selected European Immunologist to discuss recent data, future directions and setup European networks for future funding, Austria, January 2017.

Veldhoen M. Epithelial barriers: maintaining and directing T cell responses. 1<sup>st</sup> International Symposium on Immune Responses in Cancer and Infection, Lyon, France, February 2017.

Veldhoen M. Influence of nutrient-derived metabolites on lymphocyte immunity. XLII Congress of the Brazilian Society of Immunology (Mucosal Immuno 2017), Salvador, Bahia, Brazil, October 2017.

### **Communications in National Conference**

Veldhoen M. Role of Arylhydrocarbon Receptor in immunity. GSK Discovery Partnerships with Academia, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 2017.

Veldhoen M. Epithelial T cell responses. Takeda Pharmaceuticals in Lisbon Meeting, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 2017.

Veldhoen M. Epithelial T cell responses.H2020 ITN “GlycoVax”, Lisbon, Portugal, March 2017.

Veldhoen M. Epithelial barriers: Maintaining and activating resident lymphocytes. IMM Retreat, Instituto de Medicina Molecular João Lobo Antunes, Évora, Portugal, May 2017.

Veldhoen M. Session Chair. Mucosal Immunology. Portuguese Society of Immunology, i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal, June 2017.

### **Internationalisation**

We are part of several international collaborations, including France, UK, Germany and the US.

We participated in the combined Brazilian Society for Immunology and the Mucosal Immunology Society. Other meetings can be found under "conferences".

We have started a collaboration with a group in Argentina, based on mutual interest in intestinal immunity and T cell activation.

We have invited speakers as part of the ERA Chair project and the TWINNtoINFECT Twinning programme. We are part of an H2020 ITN, with one PhD student in the lab, annual meeting and summer school. We are part of a European T cell focus group, funded by EMBO, which organises an annual meeting to exchange ideas and this year we received additional funding from EFIS.

### **Advanced Teaching**

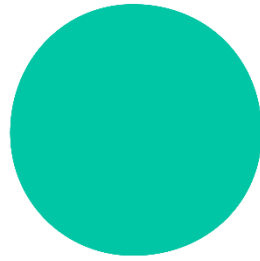
Veldhoen M. Co-coordinator. Introductory seminar Mucosal Immunology. LisbonBioMed PhD Programme, Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, February 2017.

Veldhoen M. Mucosal Immunology. Masters in Microbiologia clinica e doenças infecciosas emergentes, Biomedical Sciences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, October 2017.

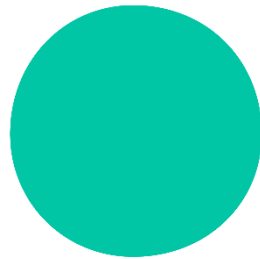
Veldhoen M. MHC, TCR, PPRs and PAMPs. Immunology. Master Course in Biomedical Sciences Instituto de Higiene e Medicina Tropical, Nova University of Lisbon (IHMT-UNL), Lisbon, Portugal, November 2017.

Ferreira C. Thymic selection, T cell differentiation. Immunology. Master Course in Biomedical Sciences Instituto de Higiene e Medicina Tropical, Nova University of Lisbon (IHMT-UNL), Lisbon, Portugal, November 2017.

Veldhoen M. Th subset diversity. Immunologie Approfondie. Pasteur Institute, Paris, France, Masters degree of three Parisian universities; University of Paris Descartes, University of Paris Pierre et Marie Curie, and University of Paris Diderot.



# Technical Facilities



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## Biobank

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### Major Interests / Objectives

Biobanco-iMM is a structure created by the Instituto de Medicina Molecular João Lobo Antunes (iMM), which receives and stores a wide collection of biological samples donated voluntarily and its correspondent clinical information in order to foster biomedical research. Biobanco-iMM aims to achieve sustainable growth, focused on improving quality, not only in samples but also in data management. Services include not only storage and processing of human samples but also Nucleic Acids Extraction, Isolation of Peripheral Blood Mononuclear Cells, Data Management and study design. In 2017, we implement a new service the Primary Cell Culture of Human Fibroblasts.

### Head of Facility

Joaquim Miguel Polido Pereira, Investigator, CHLN, MD  
 Sérgio Jerónimo Rodrigues Dias, PhD, Associate Professor

### Team

Ângela Maria Cerqueira Coelho Afonso	Master	Technician
Brígida Alexandra Amaral Mendes Riso	Master	PhD Student, Superior de Ciências do Trabalho e da Empresa
Fabiana Cândida da Rocha Rodrigues	Graduate	Technician
Susana Raquel Salsinha Ferreira	Master	Technician

### Keywords

Biobanks, Human samples, Clinical information, Biomedical research.

### Major Scientific Achievements

In 2017, we start 4 new collections. In total, there are 56 active collections in Biobanco-iMM covering all the main clinical areas. During this year, we received 28 new samples request that represents 2500 samples used for research. Samples were used for different proposes and the collection that received more requests was the “Healthy Donors” collection. During the past year, 8 new scientific papers where publish with the collaboration of the Biobanco-iMM. Biobanco-iMM is certified with ISO 9001 Quality Management System by TÜV Rheinland Portugal, as part of iMM Certification.

### Selected Publications

Rosa N, Marques J, Esteves E, Fernandes M, Mendes VM, Afonso Â, Dias S, Pereira JP, Manadas B, Correia MJ, Barros M (2016). Protein Quality Assessment on Saliva Samples for Biobanking Purposes. *Biopreservation and Biobanking*. (IF: 1.698, Citations:--).

Afonso A, Polido-Pereira J, Dias S (2014). Biobank Profile: Biobanco-iMM, Lisbon Academic Medical Centre. *Biopreservation and Biobanking* 12, 433-434. (IF: 1.698, Citations:--).

### Publications in Peer Review Journals

Perpétuo I, Caetano-Lopes J, Rodrigues A, Campanilho-Marques R, Ponte C, Canhão H, Ainola M and Fonseca JE (2017). Methotrexate and low-dose prednisolone downregulate osteoclast function by decreasing receptor activator of nuclear factor- $\kappa$ B expression in monocytes from patients with early rheumatoid arthritis. *RMD Open* 13. (IF:--, Citations:3).

Moura R, Quaresma C, Vieira A, Gonçalves M, Polido-Pereira J, Romão V, Martins N, Canhão H, Fonseca JE (2017). B-cell phenotype and IgD-CD27- memory B cells are affected by TNF-inhibitors and tocilizumab treatment in rheumatoid arthritis. *PLoS One*. (IF:2.806, Citations:1).

Guedes LC, Chan RB, Gomes MA, Conceição VA, Machado RB, Soares T, Xu Y, Gaspar P, Carriço JA, Alcalay RN, Ferreira JJ, Outeiro TF, Miltenberger-Miltenyi G (2017). Serum lipid alterations in GBA-associated Parkinson's disease. *Parkinsonism Relat Disord* 44, 58-65. (IF:4.484, Citations:--).

Perpétuo I, Caetano-Lopes J, Rodrigues AM, Campanilho-Marques R, Ponte C, Canhão H, Ainola M and Fonseca JE (2017). Effect of Tumor Necrosis Factor Inhibitor Therapy on Osteoclast Precursors in Rheumatoid Arthritis. *BioMed Research International* 2017. (IF:2.476, Citations:--).

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE (2017). Ankylosing Spondylitis Patients Have Impaired Osteoclast Gene Expression in Circulating Osteoclast Precursors. *Front Med* 4. (IF:1.634, Citations:--).

Barreto G, Sandelin J, Salem A, Nordström D, Waris E (2017). Toll-like receptors and their soluble forms differ in the knee and thumb basal osteoarthritic joints. *Acta Orthop* 88, 326–333. (IF:3.446, Citations:--).

Somovilla VJ, Bermejo IA, Albuquerque IS, Martínez-Sáez N, Castro-López J, García-Martín F, Compañón I, Hinou H, Nishimura SI, Jiménez-Barbero J, Asensio JL, Avenzoza A, Busto JH, Hurtado-Guerrero R, Peregrina JM, Bernardes GJL, Corzana F (2017). The Use of Fluoroproline in MUC1 Antigen Enables Efficient Detection of Antibodies in Patients with Prostate Cancer. *J. Am. Chem. Soc.* 139, 18255-18261. (IF: 13.858, Citations:--).

Gonçalves MJ, Mourão AF, Martinho A, Simões O, Melo-Gomes J, Salgado M, Estanqueiro P, Ribeiro C, Brito I, Fonseca JE, Canhão H (2017). Genetic Screening of Mutations Associated with Fabry Disease in a Nationwide Cohort of Juvenile Idiopathic Arthritis Patients. *Front Med* 4:12. (IF:1.634, Citations:--).

### **Invited Lectures and Seminars**

Afonso A. Apresentação Curso Investigação Centro Hospitalar Lisboa Norte - Biobanco(s), Lisbon, Portugal, May 29, 2017.

Afonso A. Tumor Banks – what are they and what for Oncobiology Seminar, Nova University of Lisbon, Lisbon, Portugal, May 25, 2017.

Afonso A. 1.º Curso Breve de Pós-Graduação em Biobancos - Biobancos de amostras biológicas para fins de investigação, Coimbra, Portugal, May 27, 2017.

### **Communications in National Conferences**

Ferreira S. Global Biobank Week - Biobanco-iMM quality assurance – Factors Involved, Stockholm, Sweden, September 2017. (Poster Presentation).

Polido-Pereira J. Réseau Européen de recherche translationnelle et innovation en oncologie- Biobanking and Cancer, Montpellier, France, December 2017. (Oral Presentation).



