

# **INSTITUTO DE MEDICINA MOLECULAR**

FACULDADE DE MEDICINA DA  
UNIVERSIDADE DE LISBOA

## **Scientific Report 2014**

Lisbon, March 2015

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## STRUCTURE AND ORGANISATION

Research and development in the Biomedical Sciences plays a central role in generating knowledge and in the application of this knowledge to improving the quality of life. ***The mission of the Institute of Molecular Medicine (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 5 former research units from the FMUL: the Biology and Molecular Pathology Centre, the Lisbon Neurosciences Centre, the Microcirculation and Vascular Pathobiology Centre, the Gastroenterology Centre and the Nutrition and Metabolism Centre. 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 associate members and meets at least once per year to analyse the scientific and finance report and to approve the plan of activities and budget for the next year.

### **Board of Directors**

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

M. Carmo-Fonseca, MD, PhD (President)  
Maria M. Mota, PhD (Executive Director)  
Bruno Silva-Santos, PhD (Vice-Director)

### **Administration Board**

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

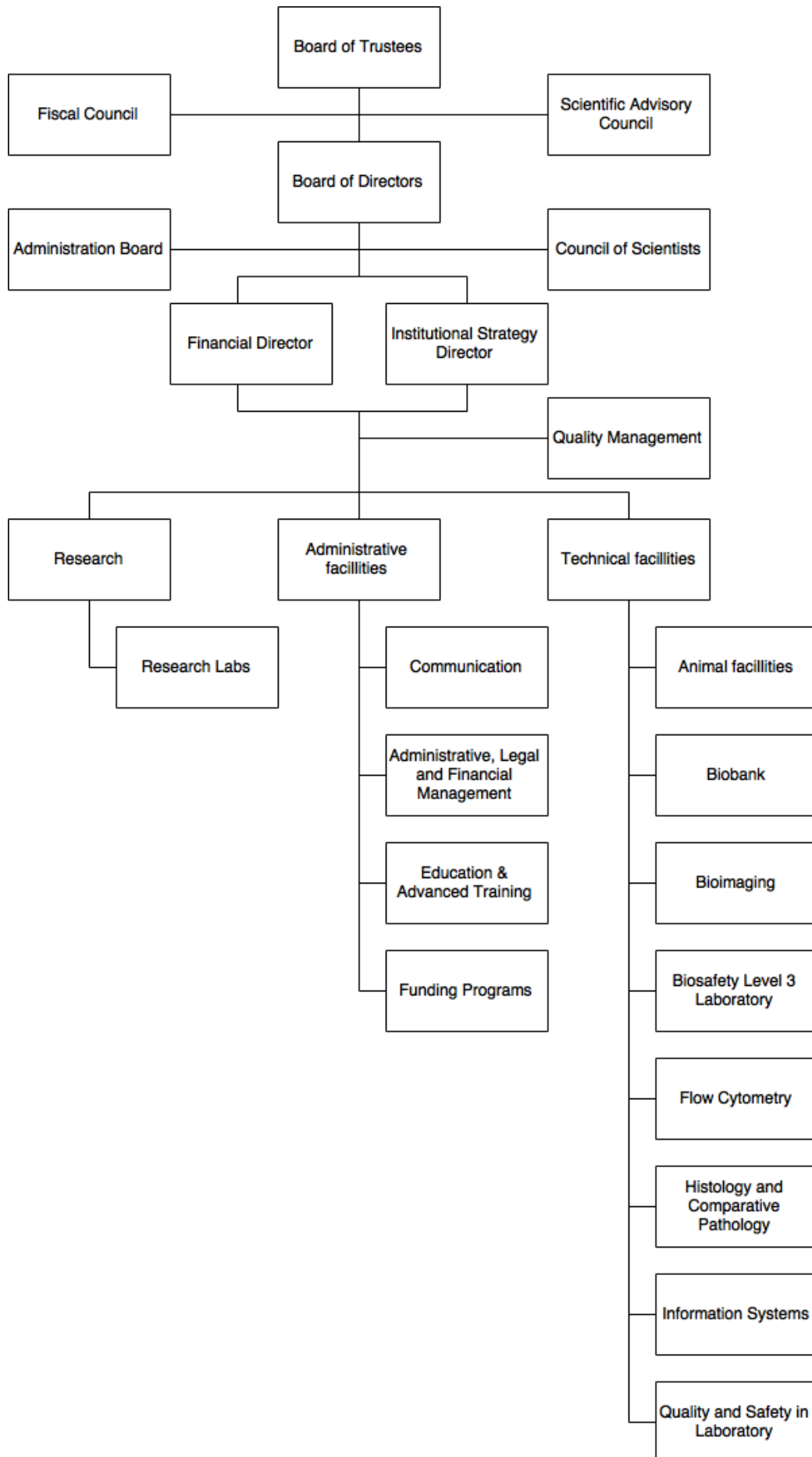
### **Council of Scientists**

The Council of Scientists is composed by all Principal Investigators. 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 Council**

Undertake periodic evaluations to the IMM specific programmes and include international experts of scientific fields analysed:

- **Carlos Caldas**, MD, PhD (Cambridge Cancer Centre, UK);
- **Gustave Moonen**, MD, PhD (Université de Liège, Belgium);
- **Paul Peter Tak**, MD, PhD (University of Amsterdam, Netherlands);
- **Philippe Sansonetti**, MD, PhD (Pasteur Institute, France);
- **Maria da Graça Carvalho** (European Parliament)



## EVALUATION REPORTS 2014

### 2013 Evaluation of FCT Research and Development Units

#### 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):

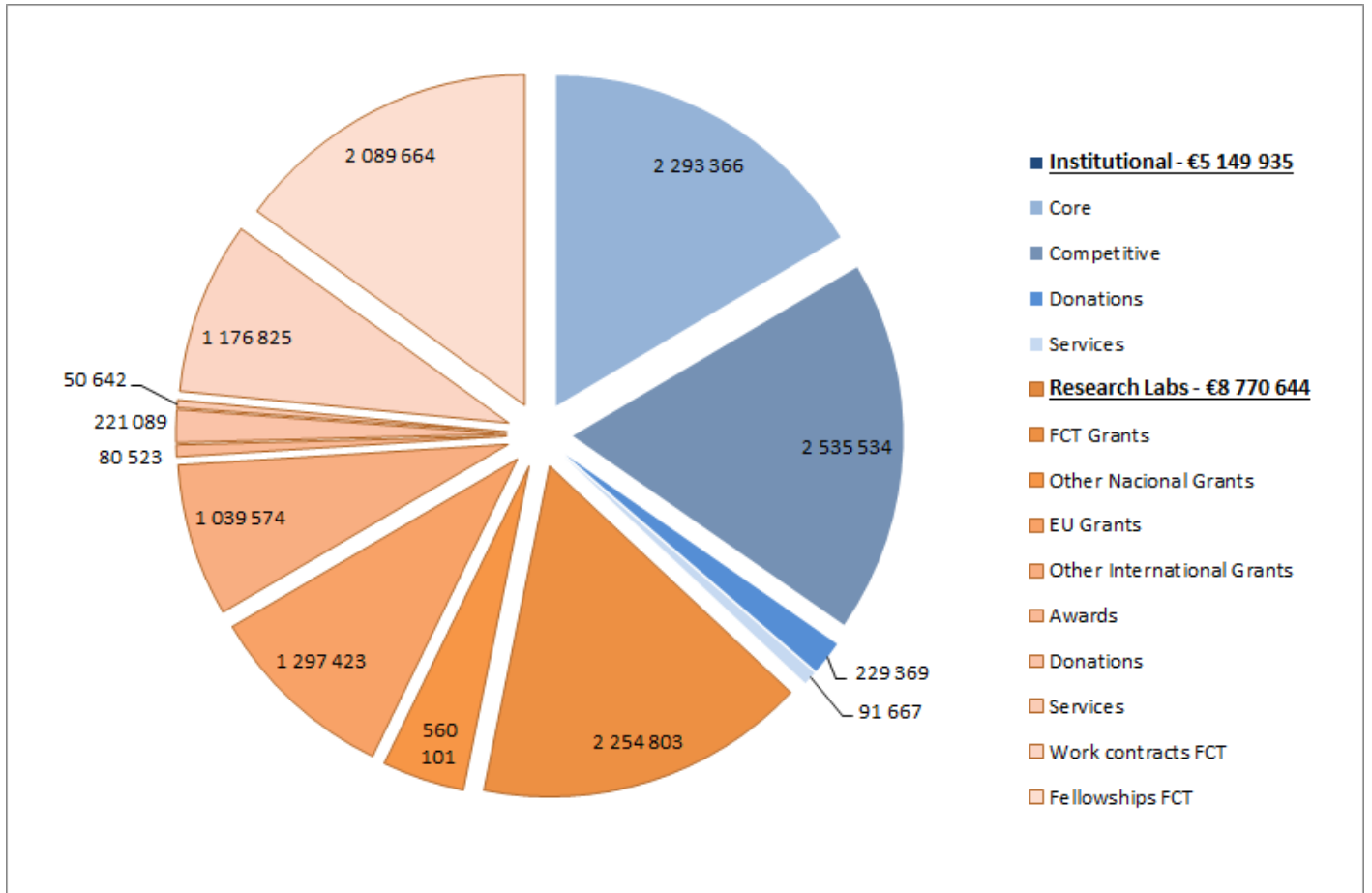
The site visit confirmed to a large extent the conclusions of the initial assessment that the unit has an excellent overall standing. It pointed out to some insufficiencies in the scientific output of a significant fraction of the integrated members listed in the initial application, and in the intensity 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. Dr 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. 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.



## RESEARCH FUNDING

### Expenditure in 2014 by Funding Source

Total Expenditure: 13.920.579 €

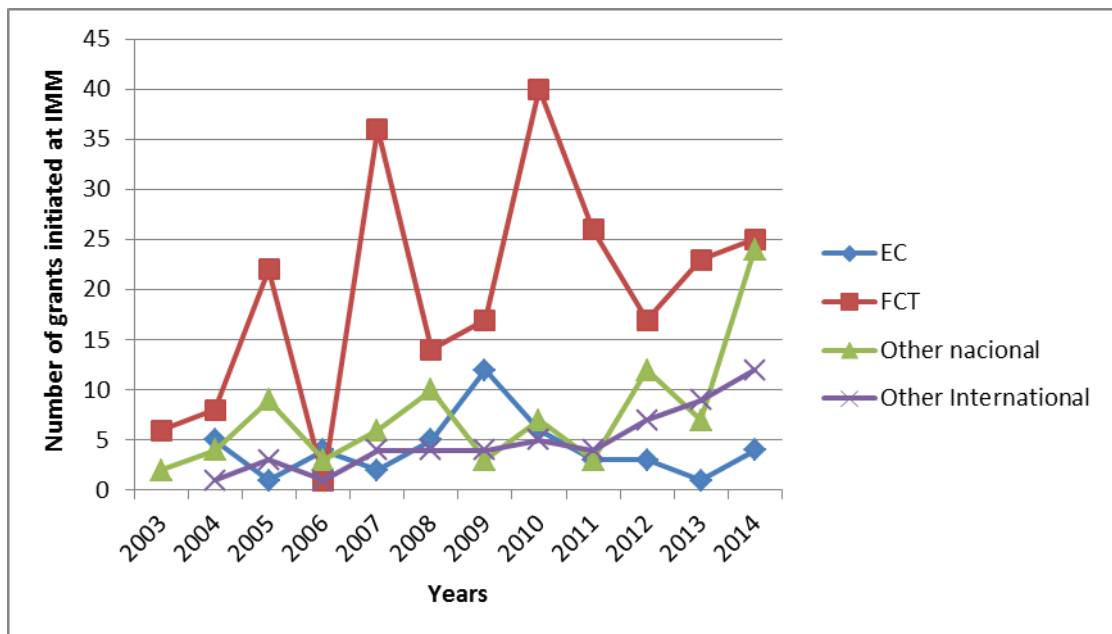


## Number of Ongoing Research Grants in 2014

### 331 Research Grants:

- Public National FCT - 114
- Public Other National - others - 8
- Public European Commission - 16
- Private National – 147
  - of which, with the industry - 53
- Private International – 46
  - of which, with the industry - 11

## Number of Research Grants initiated at IMM from 2003 to 2014



## Research Funding Initiated in 2014

### Research Grants (65)

- European Commission – 4
- Other International – 12
- FCT – 25
- Other National - 24

Agency	Researcher	IMM Budget (€)
Associação Laço	Diana Gaspar	25.000,00
Associação Portuguesa Contra a Leucemia	Haakan Norell	40.000,00
BIAL	Maria José Diógenes	49.000,00
Cell2B	João Eurico Fonseca	30.000,00
Crohn's & Colitis Foundation of America	Henrique Veiga-Fernandes	254.277,00
EMBO	Edgar Gomes	150.000,00
European Comission	Edgar Gomes	1.968.000,00
European Comission	Gonçalo Bernardes	100.000,00
European Comission	Henrique Veiga-Fernandes	149.885,00
Fundação para a Ciência e a Tecnologia	Alexandre Mendonça	125.000,00
Fundação para a Ciência e a Tecnologia	Ana Filipa Cruz	50.000,00
Fundação para a Ciência e a Tecnologia	Ana Salomé Veiga	129.209,00
Fundação para a Ciência e a Tecnologia	Ana Sofia Oliveira	89.300,00
Fundação para a Ciência e a Tecnologia	Arlindo Ferreira	100.000,00
Fundação para a Ciência e a Tecnologia	Cláudio Franco	48.488,00
Fundação para a Ciência e a Tecnologia	Daniel Carapau	50.000,00
Fundação para a Ciência e a Tecnologia	Haakan Norell	50.000,00
Fundação para a Ciência e a Tecnologia	Joaquim Ferreira	151.686,00
Fundação para a Ciência e a Tecnologia	Joaquim Ferreira	130.000,00
Fundação para a Ciência e a Tecnologia	Joaquim Ferreira	110.000,00
Fundação para a Ciência e a Tecnologia	Julie Ribot	50.000,00
Fundação para a Ciência e a Tecnologia	Kirsten Hanson	50.000,00
Fundação para a Ciência e a Tecnologia	Luís Costa	20.049,00
Fundação para a Ciência e a Tecnologia	Maria Carmo Fonseca	200.000,00
Fundação para a Ciência e a Tecnologia	Maria José Diógenes	50.000,00
Fundação para a Ciência e a Tecnologia	Marta Sofia Martins	37.700,00
Fundação para a Ciência e a Tecnologia	Miguel Castanho	99.000,00
Fundação para a Ciência e a Tecnologia	Russel Foxall	50.312,00
Fundação para a Ciência e a Tecnologia	Sales Ibiza	35.000,00
Fundação para a Ciência e a Tecnologia	Sandra Martins	49.500,00
Fundació Privada Per La Recerca Il·la Doència	Domingos Henrique	6.000,00
Hovione	Gonçalo Bernardes	93.158,07
Liga Portuguesa contra o cancro	Sandra Casimiro	10.000,00
Merck SA	Luís Costa	19.734,00
Neuropore Therapies	Miguel Castanho	20.000,00
Pfizer	Helena Canhão	40.000,00
The European Calcified Tissue Society	João Eurico-Fonseca	100.000,00

UCB Pharma , Lda	João Eurico-Fonseca	51.350,00
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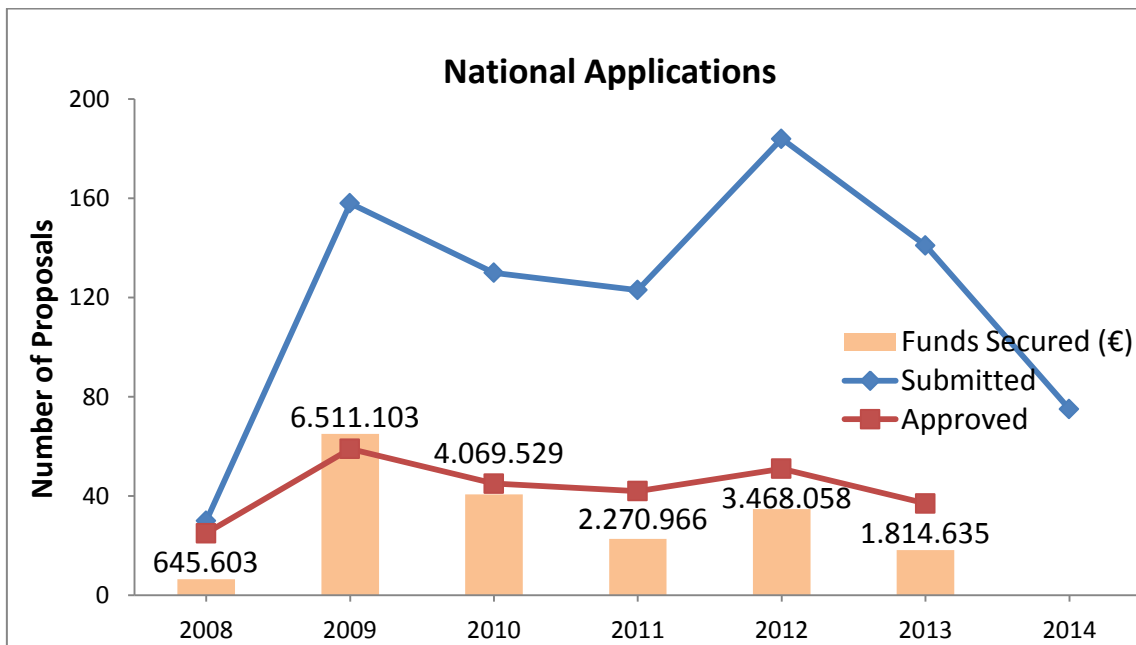
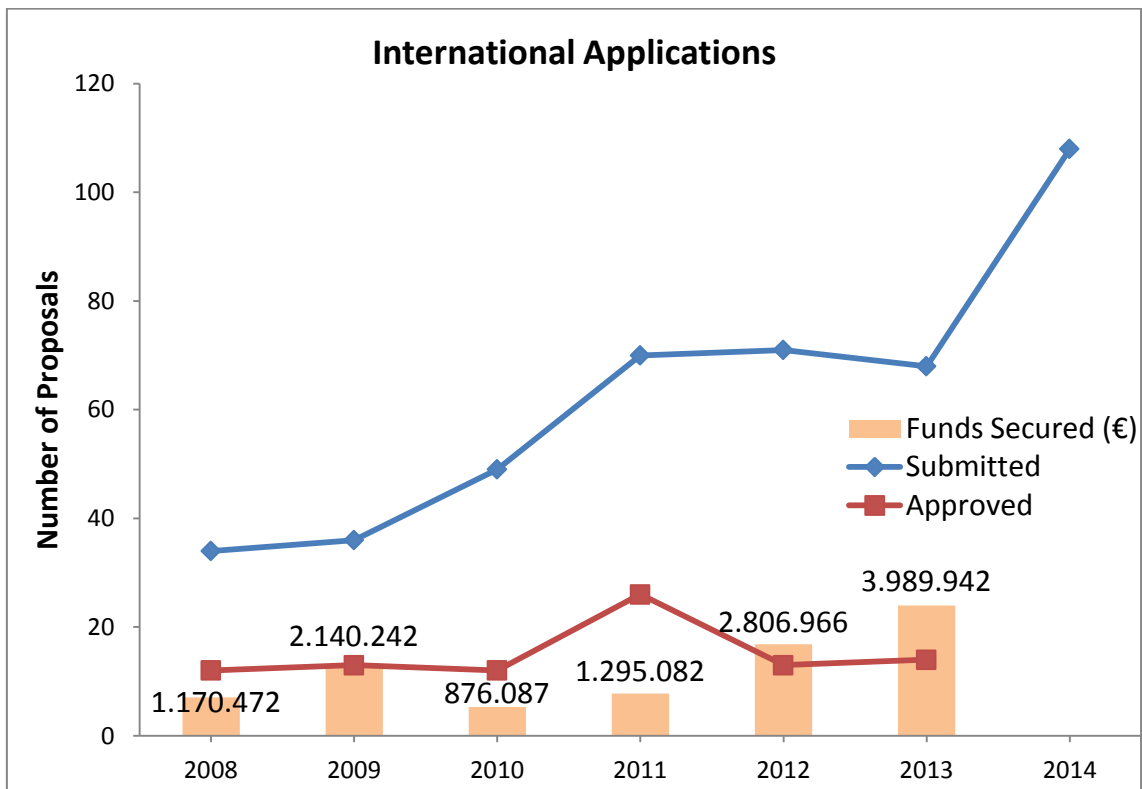
### **Protocols, Donations & Awards**

<b>Agency</b>	<b>Researcher</b>	<b>IMM Budget (€)</b>
Bayer	José Ferro	6.000,00
Eli Lilly SA	João Eurico Fonseca	5.000,00
Bristol-Myers Squibb	Bruno Silva Santos	10.000,00
EMBO	Luísa Figueiredo	8.000,00
Ana Paula Costa	Alexandre Mendonça	10.000,00
Novartis	Biobanco	5.000,00
AIDFM/Gulbenkian	Catarina Vale	2.000,00
AIDFM/Gulbenkian	Marta Bento	500,00
Centre for Experimental Medicine and Rheumatology	João Eurico Fonseca	2.235,35
Biogen Idec	José Ferro	5.000,00
Liga Portuguesa Contra o Cancro	Biobanco	9.600,00
Celgene	João Lacerda	25.000,00
Novartis Farma, S.A.	João Lacerda	2.500,00
Celgene	João Lacerda	2.500,00
EMBO	Sales Ibiza	500,00
Bristol-Myers Squibb	Bruno Silva Santos	3.000,00
Medtronic	Joaquim Ferreira	8.000,00

### **Special Projects**

<b>Agency</b>	<b>Researcher</b>	<b>IMM Budget (€)</b>
Fundação para a Ciência e a Tecnologia	UEFA	25.000,00
Fundação para a Ciência e a Tecnologia	Gonçalo Bernardes	50.000,00
European Comission	UEFA	468.280,20
Fundação para a Ciência e a Tecnologia	IMM	189.663,00
Fundação para a Ciência e a Tecnologia	Ana Fragoso	50.000,00
Fundação para a Ciência e a Tecnologia	Miguel Remondes	50.000,00
Fundação para a Ciência e a Tecnologia	Edgar Gomes	50.000,00
European Comission	Ana E. Sousa	645,55

## Number of IMM Grant Applications and Secured Funding



**Figure 1.** Total number of IMM grant applications submitted, approved, and amount of competitive funding secured per year since 2008, for international and national funding. The data rely on the registration of the funding applications received by the Funding Programs Office. Funds secured correspond to the sum of the IMM budget of the approved grants submitted in the corresponding year (still unknown regarding 2014 submissions).

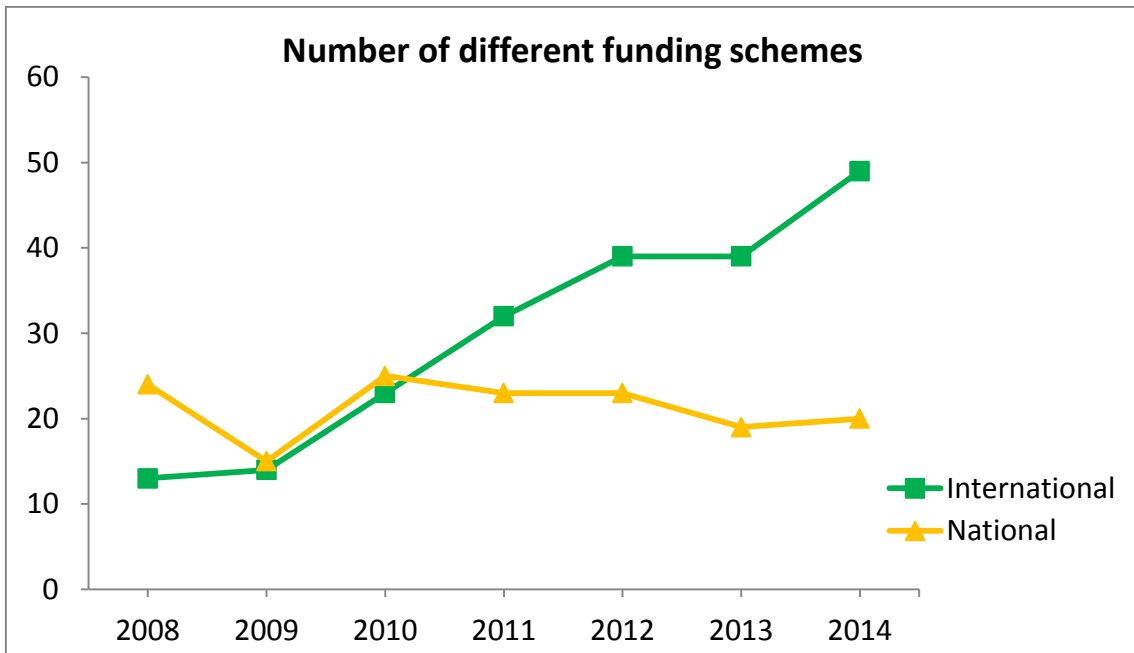
## Diversity of Funding Sources of IMM Grant Applications

In 2014, IMM researchers have submitted grants to the following funding schemes:

International	
Public	Private
ERA-Net E-Rare	Alzheimer's Association - New Investigator Research Grant (NIRG)
ERA-Net EuroNanoMed II	American Society for Bone and Mineral Research (ASBMR)
ERA-Net Infect-ERA	Axa Reserach Fund Post-doctoral Fellowship
ERA-Net Neuron II	Brain & Behavior Research Foundation (NARSAD Grants)
ERA-Net TRANSCAN	Bristol-Myers Squibb - The Partnering for Cure Programme
EU Joint Programme – Neurodegenerative Disease Research (JPND)	EMD Serono - Grant for Oncology Innovation
European Cooperation in Science and Technology (COST)	European Calcified Tissue Society - ECTS/AMGEN Bone Biology Fellowship
European Institute of Innovation and Technology (EIT) - Innovation for healthy living and active ageing	European Society for Organ Transplantation (ESOT) Junior Basic Science Research Grant
European Research Council (ERC) Advanced	European Hematology Association (EHA) - Non-Clinical Advanced Research Fellowships
European Research Council (ERC) Consolidator	Everis Foundation Entrepreneurs Award
European Research Council (ERC) Proof of Concept	Fondation Acteria - Prizes Awarded by EFIS
European Research Council (ERC) Starting	International Foundation for Research in Paraplegia
European Molecular Biology Organization (EMBO) Installation Grant	International Obsessive Compulsive Disorder Foundation
European Molecular Biology Organization (EMBO) Long-Term Fellowship	Kenneth Rainin Foundation Synergy Award
European Molecular Biology Organization (EMBO) Short-Term Fellowship	Lung Cancer Research Foundation
Horizon 2020 - Health, demographic change and wellbeing - Personalising Health and Care (PHC)	Medicines for Malaria Venture
Horizon 2020 - Leadership in enabling and industrial technologies - Information and Communications Technologies (ICT)	Mizutani Foundation for Glycoscience
Horizon 2020 - Marie-Sklodowska-Curie Actions - Individual Fellowships (IF)	Muscular Dystrophy Association
Horizon 2020 - Marie-Sklodowska-Curie Actions - Innovative Training Networks (ITN)	Parkinson's Disease Foundation
Horizon 2020 - Marie-Sklodowska-Curie Actions - Research and Innovation Staff Exchange (RISE)	Parkinson's UK

Horizon 2020 - Spreading Excellence and Widening Participation - ERA Chairs	Susan G. Komen - Career Catalyst Research Grant
Horizon 2020 - Spreading Excellence and Widening Participation - Teaming	Worldwide Cancer Research
Human Frontier Science Program (HFSP) Program Grant	
Human Frontier Science Program (HFSP) Young Investigators Grant	
Innovative Medicines Initiative (IMI)	
MIT Portugal Program - Testbed Proposals	
National Institutes of Health (NIH)	

National	
Public	Private
FCT-Argentina Bilateral Cooperation	Associação Laço - Laço Breast Cancer Grant
FCT Carnegie Mellon Portugal Programme	Associação Portuguesa contra a leucemia
FCT-DAAD Bilateral Cooperation	Associação Portuguesa Contra a Leucemia/Fundação Calouste Gulbenkian - Programa de Formação Avançada em Hemato-Oncologia
FCT-FAPESP Bilateral Cooperation	BIAL Foundation - Bursaries for Scientific Research
FCT Investigator Programme	Calouste Gulbenkian Foundation
FCT PhD Programme	Janssen-Cilag Farmacêutica - Prémios Janssen Virologia
FCT-Programa PESSOA Bilateral Cooperation	Liga Portuguesa Contra o Cancro (Bolsas LPCC-NRS-Terry Fox)
Santa Casa da Misericórdia - Prémio Neurociências	Luso-American Foundation (FLAD) - Bolsas PAPERS
	Luso-American Foundation (FLAD) - FLAD Life Science 2020
	Maratona da Saúde Association - Awards for Cancer Research
	Programa Gilead GÉNESE
	Sociedade das Ciências Médicas de Lisboa (SCML)/Laboratórios Pfizer - Pfizer Awards in Basic and Clinical Research



**Figure 2.** Diversity of international and national funding schemes of IMM grant applications, since 2008.



## 2014 IMM ACTIVITIES HIGHLIGHTS

### People in 2014

<b>Researchers</b>		<b>496</b>
	PhD researchers	202
	PhD Students	82
	M.Sc researchers	61
	Bachelor researchers	137
	Other	14
<b>Technical staff</b>		<b>97</b>
	PhD staff	7
	M.Sc staff	29
	Bachelor staff	44
	Non-Bachelor staff	17
<b>Administrative staff</b>		<b>24</b>
	PhD staff	3
	M.Sc staff	2
	Bachelor staff	14
	Non-Bachelor staff	5
<b>Total</b>		<b>617</b>

### Selection of Prizes and Awards

**Prémio Bayer:** José Ferro

**MindtheGap:** Post-Doctoral Training

**GlycoPar –Parasite Glycobiology and Anti-Parasitic Strategies:** João Rodrigues

**JPND – EU Joint Programme on Neurodegenerative Disease Research – Mamede de Carvalho**

**HIVera Projecto No âmbito do programa Europeu ERA-NET – HIVERA "European Research Projects on AIDS / HIV":** Coordinated by Miguel Castanho

**ERC Proof of Concept:** Henrique Veiga-Fernandes

**Marie Curie Career Integration Grant (European Union):** Gonçalo Bernardes and Diana Prata

**ECTS/Amgen Bone Biology Fellowship:** Bruno Vidal

**VIH FCT:** Salomé Veiga

**Bolsa Laço:** Diana Gaspar

**Prémio Pessoa 2013:** Maria M. Mota

**Senior Research Award (SRA) atribuído pela Crohn's & Colitis Foundation of America's (CCFA):** Henrique Veiga-Fernandes

**EMBO Installation Grant:** Edgar Gomes

**ERC – PhONICs** European Research Council (ERC) Consolidator Grant: Edgar Gomes

**Associação Portuguesa Contra a Leucemia (APCL):** Håkan Norell

**Kenneth Rainin Foundation (KRF) Breakthrough Award:** Henrique Veiga-Fernandes

**Horizonte 2020 – TREGeneration:** João Lacerda

**Innovative peptides against cancer and pathogenic bacteria (INPACT) :** Miguel Castanho

**Prémios Pfizer:** João Barata won on the clinical research category while Henrique Veiga-Fernandes had his award on the basic research category.

**EMBO Installation Grants :** Nuno Morais

**FCT Investigators:** Vanessa Morais, Nuno Morais, Diana Prata, Julie Ribot, Karine Serre, Bruno Bernardes, Ana Rita Grosso, Marta Martins, Luisa Figueiredo and Simão Rocha

**Liga Portuguesa contra o cancro /Terry Fox:** Sandra Casimiro

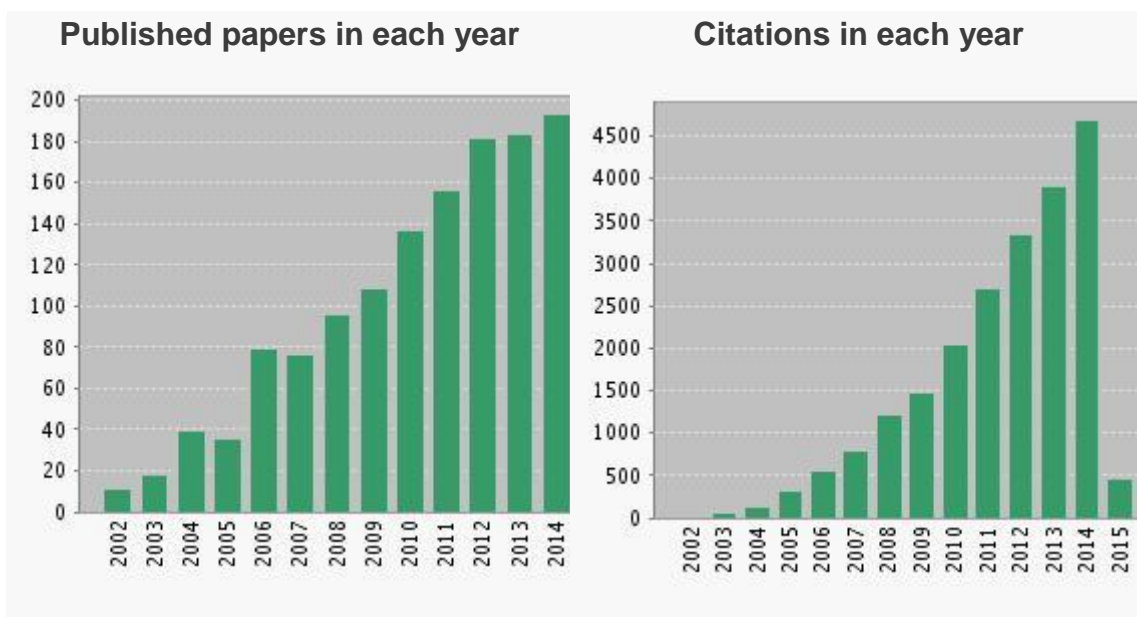
### Productivity at a glance

Publications International Journals	193
...in journals with an impact factor higher than 10	29
...in journals with an impact factor between 5 – 10	72
Book/Book Chapters International	20
Communications in International Conferences	286
Communications in National Conferences	210
Seminars and Invited Lectures	260
Organization of Conferences	59
Prizes	46
PhD Theses	17
Master Theses	58

## IMM PUBLICATIONS IN INTERNATIONAL JOURNALS

### Citation Report

(Source: ISI Web of Knowledge - Web of Science®)



**193** papers in 2014

**1.316** since 2002

Sum of the Times Cited: **21699**

Average Citations per Item: **16.49**

h-index : **64**

Query: AD=(Inst Med Mol SAME Portugal) OR AD=(Mol Med Inst SAME Portugal) OR AD=(Inst Mol Med SAME Portugal)

Refined by: ( Excluding) Document Type=( REVIEW OR EDITORIAL OR CORRECTION OR ABSTRACT OR MEETING OR BOOK )

Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, 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 2002-2014

Emre, Murat; Aarsland, Dag; Brown, Richard; et al. (2007) Clinical diagnostic criteria for dementia associated with Parkinson's disease. *MOVEMENT DISORDERS* . **22**, (12 ) 1689-1707 (Citation: 604) ( Journal IF: 5.63)

Healy, Daniel G.; Falchi, Mario; O'Sullivan, Sean S.; 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 (Citation: 346) (Journal IF: 21.66)

Fearon, Kenneth; Strasser, Florian; Anker, Stefan D.; et al. (2011) Definition and classification of cancer cachexia: an international consensus. *LANCET ONCOLOGY* . **12**, (5) 489-495 (CITATION: 319) (JOURNAL IF: 24.72)

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 (CITATION: 288) (JOURNAL IF: 5.36)

Duarte, A; Hirashima, M; Benedito, R; et al. (2004) Dosage-sensitive requirement for mouse D114 in artery development. *GENES & DEVELOPMENT* . **18** (20) 2474-2478 (Citation: 274) (Journal IF: 12.63)

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 (Citation: 273) (Journal IF: 39.20)

Ribeiro, JA; Sebastiao, AM; de Mendonca, A. (2002) Adenosine receptors in the nervous system: pathophysiological implications. *PROGRESS IN NEUROBIOLOGY* . **68** (6) 377-392 (Citation: 269) (Journal IF: 10.30)

Henry, David H.; Costa, Luis; Goldwasser, Francois; 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 (Citation: 260) (Journal IF: 17.96)

Ratziu, Vlad; Bellentani, Stefano; Cortez-Pinto, Helena; et al. (2010) A position statement on NAFLD/NASH based on the EASL 2009 special conference. *JOURNAL OF HEPATOLOGY* ,**53** (2) 372-384 (Citation: 231) (Journal IF: 10.40)

Santos, NC; Figueira-Coelho, J; Martins-Silva, J; et al. (2003) Multidisciplinary utilization of dimethyl sulfoxide: pharmacological, cellular, and molecular aspects. *BIOCHEMICAL PHARMACOLOGY* , **65** (7) 1035-1041 (Citation: 218) (Journal IF: 4.65)

## MOST RELEVANT PAPERS 2014 (JOURNAL IF > 10)

Cunha C, Aversa F, Lacerda, JF, Busca A, Kurzai O, Grube M, Löffler J, Maertens JA, Bell AS, Inforzato A, Barbati E, Almeida B, Sousa PS, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano L, Luppi M, Montovani 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):421-32. doi: 10.1056/NEJMoa1211161. (Journal IF: 54.42, Citation: 10)

Gonçalves MJ, Romão VC. Images in clinical medicine. (2014) Saber tibia in Paget's disease of bone. *N Engl J Med.* **18**, 371(25):2417. (Journal IF: 54.420, Citations: 0)

van de Pavert, S.A., Ferreira, M., Domingues, R.G., Ribeiro, H., Molenaar R., Moreira-Santos L., Almeida, F.F., Ibiza, S., Barbosa I., Goverse, G., Labão-Almeida C., Godinho-Silva, C., Konijn, T., Schooneman, D., O'Toole, T., Mizee, M.R., Habani, Y., Haak. E., Santori F.R., Littman D.R., Schulte-Merker S., Dzierzak, E., Simas, J.P., E. Mebius, R., Veiga-Fernandes, H. (2014). (2014) Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. *Nature* **508**, 123-127. <http://www.nature.com/nature/journal/v508/n7494/full/nature13158.html>. (Journal IF: 42.351, Citations: 12)

Fonseca-Pereira, D., Arroz-Madeira, S., Rodrigues-Campos M., Barbosa I. A., Domingues R. G., Bento T., Almeida A. R., Ribeiro H., Potocnik A. J., Enomoto H., Veiga-Fernandes H. (2014) The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function. *Nature* **214**, 98–101. <http://www.nature.com/nature/journal/v514/n7520/full/nature13498.html>. (Journal IF: 42.351, Citations: 0)

Munafò M, Noble S, Bowne WJ, Brunner D, Button K, Ferreira J, Holmans P, Langbehn D, Lewis G, Lindquist M, Tilling K, Wagenmakers EJ, Blumesstein R, (2014) Scientific rigor and the art of motorcycle maintenance. *Nature Biotechnology* **32**(9), 871-873. (Journal IF: 39.080, Citations: 0)

Klose C.S., Flach M., Möhle L., Rogell L., Hoyler T., Ebert K., Fabiunke C., Pfeifer D., Sexl V., Fonseca-Pereira D., Domingues R.G., Veiga-Fernandes H., Arnold S.J., Busslinger M., Dunay I.R., Tanriver Y., Diefenbach A. (2014) Differentiation of type 1 ILCs from a common progenitor to all helper-like innate lymphoid cell lineages. *Cell* **157**, 340-356. <http://www.sciencedirect.com/science/article/pii/S009286741400405X>. (Journal IF: 33.116, Citations: 20)

Shimanovich U, Bernardes GJL\*, Knowles TJ, Cavaco-Paulo A (2014) Protein Micro and Nano Capsules for Biomedical Applications.. *Chem. Soc. Rev* **43**, 1361. (Journal IF: 30.425, Citations: 4)

Hauser CA, Maurer-Stroh S, Martins IC (2014) Amyloid-Based Nanosensors and Nanodevices. *Chem. Soc. Rev.*, **43**, 5326-5345. (Journal IF: 30.425, citations: 5)

Fernandes R, Hartling L, (2014), Glucocorticoids for Acute Viral Bronchiolitis in Infants and Young children, *Jama*, **311**(1): 87-88. (Journal IF: 29.978, Citations: 0)

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** (1), 47-53. (Journal IF: 28.05, Citations: 7)

Costa L (2014) Which bisphosphonate to treat bone metastases?. *Lancet Oncology* **15**, 16. (Journal IF: 24.725, Citations: 0)

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. Nat Cell Biol. 2014 Apr;16(4):309-21. doi: 10.1038/ncb2926. Epub 2014 Mar 23. (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>. (Journal IF: 20, Citations: 23)

Hänscheid T, Rebelo M, Grobusch MP. 2014. Point-of-care tests: where is the point? *Lancet Infect Dis* **14**, 922. (Journal IF:19.446, Citation: 0)

Vaz-Luis I, Ottesen RA, Hughes ME et al. (2014) Outcomes by Tumor Subtype and Treatment Pattern in Women With Small, Node-Negative Breast Cancer: A Multi-Institutional Study. *JCO*, **32**(20): 2142 (Journal IF: 17.96 Citations: 3)

Vaz-Luis I, Keating NL, Lin NU, Lii HC, Winer EP, Freedman RA (2014) Duration and Toxicity of Adjuvant Trastuzumab in Older Patients With Early-Stage Breast Cancer: A Population-Based Study. *JCO*, **32**(9): 927 (Journal IF: 17.96 Citations: 3)

Bocchetta M, Galluzzi S, Kehoe PG, Aguera E, Bernabei R, Bullock R, Ceccaldi M; Dartigues J-F, de Mendonça A, Didic M, Eriksdotter M, Félician O, Frölich L, Gertz H-J, Hallikainen M, Hasselbalch SG, Hausner L, Heuser I; Jessen F, Jones RW, Kurz A, Lawlor B, Lleo AB, Martinez-Lage P, Mecocci P, Mehrabian S, Monsch A, Nobili F, Nordberg A, Rikkert MO, Orgogozo J-M, Pasquier F, Peters O, Salmon E, Sánchez-Castellano C, Santana I, Sarazin M, Traykov L, Tsolaki M, Visser PJ, Wallin ÅK; Wilcock G, Wilkinson D, Wolf H, Yener G, Zekry D, Frisoni GB. (2014) The Use of Biomarkers for the Etiologic Diagnosis of MCI in Europe: an EADC Survey. *Alzheimers Dement* (Journal IF: 17.472, Citations: 1)

Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, Prieto-Merino D, Dehghan A, Trompet S, Wong A, Cavadino A, Drogan D, Padmanabhan S, Li S, Yesupriya A, Leusink M, Sundstrom J, Hubacek JA, Pikhart H, Swerdlow DI, Panayiotou AG, Borinskaya SA, Finan C, Shah S, Kuchenbaecker KB, Shah T, Engmann J, Folkersen L, Eriksson P, Ricceri F, Melander O, Sacerdote C, Gamble DM, Rayaprolu S, Ross OA, McLachlan S, Vikhireva O, Sluijs I, Scott RA, Adamkova V, Flicker L, Bockxmeer FM, Power C, Marques-Vidal P, Meade T, Marmot MG, Ferro JM, Paulos-Pinheiro S, Humphries SE, Talmud PJ, Mateo Leach I, Verweij N, Linneberg A, Skaaby T, Doevendans PA, Cramer MJ, van der Harst P, Klungel OH, Dowling NF, Dominiczak AF, Kumari M, Nicolaidis AN, Weikert C, Boeing H, Ebrahim S, Gaunt TR, Price JF, Lannfelt L, Peasey A, Kubinova R, Pajak A, Malyutina S, Voevoda MI, Tamosiunas A, Maitland-van der Zee

AH, Norman PE, Hankey GJ, Bergmann MM, Hofman A, Franco OH, Cooper J, Palmen J, Spiering W, de Jong PA, Kuh D, Hardy R, Uitterlinden AG, Ikram MA, Ford I, Hyppönen E, Almeida OP, Wareham NJ, Khaw KT, Hamsten A, Husemoen LL, Tjønneland A, Tolstrup JS, Rimm E, Beulens JW, Verschuren WM, Onland-Moret NC, Hofker MH, Wannamethee SG, Whincup PH, Morris R, Vicente AM, Watkins H, Farrall M, Jukema JW, Meschia J, Cupples LA, Sharp SJ, Fornage M, Kooperberg C, LaCroix AZ, Dai JY, Lanktree MB, Siscovick DS, Jorgenson E, Spring B, Coresh J, Li YR, Buxbaum SG, Schreiner PJ, Ellison RC, Tsai MY, Patel SR, Redline S, Johnson AD, Hoogeveen RC, Hakonarson H, Rotter JI, Boerwinkle E, de Bakker PI, Kivimaki M, Asselbergs FW, Sattar N, Lawlor DA, Whittaker J, Davey Smith G, Mukamal K, Psaty BM, Wilson JG, Lange LA, Hamidovic A, Hingorani AD, Nordestgaard BG, Bobak M, Leon DA, Langenberg C, Palmer TM, Reiner AP, Keating BJ, Dudbridge F, Casas JP; InterAct Consortium. (2014) Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. *BMJ* **349**, G4164. (Journal IF: 16.378, Citations: 4)

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 ahead of print] . (Journal IF: 15.7, Citations: NA)

Hill DLG, Scharwz AJ, Isaac M, Pani L, Vamvakas S, Hemmings R, Carrillo MC, Yu P, Sun J, Beckett L, Boccardi M, Brewer J, Brumfield M, Cantillon M, Cole PE, Fox N, Frisoni GB, Jack C, Kelleher T, Luo F, Novak G, MAguite P, Meibach R, Patterson P, Bain L, Sampaio C, Raunig D, Soares H, Suhy J, Wang HL, Wolz R, Stephenson D, (2014), Coalition against major diseases/European medicines agency biomarker qualification of hippocampal volume for enrichment of clinical trials in predementia stages of Alzheimer' disease. *Alzheimer's and Dementia*, **10**, 4: 421-429. (Journal IF: 14.472; Citations: 1)

Caldeira D, Barra M, Santos AT, de Abreu D, Pinto FJ, Ferreira JJ, Costa J, (2014), Risk of drug-induced liver injury with the new oral anticoagulants: systematic review and meta-analysis. *Heart*, **100**(7):550-6. (Journal IF: 13.857; Citations: 2)

Cruz-Oliveira C, Freire JM, Conceição TM, Higa LM, Castanho MARB, and Da Poian AT. (2014) Receptors and routes of dengue virus entry into the host cells. *FEMS Microbiol. Rev.* **1-19**. doi:10.1093/femsre/fuu004 (Journal IF: 13.81, Citations: 0)

Cal PMSD, Bernardes GJL\*, Gois PMP (2014) Cysteine Selective Reactions for Antibody Conjugation. *Angew. Chem. Int. Ed.* **53**, 10585. (Journal IF: 11.336, Citations: 2)

Tsuji S, Stein L, Kamada N, Nuñez G, Bram R, Vallance BA, Sousa AE, Platt JL, Cascalho M. (2014) TACI deficiency enhances antibody avidity and clearance of an intestinal pathogen. *J Clin Invest.* **124**:4857-66. (Journal IF: 13.765).

García-Gallego S, Bernardes GJL\* (2014) Carbon-monoxide releasing molecules for the delivery of therapeutic CO in vivo. *Angew. Chem. Int. Ed.* **53**, 9712. (Journal IF: 11.336, Citations: 4)

Krall N, Pretto F, Decurtins W, Bernardes GJL, Supuran CT, Neri D (2014) A Small Molecule Drug Conjugate for the Treatment of Carbonic Anhydrase IX Expressing Tumors. *Angew. Chem. Int. Ed.* **53**, 4231. (Journal IF: 11.336, Citations: 11)

Marciano BE, Huang C, Joshi G, Rezaei N, Carvalho BC, Allwood Z, Ikinciogullari A, Reda SM, Gennery A, Thon V, Espinosa-Rosales F, Al-Herz W, Porras O, Shcherbina A, Szaflarska A, Kilic S, Franco JL, Gomez Raccio AC, Roxo P, Esteves I, Galal N, Grumach AS, Al-Tamemi S, Yildiran A, Orellana JC, Yamada M, Morio T, Liberatore D, Ohtsuka Y, Lau Y, Nishikomori R, Torres-Lozano C, Mazzucchelli JTL, Vilela MMS, Tavares FS, Cunha L, Pinto JA, Espinosa-Padilla SE, Hernandez-Nieto L, Elfeky RA, Ariga T, Toshio H, Dogu F, Cipe F, Formankova R, Nuñez-Nuñez ME, Bezrodnik L, Marques JG, Pereira MI, Listello V, Slatter MA, Nademi Z, Kowalczyk D, Fleisher TA, Davies G, Neven B, and Rosenzweig SD (2014). BCG vaccination in patients with severe combined immunodeficiency: Complications, risks, and vaccination policies. *J Allergy Clin Immunol* **133**, 1134-41. (Journal IF: 11,248).

Sousa T, Pinto S, Lucas S D, Moreira R, Coutinho A, Castro R E, Rodrigues C M, Prieto M and Fernandes F (2014) Interaction of apoptotic and cytoprotective bile acids with biomembranes. *Journal of Hepatology* **60** (1):S105. (Journal IF: 10.40, Citations: 0)

Mendes R.V., Martins G.G., Martins A.M. and 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. (Journal IF: 10,366, Citations: 0)



## SEMINARS AND WORKSHOP

### IMM Internal Seminar

15-01-2014

**Maria Carmo-Fonseca**, head of Lab, IMM

“Combining maths with live cell imaging to measure dynamics of single RNA molecules”

29-01-2014

**Luís Moita**, head of Lab, IMM

“Anthracyclines Induce DNA Damage Response-Mediated Protection against Severe Sepsis”

12-02-2014

**Sérgio Almeida**, head of Lab, IMM

“Chromatin dynamics and the genome integrity network”

12-03-2014

**Miguel Prudêncio**, head of Lab, IMM

“Thinking outside the species: a new vaccine against malaria”

26-03-2014

**Ana Sebastião**, head of Lab, IMM

“Control of neuronal inhibitory communication”

09-04-2014

**Iris Caramalho**, Ana Espada de Sousa Lab, IMM

“Regulating the development of the regulators”

16-04-2014

**Bruno Silva-Santos**, head of lab, IMM

"Differentiation and pro-inflammatory functions of gamma-delta T cells"

23-04-2014

**Miguel Castanho**, head of lab, IMM

"From analgesia to Alzheimer's: The neuropeptide kyotorphin in nature and pharmacology"

07-05-2014

**Pedro Simas**, head of lab, IMM

“Structural-based viral pathogenesis”

21-05-2014

**Sérgio Dias**, head of lab, IMM

"Cholesterol and tumor progression: (our) current views"

18-06-2014

**Nuno Santos**, head of lab, IMM

"New antiviral strategies against HIV and dengue virus"

02-07-2014

**Carlota Saldanha**, head of lab, IMM

"Acetylcholine"

24-09-2014

**Several Speakers**, GenoMed, TechnoPhage e LymphAct

"Meet the Start-Up"

15-10-2014

**Miguel Remondes**, head of lab, IMM

"Brain maps for decision-making"

29-10-2014

**Cristina Pina**, PhD, Department of Haematology, University of Cambridge

"Noise, nodes and networks in haematopoietic lineage decisions"

Host: Sérgio Dias & João Barata

12-11-2014

**Ana E Sousa**, head of Lab, IMM

"Human Immune Homeostasis and Immunodeficiency"

#### Neurosciences Seminar

13-01-2014

**Haíssa de Castro**, Master Student,

Ana Sebastião Lab, IMM

"mgluR5- mediated calcium signaling: modulation by Adenosine A1 and A2A receptors in cortical astrocytes"

20-01-2014

**Gabriela Antunes**, Posdoc

Ana Sebastião Lab, IMM

"Computational systems biology in neuroscience"

27-01-2014

**Pedro Avelar**, Master Student

Ana Sebastião Lab, IMM

"Influence of Brain-Derived Neurotrophic Factor on the effect of amyloid-beta peptide upon calcium signaling in astrocytes"

10-02-2014

**Cátia Palminha**, Master Student

Ana Sebastião Lab, IMM

"Characterization of Adenosine Receptors in a Rett Syndrome Model"

24-02-2014

**Tiago Rodrigues**, MD Student

Ana Sebastião Lab, IMM

"A $\beta$  species-mediated impairment of long-term plasticity and BDNF signaling at the hippocampus"

10-03-2014

**Alexandre de Mendonça**, Professor

José Ferro Lab, IMM

"Demência de início precoce"

17-03-2014

**Diogo Rombo**

Ana Sebastião Lab, IMM

"New sights on adenosine control of excitability"

24-03-2014

**Francisco Mouro**

Ana Sebastião Lab, IMM

"Interaction between A2a receptors and CB1 receptors in the hippocampus: consequences for memory"

31-03-2014

**Monika Lezanska**

Ana Sebastião Lab, IMM

"Deciphering the role of GlyR in astrocytes"

07-04-2014

**David Pedras**, Master student

Tiago Outeiro Lab, IMM

"Alpha-synuclein phosphorylation role in Parkinson's disease"

14-04-2014

**Sofia Duarte**, PhD student

Domingos Henrique Lab, IMM

"Synaptic Dysfunction in Neurodevelopmental Disorders with Epilepsy and Autism"

28-04-2014

**Sara Xapelli**, Post-Doc

Ana Sebastião Lab, IMM

"Modulating cannabinoid receptors to induce neurogenesis and oligodendrogenesis"

05-05-2014

**Luísa Lopes**, head of Lab, IMM

"Glucocorticoid receptor involvement in age-related hippocampal dysfunction"

12-05-2014

**Filipe Nascimento**, Master

Ana Sebastião Lab, IMM

"Adenosinergic modulation at the neuromuscular junction of the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis: insights from the pre-symptomatic and symptomatic stages"

19-05-2014

**Isa Pinto**, Master student

Ana Sebastião Lab, IMM and Faculdade de Ciências da Saúde, Universidade da Beira Interior

"The role of cGMP on A1 receptor-mediated inhibition of synaptic transmission in the hippocampus"

26-05-2014

**Noémia Pereira**, Master student

Ana Sebastião Lab, IMM

"Epileptiform activity in organotypic slice cultures: electrophysiological and molecular features"

02-06-2014

**Rita Aroeira**, PhD student

Ana Sebastião Lab, IMM

"Deciphering the glycine-mediated neurotransmission in rat brain"

09-06-2014

**Ana Rita Vaz**, PhD

Neuron Glia Biology in Health and Disease

"Motoneuron degeneration and glial reactivity in ALS: insights from cellular to animal models"

16-06-2014

**Raquel Dias**

Ana Sebastião Lab, IMM

"Homeostatic Plasticity induced by Brief Activity Deprivation Enhances Long-Term Potentiation in the Mature Rat Hippocampus"

23-06-2014

**Pedro F. Jacob**, PhD Student

Department of Zoology, University of Cambridge, United Kingdom Champalimaud Neuroscience Program, Champalimaud Centre for the Unknown, Portugal

"Evolution of species-specific behaviours: analysis of the singing central pattern generator in crickets"

30-06-2014

**Hugo Miranda**, PhD

Tiago Outeiro Lab, IMM

"The sour side of Parkinson's Disease"

07-07-2014

**Paula Pousinha**, PhD

Inst. Pharmacologie Moléculaire et Cellulaire, UMR7275 CNRS, France

"In Vivo APP intracellular domain (AICD) expression impairs synaptic plasticity in CA1 hippocampal neurons, by increasing GluN2B-containing NMDARs currents"

14-07-2014

**Several Speakers**

"Overview of FENS meeting"

21-07-2014

**Joana Xavier**, PhD student

Faculdade de Farmácia, Cellular Function and Therapeutic Targeting, iMed.UL/FFUL, University of Lisbon

"Nuclear and mitochondrial control of neural stem cell fate"

01-09-2014

**Júlio Licínio**

South Australian Health and Medical Research Institute, School of Medicine, Flinders University

"Antidepressants: Mechanisms of action, pharmacogenomics, and new targets"

08-09-2014

**André Santos**, PhD student

Ana Sebastião Lab, IMM

"BDNF and adenosine signalling on amyloid-beta peptide toxicity."

15-09-2014

**Vânia Batalha**, PhD student

Luísa Lopes Lab, IMM

"Interaction between glucocorticoid and adenosine A2A receptors in the hippocampus – implications for learning and memory."

29-09-2014

**Sandra Tenreiro**, PhD

Tiago Outeiro, Lab

"Using yeast models to probe the molecular basis of Parkinson's disease."

06-10-2014

**Rita Oliveira**, PhD

Tiago Outeiro Lab, IMM

"SIRT2: crossing the bridge between ageing and neurodegeneration."

13-10-2014

**Professora Dora Brites**

Research Institute for Medicines and Pharmaceutical Sciences iMed.Ulisboa/FFUL

"Glia-centered pathogenesis in neurodegeneration"

20-10-2014

**Raquel Dias**, PhD

Ana Sebastião Lab, IMM

"Homeostatic plasticity and LTP: fast and slow synapse regulation meet somewhere in the between."

27-10-2014

**Rita Ramalho**, PhD

Ana Sebastião Lab, IMM

"BDNF neuroprotection loss in Alzheimer's disease - are extrasynaptic NMDA receptors the bad guys?"

03-11-2014

**Onintza Sagredo**, PhD

Complutense University, Madrid, Spain

"Cannabinoid drugs for Huntington's disease: from the laboratory to the clinic."

10-11-2014

**Cátia Palminha**, Master Student

Ana Sebastião Lab

"Cannabinoid drugs for Huntington's disease: from the laboratory to the clinic."

17-11-2014

**Joana Coelho**, PhD

Luisa Lopes Lab, IMM

"Epigenetic dysregulation of Hairy and Enhancer of Split 4 (HES4) is associated with striatal degeneration in human postmortem Huntington brains."

24-11-2014

**Miguel Remondes**, PhD, head of lab, IMM

"Brain maps for decision-making"

01-12-2014

**Cláudia Valente**, PhD

Ana Sebastião Lab, IMM

"Epileptic-like electrophysiological and molecular features of cultured organotypic slices."

15-12-2014

**Daniela Magalhães**, Master student

Ana Sebastião Lab, IMM

"Deciphering the role of inflammation in the organotypic hippocampal slice model of epileptogenesis"

#### IMM Monday Lectures

06-01-2014

"Zooming in on single virus entry and fusion with a host cell"

**Gregory Melikyan**, Professor, PhD

Emory University, Atlanta, USA

Host: Nuno Santos

13-01-2014

"Hypoxia driven inflammation - a molecular paradox"

**Douglas Veale**, Professor

University College, Dublin

Host: João Eurico Fonseca

20-01-2014

"Machado-Joseph disease: from mechanism to disease-modifying therapies"

**Luís Pereira de Almeida**, PhD

Center for Neuroscience and Cell Biology, University of Coimbra

Host: Luísa Lopes

27-01-2014

"Vascular targeting in cancer and in chronic inflammation: from the bench to the clinic"

**Dario Neri**, Professor

ETH Zürich

Host: Gonçalo Bernardes

03-02-2014

"Gut reactions: Immune pathways in the intestine in health and disease"

**Fiona Powrie**, Professor

University of Oxford, John Radcliffe Hospital, Oxford

Host: Luís Graça

10-02-2014

"This seminar will be postponed for Tuesday, February 11th, at noon"

**David Fidock,**

Columbia University

Host: Maria Mota and Miguel Prudêncio

17-02-2014

"How quickly a friend can evolve into a foe: Escherichia coli adaptation to macrophages"

**Isabel Gordo,** Professor

IGC, Oeiras

Host: Mário Ramirez

24-02-2014

"Using Vaccinia virus to understand signalling, cytoplasmic transport and cytoskeletal dynamics"

**Michael Way,** Professor

London Research Institut, UK

Host: Edgar Gomes

17-03-2014

"Epigenetic control of thymic and peripheral development of Foxp3 regulatory T cells"

**Professor Jochen Huehn**

Helmholtz Centre for Infection Research - Braunschweig - Germany

Host: Luís Graça

24-03-2014

"How are regulators of intracellular trafficking risk-factors for Alzheimer's disease?"

**Cláudia Almeida,**

CEDOC, Oeiras

Host: Domingos Henrique

31-03-2014

"Tissue-specific Nuclear Envelope Protein Regulation of Genome Organization, Gene Expression, and Activation of Innate Immunity"

**Eric Schirmer**

Welcome Trust Centre for Cell Biology, Institute of Cell Biology, and Centre for Chemical and Translational Biology, University of Edinburgh

Host: Edgar Gomes



07-04-2014

"Human colour vision - key questions, some answers"

**Sérgio Nascimento**

Department of Physics, Minho University

Host: Miguel Castanho

14-04-2014

"Modulating Tau, modulating memory? Lessons from experimental models"

**David Blum**

Inserm U837 Lille France

Host: Luísa Lopes

21-04-2014

"Imaging innate immunity in action"

**Paul Kubes, Full Professor** and Director of Snyder Institute of Chronic Diseases at the University

Faculty of Medicine, University of Calgary, Canada

Host: Carlota Saldanha

28-04-2014

"Frontiers in Inflammation Research"

**Luke O'Neill, Professor**

Trinity College Dublin

Host: Maria Mota

05-05-2014

"Visualizing transcription at nucleotide resolution using nascent transcript sequencing"

**Stirling Churchman**, Assistant Professor of Genetics; Associate Member of the Broad Institute of Harvard and MIT

Harvard Medical School, Boston, USA

Host: Luisa Figueiredo

12-05-2014

"Not just for the sick : how Inflammatory signaling is essential for making fully functional T cells"

**Benedict P. Seddon, D. Phil**

MRC National Institute for Medical Research, U.K.

Host: João Barata

19-05-2014

"Cancer cell invasion and imaging therapy failure"

**Erik Sahai**, Head of Laboratory

Cancer Research UK, London Research Institute, England

Host: PDA - Ana Magalhães

26-05-2014

"Micro molecules – maximum impact in inflammatory arthritis"

**Iain McInnes**, Director of Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences

University of Glasgow, Scotland

Host: João Eurico Fonseca

02-06-2014

"The development and evolution of vertebrate morphology"

Cliff Tabin, Professor

Harvard Medical School, Boston, USA

Host: Leonor Saúde

16-06-2014

"Sugar & Proteins"

**Ben Davis**, Professor of Chemistry

University of Oxford

Host: Gonçalo Bernardes

23-06-2014

"Neisserial capsule polymerases: A gateway to vaccine development"

**Rita Gerardy-Schahn**, Professor

Hannover Medical School - Institute of Cellular Chemistry

Host: João Rodrigues

30-06-2014

"Imaging Dementia: moving towards preventive studies"

**Nick Fox**, Professor

University College of London, Dementia Research Centre, Institute of Neurology, England

Host: Alexandre Mendonça

07-07-2014

"Exploring the role of replicative stress in cancer and ageing"

**Oscar Fernández-Capetillo**

Spanish National Cancer Research Centre

Host: Sérgio Almeida

21-07-2014

"Integrated omic-based investigations of infectious disease outbreaks and pathogenicity"

**Fiona Brinkman**, Professor

Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, British Columbia, Canada

Host: Mário Ramirez/ João Carriço

15-09-2014

"Clonal evolution and cancer medicine"

**Samuel Aparicio, PhD**

University of British Columbia, Vancouver, Canada

Host: Bruno Silva-Santos & Maria Carmo-Fonseca

22-09-2014

"Environmental sensing by haematopoietic cells"

**Henrique Veiga-Fernandes**, head of Lab, IMM

29-09-2014

"Reversing the cognitive deficits associated with neurodevelopmental disorders in adults"

**Alcino Silva, PhD**

Departments of Neurobiology, Psychiatry and Psychology, UCLA Los Angeles

Host: Miguel Remondes

06-10-2014

"ER-associated protein degradation: from quality control to lipid homeostasis"

**Pedro Carvalho, PhD**

Center for Genomic Regulation, CRG Barcelona

Host: Edgar Gomes

13-10-2014

"Regulation of endothelial cell dynamics during vascular morphogenesis"

**Cláudio Franco**, head of Lab, IMM

20-10-2014

"Host-Plasmodium interactions: a tale of sensing and being sensed"

**Maria Mota**, head of Lab, IMM

27-10-2014

"Immune stimuli induce rapid and widespread changes in chromatin reorganisation"

**Gernot Längst, PhD**

Universität Regensburg - Regensburg - Germany

Host: Luísa Figueiredo

03-11-2014

"How Secretory mRNA is Anchored to the Endoplasmic Reticulum"

**Alexander Palazzo, PhD**

University of Toronto - Ontario - Canada

Host: Edgar Gomes

10-11-2014

"Checks and balances of cholinergic signaling by non-coding RNAs"

**Hermona Soreq**, PhD

The Hebrew University of Jerusalem - Jerusalem - Israel

Host: Carlota Saldanha

17-11-2014

"An ex vivo approach to study the mechanics of nuclear positioning in syncytial embryos"

**Ivo Telley**, PhD

Instituto Gulbenkian de Ciência - Lisboa - Portugal

Host: Edgar Gomes

24-11-2014

"Regulating Immunity in the Allergic Lung"

**Clare Lloyd**, PhD

Imperial College London - United Kingdom

Host: Luis Graça

01-12-2014

**Rui Martinho**, PhD

Univ. Algarve / Instituto Gulbenkian de Ciência - Portugal

"Requirement for highly efficient pre-mRNA splicing during Drosophila early embryonic development"

Host: Domingos Henrique

15-12-2014

**Dongsheng Cai**, PhD

Albert Einstein College of Medicine, New York - USA

"Hypothalamic micro-inflammation: a common basis of aging and metabolic syndrome"

Host: Luisa Lopes

Special Seminar

08-01-2014

"Deciphering the role of the histone variant macroH2A in Breast Cancer progression and iPS reprogramming"

**Alexandre Maia**

Icahn School of Medicine at Mount Sinai, N.Y. USA

22-01-2014

"Smile and kill : targeting host trafficking pathways to combat intracellular mycobacterial infections"

**Varadha Sundaramurthy**, Post-doc

Max-Planck Institute

Host: Maria Mota

27-03-2014

"The role of Jarid2 in the Xist RNA-induced targeting of Polycomb repressive complex 2 to the inactive X-chromosome"

**Simão Teixeira da Rocha**

Institut Curie, Paris, France

03-04-2014

"Peptide strategies in Leishmania chemotherapy: from piercing devices to drug smugglers"

**Luis Rivas**, Professor

Centro de Investigaciones Biologicas (CSIC), Madrid

Host: Nuno Santos

11-04-2014

"Trafficking of AMPA Receptors during synaptic plasticity: Role of the effector protein Rab11-FIP2"

**María Royo Cantabrana**

Centro de Biología Molecular "Severo Ochoa" Madrid, SPAIN

Host: Luísa Lopes

15-04-2014

"Imaging tumour metabolism using hyperpolarized 13C-MRI: Detecting response to treatment"

**Dr. Tiago Rodrigues**

Cambridge Research UK Cambridge Institute

Host: Gonçalo Bernardes

06-05-2014

"Establishing asymmetries during embryo development"

**Jeffrey Amack**, State University of New York, Upstate Medical University, Syracuse, USA

Host: Leonor Saúde

12-05-2014

"Biophysical changes of cell surface during progression to cancer: example of human cervical epithelial cells"

**Igor Sokolov**, PhD

Tufts University, Boston, MA, USA

Host: Nuno Santos

18-06-2014

"Good practices and antibodies for successful Flow Citometry results"

**Laura Schneider**, PhD

European Product Specialist, Cell Signaling Technology

20-06-2014

"Probing Mechanisms of Transcription Regulation In Cells & Across Genomes"

**John Lis**

Cornell University, New York

23-06-2014

"Mitochondrial Function in Parkinson's Disease"

**Vanessa Morais**

Laboratory of Neuronal Cell Biology and Gene Transfer K.U.Leuven and V.I.B. Leuven , Belgium

Host: Domingos Henrique

11-07-2014

"Understanding the role of the bone marrow niche in hematopoiesis and leukemic growth"

**Koen Schepers**, PhD

Department of Cell Biology, University Medical Center Utrecht, the Netherlands Department of Immunohematology and Blood Transfusion, Leiden University Medical Center, the Netherlands

Host: João Barata

08-09-2014

"Dendrophilia: Human Tree Processing in Comparative Perspective."

**W.Tecumseh Fitch**, PhD

Department of Cognitive Biology, University of Vienna

Host: Isabel Pavão Martins

12-09-2014

"Regulation of neutrophil reverse migration as a therapeutic strategy in inflammatory disease."

**Prof. Steve A. Renshaw, MA, FRCP, PhD**

Department of Infection and Immunity, University of Sheffield, UK

Host: Ângelo Calado

02-10-2014

"The role of host blood and parasite molecules in the battle between malaria and the mosquito"

**Prof. Hilary Hurd**

Keele University, Reino Unido

Host: Miguel Prudêncio

21-11-2014

"HIV targets lincp21 to evade apoptosis"

**Musa Mhlanga**, PhD

IMM and CSIR Biosciences, Pretoria, South Africa

21-11-2014

## Presentation Session of COHiTEC 2015

Host: Funding Programs Office

### Parasitology Series

07-01-2014

"Nutrient uptake and transport by Plasmodium-infected liver cells"

**Patrícia Meireles**, PhD student

Miguel Prudêncio Lab, IMM

14-01-2014

"Low liver infection: was it something the mouse ate?"

**Vanessa Luís**, Post-doc

Maria Mota Lab, IMM

21-01-2014

"Mesmerizing malaria - a new prototype magnetic device for the detection of parasites"

**Agnes Orban**, PhD student

Budapest University of Technology and Economics

28-01-2014

"Parasites and Sugars: a love affair?"

**João Rodrigues**, Principal Investigator

Gonçalo Bernardes Lab, IMM

18-02-2014

"Plasmodium liver stage infection: The relevance of host-derived lipids re-visited"

**Maurice Itoe**, Post-doc

Maria Mota Lab, IMM

25-02-2014

"Adipose Tissue invasion by Trypanosoma brucei"

**Sandra Trindade**, Post-doc

Luísa Figueiredo Lab, IMM

18-03-2014

"Deciphering iron transport in malaria parasites"

**Ksenija Slavic**, Post-doc

Maria Mota Lab, IMM

25-03-2014

"Long non coding RNAs in T. brucei : the strange case of cell differentiation"

**Fabien Guegan**, Post-doc

Luísa Figueiredo Lab, IMM

01-04-2014

"Flow cytometric detection of light depolarization: a novel assay to detect antimalarial drug effects"

**Maria Rebelo**, PhD student  
Instituto de Microbiologia, FMUL

22-04-2014

"Elucidating the molecular bases of mosquito ecology as a tool to improve malaria vector control"

**Francesco Baldini**, Post-doc  
Heather Ferguson's lab, University of Glasgow

06-05-2014

"Partners in crime: Deciphering intrahepatic host-parasite interactions"

**Cláudia Sá e Cunha**, Post-doc  
Miguel Prudêncio Lab, IMM

20-05-2014

"Integrated chemogenomic and in silico approaches to develop novel antimalarial lead compounds"

**Rui Moreira**, Professor, Group Leader  
iMed.Ulisboa, Faculdade de Farmácia

27-05-2014

"Starving the parasite might kill you: a non-lethal parasite becomes a severe malaria model in iron-deficient mice"

**Daniel Carapau**, Post-doc/Project Manager  
Maria Mota Lab

03-06-2014

"A peroxidase that turns into a chaperone: the story of a protein essential for Leishmania infectivity"

**Ana Tomás**, Group Leader  
IBMC – UP

08-07-2014

"Surviving autophagy - How Plasmodium parasites avoid host-dependent elimination during the liver stage"

**Eliana Real**, Post-doc  
Maria Mota Lab, IMM

15-07-2014



To be announced

**Kirsten Hanson**, Post-doc  
Maria Mota Lab, IMM

22-07-2014

"Plasmodium and Microbiota: Is there anything to it?"