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## Bioimaging

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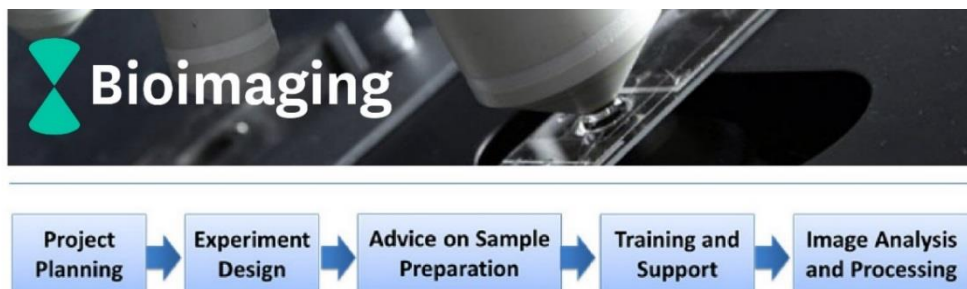
### Major Interests / Objectives

The Bioimaging Facility acts as a support structure to carry out and nurture research done with Light Microscopy inside the institute. Besides managing resources, the Facility provides iMM scientists and visitors with excellence in scientific know-how and expertise in using light microscopy methods for their research. We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques and foster interactions and collaborations between microscopy users at the iMM.

### Head of Facility

José Miguel Rino Henriques, PhD

### Graphical Abstract



### Team

Ana Margarida Santos do Nascimento	Master	Technician
António Francisco Pinção Loução Homem Temudo	Master	Technician

### Keywords / Research Areas

Fluorescence microscopy, Laser scanning confocal microscopy, Image processing and analysis, Quantification of protein dynamics and interactions, Training in microscopy.

## Major Scientific Achievements

In 2017, two new microscopy systems were added to the Bioimaging Facility: a spinning disk confocal microscope (Zeiss Cell Observer SD) and a multi-photon microscope (Leica SP8 MP). Scientific collaboration with iMM research labs resulted in one publication in which José Rino is first author (Rino J et al, *Methods Mol Biol* - PMID: 28324612) and three publications where José Rino is co-author (Ministro A et al, *Cardiovasc Res* - PMID: 28444128; Carvalho T et al, *J Cell Sci* - PMID: 28302904 and Ferreira DG et al, *Cereb Cortex* - PMID: 26534909). In 2017 the Bioimaging Facility services were used by 186 users from 40 different research labs, five of which from outside the iMM. The Bioimaging Facility is a Zeiss labs@location Partner, integrating a community of leading research facilities with expertise in specific applications of technologies that provide in depth knowledge and scientific support to Zeiss customers community.

## Selected Publications

Martin RM\*, Rino J\*, Carvalho C\*, Kirchhausen T, Carmo-Fonseca M (\*these authors have contributed equally to this work) (2013). Live-Cell Visualization of Pre-mRNA Splicing with Single-Molecule Sensitivity. *Cell Reports* 4(6), 1144-1155. <http://www.sciencedirect.com/science/article/pii/S2211124713004373#>. (IF: 8.282, Citations: 50).

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 Res* 41(5), 2881-2893. <http://nar.oxfordjournals.org/content/41/5/2881.long>. (IF: 10.162, Citations: 46).

Martins SB\*, Rino J\*, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M (\*these authors have contributed equally to this work) (2011). Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. *Nat Struct Mol Biol* 18, 1115. <http://www.nature.com/nsmb/journal/v18/n10/full/nsmb.2124.html>. (IF: 12.595, Citations: 49).

Domingues I, Rino J, Demmers JA, de Lanerolle P, Santos SC (2011). VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. *PLoS One* 6, e25668. <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0025668>. (IF: 3.394, Citations: 36).

Henriques CM, Rino J, Nibbs RJ, Graham GJ, Barata JT (2010). IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R alpha in T cells. *Blood* 115, 3269-77. <http://www.bloodjournal.org/content/115/16/3269.long?sso-checked=true>. (IF: 13.164, Citations: 55).

### **Ongoing Research Projects**

2017/2020 PPBI – Plataforma Portuguesa de Bioimagem. Coordinator: José Miguel Rino Henriques. Funding Agency: Portugal 2020. Reference: PINFRA/22122/2016. Amount: € 306 178, 00 Total Amount: € 865 695,43.

### **Publications in Peer Review Journals**

Carvalho T, Martins S, Rino J, Marinho S, Carmo-Fonseca M (2017). Pharmacological inhibition of the spliceosome subunit SF3b triggers EJC-independent NMD. *J Cell Sci* 130(9), 1519-1531. (IF: 4.431, Citations:--).

Ministro A, de Oliveira P, Nunes RJ, Dos Santos Rocha A, Correia A, Carvalho T, Rino J, Faísca P, Becker JD, Goyri-O'Neill J, Pina F, Poli E, Silva-Santos B, Pinto F, Mareel M, Serre K, Constantino Rosa Santos S (2017). Low-dose ionizing radiation induces therapeutic neovascularization in a pre-clinical model of hindlimb ischemia. *Cardiovasc Res* 113(7), 783-794. (IF: 5.878, Citations: 1).

Ferreira DG, Batalha VL, Vicente Miranda H, Coelho JE, Gomes R, Gonçalves FQ, Real JI, Rino J, Albino-Teixeira A, Cunha RA, Outeiro TF, Lopes LV (2017). Adenosine A2A Receptors Modulate alpha-Synuclein Aggregation and Toxicity. *Cereb Cortex* 27(1), 718-730. (IF: 6.559, Citations: 4).

### **Other Publications International**

Rino J, de Jesus AC, Carmo-Fonseca M (2017). Quantitative Image Analysis of Single-Molecule mRNA Dynamics in Living Cells. *Methods Mol Biol* 1563, 229-242. (IF:--, Citations:--).

### **Internationalisation**

The Bioimaging Facility is a Zeiss labs@location Partner, integrating a community of leading research facilities with expertise in specific applications of technologies that provide in depth knowledge and scientific support to Zeiss customers community.

### **Advanced Teaching**

Rino J. Lecturer (both theoretical lectures and hands-on practicals). III Quantitative Fluorescence Microscopy Course, CNC – Center for Neuroscience and Cell Biology, Coimbra, Portugal, September 18-22, 2017.

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## Biosafety Level 3 Laboratory

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### Major Interests / Objectives

The BSL3 Facility meets the highest safety standards as defined by European and International guidelines. The purpose of this facility is to enable researchers to carry out work with infectious agents that require BSL3 or ABSL3 containment conditions. The Facility is available to IMM internal and affiliated researchers, and, with the exception of ABSL3, to external researchers from academia, pharma and biotech. Work in the BSL3 Lab follows SOPs defined in the Facility's Rules and Guidelines Manual. The BSL3 Facility comprises two fully equipped tissue culture rooms and one animal experimentation room for rodents.

### Head of Facility

Joana Margarida da Silva Marques, PhD (Left December)

Pedro Simas, DVM, PhD (Started July)

### Team

Cecília Simão	Undergraduate	Technician
Daniel Corte Real Gomes da Costa	Master	Veterinary Surgeon
Iolanda Safira de Sousa Moreira	Graduate	Facility Manager

### Keywords / Research Areas

Biosafety level 3, HIV, Mycobacterium tuberculosis, ABSL3.

### Major Scientific Achievements

Merging of Rodent facility with BSL-3 Lab: in order to optimize the use and management of the Biosafety level 3 laboratory, this facility was merged with the rodent facility, allowing for an optimal use of human resources, as well as the standardization of logistics, administrative procedures and general organization and routines.

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## Flow Cytometry

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### Major Interests / Objectives

The Flow Cytometry Facility provides a state of the art flow cytometry service to iMM researchers as well as external groups from other research institutes. We aim at training researchers in the adequate use of the instruments and also on flow cytometry principles, experiment planning, as well as data analysis and interpretation. The facility is equipped with 4 cell analysers (1 BD LSRFortessa X-20, 2 BD LSRFortessa - one of them equipped with a High Throughput Sampler - and 1 BD Accuri C6), 2 cell sorters (BD FACSAria IIu and BD FACSAria III) and one imaging flow cytometer (Amnis ImageStreamX). Besides a cell sorting service, our staff ensures quality control and maintenance procedures on all instruments and the implementation of the Quality Management System, according to ISO 9001.

### Head of Facility

José Miguel Rino Henriques, PhD

### Team

Ana Isabel da Silva Vieira	Master	Technician (Left January)
Andreia Pereira Gameiro	Master	Technician (Left September)
Andreia Sofia Ramalho dos Santos	Master	Technician (Started September)
Bárbara Xavier Louro de Oliveira	Master	Technician (Started March)
Diana Leonor Constantino Macedo	PhD	Investigator (Started November)
Filipa Faria Rosa	Graduate	Technician (Left September)

### Keywords / Research Areas

Flow cytometry, High speed cell sorting, Multiparametric analysis, Imaging flow cytometry, Training in flow cytometry.

### Major Scientific Achievements

In 2017, a new cell analyzer (BD LSRFortessa X-20) and an imaging flow cytometer (Amnis ImageStreamX) were acquired by the iMM for the Flow Cytometry Facility. Scientific collaboration with an iMM research lab resulted in one publication in which José Rino is co-author: Pereira PD et al, Oncotarget (PMID: 28465489, IF: 5.312). In 2017 a total of 178 users from 35 research labs, 7 of them from outside the iMM, used the Flow Cytometry Facility.