**Ângelo Chora**, Post-doc  
Maria Mota Lab, IMM

07-10-2014

"The bittersweet role of deubiquitination during Plasmodium liver infection"

**João Vieira**, PhD student  
Maria Mota Lab, IMM

14-10-2014

"Trypanosoma brucei accelerates mouse circadian rhythm "

**Ana Filipa Ferreira**, PhD student  
Luísa Figueiredo Lab, IMM

21-10-2014

"P.berghei Mei2 like gene– a key player for malaria liver stage development "

**Ana Guerreiro**, Researcher  
Gunnar Mair Lab, IMM

28-10-2014

"Fighting Sleeping Sickness through the identification of T. brucei kinase inhibitors – A medicinal chemistry approach "

**João Seixas**, Post-Doc  
Gonçalo Bernardes Lab, IMM

04-11-2014

"N6-methyladenosine: a new modification in T. brucei "

**Idálio Viegas**, PhD student  
Luísa Figueiredo Lab, IMM

11-11-2014

"Characterization of a new malaria vaccine candidate against Plasmodium vivax using genetically modified rodent Plasmodium parasites"

**Miguel Duarte**, MSc student  
Miguel Prudêncio Lab, IMM

TBA

**Pedro Rego**, MSc student

Miguel Prudêncio Lab, IMM

18-11-2014

"Histone H1: A linker between chromatin, gene expression and fitness in Trypanosoma brucei"

**Ana Pena**, PhD student

Luísa Figueiredo Lab, IMM

25-11-2014

"Chromatin dynamics in African trypanosomes: Important for evading the immune system?"

**Francisco Branco**, PhD student

Luísa Figueiredo Lab, IMM

02-12-2014

"The immutable MicroRNAs in the host hepatocyte"

**Iset Vera**, Post-doc

Maria Mota Lab, IMM

09-12-2014

**Ana Margarida Vaz**, Researcher

"Trypanosoma brucei impairs Plasmodium berghei sporozoite's liver invasion"

Luisa Figueiredo & Miguel Prudêncio Lab, IMM

16-12-2014

**Ksenija Slavic**, Post-doc

Maria Mota Lab, IMM

"Iron transporters in malaria parasites: uptake and detox pathways"

#### Pizza Seminar

07-01-2014

"The role of adenosine A2A receptors in hippocampal neurogenesis"

**Ana Filipa Ribeiro**, PhD student

Ana Sebastião Lab, IMM

"An integrative genetic and genomics approach to Primary Spontaneous Pneumothorax susceptibility"

**Inês Sousa**, Post-Doc

Sofia Oliveira Lab, IMM

21-01-2014

"Comparação dos sistemas classificativos da frequência cardíaca fetal intraparto"

**Susana Santo**, MD, PhD student

Hospital Santa Maria

"Translational repression in Plasmodium: implications in sexual development and beyond"

**Jorge M. Santos**, MSc, PhD Student

Gunnar Mair Lab, IMM

04-02-2014

"Optimal IL-7R-mediated signaling, cell cycle progression and viability of T-ALL cells rely on CK2 activity"

**Alice Melão**, PhD student

João Taborda Barata Lab, IMM

"Hemopressin as a regulator of oligodendrogenesis in subventricular zone stem/progenitor cell cultures"

**Sara Xapelli**, Post-doc

Ana Sebastião Lab, IMM

18-02-2014

"Pathogenesis of Gammaherpesviruses Based upon Structural Data"

**Sofia Sequeira**, PhD student

Pedro Simas Lab, IMM

"Prevalence of spontaneous covRS mutations in Streptococcus pyogenes"

**Catarina Pato**, PhD student

Mário Ramirez Lab, IMM

18-03-2014

"The antigen specificity of follicular regulatory T cells"

**Ana Raquel Oliveira**, PhD student

Luís Graça Lab, IMM

"Adipose tissue invasion by Trypanosoma brucei"

**Sandra Trindade**, Post-doc

Luísa Figueiredo Lab, IMM

01-04-2014

"Dissecting the signalling pathway downstream of CD27 costimulation of Human gamma delta T-cells"

**Sérgio Ribeiro**, PhD student

Bruno Silva-Santos Lab, IMM

"Interaction between A2A receptors and CB1 receptors in the hippocampus: consequences for memory"

**Francisco Mouro**, PhD student  
Ana Sebastião Lab, IMM

22-04-2014

"Genetics of intracranial aneurysms"

**Patrícia Abrantes**, Post-Doc  
Sofia Oliveira Lab, IMM

Cancelled

**Tomás Fonseca**, PhD student  
Tiago Fleming Outeiro Lab, IMM

29-04-2014

"Monitoring antibacterial action in real time using flow cytometry"

**João Freire**, PhD student  
Miguel Castanho Lab, IMM

"Synaptic Dysfunction in Neurodevelopmental Disorders with Epilepsy and Autism"

**Sofia Duarte**, MD, PhD student  
Domingos Henrique Lab, IMM

13-05-2014

"Biophysical and nanomechanical changes of tumor cells in response to anticancer peptides' activity"

**Diana Gaspar**, Post-Doc  
Miguel Castanho Lab, IMM

"Role of endogenous cannabinoid on hippocampal LTP modulated by Adenosine receptor 1"

**Armando Cruz**, PhD Student  
Ana Sebastião Lab, IMM

27-05-2014

"Asymmetry vs Symmetry: the role of Dmrt2a in the formation of the vertebrate body plan"

**Rita Pinto**, PhD student  
Leonor Saúde Lab, IMM

Cancelled

**Paula Alexandra Oliveira**, PhD student  
Susana Constantino Lab, IMM

24-06-2014

"Development of A Novel Assay to Detect Antimalarial Drug Resistance"

**Maria Rebelo**, PhD student  
Mário Ramirez Lab, IMM

"How systemic metabolic (lipid) signals affect lymphocyte function and tumor immune surveillance in breast cancer"

**Ana de Barros**, Post-Doc  
Sérgio Dias Lab, IMM

16-09-2014

"Control of innate lymphoid cells and gut defense by neurotrophic factors"

**Bethania García Cassani**, PhD student  
Henrique Veiga-Fernandes Lab, IMM

Cancelled

**Sara Fernandes**, PhD student  
Leonor Saúde Lab, IMM

30-09-2014

"The cell's cycle around the wound"

**Telmo Pereira**, PhD student  
CEDOC

14-10-2014

"The Control of Cell Proliferation in Lupus Nephritis by miRNAs and HER2"

**Patricia Reis**, PhD  
The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, FMUL

"Flexible IL-7-mediated regulation of autophagy promotes T-cell acute lymphoblastic leukemia **cell viability**"

**Daniel Ribeiro**, PhD  
João Barata Lab, IMM

28-10-2014

"The Role of D-Glucose Uptake by Glucose Transporter 1 during the liver stage of Plasmodium Infection"

**Patricia Meireles**, PhD student  
Miguel Prudêncio Lab, IMM

"Role of the lncRNA Zeb2Nat in stemness"

**Bruno Jesus**, Post-Doc  
Maria Carmo-Fonseca Lab, IMM

11-11-2014

"Histone H1: A linker between chromatin, gene expression and fitness in Trypanosoma brucei"

**Ana Pena**, PhD student  
Luísa Figueiredo Lab, IMM

Cancelled

**Rita Vaz**, PhD student

Tecnhophage

25-11-2014

"Analysis of the dynamic properties of the pluripotency network in mouse Embryonic Stem Cells"

**Ana Guedes**, PhD student

Domingos Henrique Lab, IMM

"Control of Innate lymphoid cells and intestinal homeostasis by neurotrophic factors"

**Sales Ibiza**, Post-Doc

Henrique Veiga - Fernandes Lab, IMM

09-12-2014

**Inês Perpétuo**, PhD student

João Eurico Fonseca Lab, IMM

"Effect of TNF blocking therapy on osteoclasts from ankylosing spondylitis patients"

**Ram Srchaitanya**, PhD student

Sérgio Almeida Lab, IMM

"Catching the dangerous loops: How RNA:DNA hybrids challenge genome integrity?"

#### IMM Rheumatology Series

14-01-2014

"Looking at what matters - inside the inflamed joint"

**Douglas Veale**

University College Dublin, Ireland

Host: João Eurico – Fonseca

25-03-2014

"Diagnosing and Caring for the Autoinflammatory Syndromes – where are we now?"

**Helen J. Lachmann**

University College London, UK

Host: João Eurico – Fonseca

08-04-2014

"Adipokines in inflammatory joint diseases"

**Ulf Müller-Ladner**

Justus-Liebig University Giessen, Germany

Host: João Eurico – Fonseca

23-09-2014

"IL-23/IL-17: clinical use within reach"

**Dominique Baeten**

Amsterdam Academic Medical Centre, Netherlands

Host: João Eurico – Fonseca

04-11-2014

"Safety of kinase inhibitor in rheumatoid arthritis: A predictive model"

**Juan Gómez- Reino**

Hospital Clinico Universitario de Santiago, Spain

Host: João Eurico – Fonseca

25-11-2014

"Translational research in pediatric rheumatology"

**Alberto Martini**

Genova University, Italy

Host: João Eurico – Fonseca

02-12-2014

"Towards precision medicine using a systems biology approach"

**Tim Radstake**

University Medical Center Utrecht, Netherlands

Host: João Eurico – Fonseca

Immunology Club

06-02-2014

"Optimal IL-7-mediated signaling, cell cycle progression and viability of T-cell acute lymphoblastic leukemia cells rely on CK2 activity"

**Alice Melão**, PhD student

João Barata Lab, IMM

13-02-2014

"Is the function of master T helper transcription factors conserved amongst T cells?"

**Karine Serre**, Postdoc

Bruno Silva-Santos Lab

20-02-2014

Cancelled

**Sílvia Madeira**, PhD student

Henrique Veiga-Fernandes Lab

06-03-2014

"9G4 B cells and autoantibodies: A potencial role in Rheumatoid Arthritis"

**Rita Moura**, Post-Doc

João Eurico - Fonseca Lab

20-03-2014

"Infection of the human thymus by HIV-2"

**Helena Nunes Cabaço**, Post-Doc

Ana Espada de Sousa Lab

10-04-2014

"Role of Retinoic acid in ILC2 development and function"

**Sílvia Madeira**, PhD student

Henrique Veiga-Fernandes Lab

08-05-2014

"Key in vivo functions for the oxygen sensor PHD2 in hematopoiesis/ erythropoiesis and inflammation"

**Kristin Franke**

University of Technology, Dresden, Germany

Host: Bruno Silva-Santos

15-05-2014

"Herpesvirus Modulation of Immunological Synapses"

**Diana Fontinha**, PhD student

Pedro Simas Lab, IMM

22-05-2014

"Determining the prognostic significance of PI3K/Akt/mTOR and JAK/STAT5 signaling pathways in pediatric ALL using single-cell analysis"

**Mariana Oliveira**, Master student

João Barata Lab, IMM

12-06-2014

"Estimation of cell cycle parameters by FACS-EDU"

**Prof. Dr. João Ferreira**

Paulo Filipe Lab, IMM

19-06-2014

"The antigen specificity of follicular regulatory T cells"

**Ana Raquel Maceiras**, PhD student

Luís Graça Lab, IMM

09-10-2014

"Role of transcription factors in the functional development of gd T lymphocytes"

**Joana Martins**, MSc student



Bruno Silva-Santos Lab, IMM

23-10-2014

"Control of Innate lymphoid cells and intestinal homeostasis by neurotrophic factors"

**Sales Ibiza**, Post-Doc

Henrique Veiga-Fernandes Lab

13-11-2014

"The role of reciprocal regulation between TAL1 and miRNA expression in T-cell leukemia progression"

**Nádia Correia**, PhD student

João Barata Lab, IMM

20-11-2014

"Getting to the gut of HIV/AIDS immunopathogenesis"

**Susana M. Fernandes**, MD, PhD student

Ana E Sousa Lab

27-11-2014

"CK2 regulates CD27 receptor-costimulation in human gamma-delta T Cells"

**Sérgio T. Ribeiro**, PhD student

Bruno Silva-Santos Lab

04-12-2014

"Regulation of the Enteric Immune System by Retinoic Acid Signalling".

**Carlos Labão-Almeida**, Master student

Henrique Veiga – Fernandes Lab, IMM

#### Career Path Seminar

11-04-2014

"Careers in Academia"

**Susana Solá Cruz**

Assistant Professor at Faculdade de Farmácia - FFUL (Lisbon University School of Pharmacy)

**Sara Magalhães**

Assistant Researcher (FCT Investigator) at Faculdade de Ciências - FCUL (Lisbon University School of Sciences)

**Sara Ricardo**

Ramon y Cajal Investigator, Institut de Biologia Molecular de Barcelona (IBMB)

Host: Postdoctoral Association

23-05-2014

"Career transition to Editorial jobs"

**Celine Carret**

EMBO Journal, ex-investigadora no IMM

**Nicolau Ferreira**

Jornalista do Público

26-09-2014

"How to apply for a job: What Human Resources Departments are looking for"

**Patricia Alves**, Human Capital Senior Executive

PricewaterhouseCoopers

28-11-2014

"Careers in the Pharmaceutical Industry"

**Manuel Garrido** - Bioprocess Engineer, GenIbet Biopharmaceuticals

**Filipa Gil** - Senior Clinical Research Associate, Pharmaceutical Product Development

#### Oncology Series

16-01-2014

"Prostate Cancer: new data for an old disease"

**Chairs: Luís Costa ; Tomé Lopes**

Luis Costa, Serviço de Oncologia, CHLN, EPE – IMM; Tomé Lopes – Serviço de Urologia, CHLN,EPE

2:35 pm | Surgery in Prostate Cancer: Our experience in the past 5 years

**José Dias** – Serviço de Urologia, CHLN,EPE

3:00 pm | Translational Research in Prostate Cancer: Targeting Androgen Receptor again

**Eleni Efstathiou**- M.D. Anderson Cancer Center, Texas, USA

03:35 pm | Bone metastases in Prostate Cancer: new targets & new options

**Luís Costa**, Serviço de Oncologia, CHLN, EPE – IMM; Sandra Casimiro, Luís Costa Lab, IMM

4:00 pm | Discussion

**Carlos Rabaça**, IPO Coimbra Isabel Fernandes, Serviço de Oncologia, CHLN, EPE

4:15 pm | Coffee break & Adjourn

## Oncobiology Club

28-05-2014

"Novel Projects"

**Sérgio Dias**, Head of Lab, IMM

11-06-2014

"Quantitative analysis of clonal evolution driving relapse of acute myeloid leukemia escape variants"

**Francisco Caiado** , Post-doctoral fellow

Bruno Silva-Santos Lab, IMM

25-06-2014

"The role of Sphingosine kinase 1 in IL-7-mediated signaling and T-cell acute lymphoblastic leukemia"

**Joana Matos**, MSc Student

João Barata Lab, IMM

23-07-2014

"Could common allelic variants of the farnesyl diphosphate synthase influence the response to bisphosphonates in metastatic bone disease?"

**Irina Alho Duarte** , PhD student

Luís Costa Lab, IMM

08-10-2014

"Metabolic shift in cancer cells: insights from an acute leukemia xenotransplantation model"

**Tânia Carvalho**, PhD

Histology and Comparative Pathology Lab, in collaboration with Sérgio Dias Lab, IMM

22-10-2014

"Mechanisms of therapeutic resistance in Myeloproliferative Neoplasms"

**Bruno Cardoso**, PhD

BIOLOGY & TREATMENT OF LYMPHOID MALIGNANCIES from IPO

12-11-2014

"Nouvelles approches à CO libérant molécules en thérapie du cancer"

**Miguel Ferreira** , PhD

Gonçalo Bernardes Lab, IMM

## Computational Biology and Bioinformatics Seminars

29-01-2014

"Genomic analysis of the first Vancomycin-Resistant Staphylococcus Aureus isolated in Europe"

**João André Carriço**, PhD  
Mario Ramirez Lab, IMM

26-02-2014

"Computational Catalog of Human lincRNAs"

**Ioana Posa**, Master Student and **Joana Tavares**, Master Student  
Sérgio Almeida Lab, IMM

26-03-2014

"The Bioinformatics Unit @ IGC"

**Daniel Sobral**, Post-doc

IGC

30-04-2014

"Information theory applications for sequence analysis and collaborative projects in systems  
biomedicine"

**Susana Vinga**

IDMEC / IST-UL

28-05-2014

"Nascent transcript sequencing (NET-seq): analysis advantages and pitfalls"

**Tomás Gomes**, MSc Student

Maria Carmo-Fonseca Lab, IMM

25-06-2014

"Whole-Exome Sequencing analysis of a multiplex family with Paget's Disease of Bone"

**Patrícia Silva Santos**, Master Student

Sofia Oliveira Lab, IMM

#### Other

8th PhD Students Meeting IMM/CAML

Keynote speaker:

**Ana Cumano**, MD, PhD (Institute Pasteur, INSERM, Paris, France)

IMM Highlights

**PhD students research at IMM during 2013**

2014 CAML/IMM - PhD Projects

LisbonBioMed M2B-PhD - CAML

**IMM Alumni**

Life after PhD - Scientific and Alternative paths

Organized by: PhD Students Committee

IMM PostDoc Day

17-06-2014

Invited Speakers:

**Prof. João Lobo Antunes**, IMM

**Prof. Hélder Maiato**, IBMC

**Prof. Alexandre Quintanilha**, IBMC

Invited Speaker Seminar

22-01-2014

"Smile and kill : targeting host trafficking pathways to combat intracellular mycobacterial infections"

**Varadha Sundaramurthy**, Post-doc

Max-Planck Institute

Host: Maria Mota

Sessão Clínica

13-02-2014

"Vacina contra a malária: uma abordagem diferente para uma necessidade urgente"

**Miguel Prudêncio**, head of Lab, IMM

06-11-2014

"Em busca de novos alvos moleculares para o tratamento de leucemia"

**João Barata**, head of Lab, IMM

Statistics Workshop

03-10-2014

"A Workshop on Applied Statistics in Biology"

**Vitor Paiva**, PhD

IMAR- CMA - Marine and Environmental Research Centre Coimbra, Portugal

Host: IMM Postdoctoral Training

LisbonLymph 2014

03-10-2014

"Aggressive B-cell Lymphomas"

**Several speakers**

Biobanco-IMM

11-11-2014

Sessão Biobanco-IMM, Centro Académico de Medicina de Lisboa

PhD Dissertation Presentation

15-10-2014

"Epigenetic mechanisms of effector  $\gamma\delta$  T cell differentiation: Focus on histone modifications and microRNAs"

**Nina Schmolka**, PhD Student

Bruno Silva-Santos Lab, IMM

PhD Dissertation Presentation

15-10-2014

Brain-derived neurotrophic factor and adenosine signalling on amyloid- $\beta$  peptide induced toxicity: impact on hippocampal function

**André Jerónimo Santos**, PhD student

Ana Sebastião Lab, IMM

40th Annual Meeting of the Portuguese Society for Immunology

**13-10-2014**

**"From immune responses to immunotherapy"**

## IMM EDUCATION AND ADVANCED TRAINING

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

### Team

Executive Manager: Alexandra Manaia, Ph.D. – left July 2014

PhD Training Director: Ana Espada de Sousa, MD, Ph.D.

LisbonBioMed PhD Program Director: Domingos Henrique, Ph.D.

Postdoctoral Training Director: Luísa Figueiredo, Ph.D.

Career Development Director: Henrique Veiga Fernandes, Ph.D.

Administrative Assistant: Sónia Arroz, MSc.

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 PhD students and Postdoctoral fellows 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 e BEB) and international PhD Programs (e.g. INT, MIT-PT).

In 2013, IMM was awarded FCT funding to create the Lisbon Biomedical and Clinical Research PhD Program – LisbonBioMed, and in January 2014, we welcomed the first 10 PhD students. Furthermore, IMM is a partner in two other multi-institutional FCT PhD Programs: the Bioengineering - Cell Therapies and Regenerative Medicine (CTRM), and the Medical Biochemistry and Biophysics (M2B) PhD Programs.

In July 2014, IMM launched a call for the new Postdoctoral Programme, the Mindthegap Programme, funded by the Marie Curie Action COFUND under the EU's Seventh Framework Programme. This first call involved 2 Junior (PhDs with less than 2 years and up to 6 years prior to the publication of the call for proposals) and 1 Advanced (fellows with between 5 and 9 years post-PhD experience) positions.

Overall, the integrated management of ongoing and new 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

**In 2014, 91 PhD students conducted research at IMM: 83 Lisbon AMC PhD students plus 8 PhD students from other Programs/ Institutions**

**83 Lisbon AMC PhD students conducted research at IMM**

Besides Lisbon AMC PhD students, IMM hosted 7 PhD students from other PhD Programs/ Institutions: 1 Budapest University; 1 Karmanos Cancer Institute; 2 UNESP- Brazil; 1 Universidad Complutense de Madrid; 1 supported by Sonangol EP; 1 Research Center Borstel and 1 Carlos Chagas Filho Institute – Brazil.

**New PhD Students in 2014:**

**27 IMM /Lisbon AMC PhD Students**

**2 M2B** – Tiago Figueira and Bárbara Gomes.

**10 LisbonBioMed** – Ana Portêlo, Joana Carvalho, João Vieira, Juliana Perazzo, Mafalda Pimentel, Mariana Ferreira, Padma Akkapeddi, Raquel Freitas, Tiago Amado and Alexandra Vítor.

**15 Individual fellowships or others** – Marcelo Augusto, Mafalda Matos, Maria Dulce Neutel, Ana Cristina Alho, Válter Fonseca, Tiago Teodoro, Vasco Romão, Marco Sarmento, Luís Madeira, Daniel Caldeira, Marta Amorim, David Ângelo, Neidy Rodrigues, Viriato M'Bana and Jessica Bevan.

## Advanced Courses

A total of 7 Advanced Courses were organized

Courses organized under the CAML PhD Programme in 2014

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

#### ***Mind***

Organizers: Domingos Henrique, João Ferreira, Sérgio Dias and Isabel Pavão, IMM/FMUL

Date: Jan 6 – Feb 28 (16 ECTS)

Nº of Participants: 12

The course focused on: promotes 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 research career.

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

Organizer: Joana Marques, IMM

Date: April 1, 14, 21, 29; May 6, 7, and 8. (1,5 ECTS)

Nº of Participants: 30

The course followed the recommendations of Felasa for cat. B. 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.



### ***Clinical Research***

Organizers: António Vaz Carneiro, José Ferro and Carneiro de Moura (IMM/FMUL/HSM)  
Date: Mar 7, 8, 28 and 29; April 11, 12; May 16, 17, 23, 24; June 6,7,19 e 20; July 4 and 5 (the course includes 8 modules that could be taken independently, each module corresponding to 7.5 ECTS)

Nº of Participants: 8

Aimed at MDs and other biomedicine-related professionals with interest in conducting clinical research projects, this course provided a multidisciplinary and integrated view of clinical research focusing on the analysis of practical study cases.

### ***Bioimaging NanoCourse on Microscopy***

Organizer: José Henriques, Head of IMM Bioimaging Unit.

Date: May 15-16 (0.5 ECTS)

Nº of Participants: 45

To provide beginner/intermediate microscope users with basic theoretical background in fluorescence wide field and confocal microscopy as well as practical information on how to efficiently prepare samples, acquire data and obtain publication quality images.

### ***Quantitative evaluation of protein-ligand interactions***

Organizers: Ivo C. Martins, Axel Hollmann, and Filomena A. Carvalho

Date: September 15-18 (2 ECTS)

Nº of Participants: 10

The aim of the course is to provide participants with a solid grounding in the quantitative study of protein-ligand interactions by a wide range of biophysical techniques, with a thorough overview of basic concepts from physics, chemistry and biology, illustrating how these concepts can be combined and applied in everyday research.

### ***Nanocourse: Type-2 immune responses and allergic diseases***

Organizers: Luís Graça, Marta Monteiro, Karine Serre, Susana Lopes da Silva and Manuel Branco Ferreira.

Date: November 24-25 (0.5 ECTS)

In this course, the participants were introduced to acquire a background knowledge on type 2 immune responses, and the impact of those responses on human health. The course included an overview of the role of type 2 immune responses on allergic diseases and how a better understanding of type 2 responses can lead to the development of novel therapeutic strategies.

### Complementary skills courses:

#### ***Scientific Career Development 201***

Organizer: Joana do Rosário, MD, MDH

Date: Jan28 (0.25 ECTS)

Nº Participants: 15

These highly interactive training modules have prepared young investigators towards a successful and effective transition from the doctoral student phase into their first position as an independent scientist. Participants have analyzed and discussed choices made during their doctoral training and how to effectively use these choices to launch a productive and upward moving career. This training has used a mix delivery model, to include platform presentation, and small group individual exercises.

## PhD Students Activities

PhD students are challenged to actively suggest activities to foster both scientific and social networking between the IMM research community. Every year a group of students volunteers to form the students' commission, who is responsible for the organization of the different initiatives: "Students' Annual Retreat", the "Annual PhD Students Meeting" and a seminar series - the "Pizza Seminars".

### **2014 PhD Students committee**

Rita Aroeira, Bethania Cassani, Rita Domingues, André Faustino, Ana Filipa Guedes, Ana Marisa Guedes, Sílvia Arroz-Madeira, Tiago Amado, Diana Fernandes, Diana Fontinha, Mariana Oliveira, Mafalda Pimentel, Maria Rebelo, Ana Filipa Ribeiro e João Vieira.

### **2014 PhD Students representatives**

João Freire and Inês Perpétuo

### **Pizza Seminars**

These seminars happen every other Tuesday, at noon and pizza is served. Two students present their work and there is time for discussion.

### **VII IMM/CAML PhD Students Retreat**

Date: October 18-20

Place: Pousada da Juventude da Lousã

Participants: Total 51; PhD students (28), post-docs (4) and others (19).

Programme:

1) Canoeing; 2) Breaking the ice activities; 3) Small Hike; 4) Scientific Games.

### **VIII PhD Students Meeting IMM/CAML**

Date: March 28

Place: IMM/FMUL

Participants:

3 Opening Session, 16 New PhD students presenting their research work, 1 Keynote Speaker, 4 IMM Highlights and 7 Alumni Total: 31 participants; plus other attendants from IMM/FMUL/HSM community.

### **March 28**

#### **Opening Session**

João Lobo Antunes (President, IMM), José Fernandes e Fernandes (Director, FMUL) and Doutor Carlos Martins (Chairman, CHLN).

#### **Keynote Speaker**

Ana Cumano, MD, PhD (Institut Pasteur, INSERM, Paris, France)

#### **PhD Projects 2014**

LisbonBioMed; M2B; CAML

### **Highlights IMM**

Nina Shmolka, B Silva-Santos Lab

Epigenetic and transcriptional signatures of stable versus plastic differentiation of proinflammatory  $\gamma\delta$  T cell subsets.

**Nat Immunol.** 2013; 14(10):1093-100.

Vânia L Batalha, L Lopes Lab

Adenosine A(2A) receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation.

**Mol Psychiatry.** 2013; 18(3):320-31

Diana Carmona-Fernandes, JE Fonseca Lab

Anti-ribosomal P protein IgG autoantibodies in patients with systemic lupus erythematosus: diagnostic performance and clinical profile.

**BMC Med.** 2013; 11:98.

Nádia C Correia, J Barata Lab

Novel TAL1 targets beyond protein-coding genes: identification of TAL1-regulated microRNAs in T-cell acute lymphoblastic leukemia.

**Leukemia.** 2013

### **Alumni FMUL - IMM**

Life after PhD – Scientific and Alternative paths

Sérgio Simões, CBS Uni. Toronto, Canada

Rho GTPase and Shroom signalling direct planar polarized actomyosin contractility during convergent extension.

Ricardo Henriques, MRC LMCB, London, UK

A nanoscale view into cells through super-resolution microscopy

Ana Rita Barbosa, LRI CRUK, London, UK

From immunodeficiency to cancer: a journey on B cells

Rita Fior, IGC, Oeiras, Portugal

From Developmental Biology to Cancer, from Basic to Translational Research in Portugal

Sónia Albuquerque, Territory Manager, BioMarin, Lisbon, Portugal

Marta Campos, Clinical Trial Coordinator, CRUK Clinical Trials, Uni. Birmingham, UK

Tiago Carneiro, Biosafety and Occupational Health, IGC, Oeiras, Portugal

## **Round Table**

Alumni FMUL - IMM

## **Closing remarks & Farewell cocktail party**

## **PhD thesis**

### **17 IMM/Lisbon AMC PhD Thesis**

Margarida Filipe Dias Rodrigues (April 3, 2014). Molecular Determinants of the Cellular Internalization of Crotamine-Derived Peptides. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Nuno Santos.

Maria Leonor Lemos Pereira Miller Fleming (April 14, 2014). Deciphering the Molecular Role of DJ-1 in The Etiology of Parkinson's Disease. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Tiago Fleming Outeiro.

Angelica Vittori (April 15, 2014). Copy number variation and Huntington's disease. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Tiago Fleming Outeiro.

Rosângela Maria Rodrigues Carvalho Frita (May 19, 2014). Malaria and Tuberculosis co-infection: role for Hemozoin immunosuppression? Faculdade de Medicina da Universidade de Lisboa. Supervisor: Thomas Hänscheid.

Marcos Daniel Caetano Borges de Pinho (May 23, 2014). Lancefield group C and G streptococci in human infection: Molecular typing, virulence and antimicrobial susceptibility. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Mário Ramirez.

Carolina Góis Almeida Moreira (July 7, 2014). The Function of Drosophila Integrin Adhesion Complexes in Pupal Hemocyte Migration in vivo. Faculdade de Medicina da Universidade de Lisboa. Supervisor: António Jacinto e Leonor Saúde.

Aida Isabel Santos da Costa (July 14, 2014). From Embryonic Stem Cells to Sensory Hair Cells: a Programming Approach. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Domingos Henrique.

Maurício de Jesus Dias Martins (September 8, 2014). Language Evolution and Recursion: An Empirical investigation of Human Hierarchical Processing. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão Martins.

Sofia Ludovina Novais de Oliveira (September 12, 2014). How hydrogen peroxide and CXCL8 modulate neutrophil recruitment in vivo. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ângelo Miguel Silva Calado.

Cristina Sofia Godinho da Silva (September 24, 2014). Immune engagement thresholds for CD8+T cell control of Herpes virus-driven B cell proliferation. Faculdade de Medicina da Universidade de Lisboa. Supervisor: João Pedro Monteiro e Louro Machado de Simas.

Raquel Valente Mendes (September 29, 2014). What is the role of the cell adhesion protein N-cadherin in the molecular and morphological asymmetries of the Hensen's node. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria Leonor Tavares Saúde.

Vânia Luísa Neves Batalha (September 29, 2014). Interaction between glucocorticoid and adenosine A2A receptors in the hippocampus - implications for learning and memory. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luísa Maria Vaqueiro Lopes.

Nina Alexandra Schmolka (October 15, 2014). Epigenetic mechanisms of effector  $\gamma\delta$  T Cell differentiation: Focus on histone modifications and microRNAs. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Silva-Santos.

André Jerónimo Santos (October 15, 2014). Brain-derived neurotrophic factor and adenosine signalling on amyloid- $\beta$  peptide induced toxicity: impact on hippocampal function. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria José Diógenes.

Elisa Basso (November 25, 2014). The role of alpha-synuclein phosphorylation in synucleinopathies. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Tiago Fleming Outeiro.

Vera Lúcia Poço Geraldes (December 10, 2014). Hypothalamic and medullar mechanisms for long-term autonomic regulation of arterial blood pressure. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Rocha.

Joana Freire de Castiço Monteiro (December 18, 2014). Dissecting the Biophysical Mechanisms Underlying Regeneration of Complex Organs in Vertebrates. Faculdade de Medicina da Universidade de Lisboa. Supervisor: António Jacinto.

## RESEARCH ACTIVITY

The mission of Instituto de Medicina Molecular (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.

- Ana E. Sousa
- Ana Sebastião
- Bruno Silva-Santos
- Carlota Saldanha
- Claudio Franco
- Domingos Henrique
- Edgar Gomes
- Gonçalo Bernardes
- Henrique Veiga-Fernandes
- João Eurico-Fonseca
- João Lacerda
- João Taborda Barata
- Joaquim Ferreira
- José Ferro
- Leonor Saúde
- Luis Costa
- Luis Graça
- Luisa Figueiredo
- Luisa Lopes
- Mamede de Carvalho
- Maria Carmo-Fonseca
- Maria Mota
- Mário Ramirez
- Miguel Castanho
- Miguel Prudêncio
- Miguel Remondes
- Nuno Santos
- Paulo Filipe
- Pedro Simas
- Sérgio Almeida
- Sérgio Dias
- Sofia Oliveira
- Susana Constantino

## Ana E. Sousa Lab

### Major Interests / Objectives

UIC's 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 UIC's research effort is centered on HIV/AIDS immunopathogenesis, mainly through the study of HIV-2 infection, a naturally attenuated form of HIV disease.

UIC 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 Unit

Ana Espada de Sousa, PhD Agregação, Associate Professor, MD

### Research Team

Adriana Silva de Albuquerque	PhD	Post doctoral Investigator
Alcinda Melo	Graduate	Technician, Faculdade Medicina da Universidade de Lisboa
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 Cláudia Viseu Varandas	Undergraduate	MD/MSc Student, (started September)
Ana Isabel Gouveia Costa da Fonseca Lopes	MD/PhD	Investigator, HSM/CHLN , Clinical Specialist , Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Ana Luisa Caetano	Graduate	Technician, Faculdade Medicina da Universidade de Lisboa
Ana Rita Correia Pires	Graduate	Investigator

Andreia de Jesus Amaral Gomes Barbosa Fonseca	PhD	Post doctoral Investigator, BioFIG
Andreia Sofia Ramalho dos Santos	Graduate	Trainee, (started October)
Helena Nunes Cabaço	PhD	Post doctoral Investigator
Inês Filipa dos Santos Martins	Master	Consultant
Íris Maria Ferreira Caramalho	PhD	Investigator
Isabel Cristina e Castro de Menezes Esteves	MD	Investigator, HSM/CHLN , Clinical Specialist , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Jorge Andrade	PhD	Post-doctoral Investigator, (suspended July)
José Gonçalo Duque Pereira Monteiro Marques	MD	Investigator, HSM/CHLN , Clinical Specialist , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Maria Catarina Mota da Silva	MD	PhD Student, HSM/CHLN , Clinical Specialist
Maria da Conceição Galvão Barata Pinto Pereira dos Santos	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa
Paula Cristina Frade dos Santos Matoso	Master	Investigator
Ricardo de Mendonça Vieira	Undergraduate	Trainee, (started March) (left July)
Rui Manuel Martins Victorino	MD/PhD	Senior Investigator, Faculdade Medicina da Universidade de Lisboa, Full Professor , HSM/CHLN , Clinical Service Director
Russell Bourne Foxall	PhD	Post doctoral Investigator
Sandra Duque Maurício	Undergraduate	MSc Student, (started April)
Sara Branco Pereira da Silva	MD	Investigator, HSM/CHLN, MD
Susana Clara Barão Lopes da Silva dos Anjos	MD	PhD Student, HSM/CHLN, Clinical Specialist , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Susana Mendes Fernandes	MD	PhD Student, HSM/CHLN , Clinical Specialist , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant



Vânia Patrícia Mendes Passos	Graduate	MSc Student, (started September)
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### Keywords / Research Areas

Human T cell Homeostasis, Immune Regulation, HIV/AIDS Immunopathogenesis, HIV-2 Infection, Primary Immunodeficiencies, Immunological Reconstitution

### Major scientific achievements

1. Our study of HIV-2 infection uncovers post-transcriptional control of viral replication in human thymocytes, which may help explain why HIV-2+ individuals control viremia despite the presence of viral reservoirs.
2. Investigation of mechanisms contributing to gut recovery in HIV-1-treated individuals highlights a role for innate IL-22 compartment.
3. Regarding our Primary Immunodeficiency Centre, we reveal disturbances in two major B-cell homeostatic receptors, BAFF-R and TACI, in Common Variable Immunodeficiency.
4. Two findings relevant for autoimmune diseases worth emphasis: human regulatory T-cell development is dictated by IL-2 and IL-15 expressed in a non-overlapping pattern in the thymus; and DL1-mediated Notch signalling enhances the in vitro conversion of human memory CD4 T cells into regulatory T cells.
5. Finally, HIV/AIDS research was strengthened by the Conference "HIV-2: the forgotten virus" promoted by the Portuguese Ministry of Health that we proudly co-organized.

### Selected Publications

Rita Cavaleiro, António P. Baptista, Rui S. Soares, Rita Tendeiro, Russell B. Foxall, Perpétua Gomes, Rui M. M. Victorino, Ana E. Sousa. (2009) Major Depletion of Plasmacytoid Dendritic Cells in HIV-2 Infection, an Attenuated Form of HIV Disease. . *PLoS Pathogens* **5**, e1000667. (Journal IF: 8.057, Citations: 17)

Rita I. Azevedo, Maria V. D. Soares, João T. Barata, Rita Tendeiro, Ana Serra-Caetano, Rui M. M. Victorino, Ana E. Sousa. (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. (Journal IF: 9.775, Citations: 30)

Maria C. Pereira-Santos, António P. Baptista, Alcinda Melo, Rodrigo R. Alves, Rui S. Soares, Elisa Pedro, Manuel Pereira-Barbosa, Rui M. M. Victorino, Ana E. Sousa. (2008) Expansion of circulating Foxp3(+) CD25(bright) CD4(+) T cells during specific venom immunotherapy. .

*Clinical & Experimental Allergy* **38**, 291. (Journal IF: 4.324, Citations: 33)

Ana E. Sousa, Jorge Carneiro, Martin Meier-Schellersheim, Zvi Grossman, Rui M. M. Victorino. (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. . *The Journal of Immunology* **169**, 3400. (Journal IF: 5.362, Citations: 288)

Zvi Grossman, Martin Meier-Schellersheim, Ana E. Sousa, Rui M. M. Victorino, William E. Paul. (2002) CD4+ T-cell depletion in HIV infection: are we closer to understanding the cause?. *Nature Medicine* **8**, 319. (Journal IF: 28.054, Citations: 316)

### **Ongoing Research Projects**

2011/2014 Title: HIV/AIDS: contribute of naïve CD4 T cell homeostasis. Coordinator: Ana Espada de Sousa. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-MIC/109786/2009. Amount: 159,694€.

2013/2015 Title: Bee Venom as a tool to expand the human regulatory T-cell compartment. Coordinator: Rui Manuel Martins Victorino. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/DTP-PIC/0508/2012. Amount: 145,001€.

2013/2015 Title: Reservatórios e replicação viral nas células T CD4 de memória-central e folículas na infecção HIV-2. Coordinator: Ana Espada de Sousa. Agency: Gilead Sciences, Lda. Reference: Gilead. Amount: 14,500€.

2013/2015 Title: Plataforma Desenv Medicos-Cientistas. Coordinator: Ana Espada de Sousa. Agency: Fundação Calouste Gulbenkian. Reference: Plataforma Desenv Medicos-Cientistas. Amount: 100,000€.

2014/2014 Title: Achieving gut integrity in HIV/AIDS through IL-22. Coordinator: Russell Bourne Foxall. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/DTP-PIC/0854/2013. Amount: 50,000€.

2014/2015 Title: COST Action BM1404 “European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells (Mye-EUNITER)”. Coordinator: Ana Espada de Sousa. Agency: Comissão Europeia. Reference: COST BM1404.

### **Publications in peer review Journals**

Caramalho I, Nunes-Silva V, Pires AR, Mota C, Pinto AI, Nunes-Cabaço H, Foxall RB and Sousa AE (2014) Human regulatory T-cell development is dictated by Interleukin-2 and -15 expressed

in a non-overlapping pattern in the thymus. *J Autoimmun* Dec **3**, pii: S0896-8411(14)00166-8. doi: 10.1016/j.jaut.2014.11.002. [Epub ahead of print]. (Journal IF: 7.018).

Nunes-Cabaço H, Matoso P, Foxall RB, Tendeiro R, Pires AR, Carvalho T, Pinheiro AI, Soares RS, Sousa AE (2014) Thymic HIV-2 infection uncovers post-transcriptional control of viral replication in human thymocytes. *J Virol*. Dec **3**, pii: JVI.03047-14. [Epub ahead of print]. (Journal IF: 4.648).

Tsuji S, Stein L, Kamada N, Nuñez G, Bram R, Vallance BA, Sousa AE, Platt JL, Cascalho M. (2014) TACI deficiency enhances antibody avidity and clearance of an intestinal pathogen. *J Clin Invest*. **124**, 4857-66. (Journal IF: 13.765).

Mota C, Nunes-Silva V, Pires AR, Matoso P, Victorino RM, Sousa AE and Caramalho I. (2014) Delta-like 1-Mediated Notch Signaling Enhances the In Vitro Conversion of Human Memory CD4 T Cells into FOXP3-Expressing Regulatory T Cells. *J Immunol* **193**, 5854-62. (Journal IF: 5.362).

Fernandes SM, Pires AR, Ferreira C, Foxall RB, Rino J, Santos C, Correia L, Poças J, Veiga-Fernandes H, Sousa AE. (2014) Enteric mucosa integrity in the presence of a preserved innate interleukin 22 compartment in HIV type 1-treated individuals. *J Infect Dis*. **210**, 630-40. (Journal IF: 5.778).

Jorge I, Amaral B, Soares-Almeida LM, Foxall RB, Tendeiro R, Santos JM, Sousa AE, Victorino RM (2014) Massive hypereosinophilia and vasculitis associated with major expansion of interleukin-5-producing CD8+ T cells in HIV-1 infection. *AIDS* **28**, 1075-7. (Journal IF: 6.557).

Barbosa RR, Silva SL, Silva SP, Melo AC, Pereira-Santos MC, Barata JT, Hammarström L, Cascalho M, Sousa AE. (2014). Reduced BAFF-R and increased TACI expression in common variable immunodeficiency. *J Clin Immunol* **34**, 573-583. (Journal IF: 2.654).

Amaral AJ, Brito FF, Chobanyan T, Yoshikawa S, Yokokura T, Van Vactor D and Gama-Carvalho M (2014) Quality assessment and control of tissue specific RNA-seq libraries of *Drosophila* transgenic RNAi models. *Front. Genet.* **5**, 43. doi: 10.3389/fgene.2014.00043; (Journal IF: Not Applicable).

Marciano BE, Huang C, Joshi G, Rezaei N, Carvalho BC, Allwood Z, Ikinciogullari A, Reda SM, Gennery A, Thon V, Espinosa-Rosales F, Al-Herz W, Porras O, Shcherbina A, Szaflarska A, Kilic S, Franco JL, Gomez Raccio AC, Roxo P, Esteves I, Galal N, Grumach AS, Al-Tamemi S, Yildiran A, Orellana JC, Yamada M, Morio T, Liberatore D, Ohtsuka Y, Lau Y, Nishikomori R, Torres-Lozano C, Mazzucchelli JTL, Vilela MMS, Tavares FS, Cunha L, Pinto JA, Espinosa-Padilla SE, Hernandez-Nieto L, Elfeky RA, Ariga T, Toshio H, Dogu F, Cipe F, Formankova R, Nuñez-Nuñez ME, Bezrodnik L, Marques JG, Pereira MI, Listello V, Slatter MA, Nademi Z, Kowalczyk D, Fleisher TA, Davies G, Neven B, and Rosenzweig SD (2014). BCG vaccination in patients with severe combined immunodeficiency: Complications, risks, and vaccination policies. *J Allergy Clin Immunol* **133**, 1134-41. (Journal IF: 11,248).

Ribot JC, Ribeiro ST, Correia DV, Sousa AE, Silva-Santos B. (2014). Human gamma-delta thymocytes are functionally immature and differentiate into cytotoxic type 1 effector T cells upon IL-2/IL-15 signaling. *J Immunol.* 192:2237-43. (Journal IF: 5.362). Fernandes SM, Pires AR, Ferreira C, Tendeiro R, Correia L, Paulo SE, Victorino RMM, Sousa AE. (2014) Gut disruption in HIV-2 infection despite reduced viremia. *AIDS* **28**, 290-2. (Journal IF: 6.557).

Póvoas MI, Luís PP, Esteves I, Ferrão A (2014) Severe Langerhans cell histiocytosis in an infant: haemophagocytic syndrome association. *BMJ Case Rep.* pii: bcr2014206983. doi: 10.1136/bcr-2014-206983. (Journal IF: 2,063).

Lopes AI, Vale F F, Oleastro M. (2014) Helicobacter pylori infection. Recent developments in diagnosis. TOPIC HIGHLIGHT. *World J Gastroenterol* **20**, 9299-9313, (Journal IF: 2,433).

Fernandes SM, Pires AR, Ferreira C, Tendeiro R, Correia L, Paulo SE, Victorino RMM, Sousa AE. (2014) Gut disruption in HIV-2 infection despite reduced viremia. *AIDS* **28**,290-2. (Journal IF: 6.557).

### Other publications National

Moscoso T, Melo AC, Neto M, Pereira Santos MC. Avaliação da expressão dos marcadores CD63 e/ou CD203c em basófilos e do seu contributo no diagnóstico de hipersensibilidade ao diclofenac. *Rev Port de Imunoalergologia* 2014 **22**, (3):195-205

### Invited lectures and seminars

Sousa, AE. Infecção pelo Virus da Imunodeficiência Humana tipo 2. X Congresso Nacional VIH/SIDA, XII Congresso Nacional de Doenças Infecciosas e Microbiologia Clínica, Lisbon, Portugal, December 1, 2014

Sousa, AB. “Dilemmas in prenatal diagnosis”. Sessão sobre New challenges in prenatal diagnosis da 18ª Reunião Anual da Sociedade Portuguesa de Genética Humana. Lisboa, 19-21 Novembro 2014.

Silva, SL. Treat to Target na Imunodeficiência Comum Variável. Treat to Target nas Imunodeficiências e doença VIH. Infecção e Autoimunidade. Porto, Portugal, October 24-25, 2014

Sousa, AE. HIV Target Imunológico Reservatórios Celulares: T CD4 memória e outros. Infecção & Imunidade, Porto, Portugal, 24-25 October 2014.

Foxall, RB. “Translocação microbiana como target (HIV infection and the gut)”. T2T, Treat to Target nas imunodeficiências e doença VIH, Target virológico, imunológico, e Clínico. Infecção & Imunidade, Porto, Portugal, 24-25 October 2014.

Sousa, AB. “Face fetal”. Sessão sobre síndromes genéticas e anomalias faciais do 20º Congresso de Obstetrícia e Ginecologia organizado pela Federação de Sociedades Portuguesas de Obstetrícia e Ginecologia (FSPOG). Centro de Congressos Altis Lisboa, 2-5 Outubro 2014.

Pereira Santos, MC - Teste de activação de basófilos (TAB) no diagnóstico em alergia medicamentosa: Qual a real utilidade?- Curso Verão Actualização em alergia medicamentosa – ASIA, 20 Setembro 2014

Sousa, AE. A Portuguese experience on the way to cure – Elite controllers: what can they tell us about designing strategies for cure? Bristol-Myers Squibb, Partnering for Cure, Desafios na Virologia - Construindo Pontes rumo à Cura, Lisbon, Portugal, June 21, 2014.

Silva, SL. Reacções de hipersensibilidade e dessensibilização. IV Curso de Antimicrobianos. Sociedade de Infeciologia Pediátrica. Coimbra, Portugal, May 29-30, 2014

Victorino RMM, Clinical Research: a Driver for Improvement of Medical Care, Annual Retreat of the Program For Advanced Medical Education, April 16, 2014, Lisbon.

Fernandes, S.. Disrupting the largest barrier: HIV-2 infection of the gut. "HIV-2, the forgotten virus" meeting, Lisbon, Portugal, April 5th 2014.

Foxall, RB. Preserving peripheral homeostasis: HIV-2 impact on CD4 T cell subsets. "HIV-2, the forgotten virus" meeting, Lisbon, Portugal, April 5th 2014.

Nunes-Cabaço, H. Targeting T cells at the origin: HIV-2 infection of the human thymus. "HIV-2, the forgotten virus" meeting, Lisbon, Portugal, April 5th 2014.

Sousa, AB. "Aconselhamento genético". XLIII Conferências de Genética Doutor Jacinto Magalhães com o tema A Genética do X. Hospital de Santo António, 28 Março 2014.

Caramalho, I. Os alvos do futuro em imunoterapia e imunomodulação. V Congresso MedUBI, Covilhã, Portugal, January 10th 2014.

Lopes, AI. Terapêutica Biológica na Doença de Crohn em Idade Pediátrica. Proposta de Normas de Orientação Clínica. Reunião Anual do Grupo de Estudo da Doença Inflamatória (GEDII). Lisboa, Janeiro de 2014

Pereira Santos, MC. Novas perspectivas de diagnóstico- 1ª Jornadas de Imunoalergologia do Hospital da Luz- Do hospital à Comunidade, 24 Janeiro 2014

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

Serra-Caetano A., Barbosa R. R., Silva S. P., Barbosa M. P., Sousa A. E, Silva S. L. Exploring T-cell disturbances in Common Variable Immunodeficiency disorders, 16th Meeting of the European Society for Immunodeficiencies, Prague. Czech Republic, October 29-November 1, 2014 (Oral Presentation).

Silva S. L., Albuquerque A. S., Serra-Caetano A., Pinheiro A. S., Fernandes S. M., Foxall R. B., Ferreira J., Victorino R. M., Sousa A. E. Human naïve regulatory T-cells are maintained by IL-7, 16th Meeting of the European Society for Immunodeficiencies, Prague. Czech Republic, October 29-November 1, 2014 (Poster Presentation).

Albuquerque A. S., Silva S. L., Matoso P., Charmeteau B., Anjos R., Abecasis M., Cheynier R., Victorino R. M., Sousa A. E. Upregulation of DUSP6 in naïve CD4 T-cells of adults submitted to total thymectomy early in life, 16th Meeting of the European Society for Immunodeficiencies, Prague. Czech Republic, October 29-November 1, 2014 (Poster Presentation).

Silva S. L., Albuquerque A. S., Charmeteau B., Anjos R., Abecasis M., Victorino R. M., Cheynier R., Sousa A. E. S $\beta$ /TREC ratio in adults submitted to total or partial thymectomy in early infancy, 16th Meeting of the European Society for Immunodeficiencies, Prague. Czech Republic, October 29-November 1, 2014 (Poster Presentation).

Fernandes A, Teixeira C, Silva SL, Silva SP, Esteves I, Marques JG, Neves C, Neves JF, Faria E, Guedes M, Lemos S, Marques L. X-Linked Agammaglobulinemia: a Portuguese National Survey, 16th Biennial Meeting of the European Society for Primary immunodeficiencies. Prague. Czech Republic, October 29-November 1, 2014 (Poster Presentation).

Costa AC, Campos Melo A, Duarte F, Pedro E, Pereira-Barbosa M, Pereira Santos MC Immunoterapia sublingual específica con Pru p 3 en 10 doentes portugueses – evaluación clínica e inmunológica durante 12 meses XXIX Congreso Nacional de la Sociedad Española de Alergología e Inmunología Clínica, Salamanca, 22-25 October, 2014 (Poster Presentation). Prize of the best poster presentation

Duarte F, Costa AC, Bento ML, Pereira Santos MC, Pereira Barbosa M. Contribute of recombinant fish parvalbumin rGad<sub>c1</sub> in the characterization of fish allergic patients. Food Allergy and Anaphylaxis Meeting, Dublin, 9-11-October 2014 (Poster Presentation).

SV. Azevedo, H Loreto, Al Lopes. Immune Thrombocytopenia and Pediatric Ulcerative Colitis Management: a role for anti-TNF- $\alpha$  treatment? 3rd. International Symposium on Pediatric Inflammatory Bowel Disease, Rotterdam, September 2014, (J Crohn's Colitis suppl.) (Poster presentation)

Amaral AJ, Andrade J, Foxall R, Matoso P, Soares R, Matos AM, Tendeiro R, Gonçalves J, Gama-Carvalho M, and Sousa AE. (2014) The modulation of the microRnome of human CD4+ T cells by TCR-mediated activation and HIV infection. EMBO Fellows Meeting, EMBO, Heidelberg, Germany, June 14-16 2014 (Oral communication)

Mascarenhas MI, Costa Silva I, Campos Melo A, Pereira Santos MC, Rosado Pinto J Anaphylaxis with hydrocortisone, a rare case. XXXIII Congress of the European Academy of Allergy and Clinical Immunology, Copenhaga, 7-11 June 2014. (Poster presentation)

Brito S, Póvoas M, Dupont J, Palha A, Lobo L, Lopes AI. Peutz-Jeghers Syndrome: clinical expression, molecular findings and therapeutic implications. Congresso Asociación Española de Pediatría, Madrid, June 2014 (Poster presentation)

Nunes-Cabaço H, Matoso P, Foxall RB, Tendeiro R, Pires AR, Pinheiro AI, Soares RSS, Sousa AE; "Infection of the Human Thymus by HIV-2", 9th ENII – EFIS/EJI Immunology Summer School 2014, Porto Conte, Alghero, Sardinia, Italy, May 5th-12th 2014 (Poster presentation)

Fernandes A, Prata F, Mouzinho A, Esteves I, Marques JG. HIV drug resistance in children before initiating combined anti-retroviral treatment. 32nd Annual Meeting of the European Society for Infectious Diseases. Dublin, Ireland, 6-10 May 2014. (Poster presentation)

Morais, A. Salgado C. Silva, L.O. Silva, S. Seves, G. Esteves, I. Picard C. Marques, J.G. MyD88 Deficiency: A Clinical Case 32nd Annual Meeting of the European Society for Infectious Diseases. Dublin, Ireland, 6-10 May 2014. (Poster presentation)

Marques L, Fernandes A, Candeias F, Neves C, Prata F, Mouzinho A, Virtuoso MJ, Fraga S, Franco J, Campos T, Caldeira A, Tavares M, Rocha G, Marques JG. Portuguese Pediatric HIV Working Group. HIV Infected Children and Adolescents in Portugal – 2013. 32nd Annual Meeting of the European Society for Infectious Diseases. Dublin, Ireland, 6-10 May 2014. (Poster presentation)

Espírito Santo R, Salgado C, Pires Guerra M, Prata F, Mouzinho A, Esteves I, Quintas S, Marques JG. Cerebral toxoplasmosis in a previously "healthy" adolescent. 32nd Annual Meeting of the European Society for Infectious Diseases. Dublin, Ireland, 6-10 May 2014. (Poster presentation)

Costa AC, Duarte F, Pedro E, Pereira Santos MC, Pereira-Barbosa M. Efficacy of oral desensitization to milk in a group of Portuguese patients with persistent severe cow's milk allergy – clinical and immunological evaluation. VII World Asthma, Allergy and COPD Forum, New York, 26-29 April 2014. (Poster presentation)

Costa AC, Campos Melo A, Pereira-Barbosa M, Pereira Santos MC, Autoimmune chronic urticaria diagnosis – Contribution of the basophil activation test VII World Asthma, Allergy and COPD Forum, New York, 26-29 April 2014. (Poster presentation) Prize for the best Abstract

Costa AC, Campos Melo A, Duarte F, Pedro E, Pereira-Barbosa M, Pereira Santos MC Sublingual specific immunotherapy with Pru p 3 in 10 Portuguese patients – clinical and immunological evaluation during 12 months. VII World Asthma, Allergy and COPD Forum, New York, 26-29 April 2014. (Poster presentation)

Costa AC, Campos Melo A, Duarte F, Pedro E, Pereira-Barbosa M, Pereira Santos MC. Clinical and immunological evaluation of sublingual specific immunotherapy with Pru p 3 in 10 Portuguese patients, during 12 months. XXXIII Congress of the European Academy of Allergy and Clinical Immunology, Copenhagen, 7-11 June 2014. (Poster presentation)

Mota C, Nunes-Silva V, Sousa AE, Victorino RM, Caramalho I. Notch signaling enhances the in vitro conversion of human memory CD4 cells into Regulatory T Cells, Keystone Symposium: Inflammatory Diseases: Recent Advances in Basic and Translational Research and Therapeutic Treatments, Vancouver, Canada, January 17-22, 2014, (Poster presentation)



### Communications in National Conferences

Maurício, SD, Fernandes SM, Pires AR, Ferreira C, Sousa AE, HIV-2 Impact on Lymph Nodes. 17.º Workshop Educação pela Ciência – Dia da Investigação GAPIC/FMUL, Lisboa, Portugal, December 17, 2014 (Oral presentation).

Caramalho, I., A. Melo, E. Pedro, M. P. Barbosa, R. M. Victorino, M. C. Santos and A. E. Sousa. Bee venom enhances the differentiation of human Regulatory T cells, XL Meeting of the Portuguese Society of Immunology, Lisbon, October 13-15, 2014, (Oral presentation).

Serra-Caetano A., Barbosa R. R., Silva S. P., Barbosa M. P., Sousa A. E, Silva S. L. Exploring T-cell disturbances in Common Variable Immunodeficiency disorders, XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October, 2014 (Poster Presentation).

Marcelino J., Esteves I., Silva S. L., Serra-Caetano A., Albuquerque A.S., Melo A., Silva S. P., Sousa A. B., Marques J. G. Four cases of Hyper IgE Syndrome due to STAT3 mutations. XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October, 2014 (Poster Presentation).

Albuquerque A. S., Silva S. L., Matoso P., Charmeteau B., Anjos R., Abecasis M., Cheynier R., Victorino R. M., Sousa A. E. Upregulation of DUSP6 in naïve CD4 T-cells of adults submitted to total thymectomy early in life. XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October, 2014 (Poster Presentation).

Silva SL, Albuquerque AS, Charmeteau B, Anjos R, Abecasis M, Victorino RM, Cheynier R, Sousa AE. S $\mu$ /TREC ratio in adults submitted to total or partial thymectomy in early infancy. XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October, 2014 (Poster Presentation).

Sousa A.B., Abhyankar A. V., Albuquerque A. S., Vieira M., Carmo J. A., Silva S. L., Boisson B., Frugoni F., Notarangelo L. D., Sousa A. E., Casanova J. L., Marques J. G. Unusual presentation of X-linked SCID diagnosed by whole-exome sequencing. XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October, 2014 (Poster Presentation).

Caramalho, I., V. Nunes-Silva, A.R. Pires, C. Mota, A.I. Pinto, H. Nunes-Cabaço, R. B. Foxall and A. E. Sousa. IL-2 and IL-15 are expressed in the human thymus in a non-overlapping pattern, XL Meeting of the Portuguese Society of Immunology, Lisbon, October 13-15, 2014, (Poster presentation).

Fernandes SM, Pires AR, Matoso P, Ferreira C, Correia L, Valadas E, Poças J, Pacheco P, Sousa AE, Foxall RB. Lack of disruption of mucosal integrity in chronic HIV-2 infection. XL Annual Meeting of the Portuguese Society for Immunology, Lisbon, 13-15 October 2014. (Poster presentation).

Nunes-Cabaço H, Foxall RB, Matoso P, Pires AR, Tendeiro R, Soares RS, Pinheiro AI, Passos V, Cavaco T and Sousa AE. "Host restriction factors of retroviral replication in the human thymus", SPI'40 From Immune Responses to Therapy, IMM, Lisbon, 13-15 October 2014 (Poster presentation).

Passos VM, Sousa AE and Nunes-Cabaço H. "Quantification of Human Endogenous Retrovirus in the Human Thymus", SPI'40 From Immune Responses to Therapy, IMM, Lisbon, 13-15 October 2014 (Poster presentation).

Sousa R, Marques JG, and Gonçalves B. Sobre-prescrição de antibióticos em países em desenvolvimento – experiência dum centro de saúde em Maputo. 15º Congresso Nacional de Pediatria, Albufeira, 16 a 18 de outubro 2014. (Poster presentation).

Marcelino J, Silva P, Costa AC, Pereira Santos MC, Pereira Barbosa M. Investigação de anafilaxia de etiologia alimentar-papel dos alérgenos moleculares. XXXV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Porto 3-5 Outubro, 2014 (Oral presentation)

Aguiar R, Viegas L, Marcelino J, Costa AC, Pereira Barbosa M, Pereira Santos MC. Alergia ao camarão-caracterização do perfil de sensibilização numa população portuguesa . XXXV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Porto 3-5 Outubro, 2014 (Oral presentation)

Pestana L, Melo AC, Mendes A, Pedro E, Barbosa MP, Pereira Santos MC. Biomarcadores de sensibilização primária e reactividade cruzada em doentes alérgicos a veneno de himenópteros. XXXV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Porto 3-5 Outubro, 2014, (Oral presentation) 2º Prize of the best oral communication

Paes MJ, Fournier M, Costa AC, Pereira Santos MC, Pereira Barbosa M. Hipersensibilidade a anisakis-diagnóstico diferencial de alergia alimentar XXXV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Porto 3-5 Outubro 2014 (Poster presentation). 2º Prize of the best poster presentation

Silva SP. Workshop – complicações e prognóstico nas imunodeficiências primárias, 35º Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Porto, Portugal, 3 a 5 de Outubro, 2014 (Oral presentation)

Azevedo S, Loreto H, Lopes AI. Trombocitopenia imune e colite ulcerosa em idade pediátrica: contribuição da terapêutica biológica? Congresso Nacional Pediatria, Algarve, Outubro, 2014 (Poster presentation).

Martins C, Azevedo S, Loreto H, Mourato P, Palha A, Lopes AI. Expressão clínica e alérgica da esofagite eosinofílica em idade pediátrica - experiência de um centro terciário. Congresso Nacional Pediatria, Algarve, Outubro, 2014 (Poster presentation).

Oliveira Ramos F., Conde M., Martins F.M., Marques J.G., Esteves I., Sousa A.B., Miltenberger-

Miltenyi G., Henriques C., Farela Neves J., Cordeiro-Ferreira G., Pereira da Silva J.A., Fonseca J.E., Canhão H. "Auto-inflammatory diseases register - data from the newest Reuma.pt protocol". XVII Congresso Português de Reumatologia. Algarve, 7-10 Maio 2014. (Poster presentation).

### **Organisation of Conferences**

Sousa AE. XL Meeting of the Portuguese Society of Immunology, Lisbon, October 13-15, 2014.

Lopes AI. 1ª Reuniao Anemia na Doença Inflamatória Intestinal na criança e no jovem, Perspectiva actual e avanços terapêuticos, Lisboa, October 4, 2014

Lopes AI. President of Scientific and Organizing Committee - Reuniao Anual da Sociedade de Gastreenterologia e Nutrição Pediatrica, and Reuniao Anual da Semana Digestiva, Estoril, June 2014

Sousa AE. "HIV-2, the forgotten virus" Meeting. Programa Nacional para a Infecção VIH, Direcção Geral de Saúde. Ministry of Health. Lisbon, Portugal, April 5th 2014.

Maurício SD. 5th Annual International Medical Students Meeting, Lisboa, Portugal, March 7-9, 2014

### **Internationalisation**

Ana E Sousa: Co-Coordination of the Ebook entitled "Thymic stromal alterations and genetic disorders of immune system", *Frontiers in Immunology*.

National coordination of the COST Action BM1404 "European Network of Investigators Triggering Exploratory Research on Myeloid Regulatory Cells (Mye-EUNITER)". Agency: Comissão Europeia. Reference: COST BM1404.

Participation in the evaluation committee of the research unit Centre International de recherche en infectiologie(CIRI), at Lyon – CIRI to be coordinated by HCERES – Haute conseil de l'évaluation de la recherche et de l'enseignement supérieur. France

Establishment as Affiliated Participant of the EUROFLOW-PID Consortium - Flow Cytometry for Fast and Sensitive Diagnosis and Follow-up of Haematological Malignancies and Immune Disorders.

### **Prizes, honours and awards**

GAPIC 2nd Prize to the project HIV-2 Impact on Lymph Nodes. Lisboa, Portugal, December 17, 2014 to Mauricio, SD.

2º Prize Bial- Aristegui 2014, Sociedade Portuguesa de Alergologia e Imunologia Clinica - Imunoterapia específica sublingual com Pru p 3 numa população portuguesa com alergia grave ao pêssego – avaliação de eficácia e segurança durante 12 meses to Costa AC, Campos Melo A, Duarte F, Pedro E, Pereira-Barbosa, M Pereira Santos

### **Industry contract research**

Scientific Project entitled: Modulation of HIV replication and latency in human CD4 T cells by regulatory small RNAs. Merck Investigator Studies Program Reference: #39114, 2011/2014, 142.000€, funded by the Merck Sharp & Dome Corporation Merck & Co., Inc.. PI: Sousa AE

Scientific Project entitled: Reservatórios e Replicação Viral nas Células T CD4 de Memória-Central e Foliculares na Infecção HIV-2. 2013-2015, €14.500, funded by Gilead Sciences. PI: Sousa AE

Scientific Project entitled: Infecções crónicas por Candida albicans e defeitos intrínsecos do sistema imunitário: optimização dos cuidados de saúde através do diagnóstico de imunodeficiências primárias. 2013-2015, €20.000, funded by Gilead Sciences. PI: Silva SL.

"A Prospective, Open Label Study To Assess The Pharmacokinetics, Safety & Efficacy Of Anidulafungin When Used To Treat Children With Invasive Candidiasis, Including Candidemia" - A8851008. Ongoing at the Hospital de Santa Maria/Centro Hospitalar Lisboa Norte under the responsibility of: Marques JG.

"An Open-Label, Multicenter, Multiple-Dose Pharmacokinetic and Safety and Efficacy Trial of Maraviroc in Combination With Optimized Background Therapy for the Treatment of Antiretroviral-Experienced CCR5-Tropic HIV-1 Infected Children 2 - <18 Years of Age." Ongoing at the Hospital de Santa Maria/Centro Hospitalar Lisboa Norte under the responsibility of: Marques JG.

### **Government/Organisation contract research**

Sousa AE. Member of the National Ethical Committee for Clinical Investigation.

Victorino RMM, Chairman, and Sousa AE, Member, of the Scientific Council, Faculdade de Medicina, Universidade de Lisboa.

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

Lopes AI. Member of the Pedagogic Council, Faculdade de Medicina, Universidade de Lisboa. (since November 2014).

Sousa AE. Participation in grant evaluation, Fundação para a Ciência e Tecnologia (FCT).

Marques JG and Silva SL. Members of “Comissão Técnica de Vacinação da Direcção-Geral de Saúde”

Marques JG and Silva SL. Colaboração na elaboração da orientação da DGS nº 016/2014 de 24/09/2014 “Vacinação contra a gripe com a vacina trivalente para a época 2014/2015”.

Marques JG. Colaboração na elaboração das “Recomendações Portuguesas para o tratamento da infeção por VIH-1 e VIH- 2 2015.”

Victorino RMM. Member of the Directive Board of the Sociedade de Ciências Médicas de Lisboa.

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

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

Victorino RMM, Member of the Juri for BIAL Research Award 2014.

Victorino RMM, Member of the Evaluation Board for the Speciality Medical Training / PhD Program from Fundação para a Ciência e Tecnologia (FCT) / Ministry of Health, Portugal.

#### **Advanced teaching**

Lopes AI. Provas de Agregação (Academic Title) - Faculdade de Medicina, Universidade de Lisboa. 19-20 June, 2014.

Internships in our Lab - Specialiaty in Immunoallergology - Clinical Immunology Laboratory training period for the final degree (Ordem dos Médicos/Ministry of Health):

José Pedro – from Serviço de Imunoalergologia, Centro Hospitalar Lisboa Norte, Hospital Santa Maria, October 2013 to February 2014;

Leticia Pestana– from Serviço de Imunoalergologia, Centro Hospitalar Lisboa Norte, Hospital

Santa Maria, May to July 2014;

Rita Aguiar– from Serviço de Imunoalergologia, Centro Hospitalar Lisboa Norte, Hospital Santa Maria, October to December 2014.

Sousa AE, Pereira-Santos MC, Victorino RMM, Silva SL, Fernandes SM, and Serra-Caetano A. Clinical Immunology teaching in the core curriculum for Medical Students, Area: Medicine 2, 5th year. Faculdade de Medicina da Universidade de Lisboa.

Sousa AE, Pereira-Santos MC, Victorino RMM, Silva SL, Fernandes SM, and Serra-Caetano A. Teaching of the Discipline of Clinical Immunology of the 4th and 5th year of the Degree in Medicine – Faculdade de Medicina, Universidade de Lisboa

Sousa AE: Collaboration in the teaching of Immunology in the core curriculum for Medical Students, 2nd year. Faculdade de Medicina da Universidade de Lisboa.

Amaral AJ. Participation in the BioSys PhD program: module of Bioinformatics and Computational Modelling. Lisbon, Portugal.

Lopes AI, Regency of Disciplina Optativa de Pediatria, FMUL (5º Ano) – “Procedimentos clínicos em Pediatria” .

Marques JG. Comissão de Vacinas da SIP /SPP - Recomendações na criança imunocomprometida. 12º Encontro de Infecçologia – Sociedade de Infecçologia Pediátrica. Vila Franca de Xira, 6 de dezembro de 2014.

Marques JG. Vacinas extra Plano. Workshop do 13º Encontro Nacional de Internos e Jovens Médicos de Família. Estoril 24 de outubro de 2014.

Pereira Santos MC. Organizer and Lecturer of Workshop“Alérgenos e imunoterapia- a abordagem molecular  
Annual meeting of the Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Porto, Portugal, October 3-5, 2014

Silva SL. Organizer and Lecturer of Workshop“– complicações e prognóstico nas imunodeficiências primárias. Annual meeting of the Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Porto, Portugal, October 3-5, 2014

Sousa AB: “What about unexpected findings in chromosomal microarray analysis?” Curso da Associação Portuguesa de Diagnóstico Pré-Natal (APDPN) sobre DPN invasivo e não invasivo, satélite às Jornadas de Ginecologia e Obstetrícia do Alto Minho. Viana do Castelo, 17-18 Outubro 2014.

Lopes AI. Doença Celíaca em idade pediátrica Curso Avançado de Nutrição em Pediatria, Universidade Católica Portuguesa, Lisboa, Junho de 2014

Lopes AI. Doença Inflamatória Intestinal em idade pediátrica Curso Avançado de Nutrição em Pediatria, Universidade Católica Portuguesa, Lisboa, Junho de 2014

Marques JG. Infecções em Crianças com Imunodeficiências Primárias. Unidade Curricular “Infecções em Imunocomprometidos”. Mestrado em Saúde Tropical/Doutoramento em Medicina Tropical. Instituto de Higiene e Medicina Tropical, Lisboa, 7 de Junho de 2014.

Sousa AE. Imunodeficiência associada à infecção VIH. Instituto de Ciências Biomédicas Abel Salazar. Porto, 29 May, 2014.

Sousa AB. “A consulta de genética clínica”. Sessão Clínica do Serviço de Pediatria do Hospital de Vila Franca de Xira, 6 Maio 2014.

Sousa AE, HIV pathogenesis, GABBA PhD Program, Porto, April 28, 2014.

Marques JG. Vacinas em circunstâncias especiais. Sessão de formação do Departamento de Pediatria do Hospital de Santa Maria, CHLN. 6 de Fevereiro de 2014

Lopes AI. Organization: Curso Medical Writing, Como elaborar e publicar um artigo científico, XX Jornadas de Pediatria, Departamento de Pediatria do HSM-CHLN, Fevereiro 2014

Marques JG. Hot topics em Vacinas: painel de discussão. 9º Curso de Infeciologia Pediátrica. Coimbra, 30 e 31 de Janeiro de 2014.