The Flow Cytometry Facility is one of the founders of FLxFlow - a Portuguese network for Flow Cytometry created in 2017, which aims at bringing together the know-how of 4 core flow cytometry facilities in the Lisbon area, enabling advanced training and access to cutting edge applications to the scientific community.

### **Selected Publications**

Pereira PD, Serra-Caetano A, Cabrita M, Bekman E, Braga J, Rino J, Santus R, Filipe PL, Sousa AE, Ferreira JA (2017). Quantification of cell cycle kinetics by EdU (5-ethynyl-2'-deoxyuridine)-coupled-fluorescence-intensity analysis. *Oncotarget* 8(25), 40514-40532. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5522303/>. (IF: 5.168, Citations: 1).

### **Publications in Peer Review Journals**

Pereira PD, Serra-Caetano A, Cabrita M, Bekman E, Braga J, Rino J, Santus R, Filipe PL, Sousa AE, Ferreira JA (2017). Quantification of cell cycle kinetics by EdU (5-ethynyl-2'-deoxyuridine)-coupled-fluorescence-intensity analysis. *Oncotarget* 8(25), 40514-40532. (IF: 5.168, Citations: 1).

### **Advanced Teaching**

Rino J. Organizer and Lecturer (both theoretical lectures and hands-on practicals). 1<sup>st</sup> FLxFlow Course - Principles and Applications of Flow Cytometry. CAML Course, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, October 16-20, 2017.

## Histology and Comparative Pathology Laboratory

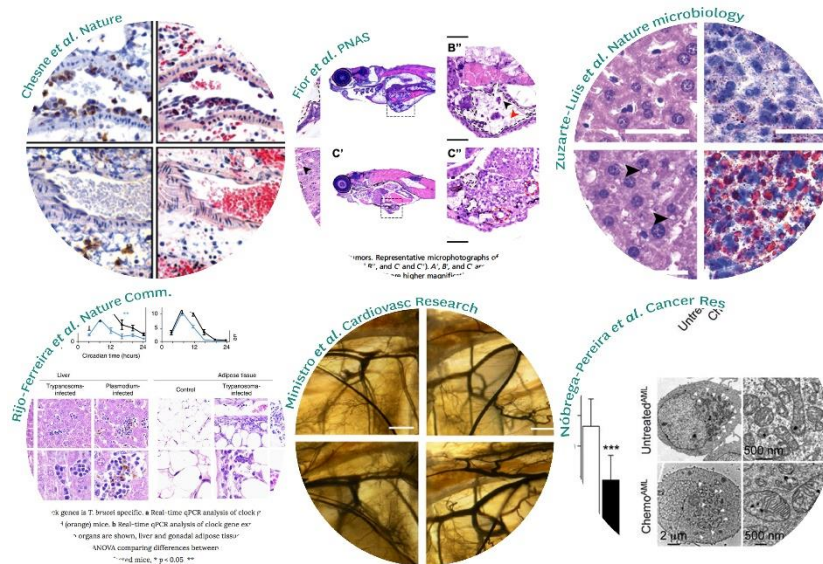
### Major Interests / Objectives

Histopathology is the art of analysing and interpreting the shape, size and architectural pattern of organelles, cells and tissues within a given clinical or research background, and can be achieved through 3 main techniques: histology, immunohistochemistry and electron microscopy, alone or in combination. At the Histology and Comparative Pathology Laboratory, this is our expertise and our mission has been to achieve the highest level of quality in supporting in-house and extramural researchers. Originality, integrity, and productivity while maintaining the highest level of technical proficiency and ethical principles is our motto; and we hope to keep up with your pace in the years to come.

### Head of Facility

Tânia Gilot Mendes de Carvalho Barão, PhD

### Graphical Abstract





### Team

Ana Margarida Biscaia Fernandes dos Santos	Graduate	Technician
Ana Rita Varanda Correia Pires	Graduate	Technician (Started October)
Andreia Lúcia do Nascimento Pinto	Master	Technician
Bruna Camila Coelho Almeida	Graduate	Trainee (Left October)
Pedro Reis Ruivo	Graduate	MSc Student (Started October)
Rute Sofia Marianito Brito	Graduate	Technician (Started July)

### Keywords / Research Areas

Histology, Comparative pathology, Transmission electron microscopy, Immunohistochemistry.

### Major Scientific Achievements

2017 has been an amazing year in what concerns our most important key performance indicators (KIPs):

- User satisfaction survey results, and
- Publications. We also increased our team by two, to meet the need for specialization and increased demand. We now have Ana Margarida Santos and Ana Rita Pires with the histology and the immunohistochemistry services; Andreia Pinto and Rute Brito with the electron microscopy service; and Tânia Carvalho with the experimental pathology, together with Pedro Ruivo, a veterinarian masters' student that joined the lab for 4 months. We also received our new/vintage transmission electron microscope and are almost ready to become totally independent in this technique.

### Selected Publications

Zuzarte-Luís V, Mello-Vieira J, Marreiros IM, et al. (2017) Dietary alterations modulate susceptibility to Plasmodium infection. *Nature Microbiology* 2, 1600-1607. (IF:--, Citations: 1).

Cardoso V, Chesne J, Ribeiro H, et al. (2017). Neuronal regulation of type 2 innate lymphoid cells via neuromedin U. *Nature*. (IF: 40.137, Citations: 7).

Fior R, Pova V, Mendes RV, et al (2017). Single-cell functional and chemosensitive profiling of combinatorial colorectal therapy in zebrafish xenografts. *Proceedings of the National Academy of Sciences of the United States of America*. (IF: 9.661, Citations: 1).

Ministro A, de Oliveira P, Nunes RJ, et al. (2017). Low-dose ionizing radiation induces therapeutic neovascularization in a pre-clinical model of hindlimb ischemia. *Cardiovascular Research*. (IF: 5.878, Citations: 1).

Graca G, Desterro J, Sousa J, et al. (2017) Identification of putative biomarkers for leptomeningeal invasion in B-cell non-Hodgkin lymphoma by NMR metabolomics. *Metabolomics*. (IF: 3.692, Citations:--).

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

Carvalho T. Translation starts with Pathology. CNC – Center for Neuroscience and Cell Biology, Coimbra, Portugal, January, 2017.

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## Information Systems

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### Major Interests / Objectives

The Information Systems Unit (USI) mission is to help researchers reach their maximum productivity by using adequate Information Technology resources. Our aims are:

- Provide state-of-the-art information technology infrastructure and support services.
- Contribute to improve productivity of researchers and research outcomes.
- Facilitate and optimize management business processes.

USI intervenes mainly in the following areas:

- Information Technology (IT) support to iMM users.
- Planning, implementation and maintenance of the infrastructure that stores, processes and protects research data.
- Design, implement and integrate information systems to facilitate scientific and management processes.

### Head of Facility

Pedro Miguel Bernardino Eleutério, Graduate

### Team

André Filipe Cardoso Gonzalez Fragoso	Undergraduate	Technician
Daniel José Vilhena Guerreiro	Graduate	Technician (Left September)
Pedro André Lozano Luiz de Castro	Graduate	Technician (Started November)
Ricardo Martinho	Undergraduate	Technician (Started April)
Ricardo Jorge Oliveira Reis	Undergraduate	Trainee (Started April)

### Keywords / Research Areas

IT support, Data protection, Information integration, Web services and applications.

### **Major Achievements**

A new HPC (High Performance Cluster) solution has been implemented successfully, which allows providing 300 cores and 3Tb of RAM for bioinformatics projects, which now have the participation of around half of iMM Labs. The upgrade of accounting and office applications to the latest 2016 version has been concluded. Windows desktops and laptops upgrade to the latest Windows 10 LTSB 1607 version has been started, 25% of this project has been concluded. USI as also implemented new video tutorials to help researchers, and facilities staff, configuring important software.

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## Laboratory Management and Safety Office

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### Major Interests / Objectives

Middle 2017, Quality and Safety in Laboratory (QSL) facility was changed to Laboratory Management (LMN) and Safety Office (SO) facilities. They operate as a support and follow-up structure to the research developed at IMM. In addition to management and maintenance of equipment and laboratories, LMN offers scientists and visitors a high level of experience in training on scientific equipment. LMN provides technical support: planning of projects for installation of new laboratories/refurnishing the existing ones and carry out acquisitions studies for new equipment. LMN have available a specialized service for washing and sterilization of materials. SO provides technical advice to labs and facilities on all aspects of OHS. The goal is to minimize the risk of injury or illness to labs and facility workers by ensuring that they have the training, information, support and equipment needed to work safely in the laboratory.

### Head of Facility

Alexandra Maralhas, Graduate

### Team

Cláudia Cavaco Guerreiro	Master	Technician (Left April)
Edna Neias F. Gomes	Graduate	Technician
Liudmila dos Santos Cupertino Borges	Undergraduate	Technician (Started November)
Maria Jardim Caramelo Dias Cabral	Master	Technician
Paula Alexandra Rodrigues Luís	Undergraduate	Technician
Sara Diana Pinheiro dos Santos	Master	Technician
Saulo de Tércio de Freitas Silva	Undergraduate	Technician

### Keywords

Infrastructure and equipments maintenance, Public procurement procedures, Health and safety, Laboratory planning and design, Purchases, Budgeting, Technical consulting.