#### **Science and society**

Mauricio SD. Young Professionals Advisory Group, The Future for Health – Everyone has a role to play, Fundação Calouste Gulbenkian, Lisboa, Portugal

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

## Ana Sebastião Lab

### Major Interests / Objectives

To fight brain diseases one has to correct abnormal synaptic function, a main challenge to Neurosciences. We aim to elucidate how the neuronal and glial components of the tripartite synapse are fine-tuned under normal and dysfunctional situations. How endogenous modulators affect the pre- post and glial components of the tripartite synapse, neuronal excitability, neuronal and glial cell renewal, neuronal and glial maturation and degeneration, under normal and pathological conditions are topics under current investigation by the Unit. As endogenous modulators we focus on neurotrophic factors, adenosine, endocannabinoids and glycine. As disease models we have been focusing on Alzheimer's and Parkinson's disease, epilepsy, amyotrophic lateral sclerosis and multiple sclerosis.

### Head of Unit

Ana M Sebastião, PhD, Full Professor

### Research Team

Ana Filipa Ferreira da Cunha Ribeiro	Master	PhD Student
Ana Iolanda d'Armada Moreira	Graduate	MSc Student, (started September)
Ana Sofia Cristovão Ferreira	PhD	Post doctoral Investigator
Ana Sofia Temudo Duarte António	Master	PhD Student (co-supervision with Domingos Henrique Lab)
André Jerónimo Santos	Master	PhD Student
António Artur da Paz Ferreira Pinto Duarte	Master	PhD Student, (left January)
Armando Dulcídio da Silva Cruz	Master	PhD Student
Catarina Miranda Lourenço	Graduate	MSc Student, (started September)
Catarina Reis Orcinha	Master	Voluntary Investigator (left in March)
Cátia Alexandra Pêgas Palminha	Graduate	MSc Student



Catia Isabel Afonso Domingos	Graduate	MSc Student, (started September)
Cláudia Alexandra dos Santos Valente de Castro	PhD	Senior Investigator
Cláudia Sofia Beltrão Cavacas	Graduate	Trainee, (started September)
Daniela Cristina Melo Magalhães	Graduate	MSc Student
Diogo Miguel Rombo	Master	PhD Student
Fabio Marques Simoes de Souza	PhD	Senior Investigator (left February)
Filipa Fiel do Carmo Glórias Ferreira	Master	Investigator
Filipe Jorge Nascimento Xavier Fernandes	Graduate	MSc Student
Francisco Melo Albuquerque Saraiva Mouro	Master	PhD Student
Frederico Simões do Couto	Graduate	Investigator, MD
Gabriela Antunes	MD/PhD	Post doctoral Investigator, (Left February)
Haíssa de Castro Abrantes	Graduate	MSc Student
Isabel Maria do Amaral Rodeia Rodrigues de Brito	Undergraduate	Trainee, (started September)
João Filipe Fonseca Gomes	Graduate	MSc Student, (started September)
João Miguel Guerreiro Covita	Master	MSc Student
Joaquim Alexandre Ribeiro	MD/PhD	Senior Investigator
Margarida Leonor Ferreira Martins	Graduate	MSc Student, (started September)
Maria Alexandra Pereira Botelho	Undergraduate	Administrative
Maria José Diógenes	PhD	Senior Investigator
Mariana Colino Oliveira	Master	PhD Student
Noémia Marisa Félix Pereira	Graduate	MSc Student
Pedro Dinis Avelar Agostinho	Graduate	MSc Student
Raquel Alice da Silva Baptista Dias	PhD	Post doctoral Investigator
Rita Cruz Coelho de Mira Ramalho	PhD	Post doctoral Investigator
Rita Isabel Pedro Aroeira	Master	PhD Student

Rui Miguel Silva Rodrigues	Graduate	MSc Student, (started September)
Sandra Cristina Henriques Vaz	PhD	Post doctoral Investigator
Sara Alves Xapelli	PhD	Post doctoral Investigator
Sara Luísa Ramalho Tanqueiro	Graduate	MSc Student, (started September)
Tatiana Pinto Morais	Graduate	MSc Student, (started September)

### Keywords / Research Areas

Tripartite synapse mechanisms, Neuronal excitation/inhibition balance, Neurodegenerative Mechanisms, Ageing, Epilepsy, Drug Abuse

### Major scientific achievements

1) Fine tune modulation of the tripartite synapse:

- a) GABAergic transmission controlled in a cell and synaptic specific way by purines (Rombo et al Hippocampus; Rombo et al Cerebral Cortex; Pires et al J Theor Biol; Jacob et al Glia);
- b) Homeostatic control of synaptic activity by adenosine kinase (Diógenes et al Cerebral Cortex).
- c) Astrocytes express GlyT2 (Aroeira et al Brain Struct Funct).

2) Synaptic plasticity modulation:

- a) Persistent changes in synaptic plasticity after prolonged manipulation of synaptic activity (Felix-Oliveira et al J Neurophysiol; Jerónimo-Santos et al Neuropharmacology; Rodrigues et al Neuropharmacology)

3) Ageing and Neurodegenerative diseases:

- a) Dysregulation of TrkB Receptors by Abeta protein (Jerónimo-santos et al Cerebral Cortex
- b) Purinergic modulation of NMT in a ALS model (Nascimento et al PLOS ONE); deregulation of NMT upon ageing (Pousinha et al PLOS ONE)
- c) Modulation of oligodendrogenesis by a CB1R ligand (Xapelli et al Front Cell Neurosc

### Selected Publications

Sebastião AM, Ribeiro J A (2009) Adenosine Receptors in the Central Nervous System . *Handbook of Experimental Pharmacology* **193**, 471-534. (Journal IF: 2,958, Citations: 119)

Fontinha BM, Diógenes MJ, Ribeiro JA, Sebastião AM (2008) Enhancement of long –term potentiation by BDNF requires adenosine A2A receptor activation by endogenous adenosine. *Neuropharmacology* **54**, 924-933. (Journal IF: 4.819, Citations: 47)

Diógenes MJ, Fernandes CC, Sebastião AM, Ribeiro JA (2004) Activation of adenosine A2A receptor facilitates BDNF modulation of synaptic transmission in hippocampal slices. *Journal of Neuroscience* **24**, 2905-2913. (Journal IF: 6.747, Citations: 88)

Dias RB, Rombo DM, Ribeiro JA, Henley JM, Sebastião AM (2013) Adenosine: setting the stage for plasticity. *Trends in Neurosciences (TINS)* **36**, 248-257. (Journal IF: 12.902, Citations: 11)

Sebastião AM, Ribeiro JA. (2000) Fine tuning neuromodulation by adenosine. *Trends in Pharmacological Sciences (TIPS)* **21**, 341-346. (Journal IF: 9.988, Citations: 171)

### Ongoing Research Projects

2011/2014 Title: Modulation of GABAergic transmission in the hippocampus by adenosine. Coordinator: Ana M Sebastião. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-NMC/110838/2009. Amount: 161,375€.

2012/2015 Title: Are microglia a new potential pharmacological target in amyotrophic lateral sclerosis (ALS)?. Coordinator: Paula Alexandra Costa Marçal Correia. Agency: Fundação Ciência e Tecnologia. Coordinator Institution: Faculdade de Farmácia, Universidade de Lisboa. Coordinator PI: Dora Brites. Reference: PTDC/SAU-FAR/118787/2010. Amount: 22,000€. Amount (total): 146,273€.

2013/2014 Title: PhD project Armand Cruz. Coordinator: Ana M Sebastião. Agency: Cardlane Ltd.. Reference: PhD project Armand Cruz. Amount: 33,044€.

2013/2014 Title: Modulation of amyloid beta-induced neuronal toxicity via JNK: a novel role for tauroursodeoxycholic acid. Coordinator: Rita Cruz Coelho de Mira Ramalho. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-NMC/112636/2009. Amount: 26,095.14€.

2014/2015 Title: Adenosine receptors: new pharmacological targets for Rett syndrome treatment. Coordinator: Maria José Diógenes. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BIM-MEC/0009/2013. Amount: 50,000€.

2014/2016 Title: Neurophysiological mechanisms of aging: novel view of old concepts. Coordinator: Maria José Diógenes. Agency: Fundação Bial. Reference: Bial fellowship programme 57/12. Amount: 49,000€.

## Other Projects

2013/2014 Adenosine A2A Receptors and Zinc: New Avenues for the Treatment of Rett. Funded: 1785€ (GAPIC). Coordinator: Maria José Diógenes.

2013/2014 Role of adenosine A2A receptors on the action of  $\beta$ -amilóide peptide upon BDNF signalling. Funded: 1785.00 € (GAPIC). Coordinator: Maria José Diógenes.

2014/2015 Microglial expression of SIRT : consequences for LTP. Funded: 650.00€ (GAPIC). Coordinator: Maria José Diógenes (collaboration with Teresa Pais from other IMM Unit).

2014/2016 Targeting selected synapses to develop new antiepileptic drugs with minimal side effects. Coordinator: Ana M Sebastião (collab. Ken Jackobson, NIH, Bethesda).

2013/2016 Adenosine kinase deficiency and epilepsy: synaptic characterization of adenosine signaling. Coordinator: Ana M Sebastião (in collab with Detlev Boison, Portland, USA).

2013/2015 GABA transport in an animal model of absence epilepsy. Coordinator: Sandra Vaz (in collab with Vecenzo Crunelli, Cardiff).

2010/2016 Amyloid beta peptide-induced toxicity: impact on hippocampal function. Coordinator: Maria José Diógenes.

2010/2016 Glycinergic neurotransmission at the hippocampus. Coordinator: Cláudia Valente.

2013/2016 Modulatory role of adenosine and cannabinoids in oligodendrogenesis and neurogenesis derived from neural stem/progenitor cells of the subventricular zone. Coordinator: Sara Xapelli.

2013/2016 Deciphering the role of inflammation in epileptogenesis. Coordinator: Claudia Valente.

2012/2015 Astrocytic Calcium signalling modulation by purines. Coordinator: Sandra Vaz.

2013/2017 Astrocytic influence of BDNF actions at the hippocampus. Coordinator: Sandra Vaz.

2013/2016 Memory dysfunction by cannabinoids: synaptic correlates and modulation by adenosine. Coordinator: Ana M Sebastião.

### Publications in peer review Journals

Rombo DM, Dias RB, Duarte ST, Ribeiro JA, Lamsa KP, Sebastião AM (2014). Adenosine A1 receptor suppresses Tonic GABAA receptor currents in hippocampal pyramidal cells and in a defined subpopulation of interneurons. *Cereb Cortex*. (ePub December 2014). (Journal IF: 8.305).

Rombo DM, Newton K, Nissen W, Badurek S, Horn JM, Minichiello L, Jefferys JG, Sebastiao AM, Lamsa KP (2014) Synaptic mechanisms of adenosine A2A receptor-mediated hyperexcitability in the hippocampus. *Hippocampus*. (Epub Nov 7). (Journal IF: 4.302).

Sebastião AM, Ribeiro J (2014) Neuromodulation and metamodulation by adenosine: Impact and subtleties upon synaptic plasticity regulation. *Brain Res*. (ePub Nov 2014). (Journal IF: 2.828).

Félix-Oliveira A, Dias RB, Colino-Oliveira M, Rombo DM, Sebastião AM (2014) Homeostatic Plasticity induced by Brief Activity Deprivation Enhances Long-Term Potentiation in the Mature Rat Hippocampus. *J Neurophysiol*. **112**, 3012-3022. (Journal IF: 3.041)

Pousinha PA, Correia AM, Sebastião AM, Ribeiro JA (2015) The giant miniature endplate potentials frequency is increased in aged rats. *Neurosci Lett*. **584C**, 224-229 (ePub October 2014). (Journal IF: 2.055).

Serpa A, Sebastião AM, Cascalheira JF (2014) Modulation of cGMP accumulation by adenosine A1 receptors at the hippocampus: Influence of cGMP levels and gender. *Eur J Pharmacol*. **744**, 83-90. (Journal IF: 2.684).

Jacob JP, Vaz SH, Ribeiro JA, Sebastião AM (2014) P2Y1 receptor inhibits GABA transport through a calcium signalling-dependent mechanism in rat cortical astrocytes. *Glia* **62**, 1211-1226. (Journal IF: 5.466).

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. (Journal IF: 8.305, Citations: 3)

Antunes G, Sebastião AM and Simões-de-Sousa (2014) Mechanisms of regulation of olfactory transduction and adaptation in the olfactory cilium. *PLoS One* **9**(8):e105531. (Journal IF: 3.534).

Nascimento, F, Pousinha PA, Marçal-Correia A; Gomes R, Sebastião AM, Ribeiro JA (2014) "Adenosine A2A receptors activation facilitates neuromuscular transmission in the pre-symptomatic phase of the SOD1(G93A) ALS mice, but not in the symptomatic phase". *PLoS ONE* **9**, (8):e104081. (Journal IF: 3.534).

Morgado AL, Xavier JM, Dionísio PA, Ribeiro MF, Dias RB, Sebastião AM, Solá S, Rodrigues CM (2014) MicroRNA-34a Modulates Neural Stem Cell Differentiation by Regulating Expression of Synaptic and Autophagic Proteins. *Mol Neurobiol*. (ePub June 2014). (Journal IF: 5.286).

Jerónimo-Santos A, Vaz SH, Parreira S, Rapaz-Lérias S, Caetano AP, Buée-Scherrer V, Castrén E, Valente CA, Blum D, Sebastião AM, Diógenes MJ (2014) Dysregulation of TrkB Receptors and BDNF Function by Amyloid- $\beta$  Peptide is Mediated by Calpain. *Cereb Cortex*. (ePub May 2014) (Journal IF: 8.305).

Assaife-Lopes N, Sousa VC, Pereira DB, Ribeiro JA, Sebastião AM (2014) Regulation of TrkB receptor translocation to lipid rafts by adenosine A2A receptors and its functional implications for BDNF-induced regulation of synaptic plasticity. *Purinergic Signalling*, **10**, 251-267. (Journal IF: 3.510, Citations: 1)

Jerónimo-Santos A, Batalha VL, Müller CE, Baqi Y, Sebastião AM, Lopes LV, Diógenes MJ. (2014) Impact of in vivo chronic blockade of adenosine A2A receptors on the BDNF-mediated facilitation of LTP. *Neuropharmacology*. **83**, 99-106. (Journal IF: 4.819, Citations: 2)

Pires M, Raischel F, Vaz SH, Cruz-Silva A, Sebastião AM, Lind PG (2014) Modeling the functional network of primary intercellular Ca<sup>2+</sup> wave propagation in astrocytes and its application to study drug effects, *Journal Theoretical Biology*, **356**, 201-212. (Journal IF: 2.303, Citations:1)

Xapelli S, Agasse F, Grade S, Bernardino L, Ribeiro FF, Schitine CS, Heimann AS, Ferro ES, Sebastião AM, De Melo Reis RA, Malva JO (2014). Modulation of subventricular zone oligodendrogenesis: a role for hemopressin? *Front Cell Neurosci* **8**, 59 e collection 2014. (Journal IF: 4.175, Citations: 3)

Rodrigues TM, Jerónimo-Santos A, Outeiro TF, Sebastião AM, Diógenes MJ (2014) Challenges and promises in the development of neurotrophic factor-based therapies for Parkinson's disease. *Drugs Aging*, **31**, 239-261. (Journal IF: 2.503, Citations: 2)

Rodrigues TM, Jerónimo-Santos A, Sebastião AM, Diógenes MJ (2014) Adenosine A2A Receptors as novel upstream regulators of BDNF-mediated attenuation of hippocampal Long-Term Depression (LTD). *Neuropharmacology*, **79**, 389-398. (Journal IF: 4.819, Citations: 1).

Sousa VC, Vital J, Costenla AR, Batalha VL, Sebastião AM, Ribeiro JA, Lopes LV (2014) Maternal separation impairs long term-potential in CA1-CA3 synapses and hippocampal-dependent memory in old rats. *Neurobiol Aging*, **35**, 1680-1685. (Journal IF: 4.853)

Aroeira RI, Sebastião AM, Valente CA (2014) GlyT1 and GlyT2 in brain astrocytes: expression, distribution and function. *Brain Struct Funct* **219**, 817-30. (Journal IF: 4.567).

Devesa P, Agasse F, Xapelli S, Almengló C, Devesa J, Malva JO, Arce VM (2014) Growth hormone pathways signaling for cell proliferation and survival in neural precursors of postnatal mice *BMC Neurosci*. **15**(1):100. doi: 10.1186/1471-2202-15-100. (Journal IF: 2.845).

Cunha-Reis D, Aidil-Carvalho MF, Ribeiro JA (2014). Endogenous inhibition of hippocampal LTD and depotentiation by vasoactive intestinal peptide VPAC1 receptors. *Hippocampus*, **24**, 1353-1363. (Journal IF: 4.302)

Coelho J.E., Alves P., Valadas JS., Schmidt T., Batalha VL., Ferreira DG., Ribeiro JA., Bader M., Cunha RA., Couto F. and Lopes LV. (2014). Overexpression of adenosine A2A receptors in rats: effects on depression, locomotion and anxiety. *Frontiers in Psychiatry* **13** June 2014 doi: 10.3389/fpsy.2014.00067. (Journal IF: ND)

Garcia-Cazorla A, Duarte ST (2014) Parkinsonism and inborn errors of metabolism. *J Inherit Metab Dis*. 2014 Jul; **37** (4):627-42.7. (Journal IF: 4.14)

Marques J, Duarte ST, Costa S, Jacinto S, Oliveira J, Oliveira ME, Santos R, Bronze-da-Rocha E, Silvestre AR, Calado E, Evangelista T (2014) Atypical phenotype in two patients with LAMA2 mutations. *Neuromuscul Disord*. 2014 May; **24**, (5):419-24 (Journal IF: 3.134)

Lee, HS, Hosuk S, Ghetti, A, Pinto-Duarte, A, Wang, X, Dziewczapolski, G, Galimi, F, Huitron-Resendiz, S, Pina-Crespo, JC, Roberts, AJ, Verma, IM, Sejnowski, TJ, Heinemann, SF (2014). Astrocytes contribute to gamma oscillations and recognition memory. *PNAS*, **111**, E3343-

E3352. (Journal IF: 9.809, Citations: 3).

#### **Other publications National**

Guimarães, S, Moura, D e Sebastião AM (2014). Mecanismos Gerais das Acções dos Fármacos. In: Terapêutica Medicamentosa e suas Bases Farmacológicas, ed., S. Guimarães, D Moura e P Soares da Silva, pp 38-50, Porto Editora, Porto.

Ribeiro, J.A. (2014). Estimulantes do Sistema Nervoso Central. Antagonistas dos receptores da adenosina: Alquilxantinas In: Terapêutica Medicamentosa e suas Bases Farmacológicas, ed., S. Guimarães, D Moura e P Soares da Silva, pp 175-180, Porto Editora, Porto.

Sebastião AM (2014). Sistema Purinérgico. In: Terapêutica Medicamentosa e suas Bases Farmacológicas, ed., S. Guimarães, D Moura e P Soares da Silva, pp 346-354, Porto Editora, Porto.

#### **Invited lectures and seminars**

AM Sebastião - Adenosine modulation of signaling at the tripartite synapse – ‘Purinergic Frontiers: From Basic Science to Clinical Challenges’, Madrid, March 2014

AM Sebastião – Invited for Discussions at the Meeting: SUDEP: Time for prevention – Evidence and Clinical Translation, Oxford, March 2014

AM Sebastião – Modulation of GABAergic inhibition in the hippocampus by adenosine - ‘Purines 2014 Conference’, Bonn, July 2014

AM Sebastião – Modulation of inhibitory synaptic transmission at the hippocampus – Faculty of Sciences, University of Lisbon, November, 2014

AM Sebastião - Synapse specific modulation of inhibitory synaptic transmission by adenosine at the hippocampus, Centro de Neurociências de Coimbra, May 2014

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

Aroeira RI, Sebastião AM and Valente CA (2014) “Characterization of BDNF role upon GlyT2-mediated glycine uptake in brain synaptosomes”. 9th Forum of European Neuroscience, July 5-9, Milan (Italy). Poster presentation.



Diógenes MJ, Jerónimo-Santos A, Batalha VL, Muller C, Hockemeyer J, Lopes LV, Sebastião AM (2014) Chronic blockade of adenosine A2A receptors prevents BDNF effect on hippocampal LTP. 9th FENS meeting, July 5-9, Milan (Italy). (Poster presentation)

Jerónimo-Santos A, Vaz SH, Parreira S, Rapaz-Lérias S, Caetano AP, Buée-Scherrer V, Castrén E, Valente CA, Blum D, Sebastião AM, Diógenes MJ (2014) Amyloid- $\beta$  peptide dysregulates TrkB receptors and BDNF function by a calpain-dependent mechanism. 9th FENS meeting, July 5-9, Milan (Italy). (Poster presentation)

Sofia T Duarte, Catia Palminha, Tiago M Rodrigues, Sara Ferreira, Ana M Sebastião, Maria José Diógenes (2014) Adenosine receptors as new pharmacological targets for Rett syndrome treatment. 9th FENS meeting, July 5-9, Milan (Italy). (Poster presentation)

Filipa F. Ribeiro, Telma E. Santos, Mónica M. Sousa, Ana M. Sebastião, The mechanisms underlying the modulation of axon elongation by adenosine A2A receptors, 9th FENS meeting, July 5-9, Milan (Italy). (Poster presentation)

Xapelli S, Ferreira FF, Ribeiro FF, Sebastião AM. Role of BDNF on endocannabinoids-modulation of neurogenesis in murine dentate gyrus stem/progenitor cell cultures. 9th FENS meeting, July 5-9, Milan (Italy). (Poster presentation)

Chazalon M, Miguelez C, Morin S, Cristóvão-Ferreira S, Vaz SH, Sebastião AM, Baufreton J (2014) Glial regulation of tonic inhibition in globus pallidus neurons. 9th Forum of European Neuroscience, 5th-9th July, Milan, Italy. (Poster presentation)

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

##### **In Meetings of Scientific Societies:**

Aroeira RI, Sebastião AM and Valente CA (2014) "Overview of the glycine-mediated neurotransmission in rat brain". XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Mouro F, Dias R.B., Rombo D.M., Ribeiro J.A., Sebastião A.M. Adenosine A2A receptor activation facilitates synaptic NMDA receptor activity in the hippocampus. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Ferreira F, Ribeiro FF, Sebastião AM, Xapelli S (2014) Unravelling the role of BDNF on endocannabinoids-modulation of neurogenesis in murine dentate gyrus stem/progenitor cell

cultures. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Santos T, Ferreira R, Maia J, Agasse F, Xapelli S, Cortes L, Bragança J, Malva JO, Ferreira L, Bernardino L. (2014) Therapeutic Potential of Retinoic Acid-Loaded Nanoparticles for Brain Repair. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Jerónimo-Santos A, Vaz SH, Parreira S, Rapaz-Lérias S, Caetano AP, Buée-Scherrer V, Castrén E, Valente CA, Blum D, Sebastião AM, Diógenes MJ (2014) Dysregulation of TrkB receptors and BDNF function by amyloid- $\beta$  peptide is mediated by calpain. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Filipa F. Ribeiro, Filipa Ferreira, Ana M. Sebastião, Sara Xapelli, The role of adenosine A2A receptors in the dentate gyrus neurogenesis of Sprague-Dawley rats, XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Rodrigues TM, Sebastião AM, Diógenes MJ (2014) BDNF mediated attenuation of hippocampal long-term depression is dependent on adenosine A2A receptors activation. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Colino-Oliveira M, Diógenes MJ, Ribeiro JA, Boison D, Sebastião AM, Synaptic modulation by adenosine on an age-dependent epilepsy model. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Nascimento F., Correia A., Gomes R., Pousinha P.A., Sebastião A.M., Ribeiro J.A. "A1 and A2A adenosine receptors functional crosstalk at the neuromuscular junction of the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis". XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Jacob PF, Vaz SH, Ribeiro JA, Sebastião AM (2014) P2Y1 receptors in astrocytes inhibit GABA transport in a calcium-signalling dependent way. XLIV Reunião Anual da Sociedade Portuguesa de Farmacologia, February 5-7, Coimbra (Portugal). (Oral presentation)

Almeida J, Vargas M, Diógenes MJ, Pais TF, Sebastião AM (2014) Effect of microglial expression of Sirt2 in LTP. 17.<sup>o</sup> Workshop "Educação pela Ciência" GAPIC, FMUL December 17, Lisboa, Portugal. (Poster and Oral Presentation)

Pedro DM, Duarte-Samartinho M, Ribeiro FF, Sebastião AM, Xapelli S (2014) Role of adenosine A2A receptor (A2Ar) and brain-derived neurotrophic factor (BDNF) on self-renewal and neurogenesis of dentate gyrus neural stem cells – 17.º Workshop “Educação pela Ciência” GAPIC, FMUL December 17, Lisboa, Portugal (Poster Presentation)

**Other Scientific Communications (national):**

Diógenes MJ - Adenosine receptors: new pharmacological targets for Rett syndrome treatment – Serviço de Neurologia, Hospital de Santa Maria, Lisboa, July 2014

Diógenes MJ - Perda da sinalização mediada pelo BDNF na Doença de Alzheimer e na Síndrome de Rett- Sessões de Farmacologia, Faculdade de Medicina, July 2014

Sebastião AM - Modulation of neuronal inhibitory transmission by adenosine – IMM Seminar, March 2014

Filipa F. Ribeiro, Filipa Ferreira, Ana M. Sebastião, Sara Xapelli, The role of adenosine A2A receptors in hippocampal neurogenesis, IMM Pizza Seminars, IMM, Lisbon, January 7th , 2014.

Xapelli S, Hemopressin as a regulator of oligodendrogenesis in subventricular zone stem/progenitor cell cultures" – IMM “Pizza Seminar, Lisbon, Feb 4th 2014

**Organisation of Conferences**

Sebastião AM: Chairperson and organizer of the symposium ‘Purinergic Control of Synaptic Transmission’ at the ‘Purines 2014 Conference’, Bonn, July 2014

Ribeiro JA: Chairperson and organizer of the symposium ‘Purinergic Signalling at the Neuromuscular system’ at the ‘Purines 2014 Conference’, Bonn, July 2014

Xapelli S: Member of the organizing committee of the “1st Joint Retreat of Postdoc fellows of IMM, IGC and CEDOC”, Sintra (Portugal), 29-31 of October 2014.

Ramalho RM: One of the organizers of the symposium “2nd IMM PostDoc Day”, Lisbon, June 2014.

## Internationalisation

Christopher Parsons (Frankfurt, Germany) within the project on Neurophysiological mechanisms of aging: novel view of old concepts, funded by the Bial Foundation.

Detlev Boison (Portland, USA) on the Functional characterization of BDNF and adenosine signalling at the hippocampus of mice with altered expression of astrocytic adenosine kinase (one paper has been already published).

Angeles García Cazorla (Barcelona, Spain), a neuropediatrician who collaborates with our group within the exploratory project funded by FCT on adenosine receptors as putative new pharmacological targets for Rett syndrome treatment.

Eero Castren (Helsinki) on Neurotrophin signalling dysfunction in Alzheimer disease models. (one paper was already published).

Jeremy Henley (Bristol)- Modulation of AMPA receptor trafficking (one paper already published).

Karri Lamsa (Oxford) on the Influence of adenosine receptors on selected hippocampal synapses and upon the neuroregulatory action of endocannabinoids in the hippocampus (two manuscripts already published).

Rafael Franco, (Pamplona) Carmen Lluís (Barcelona) and Francisco Conti (Ancona, Italy) on A1/A2A receptor heterodimers in astrocytes to control GABA transport (two papers already published).

Segi Ferré (Baltimore, USA) on galanine/dopamine interactions in the hippocampus and on A2A/GDNF interaction in the striatum (two papers already published).

Jérôme Baufreton (CNRS, Bordeaux) on GABA transport and GABAergic tonic inhibition in the Globus Pallidus: dysfunction characterization in an animal model of Parkinson's Disease.

Vicenzo Crunelli (Cardiff) on the influence of adenosine and BDNF upon GAT activity and tonic GABAergic currents in an animal model of absence epilepsy.

Karl Jaconson (NIH, Bethesda) on the characterization of the action of an antiepileptic compound at selected hippocampal synapses.

Cristha E Muller (Bonn) on the influence of adenosine upon memory impairment by cannabinoids

#### **Prizes, honours and awards**

Best work/presentation prize: Almeida J, Vargas M, Diógenes MJ, Pais TF, Sebastião AM (2014) Effect of microglial expression of Sirt2 in LTP. 17.º Workshop “Educação pela Ciência” GAPIC, FMUL December 17, Lisboa, Portugal

#### **Advanced teaching**

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

AM Sebastião – Director of the PhD Programme ‘Integrated Neurosciences’, University of Lisbon (Funded by FCT)

AM Sebastião – Member of the Scientific Board of the Ms/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa

AM Sebastião – Member of the Scientific Board Ms/PhD Programme in Cognitive Sciences, Universidade de Lisboa

Sebastião AM – Lecturer of Ms/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa and of the Ms/PhD Programme in Cognitive Sciences, Universidade de Lisboa.

Ribeiro JA - Lecturer of Ms/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa and of the Ms/PhD Programme in Cognitive Sciences, Universidade de Lisboa.

Sebastião AM – Coordinator of the Modules on ‘Molecular and Cellular Biology’, ‘Neuronal Circuits’ and ‘Neurodegeneration and Regeneration’ of the Ms/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa

Ribeiro JA - Coordinator of the Module on Neuroethics, Ms/PhD in Neurosciences.

Diógenes MJ – Coordinator of the Lab demonstrations and Journal Clubs at the Ms/PhD in Neurosciences

Lab members presented the following lectures or seminars as part of the Master and PhD Programmes in Neurosciences:

Ana Filipa Ribeiro - Modulation of neuronal outgrowth in cultured neurons , Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November, 2014

Claudia Valente – Imaging molecules by immunofluorescence, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Diogo Rombo - Evaluation of synaptic activity through electrophysiological recording Techniques, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Diogo Rombo - Synapse-specific modulation at the hippocampus, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Filipe Nascimento - Neuromuscular transmission dysfunction in ALS, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Francisco Mouro – Influence of cannabinoids upon memory: synaptic basis and behavioural evidence Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Maria José Diógenes - Neurotrophic factors: key molecules for neuronal survival and plasticity, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November, 2014

Mariana Colino-Oliveira - Receptor quantification assays: binding and Western Blot, October, 2014

Raquel Dias - Synaptic plasticity: an overview with focus upon synaptic and extrasynaptic modulation of ionotropic glutamate receptors, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Rita Aroeira - Glycine receptors and glycinergic synapses during synapse maturation, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Sandra Vaz - Calcium signalling in astrocytes: relevance for excitability control, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Sofia Cristovão-Ferreira – GABA transport modulation: implications for excitability control, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2014

Sara Xapelli - Postnatal Neurogenesis and oligodendrogenesis – role and disease implications, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December, 2014

Sofia Duarte - Modeling Neurodevelopmental Disorders with Human Induced Pluripotent Stem Cells: From Genes to Function, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 2014

André Jerónimo-Santos - Beta-Amyloid peptide, neurotrophins and neuronal death (André Santos), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 2014

Lab Members presented Lectures, under invitation at Post-graduate programmes at other Schools:

Ribeiro JA; Sebastião AM; Diogenes MJ - Mestrado em Técnicas de Diagnóstico e Intervenção Cardiovascular, Escola Superior de Tecnologia de Saúde de Lisboa, Instituto Politécnico de Lisboa, Lisbon, Portugal, 2014. Sebastião AM. - Master in Physics, Instituto Superior Técnico, Lisbon, Portugal, 2014.

Sebastião AM – Master in Neuropsychology, Universidade Católica Portuguesa Lisboa, Lisbon, Portugal, 2014. Sebastião AM – Master in Biophysics and Biomedical Engineering – Faculty of Sciences, University of Lisbon, December 2014 Ribeiro JA; Sebastião AM; Diogenes MJ – Neurosciences Course to the Master in Biomedical Engineering, IST/FMUL, University of Lisbon, October-December 2014.

Lab members presented the following ‘Neuroscience Seminars’ at IMM:

Haíssa de Castro -“mgluR5- mediated calcium signaling: modulation by Adenosine A1 and A2A receptors in cortical astrocytes.” January 13th

Gabriela Antunes - “Computational systems biology in neuroscience.” January 20th

Pedro Avelar, “Influence of Brain-Derived Neurotrophic Factor on the effect of amyloid-beta peptide upon calcium signaling in astrocytes.” January 27th

Cátia Palminha, “Characterization of Adenosine Receptors in a Rett Syndrome Model.” February 10th

Tiago Rodrigues “A $\beta$  species-mediated impairment of long-term plasticity and BDNF signaling at the hippocampus.”. February 24th

Diogo Rombo, "New sights on adenosine control of excitability." March, 17th

Francisco Mouro, "Interaction between a2a receptors and cb1 receptors in the hippocampus: consequences for memory." March 24th

Monika Lezanska, "Deciphering the role of GlyR in astrocytes." March 31st

Sofia Duarte, "Synaptic Dysfunction in Neurodevelopmental Disorders with Epilepsy and Autism." April, 14th

Sara Xapelli, Sebastião Lab (Posdoc) "Modulating cannabinoid receptors to induce neurogenesis and oligodendrogenesis." April, 28th

Filipe Nascimento, "Adenosinergic modulation at the neuromuscular junction of the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis: insights from the pre-symptomatic and symptomatic stages." May 12th

Noémia Pereira, "Epileptiform activity in organotypic slice cultures: electrophysiological and molecular features." May 26th

Rita Aroeira "Deciphering the glycine-mediated neurotransmission in rat brain." June 2nd

Raquel Dias "Homeostatic Plasticity induced by Brief Activity Deprivation Enhances Long-Term Potentiation in the Mature Rat Hippocampus." June 16th

Maria José Diógenes, "Adenosine receptors: new pharmacological targets for Rett syndrome treatment." July 28th

André Jerónimo-Santos "BDNF and adenosine signalling on amyloid-beta peptide toxicity." September 8th

Raquel Dias, " Homeostatic plasticity and LTP: fast and slow synapse regulation meet somewhere in the between." October 20th

Rita Ramalho, "BDNF neuroprotection loss in Alzheimer's disease - are extrasynaptic NMDA receptors the bad guys?" October 27th

Cátia Palminha, "Characterization of Adenosine Receptors in a Rett Syndrome Model." November 10th

Claudia Valente, " Epileptic-like electrophysiological and molecular features of cultured organotypic slices." December, 1st

Daniela Magalhães, "Deciphering the role of inflammation in the organotypic hippocampal slice model of epileptogenesis." December 1th



### Science and society

Members of the group were involved in the activities regarding the Brain Awareness Week (BAW) and Brain European Year, which included lectures and hands-on activities with the goal of increasing public awareness of the progress and benefits of brain research. These activities included an Open Day (May 14th) at IMM for the senior community and students of the secondary education.

IMM Open Day:

- “Conheces bem o teu cérebro?” – Secondary School: 60 Students.
- “Como ter um cérebro saudável?” - Senior University – 20 participants

Sessions at Schools:

School	Grade	Number of Students	Date
Escola Secundária Sebastião e Silva - Oeiras	Secundário	102	March 10
Escola EB 2º e 3º Ciclos António Gedeão - Odivelas	Básico	42	March 11
Escola Salesianos de Lisboa	Secundário	50	Mach 12
Escola Secundária António Damásio - Lisboa	Secundário	51	March 12
Agrupamento de Escolas de Alvalade - Lisboa	Secundário	98	March 13
Escola EB 2º e 3º Ciclos António Gedeão - Odivelas	Básico	54	March 13
Escola Secundária da Amadora	Secundária	50	March 28
Agrupamento de Escolas Marinha Grande Nascente	Básico	80	April 1
Agrupamento de Escolas Josefa de Óbidos	Secundária	80	March 22
Escola de Dança do Conservatório Nacional	Básico	25	June 4
Total:		632	

Sessions in Basic and High Schools included:

Aroeira RI and Xapelli S, "O Cérebro", Invited lecture on the sequence of the Brain Awareness Week held in "Escola EB 2º e 3º Ciclos António Gedeão" – Odivelas, March 11th 2014.

Xapelli S – "O Cérebro", Invited lecture on the sequence of the Brain Awareness Week held in "Colégio Laranja e Meia" – Lisboa, March 12th 2014.

Ramalho RM, "O Cérebro", Invited lecture on the sequence of the Brain Awareness Week held in Escola Secundária António Damásio, Lisboa, Março 12th, 2014

Aroeira RI, Orcinha C e Ribeiro FF, "O Cérebro", Invited lecture on the sequence of the Brain Awareness Week held in Agrupamento de Escolas Marinha Grande Nascente - Marinha Grande, Abril 1st, 2014.

Aroeira RI e Orcinha C, "O Cérebro", Invited lecture on the sequence of the Brain Awareness Week held in Escola de Dança do Conservatório Nacional em Lisboa, June 4th, 2014.

Valente CA, "Nós e o cérebro", Invited lecture on the sequence of the Brain Awareness Week held in Colégio Manuel Bernardes a alunos do 4º ano, June 6th de 2014.

Sessions at the Senior University

Aroeira RI, e Ribeiro FF, "Como ter um cérebro saudável?", seminário dado na Universidade Sénior "Academia Dos Saberes – Pólo de Loures", 16 de Maio.

Aroeira RI, e Ribeiro FF, "Como ter um cérebro saudável?", seminário dado na Universidade Sénior "Academia Dos Saberes – Pólo de Sacavém", 21 de Maio.

Aroeira RI, e Ribeiro FF, "Como ter um cérebro saudável?", seminário dado na Universidade Sénior "Academia Dos Saberes – Pólo de Sacavém", 11 de Junho.

Aroeira RI, "Como ter um cérebro saudável?", seminário dado no IMM a alunos da Universidade Sénior "Academia Sénior da Cruz Vermelha Portuguesa - Pólo de Cascais", 8 de Dezembro.

Other Science and Society activities

Rita Aroeira, Sara Xapelli and Filipa Ribeiro have been invited (March 12th) to participate in "Café de Ciência na Assembleia da República" under the subject "Mexer no Cérebro".

Diogo Rombo – Invited to participate at "3ª Edição do Conversas de Gerações na Ciência - Neuroconversas" held on Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal – November 12, 2014.

Raquel Dias – Invited to participate on the discussion of the special lecture "A construção de Realidades, na ciência e na literatura" at Instituto Superior Técnico, organized by Professor Betâmio de Almeida with Lúcia Jorge and Professor Mariano Gago

#### **PhD thesis completed**

André Jerónimo Santos 16/10/2014 Brain-derived neurotrophic factor (BDNF) and adenosine signalling on amyloid beta peptide-induced toxicity: impact on hippocampal function , Faculty of Medicine, University of Lisbon Maria José Diógenes

António Pinto-Duarte 16/01/2014 New insights into how the dysfunction of astrocytes or inhibitory circuits can lead to abnormal brain functions. PhD in Neurosciences Faculty of Medicine, University of Lisbon Joaquim Alexandre Ribeiro

**Msc thesis completed**

Sara Luísa Parreira 20/05/2014 Modulation of GABA and glutamate release by brain-derived neurotrophic factor: role of adenosine A2A receptors Faculty of Medicine, University of Lisbon Maria José Diógenes Sandra Vaz

Sofia Lérias 25/02/2014 Amyloid- $\beta$  peptide impairs BDNF effects upon GABA release from rat synaptosomes in a calpain dependent way Faculty of Medicine, University of Lisbon Maria José Diógenes Sandra Vaz

David Alexandre Correia Coelho 05/06/2014 Investigating the role of glycine in astrocyte signalling using calcium imaging of rat primary cultures of cortical astrocytes Faculty of Medicine, University of Lisbon Cláudia Valente

Noémia Marisa Félix Pereira 28/07/2014 Organotypic Hippocampal Slice Culture Model of Epileptogenesis: Electrophysiological and Molecular Features Faculty of Medicine, University of Lisbon Cláudia Valente

Cátia Palminha 21/11/2014 Characterization of adenosine receptors in a Rett syndrome model Faculty of Sciences, University of Lisbon Maria José Diógenes

## Bruno Silva-Santos Lab

### Major Interests / Objectives

We study the biology of T lymphocytes and their key roles in immunity to infection and cancer. Our projects focus on the development of these cells in the vertebrate thymus, and on their functions upon export to the periphery. We investigate differentiation and activation signals for T cells in the mouse system, which provides crucial in vivo models for infectious (such as malaria) and autoimmune diseases. We also study human peripheral blood T cells and, in particular, their recognition and elimination of lymphomas and leukemias. 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, on the one hand, and (auto)immune disorders, on the other.

### Head of Unit

Bruno Silva Santos, PhD, Associate Professor

### Research Team

Ana de Oliveira Rodrigues Amorim	Graduate	MSc Student
Ana Maria de Amarante Pamplona Dias dos Santos	PhD	Senior Investigator
Anita Raquel Quintal Gomes	PhD	Investigator, Escola Superior de Tecnologia da Saúde de Lisboa , Assistant Professor
Daniel Vargas Correia	PhD	Post doctoral Investigator
Diogo Maia e Silva	Undergraduate	Trainee
Francisco Landeck Moreira Franco Caiado	PhD	Post doctoral Investigator
Haakan Rolf Norell	PhD	Senior Investigator
Joana Luísa de Barros Martins	Graduate	MSc Student

Julie Cecile Caroline Ribot	PhD	Senior Investigator
Karine Serre	PhD	Senior Post doctoral Investigator
Maria Margarida Sousa Gonçalves Rei	PhD	PhD Student, Barts and The London School of Medicine and Dentistry , Graduate Program in Areas Of Basic and Applied Biology , (left September)
Miguel Alves Rovisco Ribeiro	Master	Trainee, (started December)
Miguel Muñoz Ruiz	Master	PhD Student
Natacha Maria Gonçalves Silva Sousa	Master	Lab manager
Nina Alexandra Schmolka	PhD	PhD Student
Rita Sofia Simões Faria	Graduate	MSc Student, (started September)
Sérgio Tiago de Freitas Ribeiro	Master	PhD Student
Sofia Mensurado Santos	Graduate	MSc Student, (started September)
Tiago Maria de Carvalho da Costa Amado	Master	PhD Student, (started March)
Tomás Laia McGuire	Graduate	Trainee

#### **Keywords / Research Areas**

T cell development/ differentiation, T cell activation, Tumour immunology, Immunopathogenesis of Severe Malaria, Leukaemia clonal evolution

#### **Major scientific achievements**

We identified a novel cellular cross-talk in ovarian cancer growth that can be exploited as a novel therapeutic target. We demonstrated that gamma delta ( $\gamma\delta$ ) T lymphocytes produce the pro-inflammatory cytokine IL-17 that mobilizes small peritoneal macrophages (SPM), which in

turn stimulate ovarian cancer proliferation in the peritoneal cavity. This research, which revealed an unexpected pro-tumor role for  $\gamma\delta$  T lymphocytes in ovarian cancer, was published in PNAS (Proceedings of the National Academy of Sciences of the USA).

We also published other 4 papers in international journals, made 9 communications in international conferences, and completed 2 PhD theses (Nina Schmolka and Margarida Rei). The application by Haakan Norell won the Research Grant from APCL – Associação Portuguesa Contra a Leucemia.

#### Selected Publications

Schmolka N\*, Serre K\*, Grosso AR, Rei M, Pennington DJ and 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. (Journal IF: 26.199, Citations: 7)

Coquet J\*, Ribot JC\*, Babala N, Middendorp S, Xiao Y, Neves JF, Fonseca-Pereira D, Jacobs H, Pennington DJ, Silva-Santos B\*\* and 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. (Journal IF: 13.216, Citations: 17)

Correia DV, Fogli M, Hudspeth K, da Silva MG, Mavilio D and 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. (Journal IF: 10.555, Citations: 30)

Lança T, Correia DV, Moita CF, Raquel H, Ferreira C, Ramalho JS, Barata JT, Moita LF, Gomes AQ and Silva-Santos B. (2010) The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to  $\gamma\delta$  T-cell cytotoxicity. *Blood* **115**, 2407-11. (Journal IF: 10.555, Citations: 34)

Ribot JC, deBarros A, Pang DJ, Neves JF, Peperzak V, Girardi M, Borst J, Hayday AC, Pennington DJ and Silva-Santos B. (2009) CD27 is a thymic determinant of the balance between IFN- $\gamma$ - and IL-17-producing  $\gamma\delta$  T cell subsets. *Nature Immunology* **10**, 427-36. (Journal IF: 26.218, Citations: 160)

### Ongoing Research Projects

2010/2015 Title: Differentiation of pro-inflammatory T cell subsets in vivo - 260352 T\_Cell(S)\_differ. Coordinator: Bruno Silva Santos. Agency: Comissão Europeia. Reference: ERC\_260352\_BSS. Amount: 1,500,000€.

2013/2014 Title: EMBO Young Scientist's Forum 2013. Coordinator: Bruno Silva Santos. Agency: EMBO. Reference: EMBO YSF 2013. Amount: 14,562.94€.

2013/2014 Title: Development of a novel adoptive cell therapy for leukemia: characterization and optimization of gamma-delta T lymphocytes for clinical application. Coordinator: Bruno Silva Santos. Agency: Fundação Ciência e Tecnologia. Reference: EXPL/BIM-ONC/0490/2012. Amount: 50,000€.

2014/2014 Title: Deciphering the outside-in mechanisms of human  $\gamma\delta$  T cell differentiation. Coordinator: Julie Cecile Caroline Ribot. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/IMI-IMU/0170/2013. Amount: 50,000€.

2014/2014 Title: Quantitative analysis of clonal evolution and characterization of tumor escape variants in relapsing Acute Myeloid Leukemia. Coordinator: Haakan Rolf Norell. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BIM-ONC/1656/2013. Amount: 50,000€.

2014/2016 Title: Preprogrammed versus stochastic clonal evolution of relapsing Acute Myeloid Leukaemia: Impact on disease development and therapeutic responses. Coordinator: Haakan Rolf Norell. Agency: Associação Portuguesa contra. Reference: APCL-SEMAPA 2013-2015. Amount: 40,000€.

### Publications in peer review Journals

Rei M, Pennington DJ and Silva-Santos B. The emerging pro-tumor role of  $\gamma\delta$  T lymphocytes: implications for cancer immunotherapy. Review. *Cancer Res*: In Press. (Journal IF: 9.284, Citations: 0)

Galluzzi L, Vacchelli E, ..., Silva-Santos B, Smyth MJ, Speiser DE, Spisek R, Srivastava PK, Talmadge JE, Tartour E, Van Der Burg SH, Van Den Eynde BJ, Vile R, Wagner H, Weber JS, Whiteside TL, Wolchok JD, Zitvogel L, Zou W, Kroemer G (2014). Classification of current anticancer immunotherapies. *Oncotarget* **5**, (24):12472-508. (Journal IF: 6.63, Citations: 0)

Bonneville M, Chen ZW, Déchanet-Merville J, Eberl M, Fournié JJ, Jameson JM, Lopes RD, Massaia M and Silva-Santos B (2014). Meeting report: Chicago 2014 – 30 years of  $\gamma\delta$  T cells. *Cell Immunol*. 2014 Nov **8**. (Journal IF: 1.87, Citations: 0)

Rei M, Gonçalves-Sousa N, Lança T, Thompson RG, Mensurado S, Balkwill FR, Kulbe H, Pennington DJ and Silva-Santos B (2014). Murine CD27(-) V  $\gamma$ 6(+) $\gamma$  $\delta$  T cells producing IL-17A promote ovarian cancer growth via mobilization of protumor small peritoneal macrophages. *Proc Natl Acad Sci U S A* **111**, (34):E3562-70. (Journal IF: 9.809, Citations: 1)

Ribot JC, Ribeiro ST, Correia DV, Sousa AE and Silva-Santos B (2014). Human  $\gamma$  $\delta$  thymocytes are functionally immature and differentiate into cytotoxic type 1 effector T cells upon IL-2/ IL-15 signaling. *J Immunol* **192**, (5):2237-43. (Journal IF: 5.362, Citations: 2)

#### **Other publications International**

Lança T, Correia DV, Silva-Santos B. 2014. Role of gamma-delta T lymphocytes in cancer immunosurveillance and immunotherapy. In *Cancer Immunology*, Vol. 2 (Nima Rezaei, editor), Springer. (Book Chapter)

#### **Other publications National**

Silva-Santos B, McGuire TL, Martins AN. 2014. Imunoterapia do melanoma metastático. In *Melanoma 2013* (Passos MJ, coordenação). Book Chapter

#### **Invited lectures and seminars**

B. Silva-Santos. Differentiation and pathogenic function of pro-inflammatory gamma-delta T cell subsets. Facultad de Medicina, Universidade Complutense, Madrid (Spain), 23 January 2014.

Håkan Norell. Immunotherapy: what is it  $\gamma$ . 8th INSPIRED, Lisbon (Portugal), 25 January 2014.

Håkan Norell. Imunologia no melanoma. PERSPECTIVAS EM ONCOLOGIA II, Porto (Portugal), 14 February 2014.

B. Silva-Santos. Oncoimmunology. Leaping Forward – Lisbon International Clinical Congress. Hospital da Luz, Lisboa (Portugal), 18 February 2014.

B. Silva-Santos. Differentiation of pro-inflammatory gamma-delta T cell subsets. European Workshop of Rheumatology Research, 22 February 2014.



B. Silva-Santos. Regulation of pro-inflammatory gamma-delta T cell responses to infection. Faculdade de Ciências, Universidade de Lisboa (Portugal), 21 March 2014.

Håkan Norell. Adoptive transfer of genetically engineered T lymphocytes. 10os Encontros da Primavera, Oncology Spring meeting, Évora (Portugal), 27 March 2014.

Håkan Norell. Cancer immunology and immunotherapy: from now to the future. 10os Encontros da Primavera, Oncology Spring meeting, Évora (Portugal), 27 March 2014.

B. Silva-Santos. Gamma-delta T cell differentiation and tumor cell recognition. Escola Superior de Tecnologia da Saúde de Lisboa, Lisboa (Portugal), 30 April 2014.

Håkan Norell. Imuno-Oncologia: o papel do sistema imunitário no cancro. 5a reunião de Oncologia da Associação Portuguesa de Farmácias Hospitalares, Porto (Portugal), 23 May 2014.

B. Silva-Santos. Molecular mechanisms of T cell differentiation. EMBO Young Scientists' Forum, Masaryk University, Brno (Czech Republic), 29 May 2014.

Håkan Norell. Immuno-Oncology across Tumours and Paradigm shift. Fórum Imuno-Oncologia II, Sociedade Portuguesa de Oncologia, Porto (Portugal), 7 June 2014.

Håkan Norell. Quantitative analysis of clonal evolution driving relapse of acute myeloid leukaemia escape variants. Conference: Invited lecturer at the University of Bergen, Bergen (Noruega), 18 June 2014.

Margarida Rei. Murine CD27(-) Vg6+ T cells producing IL-17A promote ovarian cancer growth via mobilization of small peritoneal macrophages. Oxford Immunology Group Meeting (UK), July 2014.

B. Silva-Santos. Do escape à imunoterapia nas doenças hemato-oncológicas. Hope 2014, Cascais (Portugal), 1 November 2014.

B. Silva-Santos. Immune cells in the tumor microenvironment: role in cancer progression and perspectives for immunotherapy. MD Anderson Cancer Center – Ministério da Saúde Joint Conference on Gastric and Hereditary Cancer, Lisboa, 21 November 2014.

Håkan Norell. Immunotherapy in cancer. VII Congresso Nacional Associação Portuguesa Neuro Oncologia, Lisboa (Portugal), 21 November 2014.

B. Silva-Santos. Unconventional mechanisms of effector gamma-delta T cell differentiation. The British Society for Immunology Annual Congress, Brighton (United Kingdom), 3 December 2014.

B. Silva-Santos. Molecular mechanisms of differentiation of effector gamma-delta T cell subsets. The 43rd Annual Meeting of the Japanese Society for Immunology, Kyoto (Japan), 11 December 2014.

#### Communications in International Conferences

B. Silva-Santos. Differentiation of pro-inflammatory gamma-delta T cell subsets. European Workshop of Rheumatology Research, 22 February 2014. (Invited Speaker) (Oral presentation)

Schmolka N., Gomes A.Q., and Silva-Santos B. Role of miR-146a in IL-17+ gd T cell differentiation. 6th International Gamma-Delta T-Cell Conference, Chicago (USA), 16 - 18 May 2014 (Oral presentation)

Miguel Muñoz-Ruiz, Julie C. Ribot, José R. Regueiro, Bruno Silva-Santos and Edgar Fernández-Malavé. Reduced TCR  $\gamma\delta$  signaling in CD3 $\beta$ / CD3  $\gamma$  haploinsufficient mice selectively impairs the development of IFN- $\gamma$ -producing CD27+ NK1.1+  $\gamma\delta$  T cells. 6th International Gamma-Delta T-Cell Conference, Chicago (USA), 16 - 18 May 2014 (Oral presentation)

Margarida Rei, Natacha Gonçalves-Sousa, Telma Lança, Richard G. Thompson, Frances R. Balkwilld, Hagen Kulbed, Daniel J. Pennington, and Bruno Silva-Santos. Murine CD27(-) Vg6+ T cells promote ovarian cancer growth via interleukin-17 production and mobilization of small peritoneal macrophages. 6th International Gamma-Delta T-Cell Conference, Chicago (USA), 16 - 18 May 2014 (Oral presentation)

Sérgio T. Ribeiro, Julie C. Ribot, João T. Barata and Bruno Silva-Santos. CD27 costimulation induces Casein Kinase 2 and activates pro-survival PI3K/Akt signaling in human  $\gamma\delta$  T-cells. 6th International Gamma-Delta T-Cell Conference, Chicago (USA), 16 - 18 May 2014 (Poster presentation)

Barros-Martins, J., N. Schmolka, C. Ferreira, M. Veldhoen, B. Silva-Santos and K. Serre. Unconventional functions of “master” transcription factors in  $\gamma\delta$  T cells. 6th International Gamma-Delta T-Cell Conference, Chicago (USA), 16 - 18 May 2014 (Poster presentation)

Nina Schmolka, Anita Q. Gomes, Bruno Silva-Santos. microRNAs regulate interleukin-17 and interferon-g expression during T cell development and differentiation. EBI-EMBL Workshop Networks and Pathways, Cambridge (United Kingdom), 09-13 June 2014. (Poster presentation)

B. Silva-Santos. Unconventional mechanisms of effector gamma-delta T cell differentiation. The British Society for Immunology Annual Congress, Brighton (United Kingdom), 3 December 2014. (Invited Speaker) (Oral presentation)

B. Silva-Santos. Molecular mechanisms of differentiation of effector gamma-delta T cell subsets. The 43rd Annual Meeting of the Japanese Society for Immunology, Kyoto (Japan), 11 December 2014. (Invited Speaker) (Oral presentation)

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

Francisco Caiado, Tânia Carvalho, Diogo Silva da Maia, Maria Gomes da Silva, Ton Schumacher, Bruno Silva-Santos and Håkan Norell. Quantitative analysis of clonal evolution and characterization of escape variants in relapsing acute myeloid leucemia. Hematopoiesis from bench to bedside. Braga (ICVS), 11 April 2014 (Poster and Oral presentation)

Miguel Muñoz-Ruiz, Julie C. Ribot, José R. Regueiro, Bruno Silva-Santos and Edgar Fernández-Malavé. High TCR/ CD3 expression and signaling selectively controls the development of IFN- $\gamma$ -producing  $\gamma\delta$ T cells. XL Reunião Anual da Sociedade Portuguesa de Imunologia. Lisboa, 13-15 October 2014. (Oral presentation)

Sofia Mensurado, Margarida Rei, Telma Lança, Natacha Gonçalves-Sousa, Karine Serre and Bruno Silva-Santos. In vivo inhibition of anti-tumour  $\gamma\delta$  T cell responses by polymorphonuclear Myeloid-Derived Suppressor Cells. XL Reunião Anual da Sociedade Portuguesa de Imunologia. Lisboa, 13-15 October 2014. (Poster presentation)

Sérgio T. Ribeiro, Julie C. Ribot, Daniel V. Correia, João T. Barata, Bruno Silva-Santos. Costimulation of human  $\gamma\delta$  T-cells via CD27 signaling is mediated by CK2. XL Reunião Anual da Sociedade Portuguesa de Imunologia. Lisboa, 13-15 October 2014. (Poster presentation)

Joana Barros-Martins, Nina Schmolka, Cristina Ferreira, Marc Veldhoen, Bruno Silva-Santos and Karine Serre. Lineage-specific transcriptional requirements for IFN- $\gamma$  and IL-17 production by effector  $\gamma\delta$ T cell subsets. XL Reunião Anual da Sociedade Portuguesa de Imunologia. Lisboa, 13-15 October 2014. (Poster presentation)

Francisco Caiado, Tânia Carvalho, Rita Faria, Diogo Maia e Silva, Maria Gomes da Silva, Ton Schumacher, Bruno Silva-Santos and Håkan Norell. Quantitative analysis of clonal evolution driving relapse of acute myeloid leukaemia escape variants. 1st ASPIC International Congress, Lisboa, 25-26 November 2014. (Poster presentation)

#### **Organisation of Conferences**

B. Silva-Santos organized the Oncoimmunology workshop, Encontros de Primavera em Oncologia, Hotel Évora (Portugal), 27 March 2014.

B. Silva-Santos, K. Serre and N. Gonçalves-Sousa co-organized the XL Annual Meeting of the Portuguese Society of Immunology. Instituto de Medicina Molecular, Lisboa (Portugal), 13-15 October 2014.

#### **Internationalisation**

Collaborative work with Drs. Daniel J. Pennington (Blizard Institute, Queen Mary College, London, UK), Adrian Hayday (Cancer Research UK, London, UK), Ton Schumacher (The Netherlands Cancer Institute, Amsterdam, The Netherlands), José Ramon Regueiro (Universidad Complutense, Madrid, Spain).

#### **Prizes, honours and awards**

Nina Schmolka and Sérgio T. Ribeiro were awarded individual Travel Grants from Sociedade Portuguesa de Imunologia.

Sérgio T. Ribeiro was awarded an individual Travel Grant from European Molecular Biology Organization.

#### **Advanced teaching**

B. Silva-Santos co-organized and lectured in the Immunology course of the LisbonBioMed PhD Program, IMM, 3-7 February 2014.

A. Q. Gomes and N. Schmolka. miRNAs in the immune system. Lecture in the Immunology course of the LisbonBioMed PhD Program, IMM, 3-7 February 2014.

Karine Serre. Molecular mechanisms of T cell differentiation. Lecture in the Immunology course of the LisbonBioMed PhD Program, IMM, 3-7 February 2014.

B. Silva-Santos. T cell differentiation. GABBA PhD Program course, Instituto de Biologia Molecular e Celular, Universidade do Porto, 15 April 2014.

A. Q. Gomes. miRNAs in the immune system. Master Program "Molecular Biology in Health", Escola Superior de Saúde Egas Moniz, Caparica, 21 June 2014.

B. Silva-Santos. T cell differentiation and tumor targeting in cancer immunotherapy. Universidade do Algarve, Faro, 4 July 2014.

### **Science and society**

B. Silva-Santos – media (PNAS paper): RTP, SIC, TVI (TV), Jornal de Notícias (press), Radio Renascença, Antena 1, TSF and Radio Comercial (radio).

Håkan Norell participated in the RTP1 TV show “Há Tarde”. There he discussed his research on Leukemia and was awarded the Associação Portuguesa Conta a Leucemia 2014 grant. Lisboa, 8 October 2014.

### **PhD thesis completed**

Nina Schmolka 16/10/2014 Epigenetic mechanisms of  $\gamma\delta$  effector T cell differentiation: focus on histone modifications and microRNAs Faculdade de Medicina, Universidade de Lisboa B. Silva-Santos

Margarida Rei 17/12/2014 Characterization of a pro-tumour role of interleukin-17-producing  $\gamma\delta$  T cells in ovarian cancer Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto B. Silva-Santos Daniel J. Pennington

### **Msc thesis completed**

Ana Amorim 17/11/2014 The role of microRNAs in CD8+ T cell differentiation Faculdade de Ciências, Universidade do Porto B. Silva-Santos

Rui Gonçalves 01/01/2014 Anticorpos Bloqueadores dos Checkpoints imunes no Tratamento do Cancro Faculdade de Medicina, Universidade de Lisboa B. Silva-Santos

Micael Mendes 01/01/2014 Mecanismos oncológicos de escape à vigilância do sistema imunitário Faculdade de Medicina, Universidade de Lisboa B. Silva-Santos

## Carlota Saldanha Lab

### Major Interests / Objectives

Understanding how leukocyte recruitment is governed and regulated is pivotal for the comprehension of the mechanisms underlying inflammation. We are focused on deciphering what molecular partners are targeted by fibrinogen as it modulates neutrophil action and how chemokines and hydrogen peroxide cooperate in neutrophil recruitment. We aim also to develop theoretical models to simulate phenomena occurring at the leukocyte-vascular wall interface. Under our scope are as well the study of fibrinogen-mediated signal transduction on erythrocytes bioavailability of nitric oxide and the validation of inflammatory biomarkers in vascular diseases. We expect to translate our findings towards a better understanding and management of inflammatory pathologies, like sepsis and cardiovascular diseases.

### Head of Unit

Maria Carlota Saldanha Lopes, PhD Agregação

### Research Team

Ana Rosa Miranda dos Santos Silva Herdade	Master	PhD Student
Angelo Calado	PhD	Senior Investigator
Beatriz Simões Pinheiro	Undergraduate	Trainee, (started September)
Catarina Cabrita Ramos	Master	Consultant, (left March)
Catarina Duarte Lima	Master	MSc Student, (started September)
Ekaterina Sergueevna Potapova	Graduate	MSc Student, (left May)
Giulia Andolina	Master	MSc Student, (started March) (left June)
Gonçalo José	Undergraduate	MSc Student, (started May)

Lopes da Cunha		
Inês Matos de Oliveira	Undergraduate	Technician, (started November)
Mariana Mota Castro Dias	Graduate	Internship, (left July)
Marta Filipa Paulino Silvestre	Graduate	PhD Student, (left January)
Nuno Alexandre Almeida Santos	Graduate	MSc Student, (left May)
Patrícia Alexandra Veloso Napoleão	PhD	Post doctoral Investigator
Rita Maria Santos Esteves	Graduate	Technician
Sara Louro Moleirinho	Graduate	MSc Student
Sara Maria de Almeida Beijinho	Graduate	MSc Student
Sofia Ludovina Novais de Oliveira	Graduate	PhD Student, Departamento de Biología Celular e Histología, Facultad de Biología, Universidad de Murcia, Murcia, Spain , Instituto Murciano de Investigación Biosanitaria (IMIB), Murcia, Spain , (left April)

#### **Keywords / Research Areas**

Inflammation, Microcirculation, Neutrophil, Erythrocyte, Leukocyte recruitment , Inflammation, Hemorheology, Microcirculation

#### **Major scientific achievements**

Hydrodynamic behaviour of blood cells is influenced by inflammation and thrombus. Efficient method for inducing and monitoring thrombus in mice and numerical simulations were developed.

Erythrocyte bioavailability in NO (biomarker of inflammation) depends on AChE conformation, Gi protein, band 3 and PKC. Fibrinogen and CD47 agonist peptide induce NO efflux in cAMP-

dependent and PI3K –independent manner.

Lower concentrations of sCD40L 30 days after infarct onset associate with higher prevalence of G894T eNOS polymorphism, high concentration of N-terminal BNP, compromised myocardial healing capacity at the genetic and post-transcriptional level and cardiovascular mortality. sCD40L levels decrease in sepsis patients.

In zebrafish wounding, early leukocyte recruitment requires the formation of H<sub>2</sub>O<sub>2</sub> gradients by Duox1. ATP release upon injury triggers Duox1 activation via a P2YR/PLC/Ca<sup>2+</sup> signaling pathway. Duox1-derived H<sub>2</sub>O<sub>2</sub> is able to trigger the NF- $\kappa$ B inflammatory signaling pathway.

#### Selected Publications

de Almeida VV, Calado A, Silva-Herdade AS, Rosário HS, Saldanha C. (2014) An in vitro study on the modulation of the neutrophil adhesive behavior by soluble fibrinogen. *Clin Hemorheol Microcirc* , **56**, 47-56. (Journal IF: 3.398 , Citations: 0)

de Oliveira S, López-Muñoz A, Candel S, Pelegrín P, Calado A and Mulero V. (2014) ATP modulates acute inflammation in vivo through dual oxidase 1-derived H<sub>2</sub>O<sub>2</sub> production and NF- $\kappa$ B activation. *J Immunol* **192**, 5710-9. (Journal IF: 5.362, Citations: 0)

de Almeida VV, Silva-Herdade A, Calado A, Rosário HS, Saldanha C. (2012) Fibrinogen modulates leukocyte recruitment in vivo during the acute inflammatory response. *Clin Hemorheol Microcirc* Dec 27. (Journal IF: 3.398 , Citations: 0)

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. (Journal IF: 5.000, Citations: 2)

de Almeida VV, Calado A, Rosário HS, Saldanha C. (2012) Differential effect of soluble fibrinogen as a neutrophil activator. *Microvasc Res.* **83**(3), 332-6. (Journal IF: 2.828, Citations: 0)

#### Ongoing Research Projects

2012/2014 Title: UBIMI. Coordinator: Maria Carlota Saldanha Lopes. Agency: Soc Portuguesa Hemorreologia. Reference: UBIMI. Amount: 23,575€.

2013/2016 Title: Mathematical and Computational Modeling of Human Physiology. Coordinator:



Maria Carlota Saldanha Lopes. Agency: Fundação Ciência e Tecnologia. Reference: EXCL/MAT-NAN/0114/2012. Amount: 12,100€.

#### Other Projects

2013/2015 Evaluation of inflammatory and adaptative immunity imbalance to improve prognosis of ischemic cardiovascular diseases, Liga dos Amigos do Hospital de Santa Marta. Coordinator: P. Napoleão (Liga dos Amigos do Hospital de Santa Marta/2012). Coordinator: Patricia napoleão.

2013/2015 Contribution of circulating microRNA to improve prognosis of ischemic cardiovascular diseases, Liga dos Amigos do Hospital de Santa Marta. Coordinator: P. Napoleão (Liga dos Amigos do Hospital de Santa Marta/2012). Coordinator: Patricia napoleão.

2012/2015 Evaluation of inflammation profiles in septic patients – contribution to multiple cross prognostic biomarkers, Coordinator: Carlota Saldanha.

2013/2016 “Effects of Timolol on Biochemical and Hemorheological Properties of Erythrocytes from Glaucoma Patients. Coordinator: CarLota Saldanha. Coordinator Institution: Carlos Marques-Neves FMUL Professor, ISAMB, CECU Coordenator, ALM Clinical Director.

2014/2016 Perfis da Agregação Eritrocitária e da IL-8 em sobreviventes de enfarte agudo de miocárdio. Coordinator: Carlota saldanha. Coordinator Institution: Dr. Daniel Ferreira (Hospital da Luz).

#### Publications in peer review Journals

de Oliveira S, López-Muñoz A, Candel S, Pelegrín P, Calado A and Mulero V. (2014) ATP modulates acute inflammation in vivo through dual oxidase 1-derived H<sub>2</sub>O<sub>2</sub> production and NF- $\kappa$ B activation. *J Immunol.* **192**, 5710-9. (Journal IF: 5.362, Citations: 0)

Candel S, de Oliveira S, López-Muñoz A, García-Moreno D, Espín-Palazón R, Tyrkalska SD, Cayuela ML, Renshaw SA, Corbalán-Vélez R, Vidal-Abarca I, Tsai HJ, Meseguer J, Sepulcre MP and Mulero V. (2014) Tnfa signaling through tnfr2 protects skin against oxidative stress-induced inflammation. *PLoS Biol.* **12**, e1001855. (Journal IF: 11.771, Citations: 0) Saldanha C, Lopes de Almeida JP, Silva-Herdade AS (2014) Application of a Nitric Oxide Sensor in Biomedicine. *Biosensors* **4**, 1-17 (Journal IF:NA, Citations: 0)

Saldanha C, Freitas T, Lopes de Almeida JP, Silva-Herdade AS (2014) Signal transduction pathways in erythrocyte nitric oxide metabolism under high fibrinogen levels. *Korea-Australia*

Rheology Journal 26, 217-223 (Journal IF: 0.693, Citations: 0) Vitorino de Almeida V, Calado A, Silva-Herdade AS, Rosário HS and Saldanha C. (2014) An in vitro study on the modulation of the neutrophil adhesive behavior by soluble fibrinogen. *Clin Hemorheol and Microcirc* **56**, 47 –56 (Journal IF: 2.215, Citations: 0)

Saldanha C, Silva-Herdade AS. (2014) The Ubiquity Nature of Acetylcholine. *Clinical & Experimental Pharmacology* 4, 3 (Journal IF: 2.405 , Citations: 0) Silva-Herdade AS, Freitas T, Almeida JP, Saldanha C (2014) Erythrocyte deformability and nitric oxide mobilization under pannexin-1 and PKC dependence. *Clin Hemorheol and Microcirc*, in press [Epub ahead of print] (Journal IF: 2.215, Citations: 0)

Teixeira P, Napoleão P, Saldanha C (2014). S-nitrosoglutathione efflux in the erythrocytes. *Clin Hemorheol Microcirc*; in press. [Epub ahead of print; 10.3233/CH-141855].

Saldanha C, Freitas T, Lopes de Almeida JP, Silva-Herdade AS (2014) Signal transduction pathways in erythrocyte nitric oxide metabolism under high fibrinogen levels. *Korea-Australia Rheology Journal* **26**, 217-223 (Journal IF: 0.693, Citations: 0)

Silva-Herdade AS, Freitas T, Almeida JP, Saldanha C (2014) Erythrocyte deformability and nitric oxide mobilization under pannexin-1 and PKC dependence. *Clin Hemorheol and Microcirc*, in press [Epub ahead of print] (Journal IF: 2.215, Citations: 0)

Saldanha C, Lopes de Almeida JP, Silva-Herdade AS (2014) Application of a Nitric Oxide Sensor in Biomedicine. *Biosensors* **4**, 1-17 (Journal IF:NA, Citations: 0)

#### **Invited lectures and seminars**

Saldanha C, Esteves R, Zabala L, Freitas T, Teixeira P, Napoleão P, Silva -Herdade AS, Fibrinogen effects on erythrocyte nitric oxide mobilization in presence of timolol, Workshop Ocular Microbiology Immunology, 4th International Conference on Clinical & Experimental Ophthalmology, Baltimore, USA, July 14-16 2014, Grant of Fundação Luso Americana.

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

Saldanha C, Freitas T, Lopes de Almeida, JP. Fibrinogen signalling in erythrocyte nitric oxide mobilization in presence of PI3-K and adenylyl cyclase inhibitors, XXIII International Fibrinogen Workshop, Marseille, France, July 9-11, 2014, Poster Presentation.

de Oliveira, S, Gabellini, C, Calado, A and Mulero, V. In vivo regulation of neutrophil recruitment in zebrafish acute inflammatory response: crosstalk between H2O2 and Cxcl-12,

Zebrafish Disease Models 7 Conference, Madison, USA, June 28 – July 1, 2014, Poster Presentation.

Silva-Herdade AS, Andolina C, Faggio C, Saldanha C, Platelet-Activating Factor induced inflammation: in vivo study. 87th SIBS National Congress on Peoples, Environment, Health, Turin, Italy, December 5-6, 2014, Poster presentation. Abstract published in Journal of Biological Research, 87(s1):11

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

Napoleão P, Catarina Ramos, Mafalda Selas, Francisco J. Enguita, Teresa Pinheiro, Miguel Mota Carmo, Rui Cruz Ferreira. Circulating micro-RNA profiles and patients' differentiation in ST-elevation myocardial infarction evolution. XXXV Congresso Português de Cardiologia, Albufeira, Portugal, April 27-29 2014, Poster presentation (ID 819).

Napoleão P, Francisco J. Enguita, Catarina Ramos, Mafalda Selas, Teresa Pinheiro, Miguel Mota Carmo, Rui Cruz Ferreira. Circulating microRNA profiles and patients' differentiation in ST-elevation myocardial infarction evolution. 2sd IMM Post-doc day, Lisboa, Portugal, June 17, 2014, Poster presentation.

#### **Internationalisation**

Participation with University of Murcia (Spain) in PhD thesis "How hydrogen peroxide and CXCL8 modulate neutrophil recruitment in vivo".

Participation in Lifelong learning program – ERASMUS program with University of Messina, (Italy) and development of the project "Thrombus formation and leukocyte recruitment in mice cremaster muscle: in vivo study".

#### **Advanced teaching**

Saldanha C, Silva-Herdade AS, Supervision of Lifelong learning program-ERASMUS on Thrombus formation and leukocyte recruitment in mice cremaster muscle: in vivo study. Mar-Jun 2014.

Silva-Herdade, AS. Inflammation. Lecture at Curso Livre de Bioquímica Experimental da Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, February 17, 2014

Napoleão, P. Inflammation in coronary artery disease. Lecture at Mestrado em Bioquímica da Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, 26 May 2014.

Napoleão, P. Inflammation in coronary artery disease. Lecture at Mestrado de Biologia

Humana e Ambiente da Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal, 12 March 2014.

Napoleão, P. Biomarkers of inflammation in acute coronary disease. Lecture at Curso Livre Experimental de Bioquímica da Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, 17 February 2014

#### **Science and society**

Saldanha C, President of the Portuguese Society of Hemorheology and Microcirculation (SPHM)

Editor – in - Chief of the Bulletin of the SPHM [www.hemorreologia.com](http://www.hemorreologia.com)

Saldanha C, Editorial member of Clininal Hemorheology and Microcirculation

saldanha C, Editorial member of the Sciedu Press, Case Reports in Clinical Pathology

Saldanha C, President of the 18th Conference (Lisbon 2016)

Saldanha C, “Applications and roles of acetylcholine” “Bulletin of the SPHM, (2014) Volume 29 (1), page 3-5

Saldanha C, “Hemorheology and microvesicles” Bulletin of the SPHM, (2014) Volume 29(2), page 3-4

#### **PhD thesis completed**

Sofia de Oliveira, Approved with laudation and distinction by unanimity. 12/09/2014 “How hydrogen peroxide and CXCL8 modulate neutrophil recruitment in vivo”. Lisbon Ângelo Calado (FMUL, IMM) Victoriano Mulero (University of Murcia, Spain).

#### **Msc thesis completed**

Sara Beijinho 18/12/2014 Avaliação longitudinal das concentrações solúveis de CD40L e de marcadores hemoreológicos na doença inflamatória aguda. Universidade Nova de Lisboa, Lisboa, Portugal. Patricia Napoleão

## Cláudio Franco Lab

### Major Interests / Objectives

The Vascular Morphogenesis Lab has the aim to understand the molecular mechanisms regulating coordinated endothelial cell behaviour during sprouting and remodelling phases of the angiogenic process.

Improving the knowledge on the molecular regulation of vascular morphogenesis will certainly create new possibilities for medical prevention and treatment of various human conditions.

We want to:

- Finding novel regulators of endothelial cell migration in sprouting angiogenesis
- Molecular regulation of endothelial cell axial polarity
- Effects of haemodynamic forces in vascular patterning
- Novel anti-angiogenic therapies blocking tumour angiogenesis

### Head of Unit

Claudio Areias Franco, PhD

### Research Team

Aida Andreia Pereira Pires Lima	Graduate	MSc Student, (started September)
Ana Cláudia Bernardino Raposo Alves	Master	Lab manager, (started May)
Catarina Gonçalves Fonseca	Master	Technician, (started November)
Felícia Margarida Correia Fonseca Lopes	Graduate	MSc Student, (started September)
Joana Cristina Reino Carvalho	Master	PhD Student

### Keywords / Research Areas

Angiogenesis, cell migration, tumour angiogenesis, endothelial cells, vascular patterning

### Major scientific achievements

We started to build our team during 2014, and we recruited 1 PhD student (Joana Carvalho), 1 Lab technician (Ana Alves), 2 Master Students (Felicia Lopes e Aida Lima) and 1 Research assistant (Catarina Fonseca). We published 2 main papers: one in *Nature Cell Biology*; and one in the multidisciplinary Journal of the Royal Society, *Interface*, this as a joint last author. We also had an oral communication at the prestigious Kloster-Seeon Conference on Angiogenesis in September 2014.

### Selected Publications

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. (Journal IF: 20, Citations: 23)

Bernabeu MO, Jones M, Nielsen JH, Kruger T, Nash RW, Groen D, Hetherington J, Gerhardt H, Franco CA, Coveney PV (2014) Computer simulations reveal complex distribution of haemodynamic forces in a mouse retina model of angiogenesis. *J R Soc Interface* **11**, <http://rsif.royalsocietypublishing.org/content/11/99/20140543.long>. (Journal IF: 3.856, Citations: 0)

### Ongoing Research Projects

2014/2015 Title: Decrypting SRF/MRTF-regulated transcriptome in endothelial tip cells. Coordinator: Claudio Areias Franco. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BEX-BCM/2258/2013. Amount: 48,488€.

2013/2018 Title: Exploratório - IFCT. Coordinator: Claudio Areias Franco. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: Exploratório Cláudio Franco. Amount: 50,000€.

### **Invited lectures and seminars**

Franco CA. Regulation of endothelial cell dynamics in vascular morphogenesis. IBIDELL, Barcelona, Spain (host: Mariona Graupera). December 2014.

Franco CA. Regulation of endothelial cell dynamics in vascular morphogenesis. IBILI, Coimbra, Portugal (host: Francisco Ambrósio). December 2014.

Franco CA. Wnt signalling and vascular patterning. VBL Symposium: 10 years, Arholma, Sweden (host: Holger Gerhardt). September 2014.

Franco CA. Regulation of endothelial cell dynamics in vascular morphogenesis. Karolinska Institute, Stockholm, Sweden (host: Lars Jakobsson). September 2014.

Franco CA. Regulation of endothelial cell dynamics in vascular morphogenesis. Max Planck Institute, Bad Nauheim, Germany (host: Michael Potente). March 2014.

### **Communications in International Conferences**

Franco CA, Bernabeu MO, Lenard A, Jones M, Coveney P, Affolter M, Gerhardt H. Of blood flow patterns, endothelial cell polarization and vessel regression in the mouse retina. 8th International Kloster Seeon Meeting Angiogenesis. Kloster Seeon, Germany. September 19-23, 2014. (Oral Presentation).

## Domingos Henrique Lab

### Major Interests / Objectives

A central question in developmental biology is how cells decide which differentiation paths they follow to generate tissues and organs during embryonic development. 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 progenitors acquire their multipotent character and generate the variety of neurons that compose the mature retina. The main goal is to understand the mechanisms governing the decision processes that stem/progenitor cells employ to exit the pluri/multipotent state and differentiate along various paths, thereby generating correctly patterned tissues and organs.

### Head of Unit

Domingos Manuel Pinto Henrique, PhD

### Research Team

Aida Isabel Santos da Costa	Graduate	PhD Student
Alexandra Isabel Freitas Rosa	PhD	Post doctoral Investigator
Ana Marisa Mendes Gonçalves Vinhais Guedes	Master	PhD Student
Ana Rita Ponce Álvares de Águeda Pedrosa	Master	PhD Student
Ana Sofia Temudo Duarte António	Master	PhD Student
Andreia Sofia Faria Pereira	Graduate	MSc Student, (started September)
Cláudia Sofia Cardoso Gaspar	PhD	Post doctoral Investigator
DUSAN DJOKOVIC	MD/PhD	Post doctoral Investigator, MD
Elsa Margarida Cavaco Abranches	PhD	Post doctoral Investigator
Evguenia Pavlovna Bekman	PhD	Post doctoral Investigator, ISCSEM , Assistant Professor



Pedro Miguel Branco Barbacena	Master	MSc Student
Sanja Ivkovic	PhD	Post doctoral Investigator
Sara Sofia Gasalho Ferreira	Graduate	Technician

#### Keywords / Research Areas

Stem cells, Notch signalling, Pluripotency, neurogenesis, Gene regulatory Networks, Systems Biology

#### Major scientific achievements

One of the major aims of our work is to understand how the pluripotent state is regulated, and how cells exit this state to initiate their progression into lineage commitment. Our approach involves a detailed quantitative analysis of the pluripotency network at the single-cell level in ESCs, and we have recently shown that fluctuations in Nanog expression is a cell-intrinsic property of ESCs that allow them to explore available lineage options in the pluripotent space (Abranches et al, Development 2014).

Another achievement of the lab was the identification of a combination of 3 TFs that can promote a direct transdifferentiation towards inner ear hair cells (HCs), opening new perspectives on the regulation of HC production and how these can be used for human cellular therapies aimed at curing deafness (Aida Costa et al, Development, in press).

#### Selected Publications

Abranches, E., Bekman, E., Henrique, D. (2013) Generation and characterization of a novel mouse embryonic stem cell line with a dynamic reporter of Nanog expression. *PlosOne* 8, e59928. (Journal IF: 3,534, Citations: 9)

Vilas-Boas, F., Fior, R., Swedlow, J.D., Storey, K.G., Henrique, D. (2011) A novel Reporter of Notch Signalling indicates regulated and random Notch Activation during Vertebrate Neurogenesis. *BMC Biology* 9, 58. [www.biomedcentral.com/1741-7007/9/58](http://www.biomedcentral.com/1741-7007/9/58). (Journal IF: 5,841, Citations: 14)

Abranches, E., Silva, M., Pradier, L., Schulz, H., Hummel, O., Henrique, D., Bekman, E. (2009) Neural Differentiation of Embryonic Stem Cells in vitro: a Road Map to Neurogenesis in the Embryo. *PLoS ONE* e6286. (Journal IF: 4,537, Citations: 65)

Rocha, S.F, Lopes, S.S., Gossler, A. and Henrique, D. (2009) Dll1 and Dll4 function sequentially

in the retina and pV2 domain of the spinal cord to regulate neurogenesis and create cell diversity. *Developmental Biology* **328**, 54.. (Journal IF: 4,407, Citations: 22)

Fior, R., Henrique, D. (2005) A novel hes5/hes6 circuitry of negative regulation controls Notch activity during neurogenesis. *Developmental Biology* (Journal IF: 4,407, Citations: 70)

#### **Ongoing Research Projects**

2012/2015 Title: The V2 domain of the spinal cord as a model to study neuronal fate decisions. Coordinator: Domingos Manuel Pinto Henrique. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-BID/121846/2010. Amount: 139,755€.

2014/2015 Title: Rett Syndrome. Coordinator: Domingos Manuel Pinto Henrique. Agency: Fundació Privada Per La Recerca i la Doència. Reference: Rett Syndrome. Amount: 6,000€.

#### **Publications in peer review Journals**

Abranches, E., Guedes, A.M.V., Moravec, M., Maamar, H., Svoboda, P., Raj, A., Henrique, D. (2014) Stochastic NANOG fluctuations allow mouse embryonic stem cells to explore pluripotency, *Development*, **141**, 2770-9. (Journal IF: 6.27 / Citation: 1)

#### **Internationalisation**

Our lab has established and productive collaborations with the following international groups:

- Arjun Raj, Penn University, Dept Engineering, Philadelphia, USA.
- Nicolas Daudet and Jonathan Gale's laboratories, UCL Ear Institute, London, UK
- Ana Pombo, The Berlin Institute for Medical Systems Biology, Berlin, Germany
- Nacho Molina, University of Edinburgh, UK

#### **Advanced teaching**

Domingos Henrique is Director of the LisbonBioMed PhD program, at IMM/FMUL. Co-organized 8-week Course "Towards a Creative and Critical Mind", January/February 2014.

Domingos Henrique is also member of scientific board of the PhD Program Bioengineering - Cell Therapies and Regenerative Medicine, coordinated by IST and with participation of IMM. Co-organized a 2-week Course on Stem Cell Biology (April 2014).

**PhD thesis completed**

AIDA COSTA 14/07/2014 FROM EMBRYONIC STEM CELLS TO SENSORY HAIR CELLS: A PROGRAMMING APPROACH FACULDADE DE MEDICINA DE LISBOA. DOMINGOS HENRIQUE

## Edgar Gomes Lab

### 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 Unit

Edgar Rodrigues Almeida Gomes, PhD

### Research Team

Cátia Alexandra da Silva Janota	Master	Investigator, (started October)
Mafalda Ramos de Melo Pimentel	Master	PhD Student
Maria Judite Sousa Costa	PhD	Post doctoral Investigator, (started May)
Rute Miriam Santos Morais	Graduate	MSc Student, (started August)
Telma Cristina Lourenço Carrilho	Master	Technician
Tiago Maria de Carvalho da Costa Amado	Master	Technician, (left April)
Vânia Raquel Gomes Glória	Master	PhD Student, (started August)

### Keywords / Research Areas

Cell Biology, Cytoskeleton, Cell Migration, Skeletal Muscle

### Major scientific achievements

Awards and Honors:

Investigador FCT Consolidation Grant to Edgar Gomes

EMBO Installation Grant to Edgar Gomes

ERC Consolidator Grant

Publications:

Sestina Falcone, William Roman, Karim Hnia, Vincent Gache, Nathalie Didier, Jeanne Lainé, Frederic Aurade, Isabelle Marty, Ichizo Nishino, Nicolas Charlet-Berguerand, Norma Romero, Giovanna Marazzi, David Sassoon, Jocelyn Laporte, Edgar R. Gomes. 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 (2014)

Cadot, B., Gache, V., and Gomes, E.R. Fast, Multi-Dimensional and Simultaneous Kymograph-Like Particle Dynamics (SkyPad) Analysis. *PLoS ONE* 9, e89073. (2014).

Book Chapters:

Daniel S. Osorio, Edgar R. Gomes “Connecting the nucleus to the cytoskeleton for nuclear positioning and cell migration”, *Cancer Biology and the Nuclear Envelope*, Springer, 2014

### Selected Publications

Sestina Falcone, William Roman, Karim Hnia, Vincent Gache, Nathalie Didier, Jeanne Lainé, Frederic Aurade, Isabelle Marty, Ichizo Nishino, Nicolas Charlet-Berguerand, Norma Romero, Giovanna Marazzi, David Sassoon, Jocelyn Laporte, Edgar R. Gomes. 6, 1455–1475 (2014) (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.. (Journal IF: 8.245, Citations: 1)

Cadot, B., Gache, V., and Gomes, E.R. (2014) Fast, Multi-Dimensional and Simultaneous Kymograph-Like Particle Dynamics (SkyPad) Analysis. *Plos ONE* (Journal IF: 3.5, Citations: 0)

### **Ongoing Research Projects**

2014/2017 Title: EMBO Installation Grant. Coordinator: Edgar Rodrigues Almeida Gomes. Agency: EMBO. Reference: EMBO Installation Grant - Edgar Gomes. Amount: 150,000€.

2014/2019 Title: Positioning the nucleus for cell migration and muscle fiber function - GA617676 - ERC . Coordinator: Edgar Rodrigues Almeida Gomes. Agency: Comissão Europeia. Reference: ERC - PhONICs. Amount: 1,968,000€.

2014/2019 Title: Exploratório - IFCT. Coordinator: Edgar Rodrigues Almeida Gomes. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: Exploratório Edgar Gomes. Amount: 50,000€.

### **Other Projects**

2014/2019 Positioning the nucleus for cell migration and muscle fiber function. Coordinator: Edgar Gomes.

2014/2019 Positioning the nucleus for cell migration and muscle fiber function - ERC consolidator grant. Coordinator: Edgar Gomes.

2014/2017 Positioning the cell nucleus. Coordinator: Edgar Gomes.

2014/2017 Positioning the cell nucleus - EMBO Instalation Grant. Coordinator: Edgar Gomes.

2014/2019 Positioning the nucleus for cell migration and muscle fiber function -ERC consolidator. Coordinator: Edgar Gomes.

### **Publications in peer review Journals**

Sestina Falcone, William Roman, Karim Hnia, Vincent Gache, Nathalie Didier, Jeanne Lainé, Frederic Aurade, Isabelle Marty, Ichizo Nishino, Nicolas Charlet-Berguerand, Norma Romero, Giovanna Marazzi, David Sassoon, Jocelyn Laporte, Edgar R. Gomes. 6, 1455–1475 (2014) (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. (Journal IF: 8.245, Citations: 1) .

Cadot, B., Gache, V., and Gomes, E.R. (2014) Fast, Multi-Dimensional and Simultaneous Kymograph-Like Particle Dynamics (SkyPad) Analysis. *Plos ONE* (Journal IF: 3.5, Citations: 0) .

#### **Other publications International**

Daniel S. Osorio, Edgar R. Gomes “Connecting the nucleus to the cytoskeleton for nuclear positioning and cell migration”, *Cancer Biology and the Nuclear Envelope*, Springer, 2014

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

13th International Congress on Neuromuscular Diseases, July 2014, Nice, France (Oral presentation)

## Gonçalo Bernardes Lab

### 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 Unit

Gonçalo José Lopes Bernardes, PhD, Assistant Professor

### Research Team

Eleonora Aquilini	PhD	Post doctoral Investigator, (started September)
Jessica Grace Morgan Bevan	Master	PhD Student, (started September) (left September)
João Alexandre Guarita da Silva Rodrigues	PhD	Senior Investigator, (left August)
João Daniel da Silva Seixas	PhD	Post doctoral Investigator, (started October)
Maria Inês Sousa de Albuquerque	Master	Investigator, (started June)
Miguel Correia Botelho Chaves Ferreira	PhD	Technician, (left November)
Padma Akkapeddi	Master	PhD Student
Rui Traquete	Master	PhD Student, (started June)



### Keywords / Research Areas

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

### Major scientific achievements

Dr Bernardes was awarded the 2014 Silver Medal of the European Young Chemist Award (September) and the 2014 European Prize of the RSEQ Chemical Biology Division (December).

Publications include:

- Cal PMSD; Bernardes GJL\*; Gois PMP. Cysteine Selective Reactions for Antibody Conjugation. *Angew. Chem. Int. Ed.* 2014, 53, 10585-10587
- Krall N; Pretto F; Decurtins W; Bernardes GJL; Supuran CT; Neri D. A Small Molecule Drug Conjugate for the Treatment of Carbonic Anhydrase IX Expressing Tumors. *Angew. Chem. Int. Ed.* 2014, 53, 4231-4235
- Liu F; Vijayakrishnan B; Faridmoayer A; Taylor TA; Parsons TB; Bernardes GJL; Kowarik M; Davis BG. Rationally Designed Short Polyisoprenol-linked PglB Substrates for Engineered Polypeptide N-Glycosylation. *J. Am. Chem. Soc.* 2014, 136, 566-569
- Shimanovich U; Bernardes GJL\*, Knowles TJ; Cavaco-Paulo A. Protein Micro and Nano Capsules for Biomedical Applications. *Chem. Soc. Rev.* 2014, 43, 1361-1371

### Selected Publications

Shimanovich U, Bernardes GJL\*, Knowles TJ, Cavaco-Paulo A (2014) Protein Micro and Nano Capsules for Biomedical Applications.. *Chem. Soc. Rev* **43**, 1361. (Journal IF: 30.425, Citations: 4)

Krall N, Pretto F, Decurtins W, Bernardes GJL, Supuran CT, Neri D (2014) A Small Molecule Drug Conjugate for the Treatment of Carbonic Anhydrase IX Expressing Tumors. *Angew. Chem. Int. Ed.* **53**, 4231. (Journal IF: 11.336, Citations: 11)

Cal PMSD, Bernardes GJL\*, Gois PMP (2014) Cysteine Selective Reactions for Antibody Conjugation. *Angew. Chem. Int. Ed.* **53**, 10585. (Journal IF: 11.336, Citations: 2)

García-Gallego S, Bernardes GJL\* (2014) Carbon-monoxide releasing molecules for the delivery of therapeutic CO in vivo. *Angew. Chem. Int. Ed.* **53**, 9712. (Journal IF: 11.336, Citations: 4)

Liu F, Vijayakrishnan B, Faridmoayer A, Taylor TA, Parsons TB, Bernardes GJL, Kowarik M, Davis BG (2013) Rationally Designed Short Polyisoprenol-linked PglB Substrates for Engineered Polypeptide N-Glycosylation. *J. Am. Chem. Soc.* **15**, 566. (Journal IF: 11.444, Citations: 0)

#### Ongoing Research Projects

2014/2014 Title: Exploratório - IFCT. Coordinator: Gonalo Jose Lopes Bernardes. Agency: Fundao para a Cincia e a Tecnologia, IP. Reference: Exploratrio Gonalo Bernardes. Amount: 50,000.

2014/2018 Title: PerBioImage— Exploring pericyclic reactions for bioorthogonal imaging of biological - GA 630731CIG. Coordinator: Gonalo Jose Lopes Bernardes. Agency: Comisso Europeia. Reference: PerBioImage. Amount: 100,000.

#### Other Projects

2014/2017 Marie Curie Career Installation Grant. Coordinator: Gonalo Bernardes.

2013/2017 Marie Curie Career Installation Grant. Coordinator: Goncalo Bernardes.

#### Publications in peer review Journals

Perrino E; Steiner M; Krall N; Bernardes GJL; Pretto F; Casi G; Neri D (2014) Curative properties of noninternalizing antibody-drug conjugates based on maytansinoids. *Cancer Research*, **74**, 2569-2578 (Journal IF: 9.284, Citations: 0)

Bernardes GJL\*; Lawrence AL (2014) Highlights from the 49th EUCHEM conference on stereochemistry, Brgerstock, Switzerland, *May Chem Comm.* (Journal IF: 6.718, Citations: 0)

#### Invited lectures and seminars

Bernardes, GJL, November 2014, Department of Chemistry, University of Cambridge (UK)

Bernardes, GJL, October 2014, Center for Research in Biological Chemistry and Molecular Materials (CIQUS) – Universidade de Santiago de Compostela (Spain)

Bernardes, GJL, May 2014, Institute of Biological Chemistry, Faculty of Sciences, University of Vienna (Austria)

Bernardes, GJL, April 2014, Broad Institute - The Science of Therapeutics, Boston (US)

Bernardes, GJL, April 2014, Weizmann Institute of Science (Israel)

Bernardes, GJL, January 2014, Instituto Gulbenkian de Ciência, Oeiras (Portugal)

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

Bernardes, GJL, Protein and Antibody Engineering Europe PEGS, Cancer Biotherapeutics, November 2014, Lisbon (Portugal) Oral Presentation

Albuquerque, IS; Bernardes, GJL, A modular approach to a synthetic glycoprotein vaccine candidate against Plasmodium sp., EMBO Practical Course on "Protein expression, purification, and characterization (PEPC9)", Hamburg, Germany, 8 – 16 September 2014 – (Poster and Oral Presentation)

Bernardes, GJL, September 2014, 5th EuCheMS Chemistry Congress, Istanbul (Turkey) (Oral Presentation)

Bernardes, GJL, September 2014, European Young Chemist Award @ 5th EuCheMS, Istanbul (Turkey) (Oral Presentation)

Bernardes, GJL, June 2014, Hovione & MIT Portugal Symposium, Lisbon (Portugal) (Oral Presentation)

Bernardes, GJL, June 2014, Novartis Vaccines, Siena (Italy) (Oral Presentation)

Bernardes, GJL, March 2014, AstraZeneca - MedImmune Cambridge Cancer Science Symposium, Cambridge (UK) (Oral Presentation)

Bernardes, GJL, February 2014, 4th World ADC Frankfurt (Germany) (Oral Presentation)

#### **Internationalisation**

The GBernardes Lab is a joint group between the IMM and the University of Cambridge. Moreover, the group collaborates with various international partners:

- Drs Francesco Berti and Roberto Adamo, Novartis Vaccines, Siena, Itália
- Dr Pedro Pissarra, Biotechnol Inc., New Jersey, US
- Dr Tuomas Knowles, University of Cambridge, UK

- Prof Anne S. Ulrich, Karlsruhe Institute of Technology, Germany
- Dr Angela Koehler, MIT, US
- Profs Antonio Braga and Ademir Neves, UFSC, Brazil

## Henrique Veiga-Fernandes Lab

### Major Interests / Objectives

The immune system is a key player in the resolution and prevention of severe pathologies, such as infectious and inflammatory diseases. To accomplish their function throughout life, immune cells interact with each other and with their external environment. Thus, all immune cell processes, ranging from haematopoiesis to immune cell response to pathogens, require the establishment of effective cellular and molecular interactions. However, the mechanisms that underpin immune cell function and communication with their environment remain largely elusive. Our research is centered on novel communication pathways that determine immune cell fate and disease progression in the context of lymphoid organogenesis and lymphoid cell development and function.

### Head of Unit

José Henrique Veiga Fernandes, PhD

### Research Team

Afonso Rocha Martins de Almeida	PhD	Post doctoral Investigator, Consultant , (left August)
Bethania García Cassani	Master	PhD Student
Bruno Miguel Belchior Raposo	Graduate	MSc Student, (started September)
Carlos Diogo Labão Alpiarça Sousa de Almeida	Master	MSc Student, (left November)
Cristina Sofia Godinho da Silva	No degree	Investigator, (started November)
Diogo da Fonseca Pereira	PhD	Post doctoral Investigator
Fátima Sofia dos Santos Cardoso	Graduate	Intern, (left January)
Hélder Manuel Piedade Ribeiro	Master	Technician
Luís Miguel Ferreira de Almeida	Graduate	MSc Student, (started July)
Manuela Cristina Fernandes Ferreira	PhD	Post doctoral Investigator

Rita Gomes Domingues	Master	PhD Student
Sales Ibiza	PhD	Post doctoral Investigator
Silvia Moura Arroz Nobre Madeira	Master	PhD Student

#### Keywords / Research Areas

Lymphoid organogenesis, Haematopoiesis, Innate Lymphoid Cells, Lymphocyte function

#### Major scientific achievements

Fonseca-Pereira, D., Arroz-Madeira, S. et al. (2014). The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function. *Nature* 514:98-101.

van de Pavert, S. A., Ferreira, M. et al. (2014). Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. *Nature* 508:123-127.

Klose, C. S., et al. (2014). Differentiation of Type 1 ILCs from a Common Progenitor to All Helper-like Innate Lymphoid Cell Lineages. *Cell* 157:340-356.

Senior research award. Crohn's and Colitis Foundation of America, USA

Breakthrough Award. Kenneth Rainin Foundation, USA

Pfizer prize 2014. Basic science. Pfizer/SCML. Portugal

#### Selected Publications

van de Pavert, S.A., Ferreira, M., Domingues, R.G., Ribeiro, H., Molenaar R., Moreira-Santos L., Almeida, F.F., Ibiza, S., Barbosa I., Goverse, G., Labão-Almeida C., Godinho-Silva, C., Konijn, T., Schooneman, D., O'Toole, T., Mizee, M.R., Habani, Y., Haak. E., Santori F.R., Littman D.R., Schulte-Merker S., Dzierzak, E., Simas, J.P., E. Mebius, R., Veiga-Fernandes, H. (2014). (2014) Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. *Nature* **508**, 123-127. <http://www.nature.com/nature/journal/v508/n7494/full/nature13158.html>. (Journal IF: 42.351, Citations: 12)

Fonseca-Pereira, D., Arroz-Madeira, S., Rodrigues-Campos M., Barbosa I. A., Domingues R. G., Bento T., Almeida A. R., Ribeiro H., Potocnik A. J., Enomoto H., Veiga-Fernandes H. (2014) The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function. *Nature* **214**, 98–101. <http://www.nature.com/nature/journal/v514/n7520/full/nature13498.html>. (Journal IF: 42.351, Citations: 0)

Klose C.S., Flach M., Möhle L., Rogell L., Hoyler T., Ebert K., Fabiunke C., Pfeifer D., Sexl V., Fonseca-Pereira D., Domingues R.G., Veiga-Fernandes H., Arnold S.J., Busslinger M., Dunay I.R., Tanriver Y., Diefenbach A. (2014) Differentiation of type 1 ILCs from a common progenitor to all helper-like innate lymphoid cell lineages. *Cell* **157**, 340–356. <http://www.sciencedirect.com/science/article/pii/S009286741400405X>. (Journal IF: 33.116, Citations: 20)

Almeida A.R., Fonseca-Pereira D., Arroz-Madeira S., Ribeiro H., Labão-Almeida C., Veiga-Fernandes H. (2014) The neurotrophic factor receptor RET regulates IL-10 production by in vitro polarised T helper 2 cells. *Eur J Immunol* **44**, 3605–3613. <http://onlinelibrary.wiley.com/doi/10.1002/eji.201344422/abstract;jsessionid=5FEF8A12FB92049783395D3736AD4E30.f02t03>. (Journal IF: 4.518, Citations: 0)

Ferreira, M., Veiga-Fernandes, H. (2014) Pre-birth world and the development of the immune system: Mum's diet affects our adult health: New insight on how the diet during pregnancy permanently influences offspring health and immune fitness. *Bioessays* **36**, 1213–1220. <http://onlinelibrary.wiley.com/doi/10.1002/bies.201400115/abstract>. (Journal IF: 4.927, Citations: 0)

### Ongoing Research Projects

2012/2015 Title: Stromal Cell - Immune cell interactions in health and disease - PITN-GA-2011-289720. Coordinator: José Henrique Veiga Fernandes. Agency: Comissão Europeia. Reference: Stroma. Amount: 220,204.56€.

2012/2014 Title: Modulation of RET. Coordinator: José Henrique Veiga Fernandes. Agency: National Blood Foundation. Reference: Modulation of RET. Amount: 58,088.32€.

2013/2016 Title: Control of Innate Lymphoid Cell function and intestinal homeostasis by neurotrophic factors. Coordinator: José Henrique Veiga Fernandes. Agency: Fundação Ciência e Tecnologia. Reference: FCT-ANR/IMI-IMU/0094/2012. Amount: 250,000€.

2013/2014 Title: Control of Innate Lymphoid Cell function and intestinal homeostasis by neurotrophic factors. Coordinator: José Henrique Veiga Fernandes. Agency: Kenneth Rainin Foundation. Reference: Innovator Awards Program Kenneth Rainin. Amount: 189,475.8€.

2014/2014 Title: Control of natural helper cells through the neuroregulator RET. Coordinator:

Sales Ibiza. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/IMI-IMU/0874/2013. Amount: 35,000€.

2014/2015 Title: A novel solution to efficient Haematopoietic Stem Cell regeneration - 207057 - RetImmuneFunction. Coordinator: José Henrique Veiga Fernandes. Agency: Comissão Europeia. Reference: StemCell2max - ERC-PoC. Amount: 149,885€.

2014/2017 Title: Regulation of Innate Lymphoid Cell function and intestinal defense by neuroregulatory factors. Coordinator: José Henrique Veiga Fernandes. Agency: Cronh's & Colitis . Reference: Lymphoid Cell Function - CCFA. Amount: 254,277€.

2014/2015 Title: EMBO Conference Poster Award. Coordinator: Sales Ibiza. Agency: Bio-Techne. Reference: EMBO Conference Poster Award. Amount: 500€.

#### **Publications in peer review Journals**

Godinho-Silva C., Marques S., Fontinha D., Veiga-Fernandes H., Stevenson P.G., Simas J.P. (2014). Defining Immune Engagement Thresholds for In Vivo Control of Virus-Driven Lymphoproliferation. *PLoS Pathog.* Jun 2014; **10**(6): e1004220. (Journal IF: 8.057, Citations: 0)

Fernandes S.M., Pires A.R., Ferreira C., Foxall R.B., Rino J., Santos C., Correia L., Poças J., Veiga-Fernandes H., Sousa AE. (2014 ). Enteric mucosa integrity in the presence of a preserved innate interleukin 22 compartment in HIV type 1-treated individuals. *J Infect Dis.* 2014 Aug **15**, 210(4):630-40.(Journal IF: 5.778, Citations: 40)

#### **Invited lectures and seminars**

Henrique Veiga-Fernandes, "Seminars in Clinical Research series", NY, USA, September 15-17th 2014.



### **Communications in International Conferences**

Participation in international conferences:

Henrique Veiga-Fernandes, "2014 Innovations Symposium - Taming the Microbiome", San Francisco, USA, July 14-17th, 2014.

Henrique Veiga-Fernandes, "Embo conference on Innate Lymphoid Cells, Institut Pasteur, Paris, France, September 29th to October 1st 2014.

Henrique Veiga-Fernandes, "X Meeting Spanish Society for Developmental Biology", Madrid, Spain, October 12-13th 2014.

Henrique Veiga-Fernandes, "British Society for Immunology ", Edinburgh, UK, November 12-14th 2014.

Henrique Veiga-Fernandes, "Catalan Immunology Congress (SCI)", Barcelona, Spain, November 19-20th 2014.

EMBO conference on Innate Lymphoid Cells September 29th –October 1st 2014, Institut Pasteur, Paris, France: Rita Domingues, Silvia Madeira, Bethania Cassani, Manuela Ferreira, Sales Ibiza.

Manuela Ferreira. Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. EMBO conference on Innate Lymphoid Cells September 29th –October 1st 2014, Institut Pasteur, Paris, France, (Poster Presentation)

Rita G. Domingues, Wei Xu, Diogo Fonseca-Pereira, Manuela Ferreira, Hélder Ribeiro, Silvia Lopez-Lastra, Yasutaka Motomura, Lara Moreira-Santos, Franck Bihl, Véronique Braud, Barbara Kee, Hugh Brady, Mark C. Coles, Christian Vosshenrich, Masato Kubo, James P. Di Santo and Henrique Veiga-Fernandes. NFIL3 is a central orchestrator of innate lymphoid cell development. EMBO conference on Innate Lymphoid Cells September 29th –October 1st 2014, Institut Pasteur, Paris, France (Poster Presentation).

### **Communications in National Conferences**

Participation in national conferences:

Henrique Veiga-Fernandes, "Lymphoid organogenesis", GABBA program for 2014, 16th April.

XL Annual Meeting of the Portuguese Society of Immunology, "From immune responses to

immunotherapy”, Lisboa, Portugal: Diogo Pereira, Silvia Madeira, Rita Domingues, Hélder Ribeiro, Manuela Ferreira, Bruno Raposo, Luís Almeida, Carlos Almeida.

VIII PhD Students Meeting 28 March 2014 Lisbon Academic Medical Centre, Lisbon, Portugal: Rita Domingues, Silvia Madeira, Bethania Cassani.

Manuela Ferreira et al., Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. Oral Presentation at SPI’40 – XL Annual Meeting of the Portuguese Society of Immunology. Instituto de Medicina Molecular, Lisboa, Portugal, October, 3-5 2014 (Oral presentation)

Rita G. Domingues; NFIL3 is a central orchestrator of the common innate lymphoid cell progenitor. Oral Presentation at SPI’40 – XL Annual Meeting of the Portuguese Society of Immunology. Instituto de Medicina Molecular, Lisboa, Portugal, October, 3-5 2014 2014 (Oral presentation)

Fonseca-Pereira, D., Arroz-Madeira, S. et al., The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function. Oral Presentation at SPI’40 – XL Annual Meeting of the Portuguese Society of Immunology. Instituto de Medicina Molecular, Lisboa, Portugal, October, 3-5 2014 2014 (Oral presentation)

#### **Organisation of Conferences**

Ribeiro H. Organizer of STROMA ITN 3rd Network Meeting from Stroma, Lisboa, Portugal, Setembro 2014.

#### **Prizes, honours and awards**

Best poster presentation Award 2014 to Bethania Cassani and Sales Ibiza in the EMBO Conference on Innate Lymphoid Cells, “Control of Innate lymphoid cells and intestinal homeostasis by neurotrophic factors”, Institute Pasteur, Paris, France.

Mario Arala Chaves Immunology Excellence Award 2014 to Bethania Cassani for the best poster in the XL annual meeting of the Portuguese Immunology Society "Stroma -innate lymphoid cell interaction in enteric lymphoid tissue formation", Instituto de Medicina Molecular, Lisbon, Portugal.

Senior research award 2014, Crohn's and Colitis Foundation of America, USA to Henrique

Veiga-Fernandes.

Breakthrough Award 2014, Kenneth Rainin Foundation, USA to Henrique Veiga-Fernandes.

Pfizer prize Basic science 2014, Pfizer/SCML. Portugal to Henrique Veiga-Fernandes.

SPI Best Paper Award 2014, Distinguished by Portuguese Society of Immunology to Manuela Ferreira.

#### **Patents/prototypes**

PCT/IB2013/055261 "THE USE OF RET AGONIST MOLECULES FOR HAEMATOPOIETIC STEM CELL EXPANSION PROTOCOLS AND TRANSPLANTATION THERAPY AND A RET AGONIST KIT"  
*"Entering National/Regional Phase"*

#### **Advanced teaching**

Arroz-Madeira, S. organized the "VII PhD Students Retreat", Lousã, October 18-20th, 2014

Domingues R.G., organized the "VII PhD Students Retreat", Lousã, October 18-20th, 2014

Bethania García Cassani, organized "Pizza seminars" during 2014

#### **Science and society**

Bethania Cassani (2014) "Industrial secondment at Miltenyi Biotec GmbH", 19-30 May 2014  
Cologne, Germany

Bethania Cassani (2014) "3rd Stroma ITN Network Meeting", 18 September 2014, Instituto de Medicina Molecular, Lisbon, Portugal

Bethania Cassani (2014) "Light sheet microscope training", Carl Zeiss Microscopy GmbH, Microscopy labs, 27th November 2014, Munich, Germany

Bethania Cassani (2014) "Academic secondment at the Center for Immunology and Infection",  
17-20 November 2014 University of York, UK

**Msc thesis completed**

Hélder Manuel Piedade Ribeiro 26/11/2014 Interplay of Intestinal Microbiota and Innate  
Lymphoid Cells Universidade de Lisboa Henrique Veiga-Fernandes Sales Ibiza

Carlos Labão-Almeida 24/01/2014 Regulation of the Enteric Immune System by Retinoic acid  
signaling Universidade do Algarve - Faculdade de Ciências Henrique Veiga-Fernandes

## João Eurico-Fonseca Lab

### 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. 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 Unit

João Eurico Fonseca, MD/PhD

### Research Team

Ana Cláudia Dinis Pereira	Graduate	Technician, (started September)
Ana Filipa Mourão	No degree	Investigator
Ana Filipa Rodrigues Lopes	Master	Lab manager
Ana Henrique Baptista Daniel	Graduate	MSc Student
Ana Maria Ferreira Rodrigues	Graduate	PhD Student
Ana Rita Cascão Rodrigues	PhD	Post doctoral Investigator, (started December)
Ana Rita Fernandes Vieira	Graduate	MSc Student
António José Nicolau Marques Fernandes	Graduate	MSc Student
Bruno Miguel Costa Vidal	Graduate	PhD Student

Cláudia Cristina Valente Quaresma	Graduate	MSc Student
Daniela Filipa Martins Silva	No degree	Trainee, (started November)
Diana de Almeida Carmona Fernandes	Master	PhD Student
Elsa Cristina Vieira de Sousa	Graduate	Investigator
Eunice Ribeiro João Silva Paisana	Graduate	Trainee, (started October)
Filipe Carlos Pereira dos Reis Cortes Figueiredo	No degree	MSc Student
Helena Cristina de Matos Canhão	MD/PhD	Senior Investigator
Inês Alexandra Pascoal Lopes	Graduate	MSc Student, (started May)
Inês Pedro Perpétuo	Master	PhD Student
Joana Margarida Rodrigues de Sá	Undergraduate	Technician, (started February)
Joana Ribeiro Caetano Lopes	PhD	Post doctoral Investigator
Joaquim Miguel Polido Pereira	No degree	Investigator
Luísa Sofia Campos Magalhães Garcia	Graduate	MSc Student
Marco Aurélio Carmelino Cardoso Sarmiento	Graduate	Investigator
Maria Helena Regalo da Fonseca	MD/PhD	Senior Investigator
Maria João Gonçalves	Master	Investigator, MD
Maria José Parreira dos Santos	MD/PhD	Investigator, Associate Professor
Natacha Pombinho Leonardo	Graduate	MSc Student, (started September)
Renata Inês Proença Casimiro	Graduate	MSc Student, (started September)
Rita Alexandra Pedra Aguiar de Moura	PhD	Post doctoral Investigator
Rita Maria Mendes Raposeiro	Graduate	MSc Student
Soraia Patrícia Caetano da Silva	Graduate	MSc Student, (started September)
Vasco Madeira Crispim Romão	Master	Investigator

## Keywords / Research Areas

Joint inflammatory diseases - pathogenesis, early diagnosis, prognosis and pharmacogenetics- Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing spondylitis and Juvenile Idiopathic Arthritis, Systemic effects of inflammation and effects of inflammation on bone- Osteoporosis, Osteoarthritis and Rheumatoid Arthritis, Bone biology, structure, biomechanics, Chronic Inflammation and cardiovascular risk- atherosclerosis and bone, Epidemiology of Rheumatic Diseases, Cohorts, Registries and Databases. Recommendations and Guidelines, Collaboration in Clinical Trials

## Major scientific achievements

- 1- Describe the gene expression pattern involved in bone fragility induced by rheumatoid arthritis
- 2- Preclinical development of an arthritis treatment intervention with novel compounds inhibiting IL1 and TNF
- 3- B cell gene expression in early arthritis
- 4- Anti ribosomal P antibodies as potential diagnostic markers for Lupus
- 5- Development of published protocols for mechanical and structural assessment of bone
- 6- New genetic risk factors for rheumatoid arthritis and spondylarthritis
- 7- Coordination of the Portuguese national registries of the Portuguese Society of Rheumatology and coordination of the Portuguese Rheumatology Biobank, a part of the IMM biobank.
- 8- Participation in multinational clinical trials as national coordinators allowing refractory patients to have access to the state of art in biotechnological therapies.
- 9- International collaborations have been set and strengthened, allowing the development of networking, collaborative projects and publications.

## Selected Publications

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE. (2010) Neutrophils in rheumatoid arthritis: More than simple final effectors. *Autoimmun Rev.* **9**, 531-535. (Journal IF: 7.095, Citations: 47)

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. (Journal IF: 4.117, Citations: 24)

Fonseca JE, Santos MJ, Canhão H, Choy E. (2009) Interleukin-6 as a key player in systemic

inflammation and joint destruction.. *Autoimmun Rev* **8**. 538-542, (Journal IF: 7.095, Citations: 122)

Caetano-Lopes J, Canhão H, Fonseca JE. (2009) Osteoimmunology--the hidden immune regulation of bone. *Autoimmun Rev* **8**(3), 250-5. (Journal IF: 7.095, Citations: 36)

Fonseca JE, Carvalho T, Cruz M, Nero P, Sobral M, Mourão AF, Cavaleiro J, Abreu I, Carmo Fonseca M, Branco JC. (2005) Polymorphism at position -308 of the tumor necrosis factor alpha gene and rheumatoid arthritis pharmacogenetics.. *Ann Rheum Dis* **64**, 793-794. (Journal IF: 9.270, Citations: 38)

### Ongoing Research Projects

2011/2014 Title: A National Genome Wide Association to Predict the Response to Anti-TNF Treatment in Rheumatoid Arthritis. Coordinator: Helena Cristina de Matos Canhão. Agency: Abbott Laboratorios, Lda. Reference: GWAS Abbott. Amount: 104,000€.

2012/2014 Title: Understanding physician's decision to switch or keeping treatment regimen - is it dependent on patient's outcome measures. Coordinator: Helena Cristina de Matos Canhão. Agency: Laboratórios Pfizer, Lda. Reference: Pfizer WS2120109. Amount: 84,900€.

2013/2014 Title: ASPIRE EU inflammation\_Inhibition of bone and cartilage degradation in rat induced arthritis treated with tofacitinib. Coordinator: João Eurico Fonseca. Agency: Laboratórios Pfizer, Lda. Reference: Aspire - Pfizer WI 180320. Amount: 60,000€.

2013/2014 Title: Go-Dact - A multicentre, randomized, double blind, parallel group study to compare the efficacy of golimumab in combination with methotrexate (MTX) versus MTX monotherapy in improving dactylitis and enthesitis in MTX naïve psoriatic arthritis patient. Coordinator: Elsa Cristina Vieira de Sousa. Agency: Merck Sharp & Dohme. Reference: GO-DACT . Amount: 144,350€.

2014/2014 Title: EWRR. Coordinator: João Eurico Fonseca. Agency: Eli Lilly SA. Reference: EWRR. Amount: 5,000€.

2014/2015 Title: Linking Biomechanics, Inflammation and Bone Formation in Psoriatic Arthritis. Coordinator: João Eurico Fonseca. Agency: UCB Pharma , Lda. Reference: UCB ES. Amount: 51,350€.

2014/2015 Title: Estudo aleatorizado, aberto, para investigar os mecanismos de resposta-resistência ao rituximab versus tocilizumab em doentes com artrite reumatóide com resposta inadequada aos antagonistas do TNF (R4RA). Coordinator: João Eurico Fonseca. Agency: Centre for Experimental Medicine and Rheumatology. Reference: R4RA. Amount: 2,235.35€.



2014/2017 Title: European Calcified Tissue Society/Amgen Bone Biology Research Fellowship. Coordinator: João Eurico Fonseca. Agency: ECTS Ltd. Reference: ECTS - Bruno Vidal. Amount: 100,000€.

2014/2014 Title: Ensaio pré-clínico para a avaliação do potencial terapêutico do ImmuneSafe no tratamento de patologias reumáticas. Coordinator: João Eurico Fonseca. Agency: Cell2B. Reference: Cell2B. Amount: 30,000€.

2014/2016 Title: Post-transcriptional regulation of response to Etanercept in patients with rheumatoid arthritis. Coordinator: Helena Cristina de Matos Canhão. Agency: Laboratórios Pfizer, Lda. Reference: Pfizer - W1187429. Amount: 40,000€.

#### Other Projects

2011/2014 Portuguese Epidemiologic Study of Rheumatic Diseases – EpiReumaPt. . Coordinator: Helena Canhão.

#### Publications in peer review Journals

Gonçalves MJ, Romão VC. Images in clinical medicine. (2014) Saber tibia in Paget's disease of bone. *N Engl J Med.* **18**, 371(25):2417. (Journal IF: 54.420, Citations: 0)

Cascão R, Vidal B, Raquel H, Neves-Costa A, Figueiredo N, Gupta V, Fonseca JE, Moita LF. (2014) Potent anti-inflammatory and antiproliferative effects of gambogic acid in a rat model of antigen-induced arthritis. *Mediators Inflamm.* 2014, 195327. (Journal IF: 2.417, Citations: 0)

Alonso-Perez E, Suarez-Gestal M, Calaza M, Blanco FJ, Suarez A, Santos MJ, Papasteriades C, Carreira P, Pullmann R, Ordi-Ros J, Marchini M, Skopouli FN, Bijl M, Barrizone N, Sebastiani GD, Migliaresi S, Witte T, Lauwerys BR, Kovacs A, Ruzickova S, Gomez-Reino JJ, Gonzalez A; European Consortium of SLE DNA Collections. (2014) Lack of replication of higher genetic risk load in men than in women with systemic lupus erythematosus. *Arthritis Res Ther* **19**, 16:R128. (Journal IF: 4.107, Citations: 0)

Freira S, Fonseca H, Ferreira PD, Vasconcelos P, Eurico Fonseca J.(2014) SAPHO Syndrome in an Adolescent: A Clinical Case With Unusual Severe Systemic Impact. *J Adolesc Health.* **9**, pii: S1054-139X(14)00072-X. (Journal IF: 2.748, Citations: 0)

Sanches BF, Martins T, Santos MJ, Azeredo P. Acute acalculous cholecystitis in a patient with juvenile dermatomyositis. (2014) *BMJ Case Rep.* **19**, pii: bcr2014205066 (Journal IF: NA,

Citations: 0)

Romão VC, Lima A, Bernardes M, Canhão H, Fonseca JE. (2014) Three decades of low-dose methotrexate in rheumatoid arthritis: Can we predict toxicity? *Imunol Res.* **60**, (2-3):289-310 (Journal IF: 3.525, Citations: 0)

Mourão AF, Santos MJ, Melo-Gomes J, Martins FM, Costa JA, Ramos F, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues A, Salgado M, Sousa M, Branco JC, Fonseca JE, Canhão H. (2014) Using the juvenile arthritis disease activity score based on erythrocyte sedimentation rate or C-reactive protein level: results from the portuguese register. *Arthritis Care Res (Hoboken)*. **66**, (4):585-91. (Journal IF: 4.039, Citations: 0)

Gonçalves MJ, Sousa S, Inês LS, Duarte C, Borges J, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Barcelos A, Macieira C, Canas da Silva J, Costa L, Pereira da Silva JA, Cunha-Miranda L, Da Silva JA, Canhão H, Santos MJ. (2014) Characterization of damage in Portuguese lupus patients: analysis of a national lupus registry. *Lupus* **15**, pii: 0961203314555172. [Epub ahead of print] (Journal IF: 2.481, Citations: 0)

Cambridge G, Moura RA, Santos T, Khawaja AA, Polido-Pereira J, Canhão H, Leandro MJ, Fonseca JE. (2014) Expression of the inherently autoreactive idiotope 9G4 on autoantibodies to citrullinated peptides and on rheumatoid factors in patients with early and established rheumatoid arthritis. *PLoS One.* **15**, 9(9):e107513. (Journal IF: 3.534, Citations: 0)

Martins FM, da Silva JA, Santos MJ, Vieira-Sousa E, Duarte C, Santos H, Costa JA, Pimentel-Santos FM, Cunha I, Cunha Miranda L, Nóvoa T, Cruz M, Bernardes M, Araujo D, Pereira Silva JA, Silva JC, Branco JC, Gomes JA, Faustino A, Fonseca JE, Canhão H. (2014) DAS28, CDAI and SDAI cut-offs do not translate the same information: results from the Rheumatic Diseases Portuguese Register Reuma.pt. *Rheumatology (Oxford)* **29**, pii: keu313. (Journal IF: 4.435, Citations: 0)

Lucas R, Ramos E, Prata M, Rodrigues AM, Costa L, Severo M, Canhão H, Fonseca JE, Barros H. (2014) Changes in serum RANKL and OPG with sexual development and their associations with bone turnover and bone mineral density in a cohort of girls. *Clin Biochem* **47**, (12):1040-6. (Journal IF: 2.229, Citations: 0)

Okada Y, Diogo D, Greenberg JD, Mouassess F, Achkar WA, Fulton RS, Denny JC, Gupta N, Mirel D, Gabriel S, Li G, Kremer JM, Pappas DA, Carroll RJ, Eyler AE, Trynka G, Stahl EA, Cui J, Saxena R, Coenen MJ, Guchelaar HJ, Huizinga TW, Dieudé P, Mariette X, Barton A, Canhão H, Fonseca JE, de Vries N, Tak PP, Moreland LW, Bridges SL Jr, Miceli-Richard C, Choi HK, Kamatani Y, Galan P, Lathrop M, Raj T, De Jager PL, Raychaudhuri S, Worthington J, Padyukov L, Klareskog L, Siminovitch KA, Gregersen PK, Mardis ER, Arayssi T, Kazkaz LA, Plenge RM. (2014) Integration of sequence data from a Consanguineous family with genetic data from an outbred population

identifies PLB1 as a candidate rheumatoid arthritis risk gene. *PLoS One* **10**, 9(2):e87645. (Journal IF: 3.534, Citations: 1)

Campanilho-Marques R, Ramos F, Canhão H, Fonseca JE. (2014) Remission induced by infliximab in a childhood polyarteritis nodosa refractory to conventional immunosuppression and rituximab. *Joint Bone Spine* **81**, (3):277-8. (Journal IF: 3.218, Citations: 0)

Madruga Dias JA, Rosa RS, Perpétuo I, Rodrigues AM, Janeiro A, Costa MM, Gaião L, Pereira da Silva JA, Fonseca JE, Miltenberger-Miltenyi G.(2014) Pachydermoperiostosis in an African patient caused by a Chinese/Japanese SLCO2A1 mutation-case report and review of literature. *Semin Arthritis Rheum* **43**, (4):566-9 (Journal IF: 3,629, Citations: 0)

Kearsley-Fleet L, Závada J, Hetland ML, Nordström DC, Aaltonen KJ, Listing J, Zink A, Gati T, Rojkovich B, Iannone F, Gremese E, van Riel PL, van de Laar MA, Lie E, Kvien TK, Canhão H, Fonseca JE, Rotar Z, Loza E, Carmona L, Askling J, Johansson K, Finckh A, Dixon WG, Hyrich KL; on behalf of the EULAR Study Group for Registers and Observational Drug Studies. (2014) The EULAR Study Group for Registers and Observational Drug Studies: comparability of the patient case mix in the European biologic disease modifying anti-rheumatic drug registers. *Rheumatology (Oxford)* **27**, pii: keu446. (Journal IF: 4.435, Citations: 0)

Campanilho-Marques R, Bogas M, Ramos F, Santos MJ, Fonseca JE. (2014) Prognostic value of antinuclear antibodies in juvenile idiopathic arthritis and anterior uveitis. Results from a systematic literature review. *Acta Reumatol Port* **39**, (2):116-22. (Journal IF: 0.831, Citations: 0)

Araújo F, Cordeiro I, Teixeira F, Rovisco J, Ramiro S, Mourão AF, Costa JA, Pimentão JB, Malcata A, Santos MJ, Branco JC. (2014) Portuguese Recommendations for the Diagnosis and Management of Gout. *Acta Reumatol Port* **39**, (2):158-71 (Journal IF: 0.831, Citations: 0)

Araújo F, Cordeiro I, Teixeira F, Gonçalves J, Fonseca JE.(2014) Pharmacology of biosimilar candidate drugs in rheumatology: a literature review. *Acta Reumatol Port.* **39**, (1):19-26. (Journal IF: 0.831, Citations: 0)

Dias JM, Costa MM, Canhão H, Saraiva F, Silva JA. (2014) Musculoskeletal ultrasound in Paediatric Rheumatology: a retrospective analysis. *Acta Reumatol Port.* **30**, [Epub ahead of print]. (Journal IF: 0.831, Citations: 0)

Fonseca JE, Gonçalves J, Araújo F, Cordeiro I, Teixeira F, Canhão H, da Silva JA, Garcês S, Miranda LC, Ramiro S, Roxo A, Pimentel-Santos FM, Tavares V, Neto A, Sepriano A, Malcata A, Faustino A, Silva C, Ambrósio C, Duarte C, Miguel C, Barcelos F, Santos H, Cunha I, Ramos JC,

Gomes JA, Pimentão JB, Costa L, Maurício L, Silva M, Bernardes M, Bogas M, Coelho PC, Monteiro P, Aguiar R, André R, Leitão R, Pimenta S, Meirinhos T, Fernandes S, Las V, Castelão W; Sociedade Portuguesa de Reumatologia. (2014) The Portuguese Society of Rheumatology position paper on the use of biosimilars. *Acta Reumatol Port.* **39**(1):60-71. (Journal IF: 0.831, Citations: 0)

Fonseca JE.(2014) Revisiting rheumatic diseases and cancer.*Acta Reumatol Port.***39**, **1**. 9-10. (Journal IF: 0.831, Citations: 0)

Ferraria N, Marques JG, Ramos F, Lopes G, Fonseca JE, Neves MC.(2014) Chronic recurrent multifocal osteomyelitis: case series of four patients treated with biphosphonates. *Acta Reumatol Port.* **39**, **1**:38-45

Caetano-Lopes J, Rodrigues A, Lopes A, Vale AC, Pitts-Kiefer MA, Vidal B, Perpétuo IP, Monteiro J, Konttinen YT, Vaz MF, Nazarian A, Canhão H, Fonseca JE.(2014) Rheumatoid arthritis bone fragility is associated with upregulation of IL17 and DKK1 gene expression. *Clin Rev Allergy Immunol* **47**, (1):38-45. (Journal IF: 4.728, Citations: 0)

#### **Other publications International**

Fonseca JE, Viera Sousa E, Taylor P. Management of Rheumatoid Arthritis, EULAR textbook on Rheumatic Diseases and EULAR COURSE ONLINE for the period 2013-2016.

Romão VC, Gonçalves MJ, Fernandes S, Furtado C, Fonseca JE, Romeu JC, Pereira da Silva JA. Síndrome de SAPHO. *Acta Reumatol Port.* **39**(1): Ficha de imagens colecionável nº 5.

#### **Other publications National**

Canhão H, Faustino A, Fonseca JE. Registo Nacional de Doentes Reumáticos, Reuma.pt. Canhão H, Fonseca JE. Investigação Translacional em Doenças Reumáticas. in: Doenças Reumáticas em Portugal: da Investigação às Políticas de Saúde. Observatório Nacional das Doenças Reumáticas, Ed. 2014.

### Invited lectures and seminars

Canhao H. Reuma.pt and Liver.pt. Congresso Português de Hepatologia, Cascais, Portugal Fevereiro 13-14, 2015.

Fonseca JE. Mecanismos doenças imunomediadas, o exemplo AR. Universidade da Beira Interior, Covilhã, Portugal, January 9, 2014

Fonseca JE. Perspectivas da reumatologia os argumentos. Biológicos e Biossimilares: Os Desafios, Lisbon, Portugal, January 31, 2014

Fonseca JE. Oportunidades de investigação para alunos – AEFML (docente)  
Romão VR. Oportunidades de investigação para alunos – AEFML (aluno de doutoramento).  
17.º Workshop “Educação pela Ciência”, Faculdade de Medicina de Lisboa, Lisboa, Portugal, February 27, 2014

Fonseca JE. Biossimilares o contexto atual.  
Vieira Sousa E. Artrite psoriática, regras de ouro. Pfizer summit inflammation, Obidos, Portugal, February 2, 2014

Fonseca JE. Opening of EWRR 2014 and Closing Remarks  
Canhao H. Chair the session Closing Lecture.  
34th European Workshop for Rheumatology Research (EWRR), February 20-22, 2014, Lisbon, Portugal

Vieira Sousa ES. Sequential therapy for osteoporosis.  
Fonseca JE. Inflamação e doença óssea.  
IX Congresso Português de Osteoporose, Aveiro, Portugal, February 27- March 1, 2014

Fonseca JE. Chairman in lecture Nanoinflammation: bridges between Bone and Vessel  
Vidal B. How early inflammatory events affect bone nano - properties at rheumatoid  
Carmona-Fernandes D. Coupling of atherosclerosis progression and bone disturbances.  
12th Medinterna International Meeting, Porto, Portugal, February 27, 2014,

Canhao H. Do “enough” user-developed innovations diffuse? Evidence from Finland, plus preliminary insights regarding the diffusion of valuable patient-developed medical innovations. MIT Innovation Lab Meeting, March 5-6, 2014

Fonseca JE and Romão VC. Predictive factors for MTX response.  
Fonseca JE. Animal models in autoimmune diseases.  
Fonseca JE. Chair in sessions: Plenary session IV and Animal models in autoimmune diseases.  
9th Autoimmunity Congresso, Nice, France, March 26-30, 2014

Santos MJ. AR - Para além da articulação "O Coração".

Vieria Sousa E. Chair the session “Melhorar o Conhecimento do Doente: genéricos e biosimilares são todos iguais?” XIV Jornadas da ANDAR, Lisboa, Portugal, April 10, 2014

Fonseca JE. Chairman in lecture Long term treatment: Beyond Efficacy & Safety.

Rodrigues A. Novas vias fisiopatológicas na Osteoporose.

Santos MJ. A biotecnologia abre novo ciclo na terapêutica do LES.

Vieria Sousa E. Controlar a inflamação, controlar a ossificação: identificar intervenientes.

XVII Congresso Português de Reumatologia, Albufeira, Portugal, May 7-10, 2014

Fonseca JE. Understanding the early effects of inflammation on bone: treatment perspectives.

40th Annual General Meeting. Santiago de Compostela, Spain, May 21, 2014

Canhao H. Chair the session Health, Demographic Change and Well-being. 3 Program - Conference Theme: ‘Millennial Generation: Lost or Found?’ Pavilion of Knowledge – Ciência Viva, Lisbon, Portugal, May 22-23, 2014

Vieira Sousa E. The gut, the skin and the joints: should we change diet? Connecting for the Future II, Porto, Portugal, May 24, 2014

MJ Santos. Agentes biológicos nas AIJs: Anti-TNF. XIV Jornadas Internacionais de Reumatologia Pediátrica, Lisboa, Portugal, May 29, 2014

Santos MJ. Chair in session Immune Intervention.

Santos MJ. "SLE, SS, APS - clinical aspects" – abstract session.

Vieira Sousa ES. Chair in session Novel non-TNF biologics treatment of RA.

Rodrigues AM. Chair in session Scleroderma and myositis -clinical aspects.

Fonseca JE. Chair in session RA - non biologic and small molecules.

Annual European Congress of Rheumatology EULAR 2014, Paris, France, June 11-14, 2014

Fonseca JE. Biobanco: estudar a psoríase desde a sua génese.

Canhao H. O conhecimento atual sobre as espondilartrites e a artrite psoriática em Portugal.

Vieira Sousa ES. Modelo de cooperação entre Dermatologia e Reumatologia na psoríase. Psoríase 2014, Lisboa, June 21, 2014

Fonseca JE. Biobanco-IMM e desafios para a investigação em tecidos humanos. Fisiopatologia da Artrite Reumatoide. Sessão Clínica Semanal do Hospital, Hospital Pequeno Príncipe, Curitiba, Brasil, July 31, 2014

Fonseca JE. Fisiopatologia da Artrite Reumatoide. Atualização em Artrite Psoriática.

Congresso de Reumatologia do Cone Sul, Gramado, Brasil, August 1-2, 2014

Fonseca JE. Sessão clínica Reumatologia Pediátrica- Reuma.pt. Sessão clínica Reumatologia - Reuma.pt.

Artrite psoriática e psoríase. Hospital da Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brasil, August 4-8, 2014

Canhao H. Projecto Patient-Innovation e a inovação e difusão de soluções por doentes com doenças raras. Experiências e Trajetórias de Cuidados de Saúde: as Doenças Raras em Debate. CES-Coimbra, Portugal, September 23, 2014

MJ Santos. Lúpus Eritematoso Sistemico 7º Curso de Reumatologia Prática, Lisboa, Portugal, September 18, 2014

Canhao H. EpiReumaPt – metodologia. Apresentação dos resultados do Estudo Epidemiológico de Doenças Reumáticas em Portugal, Lisbon, Portugal, September 22, 2014

MJ Santos. Metabolic comorbidities: The immune system, Inflammation, Metabolic syndrome. Porto's Autoimmune meeting Porto, Portugal, September 25, 2014

Canhao H. Inovação por doentes. Amba saber +, Lisbon, Portugal, September 25, 2014

Fonseca JE. Long term data on infliximab. Simposio sociedade Romena de Reumatologia, Brasov, Roménia, October 1, 2014

Canhao H. Reuma.pt e Resultados EpiReumapt. Jornadas Outono Vimeiro, Vimeiro, Portugal, October 3-5, 2014

Canhao H. Eficácia e segurança de fármacos anti-OP nos idosos. 34º Congresso Nacional de Ortopedia  
Albufeira, October 3- 5, 2014

Canhao H. OP nas crianças nas doenças crónicas e exercício. Osteoporose - doença crónica e exercício. 15º Congresso Nacional de Pediatria. Albufeira, October 16-18, 2014

Fonseca JE. Biosimilars the medical perspective. RA Advocacy Summit, October 29, 2014.

Canhao H. Case studies of patient innovations. Advisory Board Patient Innovation MIT, Cambridge, Boston, October 31, 2014

Canhao H. Patient Innovation: When Patients Set Out to Help Themselves and End Up Helping Many. Patient Innovation Forum. Medical Industry Leadership Institute (MILI) and University of Minnesota Carlson School of Management. Minneapolis, November 3, 2014

Moura RA. Chair in session Session VII: Inflammation.

Santos MJ. Chair in session Immune Intervention.

8th European Workshop on Immune-Mediated Inflammatory, Funchal, Madeira, Portugal  
November 5-7, 2014

MJ Santos. "Back to the basics" Definição de conceitos, criação de linguagem comum e referenciação. XXII Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon Portugal, November 2-8, 2014

Canhao H. Osteoporose - Estratégias de diagnóstico e intervenção. VII Jornadas de Saúde do Idoso / XI Congresso Hispano Luso de Gerontologia, Faculdade de Ciências da Saúde da Universidade da Beira Interior, Covilhã, Portugal, November 5-8, 2014

Fonseca JE. Size does matter? A Physician's considerations towards Biosimilars , 1st National Bio-therapeutics congresso, Kuala Lumpur Malasia, November 22, 2014.