## Major Achievements

The services were actively involved in several re-modeling works of laboratory spaces such as, new laboratory spaces for research groups – Insectary Facility (3 rooms): a Mosquito Rearing Area, a Tissue Culture Room (Blood Room) and an Infection and Dissection Room; New dark room and a New common bacterial room. The equipment management (acquisition, maintenance and repair) was improved with the ongoing inventory of all iMM equipments, required for an excellent level of support to over 350 equipments with maintenance contracts. 2017 was also marked by changes in the Public Procurement law and simultaneous improvements in all iMM acquisition procedures. We continue committed to our health and safety policies and updated risk assessment procedures, focused on the work developed in the laboratories.

The LMN and SO facilities were contracted to carry out external consultancy work, that are still in progress: a) for Siderurgia Nacional, Megasa Group (entitled: Inventory and implementation of good practices for the reception, storage and lifting of solid and liquid chemical products at the main warehouse) and for the Bento Rocha Cabral Institute (entitled: Analysis, selection and elimination of solid and liquid chemicals and radioactive materials).

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## Rodent Facility

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### Major Interests / Objectives

The rodent facility supports state-of-the-art animal research. We provide housing and care of laboratory rodents. We also support training and education in Laboratory Animal Science. The Rodent Facility strictly follows Portuguese and international laws and recommendations governing good practices and animal welfare. Namely, we follow 3R's principles, i.e., Replacement, whenever possible, of the animal model by alternative methods, Reduction of the number of animals used and, Refinement of experimental methodologies and animal care procedures.

### Head of Facility

Joana Margarida da Silva Marques, PhD (Left December)

Pedro Simas, DVM, PhD (Started July)

### Team

Bruno Miguel da Conceição Novais	Master	Animal Technician
Cecilia Simão	Undergraduate	Animal Technician
Daniel Corte Real Gomes da Costa	Master	Veterinary Surgeon
Felícia Maria Augusto Ramos	Undergraduate	Animal Caretaker
Filipe Fernandes Delgado	Graduate	Animal Technician
Iolanda Safira Sousa Moreira	Graduate	Facility Manager
Márcia Pereira da Silva	Master	Animal Welfare Officer
Mihaela Elena Morari	Undergraduate	Animal Caretaker
Olena Pavlovska Borges de Pinho	Undergraduate	Animal Caretaker
Patrícia Andrade da Fonseca Brites	Undergraduate	Animal Caretaker
Patrícia Almeida	Master	Animal Caretaker
Pedro Manuel Nogueira dos Santos	Undergraduate	Colony Manager
Sara Ghirelli	Undergraduate	Animal Caretaker

### Keywords / Research Areas

Rodents, Laboratory animal science, Animal welfare.

### Selected Publications

Maceiras A., Almeida S, Mariotti-Ferrandiz E, Chaara W., Jebbawi F, Six A, Hori S, Klatzmann D, Faro J, Graça L (2017). T follicular helper and T follicular regulatory cells have different TCR specificity. *Nature Communications*. (IF: 12.124, Citations:4).

Ribeiro ST, Tesio M, Ribot JC, Macintyre E, Barata JT, Silva-Santos B (2017) Casein kinase 2 controls the survival of normal thymic and leukemic  $\gamma\delta$  T cells via promotion of AKT signaling. *Leukemia*. (IF: 11.702, Citations: 2).

Cardoso V, Chesné J, Ribeiro H, García-Cassani B, Carvalho T, Bouchery T, Shah K, Barbosa-Morais N, Harris N, Veiga-Fernandes H (2017). Neuronal regulation of type 2 innate lymphoid cells via neuromedin U. *Nature* 549, 277. (IF: 40.137, Citations: 7).

Verdohm M (2017) Interleukin 17 is a chief orchestrator of immunity. *Nature Immunology* 18, 612-621. (IF: 21.506, Citations: 24).

Papotto PH, Ribot JC, Silva-Santos B (2017). IL-17+  $\gamma\delta$  T cells as kick-starters of inflammation. *Nat Immunol.* 18(6):604-611. Review. (IF: 21.506, Citations: 10).

Mancio-Silva L, Slavic K, 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, Bilker O, Mota MM (2017). Nutrient sensing modulates malaria parasite virulence. *Nature*, 13, 213-216. (IF: 40.137, Citations: 6).

Zuzarte-Luís V, Mello-Vieira J, Marreiros IM, Liehl P, Chora ÂF, Carret CK, Carvalho T, Mota MM (2017). Dietary alterations modulate susceptibility to Plasmodium infection. *Nat Microbiol.* 2, 1600-1607. (IF:--, Citations: 1).

Fonseca VR, Agua-Doce A, Maceiras AR, Pierson W, Ribeiro F, Romão VC, Pires AR, da Silva SL, Fonseca JE, Sousa AE, Linterman MA, Graca L (2017). Human blood Tfr cells are indicators of ongoing humoral activity not fully licensed with suppressive function. *Sci Immunol.* 2(14). pii: eaan1487. doi: 10.1126/sciimmunol.aan1487. (IF:--, Citations: 9).

Rijo-Ferreira F, Pinto-Neves D, Barbosa-Morais NL, Takahashi J, Figueiredo LM (2017). *Trypanosoma brucei* metabolism is under circadian control. *Nature Microbiology.* 2:17032, doi: 10.1038/nmicrobiol.2017.32. (IF:--, Citations: 6).



### **Ongoing Research Projects**

2017/2020: CONGENTO - Consórcio para Organismos Geneticamente Manipuláveis. Coordinator: João Pedro Louro Machado Simas. Funding Agency: Portugal 2020. Reference: PINFRA/22170/2016. Amount: € 560 085, 00 Total Amount: € 1 363 313,52.

CONGENTO will contribute to Partnerships by implementing a centralized database with all existing lines and services developed by all CONGENTO partners. It will also be involved in important partnerships with several Universities providing opportunities for Master and PhD students to develop their thesis work under a highly competitive environment where new technologies will be developed.

CONGENTO will contribute to Knowledge and transformation of knowledge through research and technological development of new tools and information that will add value to all CONGENTO members and beyond, by generating world expertise not in competition but in synergy to successfully implement the first infrastructure in the world to synergize technology development across these 3 model species.

CONGENTO will contribute to Services critically needed in Portugal: 1) maintenance and hosting of genetically modified lines from the 3 model species, either live or cryopreserved, 2) generation of new genetic lines and technologies in the different species, and 3) continuous education and certification in animal research and technology.

CONGENTO will contribute to Industry in particular by implementing several services of great interest to the health and biomedical industry (e.g. the generation of specific genetically modified animal models, large-scale drug screens, and reliable cryopreserved animal stocks).

CONGENTO implementation will contribute to strengthen the regional competitiveness by increasing innovation, R&D and services in the biomedical field contributing to the positioning of Lisbon as an international center of excellence for animal research.

### **Advanced Teaching**

Laboratory Animal Science course (according to FELASA cat. B).

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## Zebrafish Facility

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### Major Interests / Objectives

Provide a fully functional facility to be used by the iMM research units. Provide technical assistance to facilitate the use of zebrafish in a wide range of experimentation sets.

### Head of Facility

Maria Leonor Tavares Saúde, PhD, Invited Assistant Professor

### Team

Aida Gonçalves Lino Barros	Undergraduate	Technician
Lara Carvalho	Master	Lab Manager

### Keywords / Research Areas

Zebrafish, Development, Regeneration, Disease models, Small molecules screening.

### Major Scientific Achievements

The facility integrated the National Route of Scientific Infrastructures, a Consortium for GMO – CONGENTO - PINFRA/22170/2016.

The facility accommodated a new research group from iMM that brought a new challenge, the maintenance of immunocompromised zebrafish lines.

The facility collaborated with an external group from FCT-UNL assisting in a nanoparticles screening resulting in a publication Cordeiro M, Carvalho L, Silva J, Saúde L, Fernandes AR and Baptista PV. Gold Nanobeacons for Tracking Gene Silencing in Zebrafish. *Nanomaterials* (2017), 7(1), 10; doi:10.3390/nano7010010. The facility started a collaboration with the laboratory of Lino Ferreira (Biocant-UC) on a nanoparticle toxicity screen.

### **Selected Publications**

Ribeiro A, Monteiro JF, Certal AC, Cristovão AM, Saúde L (2017). Foxj1a is expressed in ependymal precursors, controls central canal position and is activated in new ependymal cells during regeneration in zebrafish. *Open Biology* 7(11): 170139. doi: 10.1098/rsob.170139. (IF: 3.481, Citations:--).

Cordeiro M, Carvalho L, Silva J, Saúde L, Fernandes AR, Baptista PV (2017). Gold Nanobeacons for Tracking Gene Silencing in Zebrafish. *Nanomaterials* 7(1), 10; doi:10.3390/nano7010010. (IF: 3.553, Citations: 2).

Fior R, Maxwell AA, Ma TP, Vezzano A, Moens CB, Amacher SL, Lewis J, Saúde L (2012). Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by Mesogenin1. *Development* 139(24), 4656-65. (IF: 5.843, Citations: 26).

Sousa S, Afonso N, Bensimon-Brito A, Fonseca M, Simões M, Leon J, Roehl H, Cancela ML, Jacinto A (2011). Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. *Development* 138(18), 3897-905. (IF: 5.843, Citations: 64).

Azevedo AS, Grotek B, Jacinto A, Weidinger G, Saúde L (2011). The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. *PloS ONE* 6(7), e22820. (IF: 2.806, Citations: 28).

### **Other Projects**

2017/2020 CONGENTO - Consórcio para Organismos Geneticamente Manipuláveis. Coordinator: João Pedro Louro Machado Simas. Funding Agency: Portugal 2020. Reference: PINFRA/22170/2016. Amount: € 560 085, 00 Total Amount: € 1 363 313,52.