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

Barreira S, Carmona-Fernandes D, Castro A, Santos P, Nicolau Fernandes A, Mendes Pedro L, Canhão H, Fonseca JE, Santos MJ. Osteoporosis in patients with severe carotid atherosclerosis. (Poster presentation)

Oliveira Santos P, Carmona-Fernandes D, Barreira S, Nicolau Fernandes A, Mendes Pedro L, Castro A, Fonseca JE, Canhão H, Santos MJ. Vitamin D - a link between atherogenesis and bone mass? (Poster presentation)

Sepriano A, Gonçalves MJ, Rodrigues A, Lopes A, Caetano-Lopes J, Fonseca JE, Canhão H. Chronic kidney disease associates with worse trabecular mechanical performance in hip osteoarthritis patients independently of bone mineral density (Poster presentation)

Rodrigues AM, Reis JE, Santos C, Pereira MP, Loureiro C; Martins F, Fonseca JE, Canhão H. Obesity is a Risk Factor for Worse Treatment Response in Rheumatoid Arthritis Patients - Results from Reuma.pt (Poster presentation)

Moura RA, Canhão H, Polido-Pereira J, Leandro MJ, Cambridge G, Fonseca JE. Serum levels of CXCL13 are increased in untreated patients with rheumatoid arthritis from the first weeks of disease development (Poster presentation)

Vieira-Sousa E, Rodrigues AM, Caetano-Lopes J, Capela S, Ramos F, Figueira R, Polido- Pereira J, Ponte C, Campanilho-Marques R, Barros R, Romeu JC, Da Silva JAP. Zoledronate efficacy and safety in active Paget's disease: long-term follow-up and retreatment in clinical practice (Poster presentation)

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE,. RANK expression is reduced in circulating monocytes from ankylosing spondylitis patients. (Poster presentation)

Ávila-Ribeiro P, Vieira-Sousa E, Canhão H, Fonseca JE. Tapering infliximab in ankylosing spondylitis: can we reduce costs? (Poster presentation)

Rodrigues AM, Caetano-Lopes J, Oliveira V, Vidal B, Gonçalves MJ, Sepriano A, Sarmento M, Monteiro J, Fonseca JE, Canhão H. Differences of bone WNT regulators expression between fragility fractures and osteoarthritis patients( Poster presentation)



Gonçalves MJ, Sepriano A, Rodrigues A, Lopes A, Caetano-Lopes J, Fonseca JE, Canhão H. Procollagen type 1 amino-terminal propeptide is negatively associated with bone stiffness in subpopulations of patients submitted to hip replacement surgery( Poster presentation)

Vieira-Sousa E, Narciso L, Saraiva F, Pereira da Silva JA, Fonseca JE. Are arthroscopic guided synovial biopsies still relevant in rheumatology practice? (Poster presentation)

34th European Workshop for Rheumatology Research, February 20-22, 2014, Lisbon, Portugal. (Poster presentation)

Traunecker E, Gardner R, J Polido J, Seitz M, Villiger PM, Fonseca JE, Giandomenica Iezzi, Padovan E. Human CD14+ CD16++ nonclassical monocytes negatively impact on Th17 expansion through LFA-1. World Immune Regulation Meeting – VIII. Davos, Switzerland, March 19-22, 2014 (Oral presentation)

Romão VC. Clinical, Pathobiological and Immunogenetic Differences in Elderly- and Young-onset Rheumatoid Arthritis. Romão VC. Tuberculosis prevention and anti-TNF therapy: the Portuguese experience. Clinical Postgraduate Meeting, Centre for Experimental Rheumatology & Medicine, Barts Health Trust, Queen Mary University of London, London, United Kingdom, March, 2014 (Oral presentation)

Agripino A, de Mello-Sampayo C, Stilwell D, Vidal B, Lopes A, Vaz MF, Vale AC, Canhão H, Silva-Lima B, Marques MC. Could ovariectomy exert different effects on biomechanical properties of diabetic and non-diabetic rat's bones? (Poster presentation)

Agripino A, de Mello-Sampayo C, Stilwell D, Vidal B, Lopes A, Vaz MF, Vale AC, Canhão H, Silva-Lima B, Marques MC. Is bone structure and bone turnover of oestrogen deficient rats affected by diabetes. ( Poster presentation)

World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases), FIBES SEVILLA Palacio de Exposiciones y Congresos, Seville, Spain, April 2 - 5, 2014 (Oral presentation)

Agripino A, de Mello-Sampayo C, Stilwell D, Vidal B, Lopes A, Canhão H, Silva-Lima B, Marques MC. Effects of ovariectomy on the bone structure and bone turnover in diabetic female rats. 2nd Annual International Conference on Pharmaceutical Sciences, Athens, Greece, May 5-8, 2014 (Oral presentation)

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R,, Ponte C, Canhão H,, Ainola M, Fonseca JE. RANK expression is reduced in circulating monocytes from ankylosing spondylitis patients 41st ECTS Congress, Prague, May 17-20, 2014 (Poster presentation)

Zejnilovic L, Oliveira P, Canhão H. Patient Innovation under Chronic Need: An Empirical Investigation of Innovation Efforts by Patients of Rare Diseases and their Caregivers. Medical User Innovation and Medical Commons, New York, USA, 28-30 May, 2014 (Oral presentation)

Romão VC, Pereira e Silva R, Rodrigues T, Oliveira S, Brites J, Neves M, GarciaR, Palma dos Reis J, Pereira da Silva JA, Lopes T. Increased overactive bladder symptom bother in autoimmune patients: systemic lupus erythematosus may be the answer. Global Congress on Lower Urinary Tract Dysfunction, Brussels, Belgium, June 2014. (Poster presentation)

Sousa S, Gonçalves MJ, Ines LS, Duarte C, Fernandes S, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda L, Da Silva JAP, Canhão H, Santos MJ. REUMA.PT/LES: The Portuguese Lupus Register (Poster presentation)

Gonçalves MJ, Sousa S, Ines LS, Duarte C, Borges J, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda L, Da Silva JAP, Canhão H, Santos MJ. Damage Predictors In Patients From The Portuguese Lupus Registry (Poster presentation)

Santos MJ, Gonçalves MJ, Inês L, Nero P, Oliveira M, Cerqueira M, Sousa S, Romão VC, Da Silva JAP, Canhão H. Serologically Active Clinically Quiescent Systemic Lupus: Results From The Portuguese Registry REUMA.PT/LES (Poster presentation)

9th European Lupus Meeting, Atenas May 23-26, 2014

Sousa S, Gonçalves MJ, Inês LS, Duarte C, Fernandes S, Terroso G, Romão VC, Cerqueira M, Raposo A, Couto M, Nero P, Nóvoa T, Pinto P, Melo Gomes JA, Canas da Silva J, Costa L, Pereira da Silva JA, Cunha-Miranda L, Da Silva JAP, Canhão H, Santos MJ. Greater diagnostic delay in early-onset than in late-onset systemic lupus erythematosus - data from Reuma.pt/LES (Poster presentation)

Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Pimentel-Santos FM, Barcelos F, Costa L, Melo Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, Da Silva JAP, Fonseca JE, Canhão H. Tocilizumab is associated with higher CDAI/SDAI remission in biologic-naïve rheumatoid arthritis patients – data from Reuma.pt (Oral presentation)

Gonçalves MJ, Sousa S, Inês LS, Duarte C, Borges J, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda L, Da Silva JAP, Canhão H, Santos MJ. The weaker sex: characterization of gender disparities in a nationwide lupus registry (Reuma.pt LES) (Poster presentation)

Inês L, Silva C, Galindo M, López-Longo F, Terroso G, Romão V, Rúa-Figueroa I, Santos MJ, Pego-Reigosa JM, Nero P, Cerqueira M, Duarte C, Miranda LC, Almaraz ER, Bernardes M, Gonçalves MJ, Mouriño-Rodríguez C, Araújo F, Raposo A, Barcelos A, Sequeira G, Nóvoa T, Couto M, Abreu P, Otón-Sánchez T, Macieira C, Ramos F, Branco JC, Silva JAP, Canhão H, Calvo-Alén J. The SLICC 2012 Classification Criteria have Higher Sensitivity for SLE than the ACR 1997 Criteria. A Study of 2055 patients from a Real-life, Multicenter, International SLE Cohort(Poster presentation)

Sepriano A, Araújo F, Aguiar R, Vieira R, Sousa E, Pimentel-Santos F, Sequeira G, Canhão H, Santos H, Garcia J, Alberto Pereira Silva J, Canas Silva J, Miranda L, Oliveira M, Salvador MJ, Bernardes M, Monteiro P, Nóvoa T, Branco JC. Retention rate and predictive factors of TNF- $\alpha$  inhibitor discontinuation in patients with ankylosing spondylitis - results from the rheumatic diseases portuguese Register REUMA.PT (Abstract book)

Gabay C, Riek M, Hetland M, Hauge E.M, Pavelka K, Tomsic M, Canhao H, Chatzidionysiou K, Vollenhoven R. van; Lukina G, Nordstrom D, Lie E, Ancuta I, Santamaria E. Loza, Riel P. van, Kvien T. Retention of Tocilizumab therapy: a comparison between Tocilizumab in monotherapy and in combination with DMARDs based on the TOCERRA collaboration (Poster presentation)

Canet LM, Caliz R, Lupianez CB, Canhao H, Escudero A, Filipescu I, Segura J, Soto-Pino MJ, Ferrer M, Garcia A, Romani L, Perez-Pampin E, Gonzalez-Utrilla A, Lopez-Nevot M, Collantes E, Fonseca JE, Sainz J. Association of IL4 IL4R and IL8RB gene polymorphisms with the risk of developing rheumatoid arthritis (Poster presentation)

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE. RANK expression is reduced in circulating monocytes from ankylosing spondylitis patients. (Abstract book)

Moura RA, Canhão H, Polido-Pereira J, Leandro MJ, Cambridge G, Fonseca JE. Serum levels of CXCL13 are increased in untreated patients with rheumatoid arthritis from the first weeks of disease development. (Poster presentation)

Romão VC, Saavedra MJ, Costa M, Macieira C, Vieira-Sousa E, Ramos F, Resende C, Capela S, Barros R, Polido-Pereira J, Rodrigues AM, Madruga-Dias J, Marques R, Ponte C, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Hepatitis B serologic profile and reactivation in rheumatic patients treated with biological therapies: single centre experience (Abstract book)

Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Pimentel-Santos FM, Barcelos F, Costa L, Melo Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, Da Silva JAP, Fonseca JE, Canhão H. Changes in DAS28, CDAI and SDAI are associated with biologic class, gender, previous biologic therapy and ACPA/RF status – Results from Reuma.pt (Abstract book)

Mourão AF, Santos MJ, Melo Gomes JA, Martins FM, Ramos F, Fernandes S, Salgado M, Guedes M, Carvalho S, Costa JA, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues A, Sequeira G, Sousa M, Branco JC, Fonseca JE, Canhão H. Biologic disease modifying anti-rheumatic drug use in the treatment of juvenile idiopathic arthritis: data from the Rheumatic Diseases Portuguese Register, Reuma.pt (Abstract book)

Romão VC, Pereira e Silva R, Rodrigues T, Oliveira S, Brites J, Neves M, Garcia R, Ramos F, Palma dos Reis J, Pereira da Silva JA, Lopes T. Overactive bladder symptom bother is increased

in patients with systemic lupus erythematosus and Sjögren's syndrome EULAR 2014, Paris, June 11-13, 2014 (Poster presentation)

Schulte-Pelkum J, Carmona-Fernandes D, Santos MJ, Albesa R, Mahler M. Utility of anti-ribosomal P and anti-Ku antibodies detected by novel chemiluminescent assays in the diagnosis of systemic lupus erythematosus. 12th International Workshop on Autoimmunity and Autoantibodies, São Paulo, Brazil, August 28-30, 2014. (Poster presentation)

Sousa S, Fernandes S, Estanqueiro P, Zilhão C, Resende C, Ramos F, Salgado M, Guedes MJ, Melo –Gomes J, Santos MJ. Juvenile systemic sclerosis: review of 15 patients. Pediatric Rheumatology European Society, Belgrado, September 17-12, 2014 (Poster presentation)

Schulte-Pelkum J, Carmona-Fernandes D, Santos MJ, Albesa R, Mahler M. Added value of the determination of anti-ribosomal and anti-Ku antibodies for diagnosis of systemic lupus erythematosus. (Poster presentation)

Mercer L, Mariette X, Dixon W, Baecklund E, Hellgren K, Dreyer L, Hetland ML, Mellekjær L, Hyrich K, Strangfeld A, Zink A, Canhao H, Martins F, Hernández V, Tubach F, Gottenberg JE, Morel J, Zav J. First Results of a European Registries Collaborative Project to Compare the Spectrum of Lymphomas Between Different Exposure Groups in Rheumatoid Arthritis. (Oral presentation)

Walker UA, Jaeger VK, Chatzidionysiou K, Hetland ML, Hauge EM, Pavelka K, Nordström DC, Canhao H, Tomsic M, van Vollenhoven R, Gabay C. Rituximab Done! What's Next in RA? (Poster presentation)

Chatzidionysiou K, Lie E, Nasonov E, Lukina G, Hetland ML, Hauge E, Pavelka K, Gabay C, Nordström D, Canhão H, Tomsic M, Piet van Riel P, Gomez-Reino J, Ancuta I, Kvien T, van Vollenhoven R, Saevarsdottir S. Smoking and Response to Rituximab in Anti-CCP Positive and Negative Rheumatoid Arthritis – Results from an International European Collaboration (Poster presentation)

Canhã H, Martins F, Melo Gomes JA, Santos MJ, Faustino A, Costa JA, Allaart C, Gvozdenovic E, Machado P, Branco JC, Fonseca JE, Pereira Da-Silva. Comparative Study of Rheumatoid Arthritis Disease Activity Indices in Two Populations of Meteor Database. (Poster presentation)

Finckh A, Neto D, Hernández MV, Iannone F, Lie E, Canhao H, Pavelka K, Turesson C, Mariette X, Hetland ML, Gottenberg J. Abatacept after Rituximab in Rheumatoid Arthritis. a Pan-European Collaboration of RA Registries Mercer L, Askling J, Raaschou P, Dixon W, Dreyer L, Hetland ML, Mellekjær L, Strangfeld A, Zink A, Iannone F, Finckh A, Zavada J, Canhao H, Martins F, Mariette X, Jacques Morel J, Jacques-Eric Gottenberg JE, Adele Green A, Victoria Hernández V, Tubach F, van Riel P, Hyrich K, Listing J. No Increased Risk of Developing a First

Invasive Melanoma in Rheumatoid Arthritis Patients Treated with Biologics: Results of a Collaborative Project of 11 European Biologics Registers (Oral presentation)

ACR/ARHP Annual Meeting, Boston, MA, November 14-19, 2014

Carmona-Fernandes D, Schulte-Pelkum J, Albesa R, Mahler M, Santos MJ. Anti-ribo-P and anti-Ku antibodies as systemic lupus erythematosus diagnostic biomarkers. (Poster presentation)

Nicolau-Fernandes A, Carmona-Fernandes D, Cortes-Figueiredo F, Barreira S, Oliveira Santos P, Amaro Gonçalves C, Pedro LM, Fonseca JE, Canhão H, Santos MJ. Osteoprotegerin, RANKL and Bone Mineral Density in patients with advanced carotid atherosclerosis. (Poster presentation)

Moura RA, Leandro MJ, Reddy V, Fonseca JE, Cambridge G. Rheumatoid arthritis patients have alterations in inherently autoreactive 9G4+ B-cell subpopulations in peripheral blood (Oral presentation)

Moura RA, Quaresma C, Vieira AR, Gonçalves MJ, Polido-Pereira J, Romão V, Martins N, Canhão H, Fonseca JE. B-cell markers expression is affected by tnf-inhibitors and tocilizumab treatment in rheumatoid arthritis (Oral presentation)

Vidal B, Cascão R., Vale A.C., Cavaleiro I., Vaz M.F., Brito J.A., Canhão H., Fonseca J.E. Arthritis induces early bone high turnover, structural degradation and mechanical weakness. (Poster presentation)

Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE Receptor activator of NF-KB expression is reduced in circulating monocytes from ankylosing spondylitis patients (Poster presentation)

Vieira-Sousa E, Narciso L, Saraiva F, Pereira da Silva JA, Fonseca JE Are arthroscopic guided synovial biopsies still relevant in rheumatology practice? (Poster presentation)

Romão VC, DiCicco M, Mahto A, Lazarou I, Fonseca JE, Kelly S, Humby F, Pitzalis C Clinical and pathological differences of elderly- and younger-onset rheumatoid arthritis in an early arthritis cohort (Poster presentation)

Furtado C, Fernandes S, Rodrigues AM, Martins F, Miranda Rosa C, Pereira da Silva JA, Vieira-Sousa E. Predictors of remission in axial spondyloarthritis patients treated with non-steroidal anti-inflammatory drugs (Poster presentation)

Romão VC, Saavedra MJ, Costa M, Macieira C, Vieira-Sousa E, Ramos F, Resende C, Capela S, Barros R, Polido-Pereira J, Rodrigues AM, Madruga-Dias J, Marques R, Ponte C, Castro A,

Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Hepatitis B serologic profile and reactivation in rheumatic patients treated with biological therapies: single centre experience (Poster presentation)

8th European Workshop on Immune-Mediated Inflammatory Diseases, Funchal – Madeira, Portugal November 5-7, 2014

Laires PA, Canhão H, Gouveia M. Early Retirement Indirect Costs Attributable to Rheumatic Diseases in Portugal. (Poster presentation)

Laires PA, Canhão H, Gouveia M. A Comparison of the Impact of Rheumatic Diseases and Other Chronic Diseases on Early Retirement in Portugal. (Poster presentation)

ISPOR 17th Annual European Congress, Amsterdam, The Netherlands, November 8-12, 2014

Santos C, Fonseca M, Corregidor V, Guerra M, Vidal B, Alves LC, Silva H, Carvalho M, Santos JP, Branco J, Jesus AP. Investigation of elemental distribution in human femoral head. 14th International Conference on Nuclear Microprobe Technology and Applications. Palazzo del Bo and Centro Culturale San Gaetano, Padova, July 6-11, 2014 (Poster presentation)

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

Cortes-Figueiredo F, Carmona-Fernandes D, Nicolau-Fernandes A, Barreira S, Santos P, Goncalves C, Pedro LM, Canhao H, Fonseca JE, Santos MJ. Adiponectin and IL-6 in established atherosclerosis: what relationship to bone mineral density? (Oral presentation)

Nicolau-Fernandes A, Carmona-Fernandes D, Cortes-Figueiredo F, Barreira S, Oliveira Santos P, Amaro Gonçalves C, Pedro LM, Fonseca JE, Canhão H, Santos MJ. Osteoprotegerin, RANKL and Bone Mineral Density in patients with advanced carotid atherosclerosis. 17.<sup>o</sup> Workshop “Educação pela Ciência”, Faculdade de Medicina de Lisboa, Lisboa, Portugal, February 27, 2014 (Oral presentation)

Gonçalves MJ, Sousa S, Inês LS, Duarte C, Borges J, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Macieira C, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda L, Da Silva JAP, Canhão H, Santos MJ. Damage predictors in SLE patients from the portuguese lupus registry (Oral presentation)

Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Pimentel-Santos FM, Barcelos F, Costa L, Melo Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, Da Silva JAP, Fonseca JE, Canhão H. Changes in DAS28, CDAI and SDAI are associated with biologic class, gender, previous biologic therapy and ACPA/RF status – Results from Reuma.pt (Oral presentation)

Mourão AF, Santos MJ, Melo Gomes JA, Martins FM, Ramos F, Fernandes S, Salgado M, Guedes M, Carvalho S, Costa JA, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues A, Sequeira G, Sousa M, Branco JC, Fonseca JE, Canhão H. Biologic disease modifying anti-rheumatic drug use in the treatment of juvenile idiopathic arthritis: data from the Rheumatic Diseases Portuguese Register, Reuma.pt (Oral presentation)

Gouveia N, Rodrigues A, Mendonça S, Costa LP, Canhão H, Branco JC. Low Back Pain and Fibromyalgia – EpiReumaPt survey results (Oral presentation)

Romão VC, Saavedra MJ, Costa M, Macieira C, Vieira-Sousa E, Ramos F, Resende C, Capela S, Barros R, Polido-Pereira J, Rodrigues AM, Madruga-Dias J, Marques R, Ponte C, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Hepatitis B serologic profile and reactivation in rheumatic patients treated with biological therapies: single centre experience (Oral presentation)

Sepriano A, Araújo F, Aguiar R, Vieira R, Sousa E, Pimentel-Santos F, Sequeira G, Canhão H, Santos H, Garcia J, Alberto Pereira Silva J, Canas Silva J, Miranda L, Oliveira M, Salvador MJ, Bernardes M, Monteiro P, Nóvoa T, Branco JC. Retention rate and predictive factors of TNF- $\alpha$  inhibitor discontinuation in patients with ankylosing spondylitis - results from the rheumatic diseases Portuguese Register REUMA.PT (Oral presentation)

Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Pimentel-Santos FM, Barcelos F, Costa L, Melo-Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, da Silva J, Fonseca JE, Canhão H. Tocilizumab is associated with higher CDAI/SDAI remission in biologic-naïve rheumatoid arthritis patients – data from Reuma.pt. (Poster presentation)

Mourão AF, Santos MJ, Martins FM, Melo Gomes JA, Mendonça S, Ramos F, et al. Retention rate of biologics in the treatment of juvenile idiopathic arthritis: data from the Rheumatic Diseases Portuguese Register reuma.pt (Poster presentation)

S Sousa, I Cordeiro, MJ Santos, P Gonçalves, A Cordeiro, S Garcês, F Godinho, F Vinagre, R Roque, V Tavares, J Canas da Silva. Abatacept: 5 anos de experiência clínica num serviço de reumatologia (Poster presentation)

Vieira-Sousa E, Polido-Pereira J, Ribeiro AL, Antunes J, Oliveira ME, Pereira da Silva JA, Fonseca JE. *Lipoma arborescens* and the hidden psoriatic arthritis (Poster presentation)

Castro A, Ferreira C, Vieira Sousa E, Miranda-Rosa C, Pereira da Silva JA. Frosted branch angiitis: uma vasculite ocular rara associada a espondilite anquilosante (Poster presentation)

Pimentel-Santos FM, Céu M, Mourão AF, Barcelos A, Ribeiro C, Vieira-Sousa E, Sequeira G, Santos H, Costa JA, Pinto P, Tavares V, Fonseca JE, Branco JC, Barros P. Reforma antecipada e absentismo nos doentes com espondilite anquilosante: que factores estão associados? (Poster presentation)

presentation)

Romão VC, Gonçalves MJ, Gonçalves A, Ramos F, Saraiva F, Romeu JC, Pereira da Silva JA. Poliarterite nodosa associada a infecção a *Coxiella burnetii*. Predictive factors of treatment response to a second TNF? inhibitor in patients with ankylosing spondylitis – results from the Portuguese Register Reuma.pt (Poster presentation)

Sousa S, Gonçalves MJ, Inês LS, Duarte C, Fernandes S, Silva C, Romão VC, Terroso G, Bernardes M, Cerqueira M, Raposo A, Sequeira G, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda L, Da Silva JAP, Canhão H, Santos MJ. REUMA.PT/LES: The Portuguese Lupus Register (Poster presentation)

Sousa S, Gonçalves MJ, Inês LS, Duarte C, Fernandes S, Terroso G, Romão VC, Cerqueira M, Raposo A, Couto M, Nero P, Nóvoa T, Pinto P, Melo Gomes JA, Canas da Silva J, Costa L, Pereira da Silva JA, Cunha-Miranda L, Da Silva JAP, Canhão H, Santos MJ. Greater diagnostic delay in early-onset than in late-onset systemic lupus erythematosus - data from Reuma.pt/LES (Poster presentation)

Gonçalves MJ, Sousa S, Inês LS, Duarte C, Borges J, Silva C, Romão VC, Terroso G, Cerqueira M, Raposo A, Bernardes M, Macieira C, Sequeira G, Barcelos A, Canas da Silva J, Costa L, Pereira da Silva JA, Miranda LC, da Silva JAP, Canhão H, Santos MJ. The weaker sex: characterization of gender disparities in a nationwide lupus registry (Reuma.pt/LES). (Poster presentation)

Romão VC, Pereira e Silva R, Rodrigues T, Oliveira S, Brites J, Neves M, Garcia R, Ramos F, Palma dos Reis J, Pereira da Silva JA, Lopes T. Overactive bladder symptom bother is increased in patients with systemic lupus erythematosus and Sjögren's syndrome. (Poster presentation)

Ponte C, Luqmani RA, Mendonça S, Martins FM, Fonseca JE, Canhão H. Reuma.pt: moving forward to vasculites. (Poster presentation)

Gonçalves MJ, Romão VC, Soares de Almeida L, Gonçalves AR, Crujo MC, Cortez Pinto H, Saraiva F, Canhão H, Romeu JC, Kutzner H, Pereira da Silva JA. Erythema elevatum et diutinum – uma vasculite rara, uma associação raríssima. (Poster presentation)

Sepriano A, Araújo F, Pimentel-Santos F, Nero P, Rodrigues A, Gouveia N, Mendonça S, Costa LP, Canhão H, C. Branco JC Health Care Resource Consumption and Health-Related Quality of Life in Knee Osteoarthritis - EpiReumaPt survey results. (Poster presentation)



Sepriano A, Gonçalves MJ, Rodrigues A, Lopes, Caetano-Lopes J, Fonseca JE, Canhão H. Chronic kidney disease associates with worse trabecular mechanical performance in hip osteoarthritis patients independently of bone mineral density. (Poster presentation)

Santos MJ, Carmona-Fernandes D, Rodrigues A, Gouveia N, Mendonça S, Costa LP, Canhão H, Branco J. Bidirectional relationship between low impact fractures and heart disease - analysis upon self-reported data from EpiReuma.pt. (Poster presentation)

Rodrigues AM, Caetano-Lopes J, Oliveira V, Vidal B, Gonçalves MJ, Sepriano A, Sarmento M, Monteiro J, Fonseca JE, Canhão H. Differences of bone WNT regulators expression between fragility fractures and osteoarthritis patients. (Poster presentation)

Romão VC, Gonçalves MJ, Fernandes S, Furtado C, Barros R, Romeu JC, Pereira da Silva JA. Terapêutica com teriparatida numa consulta de Doenças Ósseas Metabólicas (Poster presentation)

Gouveia, N, Mourão, AF, Silva, I, Machado, P, Laires, PA, Ramiro, S, Canhão, H, Branco, JC. EpiReumaPt – the end of recruitment. (Poster presentation)

Oliveira Ramos F, Conde M, Martins FM, Marques JG, Esteves I, Sousa AB, Miltenberger-Miltenyi G, Henriques C, Farelá Neves J, Cordeiro-Ferreira G, Pereira da Silva JA, Fonseca JE, Canhão H. Auto-inflammatory diseases register - data from the newest Reuma.pt protocol  
Cunha-Miranda L, Faustino A, Rodrigues A, Gouveia N, Mendonça Sílvia, Costa LP, Canhão H, Branco JC, Rheumatology Investigators. Nationwide occupational impact of rheumatic diseases: data from EpiReumaPt. (Poster presentation)

Vieira-Sousa E, Narciso L, Saraiva F, Pereira da Silva JA, Fonseca JE. Are arthroscopic guided synovial biopsies still relevant in rheumatology practice? XVII Congresso Português de Reumatologia Albufeira, May 7-10 2014. (Poster presentation)

Araujo GR, Fujimura PT, Cunha U, Junior JP, Silva CH, Mourão AF, Canhão H, Fonseca JE, Goulart LR, Gonçalves J, Ueira-Vieira C. Detection and avidity of antiCollagen type II antibodies in patients with juvenile idiopathic arthritis. 6th iMed.ULisboa Postgraduate Students Meeting, July 2, 2014. (Poster presentation)

Sousa S, Gonçalves MJ, Romão VC, Terroso G, Bernardes M, Canas da Silva J, Costa L, Macieira C, Pereira da Silva JA, Canhão H, Santos MJ. Comorbidities profile of SLE patients from the registry Reuma.pt/LES. Porto's Autoimmune Meeting. Porto, September 27, 2014 (Oral presentation)

Casimiro RI, Carmona-Fernandes D, Canhão H, Fonseca JE, Santos MJ. Coupling of atherosclerosis progression and bone disturbances in a mouse model of arthritis. (Poster presentation)

Cortes-Figueiredo F, Carmona-Fernandes D, Nicolau-Fernandes A, Barreira S, Santos P, Goncalves C, Pedro LM, Canhao H, Fonseca JE, Santos MJ. Adiponectin and IL-6 in established atherosclerosis: what relationship to bone mineral density. (Poster presentation)

Leonardo NP, Carmona-Fernandes D, Pedro LM, Ivo M, Canhão H, Fonseca JE, Santos MJ. The role of inflammation in the coupling of atherosclerosis and osteoporosis. (Poster presentation)

Nicolau-Fernandes A, Carmona-Fernandes D, Cortes-Figueiredo F, Barreira S, Oliveira Santos P, Amaro Gonçalves C, Pedro LM, Fonseca JE, Canhão H, Santos MJ. Osteoprotegerin, RANKL and Bone Mineral Density in patients with advanced carotid atherosclerosis. (Poster presentation)  
iMed Conference, Lisbon, Portugal, October 10-12, 2014

Oliveira I, Gonçalves MJ, Pereira N, Freixo J. Dor articular no adolescente- um desafio diagnóstico. (Poster presentation)

Oliveira Ramos F, Conde M, Martins FM, Marques JG, Esteves I, Sousa AB, Miltenberger-Miltenyi G, Henriques C, Fabela Neves J, Cordeiro-Ferreira G, Pereira da Silva JA, Fonseca JE, Canhao H. Auto-inflammatory diseases register - data from the newest Reuma.pt protocol. 15<sup>o</sup> Congresso Nacional de Pediatria, Albufeira, Portugal, October 16-18, 2014. (Oral presentation)

Fernandes S, Furtado C, Saavedra MJ, Vieira-Sousa E, Costa M, Polido-Pereira J, Ramos F, Macieira C, Capela S, Resende C, Barros R, Madruga-Dias J, Ponte C, Romão VC, Gonçalves MJ, Canhão H, Romeu JC, Fonseca JE, Pereira da Silva JA. Terapêutica com imunoglobulina humana endovenosa: relato da experiência de 10 anos no hospital de dia do Serviço de Reumatologia e Doenças Ósseas Metabólicas do Hospital de Santa Maria. XXII Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon Portugal, November 2-8, 2014 (Poster presentation)

#### **Organisation of Conferences**

Fonseca JE. Chair of the 34th EWRR.

Caetano Lopes J, Perpetuo IP. Local Organizing Committee 34th EWRR. 34th European Workshop for Rheumatology Research (EWRR), February 20-22, 2014, Lisbon, Portugal

Fonseca JE. Chair of the Ewimid'14. Welcome Address. 8th European Workshop on Immune-

Mediated Inflammatory, Funchal, Madeira, Portugal November 5-7, 2014

Perpetuo IP. Elected representative for the IMM/CAML PhD students community for the 2013 - 2015 biennium

Perpetuo IP. Organization committee and member of the PhD Committee from IMM/CAML PhD Students (2011-2014)

Perpetuo IP. Organization committee VIII IMM/CAML PhD Student Meeting - 2014

JEFonseca Lab organizing a series of monthly talks "IMM Rheumatology Series " with leading international researchers in the field of Rheumatology

Vieira Sousa E. Jornadas das Espondilartrites , Atualização de "2011 Portuguese recommendations for the use of biological therapies in patients with psoriatic arthritis"».Sede da Sociedade Portuguesa de Reumatologia, December 12,2014

#### **Internationalisation**

CERRERA and TOCERRA collaboration. Coordinator: Helena Canhão.

Comparative patient outcome measures study in Dutch and Portuguese rheumatoid arthritis patients – data from Meteor Project. Coordinator: Helena Canhão.

EULAR scientific Committee. João Eurico Fonseca.

IMM Rheumatology Series, in each session we promote site visit and project discussions with the international speakers.

#### **Prizes, honours and awards Patents**

Prize for best oral communication in XVII Congresso Português de Reumatologia, Albufeira, Portugal, 2014. Alexandre R. Sepriano, Filipe Araujo, Renata Aguiar, Romana Vieira, Elsa Sousa, Fernando Pimentel-Santos, Graça Sequeira, Helena Canhão, Helena Santos, Jorge Garcia, J. Alberto Pereira Silva, J. Canas Silva, Luís Miranda, Margarida Oliveira, M. João Salvador, Miguel Bernardes, Paulo Monteiro, Teresa Nóvoa, Jaime Branco; Retention rate and predictive factors of TNF- $\alpha$  inhibitor discontinuation in patients with ankylosing spondylitis - results from the rheumatic diseases portuguese Register REUMA.PT,

ECTS/AMGEN Bone Biology Fellowship 2014 was awarded to Bruno Vidal

Honourable Mention for Oral Presentation, in XVII Congresso Português de Reumatologia , Albufeira, Portugal, 2014. Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Pimentel-Santos FM, Barcelos F, Costa L, Melo-Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, da Silva JAP, Fonseca JE, Canhão H. Changes in DAS28, CDAI and SDAI are associated with biologic class, gender, previous biologic therapy and ACPA/RF status – results from Reuma.pt.

Romão VC. EULAR Scientific Training Bursary awarded for Clinical Research Fellow position for 6 months, at the Centre for Experimental Medicine & Rheumatology, Queen Mary University of London, United Kingdom (February 2014).

#### **Industry contract research**

RRU projects are supported by unrestricted research grants from industry. We will start also a clinical trial funded by Industry.

#### **Advanced teaching**

Canhao H, Ramos F, Mourao AF, Fonseca JE. Anamnese e Exame Objectivo em Reumatologia Pediátrica – Sessão Prática. Diagnóstico Diferencial: Casos clínicos II.

Santos MJ. Doenças Difusas do Tecido Conjuntivo Juvenis

Canhao H, Ramos F, Mourao AF, Santos MJ, Fonseca JE. Diagnóstico Diferencial: Casos Clínicos

Canhao H. Registos (Reuma.pt), Biobanco (Biobanco?IMM) e Investigação em Reumatologia Pediátrica? Helena Canhão

Fonseca JE. Conclusões. “1 curso pós-graduado de actualização “Diferenciação em Pediatria – Inovação e Tecnologia (2ª Parte)” módulo XIV Reumatologia, Faculdade Medicina de Lisboa, Portugal, March 21, 2014

Canhao H. Curso investigação clinica, Funchal, Madeira, April 10- 12, 2014

Canhao H. Princípios de imunoterapia.

Mourão AF and Ramos F. Casos clínicos. VII Curso de formação em neuropediatria. Aula magna- Hospital de Santa Maria- CHLN, Lisbon, Portugal, February 27, 2014

Canhao H. Registries – Reuma.pt. Training Programme in Pharmaceutical Medicine - Medical Affairs INFARMED, Lisbon, Portugal, March 06 - 08, 2014

Canhao H. Clinical and genetic predictors of response to anti-TNF-? treatment in patients with rheumatoid arthritis. Harvard Portugal Program Workshop, Lisbon, Portugal, November 21, 2014

Carmona Fernandes D. Supervisor of a student from Instituto Politécnico de Lisboa- Escola

Superior de Tecnologia da Saúde de Lisboa with the project entitled 'Associação entre Aterosclerose e Osteoporose: Caracterização de placas ateroscleróticas' & SLIDE for the Unidade Curricular de Investigação em Farmácia – Licenciatura em Farmácia.

Lopes A. Supervisor of a student from Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa for the “ Unidade Curricular: Programa de introdução à prática profissional” , Mestrado integrado de Engenharia Biomédica

Vieira Sousa E. Diferentes Tipos de Exercício, metabolismo energético do músculo e mecanismo de contração muscular, fadiga muscular e fluxo de cálcio. 10º Curso de Pós-Graduação em Medicina Desportiva, Lisbon, Portugal, March 8, 2014

Perpétuo IP\*, Caetano-Lopes J, Vieira-Sousa E, Campanilho-Marques R, Ponte C, Canhão H, Ainola M, Fonseca JE. (\* Presenting author). RANK expression is reduced in circulating monocytes from ankylosing spondylitis patients.(Oral presentation)

Camona-Fernandes D, Santos MJ, Canhão H, Fonseca JE. Anti-ribosomal P protein IgG autoantibodies in patients with systemic lupus erythematosus: diagnostic performance and clinical profile.(Oral presentation)

Vidal B, Fonseca JE, Canhão H. How early inflammatory events affect bone nano-properties at the onset of rheumatoid arthritis. (poster presentation)

IMM Highlights VIII PhD Student Meeting IMM/CAML, Lisbon, Portugal March 28, 2014

Canhao H, Fonseca JE participated in LisbonBioMed PhD Program--Class of 2014.

### **Science and society**

Helena Canhão participated, in October 2014, in TV program, Diário da Manhã TVI talk about Osteoporosis in World Osteoporosis Day.

Helena Canhão participated, in several TV programs and radio programs talk about the Patient Innovation project.

João Eurico Fonseca participated, in several TV programs and radio programs talk about rheumatic diseases.

JEFonseca Lab received students from Escola Secundária de Aveiro and Escola João de Deus in a visit to IMM.

### Msc thesis completed

Sofia Carvalho Fernandes Barreira 03/04/2014 Osteoporosis in patients with severe carotid atherosclerosis Faculdade de Medicina de Lisboa Maria José Santos Diana Fernandes

Pedro Miguel Oliveira Santos 03/04/2014 Vitamina D em doentes com aterosclerose - um elo entre aterosclerose e massa óssea? Faculdade de Medicina de Lisboa Maria José Santos Diana Fernandes

Rita Raposeiro 27/12/2014 Osteoclast activity in ankylosing spondylitis patients before and after TNF blocking therapy. Faculdade de Ciências e Tecnologias da Universidade Nova de Lisboa. Joana Lopes Inês Perpétuo

Ana Daniel 29/12/2014 Role of Wnt pathway on Rheumatoid Arthritis Faculdade de Ciências da Universidade de Lisboa Joana Lopes Inês Perpétuo

Ana Rita Vieira 17/12/2014 B cell gene expression in rheumatoid arthritis: Effect of immunosuppressive treatment. Faculdade de Ciências da Universidade de Lisboa Rita Moura

Sofia Spencer 03/04/2014 Eficiência do MTX na Artrite Psoriática. Faculdade de Medicina de Lisboa. Elsa Sousa

Claúdia Viveiros Santos 03/04/2014 Dactilite na artrite psoriática. Faculdade de Medicina de Lisboa Elsa Sousa

Claudia Quaresma 26/12/2014 Characterization of peripheral blood B cell subpopulations in Rheumatoid Arthritis Faculdade de Ciências da Universidade de Lisboa Rita Moura

Maria Maia 15/09/2014 Bone fragility as a possible complicatio of Chronic Kidney Disease in early stages. Faculdade de Medicina de Lisboa Helena Canhão

## João Lacerda Lab

### Major Interests / Objectives

Donor-derived immune cells play a pivotal role in the protection against pathogens, such as *Aspergillus*, CMV and EBV, and in the emergence of graft-versus-host disease (GVHD) and graft-versus-leukemia effect arising after hematopoietic stem cell transplantation (HSCT). Our lab is interested in the study of immune reconstitution and in the development of strategies that modulate immune responses after HSCT. We are currently conducting a Phase I/II clinical trial with CliniMACS-selected donor regulatory T cells in patients with steroid-resistant chronic GVHD. We are also studying the genetic susceptibility for infections arising after HSCT and involved in the development of pathogen-specific T cell therapies with the ultimate goal of improving patient survival and quality of life.

### Head of Unit

João Mascarenhas Forjaz de Lacerda, MD/PhD, Associate Professor, Clinical Specialist, Hospital Santa Maria

### Research Team

António Maria Moura Tavares de Sampaio Soares	Graduate	MSc Student
António Maria Santa Marta de Soure	Master	PhD Student, (left May)
Bárbara Joana Mestre Ribeiro	Undergraduate	MSc Student, (started March)
Cláudia Alexandra Martins Lobato da Silva	PhD	Visiting Researcher, (started November)
Inês Raquel Antunes Ferreira	Master	Technician
Maria Godinho A.V. Duarte Soares	PhD	Post doctoral Investigator
Rita Isabel Silva de Azevedo	PhD	Post doctoral Investigator
Telma Raquel Martins da Palma	PhD	Post doctoral Investigator, (left August)

### Keywords / Research Areas

Immune reconstitution after hematopoietic stem cell transplantation (HSCT), 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

Our unit, officially created in July 2013, has established a multidisciplinary platform involving basic scientists, physicians and bioengineers with the aim of bringing into clinical practice adoptive cellular immunotherapy strategies for the prevention and treatment of severe complications after hematopoietic stem cell transplantation (HSCT). We are currently implementing strategies to modulate immune tolerance after HSCT with donor regulatory T cells for the treatment of chronic graft versus host disease (GVHD). Our main source of funding in 2014 derived from a collaborative research grant of Harvard Medical School Portugal Program that we have in conjunction with the Dana-Farber Cancer Institute, in Boston, and Instituto Superior Técnico, in Lisboa. Starting in 2015, we have secured the coordination of the Horizon 2020 project TREGeneration, leading a European consortium evaluating the use of regulatory T cells in both acute and chronic GVHD.

### Selected Publications

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. (Journal IF: 3.940, Citations: 2)

Gomes AQ, Correia DV, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, Silva MG, Silva-Santos B. (2010) Identification of a panel of ten cell surface protein antigens associated with immunotargeting of leukemias and lymphomas by peripheral blood gammadelta T cells. *Haematologica* **95**, 1397. (Journal IF: 5.935, Citations: 24)

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. (Journal IF: 9.06, Citations: 30)

Ciceri F, Labopin M, Aversa F, Rowe JM, Bunjes D, Lewalle P, Nagler A, Di Bartolomeo P, Lacerda JF, Lupo Stanghellini MT, Polge E, Frassoni F, Martelli MF, Rocha V. ( ) A..(9), -3581. doi: 10.1182/blood-2008-02-140095 (2008) A survey of fully haploidentical hematopoietic stem



cell transplantation in adults with high-risk acute leukemia: a risk factor analysis of outcomes for patients in remission at transplantation. *Blood* **112**, 3574. (Journal IF: 9.06, Citations: 101)

#### **Other publications International**

Lacerda JF, Oliveira SN, Ferro JM. "Chronic myeloproliferative diseases." *Handb Clin Neurol*. 2014;**120**:1073(Review)

#### **Ongoing Research Projects**

2013/2016 Title: Induction of Immune Tolerance in Human Allogeneic Hematopoietic Stem Cell Transplantation. Coordinator: João Mascarenhas Forjaz de Lacerda. Agency: Fundação Ciência e Tecnologia. Reference: HMSP-ICT/0001/2011. Amount: 293,513€. Amount (total): 563,495€.

2014/2014 Title: LisbonLymph Debate . Coordinator: João Mascarenhas Forjaz de Lacerda. Agency: Celgene Sociedade Unip., Lda.. Reference: Curso Celgene. Amount: 25,000€.

2014/2017 Title: MDS Awareness Day. Coordinator: João Mascarenhas Forjaz de Lacerda. Agency: Celgene Sociedade Unip., Lda.. Reference: MDS Awareness Day. Amount: 2,500€.

#### **Publications in peer review Journals**

Cunha C, Aversa F, Lacerda, JF, Busca A, Kurzai O, Grube M, Löffler J, Maertens JA, Bell AS, Inforzato A, Barbati E, Almeida B, Sousa PS, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano L, Luppi M, Montovani 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):421-32. doi: 10.1056/NEJMoa1211161. (Journal IF: 54.42, Citation: 10, <http://www.nejm.org/doi/full/10.1056/NEJMoa1211161>)

Gomes AM, Soares MVD, Ribeiro P, Caldas J, Pova V, Martins LR, Melão A, Serra-Caetano A, de Sousa AB, Lacerda JF\*, Barata JT\*. (\* joint final authors). (2014) Adult B-cell acute lymphoblastic leukemia cells display decreased PTEN activity and constitutive hyperactivation of PI3K/Akt pathway despite high PTEN protein levels. *Haematologica* **99**(6):1062-8. doi: 10.3324/haematol.2013.096438. (Journal IF: 5.868, Citations:2)

### **Communications in International Conferences**

Alho A, Haesook KT, Reynolds CG, Chammas MJ, McDonough S, Lazo-Kallanian S, Daley J, Nikiforow S, Cutler CS, Koreth J, Ho VT, Armand P, Soiffer RJ, Antin JH, Ritz J. Homeostatic Reconstitution of CD4+ Regulatory and Conventional T Cell Subsets in Adult Patients after Allogeneic Hematopoietic Stem Cell Transplantation (HSCT). 56th Annual Meeting of the American Society of Hematology. San Francisco CA, 2014. Blood in press. (Poster presentation)

Rita I Azevedo, Antonio S Soares, Eduardo Espada, Nadia Camacho, Carlos V Martins, Fernanda Lourenco, Clara Juncal, Raul Moreno, Jose A Carmo and Joao F Lacerda IL-7 and IL-10 Serum Levels Are Potential Immune Biomarkers for Acute Graft-Versus-Host Disease Following Unrelated Hematopoietic Stem Cell Transplantation Blood 2014, 124 (21) (Meeting Abstract)

### **Organisation of Conferences**

João Lacerda Organizer and Lecturer : LisbonLymph 2014, an international meeting focusing on Aggressive B-cell Lymphomas. Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa – October 3, 2014.

João Lacerda Organizer and Lecturer: MDS Awareness Day, a 1 day international event focusing on the diagnosis and treatment of indolent and aggressive myelodysplastic syndrome. Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa – October 24, 2014.

Bone Marrow Transplantation, University of Lisbon; September 15, 2014

Lisbon Lymph, Conundrums of aggressive B cell lymphomas; Lisbon, Oct 3, 2014

A successful proposal, Horizon 2020. Fundação para a Ciência e Tecnologia, Lisbon, November 20, 2014

### **Internationalisation**

Our Unit actively collaborated in 2014 with the following investigators:

- Prof. Jerome Ritz; Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA, under the auspices of Harvard Medical School Portugal Program
- Prof. Joaquim Cabral; IST-Universidade de Lisboa, also within the framework of Harvard

#### Medical School Portugal Program

- Drs. Cristina Cunha and Dr Agostinho Carvalho, Universidade do Minho, for the studies of genetic susceptibility for invasive fungal infections
- Prof. Arne Akbar at the Division of Infection and Immunity at University College London and Prof Andrew Sewell at the Institute of Infection and Immunity at Cardiff University School of Medicine to pursue our studies on the evaluation of immune responses to cytomegalovirus in normal individuals and in patients after HSCT
- Prof. Britta Eiz-Vesper at the University of Hanover for the generation of third-party pathogen-specific T cells to administer after HSCT

#### **Msc thesis completed**

António Maria Moura Tavares Sampaio Soares 04/06/2014 Immune biomarkers in acute graft-versus-host disease Faculdade de Medicina da Universidade de Lisboa Rita Isabel Silva Azevedo

## João Barata Lab

### Major Interests / Objectives

We aim to understand the role of cell-autonomous alterations and microenvironmental cues in the development of cancer, focusing mainly on the dissection of signaling pathways essential for tumor maintenance. To do so, we make use of patient material, as a key source of insights into the disease, and integrate different biochemical, cellular and molecular biology techniques with appropriate in vitro and in vivo models - enabling an overall appreciation of the molecular, cellular and systemic nuances associated with cancer. The basic and pre-clinical research we performed 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 Unit

João Pedro Taborda Barata, PhD

### Research Team

Alice Sofia dos Santos Melão	Master	PhD Student
Ana Rita Freitas Martins de Matos Fragoso	PhD	Senior investigator
Claudia Maria Coelho de Faria	MD/PhD	Post doctoral Investigator, (started September)
Daniel Ribeiro	Master	PhD Student
Hugo Filipe Loureiro Cadilha	Undergraduate	Trainee, (started November)
Isabel da Conceicao Alves Alcobia Principe Henriques	PhD	Senior investigator, Assistant Professor
Joana Filipa Pereira de Matos	Graduate	MSc Student
Joana Tavares Ferreira da Silva	Graduate	MSc Student, (started September)
Leila Raquel Galveias	PhD	Post doctoral Investigator

Casquinha Pires Martins		
Maria Leonor Saraiva de Carvalho Morais Sarmento	PhD	Post doctoral Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Mariana Lobato de Oliveira	Graduate	MSc Student
Nádia G. Cavaleiro Sousa Correia	Master	Investigator

#### Keywords / Research Areas

Oncobiology, Leukemia, Signal transduction, Cellular and molecular biology

#### Major scientific achievements

Previously, we showed that PI3K signaling is hyperactivated in T-ALL and CLL due to CK2-mediated inhibition of PTEN. We now showed these mechanisms are even more general and extend to adult B-ALL (Gomes et al, Haematologica).

We contributed to a nomenclature proposal to avoid ambiguities in the identification of human PTEN aminoacids (Pulido et al, Science Signaling) that could result from the discovery of a PTEN long form arising from alternative translation.

We showed that, in 8% of T-ALL patients, PTEN is inactivated by microdeletions that can be subclonal and result from illegitimate RAG activity. RAGs may generate preleukemic hits and disease clonal diversification (Mendes, Sarmento et al, Blood).

We identified CHK1 as key for T-ALL cell proliferation and viability by downmodulating replication stress. Pharmacologic inhibition of CHK1 may be a novel therapeutic alternative for T-ALL treatment (Sarmento et al, Oncogene). We received the Pfizer Award for these studies.

#### Selected Publications

P.P. Zenatti, D. Ribeiro, W. Li, L. Zuurbier, M.C. Silva, M. Paganin, J. Tritapoe, J.A. Hixon, A.B. Silveira, B.A. Cardoso, L.M. Sarmento, N. Correia, M.L. Toribio, J. Kobarg, M. Horstmann, R. Pieters, S.R. Brandalise, A.A. Ferrando, J.P. Meijerink, S.K. Durum, J.A. Yunes, J.T. Barata (2011) Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia.. *Nature Genetics* **43**, 932. (Journal IF: 29.648, Citations: 67)

A. Silva, J.A. Yunes, B.A. Cardoso, L.R. Martins, P.Y. Jotta, M. Abecasis, A.E. Nowill, N.R. Leslie, A.A. Cardoso, J.T. Barata (2008) PTEN Posttranslational Inactivation and Hyperactivation of the PI3K/Akt Pathway Sustain Primary T Cell Leukemia Viability. *Journal of Clinical Investigation* **118**, 3762. (Journal IF: 13.765, Citations: 144)

J.T. Barata, A. Silva, J.G. Brandão, L.M. Nadler, A.A. Cardoso, V.A. Boussiotis (2004) Activation of PI3K is Indispensable for Interleukin 7-Mediated Viability, Proliferation, Glucose Use, and Growth of T Cell Acute Lymphoblastic Leukemia Cells. *Journal of Experimental Medicine* **200**, 659. (Journal IF: 13.912, Citations: 116)

J.T. Barata, A.A. Cardoso, L.M. Nadler, V.A. Boussiotis (2004) Interleukin-7 promotes survival and cell cycle progression of T-cell acute lymphoblastic leukemia cells by down-regulating the cyclin-dependent kinase inhibitor p27kip1. *Blood* **98**, 1524. (Journal IF: 9.775, Citations: 100)

#### Ongoing Research Projects

2012/2015 Dissecting the impact of IL7R gain-of-function mutations in T-cell leukemia. FCT. Coordinator: J.T. Barata. PTDC/SAU-ONC/122428/2010, € 165 000

2013/2015 Do miRNAs and TAL1 crosstalk? New insights into the regulation and function of a major T-cell oncogene. FCT. Coordinator: J.T. Barata. PTDC/SAU-ONC/113202/2009, € 126 000

2015 Breakthrough Idea Grant Project “Generating the tools to explore an idea: Does in vivo aberrant IL-7R constitutive signaling promote cancer development?”. IMM Director’s Fund. Started January 2015. Coordinator: J.T. Barata. €70 000

#### Publications in peer review Journals

L.M. Sarmiento, V. Póvoa, R. Nascimento, G. Real, I. Antunes, L.R. Martins, C. Moita, P.M. Alves, M. Abecasis, L.F. Moita, R.M.E. Parkhouse, J.P.P. Meijerink, J.T. Barata (2014). CHK1 overexpression in T-cell acute lymphoblastic leukemia is essential for proliferation and survival by preventing excessive replication stress. *Oncogene Aug* **18**;0. doi: 10.1038/onc.2014.248. [Epub ahead of print]. (Journal IF: 8.559)

D. Gaspar, J.M. Freire, T.R. Pacheco, J.T. Barata, M.A. Castanho (2014). Apoptotic human neutrophil peptide-1 anti-tumor activity revealed by cellular biomechanics. *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research* **1853**, **2**, 308-316. (Journal IF: 5.297)

R. Pulido, S.J. Baker, J.T. Barata, A. Carracedo, V.J. Cid, I.D. Chin-Sang, V. Davé, J. den Hertog, P. Devreotes, B.J. Eickholt, C. Eng, F.B. Furnari, M.-M. Georgescu, A. Gericke, B. Hopkins, X. Jiang, S.-R. Lee, M. Lösche, P. Malaney, X. Matias-Guiu, M. Molina, P.P. Pandolfi, R. Parsons, P. Pinton, C. Rivas, R.M. Rocha, M.S. Rodríguez, A.H. Ross, M. Serrano, V. Stambolic, B. Stiles, A. Suzuki, S.-S. Tan, N.K. Tonks, L.C. Trotman, N. Wolff, R. Woscholski, H. Wu, N.R. Leslie (2014). A unified nomenclature and amino acid numbering for human PTEN. *Science Signaling* 7 ,**332**, pe15. (Journal IF: 6.337)

R.D. Mendes\*, L.M. Sarmiento\*, K. Canté-Barrett, L. Zuurbier, J. Buijs-Gladdines, V. Póvoa, W.K. Smits, M. Abecassis, J.A. Yunes, E. Sonneveld, M.A. Horstmann, R. Pieters, J.T. Barata\*\*, and J.P.P. Meijerink\*\* (2014). PTEN micro-deletions in T-cell acute lymphoblastic leukemia are caused by illegitimate RAG-mediated recombination events. *Blood* 124 4, 567-578. \*co-first authors; \*\* co-senior authors (Journal IF: 9.775)

R. Fragoso, J.T. Barata (2014). PTEN and leukemia stem cells. *Advances in Biological Regulation* 56 (2014): 22-29. (commissioned review) (Journal IF: N/A)

R.R. Barbosa, S.L. Silva, S.P. Silva, A.C.Melo, M.C. Pereira-Santos, J.T. Barata, L. Hammarström, M. Cascalho, A.E. Sousa (2014). Reduced BAFF-R and increased TACI expression in Common Variable Immunodeficiency. *Journal of Clinical Immunology* 34 5, 573-583. (Journal IF: 2.654)

A.M. Gomes, M.V.D. Soares, P. Ribeiro, J. Caldas, V. Póvoa, L.R. Martins, A. Melão, A. Serra-Caetano, A.B. de Sousa, J. F. Lacerda, J.T. Barata (2014). Adult B-cell acute lymphoblastic leukemia cells display decreased PTEN activity and constitutive hyperactivation of PI3K/Akt pathway despite high PTEN protein levels. *Haematologica* 99,6, 1062-1068. (Journal IF: 5.868)

L.R. Martins, Y. Perera, P. Lúcio, S.E. Perea, M.G. Silva, J.T. Barata (2014). Targeting chronic lymphocytic leukemia using CIGB-300, a clinical-stage CK2-specific cell-permeable peptide inhibitor. *Oncotarget* 5, 1, 258-263. (Journal IF: 6.627)

A. Lonetti\*, I.L. Antunes\*, F. Chiarini, E. Orsini, F. Buontempo, F. Ricci, P.L. Tazzari, P. Pagliaro, F. Melchionda, A. Pession, A. Bertaina, F. Locatelli, J.A. McCubrey, J.T.Barata\*\*, A.M. Martelli\*\* (2014). Activity of the pan-class I phosphoinositide 3-kinase inhibitor NVP-BKM120 in T-cell acute lymphoblastic leukemia. *Leukemia* 28, 6, 1196–1206. \*co-first authors; \*\* co-senior authors (Journal IF: 9.379)

F. Buontempo, E. Orsini, L.R. Martins, I. Antunes, A. Lonetti, F. Chiarini, G. Tabellini, C. Evangelisti, C. Evangelisti, F. Melchionda, A. Pession, A. Bertaina, F. Locatelli, J.A. McCubrey, A. Cappellini, J.T. Barata, A.M. Martelli. (2014). Cytotoxic activity of the casein kinase 2 inhibitor

CX-4945 against T-cell acute lymphoblastic leukemia: targeting the unfolded protein response signaling. *Leukemia* 28, **3**, 543–553. (Journal IF: 9.379)

N.C. Correia, A. Gírio, I. Antunes, L.R. Martins, J.T. Barata (2014). The multiple layers of non-genetic regulation of PTEN tumor suppressor activity. *European Journal of Cancer* 50, **1**, 216-225. (review) (Journal IF: 4.819)

L.R. Martins, P. Lúcio, A. Melão, I. Antunes, B.A. Cardoso, R. Stansfield, M.T. Bertilaccio, P. Ghia, D. Drygin, M.G. Silva, J.T. Barata (2014). Activity of the clinical-stage CK2-specific inhibitor CX-4945 against chronic lymphocytic leukemia. *Leukemia* 28 **1**, 179–182. (Journal IF: 9.379)

#### **Invited lectures and seminars**

J.T. Barata. T-cell development gone wrong: cell autonomous and microenvironmental signals promoting leukemia, SPI workshop HEMATOPOIESIS: FROM BENCH TO BEDSIDE, University of Minho, Braga, Portugal, 11 April 2014.

J.T. Barata. Na fronteira entre a Imunologia e a Oncologia: citocinas e leukemia [At the frontier between Immunology and Oncology: cytokines and leukemia, V MedUBI Congress, University of Beira Interior, Covilhã, Portugal, 9-10 January 2014.

R. Fragoso. Human T-ALL leukemia initiating cells: molecular, phenotypic and functional characterization. UIPM, Portuguese Institute of Oncology, Lisbon, Portugal, 26 February 2014.

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

B.A. Cardoso, H. Belo, A.I. Oliveira, O. Pereira., J.T. Barata, A. Almeida (2014). Bone Marrow Stroma Protects BCR-ABL-Negative Myeloproliferative Neoplasms from Ruxolitinib- and Vorinostat-Induced Apoptosis. The American Society of Hematology 56th Annual Meeting, San Francisco, CA, USA, 6-9 December. (Poster presentation)

D. Ribeiro, I. Lopes, M. Abreu, J.T. Barata (2014). Flexible IL-7-mediated regulation of autophagy promotes T-cell acute lymphoblastic leukemia cell viability. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November. (Oral communication)

A. Melão\*, J. Matos\*, J.T. Barata (2014). Sphingosine Kinase is Required for IL-7-Mediated Signaling in T-cell Acute Lymphoblastic Leukemia. 1st ASPIC International Congress, Lisboa,



Portugal, 25-26 November. \*co-first authors (Poster presentation)

M.T. Fernandes, M.N. Ghezso, V. Póvoa, A.R. Ribeiro, E. Dejardin, N.L. Alves, J. Ghysdael, J.T. Barata, N.R. dos Santos. (2014). LT $\beta$ R in microenvironmental cells modulates surface lymphotoxin expression on leukemic T cells and promotes leukemogenesis. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November. (Poster presentation)

M.L. Oliveira, A.M. Gomes, L.R. Martins, J. Duarte, J.T. Barata (2014). Prognostic significance of PI3K/Akt/mTOR pathway using phosphoflow in pediatric acute lymphoblastic leukemia—preliminary results. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November. (Poster presentation)

A. Cardoso, H. Belo, J.T. Barata, A.M. Almeida (2014). Bone Marrow protects BCR-ABL-Negative Myeloproliferative Neoplasms from Ruxolitinib- and Vorinostat-Induced Apoptosis. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November. (Poster presentation)

D. Gaspar, J.M. Freire, T.R. Pacheco, J.T. Barata, M.A.R.B. Castanho (2014). Evaluation of tumor cells' biomechanical properties for assessing the chemotherapy efficacy of anticancer peptides. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November. (Poster presentation)

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

B.A. Cardoso, H. Belo, J.T. Barata, A.M. Almeida (2014). A medula óssea protege células de neoplasias crónicas BCR-ABL-negativas dos efeitos citotóxicos induzidos por ruxolitinib e vorinostat [The bone marrow protects cells from chronic BCR-ABL-negative myeloproliferative neoplasias from the cytotoxic effects of Ruxolitinib and Vorinostat]. Annual Meeting of the Portuguese Society of Hematology, Évora, Portugal, 20-22 November. (Oral presentation)

J. Matos, A. Melão, J.T. Barata (2014). Sphingosine Kinase Modulates IL-7-Mediated Signaling in T-cell Acute Lymphoblastic Leukemia. Symposium "Sphingolipids in Health and Disease", IBMC, Porto, Portugal, 18 September. (Oral presentation)

J. Matos, A. Melão, J.T. Barata (2014). Sphingosine Kinase-1 Modulates IL-7-Mediated Signaling in T-cell Acute Lymphoblastic Leukemia. SPI workshop HEMATOPOIESIS: FROM BENCH TO BEDSIDE, University of Minho, Braga, Portugal, 11 April. (Poster presentation)

### **Organisation of Conferences**

J.T. Barata was member of the Scientific Committee and co-chair of Symposium IV “Mechanisms and implications of tumor heterogeneity”, 1st ASPIC International Congress, Lisboa, Portugal, 25-26 November 2014.

R. Fragoso was member of the Organizing committee and co-chair of the 1st joint IGC/CEDOC/IMM Post-doctoral Retreat, Sintra, Portugal, 29-31 October 2014.

R. Fragoso was co-chair of the VIII IMM/CAML PhD meeting, Lisbon, Portugal, 28 March 2014.

C. Faria was member of the Scientific Committee and co-chair of Symposium 1 “Research in Neurooncology”, VII Congresso Nacional da Associação Portuguesa de Neuro-oncologia, Lisboa, Portugal, 21-22 November 2014.

### **Internationalisation**

All our projects involve to some extent collaborative work with international research groups in Europe, US and Brazil. Our publication track record illustrates this extensively and our FCT funded projects systematically include foreign researchers as consultants or participants.

Current international collaborators include: J. Andres Yunes (Centro Infantil Boldrini, Campinas, SP, Brazil), Paul Coffey (Utrecht University Medical Center, The Netherlands), Jules Meijerink (Erasmus MC Rotterdam, The Netherlands), Ben Seddon (NIMR, London, UK), Adolfo Ferrando (Columbia University, New York, NY, USA), Scott Durum (NCI, Frederick, MD, USA), David Langenau (Harvard Stem Cell Institute, Cambridge, MA, USA), Silvio Perea (CIGB, Havana, Cuba) and Alberto Martelli (University of Bologna, Italy).

### **Prizes, honours and awards**

2014 Pfizer Award on Clinical Research from Sociedade das Ciências Médicas de Lisboa to L.M. Sarmento, J.T. Barata, and collaborators.

### **Advanced teaching**

J.T. Barata lectured the topic “Cell cycle & checkpoints – I (G1/S)”, Advanced Course on Molecular Oncology: Cancer Biology and Emerging Therapies. Instituto Português de Oncologia de Coimbra Francisco Gentil, Coimbra, Portugal. 24 October.

J.T. Barata was coordinator (together with Sérgio Dias and Gonçalo Bernardes) and faculty of the “Tissues and Tumors” week (27-31 January 2014), LisbonBioMed International FCT PhD Program, IMM, Faculty of Medicine of Lisbon University, Lisbon, Portugal.

### **Science and society**

J.T. Barata was interviewed on public broadcast TV, radio and press concerning the work conducted in his lab, and particularly because of the studies published in Oncogene and the Pfizer Award that his team received.

Several members of the lab were involved in IMM laboratories’ showcase for medical students during the FMUL students’ day.

The lab joined the Brain Tumor Team (BTT) on 14 December 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.

### **Msc thesis completed**

Joana Matos 16/09/2014 The role of sphingosine kinase in IL-7-mediated signaling and T-cell acute lymphoblastic leukemia University of Coimbra João T. Barata

## Joaquim Ferreira Lab

### Major Interests / Objectives

The main mission of the Joaquim Ferreira Lab is to contribute to the development of effective and safe therapeutic interventions through the establishment of optimized methodologies for the design, conduction, analysis and report of clinical trials.

The main clinical pharmacology domains of interest are clinical trials methodology, outcomes, systematic reviews, safety, pharmaco MRI and drug utilization. The emphasis is mainly on novel, early phase

proof-of-principle clinical studies and new methodological and trial designs but the scope extends throughout the clinical development spectrum. We also envision collaborations with the pharmaceutical industry, facilitating the conduction of clinical trials to a shared role in the early stages of drug and planning of clinical development.

### Head of Unit

Joaquim Ferreira, MD/PhD, Clinical Specialist, Associate Professor, Faculdade Medicina da Universidade de Lisboa

### Research Team

Adriana Filipa da Silva Ferreira	Graduate	MSc Student, (started September)
Ana Cláudia Marques Salgueiro	Master	Trainee
Ana Isabel Santos Augusto	Graduate	Trainee, (started October)
Ana Margarida Faisca do Carmo Pires de Noronha	Graduate	Administrative
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 Rita Simões Cardoso	Graduate	MSc Student, Campus Neurologico Senior (CNS) , (left November)

Ana Teresa Martins Sousa Santos	Master	Lab Manager
Anabela Ferreira Valadas	Graduate	Investigator, Hospital São Bernardo, Setúbal , MD
André Filipe da Silva Lopes Cardoso	Graduate	Trainee
Andreia Assunção Sousa da Rocha	Graduate	MSc Student, (started September)
Carla Filipa Ferreira Rodrigues	Graduate	Trainee, (started September)
Catarina Afonso Godinho	PhD	Investigator, Campus Neurologico Senior (CNS) , Instituto Superior de Ciências da Saude Egas Moniz , 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 , CHDI
Daisy Andreína Vieira De Abreu	Master	Investigator
Daniel Gomes Caldeira	Graduate	PhD Student, Hospital Garcia de Orta , MD , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Ema Roque	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa
Helena Isabel Vicente dos Santos	Graduate	Technician, (started November)
Isabel Boaventura	Graduate	Investigator, Celgene , MD , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
João Costa	MD/PhD	Investigator, Hospital da Luz , MD , Faculdade Medicina da Universidade de Lisboa , Assistant Professor
João Franco	João Franco	Investigator

Josefa Domingos	Master	PhD Student, Campus Neurologico Senior (CNS)
Leonor Correia Guedes	Master	PhD Student, CHLN , MD
Márcio Correia Barra	Master	Trainee
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 Dulce dos Santos Neutel	Graduate	Investigator, Hospital do Espírito Santo, Évora , MD
Maria Finisterra	Graduate	Administrative
Mário Miguel Coelho da Silva Rosa	Graduate	PhD Student, CHLN , MD , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Miguel Coelho	Graduate	PhD Student, CHLN , MD
Nádia Espada	Master	Investigator, Faculdade Medicina da Universidade de Lisboa
Nilza Karina Cabral Gonçalves	Master	Investigator
Olga Sofia de Oliveira Caetano	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa , (started November)
Raquel José Ladeira Lobo	Master	Investigator, (started August)
Ricardo Miguel Ribeiro Marques Cunha Fernandes	Graduate	PhD Student, CHLN , MD , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Sofia Cristina Pereira Coutinho Reimao	Master	PhD Student, CHLN , MD , Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Tiago Mestre	Master	PhD Student, University of Ottawa , Assistant Professor , University of Ottawa ,

		MD
Tiago Rodrigues Teodoro	Master	PhD Student, CHLN , MD
Tiago Soares	Graduate	MSc Student
Vanda Filipa Viseu Cândido Freitas Castro	Master	Investigator, Campus Neurologico Senior (CNS) , Clinical Specialist

#### Keywords / Research Areas

Parkinson's disease, Huntington Disease, Movement Disorders, Neuropharmacology, Clinical trials, Systematic reviews

#### Major scientific achievements

The Joaquim Ferreira Lab was formally created on the 1st of July 2013 based on the research team from the Neuropharmacology Unit of the Neurological Clinical Research Unit and the members of the Laboratory of Clinical Pharmacology (Faculty of Medicine). During the first year the research team was enlarged mainly with new MSc and PhD students.

The Drug Evaluation and Systematic Reviews Sub-Unit (Movement Disorders Cochrane Collaboration Review Group) was consolidated and The Safety and Drug Utilization Research Unit (Pharmacovigilance Regional Unit) gained sustainability with a revised service contract with INFARMED. Additionally, a Biostatistics and Methodological Sub-Unit was developed. Funding for the next 3 years was guaranteed with the success in three international research grants.

More recently, a Pharmaco MRI sub-unit was created. With the application of neuroimaging techniques we believe it will be possible to detect micro-structural, functional and biochemical in central nerv

#### Selected Publications

Caldeira D, Barra M, Santos AT, de Abreu D, Pinto FJ, Ferreira JJ, Costa J, (2014), Risk of drug-induced liver injury with the new oral anticoagulants: systematic review and meta-analysis. *Heart*, **100**(7):550-6. (Journal IF: 13.857; Citations: 2)

Fernandes R, Hartling L, (2014) Glucocorticoids for Acute Viral Bronchiolitis in Infants and Young children. *JAMA* **311**(1), 87-88. (Journal IF: 29.978, Citations: 0)

Munafò M, Noble S, Bowne WJ, Brunner D, Button K, Ferreira J, Holmans P, Langbehn D, Lewis

G, Lindquist M, Tilling K, Wagenmakers EJ, Blumesntein R, (2014) Scientific rigor and the art of motorcycle maintenance. *Nature Biotechnology* **32**(9), 871-873. (Journal IF: 39.080, Citations: 0)

Hill DLG, Scharwz AJ, Isaac M, Pani L, Vamvakas S, Hemmings R, Carrillo MC, Yu P, Sun J, Beckett L, Boccardi M, Brewer J, Brumfield M, Cantillon M, Cole PE, Fox N, Frisoni GB, Jack C, Kelleher T, Luo F, Novak G, MAguite P, Meibach R, Patterson P, Bain L, Sampaio C, Raunig D, Soares H, Suhy J, Wang HL, Wolz R, Stephenson D, (2014) Coalition against major diseases/European medicines agency biomarker qualification of hippocampal volume for enrichment of clinical trials in predementia stages of Alzheimer' disease. *Alzheimer's and Dementia*, **10**, 421-429. (Journal IF: 14.472, Citations: 1)

Reimão S, Pita Lobo P, Neutel D, Correia Guedes L, Coelho M, Rosa MM, Ferreira J, Abreu D, Gonçalves N, Morgado C, Nunes RG, Campos J, Ferreira JJ, (2014) Substantia nigra neuromelanin magnetic resonance imaging in de novo Parkinson's disease patients. *European Journal of Neurology* doi: 10.1111/ene.12613. (Journal IF: 3.852, Citations: 0) (Epub ahead of print).

#### **Ongoing Research Projects**

2011/2014 Title: SensePark: Supporting and empowering parkinson patients in their home environment using a Novel Sensory information system that monitors daily-life-relevant parameters of Parkinson disease -. Coordinator: Joaquim Ferreira. Agency: Comissão Europeia. Reference: Sense Park. Amount: 209,720€.

2014/2017 Title: Avaliação Abrangente e Não Enviesada de Fatores de Risco Genéticos e Ambientais para a Doença de Parkinson. Coordinator: Joaquim Ferreira. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: JPND-RF/0001/2012. Amount: 130,000€.

2014/2017 Title: Cuidados para Parkinsonismo em Estádio Avançado. Coordinator: Joaquim Ferreira. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: JPND-HC/0002/2012. Amount: 110,000€.

2013/2016 Title: Research Design and Data Analysis in Support of Clinical Trial Design and Clinical Research Projects. Coordinator: Joaquim Ferreira. Agency: CHDI Foundation, Inc.. Reference: CHDI. Amount: 525,762€.

2014/2016 Title: Ablynx N.V.. Coordinator: Ricardo Miguel Ribeiro Marques Cunha Fernandes. Agency: Ablynx N.V.. Reference: Ablynx. Amount: 3,000€.

2014/2015 Title: 1St IMM Teaching Course on DBS Movement Disorders. Coordinator: Joaquim Ferreira. Agency: Medtronic Portugal, Lda. Reference: 1St IMM Teaching Course on DBS Movement Disorders. Amount: 8,000€.



### Other Projects

2013/2014 Imaging of Basal Ganglia from Magnetic Induction Tomography. Coordinator: Joaquim Ferreira. Coordinator Institution: Instituto Superior Técnico. Coordinator PI: Raul Carneiro Martins.

2013/2014 Epidemiological study to assess the prevalence of Parkinson's disease in Portugal. . Coordinator: Joaquim Ferreira. Coordinator Institution: Instituto Superior Técnico. Coordinator PI: Raul Carneiro Martins.

2013/2014 Glucocerebrosidase in Parkinson's disease: from risk factor to biomarker. Coordinator: Joaquim Ferreira. Coordinator Institution: Instituto de Medicina Molecular. Coordinator PI: Gabriel Miltenberger-Miltenyi.

### Publications in peer review Journals

Reimão S, Pita Lobo P, Neutel D, Correia Guedes L, Coelho M, Rosa MM, Ferreira J, Abreu D, Gonçalves N, Morgado C, Nunes RG, Campos J, Ferreira JJ, (2014) Substantia nigra neuromelanin magnetic resonance imaging in de novo Parkinson's disease patients. *European Journal of Neurology*, doi: 10.1111/ene.12613. (Epub ahead of print)

Coelho M, Marti MJ, Sampaio C, Ferreira JJ, Valldeoriola F, Rosa MM, Tolosa E. (2015), Dementia and severity of parkinsonism determines the handicap of patients in late-stage Parkinson's disease: the Barcelona-Lisbon cohort. *European Journal of Neurology*, **22** (2):305-12. (Journal IF: 3.852, Citations: 0)

Caldeira D, Lopes R, Cruz I, Almeida AR, Gomes C, Stuart B, Almeida S, Brandão L, Pereira H, (2014), The burnout stage of an epical hypertrophic cardiomyopathy. *International journal of cardiology*, **177**(3):179-80. (Journal IF:6.175; Citations:0)

Caldeira D, Costa J, Ferreira JJ, Pinto FJ, (2014), Thromboembolic risk in the initiation, switch and interruption/re-initiation of oral anticoagulants: do newcomers improve outcomes? Insights from a meta-analysis of RCTs. *International Journal of Cardiology*. **177**, 117–119. (Journal IF: 2.298; Citations: 1)

Caldeira D, Costa J, Ferreira JJ, Pinto FJ, (2014), Thromboembolic risk in the initiation, switch and interruption/re-initiation of oral anticoagulants: do newcomers improve outcomes?

Insights from a meta-analysis of RCTs. *International Journal of Cardiology*. **177**, 117–119. (Journal IF: 2.298)

Caldeira D, Vaz-Carneiro A, Costa J, (2014), Cochrane Corner: What is the clinical impact of oxygen therapy for acute myocardial infarction? Evaluation of a Cochrane systematic review. *Revista Portuguesa de Cardiologia* . (Journal IF: 0.525, Citations: 0)

Fernandes RM, Oleazczuk, Woods CR, Rowe BH, Cates CJ, Hartling L, (2014) The Cochrane Library and safety of systemic corticosteroids for acute respiratory conditions in children: an overview of reviews. *Evidence-Based Child Health* **9**,(3):733-747 (Journal IF: NA)

Mestre TA, Teodoro T, Reginold W, Graf J, Kasten M, Sale J, Zurowsky M, Miasaki J, Ferreira JJ, Marras C, (2014), Reluctance to start medication for Parkinson's disease: A mutual misunderstanding by patients and physicians. *Parkinsonism and Related Disorders*, **20**,(6): 608-612. (Journal IF: 3.274; Citations: 0)

Caldeira D, Costa J, Fernandes RM, Pinto FJ, Ferreira JJ, (2014), Performance of the HAS-BLED high bleeding-risk category, compared to ATRIA and HEMORR2HAGES in patients with atrial fibrillation: a systematic review and meta-analysis. *Journal of Interventional Cardiac Electrophysiology*, **40**,(3):277-84. (Journal IF: 1.552; Citations: 0)

Taylor C, Cowan P, Desjardins P, Dimitrova R, Dionne R, Farrar JT, Hewitt DJ, Iyengar S, Jat GW, Kalso E, Kerns RD, LEff R, Leong M, Petersen KL, Ravina MB, Rauschkolb C, Rice ASC, Rowbotham MC, Sampaio C, Sindrup SH, Stauffer JW, Steigerwald I, Stewart J, Tobias J, Treede RD, Wallace3 M, White RE, (2014), Research designs for proof-of-concept chronic pain clinical trials: IMMPACT recommendations. *Pain*, **155**,(9): 1686-1695 (Journal IF: 5.836; Citations: 3)

Hill DLG, Scharwz AJ, Isaac M, Pani L, Vamvakas S, Hemmings R, Carrillo MC, Yu P, Sun J, Beckett L, Boccardi M, Brewer J, Brumfield M, Cantillon M, Cole PE, Fox N, Frisoni GB, Jack C, Kelleher T, Luo F, Novak G, MAguite P, Meibach R, Patterson P, Bain L, Sampaio C, Raunig D, Soares H, Suhy J, Wang HL, Wolz R, Stephenson D, (2014), Coalition against major diseases/European medicines agency biomarker qualification of hippocampal volume for enrichment of clinical trials in predementia stages of Alzheimer' disease. *Alzheimer's and Dementia*, **10**, 4: 421-429. (Journal IF: 14.472; Citations: 1)

Dodel R, Jonsson B, Reese JP, Winter Y, Martinez-Martin P, Holloway R, Sampaio C, Ruzicka E, Hawthorne G, Oertel W, Poewe W, Stebbins G, Rascol O, Goetz CG, Schrag A, (2014), Measurement of costs and scales for outcome evaluation in health economic studies of Parkinson's disease. *Movement Disorders*, **29**,(2): 169-176. (Journal IF: 5.634; Citations: 2)

Caldeira D, Costa J, Barra M, Pinto JF, Ferreira JJ, (2015), How safe is acetaminophen use in patients treated with vitamin K antagonists? A systematic review and meta-analysis, *Thrombosis Research*, **135**, (1):58-61 (Journal IF: not indexed;; Citations: 0)

Caldeira D, Vaz-Carneiro A, Costa J, (2014), The impact of dosing frequency on medication adherence in chronic cardiovascular disease: Systematic review and meta-analysis.[Analysis of the Cochrane review: Anticoagulation versus placebo for heart failure in sinus rhythm. Cochrane Database Syst Rev. 2014;3:CD003336] *Acta Med Port.* **27**(3):284-6. (Journal IF: 0.281; Citations: 0)

Stout JC, Queller S, Baker KN, Cowlshaw S, Sampaio C, Fitzner-Attas C, Borowsky B, (2014), HD-CAB: a cognitive assessment battery for clinical trials in Huntington's disease 1,2,3. *Movement Disorders*, **29**, 6: 1281-1288. (Journal IF: 5.634; Citations: 1)

Sampaio C, Borowsky B, Reilmann R, (2014) Clinical trials in Huntington's Disease: interventions in early clinical development and newer methodological approaches. *Movement Disorders*, **29**, (11): 1419-1428 (Journal IF: 5.634; Citations: 1)

Azevedo P, Costa J, Vaz-Carneiro A, (2014) [Analysis of the Cochrane Review: Use of Systemic Corticosteroids for Acute Exacerbations of Chronic Obstructive Pulmonary Disease. Cochrane Database Syst Rev. 2014, 9:CD001288]. *Acta Med Port.* **27**(5):537-40. *Acta Médica Portuguesa*, **27**, (3):284-6. (Journal IF: 0.281; Citations: 0)

Caldeira D, Costa J, Ferreira JJ, Pinto FJ, (2014), Net clinical benefit outcome should be standardized in trials evaluating antithrombotic drugs: the example of NOACs in atrial fibrillation. *International Journal of Cardiology*, **174**, (2):405-6. (Journal IF: 6.175; Citations: 0)

Caldeira D, David C, Santos AT, Costa J, Pinto FJ, Ferreira JJ, (2014), Efficacy and safety of low molecular weight heparin in patients with mechanical heart valves: systematic review and meta-analysis. *Journal of Thrombosis Haemost*, **12**, (5):650-9.(Journal IF: 5.550; Citations: 0)

Caldeira D, Barra M, Santos AT, de Abreu D, Pinto FJ, Ferreira JJ, Costa J, (2014), Risk of drug-induced liver injury with the new oral anticoagulants: systematic review and meta-analysis. *Heart*, **100**(7):550-6. (Journal IF: 13.857; Citations: 2)

Cardoso AT, Nanji L, Costa J, Vaz-Carneiro A, (2014) [Analysis of the Cochrane Review: Vitamin D supplementation for prevention of cancer in adults. Cochrane Database Syst Rev. 2014, 6:CD007469]. *Acta Médica Portuguesa*, **27**(4):411-3. (Journal IF: 0.281; Citations: 0)

Caldeira D, Barra M, David C, Costa J, Ferreira JJ, Pinto FJ, (2014), The prevalence of oral anticoagulation in patients with atrial fibrillation in Portugal: Systematic review and meta-analysis of observational studies. *Revista Portuguesa de Cardiologia*, 33, (9):555-560. (Journal IF: 0.525; Citations: 0)

Caldeira D, Costa J, Pinto FJ, Ferreira JJ, (2014), The risk of infection with new oral anticoagulants: a meta-analysis. *International journal of Cardiology*, 72, (1):267-8. (Journal IF: 6.175; Citations: 0)

Sidiropoulos C, Masani K, Mestre T, Milosevic M, Poon YY, Fallis M, Shah BB, Kalia SK, Popovic MR, Lozano AM, Moro E, (2014) Spinal cord stimulation for gait impairment in spinocerebellar ataxia 7. *Journal of Neurology*, 261(3):570-574. (Journal IF: 3.578; Citations: 0)

Lines M, Jobling R, Brady L, Marshall, CR, Stephen W, Rodriguez AR, Lee L, Lang A, Mestre T, Wanders R, Ferdinandusse S, Tarnopolsky M, Canadian Pediatric Genetic Disorders Sequencing Consortium (FORGE Canada), (2014), Peroxisomal D-bifunctional protein deficiency: Three adults diagnosed by whole-exome sequencing. *Neurology*, 82 (11):63-8. (Journal IF: 8.249; Citations: 0)

Hartling L, Vandermeer B, Fernandes RM, (2014), Systematic reviews, overviews of reviews and comparative effectiveness reviews: a discussion of approaches to knowledge synthesis. *Evidence-Based Child Health: a Cochrane Review Journal*, 9:486-494. (Journal IF: not indexed, Citations:)

Sousa R, Costa J, Vaz Carneiro A, Fernandes RM, (2014,) Cochrane Corner: Terapêutica combinada e alternada com paracetamol e ibuprofeno para crianças com febre. *Acta Pediátrica Portuguesa*, 2014; 45, 64-66. (Journal IF: NA)

Magalhães M, Costa J, Vaz Carneiro A, Fernandes RM, (2014) Cochrane Corner: overview de revisões sobre o tratamento da laringotraqueíte (CROUP). *Acta Pediátrica Portuguesa*, 2014; 45:168-171. (Journal IF: NA)

Conceição I, Costa, J, Castro J, de Carvalho M, (2014), Invasive fibroblasts: Fundamental difference between sporadic inclusion body myositis and polymyositis, *Muscle & Nerve*, 49(2):181-186. (Journal IF: 2.314; Citations: 2)

Luis L, Zhu H, Costa J, Valls-Solé J, Brandt T, Zhou W, Schneider E, (2014), Reply to the commentary on Luis et Al. "Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials". *Otology & Neurotology*, 35(2):379-83. (Journal impact factor: 1.598, Citations: 0)

Fernandes R, Hartling L, (2014), Glucocorticoids for Acute Viral Bronchiolitis in Infants and Young children, *Jama*, **311**(1): 87-88. (Journal IF: 29.978, Citations: 0)

Gil J, Costa J, Vaz Carneiro A, Fernandes RM, (2014) Imuno-estimulantes na prevenção de infeções respiratórias em crianças. *Acta Pediátrica Portuguesa*, 2014; **45**, 253-255. (Journal IF:NA)

Hartling L, Hamm MP, Fernandes RM, Dryden DM, Vandermeer B, (2014) Quantifying Bias in Randomized Controlled Trials in Child Health: A Meta-Epidemiological Study. *PLoS ONE*, 9: **2**. (Journal IF: 3.534, Citations: 1)

Albuquerque L, Coelho M, Martins M, Guedes LC, Rosa MM, Ferreira JJ, Cattoni MB, Carvalho H, Ferreira AG, Martins IP, (2014), STN-DBS does not change emotion recognition in advanced Parkinson's disease, *Parkinsonism & Related Disorders*, **20** (2): 166-169. (Journal IF: 3.274, Citations: 0)

Conceição I, Costa J, Castro J, de Carvalho M, (2014), Neurophysiological techniques to detect early small-fiber dysfunction in transthyretin amyloid polyneuropathy. *Muscle & Nerve*, **49**(2):181-6. (Journal IF: 2.314, Citations: 3)

Vaz Carneiro A, Costa J. [Analysis of the Cochrane review: Multimedia educational interventions for consumers about prescribed and over-the-counter medications. Cochrane Database of Systematic Reviews 2013;4:CD008416]. *Acta Médica Portuguesa*: **4-5**. (Journal IF: 0.281, Citations: 0)

Vaz-Carneiro A, Luz R, Borges M, Costa J, (2014), [Primary and secondary outcomes in oncology clinical trials: definitions and uses]. *Acta Médica Portuguesa*, **27**(4):498-502. (Journal IF: 0.281; Citations: 0)

Munafò M, Noble S, Bowne WJ, Brunner D, Button K, Ferreira J, Holmans P, Langbehn D, Lewis G, Lindquist M, Tilling K, Wagenmakers EJ, Blumesstein R, (2014), Scientific rigor and the art of motorcycle maintenance. *Nature Biotechnology*, **32**(9): 871-873. (Journal IF: 39.080; Citations: 0)

Caldeira D, Loureiro MJ, Costa J, Pinto FJ, Ferreira JJ, (2014), Oral anticoagulation for pulmonary arterial hypertension: systematic review and meta-analysis. *Canadian Journal of*

Cardiology, 30(8):879-87. (Journal IF: 3.940; Citations: 1)

#### Invited lectures and seminars

Fernandes R, Investigação em Pediatria. Curso Investigação Clínica: do desenho do projecto à publicação. 15º Congresso Nacional de Pediatria, Sociedade Portuguesa de Pediatria. Albufeira, 16-18 October, 2014.

Borges M. Custos do tratamento do carcinoma pulmonar de não pequenas células em Portugal. 6º Congresso Português do Cancro do Pulmão. Grupo de Estudos do Cancro do Pulmão. Lisboa, Out 2014.

Ferreira JJ, Evolution of PD motor and non motor features. 7th Annual MDS-ES Summer School for Young Neurologists, Barcelona, Spain, July 18-20, 2014.

Fernandes R, Corticoides inalados em contínuo ou em S.O.S. I Curso Pós-Graduado de Actualização Diferenciação em Pediatria - Inovação e Tecnologia - Módulo XVII –Pneumologia + Alergologia, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 20 June 2014.

Fernandes R, Corticoides inalados em contínuo ou em S.O.S. 2º Congresso de Alergologia Pediátrica, Sociedade Portuguesa de Alergologia Pediátrica, Braga, 13 June, 2014.

Ferreira JJ, An update on Huntington's disease: from pathophysiology to new treatments, 18th International Congress of Parkinson's Disease and Movement Disorders, Stockholm, Sweden, June 8-12, 2014.

Ferreira JJ, What to expect from recent methodological issues, 18th International Congress of Parkinson's Disease and Movement Disorders, Stockholm, Sweden, June 8-12, 2014.

Ferreira JJ, Key learnings from recent movement disorders clinical trials, 18th International Congress of Parkinson's Disease and Movement Disorders, Stockholm, Sweden, June 8-12, 2014.

Ferreira JJ, Course in Clinical Research, 5Th module: Clinical trials, May, 23 th-24th, Faculdade de Medicina de Lisboa, Lisboa.

Ferreira JJ, Update on symptomatic and disease modifying treatments in HD, International Expert meeting on Agitation and Hyperkinetic Movement Disorders, Valencia, May 15-18, 2014

Fernandes R, Oxigenoterapia de alto fluxo na Urgência Pediátrica. 2.ª Reunião da EuSPP - Sociedade de Urgência e Emergência Pediátrica, Coimbra, 17 May, 2014.

Costa J. Exames Complementares de Diagnóstico - Papel da Neurofisiologia. Sociedade Portuguesa Doenças do Movimento. Vimeiro, Mar 2014.

Ferreira JJ, Prática médica e investigação em neurociências, Dois dedos de conversa, ATV, Torres Vedras, 22 de Março, 2014.

Ferreira JJ, Systematic Review and Meta-Analysis: Clinical Data Management and Analysis, University of Aveiro, Aveiro, March 20 th – 24 th, 2014.

Costa J. Portuguese Branch of the Iberoamerican Cochrane Network. Congresso de Neurologia 2014. Lisboa, Nov 2014.

Ferreira JJ, Video Diagnosis of Movement Disorders, 5Th AIMS Meeting Organizing Committee, Faculty of Medicine, University of Lisbon, March 8-10, 2014.

Fernandes R, Systematic reviews: The Cochrane Collaboration. Training Programme in Pharmaceutical Medicine, Module: Systematic Review and Meta-Analysis: Clinical Data Management and Analysis (M07), Health Sciences Department, University of Aveiro, Aveiro, 21 March, 2014.

Fernandes R, Gomes C, Bandeira T, Bronquiolite revisitada: estudos ABBA, SABIO, TABU e PERN. Sessão Núcleo de Investigação, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 20 March, 2014.

Fernandes R, Diagnostico laboratorial em alergia alimentar: fiabilidade dos testes. 1ª Reunião Temática da Sociedade Portuguesa de Alergologia Pediátrica, Porto, 22 February, 2014.

Fernandes R, Alergia medicamentosa: testes de provocação. XX Jornadas de Pediatria, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 13 February, 2014.

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

M. Borges, M. Gouveia, J. Alarcão, R. Sousa, E. Teixeira, F. Barata, E. Laranjeira, F. Lopes, B. Parente, L. Pinheiro, A. Vaz-Carneiro, J. Costa. Cost and Burden of Non-Small Cell Lung Cancer's in Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

M. Gouveia, M. Borges, M. Augusto, D. Caldeira, J. Alarcão, L. Pinheiro, R. Sousa, F. Fareleira, R. Ascensão, J. Costa, P. Laires, M. Fiuza, N.C. Dias, S. Martins, A. Belo, A. Vaz-Carneiro. Cost and Burden Of Hypercholesterolemia In Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

M Inês, F. Rodrigues, J. Saraiva, J. Costa. Pre-Symptomatic Genetic Testing In Familial Amyloid

Polyneuropathy: The Reproductive Options. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

Gouveia M, Borges M, Augusto M, Caldeira D, Alarcão J, Pinheiro L, Sousa R, Fareleira F, Ascensão R, Costa J, Laires P, Fiuza M, Dias N, Martins S, Belo A, Vaz-Carneiro A. Cost and Burden of Hypercholesterolemia In Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands, Nov 2014. (Poster presentation)

Borges M, Gouveia M, Alarcão J, Sousa R, Teixeira E, Barata F, Laranjeira E, Lopes F, Parente B, Pinheiro L, Vaz-Carneiro A, Costa J. Cost and Burden of Non-Small Cell Lung Cancer's in Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands, Nov 2014. (Poster presentation)

Augusto M, Gouveia M, Borges M, Campioni M. Cost-Effectiveness of Romiplostim for The Treatment of Chronic Immune Trombocytopenia in Portugal. . ISPOR 17th Annual European Congress. Amsterdam, The Netherlands, Nov 2014. (Poster presentation)

Foisy M, Thomson D, Dryden DM, Fernandes RM, Hartling L. Conducting overviews of reviews: lessons learned since 2006. 22nd Cochrane Colloquium. Cochrane Collaboration. Hyderabad, 21-26 September 2014. Oral session 19. (Oral presentation)

Foisy M, Dryden DM, Fernandes RM, Hartling L. Multiple systematic reviews published on the same topic area: an analysis of systematic reviews that overlap in content. 22nd Cochrane Colloquium. Cochrane Collaboration. Hyderabad, 21-26 September 2014. Oral session 19. (Oral presentation)

Hartling L, Wingert A, Crick K, Fernandes R, Thomson D, Williams K. An evaluation of harvest plots to display results of meta-analyses in overviews of reviews. 22nd Cochrane Colloquium. Cochrane Collaboration. Hyderabad, 21-26 September 2014. P41 (Poster presentation)

Foisy M, Fernandes RM, Dryden DM, Hartling L. Grading the quality of evidence in existing systematic reviews: challenges and considerations. 22nd Cochrane Colloquium. Cochrane Collaboration. Hyderabad, 21-26 September 2014. P99 (Poster presentation)

Constant C, Magalhães M, Andrade MG, Malveiro D, Azevedo I, Sousa E, Salgado R, Bandeira T, Fernandes RM. Perspectives of pediatricians and general practitioners on diagnosis and treatment of bronchiolitis. ERS 2014 Congress, Munich, 6-10 September 2014. P1237. (Poster presentation)

Fernandes RM, Abreu D, Andrade MG, Constant C, Malveiro D, Magalhães M, Azevedo I, Sousa E, Salgado R, Bandeira T. Perspectives of pediatricians and general practitioners on definition and important outcomes in bronchiolitis. ERS 2014 Congress, Munich, 6-10 September 2014. P1257 (Poster presentation)



Fernandes RM, Plint AC, Terwee CB, Klassen TP, Offringa M, van der Lee JH. Measurement properties of RDAI and RACS and their suitability as outcome measures in bronchiolitis trials. ERS 2014 Congress. European Respiratory Society. Munich, 6-10 September 2014. P1256 (Poster presentation)

Luis L, Costa J, Muñoz E, Schneider E, Valls-Solé J. Vestibular ocular reflex dynamics during passive head-impulses: slow phase and quick-eye movements in Huntington's disease. European Huntington's Disease Network Meeting. Barcelona, Spain: Sep 2014. (Poster presentation)

Borges M, Gouveia M, Alarcão J, Sousa R, Barata F, Laranjeira E, Lopes F, Parente B, Pinheiro L, Teixeira E, Vaz-Carneiro A, Costa J Non-small cell lung cancer's burden of disease in Portugal. 39 th European Society for Medical Oncology Congress. Madrid, Sept 2014. (Poster presentation)

Luis L, Costa J, Muñoz E, de Carvalho M, Lehnen N, Schneider E. Vestibular ocular reflex dynamics with head-impulses in hereditary cerebellar ataxias. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014. (Poster presentation)

Luis L, Lehnen N, Muñoz E, de Carvalho M, Schneider E, Valls-Solé J, Costa J. Anticomensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmus. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014. (Poster presentation)

Castro J, Costa J, Pinto S, de Carvalho M. Motor unit number index (MUNIX) in amyotrophic lateral sclerosis: a prospective cohort study. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014. (Poster presentation)

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

Caldeira D, Barra M, Pinto FJ, Ferreira JJ, Costa J. Risco de hemorragia intracraniana com os novos anticoagulantes orais: revisão sistemática e meta-análise. 15º Congresso do NEDVC. Porto Nov 2014. (Oral presentation)

Cardoso R. Terapia da Fala no espectro do Parkinsonismo, Congresso Nacional de Terapia da Fala 2014, pelo caminho da ciência ao encontro da Prática, Lisbon, November, 2014 (Oral presentation)

Lobo PP, Coelho M, Cattoni B, Guedes LC, Carvalho H, Ferreira JJ, Rosa MM, Gonçalves Ferreira A, Tratamento da distonia tardia dos neurolépticos por cirurgia de estimulação cerebral profunda do globo pálido interno, Congresso Nacional da Sociedade portuguesa das Doenças

do Movimento, Vimeiro, 28-30 Março 2014 (Poster presentation)

Morgado S, Coelho M, Guedes LC, Sinal do “olho de tigre” em doente com atrofia dentato-rubro-pálido-luisiana, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Franco A, Lobo PP, Coelho M, Geraldés R, Pinho e Melo T, Monocoreia-balismo como forma de apresentação do acidente vascular cerebral isquémico do território vertebro-basilar, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Oral presentation)

Miranda HV, Cássio R, Penque D, Guedes LC, Soares T, Coelho M, Rosa MM, Ferreira JJ, Outeiro T, Alpha-synuclein as a blood biomarker for Parkinson Disease, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Oral presentation)

Reimão S, Lobo PP, Neutel D, Nunes R, Ferreira J, Campos J, Ferreira JJ, Locus ceruleus and substantia nigra magnetic resonance imaging in patients with early Parkinson's disease, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Castro Caldas A, Guedes LC, Ferreira JJ, Coelho M, Distonia do músico como apresentação inicial de doença de Parkinson, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Ferreira JJ, Teodoro T, Geraldés R, Guedes LC, Alterações cognitivas, síndrome parkinsónica e ataxia cerebelosa resultante de calcinose cerebral extensa num doente com LES, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Teodoro T, Nzwalo H, Guedes LC, Coelho M, Rosa MM, Ferreira JJ, Comportamentos suicidas em ensaios clínicos com fármacos anti-parkinsónicos para doença de Parkinson, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Teodoro T, Nzwalo H, Guedes LC, Coelho M, Rosa MM, Ferreira JJ, Risco de comportamentos suicidas em doentes incluídos em ensaios clínicos de ECP para a doença de Parkinson, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Godinho C, Ferret-Sena V, Brito J, Dias M, Calado A, Semedo C, Domingos J, Melo F, Controlo postural na doença de Parkinson: alterações características em função dos diferentes estádios

de evolução da doença, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Oral presentation)

Godinho C, Ferret-Sena V, Brito J, Dias M, Calado A, Semedo C, Domingos J, Melo F, Efeito da estimulação cerebral profunda sobre o controlo motor em doentes com doença de Parkinson – estudo preliminar, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Caníça V, Domingos J, Godinho C, Pinho a, Guerreiro D, Queimado F, Martins P, Cardoso R, Loureiro R, Ferreira JJ, Avaliação da aplicabilidade de programa intensivo de reabilitação para indivíduos com doença de Parkinson, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Teodoro T, Nzwalo H, Guedes LC, Coelho M, Rosa MM, Ferreira JJ, A ECP-NST para doença de Parkinson induz comportamentos suicidas? Meta-análise de ensaios clínicos, Congresso Nacional da Sociedade portuguesa das Doenças do Movimento Vimeiro, 28-30 Março 2014 (Poster presentation)

Gouveia M, Borges M, Augusto M, Caldeira D, Alarcão J, Pinheiro L, Sousa R, Fareleira F, Ascensão R, Costa J, Laires P, Fiuza M, Dias NC, Martins S, Belo A, Vaz Carneiro A. The cost of hypercholesterolemia in Portugal. XV Congresso Português Endocrinologia. Vilamoura, Jan 2014. (Poster presentation)

Gouveia M, Borges M, Augusto M, Caldeira D, Alarcão J, Pinheiro L, Sousa R, Fareleira F, Ascensão R, Costa J, Laires P, Fiuza M, Dias NC, Martins S, Belo A, Vaz Carneiro A. The cost of hypercholesterolemia in Portugal. XV Congresso Português Endocrinologia. Vilamoura, Jan 2014. (Poster presentation)

#### **Organisation of Conferences**

Coelho M. Organized the 1st Teaching Course on DBS Movement Disorders. Faculdade de Medicina de Lisboa, Instituto de Medicina Molecular. Lisbon, October 22, 2014.

Godinho C. Co-organized MDS 2nd Allied Health Professional Summer School: physiotherapy for people with Parkinson's disease. Torres Vedras, Portugal, September 25-27,2014.

Ferreira JJ, Godinho C. Co-organized MDS 2nd Allied Health Professional Summer School: physiotherapy for people with Parkinson's disease. Torres Vedras, Portugal, September 25-27,2014.

Costa J. Vestibular Diagnosis, Treatment and Rehabilitation Course (2nd edition). Hospital de Santa Maria and Clinical Physiology Translational Unit IMM. Lisbon, 15-17 September 2014.

Costa J. Curso Revisões Sistemáticas como Projecto de Investigação Clínica. Faculdade de Medicina da Universidade de Lisboa. 11-12 Setembro 2014.

Costa J. Inauguration of the Portugueses Branch of the Iberoamerican Cochrane Network, Lisboa, 28-29 June 2014.

Ferreira JJ, Course in Clinical Research, 5Th module: Clinical trials, Faculdade de Medicina de Lisboa, Lisboa, May, 23 th-24 th, 2014.

Ferreira JJ. Co-organized Congresso Nacional da Sociedade Portuguesa das Doenças do Movimento, Vimeiro, Portugal, March 28th-30th, 2014.

Neutel D. Co-organized Congresso Nacional da Sociedade Portuguesa das Doenças do Movimento, Vimeiro, Portugal, March 28th-30th, 2014.

Costa J. Vestibular Diagnosis, Treatment and Rehabilitation Course. Hospital de Santa Maria and Clinical Physiology Translational Unit IMM. Lisbon, 27–29 January 2014.

#### **Industry contract research**

Infarmed, Unidade de Farmacovigilância de Lisboa e Vale do Tejo. 67.444,44 €

Fundação Merck, Sharp & Dohme, Base Editorial do Cochrane Movement Disorders Group.7.500€

#### **Advanced teaching**

Ferreira JJ. Ensaios clínicos. Mestrado em Cuidados Paliativos. Lisboa, 18-20 Dezembro 2014.

Ferreira JJ. Parkinson's Disease: diagnosis, clinical features and motor complications. Movement disorders Course, Plovdiv, Bulgária, 12-13 December 2014.

Ferreira JJ. Non-motor symptoms in Parkinson's disease. Movement disorders Course, Plovdiv, Bulgária, 12-13 December 2014.

Ferreira JJ. Multiple system atrophy, Movement disorders Course, Plovdiv, Bulgária, 12-13 December 2014.

Ferreira JJ. Porque precisamos de ensaios clínicos? I Jornadas do Internato Médico, Faculdade de Medicina de Lisboa, Lisboa, 15 e 16 de Novembro 2014

Foisy M, Dryden D, Fernandes R, Hartling L. Workshop: Advancing methods for overviews of reviews: a discussion of challenges and potential solutions. 22nd Cochrane Colloquium.,Cochrane Collaboration. Hyderabad, 21-26 September 2014.

Fernandes R. Análise crítica / Avaliação qualidade dos artigos incluídos. Curso Revisões Sistemáticas como Projecto de Investigação Clínica, Faculdade de Medicina, Universidade de Lisboa, 11 and 13 September 2014.

Ferreira JJ. Progressão da Doença de Parkinson, Curso em Doenças do Movimento, Doença de Parkinson, Sintra, 11 de Outubro 2014.

Ferreira JJ. Quando e como começar a tratar a Doença de Parkinson, Curso em Doenças do Movimento, Doença de Parkinson, Sintra, 11 de Outubro 2014.

Ferreira JJ. Caso clínico: Doente de novo, Curso em Doenças do Movimento, Doença de Parkinson, Sintra, 11 de Outubro 2014.

Ferreira JJ. Evolution of PD motor and non motor features, 7th Annual MDS-ES Summer School for Young Neurologists, Barcelona, Spain, July 18-20, 2014

Ferreira JJ. Progression in Parkinson's disease, 7th Annual MDS-ES Summer School for Young Neurologists, Barcelona, Spain, July 18-20, 2014

Fernandes R. Tipos de Revisões Sistemáticas: Intervenção, Diagnóstico e Prognóstico. Systematic Reviews Module, Introduction to Clinical Research: a practical course, Lisbon Academic Medical Centre - CAML Doctoral Program, Lisboa, 27 June 2014.

Ferreira JJ. Key learnings from recent movement disorders clinical trials, Parkinson's Disease Educational Course for Industry Professionals, International Parkinson and Movement Disorder Society, Stockholm June 10, 2014

Ferreira JJ. An update on Huntigton's disease: from pathophysiology to new treatments, Parkinson's Disease Educational Course for Industry Professionals, International Parkinson and Movement Disorder Society, Stockholm June 10, 2014

Ferreira JJ. Management of Advanced Parkinson's Disease: Medical Treatments and Outcome Measures, What is Parkinson's Disease? Differential diagnosis and pathophysiology, Parkinson's Disease Educational Course for Industry Professionals, International Parkinson and Movement Disorder Society, Stockholm June 7, 2014.

Ferreira JJ. What is Parkinson's Disease? Differential diagnosis and pathophysiology, Parkinson's Disease Educational Course for Industry Professionals, International Parkinson and Movement Disorder Society, Stockholm June 7, 2014.

Fernandes R. Clinical outcomes and biomarkers. Module Therapeutic Research in Neurosciences, Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisboa, 5 June 2014.

Ferreira JJ. Therapeutic strategies for atypical parkinsonian conditions, Update on atypical Parkinson's disease, Joint congress Istanbul 2014, Istanbul, Turkey, 31 May - 3 June, 2014.

Fernandes R. Clinical trial design and methodology. Clinical Trials Module, Introduction to Clinical Research: a practical course, Lisbon Academic Medical Centre - CAML Doctoral Program, Lisboa, 23 May 2014.

Fernandes R. Reações Adversas Medicamentosas em Pediatria. Curso Básico de Farmacovigilância, Unidade de Farmacovigilância de Lisboa e Vale do Tejo, Lisboa, 13 May 2014.

Ferreira JJ. Experimentação médica, I Curso Pós-Graduado de actualização sobre Direito da Medicina & Justiça Penal, Faculdade de Direito, Universidade de Lisboa, Maio de 2014.

Godinho, C. Physical Activity, Exercise and Health. Post-Graduation Course. Cooperativa de Ensino Superior Egas Moniz. May 2014.

Godinho, C. Physiology and impact of physical activity in the human body. Post-Graduation Course. Cooperativa de Ensino Superior Egas Moniz. May 2014.

Fernandes R. Allergy testing: an evidence-based approach for respiratory disorders. International Course on Pediatric Pulmonology ICPP 10, Lisboa, 11 April 2014.

Fernandes R. Utilização racional de broncodilatadores. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo XII Terapêutica Farmacológica Das Doenças Respiratórias na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 4 April 2014.

Fernandes R. Utilização racional de corticoesteróides e outros anti-inflamatórios. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo XII Terapêutica Farmacológica Das Doenças Respiratórias na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 4 April 2014.

Rosario F, Fernandes R, Bandeira T, Adesão terapêutica. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo XII Terapêutica Farmacológica Das Doenças Respiratórias na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 4 April 2014.

Fernandes R. Princípios de farmacologia clínica e prescrição racional em doenças respiratórias pediátricas. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo XII Terapêutica Farmacológica Das Doenças Respiratórias na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 3 April 2014.

Costa J. Teacher. Module XII - "Terapêutica Farmacológica Das Doenças Respiratórias na Criança no Curso de Especialização Doenças Respiratórias e do Sono na Criança". Faculdade de Medicina da Universidade de Lisboa. 3-5 Abril de 2014.

Ferreira JJ. When to start treatment in Parkinson's disease, 3rd International Movement Disorders Teaching Course, Brasov, Romania, April 3-4, 2014

Ferreira JJ. Development of a meta-analysis protocol – a practical exercise, Systematic review and meta-analysis: clinical management and analysis, Training programme in Pharmaceutical Medicine, Universidade de Aveiro, March 20, 2014

Ferreira JJ. Critical appraisal of clinical trials papers – a practical exercise, Systematic review and meta-analysis: clinical management and analysis, Training programme in Pharmaceutical Medicine, Universidade de Aveiro, March 20, 2014

Ferreira JJ. Define the objective and selection criteria of the meta-analysis, Systematic review and meta-analysis: clinical management and analysis, Training programme in Pharmaceutical Medicine, Universidade de Aveiro, March 20, 2014

Ferreira JJ. Principles of evidence – based medicine (EBM), Systematic review and meta-analysis: clinical management and analysis, Training programme in Pharmaceutical Medicine, Universidade de Aveiro, March 20, 2014

Godinho, C. Physical Activity and Exercise in Clinical Nutrition. Seminar in Master Degree Course of Clinical Nutrition. Cooperativa de Ensino Superior Egas Moniz. March 2014.

Godinho, C. Principles of sport training. Seixal Clinic, FISIOBASKET. February 2014

Fernandes R. Epidemiologia, Factores De Risco E Desencadeantes Na Asma. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo III - Doença Pulmonar Crónica na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 11 January 2014.

Fernandes R. Sibilância no pré-escolar. Curso de Especialização Doenças Respiratórias e do Sono na Criança, Módulo III - Doença Pulmonar Crónica na Criança, Departamento de Pediatria, Hospital de Santa Maria, Lisboa, 9 January 2014.

Costa J. Former: "Da epidemiologia do medicamento à Farmacoterapia e à decisão clínica". Promotor: Comissão de Farmácia e Terapêutica ARSLVT 201

Costa J. Responsible for the Module of Market Access at “Leading Pharma”. Program of Management for the Pharmaceutical industry. Catolica Executive Education Lisbon.

Costa J. Coordinator of the Module: Clinical epidemiology - Program Educacional MANAGE. Escola Nacional Superior de Saúde. Universidade Nova de Lisboa.

#### **Science and society**

Ferreira, JJ (2014) Sociedade Civil: Resposta dos Parceiros. RTP2

Valadas, A (2014) A Tarde E Sua: A Doença De Parkinson. TVI

Ferreira, JJ (2014) Edicao Da Manha. SIC

Domigos, J; Ferreira, JJ (2014) Bom Dia Portugal. RTP

Domingos, J (2014) Praca Da Alegria. RTP

Domingos, J; Valadas, A (2014) Portugal No Coração: Doença De Parkinson. RTP1

Domingos, J (2014) Jornal da Noite. SIC

#### **Msc thesis completed**

Ana Cláudia Marques Salgueiro 19/12/2014 Training in Coordination of Clinical Trials in a Clinical Reserach Unit Universidade de Aveiro Joaquim Ferreira, Md, PhD, Joana Gomes da Silva, MD, PhD

André Cardoso 25/07/2014 Training in Coordination of Clinical Trials in a Clinical Research Unit Universidade de Aveiro Joaquim ferreira, MD, PhD

Márcio Barra 25/07/2014 Training in Coordination of Clinical Trials in a Clinical Research Unit Universidade de Aveiro Joaquim Ferreira, Md, PhD

João Valente Jorge 22/05/2014 Normas de orientação clínica portuguesas. Abordagem terapêutica de doenças e factores de risco cardiovasculares. Que evidência, que método e que impacto? Faculdade de Medicina de Lisboa Joaquim Ferreira MD, PhD João Costa, MD, PhD

Raquel Paulinetti Câmara 22/05/2014 The magnitude of placebo effect in Restless Legs syndrome, Faculdade de Medicina de Lisboa Ricardo Fernandes, MD

Ivo Miguel Santos Duarte 22/05/2014 Clinical practice guidelines for management of Parkinson’s disease: a systematic critical appraisal Faculdade de Medicina de Lisboa Mário Miguel Rosa, MD

Guilherme Manuel Coelho Santiago Violante da Cunha 22/05/2014 A systematic review of caracteristics and validity of monitoring technologies to assess Parkinson’s disease symptoms



and signs Faculdade de Medicina de Lisboa Joaquim Ferreira, MD, PhD

Linda Maria Azevedo Kauppila 22/05/2014 Characterization of adverse drug reactions with neuropsychiatric clinical manifestations reported spontaneously to the Portuguese Pharmacovigilance system in the greater Lisboa area Faculdade de Medicina de Lisboa Mário Miguel Rosa, MD João Costa, Md, PhD

## José Ferro Lab

### Major Interests / Objectives

The general objective of UNIC is to increase the knowledge and foster the prevention and treatment of major prevalent and disabling disorders involving the brain, such as stroke and Alzheimer's disease. The main advantage of the unit 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 of UNIC conducted clinical trials and assessed the clinical impact of different interventions in multinational efforts to get new treatments for these prevalent and disabling brain disorders.

### Head of Unit

José Manuel Morão Cabral Ferro, MD, PhD, Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria

### Research Team

Alcina Fraga Luz	No degree	Investigator
Alexandre Valério de Mendonça	PhD	Senior Investigator
Ana Catarina Gaspar Fonseca	Master	PhD Student
Ana Isabel Figueira Verdelho	MD/PhD	Investigator
Ana Sofia Valentim Rodrigues	Graduate	Investigator, (started March)
Bruno André e Silva Miranda	Master	PhD Student
Carolina Pires Maruta	Master	PhD Student
Catarina Beatriz Silva Ferreira	Graduate	MSc Student, (started June)
Catarina Carapeto da Silva Chester	Graduate	MSc Student
Elisabete Mendes Lopes	No degree	Investigator
Fátima Soares	No degree	Investigator

Frederico Simões do Couto	Graduate	Investigator, MD
Helena Sofia Garrido Bárrios	Master	Investigator, Hospital do Mar , MD
Inês Isabel Dias Simões Manita Mares	Graduate	MSc Student
Isabel Pavão Martins	PhD	Investigator
José Manuel Borges Fonseca	Master	PhD Student
Lara Isabel Pires Melo Caeiro	Master	PhD Student
Luisa Farrajota	No degree	Investigator
Madalena Cristina Rocha Martins	PhD	Post doctoral Investigator, (left January)
Maria Gabriela Mariano Leal	Graduate	Investigator
Maria Luisa Albuquerque	No degree	Investigator
Maria Luisa Mendonça Correia Pires	Undergraduate	Administrative
Maria Manuela Gil Guerreiro	PhD	Investigator
Marisa Marina Fatuda Costa	Undergraduate	Administrative
Mauricio de Jesus Dias Martins	Master	PhD Student
Patrícia Canhão	No degree	Investigator
Paulo Maciel Mendes Batista	Graduate	Investigator
Raquel Santos Gil Gouveia	Master	PhD Student
Ruth Isabel de Gusmão Fernandes Geraldes Ramos Dias	Master	Investigator
Sara Cunha Leal Rocha Coelho	Master	PhD Student
Sofia Madureira	Master	PhD Student
Teresa Pinho e Melo	No degree	Investigator
Vanda Filipa Viseu Cândido De Freitas	Master	MSc Student
Vitor Oliveira	No degree	Investigator

### Keywords / Research Areas

Stroke, Parkinson's disease, Cognitive decline, Complex diseases, Genetics, Clinical trials

### Major scientific achievements

The researchers of UNIC made in 2014 significant scientific contributions expressed in full papers published in international peer-reviewed journals. Important results were obtained regarding age-related white matter changes, namely on the relationship between cerebral small vessel disease and brain atrophy, cognitive decline and depression in the elderly. Advances were made on the study of cognitive aging in primary care, the understanding of subjective memory complaints, evaluation of quality of life and determination of the prognosis of elderly people with cognitive complaints. New data were published using traditional genetic approaches, like linkage and association, as well as new approaches, namely genome-wide association studies, exome sequencing and microRNA expression profiling, to identify susceptibility genes in neurological disorders. Novel genetic risk factors for ischaemic stroke and its subtypes were identified, and new mutations in genes involved in complex neurodegenerative disorders were characterized.

### Selected Publications

Fitch W, Martins MJ. (2014) Hierarchical processing in music, language, and action: Lashley revisited. *Ann Ny Acad Sci* **1316**, 87-104. (Journal IF: 4.039, Citations: 0)

Fonseca AC, Brito D, Pinho e Melo T, Geraldés R, Canhão P, Caplan LR, Ferro JM. (2014) , N-terminal pro-brain natriuretic peptide shows diagnostic accuracy for detecting atrial fibrillation in cryptogenic stroke patients. . *Int J Stroke* **9**, 419-425. (Journal IF: 4.029, Citations: 1)

Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, Prieto-Merino D, Dehghan A, Trompet S, Wong A, Cavadino A, Drogan D, Padmanabhan S, Li S, Yesupriya A, Leusink M, Sundstrom J, Hubacek JA, Pikhart H, Swerdlow DI, Panayiotou AG, Borinskaya SA, Finan C, Shah S, Kuchenbaecker KB, Shah T, Engmann J, Folkersen L, Eriksson P, Ricceri F, Melander O, Sacerdote C, Gamble DM, Rayaprolu S, Ross OA, McLachlan S, Vikhireva O, Sluijs I, Scott RA, Adamkova V, Flicker L, Bockxmeer FM, Power C, Marques-Vidal P, Meade T, Marmot MG, Ferro JM, Paulos-Pinheiro S, Humphries SE, Talmud PJ, Mateo Leach I, Verweij N, Linneberg A, Skaaby T, Doevendans PA, Cramer MJ, van der Harst P, Klungel OH, Dowling NF, Dominiczak AF, Kumari M, Nicolaidis AN, Weikert C, Boeing H, Ebrahim S, Gaunt TR, Price JF, Lannfelt L, Peasey A, Kubinova R, Pajak A, Maljutina S, Voevoda MI, Tamosiunas A, Maitland-van der Zee AH, Norman PE, Hankey GJ, Bergmann MM, Hofman A, Franco OH, Cooper J, Palmen J, Spiering W, de Jong PA, Kuh D, Hardy R, Uitterlinden AG, Ikram MA, Ford I, Hyppönen E, Almeida OP,

Wareham NJ, Khaw KT, Hamsten A, Husemoen LL, Tjønneland A, Tolstrup JS, Rimm E, Beulens JW, Verschuren WM, Onland-Moret NC, Hofker MH, Wannamethee SG, Whincup PH, Morris R, Vicente AM, Watkins H, Farrall M, Jukema JW, Meschia J, Cupples LA, Sharp SJ, Fornage M, Kooperberg C, LaCroix AZ, Dai JY, Lanktree MB, Siscovick DS, Jorgenson E, Spring B, Coresh J, Li YR, Buxbaum SG, Schreiner PJ, Ellison RC, Tsai MY, Patel SR, Redline S, Johnson AD, Hoogeveen RC, Hakonarson H, Rotter JJ, Boerwinkle E, de Bakker PI, Kivimaki M, Asselbergs FW, Sattar N, Lawlor DA, Whittaker J, Davey Smith G, Mukamal K, Psaty BM, Wilson JG, Lange LA, Hamidovic A, Hingorani AD, Nordestgaard BG, Bobak M, Leon DA, Langenberg C, Palmer TM, Reiner AP, Keating BJ, Dudbridge F, Casas JP; InterAct Consortium. (2014) Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. *BMJ* **349**, G4164. (Journal IF: 16.378, Citations: 4)

van der Zee J, Langenhove TV, Kovacs GG, Dillen L, Deschamps W, Engelborghs S, Matej R, Vandenbulcke M, Sieben A, Dermaut B, Smets K, Van Damme P, Merlin C, Laureys A, Van Den Broeck M, Mattheijssens M, Peeters K, Benussi L, Binetti G, Ghidoni R, Borroni B, Padovani A, Archetti S, Pastor P, Razquin C, Ortega-Cubero S, Hernández I, Boada M, Ruiz A, de Mendonça A, Miltenberger-Miltényi G, Simões do Couto F, Sorbi S, Nacmias B, Bagnoli S, Graff C, Chiang H-H, Thonberg H, Pernecky R, Diehl-Schmid J, Alexopoulos P, Frisoni GB, Bonvicini C, Synofzik M, Maetzler W, vom Hagen JM, Schöls J, Haack TB, Strom TM, Prokisch H, Dols-Icardo O, Clarimón J, Lleó A, Santana I, Almeida MR, Santiago B, Heneka MT, Jessen F, Ramirez A, Sanchez-Valle R, Llado A, Gelpi E, Sarafov S, Tournev I, Jordanova A, Parobkova E, Fabrizi GM, Testi S, Salmon E, Ströbel T, Santens P, Robberecht W, De Jonghe P, Martin J-J, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Sleegers K, Van Broeckhoven C. (2014) Rare mutations in SQSTM1 modify susceptibility to frontotemporal lobar degeneration. *Acta Neuropathologica* **128**, 397-410. (Journal IF: 9.777, Citations: 1)

Bocchetta M, Galluzzi S, Kehoe PG, Aguera E, Bernabei R, Bullock R, Ceccaldi M; Dartigues J-F, de Mendonça A, Didic M, Eriksdotter M, Félician O, Frölich L, Gertz H-J, Hallikainen M, Hasselbalch SG, Hausner L, Heuser I; Jessen F, Jones RW, Kurz A, Lawlor B, Lleo AB, Martinez-Lage P, Mecocci P, Mehrabian S, Monsch A, Nobili F, Nordberg A, Rikkert MO, Orgogozo J-M, Pasquier F, Peters O, Salmon E, Sánchez-Castellano C, Santana I, Sarazin M, Traykov L, Tsolaki M, Visser PJ, Wallin ÅK; Wilcock G, Wilkinson D, Wolf H, Yener G, Zekry D, Frisoni GB. (2014) The Use of Biomarkers for the Etiologic Diagnosis of MCI in Europe: an EADC Survey. *Alzheimers Dement* (Journal IF: 17.472, Citations: 1)

### **Ongoing Research Projects**

2010/2014 Title: TIA Registry. Coordinator: Patrícia Canhão. Agency: SOS Ataque Cérébrale. Reference: TIA Registry. Amount: 8,620€.

2014/2016 Title: Metastroke. Coordinator: José Manuel Morão Cabral Ferro. Agency: Bayer Portugal, S.A.. Reference: Bayer. Amount: 6,000€.

2014/2017 Title: Avaliação de Intervenções e Estratégias na Demência do Jovem. Coordinator: Alexandre Valério de Mendonça. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: JPND-HC/0003/2012 - Rhapsody. Amount: 125,000€.

2014/2017 Title: Setting the stage for prevention trials in Genetic Frontotemporal Lobar Degeneration. Coordinator: Alexandre Valério de Mendonça. Agency: Ana Paula dos Santos Marques da Costa. Reference: GenFi. Amount: 10,000€.

2013/2017 Title: ISCVT-2. Coordinator: José Manuel Morão Cabral Ferro. Agency: Congrex Schweiz AG. Reference: ISCVT-2. Amount: 155,000€.

2014/2017 Title: Formação Jovens Neurologistas. Coordinator: José Manuel Morão Cabral Ferro. Agency: Biogen Idec. Reference: Formação Jovens Neurologistas. Amount: 5,000€.

### **Other Projects**

2010/2014 Mindful aging. Avoiding age related cognitive decline. Coordinator: Isabel Pavão Martins.

2014/2014 Hemispatial Neglect and the Pulvinar Nucleus: an alternative pathway for selective attention . Coordinator: Isabel Pavão Martins.

2010/2014 BIOMARKAPD – Biomarkers for Alzheimer’s disease and Parkinson’s disease. Coordinator: Alexandre Mendonça.

2010/2014 Estudo Necrópsico de Doentes com Formas Familiares ou Atípicas de Demência. Coordinator: Ana Verdelho.

2011/2014 NEUROCLINOMICS - Understanding NEUROdegenerative diseases through CLINical and OMICS data integration. Coordinator: Sara Madeira.

2009/2014 Pesquisa de Novas Mutações em Genes Responsáveis por Demência Familiar. Coordinator: Alexandre Mendonça.

2009/2014 QREN Do-it – PPS3 – sdAb+péptido – Investigação translacional em Alzheimer.  
Coordinator: Alexandre Mendonça.

2012/2015 Subjective Memory Complaints in the Early Diagnosis of Mild Cognitive Impairment.  
Coordinator: Manuela Guerreiro.

#### Publications in peer review Journals

Aguiar de Sousa D, Ferro JM, Canhão P, Barinagarrementeria F, Bousser MG, Stam J, Nogueira Pinto A, Viana Baptista M, Béjot Y, Dequatre-Ponchelle N. (2014) Cerebral venous thrombosis causing posterior fossa lesions: Description of a case series and assessment of safety of anticoagulation. *Cerebrovascular Diseases* **38**, 384-388. (Journal IF: 3.698, Citations: 0) .

Albuquerque L, Coelho M, Martins M, Guedes LC, Rosa MM, Ferreira JJ, Cattoni MB, Carvalho H, Ferreira AG, Martins IP. (2014) STN-DBS does not change emotion recognition in advanced Parkinson's disease. letter to the editor. *Parkinsonism and Related Disorders. Parkinsonism Relat D* **20**, 564-565. (Journal IF: 4.126, Citations: 0) .

Alexandrino GM, Damásio J, Canhão P, Geraldés R, Melo TP, Correia C, Ferro JM. (2014) Stroke in sports: a case series. *J Neurol* **261**, 1570-1574. (Journal IF: 3.841, Citations: 0) .

Barra L, Ha A, Sun L, Fonseca C, Pope J. (2014) Efficacy of biologic agents for improving the Health Assessment Questionnaire (HAQ) Score in established and early rheumatoid arthritis: A meta-analysis with indirect comparisons. *Clin Exp Rheumatol* **32**, 333-341. (Journal IF: 2.973, Citations: 1) .

Cardoso S, Silva D, Maroco J, de Mendonça A, Guerreiro M. 2014 14 222-228. (2014) Non – Literal Language deficits in Mild Cognitive Impairment. *Psychogeriatrics* **14**, 222-228. (Journal IF: 1.219, Citations: 0) .

Castro Caldas A, Geraldés R, Neto L, Canhão P, Melo TP. (2014) Central Nervous System Vasculitis associated with Hepatitis C vírus Infection: a brain MRI-supported diagnosis. *J Neurol Sci* **336**, 152-154. (Journal IF: 2.262, Citations: 0) .

Crespo AC, Silva B, Marques L, Marcelino E, Maruta C, Costa S, Timóteo A, Vilares A, Couto FS, Faustino P, Correia AP, Verdelho A, Porto G, Guerreiro M, Herrero A, Costa C, de Mendonça A, Costa L, Martins M. (2014) Genetic and biochemical markers in patients with Alzheimer's disease support a concerted systemic iron homeostasis dysregulation. *Neurobiol Aging* **35**,

777-785. (Journal IF: 4.853, Citations: 7)

Ferro JM, Fonseca C. (2014) Stroke: an update-. *J Neurol* **261**, 1837–1841. (Journal IF: 3.841, Citations: 0) .

Fitch W, Martins MJ. (2014) Hierarchical processing in music, language, and action: Lashley revisited. *Ann Ny Acad Sci* **1316**, 87-104. (Journal IF: 4.039, Citations: 0)

Fonseca AC, Brito D, Pinho e Melo T, Geraldles R, Canhão P, Caplan LR, Ferro JM. (2014) , 9, 419-425. (Journal IF: 4.029, Citations: 1). (2014) N-terminal pro-brain natriuretic peptide shows diagnostic accuracy for detecting atrial fibrillation in cryptogenic stroke patients. . *Int J Stroke* , **9**, 419-425. (Journal IF: 4.029, Citations: 1) .

Geraldles R, Sousa, PR, Fonseca AC, Falcão F, Canhão P, Pinho e Melo T. (2014) Non-traumatic convexity subarachnoid haemorrhage: different aetiologies, different outcomes. *J Stroke Cerebrovasc Dis* **23**, e23-30. (Journal IF: 1.993, Citations: 2)

Geraldo AF, Silva C, Neutel D, Neto LL, Albuquerque L. (2014) Delayed leukoencephalopathy after acute carbon monoxide intoxication. *J Radiol Case Rep* **31**, 1-8. *J Radiol Case Rep*. **8**, 2014 May 31 (5 (Journal IF: , Citations: ) .

Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, Prieto-Merino D, Dehghan A, Trompet S, Wong A, Cavadino A, Drogan D, Padmanabhan S, Li S, Yesupriya A, Leusink M, Sundstrom J, Hubacek JA, Pikhart H, Swerdlow DI, Panayiotou AG, Borinskaya SA, Finan C, Shah S, Kuchenbaecker KB, Shah T, Engmann J, Folkersen L, Eriksson P, Ricceri F, Melander O, Sacerdote C, Gamble DM, Rayaprolu S, Ross OA, McLachlan S, Vikhireva O, Sluijs I, Scott RA, Adamkova V, Flicker L, Bockxmeer FM, Power C, Marques-Vidal P, Meade T, Marmot MG, Ferro JM, Paulos-Pinheiro S, Humphries SE, Talmud PJ, Mateo Leach I, Verweij N, Linneberg A, Skaaby T, Doevendans PA, Cramer MJ, van der Harst P, Klungel OH, Dowling NF, Dominiczak AF, Kumari M, Nicolaidis AN, Weikert C, Boeing H, Ebrahim S, Gaunt TR, Price JF, Lannfelt L, Peasey A, Kubinova R, Pajak A, Malyutina S, Voevoda MI, Tamosiunas A, Maitland-van der Zee AH, Norman PE, Hankey GJ, Bergmann MM, Hofman A, Franco OH, Cooper J, Palmén J, Spiering W, de Jong PA, Kuh D, Hardy R, Uitterlinden AG, Ikram MA, Ford I, Hyppönen E, Almeida OP, Wareham NJ, Khaw KT, Hamsten A, Husemoen LL, Tjønneland A, Tolstrup JS, Rimm E, Beulens JW, Verschuren WM, Onland-Moret NC, Hofker MH, Wannamethee SG, Whincup PH, Morris R, Vicente AM, Watkins H, Farrall M, Jukema JW, Meschia J, Cupples LA, Sharp SJ, Fornage M, Kooperberg C, LaCroix AZ, Dai JY, Lanktree MB, Siscovick DS, Jorgenson E, Spring B, Coresh J, Li YR, Buxbaum SG, Schreiner PJ, Ellison RC, Tsai MY, Patel SR, Redline S, Johnson AD, Hoogeveen RC, Hakonarson H, Rotter JI, Boerwinkle E, de Bakker PI, Kivimaki M, Asselbergs FW, Sattar N, Lawlor DA, Whittaker J, Davey Smith G, Mukamal K, Psaty BM, Wilson JG, Lange LA, Hamidovic A, Hingorani AD, Nordestgaard BG, Bobak M, Leon DA, Langenberg C, Palmer TM, Reiner AP,



Keating BJ, Dudbridge F, Casas JP; InterAct Consortium. (2014) Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. *BMJ* **349**, g4164. (Journal IF: 16.378, Citations: 4) .

João AA, Goucha TB, Martins IP. (2014) Aura status: a not so frequent aura. *Cephalalgia* **34**, 1150-1162. (Journal IF: 4.121 , Citations: 0) .

Lanthier S, Calabrese LH, Ferro JM, Putaala J, Strbian D, Chagnon M, Frosch MP, Singhal AB, Salvarani C, Létourneau-Guillon L, Poppe AY, Guilbert F, Raymond J, Muccilli A; INTERSPACE investigators. (2014) The INTERNational Study on Primary Angiitis of the CEntral nervous system--a call to the world. *Int J Stroke* **9**, e23. (Journal IF: 4.029 , Citations: 0) .

Lobo S, Ferro JM, Barinagarrementeria F, Bousser MG, Canhão P, Stam J. (2014) Shunting in Acute Cerebral Venous Thrombosis: A Systematic Review. *Cerebrovasc Dis* **37**, 38-42. (Journal IF: 3.698, Citations: 1) .

Martins MJ, Fischmeister FP, Puig-Waldmüller E, Oh J, Geißler A, Robinson S, Fitch WT, Beisteiner R. (2014) Fractal image perception provides novel insights into hierarchical cognition. *Neuroimage* **96**, 300-308. (Journal IF: 6.132, Citations: 0) .

Martins MJ, Laaha S, Freiburger EM, Soonja C Fitch WT. (2014) How children perceive fractals: Hierarchical self-similarity and cognitive development. *Cognition* **133**, 10-24. (Journal IF:NA Citations: 0) .

Maruta C, Makhmood S, Downey LE, Golden HL, Fletcher PD, Witoonpanich P, Rohrer JD, Warren JD. (2014) Delayed auditory feedback simulates features of nonfluent primary progressive aphasia. *J Neurol Sci* , **347**, 345-348. (Journal IF: 2.262, Citations: 0) .

Neutel D, Biscoito L, Campos J, e Melo TP, Albuquerque L (2014). Giant cell arteritis with symptomatic intracranial stenosis and endovascular treatment. *Neurol Sci* **35**, 609-610. (Journal IF: 1.495, Citations: 1) .

Poggesi A, Gouw A, van der Flier W, Pracucci G, Chabriat H, Erkinjuntti T, Fazekas F, Ferro JM, Blahak C, Langhorne P, O'Brien J, Schmidt R, Visser MC, Wahlund LO, Waldemar G, Wallin A, Scheltens P, Inzitari D, Pantoni L. (2014) Neurological abnormalities predict disability: the LADIS (Leukoaraiosis And DISability) study. *J Neurol* **261**, 1160-1169. (Journal IF: 3.841, Citations: 0)

Silva D, Guerreiro M, Faria C, Maroco J, Schmand BA, Mendonça A. (2014) Significance of subjective memory complaints in the clinical setting. *J Geriatr Psychiatry Neurol* **27** 259-265.

(Journal IF: 1.629, Citations: 0) .

Teodoro T, Geraldles R, Melo TP. (2014) Symptomatic internal carotid artery thrombosis in acute carbon monoxide intoxication. *Am J Emerg Med*; **32**, 684 e5-6. (Journal IF: 1.152, Citations: 0) .

Teodoro T, Nagel MA, Geraldles R, White T, Mahalingam R, Batista P, Wellish M, Pimentel J, Khmeleva N, Heintzman A, Albuquerque L, Boyer PJ, Choe A, Peralta R, Gilden D. (2014) Biopsy-negative, varicella zoster virus (VZV)-positive giant cell arteritis, zoster, VZV encephalitis and ischemic optic neuropathy, all in one. *J Neurol Sci*; **343**, 195-197. (Journal IF: 2.262, Citations: 0).

van der Zee J, Langenhove TV, Kovacs GG, Dillen L, Deschamps W, Engelborghs S, Matej R, Vandenbulcke M, Sieben A, Dermaut B, Smets K, Van Damme P, Merlin C, Laureys A, Van Den Broeck M, Mattheijssens M, Peeters K, Benussi L, Binetti G, Ghidoni R, Borroni B, Padovani A, Archetti S, Pastor P, Razquin C, Ortega-Cubero S, Hernández I, Boada M, Ruiz A, de Mendonça A, Miltenberger-Miltényi G, Simões do Couto F, Sorbi S, Nacmias B, Bagnoli S, Graff C, Chiang H-H, Thonberg H, Pernecky R, Diehl-Schmid J, Alexopoulos P, Frisoni GB, Bonvicini C, Synofzik M, Maetzler W, vom Hagen JM, Schöls J, Haack TB, Strom TM, Prokisch H, Dols-Icardo O, Clarimón J, Lleó A, Santana I, Almeida MR, Santiago B, Heneka MT, Jessen F, Ramirez A, Sanchez-Valle R, Llado A, Gelpi E, Sarafov S, Tournev I, Jordanova A, Parobkova E, Fabrizi GM, Testi S, Salmon E, Ströbel T, Santens P, Robberecht W, De Jonghe P, Martin J-J, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Sleegers K, Van Broeckhoven C. (2014) Rare mutations in SQSTM1 modify susceptibility to frontotemporal lobar degeneration. *Acta Neuropathologica*; **128**, 397-410. (Journal IF: 9.777, Citations: 1).

Viegas LD, Stolz E, Canhão P, Ferro JM. (2014) Systemic Thrombolysis for Cerebral Venous and Dural Sinus Thrombosis: A Systematic Review. *Cerebrovasc Dis*; **37**, 43-50. (Journal IF: 3.698, Citations: 1).

Gil-Gouveia R, Oliveira A, Martins IP. (2014) Assessment of cognitive dysfunction during migraine attacks: A systematic review. *J Neurol* (Journal IF: 3.841, Citations: 1). [Epub ahead of print]

Martins IP. (2014) Cyclic nocturnal awakening: A warning sign of a cluster bout. *Cephalalgia* (Journal IF: 4.121, Citations: 1). [Epub ahead of print]

Bocchetta M, Galluzzi S, Kehoe PG, Aguera E, Bernabei R, Bullock R, Ceccaldi M, Dartigues J-F, de Mendonça A, Didic M, Eriksdotter M, Félician O, Frölich L, Gertz H-J, Hallikainen M, Hasselbalch SG, Hausner L, Heuser I, Jessen F, Jones RW, Kurz A, Lawlor B, Lleo AB, Martinez-

Lage P, Mecocci P, Mehrabian S, Monsch A, Nobili F, Nordberg A, Rikkert MO, Orgogozo J-M, Pasquier F, Peters O, Salmon E, Sánchez-Castellano C, Santana I, Sarazin M, Traykov L, Tsolaki M, Visser PJ, Wallin ÅK; Wilcock G, Wilkinson D, Wolf H, Yener G, Zekry D, Frisoni GB. (2014) The Use of Biomarkers for the Etiologic Diagnosis of MCI in Europe: an EADC Survey. *Alzheimers Dement* (Journal IF: 17.472, Citations: 1). [Epub ahead of print]

#### **Other publications International**

Antunes P, Teodoro T, Geraldes R. Acute myocardial infarction during thrombolysis. in *More Case Studies in Stroke: Common and Uncommon presentations*. Cambridge University Press. 2014:108-113

Biller J, Ferro JM (eds). Neurologic aspects of systemic disease, Part I. *Handbook of Clinical Neurology*. Aminoff MJ, Boller F, Swaab DF (eds) Elsevier, Edinburgh 2014; vol 119

Biller J, Ferro JM (eds). Neurologic aspects of systemic disease, Part II. *Handbook of Clinical Neurology*. Aminoff MJ, Boller F, Swaab DF (eds) Elsevier, Edinburgh 2014; vol 120

Biller J, Ferro JM (eds). Neurologic aspects of systemic disease, Part III. *Handbook of Clinical Neurology*. Aminoff MJ, Boller F, Swaab DF (eds) Elsevier, Edinburgh 2014; vol 121

de Lacerda JF, Oliveira SN, Ferro JM. Chronic myeloproliferative diseases. *Handb Clin Neurol*. 2014;120:1073-81.

Ferro JM, Canhão P. Cerebral venous sinus thrombosis: update on diagnosis and management. *Curr Cardiol Rep*. 2014;16:523.

Ferro JM, Canhão P. Identification, differential diagnosis and therapy for cerebral venous thrombosis. Schwab S, Hanley D, Mendelow AD (eds). *Critical care of the stroke patient*. Cambridge University Press, 2014:501-514.

Ferro JM, Fonseca AC. Infective endocarditis. *Handb Clin Neurol*. 2014;119:75-91.

Ferro JM, Fonseca C. Clinical features of acute stroke. Norrving B (ed). *Oxford textbook of stroke and cerebrovascular disease*. Oxford University Press, 2014:85-93.

Ferro JM, Martins IP, Caeiro L. Behavioral Neurology of Stroke. Brainin M, Heiss W-D (eds). *Textbook of Stroke Medicine*. Cambridge University Press, 2014: 236-254.

Ferro JM, Oliveira S. Neurologic manifestations of gastrointestinal and liver diseases. *Curr Neurol Neurosci Rep*. 2014;14:487

Ferro JM, Oliveira SN, Correia L. Neurologic manifestations of inflammatory bowel diseases.

Handb Clin Neurol. 2014;120:595-605.

Ferro JM, Verdelho A, Madureira S. Cognitive consequences of small vessel disease. Pantoni L, Gorelick PB (eds) Cerebral small vessel disease. Cambridge University Press, 2014:\236-250.

Ferro JM. Neurologic manifestations of inflammatory bowel disease. Gastroenterology and Hepatology 2014;10:599-600.

Verdelho A. The role of cerebrovascular disease in cognitive decline. In: Galimberti D, Scarpini E (eds). Neurodegenerative Disease. Clinical aspects, molecular genetics and biomarkers. Springer-Verlag, London 2014:65-76.

#### **Other publications National**

Leal, G., Sancho, A. (2014) Validação portuguesa da escala Functional Assessment of Communication Skills for Adults (ASHA -FACS) numa população de pessoas com afasia. Cadernos de Saúde, Vol . 5, N. º 1 e 2, 2012 p. 15-30.

Verdelho A. Actividade física e lazer. Revista Alzheimer Portugal 2014;55:6-7

#### **Invited lectures and seminars**

Albuquerque L, Viana P, Sousa D, Peralta P, Bentes C, Pimentel J. Estado de Mal não Convulsivo. Sessão Clínica Universitária de Neurologia. Aula Magna Faculdade de Medicina de Lisboa, 23 January 2014

Canhão P. Questões práticas na prevenção secundária do AVC com Rivaroxabano. 8º Congresso Português do AVC. Porto, 7 February 2014.

Ferro JM. Acute Stress and cerebrovascular disease. The 2nd International Conference on Heart and Brain, Paris, 27 February -1 March, 2014

Ferro JM. Cerebral Venous Thrombosis. Current Guidelines. 9th World Stroke Congress. Istanbul, 22-25 October 2014

Ferro JM. Dissecções cérvico-cefálicas – tratamento – evidência e recomendações. 8º Congresso Português do AVC. Porto, 6 February 2014.

Ferro JM. Sinus venous thrombosis – presentation of updated guidelines. Stroke update 2014. Stockholm, 16-18 November 2014.

Ferro JM. Stroke prevention: Are we focused on the brain? III Thrombosis Forum Portugal 2014, Lisbon, 11 October 2014

Ferro JM. Poststroke mood disorders. The relevance and management of these sequelae in stroke patients. XXIII European Stroke Conference. Nice, 8 May 2014.

Ferro JM. ESO Guidelines. Sinus venous thrombosis. XXIII European Stroke Conference. Nice, 8 May 2014.

Fonseca C. Heroin, cocaine and other drugs – Alcohol, drugs and stroke. XXIII European Stroke Conference. Nice, 8 May 2014.

Fonseca C. Importância da adesão a terapêutica para protecção do doente. 8º Congresso Português do AVC. Porto, 7 February 2014.

Fonseca C. Nt-pro BNP as a biomarker of cardioembolic stroke. Harvard Medical School Portugal Fellows Forum. Lisbon, 13 November 2014.

Geraldes R. Esclerose Múltipla e Neuromielite Óptica: critérios de diagnóstico e novas terapêuticas. Reunião de Inverno da Sociedade Portuguesa de Neuropediatria. Lisbon, 28 February 2014.

Geraldes R. Diagnostic Complementary investigation and diagnostic criteria in Multiple Sclerosis. EMin lecture. Multiple sclerosis for residents Biogen Idec Program, 25 January 2014.

Geraldes R. Stroke and Connective tissue disorders. European Stroke Conference. Nice, 6 May 2014.

Geraldes R. Vasculites e AVC. Curso de Pós-graduação em AVC. Escola Superior de Enfermagem São Francisco das Misericórdias. Lisbon, 10 May 2014.

Geraldes R. Vertigem e AVC. Reunião de Otoneurologia. Évora, February 2014.

Madureira S. Estratégias de intervenção não farmacológica em doentes com demência. VII Congresso Nacional de Cuidados Paliativos, Carvoeiro, 27-29 March 2014.

Martins IP. Actualização terapêutica em cefaleias em salvas. Sessão do Serviço de Neurologia, Anfiteatro Almeida Lima, Serviço de Neurologia. Hospital de Santa Maria, Lisbon, 9 October 2014.

Martins IP. Organização cerebral da linguagem. Sessão dos internos, Anfiteatro Almeida Lima, Serviço de Neurologia. Hospital de Santa Maria, Lisbon, 26 September 2014.

Martins IP. The art of scientific writing. First Summer course of the European Federation of Neuropsychological Societies. Freie Univ Berlin, Germany, September 2014.

Martins IP. The art of scientific writing. Sessão dos internos, Anfiteatro Almeida Lima, Serviço de Neurologia. Hospital de Santa Maria, Lisbon, 10 October 2014.

Martins IP. Aspectos clínicos e avaliação do défice cognitivo vascular. Curso de Pós-Graduação em Acidente Vascular Cerebral Neurologia comportamental e disfunção cognitiva na doença vascular cerebral, Escola Superior de Enfermagem São Francisco das Misericórdias, Lisbon, 15 March 2014.

Martins IP. Raising a Scientific Question. Programa Doctoral Lisbon BioMed. Faculdade de Medicina de Universidade de Lisboa, Lisbon, 23 January 2014.

Melo TP. Acidente vascular cerebral. I Jornadas do Internato Médico. Lisbon, 14-16 November 2014.

Melo TP. Trombólise fora da indicação aprovada pela EMA. 8º Congresso Português do AVC. Porto, 7 February, 2014.

Santos AC. Evidência actual para a estimulação/reabilitação cognitiva do defeito cognitivo vascular. 8º Congresso Português do AVC. Porto, 7 February 2014.

Sousa D, Martins, IP. Apraxia. Sessão do Serviço de Neurologia, Anfiteatro Almeida Lima, Serviço de Neurologia. Hospital de Santa Maria, Lisbon. Nov 2014.

Verdelho A. Multidisciplinary teams in dementia care. Leaping Forward, Lisboa, 19 February 2014.

Verdelho A. Vascular dementia. Joint EFNS-ENS Congress. Istanbul 3 June 2014.

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

Abreu LP, Teodoro T, Canhão P, Geraldés R. Intracranial varicella zoster virus vasculopathy manifesting as transient ischaemic attacks. Joint Congress of European Neurology, Istanbul, Turkey, 31 May-3 June 2014 (Poster presentation)

Aguiar de Sousa D, Barata Tavares J, Filipa, Geraldo A, Reimaão S, Peralta R, Geraldés R, Albuquerque L. Multiphasic disseminated encephalomyelitis associated with *Campylobacter jejuni* infection. Joint Congress of European Neurology, Istanbul, Turkey, 31 May-3 June 2014 (Poster presentation)

Aguiar de Sousa D, Ferro JM, Canhão P, Barinagarrementeria F, Boussier M-G, Stam J, the ISCVT Investigators. Acetazolamide in acute cerebral venous thrombosis: a case control study. XXIII European Stroke Conference. Nice, 6-9 May 2014. (Poster presentation)

Amarenco P, Lavallée PC, Labreuche J, Albers GW, Bornstein N, Caplan LR, Donnan GA, Ferro J, Hennerici MG, Molina C, Rothwell PM, Steg PG, Uchiyama S, Wong KSL. Baseline characteristics and one-year outcome in 4789 patients included in the TIA registry.org. XXIII European Stroke Conference. Nice, 6-9 May 2014. (Oral presentation)

Castro Caldas A, Silva C, Pimentel J, Ferro J.M. Cerebral amyloid angiopathy-related inflammation. A systematic review of individual reported cases. Joint Congress of European Neurology, Istanbul, Turkey, 31 May-3 June 2014 (Oral presentation)

Coutinho JM, Ferro JM, Canhão P, Barinagarrementeria F, Bousser M-G, Stam J for the ISCVT Investigators. Cerebral venous thrombosis in the absence of headache: a post-hoc analysis of the ISCVT study. XXIII European Stroke Conference. Nice, 6-9 May 2014. (Oral presentation)

Fonseca AC, Geraldes R, Pinho e Melo T, Canhão P, Ferro JM. Wake-up stroke not linked to newly diagnosed atrial fibrillation. XXIII European Stroke Conference. Nice, 6-9 May 2014. (Poster presentation)

Franco AC, Pita Lobo P, Coelho M, Geraldes R, Melo TP. Ischemic stroke presenting with lower limb monochorea/ballism. Joint Congress of European Neurology, Istanbul, Turkey, 31 May -3 June 2014 (Poster presentation)

Gil-Gouveia R, Oliveira AO, Martins IP. The impact of cognitive symptoms on migraine attack related disability. 4th European Headache and Migraine Trust International Congress 2014, Copenhagen, 18-21 September 2014 (Poster presentation)

Henriques I, Gutierrez-Fernandez M, Rodriguez-Frutos B, Ramos J, Ortega L, Navarro I, Cerdan S, Ferro J, Diez-Tejedor E. ADC heterogenetics within acute ischemic lesion predict better functional outcome in experimental stroke. XXIII European Stroke Conference. Nice, 6-9 May 2014. (Oral presentation)

Lanthier S. Ferro J M, Calabrese, Putaala J, Strbian D, Letourneau-Guillon L, Chagnon M, Singhal AB, Salvarani C, Frosch, MP, Guilbert, F, Raymond, J. The International Study on Primary Angiitis of the Central Nervous System (INTERSPACE) Needs More Study Sites: a Special Invitation to Canada. Canadian Stroke Congress Local, Vancouver, Canada, 04-07 October 2014. (Poster presentation)

Martins IP. Mindful aging. Avoiding age related cognitive decline. 10º Simpósio da Fundação Bial "Aquém e Além do Cérebro". Bial Foundation. 10th Symposium "Behind and Beyond the Brain", Casa do Médico, Porto, 26-29 March 2014 (Oral presentation)

### Communications in National Conferences

Abad A, Pompili A, Trancoso I, Fonseca J. "VITHEA - O potencial das tecnologias da fala no tratamento da afasia". IV Workshop "Linguistics, Language Development and Impairment". Faculdade de Letras da Universidade de Lisbon, 31 January 2014. (oral presentation)

Abreu LF, Canhão P, Fonseca AC, Pinho e Melo T. Síndrome de Cotard em doentes cerebrovasculares. Congresso de Neurologia 2014. Lisbon, 12-15 November 2014 (oral presentation)

Abreu LF, Fonseca C, Pinho e Melo T. Canhão P, Magalhães FG. Síndrome de Cotard após acidente vascular cerebral hemorrágico. 8º Congresso Português do AVC. Porto, 6-8 February 2014 (poster presentation)

Abreu LF, Teodoro T, Canhão P. Acidentes isquémicos transitórios como manifestação de vasculopatia intracraniana por vírus varicela zoster. 8º Congresso Português do AVC. Porto, 6-8 February 2014 (oral presentation).