### **Publications in Peer Review Journals**

Cordeiro M, Carvalho L, Silva J, Saúde L, Fernandes AR, Baptista PV (2017). Gold Nanobeacons for Tracking Gene Silencing in Zebrafish. *Nanomaterials* 7(1), 10; doi:10.3390/nano7010010. (IF: 3.553, Citations: 2).

### **Invited Lectures and Seminars**

Carvalho L. Maintenance and Husbandry in Zebrafish. Course in Laboratory Animal Science (Cat. B), Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, April 2017.

Carvalho L. Maintenance and Husbandry in Zebrafish. Course in Laboratory Animal Science (Cat. B), Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 2017.

### **Science and Society**

The Fish facility was visited by:

February 20 - Biochemistry Course.

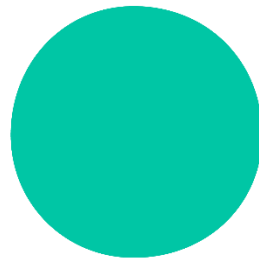
March 20 - Escola Secundária Camões, Portugal (25 students).

May 10 - Dia do Candidato Faculty of Medicine, University of Lisbon.

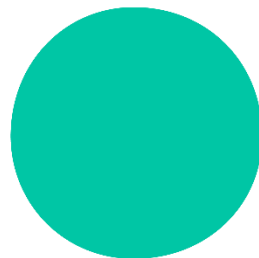
May 23 - Escola Secundária, Secondary Education (25 students).

July 27 - USA students to visit IMM (18 students).

ReTubi Event “Oncology: Talking with scientists”. Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 8, 2017. (Poster Presentation).



# **Administrative Facilities**



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## Career Development

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### Major Interests / Objectives

General Aim: Provide training opportunities for success in science to researchers at different stages in their careers.

Ongoing Activities:

- Ensure full running of ongoing Master, PhD (CAML, LisbonBioMed) and Postdoctoral Programs: Launch Calls; Administrative execution; Managerial support to PhD students/Postdoctoral researchers' activities; Support MSc/PhD students and Postdoctoral researchers throughout their training.
- Run Advanced Courses, scheduled upon CAML & LisbonBioMed Scientific Boards approval; cover all organizational aspects.
- Organize the Monday Lectures seminar series.
- Support applications to the FCT Call for PhD fellowships.
- Implement the "Training Program for the Next Step".

### Head of Facility

Ana Filipa Duarte Nunes Almeida, PhD

### Keywords / Research Areas

Advanced-Training, Master-Program, PhD-Program, Postdoctoral-Program, Career development, Advanced courses.

### Major Achievements

Specific Achievements:

- Overall managerial and administrative execution of the LisbonBioMed PhD Program: international call launch, info dissemination, applications management, coordination of the selection and admission process, production of overall program metrics and statistics and reporting, grounding the 8-week initial training program and its implementation;
- Implementation of the "Master Programme @ IMM Lisboa" (assembly and dissemination of IMM's Master project proposals/vacancies; "Open Afternoon"; "Best Master Thesis" Awards);
- Implementation of the "Training Program for the Next Step";

- Support training in bioinformatics;
- Organization of traineeships at iMM (e.g. Summer Internships, CoLab Sessions);
- Support to the FCT Call for PhD fellowships (21 applications in 2017 call).

Transversal managerial support to:

- FCT fellowships: renewals, periods abroad, thesis committees, general queries;
- PhD students/Postdocs-driven initiatives, advanced courses, Monday Lectures and other scientific events.

### **Advanced Teaching**

Nunes F. Organizer. Intellectual Property Protection: Creating Value from Research Seminar by Dr. John Van Amsterdam, Chair of the Biotechnology Group at Wolf Greenfield & Sacks, Intellectual Property Law (USA), Instituto de Medicina Molecular João Lobo Antunes, May 2017.

Nunes F. Organizer. Seminar “iMM Best Master Thesis”, by the 3 winners of the iMM “Best Master Thesis” Awards, Instituto de Medicina Molecular João Lobo Antunes, December 4, 2017.

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## Communication

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### Major Interests / Objectives

The Communication is iMM's first line of interaction with society providing updated, reliable and relevant information on all of iMM's thematic areas, as well as promoting the very best scientific successes made by its research teams. Its mission is to support the internal and external communication of iMM's activities as well to advice iMM Direction on Public Affairs issues.

With the firm belief that science should inform decisions because it impacts everyone's lives, the Communication targets a wide range of audiences (policy makers, public opinion, patients associations, medical societies, schools, academia, industry, media, arts, amongst others). It serves as spokesman for the institute and it's responsible to manage iMM's image aligned with the institute values and mission.

### Head of Facility

Ana Maria Matias de Barros, PhD

### Team

Ana Cláudia Silva	Graduate	Administrative
Sandra Isabel Gertrudes	Graduate	Administrative

### Keywords

Corporate and institutional communication, Science communication, Public affairs, Digital communication.



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## Human Resources

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### Major Interests / Objectives

Initially included in the Management, the Human Resources Office became an independent Facility in July 2017 through the hiring of a Human Resources Director. The purpose of the Human Resources Office is to develop, implement, and support programs and processes that add value to iMM and its employees, leading to improvements in employee well-being, empowerment, and growth, while committed to key iMM activity: Research. The mission is to provide effective human resource management through the development and implementation of policies, programs and services that contribute to the pursuit of the iMM Vision "to promote individual freedom and ambition, not a culture of individuality", and the common goal of "creating new knowledge that will impact human health".

### Head of Facility

Sofia Isabel Lopes dos Santos Vicente dos Santos, (Started July)

### Team

Cláudia Aurora Mira Soeiro	Graduate	Administrative
Susana Isabel dos Santos Pedroso	Undergraduate	Administrative

### Keywords / Research Areas

Human resources team has solid technical and soft skills with the aim to promote Talent. Our goal is to select and support the most prepared candidates to maintain the excellence of iMM, whether is a researcher or support staff.

### Major Achievements

The year of 2017 was a structuring year and some changes have taken place due to the implementation of new procedures and measures that have begun to have an impact on the management of iMM. The Human Resources Office started to play a strategic role through the professionalization of Recruitment, Integration, Development and Evaluation of the elements.

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## Management

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### Major Interests / Objectives

In 2017, some important changes have occurred within the Management Unit.

Firstly, Instituto de Medicina Molecular João Lobo Antunes would like to address a truthful thank you note to Margarida Pinto Gago that decide to leave iMM in June 2017. Margarida joined iMM from its beginning leaving behind an important legacy that shall be remembered and appreciated. Fausto Lopo de Carvalho joined iMM in June 2017 and is currently head of the Management Unit facility.

Regarding its organizational structure, some important changes must be highlighted: Purchasing Office joined this facility in July and, in September, the Funding Office Team also joined the Management Unit ceasing to exist as a standalone facility. Alongside with Accounting, Projects and Legal, the Management Unit has now extended capabilities and vision over the Pre-Grant/Post-Grant process.

**Funding Office** – Proposal design support; Support in consortium formation - identifying missing competences; Liaison with funding agency; Administrative and financial grant support; Support to grant writing namely impact (dissemination, communication, exploitation) and implementation sections; Budgeting support and validation; Ethics compliance advice.

**Accounting** – iMM statutory accounts and tax returns; cost accounting; Reporting and compliance with DGO (Direcção Geral do Orçamento) regarding budget submission and execution.

**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.

**Purchasing Office** – Tendering according to Portuguese and European legislation; Verification of the validity of expenses in the research project; Placing the order to the supplier, tracking delivery times and updating the researcher on lead times.

**Legal** – Institutional and Researcher's support; Main areas of expertise: Intellectual Property; Consortium Agreements; Public Law and Employment.

The Management Unit 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 in DGO and for setting up, while following, the execution of the operational budget of all iMM facilities. The Management unit is also requested to give support in matters concerning inter-institutional collaborations. Finally, the Management Unit is accountable for promoting Quality Management System actions regarding up to date procedures, reports and assessments per facility and fulfillment of ISO 9001 requirements.

### Head of Facility

Maria Margarida Mendonça Correia Pires Pinto Gago, Graduate (Left June)

Fausto da Costa Santos Lopo de Carvalho, MBA (Started June)

### Team

#### Board of Directors Assistant:

Ana Clara Pereira Faria Artur	Graduate	Administrative
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#### Funding:

Afonso Miguel dos Santos Duarte	PhD	Pre-Award Manager (Started April)
Bárbara Sofia Lopes Gomes	Master	Pre-Award Manager (Started November)
Joana Cristina Costa	PhD	Senior Manager
Marija Petkovic Garcia	PhD	Pre-Award Manager

#### Projects:

Andreia Sofia Gonçalves Almeida Vaz Veiga	Graduate	Project Manager
David Abreu	Master	Project Manager (Left June)
Isabel Pequenino Roque	Graduate	Project Manager
Maria José Flores Marques Antunes	Graduate	Project Manager
Maria Rosa Vieira Ventura	Graduate	Project Manager
Mónica Aurora Malheiro Vieira	Graduate	Project Manager (Left May)
Tiago José Ramos Reis	Graduate	Project Manager

**Purchases:**

Alexandre Manuel Raposo de Jesus	Master	Manager
Ana Rita Fonseca Vicente	Graduate	Technician
Cláudia Sofia Palmeiro Alves da Costa	Graduate	Technician
Rita Santinho Grenho	Master	Technician (Started September)
Sandra Isabel Francisco Lopes	Graduate	Technician
Sara Marisa Caseiro Rebelo	Graduate	Technician
Vânia Isabel Esteves Polido Marques Paula	Graduate	Technician

**Accounting:**

Ana Filipa de Almeida Pereira	Graduate	Administrative
Cláudia Filipa Dias Marques	Graduate	Administrative (Started September)
Eduarda Maria Seabra Rosmaninho	Master	Administrative
Pedro Miguel da Rosa Santos	Graduate	Administrative (Started October)
Pedro Gaspar Rebelo Lopes Moura	Master	Administrative
Sandra Paula da Silva Duarte	Graduate	Accountant
Vera Cristina Felício Conceição Rego	Undergraduate	Administrative

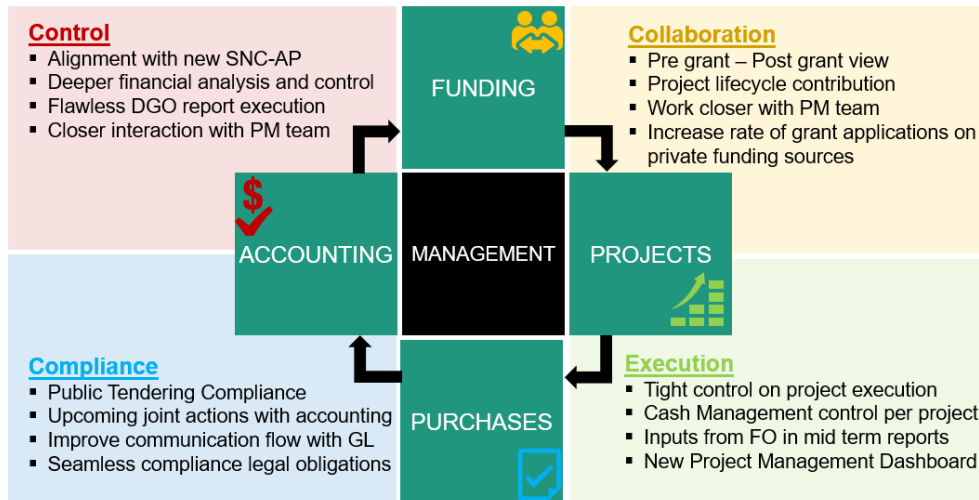
**Legal:**

André Rebelo da Silva Fialho	Graduate	Lawyer
Ricardo Caetano Dias Cotrim	Graduate	Administrative (Left April)

**Front Office:**

Joana Andrade de Sousa Lamas	Graduate	Administrative (Started December)
Lúcia Cristina Manso Alves	Graduate	Administrative

## Keywords / Research Areas



## Major Achievements

**Funding Office:** Dissemination of nearly 300 funding opportunities; Increased compliance between iMM researchers and Funding Office; Support to 215 applications to 42 different International and to 19 different National Funding Programs, namely in eligibility, ethical, legal, technical and administrative aspects; Support and management of the iMM’s Director’s Fund schemes; Technical coordination of seven institutional projects.

**Accounting:** Compliance with new demands from DGO (Direcção geral do Orçamento) – monthly execution reports against approved budget. Analysis by funding source and economic items; New skills on management financials besides the normal accounting records; Shorter periods for monthly closings; Preparation work for new SNC-AP module on iMM IT platform; Improved team dynamics and leadership model.

**Purchasing Office:** Improved capabilities regarding new adaptation for public tendering Law within Public Contract Code (CCP); Additional process agility gained through a successful implementation of an effective functional flowchart; Successful collaboration with Legal entities to better comprehend CCPs scope of action; Visible team improvement with a new Leadership model.

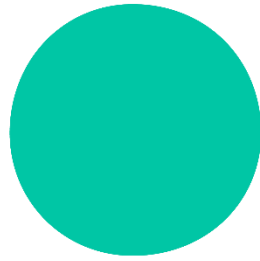
**Project Management:** Accurate deadline of report submission control; Improvements on project control metrics; improved capabilities to better deal with changes in cost eligibility and expenses submission; Good team alignment with funding office members regarding the institutional European projects.

**Legal:** Continuous support of complex process regarding iMM capability to deal with CCPs; accurate support on new ventures and Start-Ups regarding PI registration and support.

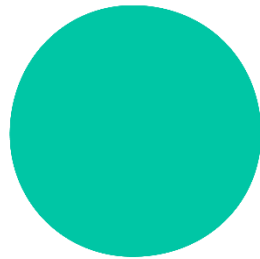
**Quality Management System:** Successful audit in 2017, SWOT and annual satisfaction survey completed for iMM.

In 2017, Management Unit underwent some structural changes that directly or indirectly affected iMM's scientific community and board of directors. Besides the new leadership model, with a new Director in functions from June on, other organizational changes were put in place with the single goal of building a more effective and responsive structure to address iMM's main goal – to pave the way for groundbreaking science by providing an environment that fosters freedom to chase key questions and embrace creativity.

The legal macro environment surrounding iMM affected severely some processes. One positive consequence could be taken away – the need to address a higher set of demands created a positive pressure to revisit the existing models while promoting the necessary team spirit to be more assertive. Financial analysis and reporting are now more demanding enabling for more accurate state of the art reports and predictive analysis. Purchases are being tracked and registered in a way that allows for timely status on top suppliers regarding the volume ordered and a more close communication with accounting and general management. 2017 ended with a more robust management unit with extended capabilities giving a very positive sign to address the challenges ahead in 2018.



# Startups



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## GenoMed

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### Major Interests / Objectives

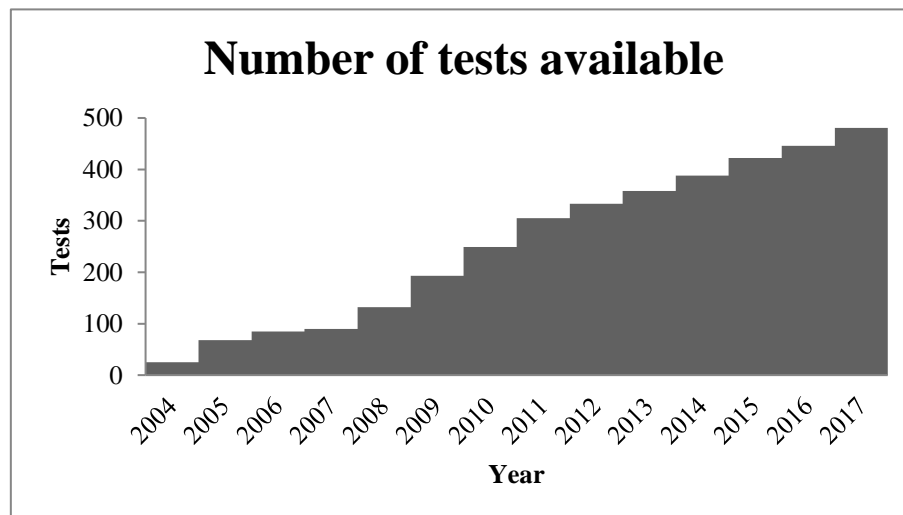
GenoMed is a spin-off company of iMM created in 2004. GenoMed's mission is to provide cutting-edge technology transfer services relevant for medical applications. Currently, GenoMed offers 480 different tests that are used in diagnosis, prognosis and therapeutic follow up. The main medical areas covered include Oncology, Hematology, Cardiology, Neurology, Gastroenterology/Hepatology, Nephrology, Endocrinology/Metabolic diseases, Obstetrics/Gynecology, Pneumology, Dermatology, Ophthalmology, Otorhinolaryngology, Pediatrics, Urology and Pharmacogenetics. Additionally, GenoMed provides parental and ancestry DNA testing.

### Head

Teresa Porta Nova, MSc – Executive Director/Technical Director

Marta Zegre Amorin, MD – Clinical Director

### Graphical Abstract





### Team

Ana Coutinho	MSc	Area Manager, Technician
Ana Carla Sousa	Graduate	Technician
Ana Clemente	MSc	Business Developer
Ana Flores	Undergraduate	Management Assistant
Ana Rita Dário	MSc	Technician (Started July)
André Janeiro	Graduate	Technician
Andreia Pereira	MSc	Technician (Started June)
Catarina Reis	Graduate	Technician (Started July)
Catarina Silveira	MSc	Technician, PhD Student BDE
Fernanda Barbosa	Undergraduate	Direction Assistant
Hélia Guerreiro	MSc	Technician
Inês Silva	MSc	Technician, Quality Manager
Joana Lopes	MSc	Technician
Joana Tavares	MSc	BioInformatic
Paula Borralho Nunes	MD/PhD	Clinical Pathologist
Paula Costa	Graduate	Technician
Renata Casimiro	MSc	Technician (Started March)
Rita Raposeiro	MSc	Technician
Sandra Matos	MSc	Technician
Sara Malveiro	Graduate	Technician
Sara Castro	MSc	Technician (Started November)
Sofia Fernandes	MSc	Technician (Left May)
Sónia Matos	MSc	Area Manager, Technician
Sónia Santos	PhD	Area Manager, Technician
Vânia Martins	Graduate	Technician

### Keywords / Research Areas

Molecular diagnosis, Oncology, Genetics, Rare diseases.

### Major Scientific Achievements

In 2017, we implemented 26 new NGS panels, designed together with the clinicians and responding to their patient's needs.

GenoMed received a positive outcome to our project proposal MyCardioGene Test, financed by Lisboa2020 program, with two major objectives: Develop new bioinformatic workflow that allows the analysis of complete genes (introns and exons) to discover potential new alterations which cause hypertrophic cardiomyopathy; and to construct new cellular models using CRISPR/Cas9, which will allow the evaluation of the mutations in the expression of the proteins in the cardiac muscle.