Aguiar de Sousa D, J.M. Ferro, P. Canhão, F. Barinagarrementeria, M.-G. Bousser, J. Stam. Acetazolamide in acute cerebral venous thrombosis: a case-control study. XXIII European Stroke Conference. Nice, France. 6 – 9 May 2014 (poster presentation)

Aguiar de Sousa D, Patrícia Canhão, José M. Ferro. Segurança da Gravidez após Trombose Venosa Cerebral: Revisão Sistemática. Congresso de Neurologia 2014 – Neurologia do Futuro. Lisboa, 13-15 November 2014 (oral presentation)

Alexandrino G, Damásio J, Canhão P, Geraldês R, Melo TP, Correia C, Ferro J. Acidente vascular cerebral no desporto. 8º Congresso Português do AVC. Porto, February 6-8, 2014 (oral presentation)

Alves P, de Carvalho M, Peralta R, Geraldês R, Fonseca AC, Pinho e Melo T. Mioclonias axiais após acidente vascular cerebral isquémico. Congresso de Neurologia 2014. Lisbon, 12-15 November 2014 (poster presentation)

Alves P, Silva C, Baptista J, Fonseca AC. Lateralidade da pneumonia em doentes com acidente vascular cerebral. Congresso de Neurologia 2014. Lisbon, 12-15 November 2014 (oral presentation)

Alves P, Silva H, Geraldês R, Fonseca C. IV e V pares como forma de apresentação de Siderose Superficial do Sistema Nervoso Central. Forum de Neurologia 2014. Coimbra, 15-17 May 2014 (poster presentation)

Baeta E, Rocha R, Brito C, Martins IP. Calculo e Processamento de Números pela numa População Saudável. Reunião da Secção de Neurologia do Comportamento. Fórum de



Neurologia, Hotel Vila Galé, Coimbra, 16 May 2014 (Oral presentation)

Castro Caldas A, Martins I, Soares AP, Canhão P. AVC isquémico secundário a síndrome de hiperestimulação do ovário. 8º Congresso Português do AVC. Porto, 6-8 February 2014 (poster presentation)

Cipriano M, Maruta C, Freitas V, Martins IP. Contributo de um teste de memória de cinco palavras na avaliação cognitiva. Reunião da Secção de Neurologia do Comportamento. Fórum de Neurologia, Hotel Vila Galé, Coimbra, 16 May 2014 (Oral presentation)

Farrajota L, Fonseca J, Leal G, Martins IP. Quando a segunda língua emerge na afasia. Características do discurso em dois casos clínicos. Reunião do Grupo da Neurologia do Comportamento. Congresso de Neurologia, Lisboa, 12-15 November 2014 (Oral presentation)

Fonseca J, Leal G, Farrajota L, Pinho e Melo T, Fonseca AC, Morgado J, Miranda F, Martins IP. Afasia no Acidente Vascular agudo: uma série de 350 casos. Reunião do Grupo de Neurologia do comportamento. Lisbon, 12 November 2014 (oral presentation).

Fonseca AC, Canhão P, Martins IP. Dois casos de amnesia. Reunião do Grupo da Neurologia do Comportamento. Congresso de Neurologia, Lisboa, 12-15 November 2014 (Oral presentation)

Fonseca J. As pessoas com afasia submetidas a trombólise são diferentes? VII Congresso Nacional da Associação Portuguesa de Terapeutas da Fala Fundação Portuguesa das Comunicações, Lisboa, 14-15 November 2014 (Oral presentation)

Fonseca J. O que é que os terapeutas da fala pensam acerca da relação entre afasia e trombólise. VII Congresso Nacional da Associação Portuguesa de Terapeutas da Fala Fundação Portuguesa das Comunicações, Lisboa, 14-15 November 2014 (Oral presentation)

Fonseca J, Leal G, Farrajota L, Martins IP. A plataforma VITHEA – para o tratamento online da afasia. 8º Congresso Português do AVC. Porto, 6-8 February 2014 (Poster presentation).

Fonseca J, Maruta C, Campos AR, Farias JP, Martins IP. Mapeamento intra-operatório da linguagem em doentes operados acordados a tumores cerebrais. Simpósio “Terapia da Fala: a diversidade de uma Profissão” Escola Superior de Saúde de Alcoitão, Alcoitão, 6 June 2014. (Oral presentation)

Franco A, Abreu LF, Lobo PP, Coelho M, Geraldês R, Melo TP. Monocoreia/balismo como forma de apresentação de acidente vascular cerebral isquémico do território vertebro-basilar. 8º Congresso Português do AVC. Porto, February 6-8, 2014 (Oral presentation)

Gil-Gouveia R, Pinto J, S, Figueiredo P, Vilela P, Martins IP. Perfusão Cerebral durante a crise de Enxaqueca sem Aura por Ressonância Magnética com a técnica ASL. Congresso de Neurologia, Lisboa, 12-15 November 2014 (Oral presentation)

Henriques I, Gutiérrez-Fernández M, Rodríguez-Frutos B, Ramos J, Díez-Tejedor E, Ferro J. Menor tamanho e melhor resultado funcional com sulfuro de hidrogéneo após enfarte cerebral: mecanismo de protecção inclui regulação das espécies reactivas de oxigéneo. 8º Congresso Português do AVC. Porto, February 6-8, 2014 (Oral presentation)

Homem C, Geraldés R, Fonseca AC, Pinho e Melo T. Ressonância Magnética crânio-encefálica com sequência de difusão negativa:exclui o diagnóstico de acidente vascular cerebral isquémico em fase aguda? Forum de Neurologia 2014. Coimbra, May 15-17, 2014 (Poster presentation)

Lobo Antunes M, Fonseca AC, Pacheco E, Pinho e Melo T. Acidente Vascular Cerebral no ar. Forum de Neurologia 2014. Coimbra, May 15-17, 2014 (Poster presentation)

Mares I, Smith M, Johnson MH, Senju A. Detecção e processamento do contacto ocular: um estudo de potenciais evocados. Reunião da Secção de Neurologia do Comportamento. Fórum de Neurologia, Hotel Vila Galé, Coimbra, 16 May 2014 (Oral presentation)

Martins IP, Maruta C, Fonseca AC, Canhão P. Dois casos de amnésia. Reunião do Grupo de Neurologia do comportamento. Lisbon, 12 November 2014 (Oral presentation).

Martins IP. Enxaqueca e vertigem. Reunião anual da APO-Associação Portuguesa de Otoneurologia. Salgados Grande Hotel, Albufeira, 20-21 June 2014 (Oral presentation)

Martins IP. Vertigem migranosa. Síndrome Vestibular Agudo, VI Reunião de Inverno da APO. Ecorkhotel, Évora, 8 February 2014 (Oral presentation)

Maruta C, Ferreira C, Guerreiro M, Castelo-Branco M, Miltenyi G, Almeida MR, Santiago B, de Mendonça A. Understanding the initial phases of genetic frontotemporal lobar degeneration - setting the stage for prevention trials. 28th Grupo de Estudos de Envelhecimento Cerebral e Demências Meeting, Aveiro, 27-28 June 2014 (Oral presentation)

Maruta C, Maroco J, de Mendonça A, Guerreiro M. Alterações do comportamento na Afasia Primária Progressiva. Reunião do Grupo da Neurologia do Comportamento. Congresso de Neurologia, Lisboa, 12-15 November 2014 (Oral presentation)

Maruta C, Pereira T, Madeira S, De Mendonça A, Guerreiro M. Classification of Primary Progressive Aphasia: Do unsupervised data-mining methods support a logopenic variant?. 28th Grupo de Estudos de Envelhecimento Cerebral e Demências Meeting, Aveiro, 27-28 June 2014 (Oral presentation)

Mota E, Magalhães A, Santos M, Canhão P, Fonseca AC. Associação entre arterite das células gigantes, polimialgia reumática e acidente isquémico transitório: a proposito de um caso clinico. 15º Congresso do núcleo de estudos da doença vascular cerebral. Porto, 28-29 November 2014 (Poster presentation)

Oliveira Santos M, Geraldés R, Melo TP. Acidente vascular cerebral isquémico como manifestação inaugural de neoplasia do pulmão. Congresso de Neurologia 2014. Lisbon, 12-15 November 2014 (Poster presentation)

Sousa D, Almeida J, Martins IP. Apraxias. Sessão do Serviço de Neurologia, Anfiteatro Almeida Lima, Serviço de Neurologia. Hospital de Santa Maria, Lisboa, 20 November 2014. (Oral presentation)

### **Organisation of Conferences**

Martins IP (organizing Committee). From Clinic to Research: Design, Analysis, Ethics. First Summer School of the Federation of the European Societies of Neuropsychology, Berlin, September 1-4, 2014.

Martins IP – organizer “Dendrophilia: Human Tree Processing in Comparative Perspective” palestrante: W Tecumseh Fitch, University of Vienna. Language Evolution Seminar. Faculdade de Medicina da Universidade de Lisboa, edifício Egas Moniz, Lisboa, September, 8, 2014,

Martins, I.P., Maruta, C. organizer- I Curso Pós-Graduado de Actualização - AVALIAÇÃO NEUROPSICOLÓGICA. Laboratório de Estudos de Linguagem, Faculdade de Medicina da Universidade de Lisboa, November 7-8, December 5-6 2014 and January 9, 2015

Canhão P - Comissão Organizadora. 8º Congresso de Acidente Vascular Cerebral, Porto, February 6-8, 2014.

Ferro JM - Comissão Organizadora. Leaping Forward. Lisbon International Clinical Congress, Lisbon 13-19 February 2014.

Ferro JM, Verdelho A - Comissão Organizadora., Leaping Forward - Módulo – Mind, Cognition and Neurodegeneration. Lisbon February 13-19, 2014.

### **Internationalisation**

Ana Catarina Fonseca - Member of the Young stroke physicians committee da European Stroke Organization

José M. Ferro - Member of the Scientific Panel for Health do Directorate- General for Research and Innovation (Directorate E – Health) EU- Horizon 2020

### **Prizes, honours and awards**

Winner of the 2013 International Journal of Language and Communication Disorders Article Prize. Martins, I.P., Leal, G., Fonseca, I., Farrajota, L., Aguiar, M., Fonseca, J., Lauterbach, M., Gonçalves, L., Cary, M.C., Ferreira, J.J., Ferro, J.M. (2014) A randomized, rater-blinded, parallel trial of intensive speech therapy in sub-acute post-stroke aphasia: the SP-I-R-IT study.

2º prémio Cefaleias. Sociedade Portuguesa de Cefaleias. Gil-Gouveia, R., Oliveira, A, Martins, I.P. (2014) A short battery for cognitive assessment migraine.

3º prémio Cefaleias. Sociedade Portuguesa de Cefaleias. Gil-Gouveia, R., Oliveira, A, Martins, I.P. (2014) Clinical utility of the Mig-SCog.

Prémio João Lobo Antunes 2014 atribuído pela Sociedade Portuguesa de Neurologia – Ana Catarina Fonseca

### **Industry contract research**

Clinical trial TAMIGA - A double-blind, placebo-controlled, randomised, Phase IIIb trial evaluating the efficacy and safety of standard of care (SOC)+/-continuous bevacizumab treatment following progression of disease (PD) in patients with glioblastoma (GBM) after first (1st)-line treatment with radiotherapy, temozolomide and bevacizumab.

Clinical trial with the H3 histamine antagonist in Alzheimer's disease (SCL-38093-012).

Clinical trial the monoclonal antibody against B-amyloid, gantenerumab (Scarlet Road study and Marguerite study).

Clinical trial and the B-secretase inhibitor, MK-8931, in Alzheimer's disease.

GLORIA, Bi Trial nº 1160.136, Phase II-III - Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation. (Boehringer Ingelheim)

LIFE, Protocol F02695 LP 2 05 - Effect of 3-month treatment with F2695 (75 mg OD) on improving functional recovery of patients with ischemic Stroke. A Multicenter, Randomised, Double-blind, Parallel-group, Placebo-Controlled Study. (Pierre Fabre Médicament)

XANTUS, Protocolo XA1101–Impact nº 15914– Xarelto® on prevention of stroke and non-central nervous system systemic embolism in patients with non-valvular atrial fibrillation (Bayer Portugal, SA)

TO ACT – Project nº 1227201 Trómbolise ou Anticoagulação para Trombose Venosa Cerebral/

Thrombolysis Or Anticoagulation for Cerebral venous Thrombosis (Eurotrials)

ORATÓRIO - A Phase III, multicenter, randomized, parallel-group, double-blinded, placebo controlled study to evaluate the efficacy and safety of ocrelizumab in adults with Primary Progressive Multiple Sclerosis. (Roche)

EXPAND - A multicenter, randomized, double-blind, parallel-group, placebo-controlled variable treatment duration study evaluating the efficacy and safety of Siponimod (BAF312) in patients with secondary progressive multiple sclerosis. (Novartis)

MOVE 1 – Melhorias de Mobilidade (MObility ImProVEments) com Espasticidade em Esclerose Múltipla. Recolha de dados retrospectiva sobre a prestação de cuidados e a satisfação com o tratamento de doentes com esclerose múltipla com espasticidade. (Almirall)

ORACLE - A Phase III, randomized, double-blind, placebo-controlled, multicenter clinical trial of oral cladribine in subjects with a first clinical event at high risk of converting to MS (Merck)

#### **Science and society**

Abad A, Pompili A, Trancoso I, Martins IP, Fonseca J. (2014) VITHEA – Terapia Virtual. Exposição Loucura - Ciência Viva, Pavilhão do Conhecimento. October to September 2015. [www.pavconhecimento.pt/visite-nos/exposicoes/detalhe.asp?id\\_obj=3076](http://www.pavconhecimento.pt/visite-nos/exposicoes/detalhe.asp?id_obj=3076).

Patricia Canhão - Participação na Organização das comemorações do dia Nacional do Doente com AVC 2014

Ruth Geraldés – Participação na reunião de doentes com Esclerose múltipla Academia 35 com a apresentação “O que significa correr riscos na esclerose múltipla?” , organizada pela Sociedade Portuguesa de Esclerose Múltipla. Divulgação da referida reunião através dos meios de comunicação social – entrevista no Correio da Manhã TV e na TVI

#### **PhD thesis completed**

Ana Catarina Gaspar Fonseca 25/02/2014 Papel do peptídeo natriurético cerebral de tipo B na classificação do tipo de AVC isquémico Universidade de Lisboa José M. Ferro

João Carlos Correia de Sá 19/03/2014 Captura recaptura como método epidemiológico a aplicar à Esclerose Múltipla Universidade de Lisboa José M. Ferro

Mauricio de Jesus Dias Martins 08/09/2014 Language Evolution and Recursion: Developing Analyses Methods for Recursive Patterns Recognition. Universidade de Lisboa Tecumseh Fitch Isabel Pavão Martins

### **Msc thesis completed**

Gonçalo Alexandrino 27/06/2014 Acidente Vascular Cerebral e Desporto: Um Estudo Multicêntrico em Portugal. Série de casos retrospective Universidade de Lisboa José M. Ferro

Rita Pimenta 27/06/2014 Vasculites Cerebrais na Doença Inflamatória Intestinal Universidade de Lisboa José M. Ferro

Carla Ferreira 27/06/2014 Moya Moya disease: Literature review and case report Universidade de Lisboa José M. Ferro

Catarina de Oliveira Pinho 27/06/2014 Prognóstico de Acidentes Neurológicos Transitórios com sintomas atípicos Universidade de Lisboa Patrícia Canhão

Filipa Isabel Moreira Bárbara Fidalgo Carioca 27/06/2014 Blood biomarkers and stroke recurrence in patients with transient ischemic attack Universidade de Lisboa Patricia Canhão

## Leonor Saúde Lab

### Major Interests / Objectives

We would like to understand the cellular and molecular mechanisms controlling the left-right asymmetric placement of internal organs and the bilateral symmetric formation of musculoskeletal elements in vertebrates. In addition we are interested in making the bridge between the fundamental developmental processes that we have been studying with the mechanisms that have to be activated during regeneration upon severe injury.

### Head of Unit

Maria Leonor Tavares Saúde, PhD, Invited Assistant Professor

### Research Team

Ana Catarina Esteves Ribeiro	PhD	Post doctoral Investigator
Ana Margarida Pereira Cristovão Pinto	Graduate	Technician
Ana Rita Isidro Farinho	Master	Technician, (started February)
António José Fernandes da Silva Francisco	Graduate	PhD Student, Faculdade Medicina da Universidade de Lisboa , Teaching Assistant
Dalila Maria Neves Silva	Undergraduate	Trainee, (started February)
Diana Martins Bordalo	Graduate	MSc Student, (started July)
Henrique Caldeilla Sentieiro Lyon de Castro	Graduate	MSc Student, (started September)
Marta Sofia da Silva Rodrigues	Graduate	MSc Student, (started June)
Raquel Valente Mendes	Graduate	PhD Student
Rita Alexandra Rodrigues Pinto	Master	PhD Student

Rita Joana Soares Serrano	Graduate	MSc Student, (left May)
Sara Maria Ferreira Fernandes	Master	PhD Student
Susana Alexandra Rodrigues Pascoal	PhD	Post doctoral Investigator

#### Keywords / Research Areas

Left-right asymmetry, Somite formation, Tissue/organ regeneration

#### Major scientific achievements

We uncovered the mechanism that helps to lock the Left and the Right identities once these are established in the vertebrate embryo and published these findings in a *Developmental Cell* paper in the summer.

Raquel V. Mendes, a PhD student in the unit, graduated successfully and will continue her postdoctoral training at the Champalimaud Foundation.

#### Selected Publications

Mendes R.V., Martins G.G., Martins A.M. and 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. (Journal IF: 10,366, Citations: 0)

Fior R., Maxwell A.A., Ma T.P., Vezzano A., Moens C.B., Amacher S.L., Lewis J. and Saúde L. (2012) Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by *Mesogenin1*. *Development* **139**(24), 4656-65. (Journal IF: 6,273, Citations: 10)

Azevedo A.S., Sousa S., Jacinto A. and Saúde L. (2012) An amputation resets positional information to a proximal identity in the regenerating zebrafish caudal fin. *BMC Developmental Biology* **12**(1), 24. (Journal IF: 2,752, Citations: 5)

Azevedo A.S., Grotek B., Jacinto A., Weidinger G. and Saúde L. (2011) The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. *PLoS ONE* Vol. **6**(7), e22820. (Journal IF: 3,534, Citations: 11)



Lopes S.S., Lourenço R., Pacheco L., Moreno N., Kreiling J. and Saúde L. (2010) Notch signalling regulates left-right asymmetry through ciliary length control. *Development*, **21**, Vol.1373 625-32. (Journal IF: 6,273, Citations: 36)

#### **Ongoing Research Projects**

2012/2015 Title: Uncover the molecular mechanism downstream of Dmrt2a/Terra that coordinates symmetry versus asymmetry along the left-right axis. Coordinator: Maria Leonor Tavares Saúde. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-BID/119627/2010. Amount: 109,755€.

2013/2015 Title: Prémio L’Oreal 2012. Coordinator: Maria Leonor Tavares Saúde. Agency: L’Oreal Portugal Lda. Reference: Prémio L’Oreal 2012. Amount: 20,000€.

2013/2015 Title: Uncovering cellular mechanisms of spinal cord regeneration in zebrafish and their modulation with aging. Coordinator: Maria Leonor Tavares Saúde. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/BIM-MED/1375/2012 . Amount: 181,199€.

#### **Publications in peer review Journals**

Mendes R.V., Martins G.G., Martins A.M. and 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. (Journal IF: 10,366, Citations: 0)

#### **Invited lectures and seminars**

Saúde, L. Cell movement choreographies that shape the vertebrate body plan. Departamento de Ciências Biomédicas e Medicina da Universidade do Algarve, Faro, Portugal, January 16, 2014

Saúde, L. The amazing regenerative capacity of the zebrafish. Encontro ENEBioq FCT-UNL, Monte da Caparica, Portugal, April 12, 2014

Saúde, L. The zebrafish in Biomedical Research. Serviço de Neurologia, Hospital de Santa Maria, Lisboa, Portugal, April 23, 2014

Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen’s node cells. Simpósio Anual do GABBA 2014, ICBAS, Porto, Portugal, July 17, 2014

Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. X Meeting Spanish Society for Developmental Biology, Madrid, Spain, October 13, 2014

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

Saúde, L. Quaking A, a post-transcriptional regulator of early patterning in zebrafish, The 3rd European PI Meeting, Ein Gedi, Israel. 30 March-3 April (Poster Presentation)

Ribeiro, A & Saúde, L. Foxj1a-positive cells at the center of spinal cord regeneration in zebrafish. Development and Regeneration of the Spinal Cord, EMBO Workshop, Sitges, Spain. 1-4 October (Poster Presentation)

Pinto, R., Almeida-Santos, J. & Saúde, L. Asymmetry versus Symmetry: the role of Dmrt2a in the formation of the vertebrate body plan, X Meeting of the Spanish Society of Developmental Biology, Madrid, Spain. 13-15th October (Poster Presentation)

#### **Advanced teaching**

Saúde, L. lectured "EMT/MET processes in vertebrate development", Pro-RegeM - PhD PROGRAMME in MECHANISMS of DISEASE and REGENERATIVE MEDICINE, Universidade do Algarve, Faro. January 16, 2014

Saúde, L. lectured "The importance of Cilia in Development and Disease", BioSys - PhD in Biology/Biochemistry, Faculdade de Ciências da Universidade de Lisboa. February 10, 2014

Saúde, L. lectured "The timing of progenitor differentiation during somitogenesis", IGC PhD Programme - Integrative Biology and Biomedicine, IGC, Oeiras. February 19, 2014

Saúde, L. co-organized and lectured the course "Genetics & Development", Programa de Pós-Graduação Ciência para o Desenvolvimento, Praia, Santiago, Cape Verde. March 3-7, 2014

Saúde, L. lectured "Left-Right Patterning", GABBA PhD Programme, IBMC, Porto. March 12, 2014

Saúde, L. lectured "The amazing regenerative capacity of the zebrafish", GABBA PhD Programme, IBMC, Porto. June 16, 2014

Saúde, L. lectured "Left-Rigth Patterning", Mestrado em Biologia Evolutiva e do Desenvolvimento, FCUL, Lisboa. November 11, 2014

### **PhD thesis completed**

Raquel Valente Mendes 29/10/2014 What is the role of the cell adhesion N-cadherin in the molecular and morphological asymmetries of the Hensen's node Faculdade de Medicina da Universidade de Lisboa Leonor Saúde

### **Msc thesis completed**

Tiago Maçarico 18/12/2014 Uncovering the effect of low doses of ionizing radiation in angiogenesis during spinal cord regeneration Faculdade de Ciências da Universidade de Lisboa Ana Ribeiro

Rita Serrano 09/05/2014 The Role of Hedgehog Signalling during Larvae Fin Fold Regeneration Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa Susana Pascoal

### **Science and society**

Leonor Saúde. Collaboration with artist Herwig Turk in "Conversation that never took place" an installation presented in Lisbon, Coimbra and Vienna.

## Luís Costa Lab

### Major Interests / Objectives

We direct our research to address at the pre-clinical level the mechanistic effects that explain our major clinical questions. Focusing in metastasis, we aim to understand if metastases genetically and phenotypically recapitulate the primary tumors, and how important are the tumor-target organ/host interactions. Our major interests were: (I) to identify prognostic and/or predictive markers, and new therapeutic targets in bone metastases; (II) to identify a molecular signature of colorectal cancer metastization, and to determine if chemotherapy-induced cell senescence may be related with relapse; (III) to understand the role of phospholipase C epsilon in tumor progression ; and (IV) to identify new therapeutic strategies by studying the role of tumor-associated ECM in cancer progression.

### Head of Unit

Luis António Marquês da Costa, MD/PhD

### Research Team

Afonso Camilo Rodrigues Fernandes	PhD	Consultant
Arlindo Júlio Rebelo da Silva Ferreira	Master	Investigator, MD
Diana Domingos de Matos	Graduate	MSc Student
Inês Maria Duarte Vaz Luis	Graduate	Investigator, HSM , Teaching Assistant
Isabel Cristina Ferreira Fernandes Borges da Costa	Master	Investigator, chln , Clinical Specialist , Assistant Professor
Joana Maria Tato Ribeiro Costa	Graduate	Technician, (started October)
Margarida Caracol Castanho Lopes Matias Ghesquiere	Graduate	Investigator, CHLN , Clinical Specialist
Maria José Palma Bettencourt	Graduate	MSc Student, (started November)
Mário Alberto Ferreira Maia Matos	Graduate	MSc Student
Marta Sofia Alves Martins	PhD	Post doctoral Investigator, (started April)

Ricardo Castanheira Pires	Graduate	Technician
Rudolfo Pais Mendes Ferreira Francisco	Graduate	Consultant, (started September)
Sandra Cristina Cana de Anjo Casimiro	PhD	Post doctoral Investigator
Sandra Sofia Chorão Lavajo Lucas	Graduate	Administrative
Sara Santos Henriques	Graduate	MSc Student
Tânia Elisa dos Santos Silva	Graduate	Administrative, (started July)
Teresa Raquel Duarte Pacheco	PhD	Post doctoral Investigator

#### **Keywords / Research Areas**

Metastasis, bone “vicious cycle, tumor microenvironment, extracellular matrix, tumor heterogeneity, tumoral pathway-targeted therapies

#### **Major scientific achievements**

In 2014 we hosted the meeting “A choice of challenges in breast cancer” that was conceived to commemorate the 60th anniversary of Hospital de Santa Maria. In the scope of our collaboration at the Global Cancer Genomics Consortium (GCGC) we continue to develop scientific projects in the area of cancer metastases and the genomic of breast tumors. Our research line in bone metastases conducted to publications mostly focused on clinical research.

We showed that high expression of the oncogene methaderin (MTDH) can be considered a biomarker of relapse in CRC, including lung-specific relapse.

We developed a new field of research to study the role of Phospholipase C epsilon (PLC?) which was characterized as a direct effector of Ras in the progression of colorectal cancer (CRC). Detailed analysis of PLC? expression in our collection of human CRC biopsies is ongoing with the potential application as a biomarker of tumour progression.

### Selected Publications

Costa L (2014) Which bisphosphonate to treat bone metastases?. *Lancet Oncology* **15**, 16. (Journal IF: 24.725, Citations: 0)

Costa L., Casimiro S., Gupta S., Knapp S., Pillai M.R., Toi M., Badwe R., Carmo-Fonseca M., Kumar R. (2014) The global cancer genomics consortium's third annual symposium: from oncogenomics to cancer care. *Genes & Cancer* **5**, 64. (Journal IF: NA, Citations: 0)

Casimiro S, Fernandes A, Oliveira AG, Franco M, Pires R, Peres M, Matias M, Tato-Costa J, Guerra N, Ramos M, Cruz J, Costa L (2014) Metadherin expression and lung relapse in patients with colorectal carcinoma. *Clin Exp Metastasis* **31**, 689. (Journal IF: 3.725, Citations: 0)

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. (Journal IF: 9.284, Citations: 8)

Henry D, Vadhan-Raj S, Hirsh V, von Moos R, Hungria V, Costa L, Woll PJ, Scagliotti G, Smith G, Feng A, Jun S, Dansey R, Yeh H. (2013) Delaying skeletal-related events in a randomized phase 3 study of denosumab versus zoledronic acid in patients with advanced cancer: an analysis of data from patients with solid tumors. *Support Care Cancer* **22**, 679. (Journal IF: 2.495, Citations: 4)

### Ongoing Research Projects

2011/2014 Title: Synthesis, Characterization and Biological Assessment of Multi-Functional Bone-Seeking Agents. Coordinator: Luis António Marquês da Costa. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/QUI-QUI/115712/2009. Amount: 50,064€.

2011/2015 Title: Mechanisms of invasion and progression in metastatic bone disease. Coordinator: Inês Maria Duarte Vaz Luis. Agency: Fundação Ciência e Tecnologia. Reference: HMSP-ICS/0004/2011. Amount: 400,000.01€.

2013/2016 Title: Colagenio do Cancro da Mama. Coordinator: Luis António Marquês da Costa. Agency: Celgene Sociedade Unip., Lda.. Reference: Colagenio do Cancro da Mama. Amount: 4,000€.

2013/2014 Title: Caracterização Molecular de Carcinomas da Mama. Coordinator: Sandra Cristina Cana de Anjo Casimiro. Agency: Novartis Farma, S.A.. Reference: Caracterização Molecular de Carcinomas da Mama. Amount: 10,000€.

2013/2015 Title: Molecular and Nano Tools for Cancer Theranostics. Coordinator: Luis António

Marquês da Costa. Agency: Fundação Ciência e Tecnologia. Reference: EXCL/QEQ-MED/0233/2012. Amount: 33,000€.

2013/2015 Title: C-MET in Bone Metastases. Coordinator: Luis António Marquês da Costa. Agency: Merck, S.A.. Coordinator PI: Sandra Casimiro. Reference: C-MET in Bone Metastases. Amount: 21,000€. Amount (total): 21,000€.

2014/2015 Title: CancerSys - Multiscale modeling for personalized therapy of bone metastasis. Coordinator: Luis António Marquês da Costa. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/EMS-SIS/1954/2013. Amount: 20,049€.

2014/2015 Title: Mechanisms and relevance of Phospholipase C epsilon downregulation in cancer. Coordinator: Marta Sofia Alves Martins. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BIM-ONC/1048/2013. Amount: 37,700€.

2014/2015 Title: Relative effectivity of aromatase inhibitors versus tamoxifen in patients with early breast cancer. Coordinator: Arlindo Júlio Rebelo da Silva Ferreira. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: HMSP-ICJ/0007/2013. Amount: 100,000€.

2014/2015 Title: Papel da Fosfolipase C. Coordinator: Luis António Marquês da Costa. Agency: Merck, S.A.. Reference: Papel da Fosfolipase C. Amount: 4,208.4€.

2014/2016 Title: Mechanisms of invasion and progression of cancer in bone: Molecular profiling of matrix and adhesion-related molecules in metastatic disease. Coordinator: Sandra Cristina Cana de Anjo Casimiro. Agency: Liga Portuguesa Contra o Cancro. Reference: Liga Portuguesa contra o cancro /Terry Fox. Amount: 10,000€.

#### **Other Projects**

2011/2014 Mechanisms of invasion and progression in metastatic bone disease and outcomes in HER2 positive metastatic breast cancer. Coordinator: Inês Vaz Luis.

2012/2014 Activation of mTOR pathway in breast cancer: analysis of primary and metastasis tumor samples. Coordinator: Luis Costa.

2013/2014 Clinical significance of the AKT/mTOR pathway activation in KRAS-wt metastatic colorectal cancer response to EGFR-targeted therapy. Coordinator: Luis Costa.

2013/2017 Advanced breast cancer: prognosis and therapeutics. Coordinator: Sandra Casimiro.

2013/2015 Luminal-type breast cancer: prognostic value of RANK-positive lymphatic nodes. Coordinator: Sandra Casimiro.

### Publications in peer review Journals

Costa L. (2014) Which bisphosphonate to treat bone metastases?. *Lancet Oncol.* **15**, (1), 16-16. (Journal IF: 24.725, Citations: 0)

Costa L. (2014) Bisphosphonates in adjuvant setting for breast cancer: a review of the meta-analysis of bisphosphonate's effects on breast cancer recurrence presented in December 2013 at San Antonio Breast Conference Current Opinion in *Supportive & Palliative Care.* **8** (4) 414-419, 2014 (Journal IF: NA; Citations 0)

Casimiro S, Fernandes A, Oliveira AG, Franco M, Pires R, Peres M, Matias M, Tato-Costa J, Guerra N, Ramos M, Cruz J, Costa L (2014) Metadherin expression and lung relapse in patients with colorectal carcinoma. *Clin Exp Metastasis.* **31**(6):689-96. (Journal IF: 3.725, Citations: 0)

Costa L., Casimiro S., Gupta S., Knapp S., Pillai M.R., Toi M., Badwe R., Carmo-Fonseca M., Kumar R. (2014) The global cancer genomics consortium's third annual symposium: from oncogenomics to cancer care. *Genes & Cancer* **5**(3-4): 64-70. (Journal IF: NA, Citations: 0)

Fernandes C, Monteiro S, Mendes P, Gano L, Marques F, Casimiro S, Costa L, Correia JGD, Santos I (2014) Biological assessment of novel bisphosphonate-containing 99mTc/Re-organometallic complexes. *Journal of Organometallic Chemistry.* **760**:197-204. (Journal IF: 2.302, Citations: 0)

Castaldo S, da Silva A, Matos A, Inácio A, Bicho M, Medeiros R, Alho I, Bicho M: The role of CYBA (p22phox) and catalase genetic polymorphisms and their possible epistatic interaction in cervical cancer. *Tumor Biology* 2014:**1-6**. (Journal IF:2.840 Citations:0)

Gaspar D, Freire JM, Pacheco TR, Barata JT, Castanho MA. 2014. Apoptotic human neutrophil peptide-1 anti-tumor activity revealed by cellular biomechanics. *Biochim Biophys Acta.* **1853**(2):308-316 (Journal IF: 5,297 Citations: 0)

Vaz-Luis I, Keating NL, Lin NU, Lii HC, Winer EP, Freedman RA (2014) Duration and Toxicity of Adjuvant Trastuzumab in Older Patients With Early-Stage Breast Cancer: A Population-Based Study. *JCO*, **32**(9): 927 (Journal IF: 17.96 Citations: 3)

Vaz-Luis I, Ottesen RA, Hughes ME et al. (2014) Outcomes by Tumor Subtype and Treatment Pattern in Women With Small, Node-Negative Breast Cancer: A Multi-Institutional Study. *JCO*,



**32(20): 2142** (Journal IF: 17.96 Citations: 3)

Freedman RA, Vaz-Luis I, Barry WT et al. (2014) Patterns of chemotherapy, toxicity, and short-term outcomes for older women receiving adjuvant trastuzumab-based therapy. *Breast Cancer Res & Treat.* **145(2):** 491-501 (Journal IF: 4.198 Citations: 1)

Seah DS, Vaz-Luis I, Olson E, Sohl J, Litsas G, Winer EP, Lin NU, Burstein HJ. (2014) Use and duration of chemotherapy in patients with metastatic breast cancer according to tumor subtype and line of therapy. *JNCCN*, **12(1):**71-80 (Journal IF: 4.273 Citations: 1)

#### **Other publications International**

Toi M., Pillai M.R., Sudeep S., Badwe R., Carmo-Fonseca M., Costa L., Chow L.WC., Knapp S., and Kumar R.(2014) The global cancer genomics consortium's symposium: new era of molecular medicine and epigenetic cancer medicine - cross section of genomics and epigenetics" *Genes & Cancer, Advance Publications*, December 2014 (Journal IF:NA , Citations 0)

#### **Invited lectures and seminars**

*Costa L. Treatment of bone metastases from breast cancer. Innovation in Breast Cancer – IBC 2014, Madrid, Spain, February 22, 2014*

*Costa L. Re-visiting the vicious cycle in bone metastases: Host Variability and Oncodynamics. OHRI Lab Seminar*

*Costa L. Current & Novel Therapies for Bone Metastases - Moving away from bone-targeted agents? Current agents, indicators of response, sensitivity and resistance Bonus 9 Meeting organized by the Ottawa Hospital Cancer Centre. Canada, April 24-25, 2014*

*Costa L. The current status of treatment of cancer-related bone disease. Haukeland University Hospital, Bergen, Norway. May 14, 2014*

*Costa L. An update in the management of bone metastases in patients with solid tumours: overview of the clinical data and practicalities of management. Update on the Optimization of Care for Cancer Patients with Bone Metastases: a meeting for Healthcare Professionals at the Royal College of Obstetricians and Gynecologists, Regent's Park London, London, UK, June 10, 2014.*

*Costa L. Cancer Metastases: is bone a useful paradigm? 1st ASPIC International Congress. F. Calouste Gulbenkian, Lisboa, Portugal, November 26, 2014.*

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

D. Gaspar, J.M. Freire, T.R. Pacheco, J.T. Barata, M.A. Castanho. Evaluation of tumor cell's biomechanical properties for assessing the chemotherapy efficacy of anticancer peptides. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 Novembro 2014 (Poster Presentation)

Ribeiro EM, Fernandes C, Marques F, Galamba JDG, Matos D, Alho I, Casimiro S, Santos I. Block copolymer micelles for therapy of bone metastases. 1st ASPIC International Congress, Lisboa, Portugal, 25-26 Novembro 2014 (Poster Presentation)

Vaz-Luis I, Hughes ME, Cronin A, Rugo HS, Edge SB, Moy B, Theriault RT, Winer EP, Lin NU. Emerging trends in type of chemotherapy (CT) received among patients (pts) with stage I breast cancer (BC). ASCO 2014, Chicago, IL, USA, 30 May - June 3 2014 (Poster presentation)

Vaz-Luis I, Keating NL, Lin NU, Lii J, Winer EP, Freedman RA. Disparities among older women with de novo stage IV breast cancer treated with trastuzumab from 1999 to 2009. ASCO 2014, Chicago, IL, USA, 30 May - June 3 2014 (Poster presentation)

Mayer E, Vaz-Luis I, Richardson A, Perou C, Lehmann B, Fraser Symmans W, Barry W, Wolff A, Winer EP. TBCRC030: A randomized phase II study of preoperative cisplatin versus paclitaxel in patients (pts) with BRCA1/2-proficient triple negative breast cancer (TNBC): Evaluating the Homologous Recombination Deficiency (HRD) Biomarker. ASCO 2014, Chicago, IL, USA, 30 May - June 3 2014 (Poster presentation)

Freedman, R, Vaz-Luis I, Barry W, Wagle N, Isakoff S, Tung N, Galler S, Sohl J, Lowe A, Krop I, Winer EP, Lin, NL. A Phase II study of Eribulin Mesylate in Combination with Trastuzumab and Pertuzumab in Patients (pts) with Metastatic, Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer. ASCO 2014, Chicago, IL, USA, 30 May - June 3 2014 (Poster presentation)

Vaz Luis I, Hughes ME, Cronin A, Rugo H, Edge S, Moy B, Theriault R, Hassett M, Winer EP, Lin NU. Variation in the use of mastectomy (MAST) in women with small node negative breast cancer (BC) treated at US academic institutions. San Antonio Breast Cancer symposium, San Antonio, TX, USA, 9-13 December 2014 (Poster Presentation)

### **Communications in National Conferences**

Ferreira AR, Vendrell I, Alho I, Vaz-Luís I, Costa L. A influência do ambiente hormonal no turnover ósseo em doentes com cancro da mama metastático tratadas com quimioterapia e ácido zoledrónico: coorte retrospectivo exploratório. Encontros da Primavera, Évora, March 27-30, 2014.

### **Prizes, honours and awards**

Liga Portuguesa Contra o Cancro / Terry Fox Foundation Oncology Research Award 2014 to S. Casimiro

### **Advanced teaching**

Costa L. and Casimiro S. are members of the Organizing and Scientific Committee of the "Oncobiology Masters Course 2014-2015", FML

## Luís Graça Lab

### 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 Unit

Luis Graca, MD/PhD, Associate Professor

### Research Team

Ana Água-Doce	PhD	Post doctoral Investigator
Ana Raquel Maceiras Oliveira	Master	PhD Student
Joana Catarina Mendão Azeitão da Silva	Master	PhD Student, (left October)
Marta Sofia Ferreira Monteiro Coelho Antunes	PhD	Post doctoral Investigator
Raquel Filipa Reis de Freitas	Master	PhD student
Ruy Miguel Sousa Soeiro de Figueiredo Ribeiro	PhD	Senior Investigator
Sara Mulas Sá de Matos	Master	Lab manager
Sílvia Cristina de Paiva e Almeida	PhD	Post doctoral Investigator
Vanessa Alexandra Gonçalves de Oliveira Martins	PhD	Post doctoral Investigator

### Keywords / Research Areas

Immune tolerance, Regulatory T cell subsets, T follicular helper (Tfh) cells, Allergy, Autoimmunity, Transplantation

### Major scientific achievements

We found iNKT cells respond to environmental cues acquiring different types of effector responses, namely Foxp3 expression and regulatory function, and IL-17 or IL-9 production. These data challenge the dogma that all iNKT cells leave the thymus already as functional committed effectors. Furthermore, we have recently established 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.

Our studies on tolerance induction to foreign proteins, such as factor VIII in hemophilic mice, have shown induction of immune tolerance following CD4-blockade can be mediated by a Foxp3-independent mechanism that relies on IL-10. This IL-10-dependent mechanism can be exploited to facilitate transplantation tolerance.

Finally we have defined Tfh and Tfr cells in the same germinal centre have distinct antigen specificities.

### Selected Publications

Oliveira VG, Agua-Doce A, Curotto de Lafaille MA, Lafaille JJ, Graca L. (2013) Adjuvant facilitates tolerance induction to factor VIII in hemophilic mice through a Foxp3-independent mechanism that relies on IL-10. *Blood* **121**, 3936. (Journal IF: 9.775, Citations: 5)

Monteiro M, Almeida CF, Agua-Doce A, Graca L. (2013) Induced IL-17-producing invariant NKT cells require activation in presence of TGF- $\beta$  and IL-1  $\beta$  *J Immunol.* **190**, 805. (Journal IF: 5.362, Citations: 19)

Oliveira VG, Caridade M, Paiva RS, Demengeot J, Graca L. (2011) Sub-optimal CD4+ T-cell activation triggers autonomous TGF- $\beta$ -dependent conversion to Foxp3+ regulatory T cells. *Eur J Immunol.* **41**, 1249. (Journal IF: 4.518, Citations: 32)

Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira VG, Faro J, Graca L. (2011) Regulation of the germinal center reaction by Foxp3+ follicular regulatory T cells. *J Immunol.* **187**, 4553. (Journal IF: 5.362, Citations: 101)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Agua-Doce A, Wollenberg I, Silva-Santos B, Graca L. (2010) Identification of Regulatory Foxp3+ Invariant NKT Cells Induced by TGF-  $\beta$ . *J Immunol.* **185**, 2157. (Journal IF: 5.362, Citations: 57)

#### Ongoing Research Projects

2012/2014 Title: EFSD and Novo Nordisk. Coordinator: Luis Graca. Agency: EFSD. Reference: EFSD and Novo Nordisk. Amount: 100,000€.

2011/2014 Title: Bayer Hemophilia Awards - Boosting dendritic cell function to facilitate tolerance induction to recombinant clotting factors. Coordinator: Vanessa Alexandra Gonçalves de Oliveira Martins. Agency: Bayer HealthCare. Reference: Bayer. Amount: 119,299.22€.

2012/2014 Title: Regulation of germinal centre reaction by Foxp3+ follicular T cells. Coordinator: Luis Graca. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-IMU/120225/2010. Amount: 124,555€.

2014/2015 Title: ECBIO II. Coordinator: Luis Graca. Agency: ECBio, S.A.. Reference: ECBIO II. Amount: 15,000€.

#### Other Projects

2011/2014 Boosting dendritic cell function to facilitate tolerance induction to recombinant clotting factors. Coordinator: Vanessa Oliveira.

#### Publications in peer review Journals

Silva JM, Vandermeulen G, Oliveira VG, Pinto SN, Rodrigues C, Salgado A, Afonso CA, Viana AS, Jérôme C, Silva LC, Graca L, Pr at V, Florindo HF(2014) Development of functionalized nanoparticles for vaccine delivery to dendritic cells: a mechanistic approach. *Nanomedicine (Lond)*; **9**(17):2639-56. (Journal IF: 5.824, Citations: 1)

Silva JM, Zupancic E, Vandermeulen G, Oliveira VG, Salgado A, Videira M, Gaspar M, Graca L, Pr at V, Florindo HF (2014) In vivo delivery of peptides and Toll-like receptor ligands by mannose-functionalized polymeric nanoparticles induces prophylactic and therapeutic anti-tumor immune responses in a melanoma model. *J Control Release*; **198C**:91-103. (Journal IF:

7.261, Citations: 0)

Monteiro M, Graca L. (2014) iNKT cells: innate lymphocytes with a diverse response. *Crit Rev Immunol*;34 (1):81-90. Review. (Journal IF: 3.889, Citations: 3)

Martins JP, Santos JM, de Almeida JM, Filipe MA, de Almeida MV, Almeida SC, Água-Doce A, Varela A, Gilljam M, Stellan B, Pohl S, Dittmar K, Lindenmaier W, Alici E, Graça L, Cruz PE, Cruz HJ, Bárcia RN (2014) Towards an advanced therapy medicinal product based on mesenchymal stromal cells isolated from the umbilical cord tissue: quality and safety data. *Stem Cell Res Ther*;5 (1):9. (Journal IF: 4.63, Citations: 4)

#### Invited lectures and seminars

Luis Graca, "T follicular regulatory cells", European Midwinter Workshop 2014, Angerer Alm – Austria, 27 – 29 Jan 2014.

Luis Graca, "Prevention of immune pathology by specialized regulatory cell subsets", Departmental seminar, MRC-LMB, Cambridge, 28 Feb 2014.

Luis Graca, "Different regulatory mechanisms leading to immune tolerance to foreign antigens", International School for Translational Immunology, COST action, Tallin 23 – 26 Apr 2014.

Luis Graca, "Back to the Basics", Forum Imuno-Oncologia, Sociedade Portuguesa de Oncologia, Porto, 7 Jun 2014.

Luis Graca, "My self is different from your self", Notions of Self: Exploring Theories of Immunity, Porto, 30 Set 2014.

Luis Graca, "Imuno-oncologia", 6th Congresso Português de Cancro do Pulmão, Grupo de Estudos do Cancro do Pulmão, Lisboa, 9-11 Out 2014.

Luis Graca, "Cellular mechanisms underlying immune suppression and tolerance in transplantation", Congresso da Sociedade Portuguesa de Transplantação, Lisboa, 10 Out 2014.

Ana Agua-Doce, Vanessa G. Oliveira, Marta Caridade, Lisa Bergman and Luis Graca, "Identification of adjuvants leading to Foxp3-independent IL-10-mediated regulatory mechanisms that facilitate immune tolerance induction", Immunotherapy 2014, Havana, Cuba, 10-14 Nov 2014.

Luis Graca, "Back to Basics", Congresso da Sociedade Portuguesa de Oncologia, Porto 14-16

Nov –2014.

Luis Graca, "Targeting germinal centre dysregulation in allergy", Harvard Medical School – Portugal Retreat, Lisbon, 12-13 Dec 2014.

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

Maceiras A.R., Agua-Doce A., Faro J., and Graca L., "T follicular helper (Tfh) and Foxp3+ T follicularregulatory (Tfr) cells have a different TCR repertoire", 8th European Workshop On Immune-Mediated Inflammatory Diseases 2014 (EWIMID 2014), Funchal/Madeira, 05-11-2014 a 07-11-2014, (Oral presentation)

Ana Raquel Maceiras, Ana Agua-Doce, Jose Faro and Luis Graca, "Foxp3+ follicular regulatory T (Tfr) cells and T follicular helper (Tfh) cells involved in the same germinal centre response differ in their antigen specificity", The Fourth International Conference on Regulatory T Cells and T Helper Cell Subsets and Clinical Application in Human Diseases Shanghai, China, 01-11-2014 to 04-11-2014, (Oral presentation)

Ana Agua-Doce, Vanessa G. Oliveira, Lisa Bergman, Maria Curotto de Lafaille, Juan J. Lafaille, and Luis Graca, "Identification of adjuvants leading to Foxp3-independent IL-10-mediated regulatory mechanisms that facilitate immune tolerance induction", Cell-VIB-Symposium: The Multifaceted Roles of Type 2 Immunity 2014, Brugge – Belgium, 09-12-2014 a 12-12-2014, (Poster presentation)

Ana Raquel Maceiras, Ana Agua-Doce, Jose Faro and Luis Graca, "Antigen-specificity of follicular regulatory T cells", 18th Germinal Center Conference, Uddevalla, Sweden, 11-09-2014 a 14-09-2014, (Oral Presentation)

Almeida SCP, Graça, L., "FOXP3+ iNKTreg cells promote LOCAL IMMUNESUPPRESSION LEADING TO LONG-TERM SURVIVAL OF intra-portal islet ALLOGRAFTS IN DIABETIC MICE", 8th European Workshop On Immune-Mediated Inflammatory Diseases 2014 (EWIMID 2014), Funchal/Madeira, 05-11-2014 a 07-11-2014, (Poster presentation)

Marta Monteiro, Catarina F. Almeida, Ana Agua-Doce, Diogo Fonseca-Pereira, Henrique Veiga-Fernandes and Luis Graca, "IL-9 expression by invariant Natural Killer T cells is imprinted outside the thymus", 8th European Workshop On Immune-Mediated Inflammatory Diseases 2014 (EWIMID 2014), Funchal/Madeira, 05-11-2014 a 07-11-2014, (Poster presentation)



### **Communications in National Conferences**

Ana Agua-Doce, Vanessa G. Oliveira, Lisa Bergman, Maria Curotto de Lafaille, Juan J. Lafaille, and Luis Graca, "Identification of adjuvants leading to Foxp3-independent IL-10-mediated regulatory mechanisms that facilitate immune tolerance induction", XL Annual Meeting SPI'40, IMM- Lisbon/ Portugal, 13-10-2014 a 15-10-2014, (Oral Presentation)

Almeida SCP, Graça, L., "FOXP3+ iNKTreg cells promote LOCAL IMMUNESUPPRESSION LEADING TO LONG-TERM SURVIVAL OF intra-portal islet ALLOGRAFTS IN DIABETIC MICE", XL Annual Meeting SPI'40, IMM- Lisbon/ Portugal, 13-10-2014 a 15-10-2014, (Poster presentation)

Marta Monteiro, Catarina F. Almeida, Ana Agua-Doce, Diogo Fonseca-Pereira, Henrique Veiga-Fernandes and Luis Graca, "IL-9 expression by invariant Natural Killer T cells is imprinted outside the thymus", XL Annual Meeting SPI'40, IMM- Lisbon/ Portugal, 13-10-2014 a 15-10-2014, (Poster presentation)

Maceiras A.R., Agua-Doce A., Lopes D., Faro J., and Graca L., "Antigen immunization originates Tfh and Tfr populations with different TCR repertoire", XL Annual Meeting SPI'40, IMM- Lisbon/ Portugal, 13-10-2014 a 15-10-2014, Oral Presentation. (Poster presentation)

Marta Monteiro, Catarina F. Almeida, Ana Agua-Doce, Diogo Fonseca-Pereira, Henrique Veiga-Fernandes and Luis Graca, "IL-9 expression by invariant Natural Killer T cells is imprinted outside the thymus", 8th European Workshop On Immune-Mediated Inflammatory Diseases 2014 (EWIMID 2014), Funchal/Madeira, 05-11-2014 a 07-11-2014, (Poster presentation)

### **Organisation of Conferences**

Luís Graça, 8th European Workshop On Immune-Mediated Inflammatory Diseases 2014 (EWIMID 2014), Funchal/Madeira, 05-11-2014 a 07-11-2014

Luís Graça, 40th Congress of Portuguese Society for Immunology, SPI – XL, Lisbon IMM, 13-15 Out 2014

### **Prizes, honours and awards**

Best oral presentation award in the XL Annual Meeting SPI'40, IMM- Lisbon/ Portugal, 13-10-2014 a 15-10-2014 to Ana Raquel Maceiras

### **Industry contract research**

Contract research for ECBio.

### **Advanced teaching**

Marta Monteiro:

Gabba PhD Programme 17 Apr 2014

Luís Graça:

IMM PhD Program – Immunology Module 3- 7 Feb 2014

PhD Program Medicina Regenerativa, Instituto Superior Técnico, 10Apr 2014

PhD Program GABBA 17 Apr 2014

PhD Program BioSys, FCUL, 13 Mar 2014

ITQB PhD Program 7 Apr 2014

PhD Program FFUL 21 Apr 2014

### **Science and society**

Luis Graca and Silvia Almeida: Collaboration with visual artist Marta de Menezes leading to the development of an artwork named "Immortality for Two" exhibited in November 2014 in Zagreb, Croacia.

Luis Graca: collaboration with visual artist Herwig Turk for the development of the artwork "Conversation that never took place", exhibited during 2014 in Coimbra, Portugal and Vienna, Austria.

Luis Graca; Associação Portuguesa Amigos dos Castelos, Lisboa 1 Dec - Imunologia: como o nosso organismo se reconhece e se defende.

Marta Monteiro; "Functional subsets of invariant Natural Killer T cells in immune pathology: the good, the bad and the ugly" 2nd IMM Postdoc Day, IMM-Lisbon/Portugal, 17-06-2014, Oral presentation.

Sílvia Almeida “Extração do DNA de morangos”, Feira da Ciência Atlântico, Amora/Portugal, 31-03-2014 a 02-04-2014, Promotion of science among students.

## Luísa Figueiredo Lab

### Major Interests / Objectives

Parasitism is the ability of an organism to exploit its host, which may increase reproductive success of the parasite, usually by enhancing its transmission efficiency. Sleeping sickness is a fatal neglected disease caused by *Trypanosoma brucei* a unicellular parasite responsible for 10,000 deaths every year in Africa. *T. brucei* relies on sophisticated mechanisms such as antigenic variation and cell differentiation to overcome the host immune system and to ensure its transmission to a new host, respectively. *T. brucei* interferes with the host sleep pattern and other circadian rhythms. Efficient parasitism relies therefore on a cross-talk between parasite, host and environment. In our group, we use genetic, biochemical and molecular approaches to study these interactions.

### Head of Unit

Luisa Miranda Figueiredo, PhD

### Research Team

Ana Catarina Dias Pena	Master	PhD Student
Ana Filipa de Almeida Rijo Ferreira	Master	PhD Student
Ana Margarida Roque Sanches Vaz	Master	Junior Investigator
Daniel Pinto de Oliveira Gonçalves Neves	Bachelor	MSc Student
Fabien Marc Guegan	PhD	Post-doctoral Investigator
Fábio Pereira Bento	Bachelor	MSc Student (started September)
Francisco Maria dos Santos e Silva Aresta Branco	Master	PhD Student
Helena Isabel Gomes Pires Manso	PhD	Post-doctoral Investigator
Idálio de Jesus Contreiras Viegas	Bachelor	MSc Student (started July)
Leonor Duarte Pinho	Master	Lab manager
Mafalda de Ramos Pimentel	Master	Junior Investigator

Nicole Juliana Eisenhuth	Bachelor	Erasmus MSc Student (May to August)
Sandra Isabel Gonçalves Trindade	PhD	Post-doctoral Investigator

#### Glycobiology group

Eleonora Aquilini	PhD	Post-doctoral Investigator
Jessica Grace Morgan Bevan	Master	PhD student
João Alexandre Guarita da Silva Rodrigues	PhD	Senior Investigator & ITN coordinator
Miguel Correia Botelho Chaves Ferreira	PhD	Post-doctoral Investigator

#### Keywords / Research Areas

antigenic variation, infection, gene expression, parasitology, host-parasite interaction, glycobiology

#### Major scientific achievements

Publication of the first paper from our laboratory. Pena et al. show that histone H1 is important to keep chromatin compact in Trypanosomes and specifically silence Pol I transcribed genes.

Submission of our first patent to INPI request nr 20151000000904

Award of "FCT investigator 2014" to Luisa Figueiredo.

Election to be conference chair (organizer) of the Gordon Research Conference on the Biology of Host-Parasite Interactions 2018

Appointed director of IMM post-doctoral training program

Highest grade (20/20 values) awarded to Idálio Viegas for his Masters Thesis

Two Masters students associated with Luisa Figueiredo's group (Idálio Viegas and Margarida Vaz) were selected for the LisbonBioMed PhD program

#### Selected Publications

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- 63 (Journal IF: 5.0, Citations: 2)

Figueiredo LM, Cross GA (2010) Nucleosomes are depleted at the VSG expression site transcribed by RNA polymerase I in African trypanosomes. *Eukaryot Cel* **9**, 148-154. (Journal IF: 3.2, Citations: 42)

Yang X, Figueiredo LM, Espinal A, Okubo E, Li B (2009) RAP1 is essential for silencing telomeric Variant Surface Glycoprotein genes in Trypanosoma brucei. *Cell* **137**, 99-109 (Journal IF: 33.1, Citations: 71)

Figueiredo LM, Cross GAM, Janzen CJ (2009) Epigenetic regulation in African trypanosomes: a new kid on the block. *Nat Rev Microbiol* **7**, 504-513. (Journal IF: 23.3, Citations: 64)

Figueiredo LM, Janzen CJ, Cross GAM (2008) A histone methyltransferase modulates antigenic variation in African trypanosomes. *PLoS Biol* **6**, e161. (Journal IF: 11.8, Citations: 81)

#### Ongoing Research Projects

2010/2014 Title: Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes - PIRG06-GA-2009-256299. Coordinator: Luisa Miranda Figueiredo. Agency: Comissão Europeia. Reference: HistoneH1Tryp. Amount: 100,000€.

2011/2016 Title: Embo Instalation Grant. Coordinator: Luisa Miranda Figueiredo. Agency: EMBO. Reference: Embo Instalation Grant LF. Amount: 250,000€.

2011/2014 Title: The role of histone H1 in antigenic variation of African trypanosomes. Coordinator: Luisa Miranda Figueiredo. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/BIA-BCM/115864/2009. Amount: 189,828€.

2011/2014 Title: Screening of chromatin factors involved in antigenic variation in Trypanosoma brucei. Coordinator: Luisa Miranda Figueiredo. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-MIC/113225/2009. Amount: 113,407€.

2012/2017 Title: International Early Career Scientist - How Parasites Use Epigenetics to Evade Host Defenses. Coordinator: Luisa Miranda Figueiredo. Agency: Howard Hughes Medical Insti.. Reference: Howard Hughes Medical Institute. Amount: 370,310.41€.

2012/2014 Title: Embo Small Grant . Coordinator: Luisa Miranda Figueiredo. Agency: EMBO. Reference: Embo Small Grant LF. Amount: 5,000€.

2013/2015 Title: Postdoctoral Sponsorhip Agreement . Coordinator: Luisa Miranda Figueiredo. Agency: AXA SA. Reference: Postdoctoral Sponsorhip Agreement . Amount: 120,000€.

2014/2015 Title: Embo Small Grant . Coordinator: Luisa Miranda Figueiredo. Agency: EMBO.  
Reference: YIP - Small Grant . Amount: 8,000€.

#### **Publications in peer review Journals**

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), 645-63. (Journal IF: 5.026, Citations: 2)

#### **Other publications International**

Figueiredo LM and Horn D (2014). Trypanosoma brucei Subtelomeres: Monoallelic Expression and Antigenic Variation. In Subtelomeres, Louis EJ and Becker MM, eds. (Berlin Heidelberg: Springer), pp. 137-152.

#### **Invited lectures and seminars**

Figueiredo LM. Chromatin dynamics in Trypanosomes. Institut Pasteur, Paris, France, June 26, 2014.

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

Figueiredo LM. Chromatin Dynamics and Gene Expression in Trypanosoma brucei. Gordon Research Conference on the Biology of Host-Parasite Interactions, Newport, RI, United States of America, June 2014 (Oral presentation)

Rijo-Ferreira F; Takahashi JS, Figueiredo LM. Trypanosoma brucei accelerates the mouse circadian clock. Society for Research on Biological Rhythms. Big Sky, Montana, United States of America, June 2014 (Poster presentation)

Pena AC, Pimentel MR, Manso H, Vaz-Drago R, Pinto-Neves D, Aresta-Branco F, Neves D, Rijo-Ferreira AF, Guegan F, Pedro Coelho L, Carmo-Fonseca M, Barbosa-Morais NL, Figueiredo LM. Trypanosoma brucei histone H1 inhibits RNA polymerase I transcription and is important for parasite fitness in vivo. ParaFrap Congress, Marseille, France, September 2014 (Poster presentation)

presentation)

Rijo-Ferreira F and Figueiredo LM. “CleverSys HomeCageScan: what is your mouse doing when you’re not looking?” EMBO Young Investigator PhD Course 2014. EMBL campus. Heidelberg, Germany, December 2014 (Poster presentation)

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

Ferreira AF, Takahashi JS, Figueiredo LM. Trypanosoma brucei accelerates the mouse internal clock. XVII Congresso Português de Parasitologia, Coimbra, Portugal, November, 2014. (Oral presentation)

Ferreira AF, Takahashi JS, Figueiredo LM. Trypanosoma brucei accelerates mouse circadian rhythm. GABBA PhD program. Universidade do Porto, Oporto, Portugal, December, 2014. (Oral presentation)

#### **Organisation of Conferences**

Founder and organizer of the weekly institutional lectures of IMM. September, 2012 – July, 2014. Every week a renown scientist gives a lecture to a broad audience of around 100 people. Most speakers work abroad and about one third comes from a national research institute. Topics are diverse, from clinical research to basic biology. As the founder and organizer, I have established the rules of whom to invite, the logistics of the invitations, how to best host the speakers and so on. Going to the Monday Lectures has become a natural weekly routine for many researchers of IMM.

#### **Prizes, honours and awards**

Award of “FCT investigator 2014” to Luisa Figueiredo

Highest grade (20/20 values) awarded to Idálio Viegas for his Masters Thesis



### **Advanced teaching**

Figueiredo LM. GABBA PhD Program, Instituto Biologia Molecular Celular, Porto, Portugal.  
“Sleeping sickness when a parasite makes the internal clock of the host run faster.” May 2014

### **Science and society**

Figueiredo LM. Conversas de gerações na microciência. Faculdade de Ciências e Tecnologia,  
Universidade Nova de Lisboa, Monte de Caparica, Portugal, May 2014

### **Msc thesis completed**

Idálio de Jesus Viegas 12/11/2014 “N6-methyladenosine: a new modification in *T. brucei* ”.  
Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa. Luisa Figueiredo

## Luísa Lopes Lab

### 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 Unit

Luísa Maria Vaqueiro Lopes, PhD

### Research Team

Ana Inês Marques Morgado	Graduate	MSc Student, (started September)
Diana Gabriela Ribeiro Ferreira	Master	PhD Student, University Medical Center Goettingen, Department of NeuroDegeneration and Restorative Research , Faculdade Medicina da Universidade do Porto
Joana Fernandes Esteves Soares Coelho	PhD	Post doctoral Investigator
Mariana Temido Mendes Ferreira	Master	PhD Student
Rui Artur Paiva Loureiro Gomes	PhD	Investigator, Assistant Professor
Vânia Luisa Neves Batalha	PhD	PhD Student

## Keywords / Research Areas

Aging, Neurosciences, Cognition, Hippocampus

## Major scientific achievements

1) We produced, in collaboration with INSERM (Lille, France) and Univ Bonn (Bonn, Germany) an innovative study showing the benefits of using an improved caffeine analog (MSX-3) in a mouse model of Alzheimer's disease (AD). This was published in the journal *Molecular Psychiatry* (IF: 15.14), reveals that in mice with lesions associated with AD, the oral therapy with this new drug, MSX-3, significantly improved memory and reduces the Tau protein hyperphosphorylation. We found this is due to the action of the drug on a specific protein, the adenosine A2A receptor, known target for caffeine in the brain.

2) We have completed the generation of a novel transgenic mice overexpressing A2AR driven by a CamKII promoter, with the aim of characterising the outcome of A2A upsurge to brain function, started 3 years ago (in col. with INSERM, France) (Paper published *Frontiers in Psychiatry*, 2014)

3) A new exchange project with the team of Dr. Helene Marie (IPMC-CNRS, Lille, France) initiated.

## Selected Publications

Sousa VC, Vital J, Costenla AR, Batalha VL, Sebastião AM, Ribeiro JA, Lopes LV (2014) Maternal separation impairs long term-potential in CA1-CA3 synapses and hippocampal-dependent memory in old rats. *Neurobiol Aging*. **35**, 1680-5. (IF: 6.1 Citation: 0)

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 ahead of print] . (Journal IF: 15.7, Citations: NA)

Batalha VL, Pego JM, Fontinha BM, Costenla AR, Valadas JS, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV. (2013) Adenosine A<sub>2A</sub> receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *MOLECULAR PSYCHIATRY* **18**, 320. (Journal IF: 15.1, Citations: 8)

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. (Journal IF: 7.8, Citations: 17)

Chen, JF (Chen, Jiang-Fan); Sonsalla, PK (Sonsalla, Patricia K.) ; Pedata, F (Pedata, Felicitia); Melani, A (Melani, Alessia); Domenici, MR (Domenici, Maria Rosaria); Popoli, P (Popoli, Patrizia); Geiger, J (Geiger, Jonathan); Lopes, LV (Lopes, Luisa V.) ; De Mendonca, A (De Mendonca, Alexandre) (2007) Adenosine A(2A) receptors and brain injury: Broad spectrum of neuroprotection, multifaceted actions and . *PROGRESS IN NEUROBIOLOGY* **83**, 310. (Journal IF: 10.57, Citations: 111)

#### **Ongoing Research Projects**

2014/2015 Title: Prémio Gulbenkian - Best Plenary Presentation . Coordinator: Luísa Maria Vaqueiro Lopes. Agency: AIDFM. Reference: Prémio Gulbenkian - Best Plenary Presentation . Amount: 500€.

2014/2015 Title: Service-University of Macau. Coordinator: Luísa Maria Vaqueiro Lopes. Agency: Institute of Chinese Medical Sciences. Reference: Service-University of Macau. Amount: 3,000€.

#### **Other Projects**

2013/2015 Fritz Thyssen Foundation - "Adenosine A2A receptors and alpha-synuclein: Novel targets for Parkinson's disease" This project addresses the in vitro role of A2ARs to aSyn aggregation and toxicity using cellular models of aSyn aggregation. Amount: 110 000EUR. Coordinator: Luisa Lopes/Tiago Outeiro.

2011/2015 FCT - Molecular determinants of microglial activation and neuronal dysfunction in in vivo models of Parkinson's disease. Amount: 168 000 EUR. Coordinator: Teresa Pais. Coordinator Institution: IMM. Coordinator PI: Teresa Pais.

2011/2014 Bial Foundation - "Psychological indicators of stress reactivity and disease adaptation" Amount: 48 000EUR. Coordinator: Luisa Lopes/Silvia Ouaikinin. Coordinator Institution: HSM/FML Lisbon. Coordinator PI: Sílvia Ouaikinin.

#### **Publications in peer review Journals**

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](https://doi.org/10.1038/mp.2014.151). [Epub ahead of print] . (Journal IF: 15.7, Citations: NA)

Coelho JE, Alves P, Canas PM, Valadas JS, Shmidt T, Batalha VL, Ferreira DG, Ribeiro JA, Bader M, Cunha RA, do Couto FS, Lopes LV. Overexpression of Adenosine A2A Receptors in Rats: Effects on Depression, Locomotion, and Anxiety. *Front Psychiatry*. 2014 Jun **13**;5:67. (Journal IF: NA Citation: 0)

Jerónimo-Santos A, Batalha VL, Mueller CE, Baqi Y, Sebastião AM, Lopes LV, Diogenes MJ. (2014) Impact of in vivo chronic blockade of adenosine A2A receptors on the BDNF-mediated facilitation of LTP. *Neuropharmacology*. **83C**, 99-106. (Journal IF:4.81 Citation: 2)

Sousa VC, Vital J, Costenla AR, Batalha VL, Sebastião AM, Ribeiro JA, Lopes LV (2014) Maternal separation impairs long term-potential in CA1-CA3 synapses and hippocampal-dependent memory in old rats. *Neurobiol Aging*. **35**, 1680-5. (IF: 6.1 Citation: 0)

Bai G, Cheung I, Shulha HP, Coelho JE, Li P, Dong X, Jakovcevski M, Wang Y, Grigorenko A, Jiang Y, Hoss A, Patel K, Zheng M, Rogaev E, Myers RH, Weng Z, Akbarian S, Chen JF.(2014) Epigenetic dysregulation of hairy and enhancer of split 4 (HES4) is associated with striatal degeneration in postmortem Huntington brains. *Hum Mol Genet*. 2014 Dec 5. pii: ddu561. [Epub ahead of print]

Nascimento F, Pousinha PA, Correia AM, Gomes R, Sebastião AM, et al. (2014) Adenosine A2A Receptors Activation Facilitates Neuromuscular Transmission in the Pre-Symptomatic Phase of the SOD1(G93A) ALS Mice, but Not in the Symptomatic Phase. *PLoS ONE* **9**, (8): e104081. doi:10.1371/journal.pone.0104081

#### Other publications International:

Vanessa Flaten, Cyril Laurent, Joana E. Coelho, Ursula Sandau, Vanessa L. Batalha, Sylvie Burnouf, Malika Hamdane, Sandrine Humez, Detlev Boison, Luisa V. Lopes, Luc Buee, David Blum (2014) From epidemiology to pathophysiology: what about caffeine in Alzheimer's disease ?. *BIOCHEMICAL SOCIETY TRANSACTIONS*, **42**, 587-592 (Journal IF: 3.23 Citations: 2)

### Invited lectures and seminars

Luísa Lopes: "Adenosine and brain disorders"; French Society for Neurosciences – Journées Thematiques Perturbations metaboliques dans les maladies neurologiques et mentales, Lille, May 19, 2014

Luisa Lopes: "Stressed out brain: impact on memory anatomy connectivity and performance" Department of NeuroDegeneration, University Medizin Gottingen, July 23, Gottingen, Germany

Luísa Lopes: "Adenosine A2A receptors and stress – impact on cognition" Purines 2014 - Nucleotides, Nucleosides and Nucleobases, International Conference on Signalling, Drugs and Targets, Bonn (Germany): July 23-27, 2014

Luísa Lopes: "When stress messes up memory - can we revert it back?"; L'Institut de Pharmacologie Moléculaire et Cellulaire (IPMC-CNRS), October 18, Nice, France

Joana Coelho: Alterações num modelo animal de sobre expressão de receptores A2A da adenosina: efeitos em medidas experimentais de locomoção, ansiedade e depressão. X CONGRESSO NACIONAL DE PSIQUIATRIA – 13-15 Novembro 2014, Vilamoura, Portugal

### Communications in International Conferences

Ferreira DG, Coelho JE, Batalha VL, Miranda HV, Queiroz F, Real J, Cunha RA, Lopes LV and Outeiro TF, 2014 "Alpha-synuclein oligomers fail to induce synaptic dysfunction in adenosine A2A receptor knockout-mice" 9th FENS Forum of Neuroscience, July, Milan, Italy. (Poster presentation)

Batalha VL, Ferreira DG, Coelho JE, Valadas JS, Bader M, Gomes RA, Blum D, Lopes LV, Hippocampal deficits driven by overexpression of adenosine A2A receptors in forebrain neurons, 9th Federation of European Neuroscience societies forum, July, Milan, Italy. (Poster presentation)

Diógenes MJ, Jerónimo-Santos A, Batalha VL, Muller C, Hockemeyer J, Lopes LV, Sebastião AM (2014) Chronic blockade of adenosine A2A receptors prevents BDNF effect on hippocampal LTP. 9th FENS meeting, Milan, Italy. (Poster presentation)

FENS 2014:

Nádia M. Grilo<sup>1</sup>, Vânia L. Batalha<sup>2</sup>, Luisa V. Lopes<sup>2</sup>, Alexandra M. M. Antunes<sup>3</sup> and Sofia A. Pereira<sup>1</sup> Deficits in memory performance and anxiety levels induced by the anti-HIV drug

Efavirenz, 9th FENS meeting, Milan, Italy (Poster presentation)

Nádia M. Grilo<sup>1</sup>, Vânia L. Batalha<sup>2</sup>, Luisa V. Lopes<sup>2</sup>, M. Matilde Marques<sup>3</sup>, Emília C. Monteiro<sup>1</sup>, Alexandra M. M. Antunes<sup>3</sup> and Sofia A. Pereira An animal model to explore Efavirenz toxicokinetics and its relation to neurological phenotype, Eurotox 2014, 7-10 September, Edinburgh, Scotland (Oral presentation)

L. V. LOPES<sup>1</sup>, V. L. BATALHA<sup>1</sup>, D. R. FERREIRA<sup>1</sup>, J. S. VALADAS<sup>1</sup>, J. E. COELHO<sup>1</sup>, R. GOMES<sup>1</sup>, P. M. CANAS<sup>2</sup>, V. BUÉE-SCHERRER<sup>3</sup>, S. HUMEZ<sup>3</sup>, T. SHMIDT<sup>4</sup>, M. HAMDANE<sup>3</sup>, G. SADRI-VAKILI<sup>5</sup>, L. BUÉE<sup>3</sup>, T. F. OUTEIRO<sup>6</sup>, R. A. CUNHA<sup>2</sup>, M. BADER<sup>7</sup>, D. BLUM<sup>3</sup>; A novel role of adenosine A2A receptor in the modulation of the stress glucocorticoid receptor in the brain, SFN meeting, Washington, US (nov 2014) (Oral Presentation)

T. F. OUTEIRO<sup>1</sup>, H. VICENTE-MIRANDA<sup>2</sup>, E. M. SZEGO<sup>1</sup>, W. XIANG<sup>3</sup>, H. LASHUEL<sup>4</sup>, J. KLUCKEN<sup>5</sup>, M. ZWECKSTETTER<sup>6</sup>, L. V. LOPES<sup>2</sup>, F. GIORGINI<sup>7</sup>; Glycation disrupts proteostasis and promotes neurodegenerative alterations in synucleinopathies, SFN meeting, Washington, US (Nov 2014) (Oral Presentation)

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

Ferreira DG, Coelho JE, Batalha VL, Miranda HV, Queiroz F, Real J, Cunha RA, AlbinoTeixeira A, Lopes LV and Outeiro TF, 2014 “Adenosine A2A receptors modulate alphasynuclein toxicity and aggregation” 4th PhD student meeting of the Faculty of Medicine, University of Porto, Porto, Portugal.