GenoMed participated in the international collaborative study for the approval of the first international standards for KRAS mutations: Collaborative study to evaluate the proposed WHO 1<sup>st</sup> International Reference Panel for genomic KRAS codons 12 and 13 mutations.

### **Ongoing Research Projects**

2017/2021: LysoMod, funded with the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 734825.

2017/2019: MyCardioGeneTest, funded by Lisboa2020, Portugal2020 from European Regional Development Fund (FEDER).

Participation in a collaborative study with the National Institute for Biological Standards and Control (NIBSC) for the evaluation of the first international reference panel for the mutations in the codons 12 and 13 of KRAS gene, approved by ECBS (WHO Expert Committee on Biological Standardization) in October 2017.

2016/2019: Characteristics and frequency of IDH mutations in real world AML patients in Portugal. Celgene. Coordinator: Prof. Carmo-Fonseca. Participants: Sónia Matos.

### **Publications in Peer Review Journals**

Azevedo A, Mousinho F, Mendes T, Sousa e Santos P, Cerqueira R, Matos S, Santos S, Ramos S, Viana J, Lima F. Cocomitant Presence of JAK2V617F Mutation and BCR–ABL Translocation in Two Patients: a New Entity or a Variant of Myeloproliferative Neoplasms. *Blood Cells, Molecules and Diseases*, *submitted*.

### **Invited Lectures and Seminars**

Matos S. Monitorização da Resposta a Terapêutica com TKIs. Aspectos Mais Relevantes. Leucemia Mieloide Crónica - para além da 1<sup>a</sup> linha terapêutica. Lisbon, Portugal, February 17, 2017.

Santos S. Genética Aplicada à Hemato-oncologia – Citogenética. Curso de Pós-Graduação em Medicina Laboratorial (3<sup>rd</sup> edition), June 3, 2017.

Matos S. Genética Aplicada à Hemato-oncologia – Biologia Molecular. Curso de Pós-Graduação em Medicina Laboratorial (3<sup>rd</sup> edition), June 3, 2017.

Santos S. A citogenética no diagnóstico das Mielodisplasias e da Leucemia Mielomonocítica Crónica. VII Curso Internacional de Diagnóstico Laboratorial, November 10, 2017.

Matos S. A biologia molecular no diagnóstico das Mielodisplasias e da Leucemia Mielomonocítica Crónica. VII Curso Internacional de Diagnóstico Laboratorial, November 10, 2017.

Silveira C. Novas técnicas de sequenciação. Curso Nefropatias Hereditárias (Sociedade Portuguesa de Nefrologia), Porto, Portugal, March 11, 2017.

Silveira C. Novos diagnósticos, novas abordagens terapêuticas – o papel da genética. Curso de Pediátrica - Módulo de Nefrologia - Nefrologia Diferenciada, Hospital de Santa Maria, Lisbon, Portugal, November 17, 2017.

Sousa A. Imersão sobre Carcinoma do Pulmão de Não Pequenas Células. AstraZeneca, Lisbon, Portugal, June 20, 2017.

Silveira C. Programa de imersão BRCA, Programas de Imersão. AstraZeneca, Lisbon, Portugal, April 27, 2017.

#### **Communications in International Conferences**

Matos S, Martins V, Guerreiro H, Desterro J, Carmo-Fonseca M. IDH Mutations in AML patients in Portugal. 8<sup>th</sup> IRM Haematology – Celgene, Milan, Italy, April 1, 2017. (Poster Presentation).

Silveira C, Sousa AC, Janeiro A, Felizardo M, Carmo-Fonseca M. ddPCR to detect EGFR T790M. Liquid Biopsies EMBL Course, Heidelberg, Germany, October 9-13, 2017. (Poster Presentation).

#### **Communications in National Conferences**

Matos S. Next Generation Sequencing na Hemato-oncologia. Hematology and Bone Marrow Transplantation Service of Hospital de Santa Maria – Centro Hospitalar Lisboa Norte, Lisbon, Portugal, February 9 and September 28, 2017. (Oral Presentation).

Silveira C, Coutinho A, Tavares J, Ribeiro M, Carmo-Fonseca M. Whole exome sequencing for diagnosis of rare diseases. 13<sup>th</sup> International Symposium of Sociedade Portuguesa de Doenças Metabólicas, Évora, Portugal, March 16-17, 2017. (Poster Presentation).

Silveira C. Precision Oncology in breast cancer. 4<sup>a</sup> Reunião de Utilizadores de Plataformas de NGS ILC/Illumina, Porto, Portugal, October 2, 2017. (Oral Presentation).

Matos S, Desterro J, Nunes A, Gomes da Silva M, Chacim S, Mariz M, Esteves G, Raposo J, Botelho A, Espadana A, Ribeiro L, Martins V, Guerreiro H, Carmo-Fonseca M. *IDH* Mutations in AML patients in Portugal. 4<sup>th</sup> International Conference on Acute Myeloid Leukemia, Estoril, Portugal, October 5-7, 2017. (Poster Presentation).

Macedo A, Caetano G, Guerra L, Lopes C, Polo B, Valle S, Mota A, Cabral R, Cunha M, Magalhães, Santos MJ, Martins J, Santos P, Melo T, Coelho H, Montalvao A, Cerveira N, Matos S, Rodrigues J, Gírio A, Saraiva A. Evaluation of the Effectiveness, Safety and Compliance of Nilotinib in the Treatment of Newly-Diagnosed CML Patients in a “Real-Life” Setting — Preliminary Results of the PIANO-CML Study. 19<sup>th</sup> Annual John Goldman Conference on Chronic Myeloid Leukemia: Biology and Therapy, Estoril, Portugal, October 12-15, 2017. (Poster Presentation).

Polo B, Macedo A, Caetano G, Guerra L, Lopes C, Valle S, Mota A, Cabral R, Cunha M, Magalhães R, Santos MJ, Martins J, Santos P, Melo T, Coelho H, Montalvao A, Cerveira N, Matos S, Rodrigues J, Gírio A, Saraiva A. Efetividade e Segurança de Nilotinib no Tratamento de LMC Recém-Diagnosticada num Contexto de “Vida Real”: Resultados Preliminares do Estudo PIANO-CML. SPH Annual Meeting, Vilamoura, Portugal, November 16-18, 2017. (Poster Presentation).

Matos S, Desterro J, Nunes A, Gomes da Silva M, Chacim S, Mariz M, Botelho A, Esteves G, Raposo J, Martins V, Guerreiro H, Carmo-Fonseca M. Mutações *IDH* em doentes com LMA em Portugal. SPH Annual meeting, Vilamoura, Portugal, November 16-18, 2017. (Oral Presentation).

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## Lymphact S.A.

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### Major Interests / Objectives

Lymphact is a biopharmaceutical start-up focused on developing innovative personalised medical treatments. Our first product - DOT-Cells® - can target not only cancer and virus-infected cells, but also chemotherapy-resistant cancer stem cells and viral reservoirs, believed to cause disease recurrence. An improved anti-tumour function and the absence of severe associated side-effects are distinctive and unique features of our therapeutic approach.

### Head

Diogo R. Anjos, MBA – CEO

### Keywords / Research Areas

Cellular therapies, Immunology, Oncology, Immunotherapies, Start-up, Gamma-Delta.

### Recent Most Relevant Publications

Almeida AR, Correia DV, Fernandes-Platzgummer A, 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. Clin Cancer Res. 2016 Dec 1;22(23):5795-5804. (IF: 9.619, Citations: 9).

### Ongoing Research Projects

Proprietary Research.

### Patents / Prototypes

PCT IB2012/052545.

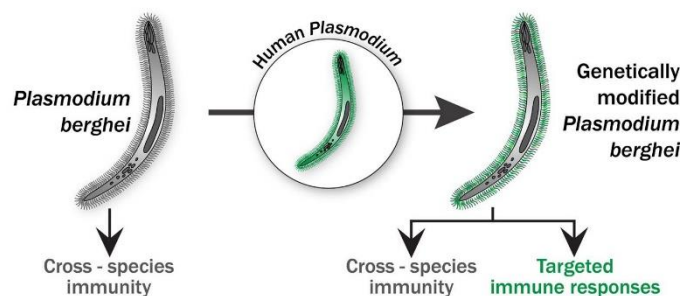
PCT EP2016/063077.

## RoPlaVac

### Major Interests / Objectives

RoPlaVac is a spin-off company of Instituto de Medicina Molecular João Lobo Antunes, created in 2014. The mission of RoPlaVac is to develop medical solutions against malaria, one of the most prevalent diseases worldwide. Malaria is caused by Plasmodium parasites, injected into their mammalian host as sporozoites, through the bite of an infected mosquito. Currently, RoPlaVac is engaged in three main endeavors: Vaccination- Development of a new whole-organism vaccine against malaria, based on the use of genetically modified rodent Plasmodium parasites; Plasmodium sporozoite cryopreservation - Development of an effective method to cryopreserve Plasmodium sporozoites for use in research and vaccination; In vitro Plasmodium sporozoite production- Development of a cell culture-based method to produce infective Plasmodium sporozoites for use in research and vaccination.

### Graphical Abstract



### Head

Miguel Prudêncio, PhD, Instituto de Medicina Molecular João Lobo Antunes, Group Leader – Prudêncio Lab

### Team

António M. Mendes	Post-Doc Fellowship, iMM
Maria M. Mota	Group Leader, iMM
Miguel Prudêncio	Group Leader, iMM

### **Keywords / Research Areas**

Malaria, Plasmodium, Vaccines, Liver infection, Sporozoites, Cryopreservation.

### **Major Scientific Achievements**

- With the support of Fundação Luso-Americana (FLAD), ROPLAVAC ensured the maintenance of its Intellectual Property regarding a new strategy for vaccination against malaria.
- The first vaccine candidate employing ROPLAVAC's patented technology entered Phase I/IIa clinical trials.
- An effective cryopreservation method for Plasmodium sporozoites is under optimization in collaboration with the company Smartfreez.
- An in vitro system for production of Plasmodium sporozoites has been developed and published, and is currently being optimized.

### **Selected Publications**

Mendes AM, Scholzen A, Mueller AK, Khan SM, Sauerwein RW, Prudêncio M (2017). Whole Organism Pre-Erythrocytic Vaccines, In: Rodriguez A. and Mota MM. (Eds) Malaria: immune response to infection and vaccination, Springer International Publishing, Cham, Switzerland.

Azevedo R, Markovic M, Machado M, Franke-Fayard B, Mendes AM, Prudêncio M (2017). A bioluminescence method for in vitro screening of Plasmodium transmission-blocking compounds. Antimicrob. Agents Chemother. 61, 202699. (IF: 4.302, Citations: 1).

Mendes AM, Albuquerque IS, Machado M, Pissarra J, Meireles P, Prudêncio M (2017). Inhibition of Plasmodium liver infection by ivermectin. Antimicrob. Agents Chemother. 61, e02005-16. (IF: 4.302, Citations: 6).

### **Ongoing Research Projects**

Prémio BES Inovação 2013.

Fundação Luso-Americana (FLAD).

### **Invited Lectures and Seminars**

Prudêncio M. Como criar uma Start-up. JORTEC Bioquímica, Faculty of Sciences and Technology, Nova University of Lisbon, Monte de Caparica, Portugal, February 9, 2017.

Prudêncio M, Mendes A. ROPLAVAC: Revolutionizing malaria vaccination. Caixa Capital, Lisbon, Portugal, March 17, 2017.

Prudêncio M. Towards a New Malaria Vaccine. GlycoVax Workshop, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, March 20-24, 2017.

Prudêncio M. A New Approach to Malaria Vaccination. BioSAM-Biological Sciences Annual Meeting, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, April 22, 2017.

Prudêncio M, Mendes A. ROPLAVAC: Revolutionizing malaria vaccination. Makara Innovation Fund & Intellectual Property Office of Singapore, Laboratório Germano de Sousa, Lisbon, Portugal, June 14, 2017.

Prudêncio M, Mendes A. A new vaccine against malaria. Technology Transfer Office - University College London, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, September 14, 2017.

Prudêncio M, Mendes A. A New vaccine against malaria. Universal Biotech Innovation Prize 2017, Semi-Finals, Paris, France, September 8, 2017.

Prudêncio M, Mendes A. ROPLAVAC: A new vaccine against malaria. Presentation for European Investment Bank, Lisbon, Portugal, October 10, 2017.

Prudêncio M. A new vaccine against malaria. Presentation for Pagliuca Harvard Life Lab, Instituto de Medicina Molecular João Lobo Antunes, Lisbon, Portugal, November 28, 2017.

### **Communications in International Conferences**

Prudêncio M. Understanding the Liver Stage of Malaria Parasite to Enable and Accelerate the Development of a Highly Efficacious Vaccine. NIAID, Rockville, USA, August 8-9, 2017.

### **Prizes, Honours and Awards**

Semi-Finalist of the Universal Biotech Innovation Prize 2017, Paris, France.



## Patents / Prototypes

"Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine" (WO 2013156949 A1, also published as CN104302313A, EP2838554A1, US20150071966).

Provisional application (Portugal) No. 20121000030819, filed 17.04.2012.

PCT international application PCT/IB2013/053050, submitted 17.04.2013, published 24.10.2013.

Patent applications filed in Angola, Australia, Brazil, China, India, Japan, Mozambique, South Africa, United States, and European Patent (Euro-PCT), November 2014.

Patent granted in India (07.08.2015), Mozambique (17.08.2015), South Africa (23.12.2015), Japan (2015), Australia (03.02.2017) and USA (15.02.2017).

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## StemCell2MAX

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### Major Interests / Objectives

StemCell2MAX is a biotechnology spin-off from Instituto de Medicina Molecular João Lobo Antunes in the field of regenerative medicine which markets a proprietary mix of neurotrophic factors that are able to stimulate the expansion of haematopoietic stem cells (HSCs), highly improving their utility in research and potential clinical use.

StemCell2MAX markets StemCell2MAX™ Mix for HSC expansion for research use only (RUO), addressing the market for blood stem cell research products with a growing sales track record. Now, following extensive proof of concept StemCell2MAX is preparing StemCell2MAX™ Med for the clinical market. The innovation is protected in the EU, USA and Japan for stem cell maintenance, expansion or transplantation, for both research and clinical use.

### Head

Maria Brandão de Vasconcelos, MBA, StemCell2MAX, CEO and Co-founder

Filipa Matos Baptista, PhD, StemCell2MAX, CMO & Co-founder

Henrique Veiga - Fernandes, PhD, StemCell2MAX, Scientific Board Director & Co-founder, Group Leader & Board Director, iMM

Francisco Ferreira dos Santos, PhD, StemCell2MAX, Chief Scientific Officer

### Team

Henrique Veiga-Fernandes, PhD	Group Leader, iMM
Diogo Fonseca-Pereira, PhD	Post-Doc Student, Harvard T.H. Chan School of Public Health
Francisco Ferreira dos Santos, PhD	Chief Scientific Officer StemCell2MAX
Silvia Arroz-Madeira	PhD Student, iMM

### Keywords / Research Areas

Biotechnology, Cellular therapy, Hematopoietic stem cells, Cord blood expansion.

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## TechnoPhage

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### Major Interests / Objectives

TechnoPhage is an innovative biopharmaceutical company committed to the R&D of new molecules - chemical and biological - in diverse therapeutic areas, such as infection, neuroscience, and immunology. TechnoPhage's strategy is based on developing new therapeutics in early phases of R&D, with a view to then enter into collaboration deals for pre-clinical and/or clinical development. TechnoPhage is developing proprietary drug discovery products from discovery to clinical stage. The company has several patents in place and successfully developed one of its products into clinical Phase I. TechnoPhage is focused on increasing its portfolio of proprietary technologies and deriving products. This is achieved through an active R&D program and collaboration agreements with national and international pharmaceutical companies, research centers and universities across the US, Europe and Asia.

The company's laboratories are located at iMM, in Lisbon, under a scientific collaboration protocol signed by both entities. Close proximity to the renowned Santa Maria Hospital and the iMM help facilitate the creation of multidisciplinary teams essential to the process of translational medicine. Furthermore, this proximity helps to facilitate access to the necessary equipment and talent required to develop full product solutions, including direct collaboration with leading experts from the clinical fields covering the therapeutic products under development.

### Head

Miguel Garcia, PharmD, PhD, MBA, TechnoPhage, SA

### Team

Ana Isabel Guedelha da Silva Neves	MSc, Engineering	Manager
Ana Raquel Martins Barbosa	MSc	Scientist
Ana Rolo	BSc	Executive Assistant
Catarina Rodrigues Amorim	BSc	Trainee
Clara Isabel Rodrigues Leandro	MSc	Senior Scientist
Daniela Jones-Dias	PhD	Scientist
Diana Sofia Chapela Duarte Pires	MSc	PhD Student
Joana Henriques Ministro	MSc	PhD Student
João Miguel Sotinho Oliveira	PharmD	Innovation Manager
Patricia Alexandra Norte Ferreira Pinto	BSc	Technician
Pedro David Pereira Mendes Fontes	BSc	MSc Student

Rita Leitão Landeiro Vaz	MSc	PhD Student
Sofia Volker Corte-Real	PhD	R&D Director
Sónia Marina Gomes Almeida	BSc Finances	Financial Director
Soraia Rafaela Santiago de Oliveira	PhD	Senior Scientist

### Keywords // Research Areas

R&D of therapeutics for human disease, Bacteriophage therapeutics, Small domain antibodies, Zebrafish models for in vivo screening.

### Major Scientific Achievements

Based on 10 years of R&D, TechnoPhage is now in a position to bring its products to commercial stage, and is entering a new growth phase, with its first authorization to enter clinical trials (IND) cleared by the FDA in 2014 for the development of bacteriophages for the treatment of chronic ulcers (TP-102).

### Selected Publications

Neves V, Silva FA, Côrte-Real S, Castanho MARB (2016). Antibody Approaches to Treat Brain Diseases. *Trends in Biotechnology* 34(1). (IF: 11.126. Citations: 7).

Proença D, Leandro C, Garcia M, et al (2015). EC300: a phage-based, bacteriolysin-like protein with enhanced antibacterial activity against *Enterococcus faecalis*. *Appl Microbiol Biotechnol* 99(12):5137-49. (IF: 3.42, Citations: 5).

Pirnay JP, Blasdel BG, Bretaudeau L, et al (2015). Quality and Safety Requirements for Sustainable Phage Therapy Products. *Pharm Res* 32(7):2173-9. (IF: 3.002, Citations: 24).

Proença D, Velours C, Leandro C, et al (2015). A two-component, multimeric endolysin encoded by a single gene. *Molecular Microbiology* 95(5), 739–753. (IF: 3.898, Citations:--).

### Ongoing Research Projects

Current projects are focused in inflammatory, neurological, infectious and rare diseases.

### Patents // Prototypes

Several patentes in National Phases, PCTs and provisionals.