Nascimento F, Correia AM, Gomes RA, Pousinha PA, Sebastião AM, Ribeiro JA (2014). A1 and A2A adenosine receptors functional crosstalk at the neuromuscular junction of the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis, XLIII Reunião Anual da Sociedade Portuguesa de Farmacologia, Universidade de Coimbra

#### **Internationalisation**

Academia/Networking: Our group benefits extensively from collaborations. They provide mentoring, critical mass but also share knowledge and technical skills. We have bilateral collaborations running with exchange and tutoring of students from France, Germany and US. These are the basis for the applications Luisa Lopes as submitted this year (as PI) to international funding agencies, such as ANR, Fritz Thyssen Foundation, Harvard Medical School-Portugal and NARSAD. LL is PhD supervisor in the EU Erasmus/Mundus “Ageing Brain” network and frequently chairs symposia and delivers lectures internationally (FENS, SFN, Purines, ICAD). Since June 2013, Luisa Lopes hosts the annual NeuroSeS symposium, which gathers foreign speakers in the Neuroscience field at IMM and fosters scientific exchange. The

research results are disseminated to the national and international scientific community via meetings and symposia (ICAD, AD/PD, FENS, SFN). Moreover, they will be exchanged during regular seminars and annual congresses organized by LABEX DISTALZ, North Dementia Pole (DN2M), FUI-funded Medialz consortium as well as to IMM and the “PurineDrugs” consortium (FP7- ITN).

#### **Prizes, honours and awards**

2014 Best Presentation Award to Diana Ferreira; 4th PhD student meeting of the Faculty of Medicine, University of Porto, Porto, Portugal.

2014 Young Investigator Training Program fellowship to Vânia Batalha (FENS)

FENS/IBRO fellowship to Vania Batalha (9th Federation of European Neuroscience Societies forum) July 2014.

Best Scientific Oral Presentation to Marta Bento (FML Gaptic Student) Annual international medical students meeting, 2014 (EURO 500) SERVIER PRIZE

#### **Industry contract research**

Established a protocol with Technophage aiming at testing novel compounds against Parkinson's disease (PD). Our role is to implement animal models of PD in rodents and screen the efficacy of promising compounds. Team: Joana Coelho and Luisa Lopes.

#### **Advanced teaching**

PhD programs as lecturer (Luisa Lopes):

Since 2013 - IMM PhD Biomed program lecturer (Neurosciences week)

Since 2012 - PhD supervisor within the NEU4EU - European PhD education and training network 'Ageing Brain' (Coordinator: Univ. Groningen)

Since 2011 – Faculty member in the Doctoral Course “Clinical Neurosciences and Neuropsychiatry” - Faculdade de Medicina do Porto, Portugal, Module: Stress and Cognition

Since 2008 - Faculty member of the Neurosciences PhD program (FML/Universidade de Lisboa)

Participation in PhD committees as opponent (Luisa Lopes):

Sara Matos (FMUL) Kytorphin peptide derivatives in the relationship between analgesia and Alzheimer's Disease, Universidade de Lisboa



Shilan Aslani Dissecting the crosstalk between stress, depression and obesity - Faculdade de Medicina, Universidade do Minho, Braga

Elisabete Augusto - Characterization of ecto-5'-nucleotidase (CD73) in the brain – role in adenosine A2A receptor activation - Faculdade de Medicina, Universidade de Coimbra

Rui Gomes:

Coordinator and lecturer of the Cell Cycle Regulation course (Master program in Molecular Biology and Genetics, Faculdade de Ciencias, Universidade de Lisboa, Lisbon, Portugal).

Coordinator and lecturer of the Molecular Biology course (Master Program in Bioinformatics and Computational Biology, Faculdade de Ciencias, Universidade de Lisboa, Portugal).

Coordinator and lecturer of the Genetics and Molecular Biology course (Biology Graduate Program, Faculdade de Ciencias, Universidade de Lisboa, Portugal).

### **Science and society**

The Brain Awareness Week (BAW) is promoted every year in March. The team has participated very actively in the activities in the last areas. These include debates in schools, public conferences or round tables, press releases and publication of several articles for the general public. Luisa Lopes is member of the board of the Portuguese Society for Neuroscience (SPN) and has coordinated the BAW activities within the Lisbon area from 2008-2013. We engage in public awareness via lectures, webpages and print material to research associations and organizations as well as industry. See please [www.spn.org.pt](http://www.spn.org.pt)

### **PhD thesis completed**

Vânia Batalha 30/09/2014 “Interaction between glucocorticoid and adenosine A2A receptors in the hippocampus – implications for learning and memory” University Lisbon - Faculty Medicine Luisa Lopes

### **Msc thesis completed**

Inês de Sousa Costa 04/12/2014 Validation of neuroprotective effect of blackberries digested metabolites in a model of neurodegeneration based on rat neurons primary culture Faculdade de Ciencias, Universidade de Lisboa, Lisbon, Portugal. Cláudia Nunes dos Santos Rui Gomes

## Mamede de Carvalho Lab

### Major Interests / Objectives

The Translational Clinical Physiology Unit investigates the motor neuron function and degeneration autonomic nervous system and cardiovascular regulation, peripheral nerve function, behaviour and imaging-neurocomputational models of brain dysfunction. This Unit has contributed to a more complete comprehension of the electrophysiological signs in motor neuron degeneration, the role of the autonomic nervous system in heart regulation and about the activity of brain structures in behaviour disturbances. In the future we aim to approach brain function and autonomic dysfunction, computational models of frontal degeneration in motor neuron disease, new techniques to evaluate small nerve fibre evaluation, and the interaction between brain and nerve excitability.

### Head of Unit

Mamede de Carvalho, MD, PhD. Institute of Physiology, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa. Department of Neurosciences, Centro Hospitalar Lisboa Norte.

### Research Team

Alberto Albino Granado Escalda	MD/PhD	Investigator, Assistant Professor
Ana Catarina dos Santos Farinha	Graduate	MSc Student, (started February)
Ana Isabel Ladeira Portêlo	Master	PhD Student, (started April)
Ana Isabel Lopes Francisco Moura Santos	PhD	Investigator, Assistant Professor
Ana Rita Mendes Londral Gamboa	Master	Investigator
Anabela Leuschner Fernandes Cardoso Pinto Noronha Sanches	MD/PhD	Senior Investigator, CHLN , Consultant , Faculdade Medicina da Universidade de Lisboa , Associate Professor

Andreia da Silva Borges Carapinha	Graduate	Technician
Andreia Leitão Tavares Ribeiro dos Santos	Graduate	PhD Student, (started February)
Andrés Díaz Campos	Graduate	Investigator
Ângela Raquel Amaro Leal	Master	MSc Student
Ângelo Rodrigo Neto Dias	Graduate	MSc Student
Anna Caroline Marques dos Anjos Braga	Master	Investigator
BENJAMIM ABRAHAM OHANA	Master	Investigator, Associate Professor , Clinical Specialist
Catarina Raquel Nunes da Silva	Graduate	MSc Student
Diana Lina Jerónimo da Cunha Reis	PhD	Post doctoral Investigator
Fernando Manuel Pinto Ferreira Domingos	MD/PhD	Investigator, Assistant Professor
Gabriela Barbu Postolache	PhD	Investigator, Assistant Professor
Inês Antunes de Santa Ana	Graduate	MSc Student
Isabel Maria dos Santos Conceição	Graduate	Investigator, Teaching Assistant , Clinical Specialist
Isabel Maria Teixeira Máxima Graça	Undergraduate	Administrative, (left April)
João Miguel Proença Abreu	Graduate	MSc Student, (started February)
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Investigator
José Pedro Almeida	Graduate	PhD Student
Lena Helene Ernst	PhD	Post doctoral Investigator, (started February)
Leonel Almeida Luis	Graduate	Investigator, Hospital de Santa Maria , Clinical Specialist
Maria Cano-Colino	PhD	Post doctoral Investigator

Maria da Conceição Jonet de Azevedo Coutinho	MD/PhD	Investigator, Associate Professor
Maria do Amparo Barros	Graduate	Technician
Maria Inês Mendes Caldeira	Master	Investigator, (started July)
Maria Isabel de Sousa Rocha	PhD	Senior Investigator
Mariana Fernandes Alves Pereira	Graduate	MSc Student, (started September)
Mario Joao Martins Oliveira	MD/PhD	Investigator
Marisa Tavares Brum	Master	MSc Student, Physician
Michael Swash	MD/PhD	Investigator
Nataniel João Gonçalves Cleto Rosa	Master	PhD Student
Pedro Jorge Filipe Pereira	Master	PhD Student
Pedro Miguel Tojais Rodrigues Alves	Graduate	Investigator, Teaching Assistant
Raquel de Sá da Silva Laires Rua	Graduate	Technician
Ricardo Duarte Ferreira Filipe	Graduate	MSc Student, (started March)
Rita Alexandra Figueira Belo	Undergraduate	MSc Student
Susana Cristina Da Costa Pinto	MD/PhD	Investigator
Tiago Vaz Maia	PhD	Technician
Vera Lúcia Poço Geraldes	Graduate	PhD Student
Victor César Ferreira de Moura Gonçalves	MD/PhD	Investigator, Assistant Professor

#### 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

International collaboration has been strengthened in different areas of research in our Unit. This approach has permitted a number of publications in high impact factor journals.

In amyotrophic lateral sclerosis advances were performed in understanding the diagnostic process, measuring progression and identifying new biomarkers towards an earlier diagnosis. We have been more active regarding media interaction taking into account the renewed societal interest in this disorder.

New data is provided related to the learning process and the role of striatum in this complex brain function. The origin of atrial fibrillation and cardiogenic syncope, as well as atrial fibrillation treatment have been extensively investigated and new concepts are proposed.

Novel research areas are approached, in particular vestibular function and direct electric current transcranial stimulation.

### Selected Publications

Turner, M. R., Hardiman, O., Benatar, M., Brooks, B. R., Chio, A., de Carvalho, M., & Kiernan, M. C. (2013) Controversies and priorities in amyotrophic lateral sclerosis. *Lancet Neurology* **322**, 310. (Journal IF: 21,823, Citations: 25)

Lamberts, R. J., Laranjo, S., Kalitzin, S. N., Velis, D. N., Rocha, I., Sander, J. W., & Thijs, R. D. (2013) Postictal generalized EEG suppression is not associated with periictal cardiac autonomic instability in people with convulsive seizures. *Epilepsia* **523-529**. (Journal IF: 4.584, Citations: 9)

Maia, T. V., & Frank, M. J (2011) From reinforcement learning models to psychiatric and neurological disorders. *Nature Neuroscience* **162**, 154. (Journal IF: 14.976, Citations: 184)

de Carvalho, M., Dengler, R., Eisen, A., England, J. D., Kaji, R., Kimura, J. & Swash, M. (2007) Electrodiagnostic criteria for diagnosis of ALS. *Clinical Neurophysiology* **503**, 497. (Journal IF: 3.647, Citations: 314)

Maia, T. V., & McClelland, J. L. (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/>. (Journal IF: 9.809, Citations: 430)

### **Ongoing Research Projects**

2012/2015 Title: Sampling and biomarker Optimization and Harmonization In Amyotrophic Lateral Sclerosis (ALS) and other. Coordinator: Mamede de Carvalho. Agency: Fundação Ciência e Tecnologia. Reference: JPND/0002/2011. Amount: 60,000€.

2012/2014 Title: Early disease markers in early symptomatic carriers of TTR V30M mutation. Coordinator: Mamede de Carvalho. Agency: Laboratórios Pfizer, Lda. Reference: Pfizer WI128568. Amount: 40,000€.

2013/2014 Title: Reinforcement Learning and Motor Biases in Children with Tourette Syndrome. Coordinator: Tiago Vaz Maia. Agency: Tourette Syndrome Association, Inc. Reference: TSA Research Award Program - Tourette Syndrome. Amount: 56,078.96€.

### **Other Projects**

2012/2014 TEMIS- TEchnologies innovantes pour quantifier et qualifier le mode de vie pour des services de Médecine Personnalisée ( [www.temis-project.eu](http://www.temis-project.eu)). Coordinator: Professora Dra Isabel Rocha.

2011/2014 Understanding Neurodegenerative Diseases Through Clinical and OMICS data Integration- Neuroclinomics . Coordinator: Sara Madeira collaboration with Mamede de Carvalho (PTDC/EIA-EIA/111239/2009)130.572,00€.. Coordinator PI: Coordinator: Sara Madeira.

2012/2016 Early Markers in Familial Amyloid Polyneuropathy. Coordinator: Dra Isabel Conceição.

2008/2018 Transthyretin-associated amyloidoses outcomes survey (THAOS). A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidoses (Fold Rx Pharmaceuticals, Inc.) Coordinator: Dra Isabel Conceição.

2012/2015 Sampling and Biomarker Optimization and Harmonization in ALS and other Motor Neuron Diseases (SOPHIA). Coordinator: Professor Dr Mamede Carvalho-100.000€.

2013/2014 Reinforcement learning and motor biases in children with Tourette syndrome. Coordinator: Professor Dr Tiago Vaz Maia - \$75.000,00

2013/2016 RSE FISIO – necessidades requisitos e barreiras de adoção de registo de saúde electrónico em fisioterapia PTDC/DTP-DFS/1661/2012). Coordinator: participant Prof Dra

Gabriela Postolache. Coordinator Institution: RSE FISIO.

2013/2015 . Fx1A303 OpenLabel Safety and Efficacy Evaluation of Fx1006A in Patients with Transthyretin Amyloidosis. (Pfizer/FoldRx Pharmaceuticals, Inc.). Coordinator: Dra. Isabel Conceição.

2014/2018 Control and reward circuits as targets for repetitive behaviors. Coordinator: Prof. Dr.TV Maia - Consultant. Coordinator Institution: National Institute of Mental Health (USA). Coordinator PI: R. Marsh & H. Blair Simpson (Co-PIs).

2014/2015 NETWORK OF COHORT ASSESSMENT in ALS (NTCALs) Coordinator: Mamede de Carvalho.

2014/2019 Neural mechanisms of sensory predictions in schizophrenia with hallucinations. Coordinator: G. Horga - Prof. Dr.TV Maia - Consultant.

#### **Publications in peer review Journals**

Conceição I, Costa J, Castro J, de Carvalho M (2014). Neurophysiological techniques to detect early small-fiber dysfunction in transthyretin amyloid polyneuropathy. *Muscle Nerve* **9**; 181-186. (Journal IF 2.311 Citation: 2 )

de Carvalho M, Turkman A, Swash M (2014). Sensitivity of MUP parameters in detecting change in early ALS. *Clin Neurophysiol*; **125**: 166-169 (Journal IF 3.144 Citation: 4 )

Pinto S, de Carvalho M (2014). Breathing new life into treatment advances for respiratory failure in ALS patients. *Neurodegen Dis Manage*; **4**: 83-102.(Journal IF: 3.454 Citation: NA)

Laborinho-Pronto AC, Pinto S, de Carvalho M (2014). Roles of vascular endothelial growth factor (VEGF) in amyotrophic lateral sclerosis. *BioMed Research International*; **2014**: 1-24 Journal IF 2.880 Citation: 1)

de Carvalho M (2014). A handful of promises. (editorial) *Clin Neurophysiol*; **125**: 5 (JournalIF: 3.144 Citation: NA).

Carilho R, de Carvalho M, Swash M, Pinto S, Pinto A, Costa J (2014). Vascular Endothelial Growth Factor and Amyotrophic Lateral Sclerosis: the interplay with exercise and non-invasive ventilation. *Muscle Nerve*; **49**: 545-550. (JournalIF: 2.311 Citation: 3).

Pinto S, de Carvalho M, Swash M (2014). Does surgery accelerate progression of amyotrophic lateral sclerosis? *J Neurol Neurosurg Psychiatry*, **85**: 643-646. (Journal IF: 5.580Citation: 5).

Lehnert S, Costa J, de Carvalho M, Kirby J, Kuzma M, Morelli C, Robbrecht W, Shaw P, Silani V, Steinacker P, Tumani H, Van Damme P, Ludolph, Otto M (2014). Multicenter quality control evaluation of different biomarker candidates for amyotrophic lateral sclerosis. *Amyotr Lat Scler Frontotemporal Degener*; **15**, 344-350. (Journal IF: 2.591 Citation: 6)

Akimoto C, Alstermark H, Birve A, Nordin A, Andersen PM, Volk AE, Tradowsky DC, Just W, Kubisch C, van Blitterswijk M, DeJesus-Hernandez M, Rademakers R, Van Broeckhoven C, Van Den Broeck M, van der Zee J, Leblond CS, Daoud H, Rouleau GA, Mouzat K, Lumbroso S, Camu W, Rattia A, Calinia D, Silani V, Konno T, Onodera O, Veldink JH, van Rheenen W, van den Berg LH, de Carvalho M, Pinto S, Weber M, Smith B., Shaw CE, Proven M, Lloyd-Jani A, Talbot K, Landers JE, Keagle P, Chesi A, Gitler AD (2014). A Comparative blinded study on the reliability of genetic testing for the GGGGCC-repeat expansion in C9orf72 reveals marked differences in results among 14 Laboratories. *Hum Mol Genet* **51**, 419-24. (Journal IF: 6.677 Citation: 2)

Lefaucheur J-P, André-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, Cantello RM, Cincotta M, de Carvalho M, Ridder DD, Devanne H, Di Lazzaro V, Filipovi? SR, Hummel FC, Jääskeläinen SK, Kimiskidis VK, Koch G, Langguth B, Nyffeler T, Oliviero A, Padberg F, Poulet E, Rossi S, Rossini PM, Rothwell JC, Schönfeldt-Lecuona C, Siebner HR, Slotema CW, Stagg CJ, Valls-Sole J, Ziemann U, Paulus W, Garcia-Larrea L (in press). European guidelines on the clinical use of repetitive transcranial magnetic stimulation (rTMS) for treatment. (Journal IF: NA Citation: 2)

Nzwalo H, de Abreu D, Swash M, Pinto S, de Carvalho M (2014). Delayed diagnosis in ALS: the problem continues. *J Neurol Sci*; **343**: 173-175. (Journal IF: 2.262 Citation: 3)

Gonçalves M, Tillack L, de Carvalho M, Pinto S, de Carvalho M, Conradt H, Costa J (in press). Phosphoneurofilament heavy chain and N-glycomics from the cerebrospinal fluid in Amyotrophic Lateral Sclerosis. *Clin Chim Acta*; **438**: 342-349 (Journal IF: 2.764 Citation: NA)

Carreiro AV, Amaral PMT, Ramalho R, Pinto S, de Carvalho M, Tomas P, Madeira SC. Prognostic prediction in patients with ALS using a patient-driven approach with time windows (in press). *Data Mining and Knowledge Discovery* (Journal IF: 1.745 Citation: NA)

de Carvalho M, Eisen A, Krieger C, Swash M (2014). Motor unit firing in amyotrophic lateral sclerosis. *Front Hum Neurosci*; **8**:719 (Journal IF: 2.9 Citation: NA)

Gomez-Vilda P, Londral A, Rodellar-Biarge V, Ferrández-Vicente JM, de Carvalho M (in press). Monitoring amyotrophic lateral sclerosis by biomechanical modeling of speech production. *Neurocomputing*. (Journal IF: 1.634 Citation: 0)

de Carvalho M (2014). Ultrasound in ALS: is it a sound method? (editorial) *Clin Neurophysiol*. (Journal IF: 3.144 Citation: 1)



Pinto S, de Carvalho M (2014). Young slow-progressing ALS patients are at higher risk of inappropriate and disease fastening surgeries (letter). *Amyotr Lat Scler Frontotemporal Degener* (Journal IF: 2.591 Citation: NA)

Maia, T. V.\* & Cano-Colino, M.\* (in press). The role of serotonin in orbitofrontal function and obsessive-compulsive disorder. *Clinical Psychological Science*. \*Authors contributed equally. (Journal IF: NA Citation: NA)

Maia, T. V. (in press). Introduction to the series on computational psychiatry. *Clinical Psychological Science*. (Journal IF: NA Citation: NA )

Horga\*, G., Maia\*, T. V., Marsh, R., Hao, X., Xu, D., Duan, Y., Tau, G. Z., Graniello, B., Wang, Z., Kangarlu, A., Martinez, D., Packard, M. G., Peterson, B. S. (in press). Changes in corticostriatal connectivity during reinforcement learning in humans. *Human Brain Mapping*. (Journal IF: NA Citation: NA )\*Authors contributed equally.

Posner, J., Marsh, R., Maia, T. V., Peterson, B. S., Gruber, A., & Simpson, H. B. (2014). Reduced functional connectivity within the limbic cortico-striato-thalamo-cortical loop in unmedicated adults with obsessive-compulsive disorder. *Human Brain Mapping*, Vol. **35**, No. 6, pp. 2852-2860. (Journal IF: 6.924 Citation: NA)

Geraldes, V., Goncalves-Rosa, N., Liu, B., Paton, J. F., & Rocha, I. (2014). Essential role of RVL medullary neuronal activity in the long term maintenance of hypertension in conscious SHR. *Autonomic Neuroscience*, **186**, 22-31. (Journal IF: NA Citation: NA)

Conceição I, Costa J, Castro J, de Carvalho M. Neurophysiological techniques to detect early small-fiber dysfunction in transthyretin amyloid polyneuropathy. *Muscle Nerve*. 2014 Feb;**49**(2):181-6.(Journal IF: NA Citation: NA)

Luis L, Zhu H, Costa J, Valls-Solé J, Brandt T, Zhou W, Schneider E. Reply to the commentary on Luis et Al. Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials. *Otol Neurotol*. 2014 Feb;**35**(2):379-83 (Journal IF: NA Citation: NA)

Laranjo, S., Oliveira, M., & Trigo, C. (2014). Successful catheter ablation of a left anterior accessory pathway from the non-coronary cusp of the aortic valve. *Cardiology in the young*, **1-3**.(Journal IF: NA Citation: NA)

Lip, G. Y., Laroche, C., Boriani, G., Dan, G. A., Santini, M., Kalarus, Z., ... & Tavazzi, L. (2014). Regional differences in presentation and treatment of patients with atrial fibrillation in Europe:

a report from the EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *Europace*, *euu201*.(Journal IF: NA Citation: 1)

Caldeira D, Barra M, Santos AT, de Abreu D, Pinto FJ, Ferreira JJ, Costa J. Risk of drug-induced liver injury with the new oral anticoagulants: systematic review and meta-analysis. *Heart* 2014 Apr;**100**(7):550-6.(Journal IF: NA Citation: NA)

Caldeira D, David C, Santos A, Costa J, Pinto F, Ferreira JJ. Efficacy and safety of low molecular weight heparin in patients with mechanical heart valves: systematic review and meta-analysis. *J Thromb Haemost*. 2014 May;**12**(5):650-9.(Journal IF: NA Citation: NA)

Geraldes, V., Gonçalves-Rosa, N., Liu, B., Paton, J. F., & Rocha, I. (2014). Chronic depression of hypothalamic paraventricular neuronal activity produces sustained hypotension in hypertensive rats. *Experimental physiology*, **99**(1), 89-100.(Journal IF: NA Citation: NA)

Caldeira D, Costa J, Ferreira JJ, Pinto FJ. Thromboembolic risk in the initiation, switch and interruption/re-initiation of oral anticoagulants: do newcomers improve outcomes? Insights from a meta-analysis of RCTs. *International Journal of Cardiology* 2014; **177**: 117–119. (Journal IF: NA Citation: NA)

Caldeira D, Costa J, Barra M, Pinto FJ, Ferreira JJ. How safe is acetaminophen use in patients treated with vitamin K antagonists? A systematic review and meta-analysis. *Thromb Res*. 2015 Jan;**135**(1):58-61(Journal IF: NA Citation: NA)

Luis L, Lehnen N, Muñoz E, de Carvalho M, Schneider E, Valls-Solé J, Costa J. Anticompensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmus. *Vest Research* 2014 (in press)

Luis L, Costa J, Yacovino D, A pragmatic strategy for positional downbeat nystagmus and vertigo. *Otol Neurotol* 2014 (in press)

Caldeira D, Loureiro MJ, Costa J, Pinto FJ, Ferreira JJ. Oral anticoagulation for pulmonary arterial hypertension: systematic review and meta-analysis. *Can J Cardiol*. 2014 Aug;**30**(8):879-87 (Journal IF: NA Citation: NA)

Caldeira D, Barra M, Pinto FJ, Ferreira JJ, Costa J. Intracranial hemorrhage risk with the new oral anticoagulants: a systematic review and meta-analysis. *J Neurol*. 2014 (Journal IF: NA Citation: NA)

Caldeira D, Costa J, Fernandes RM, Pinto FJ, Ferreira JJ. Performance of the HAS-BLED high bleeding-risk category, compared to ATRIA and HEMORR2HAGES in patients with atrial fibrillation: a systematic review and meta-analysis. *J Interv Card Electrophysiol*. 2014 Sep;**40**(3):277-84(Journal IF: NA Citation: NA)

Caldeira D, Barra M, de Abreu D, Santos A, Costa J, Ferreira JJ. Risk of Insomnia with Non-Vitamin K Oral Anticoagulants: Systematic review and Meta-analysis. *Sleep and Breathing* 2014 (in press)

Gouveia M, Sousa R, Costa J, Borges M. Economic Evaluation of Suboxone® for substitution treatment of opioid drug dependence in Portugal. *Heroin Addiction and Related Clinical Problems* Dec 20 2014 (Published Ahead-of-Print).

Caldeira D, Ferreira A, Barra M, Gonçalves N, Pinto FJ, Ferreira JJ, Costa J. Pericardial bleeding risk with non-vitamin K oral anticoagulants: a meta-analysis. *International Journal of Cardiology* 2014 (in press)

Laranjo, S., Tavares, C., Oliveira, M., & Rocha, I. (2014). Autonomic modulation in a patient with syncope and paroxysmal atrial-fibrillation. *Autonomic Neuroscience*.

Cunha-Reis, D.; Aidil-Carvalho M.F. and Ribeiro, J.A. (2014) Endogenous inhibition of hippocampal LTD and depotentiation by vasoactive intestinal peptide VPAC1 receptors, *Hippocampus*, **24**:1353–1363. (Journal IF: 5.49 Citation: NA)

Luis L, Zhu H, Costa J, et al. Reply to the commentary on Luis et Al. "Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials". *Otol Neurotol*. 2014; **35**(2):379–383. (Journal IF: 5.49 Citation: NA)

Laranjo, S., Tavares, C., Oliveira, M., Trigo, C., Pinto, F., & Rocha, I. (2014). An insight into the autonomic and haemodynamic mechanisms underlying reflex syncope in children and adolescents: a multiparametric analysis. *Cardiology in the young*, **1-8**. (Journal IF: NA Citation: NA)

#### **Other publications International**

Domingos F, Serra A: Metabolic syndrome: a multifaceted risk factor for kidney stones. *Scand J Urol*. 2014 Oct;**48**(5):414-9 Epub 2014 Apr 8

Conceição I, Costa J, Castro J, de Carvalho M. Neurophysiological techniques to detect early small-fiber dysfunction in transthyretin amyloid polyneuropathy. *Muscle Nerve*. 2014 Feb;**49**(2):181-6.

Ole B. Suhr, Isabel M. Conceicao, Onur N. Karayal, Francine S. Mandel, Pedro E. Huertas, Bogoran Ericzon. Post Hoc Analysis of Nutritional Status in Patients with Transthyretin Familial Amyloid Polyneuropathy: Impact of Tafamidis. *Neurology and Therapy: Volume 3, Issue 2* (2014), Page 101-112

de Carvalho M, Swash M (2014). Neurologic Complications of Atlanto-Axial Dislocation. In HANDBOOK OF CLINICAL NEUROLOGY – Neurologic Aspect of Systemic Diseases. Ed. Biller J, Ferro JM. *Elsevier* **119**; pp 435-448

Rodrigues F, Caldeira D, Ferreira J, Costa J. Epidemiology of caffeine and neuroprotection in Parkinson's disease, in "The Adenosinergic System - A Non-Dopaminergic Target in Parkinson's Disease", edited by Nicola Simola, Micaela Morelli and Jadwiga Wardas (Springer). Book Chapter

Luis L. 2014. The video Head Impulse Test. In: Carmona S., Asprela Libonati G., eds. Neurotology. Akadia Editorial; [CD-ROM]. Luis L. 2014. O vHIT como teste de avaliação vestibular. In: Zuma e Maia F., Mangabeira Albernaz P., Carmona S., ed. *Otoneurologia Atual. Revinter*; pp **89-104**.

Lucília N Diogo, Inês V Faustino, Ricardo A Afonso, Sofia A Pereira, Emília C Monteiro, Ana I Santos. Losartan voluntary oral administration – a less stressful approach in rats. *Journal of the American Association for Laboratory Animal Science – JAALAS*, in press).

#### **Other publications National**

Valente, B. T., Conceição, J. M., da Silva, M. N., Oliveira, M. M., Cunha, P. S., Lousinha, A., & Ferreira, R. C. (2014). Acesso femoral venoso: uma alternativa excepcional para a implantação de *i>* pacemaker *</i> definitivo. *Revista Portuguesa de Cardiologia*, 33(5), 311-e1.*

Portugal, G., Oliveira, M. M., Cunha, P. S., Ferreira, F., Lousinha, A., Fiarresga, A., ... & Ferreira, R. C. (2014). Short QT syndrome presenting as syncope: How short is too short. *Revista Portuguesa de Cardiologia*, 33(10), 649-e1

Oliveira, M., Madeira, F., Bonhorst, D., & Morais, C. (2014). Registo nacional de eletrofisiologia cardíaca (2012). *Revista Portuguesa de Cardiologia*, 33(10), 583-589.

Sousa R. Costa J, Vaz Carneiro A, Fernandes RM. Cochrane Corner: "Combined and alternating

paracetamol and ibuprofen therapy for febrile children". *Acta Pediatr Port* 2014;45:64-66

Ferreira-Magalhães M, Costa J, Vaz Carneiro A, Fernandes RM. Cochrane Corner: "Overview of reviews on the treatment of croup". *Acta Pediatr Port* 2014;45:168-171

Gil J, Costa J, Vaz Carneiro A, Fernandes RM. Cochrane Corner: "Immunostimulants for preventing respiratory and tract infection in children". *Acta Pediatr Port* 2014;45:253-255

Costa J, Sousa R, Alarcão J, Vaz Carneiro A, Filipe P. Eficácia e segurança de mebutato de ingenol no tratamento da queratose actínica: Revisão sistemática e meta-análise. *Revista da Sociedade Portuguesa de Dermatologia e Venereologia* 2014; 72 (3) (in press)

Cabanelas, N., Oliveira, M., da Silva, M. N., Cunha, P., Valente, B., Lousinha, A., ... & Ferreira, R. (2014). The proarrhythmic effect of cardiac resynchronization therapy: An issue that should be borne in mind. *Revista Portuguesa de Cardiologia (English Edition)*, 33(5), 309-e1

Vaz Carneiro A, Costa J. [Analysis of the Cochrane review: Multimedia educational interventions for consumers about prescribed and over-the-counter medications. *Cochrane Database*

Vaz Carneiro A, Costa J. [Analysis of the Cochrane Review: Direct thrombin inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in people with non-valvular atrial fibrillation. *Cochrane Database Syst Rev.* 2014;3:CD009893]. *Acta Med Port.* 2014 Mar-Apr;27(2):157-9.

Caldeira D, Vaz-Carneiro A, Costa J. [Analysis of the Cochrane review: Anticoagulation versus placebo for heart failure in sinus rhythm. *Cochrane Database Syst Rev.* 2014;3:CD003336]. *Acta Med Port.* 2014 May-Jun;27(3):284-

Vaz-Carneiro A, Luz R, Borges M, Costa J. [Primary and secondary outcomes in oncology clinical trials: definitions and uses]. *Acta Med Port.* 2014 Jul-Aug;27(4):498-502.

Cardoso AT, Nanji L, Costa J, Vaz-Carneiro A. [Analysis of the Cochrane Review: Vitamin D supplementation for prevention of cancer in adults. *Cochrane Database Syst Rev.* 2014, 6:CD007469]. *Acta Med Port.* 2014 Jul-Aug;27(4):411-3.

Caldeira D, Barra M, David C, Costa J, Ferreira JJ, Pinto FJ. The prevalence of oral anticoagulation in patients with atrial fibrillation in Portugal: Systematic review and meta-analysis of observational studies. *Rev Port Cardiol.* 2014 Sep;33(9):555-60.

Azevedo P, Costa J, Vaz-Carneiro A. [Analysis of the Cochrane Review: Use of Systemic Corticosteroids for Acute Exacerbations of Chronic Obstructive Pulmonary Disease. *Cochrane Database Syst Rev.* 2014, 9:CD001288]. *Acta Med Port.* 2014 Sep-Oct;27(5):537-40.

Gouveia M, Costa J, Alarcão J, Augusto M, Caldeira D, Pinheiro L, Vaz Carneiro A, Borges M.

Burden of Disease and Cost of Illness of Atrial Fibrillation in Portugal. Rev Port Cardiol. 2014 Dec 16. (Published Ahead-of-Print)

Caldeira D, Lopes LR, Vaz-Carneiro A, Costa J. Cochrane Corner: Corticosteroids for viral myocarditis. Rev Port Cardiol. 2014 Dec 16. (Published Ahead-of-Print)

Valente, B. T., Conceição, J. M., da Silva, M. N., Oliveira, M. M., Cunha, P. S., Lousinha, A., ... & Ferreira, R. C. (2014). Acesso femoral venoso: uma alternativa excepcional para a implantação de *i* pacemaker*/i* definitivo. Revista Portuguesa de Cardiologia, 33(5), 311-e1.

Correia PA, Domingos F: Water-electrolyte balance?and acid-base equilibrium?– A perspective on homeostatic physiology. Port J Nephrol Hypert 2014; 28(4): 290-291

Almeida M., Gonçalves P., Infante de Oliveira E., Carvalho H. Renal Denervation for Resistant Hypertension - An update on the current understanding of the role of sympathetic nervous system in blood pressure control. Rev Port Cardiol Accepted for publication Impact factor: 0.525

Infante, D. O. E. (2014). Renal sympathetic denervation-phenomenon or noumenon?. Revista portuguesa de cardiologia: orgao oficial da Sociedade Portuguesa de Cardiologia= Portuguese journal of cardiology: an official journal of the Portuguese Society of Cardiology. (Impact factor: 0.525

Jerónimo, A., Sagarrabay, A., de Sousa, V., Gonçalves, V., & Barros, E. (2014). Cordoma do clivus: Abordagem endoscópica endonasal transesfenoidal. Revista Portuguesa de Otorrinolaringologia e Cirurgia Cérvico-Facial, 52(1), 33-38.

Damásio A, Oliveira M, Cunha P, Mesquita D, Neves D, Lousinha A, Valente B, Osório P, Conceição JM, Nogueira da Silva, Ferreira R.Hematomas com necessidade de drenagem cirúrgica em doentes com dispositivos cardíacos implantáveis: prevalência e fatores de risco.XXIX Jornadas de Cardiologia do Sul e Regiões Autónomas, Évora, Outubro/2014.

Costa, J, de Carvalho, M (in press) Esclerose Lateral Amiotrófica. In NEUROCIÊNCIAS. Eds. Rego, C, Oliveira, C, Duarte, CB. Lidel. (Book)

#### **Invited lectures and seminars**

M.de Carvalho M.INSTITUTE of NEUROSCIENCES. UNIVERSITY of NEWCASTLE. Newcastle, Janeiro de 2014.

Fasciculation Potentials de Carvalho M.ATHLETICISM, CARDIOVASCULAR FITNESS and ENERGY METABOLISM in ALS. Oxford, Março de 2014.EMG as a Pre-Symptomatic Tool

de Carvalho M. 30TH INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlin. Março, 2014. Proving Upper Motor Neuron Signs in ALS

de Carvalho M. II CURSO MONOTEMÁTICO de DIABETES MELLITUS. Lisboa, Junho de 2014. Polineuropatia Diabética

de Carvalho M. REUNIÓN NEUROFISIOLOGIA CLÍNICA. Capítulo Bogota da Asociación Colombiana de Neurología. Bogota, Setembro de 2014. Enfermedad de la Neurona Motora: de Charcot a nuestros días (Magistral). Estudio Neurofisiológico de la Enfermedad de Neurona Motora (Magistral)

de Carvalho M. WORKSHOP PERSPECTIVAS EM ESTATÍSTICA BAYESIANA. Lisboa, Outubro de 2014. Statistics in Medicine.

de Carvalho M. CONGRESSO de NEUROLOGIA 2014. Lisboa, Novembro de 2014. Esclerose Lateral Amiotrófica: de Charcot ao futuro.

Conceição I, Early diagnosis of TTR-FAP: Clinical practice. ARIA III SYMPOSIUM : advances and research in TTR - improving diagnosis, improving outcomes. Póvoa do Varzim, Portugal. Feb 7-8th, 2014

Conceição I, Monitoring and assessment of patients treated with tafamidis. ARIA III SYMPOSIUM : advances and research in TTR - improving diagnosis, improving outcomes. Póvoa do Varzim, Portugal. Feb 7-8th, 2014

Conceição I, Amyloid Neuropathies- neurophysiological approach. ICCN Teaching Session. 30th International Congress on Clinical Neurophysiology (ICCN) of the IFCN and 58th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN) Mar 19, 2014 - Mar 23, 2014, Berlin, 2014

Conceição I, The story of tafamidis: what has it meant for people with TTR-FAP and their families Pfizer European Rare Disease Summit. June 3-5, 2014 London.

Conceição I, TRANSTHYRETIN FAMILIAL AMYLOID POLINEUROPATHY: pharmacological management. 18a Reunião Anual da Sociedade Portuguesa de Genética Humana. 19 – 21 Novembro, Lisboa 2014

Oliveira M., Canalopatias, 3º Curso de Revisão e Atualização em Medicina Cardiovascular, Casa do Coração, Janeiro, 2014.

Oliveira M., CDI subcutâneo - Não traz nada de novo e tem limitações significativas! ARRITMIAS 2014. Cascais, Fevereiro, 2014.

Oliveira M., Os Doentes com FA Persistente de Longa Duração Devem ser Candidatos a Ablação por Cateter? Congresso Novas Fronteiras em Cardiologia. Ericeira, Fevereiro, 2014.

Oliveira M.,Managing systems in cardiac remote monitoring. A complex challenge turned into an important clinical tool. BIOSTEC 2014, 7th International Joint Conference on Biomedical Engineering Systems and Technologies.Angers, Março,2014

Oliveira M., TOUGHT CRT/CHF CASES -. SonR solved it! New Horizons in Heart Failure. Londres, Março, 2014.

Oliveira M.,Autonomic Modulation Therapy, Meet the Masters Autonomic Nervous System and Cardiac Arrhythmias , Budapeste, Março,2014.

Oliveira M.,Terapêutica de Ressincronização Cardíaca na Insuficiência Cardíaca Ligeira” Custo-Efectividade em Cardiologia. XXXV Congresso Português de Cardiologia. Albufeira, Abril,2014.

Oliveira M., Ablação de Fibrilhação Auricular: Experiência Portuguesa-Seguimento de doentes.XXXV Congresso Português de Cardiologia

Oliveira M.,Hemodynamic Device-Based AV and VV Delays Optimization in CRT: 2 Years of Practice with Systematic Echocardiography Validation. Can a Hemodynamic Sensor in CRT Make a Difference? Seeing is Believing. Cardiostim, Nice, Junho 2014.

Oliveira M.,Managing cardiac remote monitoring - a complex challenge turned into an important evidence-based practice. Workshop - Cardiac Remote Monitoring. Summer Meeting, Lisboa, Jullho, 2014.

Oliveira M.,Alterações do Segmento ST nas perturbações da condução AV. Sessão Clínica:Hospital Santa Marta, Lisboa, Outubro, 2014.

Oliveira M.,Cardioversão: a resposta à pergunta que faltava – resultados do estudo X-Vert -O compromisso com a inovação - Novas perspectivas de Xarelto na prevenção do AVC.Coração no Centro. Coimbra, Outubro/2014.

Luís L., The vestibulo-ocular reflex in vertigo, dizziness and balance disorders (Masterclass). Brainstem Society Meeting. Berlin, 2014.

Oliveira M., Leaping Forward – Lisbon International Clinical Congress “Robotics – the new frontier to treat arrhythmia” Lisboa, Fevereiro, 2014. (Moderador)



Oliveira M., (Journal Club) Hospital Santa Marta “Dronedarone for atrial fibrillation: The limited reliability of clinical practice guidelines”: Lisboa, Março, 2014.(Moderador)

Oliveira M., New Horizons in Heart Failure “Biologic resynchronization as an adjunct to CRT” Mário Oliveira, Londres, Março, 2014.(Moderador)

Oliveira M., XXXV Congresso Português de Cardiologia “Doenças Arritmogénicas Hereditárias: da genética ao choque do CDI” Mário Oliveira, Albufeira, Abril/2014.(Moderador)

Oliveira M., XXXV Congresso Português de Cardiologia “O melhor método para tratar a fibrilhação auricular isolada (Controvérsia)” Mário Oliveira, Albufeira, Abril/2014. (Moderador)

Oliveira M.,Reunião Nacional dos Centros de Pacing "Sistema Nacional de Vigilância de Dispositivos Médicos e Registo Nacional de Pacing” Viseu, Maio/2014.(Moderador)

Oliveira M.,Summer Meeting 2014” Remote Monitoring for the clinical management of heart failure patients” Mário Oliveira, Centro Cultural de Belém, Lisboa, Julho/2014. (Moderador)

Oliveira M.,Hospital Santa Marta, “Chronic vagal stimulation for the treatment of low ejection fraction heart failure: results of the neural cardiac therapy for heart failure (NECTAR-HF) randomized controlled trial and Autonomic Regulation Therapy via Left or Right Cervical Vagus Nerve Stimulation in Patients with Chronic Heart Failure: Results of the ANTHEM-HF Trial”Mário Oliveira, Lisboa Outubro, 2014. (Moderador)

Luís L. vHIT instruction course. XXVIII Barany Conference. Buenos Aires, Argentina, 2014.(Invited speaker; member of the Scientific and Organizing Committee)

Luís L., Video Head Impulse Test. Portuguese National ENT Congress, Lisbon, 2014. (Instructional Course )

Luís L., Vestibular Update, Congresso nacional SEORL. Madrid, Spain, 2014 (Instructional course)

Pinto S, de Carvalho M., NIV in ALS - When to start?” In Amyotrophic Lateral Sclerosis, Working group 2 – Noninvasive ventilation. 15thInternational Symposium of KU Leuven - Sleep apnea. Leuven, Feb20th, 2014.

Pinto S., Investigação em Medicina Física e de Reabilitação. Reunião da SPMFR integrado na Reunião da European Academy of Rehabilitation Medicine .Coimbra, Nov2014.

Pinto A. JORNADAS INTERNACIONAIS DE REABILITAÇÃO DO CMRA, Reabilitação Respiratória em Doentes Neurológicos, Alcoitão Outubro de 2014

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

de Carvalho M., BIOSIGNALS 2014: 7th International Conference on Bio-Inspired Systems and Signal Processing. Angers, Março de 2014. (Oral presentation)

de Carvalho M., Coherence and Phase Locking Disruption in Electromyograms of Patients with Amyotrophic Lateral Sclerosis. Camara, M; de Carvalho, M; Sergio, T; Pereira, C; Gamboa, H. (Oral presentation)

Pinto, P; Alves, P; de Carvalho, M. Is diaphragm ultrasound useful in ALS? ENCALS MEETING 2014. Leuven, Maio de 2014 (Poster presentation)

Saldanha, C; Pinto, S; Laborinho-Pronto, A; Barros, MA; Freitas, T; de Carvalho, M. THE JOINT 28th EUROPEAN SOCIETY for MICROCIRCULATION – 8th EUROPEAN VASCULAR BIOLOGY ORGANISATION MEETING. Pisa, June 2014. Hemorheological and Biochemical Parameters in Amyotrophic Lateral Sclerosis. (Oral presentation)

De Carvalho, M Turkman, A; Pinto, S; Swash, M. Modulation of Fasciculation Potential Frequency in ALS. 25th INTERNATIONAL SYMPOSIUM on ALS/MND. Bruxelas. Dezembro de 2014. (Poster presentation)

Diaz Campos, A; Conceição, I; Castro, J; de Carvalho, M. Detection of Early Abnormalities in Familial Amyloid Polyneuropathy by Quantitative Sensory Testing (QST). 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Luis, L; Lehnen, N; Munoz, E; de Carvalho, M; Schneider E; Valls-Solé, J; Brandt, T; Costa, J. Anticompensatory Quick Eyes Movements after Head Impulses – a peripheral vestibular sign in spontaneous nystagmus. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Luis, L; Costa, J; Munoz, E; de Carvalho, M; Lehnen, N; Schneider E; Valls-Solé, J. J. VOR Dynamics in Hereditary Cerebellar Ataxias. 30th INTERNATIONAL CONGRESS OF CLINICAL

NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Castro, J; Costa, J; Pinto, S; de Carvalho, M. Motor Unit Number Estimation (MUNIX) in amyotrophic lateral sclerosis – a prospective cohort study. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

De Carvalho, M; Swash, M. An Original Method to Investigate the Origin of the Fasciculation Potentials. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Pugdhal, K; Johnsen, B; Tankisi, H; Camdessanche, J-P; de Carvalho, M; Fawcett, P; Liguori, R; Labarre-Vila; Nix, W; Schofield, I. Fuglsang-Fredericksen. Value of EMG in Myopathy. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Castro, J; de Carvalho, M. Influence of an Inhibitory Theta-Burst Protocol on the Cortical Silent Period Induced by Magnetic Stimulation. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

De Carvalho, M; Casanova, I; Diaz Campos; A; Brum, M; Conceição, I. Motor Excitability Measurements in Familial Amyloid Polyneuropathy – the influence of tafamidis treatment. 30th INTERNATIONAL CONGRESS OF CLINICAL NEUROPHYSIOLOGY. Berlim, Março de 2014. (Poster presentation)

Neuwirth, C; Barkhaus, PE; Burkhardt, C; Castro, J; Czell, D; de Carvalho, M; Nandedkar, S; Stalberg, S; Weber, M. Motor Unit Number Index (MUNIX): ready for clinical ALS trials: a 15-months longitudinal trial. 25th INTERNATIONAL SYMPOSIUM on ALS/MND. Bruxelas. Dezembro de 2014. (Poster presentation)

Maia T.V., Computational Modeling and Brain Imaging of Tourette Syndrome and Attention-Deficit/Hyperactivity Disorder, Wellcome Trust Centre for Neuroimaging, University College London, UK, July 4, 2014 (Poster presentation)

Maia T.V., The Catecholamines in Psychiatric Disorders”, Keynote Speaker, Zurich Computational Psychiatry Meeting: Psychiatry under the Lens of Algorithms, Zurich, Switzerland, May 19, 2014. (Oral presentation)

Maia T.V., Reinforcement Learning in Tics, Habits, and Avoidance”, Computational Psychiatry

Workshop, Computational and Systems Neuroscience (Cosyne) Meeting, Snowbird, UT, USA, March 3, 2014 (Oral presentation)

Cunha-Reis, D.Gonçalves-Rosa N, Amaro-Leal A, Nunes-da-Silva C, Rocha I., Impaired spatial memory and response to novelty in a rat model of metabolic syndrome. Communication to the 9th FORUM OF EUROPEAN NEUROSCIENCE – FENS 2014, MILAN, ITALY, 5th -9th JULY, 2014. (Oral presentation)

Serôdio J, Cunha PS, Ferreira R, Laranjo S, Tavares C, Alves S, Rocha I, Oliveira M.Acute Baroreflex Effectiveness Index reduction after cardiac resynchronization therapy.CARDIOTECHNIX 2014, Roma, Setembro/2014. (Oral presentation)

Mesquita D, Abreu A, Portugal G, Cunha P, Oliveira M, Carmo M, Santos V, Santa-Clara H, Oliveira L, Ferreira R.Cardiac autonomic dysfunction and cronic heart failure: can I-123 meta-iodobenzylguanidine scintigraphy predict arrhythmic events in patients with CRT?Heart Failure 2014, Atenas, 5/2014. (Oral presentation)

Mesquita D., Abreu A., Portugal G., Pimenta R., Cunha P., Nogueira Da Silva M., Mota Carmo M., Santa-Clara H., Oliveira L., Oliveira M., Ferreira R.Cardiac Scintigraphy with I-123 Metaiodobenzylguanidine in the Evaluation of Arrhythmic Risk in Patients with Cardiac Autonomic Dysfunction and Cronic Heart Failure.Cardiostim, Nice, 6/2014.(Oral presentation)

Abreu A., Mesquita D., Santa-Clara H., Oliveira L., Nogueira Da Silva M., Cunha P., Portugal G., Pimenta R., Ferreira R., Oliveira M.Cardiac Scintigraphy with I-123 Metaiodobenzylguanidine in the Evaluation of Arrhythmic Risk in Patients with Cardiac Autonomic Dysfunction and Cronic Heart Failure.CARDIOTECHNIX 2014, Roma, Setembro/2014. (Oral presentation)

Branco L., Galrinho A., Silva T., Feliciano J.,Teixeira P., Rio P., Alves S., Santos S., Silva M., Cunha P., Oliveira M., Ferreira R.Changes Obtained in Different Echocardiographic Parameters after ECHO Guided CRT Optimization.Cardiostim, Nice, 6/2014. (Oral presentation)

Oliveira M, Branco L, Galrinho A, Nogueira da Silva, Silva P, Valente B, Feliciano J, Pimenta R, Delgado AS, Ferreira R.Haemodynamic Device-Based Optimization in Cardiac Resynchronization Therapy: Initial Experience with Systematic Echocardiographic Assessment of AV and VV Intervals.Cardiostim, Nice, 6/2014. (Oral presentation)

Branco L., Galrinho A., Oliveira M., Feliciano J., Silva T., Soares R., Alves S., Santos S., Rio P., Cunha P., Silva M., Ferreira R.Importance of ECHO Guided CRT Optimization in Non Responder Patients and Predictors of Significant Improvement after Optimization.Cardiostim, Nice, 6/2014. (Oral presentation)

Nogueira M, Abreu A., Pinheiro T., Ramos C., Cunha P., Oliveira M., Feliciano J., Soares R., Mota Carmo M., Cruz Ferreira R.Modulation of the inflammatory response and apoptosis by cardiac resynchronization in heart failure.Congresso Europeu de Cardiologia, Barcelona, Setembro/2014. (Oral presentation)

Branco L.M., Galrinho A., Feliciano J., Oliveira M., Soares R., Alves S., Timoteo A., Cunha P., Nogueira Silva M., Cruz Ferreira R. Predictors of mortality and/or transplantation in patients submitted to echo guided CRT optimization. Congresso Europeu de Cardiologia, Barcelona, Setembro/2014. (Oral presentation)

Laranjo S., Oliveira, M., Nogueira-da-Silva L., Ferreira, F., Oliveira, J., Agapito A., Fragata J., Trigo C., Pinto F.F., Ferreira R. Prevalence of Arrhythmias and Their Risk Factors Long-Term After Surgical Repair of Tetralogy of Fallot. *Cardiostim*, Nice, 6/2014. (Oral presentation)

Feliciano J, Oliveira M, Soares R, Nogueira Silva M, Cunha P, Pereira Silva T, Branco LM, Alves S, Pimenta R, Cruz Ferreira R. Prognostic impact of long-term remote monitoring in heart failure patients with implantable devices: preliminary analysis. *Heart Failure* 2014, Atenas, 5/2014 . (Oral presentation)

Feliciano J., Oliveira M., Soares R., Nogueira da Silva M., Cunha P., Silva T., Branco L., Galrinho A., Alves S., Delgado A., Pimenta R., Ferreira R. Prognostic Impact of Long-Term Remote Monitoring in Heart Failure Patients with Implantable Devices: Preliminary Analysis. *Cardiostim*, Nice, 6/2014. (Oral presentation)

Locati E., Moya A., Brignole M., Ormaetxe J., Tanner H., Oliveira M., Lopez-Gil M., Sabate X., Rivas N., Willems R., Lunati M. Synarr-Flash Study: Monitoring of Syncope and Palpitations with External Loop Recorder. *Cardiostim*, Nice, 6/2014. (Oral presentation)

Laranjo S, Tavares C, Oliveira MM, I Rocha. The Predictive Value of a Multivariate Model of Autonomic and Baroreflex Function Applied to Patients With Reflex Syncope. *Cardiostim*, Nice, 6/2014. (Oral presentation)

Monteiro A., Oliveira M., Cunha P., Nogueira da Silva M., Feliciano J., Branco L., Rio P., Cabanelas N., Pimenta R., Delgado A., Lourenço A., Ferreira, R. Time to Left Ventricle Reverse Remodeling after Cardiac Resynchronization Therapy: Better Late than Never? *Cardiostim*, Nice, 6/2014. (Oral presentation)

Rio P., Oliveira M., Cunha P., Nogueira Da Silva M., Branco L., Galrinho A., Abreu J., Feliciano J., Monteiro A., Teixeira P., Pimenta R., Delgado A., Ferreira R. What Happens to Non-Responders in Cardiac Resynchronization Therapy? *Cardiostim*, Nice, 6/2014. (Oral presentation)

Diaz Campos (Bogotá/CO), I. Conceição, J. Castro, M. De Carvalho (Lisbon/PT) Detection of early neuropathic abnormalities in familial amyloidotic polyneuropathy by Quantitative Sudomotor Axon Reflex Test (QSART). 30th International Congress on Clinical Neurophysiology (ICCN) of the IFCN and 58th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN) Mar 19, 2014 - Mar 23, 2014. Berlin, 2014. (Oral presentation)

M. de Carvalho, I. Casanova, A. Dias, M. Brum, I. Conceição. Motor excitability measurements in familial amyloid polyneuropathy – the influence of tafamidis treatment. 30th International Congress on Clinical Neurophysiology (ICCN) of the IFCN and 58th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN) Mar 19, 2014 - Mar 23, Berlin, 2014 (Oral presentation)

Ole Suhr, David Adams, Teresa Coelho, Isabel Conceicao, Marcia Waddington-Cruz, Hartmut Schmidt, Josep Campistol, Jean Pouget, Juan Buades, John Berk, Rick Falzone, Jamie Harrop, Ricardo De Frutos, Brian Bettencourt, Jeff Cehelsky, Sara Nochur, Akshay Vaishnav, Jared Gollob. Further analysis of phase II trial of patisiran, a novel RNAi therapeutic for the treatment of familial amyloidotic polyneuropathy. XIV International Symposium on Amyloidosis April 27 – May 1, 2014 Indianapolis, IN, USA. (Oral presentation)

Arie J Stangou, Teresa Coelho, Isabel Conceicao, Maria Saraiva, Eduardo Barroso, David Adams, Didier Samuel, Teresa Antonini, Violaine Plante, David Azoulay, Giampaolo Merlini, Laura Obici, Claudio Rapezzi, Francisco Salvi, Gerd Otto, Ana Barreiros, Marcia Waddington Cruz, Steve Zeldenrust, Merrill Benson, Andrea Tzakis, Bouke Hazenberg, Shu- Ichi Ikeda, Yukio Ando, Julian Gillmore, Paolo Muesan, Philip N Hawkins, Henryk Wilzek, Marie Larsson, Ole Suhr, Laura Llado, Per Westermark, Bo-Goran Ericzon. Domino liver transplantation using familial amyloidotic polyneuropathy liver grafts; proposal for an international multicentre study to assess risk of de novo amyloidosis in the domino recipients. XIV International Symposium on Amyloidosis April 27 – May 1, 2014 Indianapolis, IN, USA. (Oral presentation)

I. Conceição, J. Castro, K. Valdez, H. Ferreira, P. Pereira, M. Cardoso, T. Coelho. Tafamidis meglumine and nerve fiber function in Portuguese patients with transthyretin familial amyloid neuropathy. Joint Congress of European Neurology, Istanbul, Turkey, May 31-June 3, 2014. (Oral presentation)

T. Coelho, I. Conceição, M. Cardoso, C. Monteiro, C. Alves, C. Rodrigues, P. Pereira, A.M. Silva. Evaluation of one year treatment with tafamidis in Portuguese patients with transthyretin familial amyloid polyneuropathy. Joint Congress of European Neurology, Istanbul, Turkey, May 31-June 3, 2014 (Poster presentation)

T. Coelho, I.M. Conceicao, F. Barroso, M. Waddington-Cruz, H.H.-J. Schmidt<sup>5</sup>, G. Rosas, F.S. Mandel, M. Stewart, P. Huertas, O.N. Karayal. Long term effects of tafamidis treatment on transthyretin familial amyloid polyneuropathy (TTR-FAP): interim results from the Fx1A-303 study. Joint Congress of European Neurology, Istanbul, Turkey, May 31-June 3, 2014 (Oral presentation)

Brum M, Castro J, Conceicao I. 13th International Congress on Neuromuscular Diseases, Nice-France 5-10 July 2014. Familial Amyloid Polineuropathy: efficacy of liver transplant versus tafamidis in nerve fiber function. (Poster Presentation)

Lima Da Silva G., Cortez-Dias N., Placido R., Ramalho A.R., Guimaraes T., Nobre Menezes M., Conceicao I., Nunes Diogo A, Azevedo Coutinho M.C. NT-proBNP: an important prognostic marker in familial amyloid polyneuropathy. European Congress of Cardiology. Barcelona 2014. M. Nobre Menezes, N. Cortez Dias, A.R.G. Francisco, R. Placido, A.R.G. Ramalho, T. Guimaraes, A. Paixao, I. Conceicao, A. Nunes Diogo, M.C. Azevedo Coutinho. Early and late onset of familial amyloid polyneuropathy: two distinct clinical phenotypes in terms of arrhythmias. European Congress of Cardiology. Barcelona 2014. (Oral presentation)

David Adams, Ole Suhr, Teresa Coelho, Isabel Conceicao, Marcia Waddington-Cruz, Hartmut Schmidt, Juan Buades, Josep Campistol, Jean Pouget, John Berk, Rick Falzone, Jamie Harrop, Ricardo De Frutos, Brian Bettencourt, Jeffrey Cehelsky, Sara Nochur, Akshay Vaishnav and Jared Gollob. Phase 2 Open-Label Extension Study of Patisiran, an RNAi Therapeutic for the Treatment of Familial Amyloidotic Polyneuropathy. American Neurological Association's 2014 Annual Meeting. Baltimore, MD, United States. Sun, Oct 12 – Tue, Oct 14, 2014 (Oral presentation)

Luís L. Anticomensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmus. XXVIII Barany Conference, Argentina, 2014  
Luís L., Vestibular ocular reflex dynamics with head-impulses in hereditary cerebellar ataxias. ICCN 2014. Berlin, 2014 (Poster presentation)

Santos, A.I. (2014) FELASA Accreditation of education and training – a mobility passport, RusLASA-ICLAS International Conference, S. Petersburg, Russia. (Oral presentation)

Lucília N Diogo, Sofia A Pereira, Inês V Faustino, Ricardo A Afonso, Ana I Santos, Emília C Monteiro. Effects of carvedilol on blood pressure and heart rate in a rat model of hypertension induced by chronic intermittent hypoxia. XLV Portuguese Society of Pharmacology (SPF) Annual Meeting, XXXIII Meeting of Clinical Pharmacology and XIV Meeting of Toxicology, Lisbon, 4-5 February 2015 (Oral presentation)

Lucília N Diogo, Inês V Faustino, Ricardo A Afonso, Sofia A Pereira, Emília C Monteiro, Ana I Santos. Oral Voluntary ingestion as a stress free alternative to orogastric gavage: the example of losartan chronic administration. EUROTOX 2014: 50th Congress of The European Societies of Toxicology. Edinburgh International Conference Centre. 07 - 10 September 2014 / United Kingdom, Edinburgh (Poster presentation)

Luís L., Anticomensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmus. ICCN 2014. Berlin, 2014. (Poster presentation)

Pinto S, Alves P, Pimentel B, Swash M, de Carvalho M. Ultrasound for assessment of diaphragm in Amyotrophic Lateral Sclerosis. Congresso de Neurologia 2014-Neurologia do Futuro. Lisboa, Nov 2014. (Oral presentation)

Pinto S, Alves P, Pimentel B, Swash M, de Carvalho M. Ultrasound and neurophysiological assessment of the diaphragm in Amyotrophic Lateral Sclerosis. 12th annual congress of the European network for the cure of ALS (ENCALS). Leuven, May 2014 (Poster presentation)

Luis L, Costa J, Muñoz E, de Carvalho M, Lehnen N, Schneider E. Vestibular ocular reflex dynamics with head-impulses in hereditary cerebellar ataxias. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014. (Poster presentation)

Luis L, Lehnen N, Muñoz E, de Carvalho M, Schneider E, Valls-Solé J, Costa J. Anticomensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous

nystagmus. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014 (Poster presentation)

Castro J, Costa J, Pinto S, de Carvalho M. Motor unit number index (MUNIX) in amyotrophic lateral sclerosis: a prospective cohort study. International Congress Clinical Neurophysiology 2014. Berlin, Germany: Mar 2014. (Poster presentation)

Luis L, Costa J, Muñoz E, Schneider E, Valls-Solé J. Vestibular ocular reflex dynamics during passive head-impulses: slow phase and quick-eye movements in Huntington's disease. European Huntington's Disease Network Meeting. Barcelona, Spain. (Poster presentation)

M. Gouveia, M. Borges, M. Augusto, D. Caldeira, J. Alarcão, L. Pinheiro, R. Sousa, F. Fareleira, R. Ascensão, J. Costa, P. Laires, M. Fiuza, N.C. Dias, S. Martins, A. Belo, A. Vaz-Carneiro. Cost and Burden Of Hypercholesterolemia In Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

Inês M, Rodrigues F., Saraiva J., Costa J.. Pre-Symptomatic Genetic Testing In Familial Amyloid Polyneuropathy: The Reproductive Options. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

Borges M., Gouveia M., Alarcão J., Sousa R., Teixeira E., Barata F., Laranjeira E., Lopes F., Parente B., Pinheiro L., Vaz-Carneiro A., Costa J.. Cost and Burden of Non-Small Cell Lung Cancer's in Portugal. ISPOR 17th Annual European Congress. Amsterdam, The Netherlands: Nov 2014. (Poster presentation)

Silva Marques, J., A. Magalhães, C. Jorge, Infante Oliveira E., Duarte J. A., Marques Da Costa J., Canas Da Silva P., Nunes Diogo A., Access Site Is an Independent Predictor of Radiation Exposure During Coronary Angiography and Pci, In EuroPCR 2014. Paris, France, 2014. (Poster presentation)



### Communications in National Conferences

Santos, M; Gomes, A; Gamboa, H; de Carvalho, M; Pinto, S; Quintão, C. FÍSICA 2014 – 19ª CONFERÊNCIA NACIONAL de FÍSICA e 24º ENCONTRO IBÉRICO para o ENSINO DA FÍSICA. Estudo do Comportamento Dinâmico do Sinal Eletromiográfico na Esclerose Lateral Amiotrófica, Lisboa, Setembro 2014 (Oral presentation)

Pinto, S; Alves, P; Pimentel, B; Swash, M; Ultrasound for Assessment of Diaphragm in ALS, CONGRESSO de NEUROLOGIA 2014. Lisboa, Novembro de 2014 (Oral presentation)

Pronto-Laborinho, AC; Barros, MA; Pinto, S; de Carvalho, Aumento da Proteína Secretoras das Células de Clara em Doentes com Esclerose Lateral Amiotrófica. CONGRESSO de NEUROLOGIA 2014. Lisboa, Novembro de 2014 (Oral presentation)

Alves, P; de Carvalho, M; Peralta, R; Gerales, R; Fonseca, AC; Pinho e Melo, T. Mioclonias Axiais após Acidente Vascular Cerebral Isquémico. CONGRESSO de NEUROLOGIA 2014. Lisboa, Novembro de 2014 (Poster presentation)

Ferreira, J; Franco, A; Peralta, R; Albuquerque, L; de Carvalho, M., Miosite Focal do Músculo Grande Adutor da Coxa Associada a Infecção à Adenovírus. CONGRESSO de NEUROLOGIA 2014. Lisboa, Novembro de 2014 (Poster presentation)

Maia T.V., Simple Neurocomputational Mechanisms in the Explanation of Complex Psychiatric Disorders”, Workshop on One, Two, and Many Brains, Champalimaud Foundation, Lisbon, Portugal, September 19, 2014 (Oral presentation)

Maia T.V., Translational Neuroscience: From Basic Science to the Clinic, Symposium on Neurodevelopmental Disorders: From Neuroscience to the Clinic, Champalimaud Centre for the Unknown, Lisbon, Portugal, May 30, 2014. (Oral presentation)

Maia T.V., Cortico-Striatal Circuits: Structure and Function” and “Cortico-Striatal Circuits in Tourette Syndrome and Obsessive-Compulsive Disorder”, Advanced Course on Neuronal Circuits & Behavior, Neurasmus Program, Center for Neuroscience and Cell Biology, University of Coimbra, Portugal, January 22, 2014 (Oral presentation)

Leal E., Oliveira M., Pais-Ribeiro J., Oliveira, E., Alves T., Ferreira R. Impacto da síncope na qualidade de vida: validação duma escala de avaliação em doentes submetidos a teste de inclinação. ARRITMIAS 2014, Cascais, Fevereiro/2014. (Oral presentation)

Oliveira M. Mechanistic exploration of molecular changes underlying autonomic-induced atrial remodeling: a new step in the comprehension of arrhythmogenic vulnerability? ARRITMIAS 2014, Cascais, Fevereiro/2014. (Oral presentation)

Oral presentation Valente B., Oliveira M, Silva Cunha P., Nogueira da Silva, Lousinha A, Conceição JM, Cruz Ferreira R., Experiência Inicial da Implementação da Técnica da Pisa na Extracção de Electrodo em Portugal. ARRITMIAS 2014, Cascais, Fevereiro/2014. (Oral presentation)

Seródio J, Oliveira M, Cunha P, Nogueira Silva M, Abreu A, Laranjo S, Tavares C, Branco L, Alves S, Pinto B, Rocha I, Ferreira R., Autonomic and Baroreflex Function in Heart Failure Patients Candidate to Cardiac Resynchronization Therapy. Arritmias 2014, Cascais, Fevereiro/2014. (Oral presentation)

Monteiro A., Oliveira M., Silva Cunha P., Nogueira da Silva, Feliciano J, Galrinho A, Rio P, Pimenta R, Delgado A, Ferreira R. , Upgrading from right ventricular pacing to biventricular stimulation in pacemaker patients with severe heart failure: long-term effects on left ventricular remodeling. Arritmias 2014, Cascais, Fevereiro/2014. (Oral presentation)

Laranjo S., Oliveira M., Nogueira Silva M., Sousa L., Ferreira F., Oliveira J., Agapito A., Fragata J., Trigo C., Pinto F.F., Ferreira R. Prevalence of Arrhythmias and Their Risk Factors Long-Term After Surgical Repair of Tetralogy of Fallot. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Pereira da Silva T, Ramos R, Oliveira M, Silva Cunha P., Nogueira da Silva, Barbosa C, Sofia A, Pimenta R, Marques H, Ferreira R. ,Influência da fibrilhação auricular recorrente na fração de esvaziamento total, ativa e passiva da aurícula esquerda. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Branco L, Galrinho V, Oliveira M, Silva T, Feliciano J, Nogueira M, Rio R, Alves S, Cunha P, Nogueira Silva M, Ferreira R. Caracterização dos resultados da otimização da programação do CRT com apoio ecocardiográfico e modificação induzida em diferentes parâmetros ecocardiográficos. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Monteiro A, Oliveira M., Lousinha A, Nogueira da Silva, Cunha P, Nogueira M, Rio P, Ferreira R., Perfuração Tardia do Ventrículo Direito após implantação de pacemaker. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Laranjo S, Tavares C, Oliveira M, I Rocha., The Predictive Value of a Multivariate Model of Autonomic and Baroreflex Function Applied to Patients with Reflex Syncope. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Oliveira M, Nogueira da Silva, Cunha P, Lousinha A, Laranjo S, Silva T, Alves T, Delgado AS, Carlos I, Ferreira R., Assessing arrhythmia burden after ablation of atrial fibrillation using an event loop recorder: is there a predictive value during the “blanking period? XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Mesquita D, Abreu A, Portugal G, Pimenta R, Cunha P, Nogueira da Silva, Oliveira M, Ferreira R. Disfunção Autonómica Cardíaca e Insuficiência Cardíaca Crónica: poderá a cintigrafia com I-123 meta-iodobenzilguanidina prever os eventos arritmicos em portadores de TRC?. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Tereno Valente B, Conceição JM, Oliveira M, Nogueira da Silva M, Silva Cunha P, Lousinha A, Rio P, Pimenta R, Ferreira R., Implementação da “Técnica de Pisa” na Extração de Eléctrodos em Portugal- Resultados dos Primeiros Procedimentos Realizados a Nível Nacional.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Lousinha A, Oliveira M, Nogueira da Silva, Silva Cunha P, Valente B, Silva T, Monteiro N, Pimenta R, Ferreira R., Catheter ablation of ventricular outflow tract arrhythmias guided by non-contact mapping system – long term results. XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Monteiro A., Oliveira M., Cunha P., Nogueira da Silva M., Feliciano J., Branco L., Rio P., Cabanelas N., Pimenta R., Delgado A., Lourenço A., Ferreira, R., Time to Left Ventricle Reverse Remodeling after Cardiac Resynchronization Therapy: Better Late than Never?XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Monteiro A, Oliveira M, Silva Cunha P, Nogueira da Silva, Feliciano J, Galrinho A, Rio P., Pimenta R., Delgado AS, Ferreira R,XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Oliveira M, Branco L, Galrinho A, Nogueira da Silva, Cunha P, Valente B, Feliciano J, Pimenta R, Delgado AS, Ferreira R.,Haemodynamic device-based optimization in cardiac resynchronization therapy: initial experience with systematic echocardiographic assessment of AV and VV intervals.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Branco L, Galrinho A, Oliveira M, Feliciano J, Silva T, Soares R, Alves S, Santos S, Rio P, Cunha P, Nogueira da Silva, Ferreira R.Benefício e fatores predizentes da melhoria da fração de ejeção no seguimento após optimização da programação guiada de CRT por ecocardiografia.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Feliciano J, Oliveira M, Soares R, Nogueira da Silva M, Cunha PS, Pereira Silva T, Branco L, Alves S, Delgado AS, Ferreira RC. Análise inicial do impacto prognóstico dos sistemas de monitorização à distância em portadores de dispositivos com terapêutica de ressincronização cardíaca.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Nogueira M, Abreu A, Pinheiro T, Ramos C, Cunha P, Oliveira M, Portugal G, Feliciano J, Soares R, Carmo M, Nogueira Silva, Ferreira R., Modulation of the inflammatory response and apoptosis by cardiac resynchronization in heart failure.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014 (Oral presentation)

Ferreira MJ, Oliveira M, Mateus C, Ferreira R, Farias F., Análise de Custo-Efectividade da

Terapêutica de Ressincronização Cardíaca: impacto da dessincronia mecânica na seleção de doentes.XXXV Congresso Português de Cardiologia, Albufeira, Abril/2014. (Oral presentation)

Serôdio J, Oliveira M, Cunha PS, Nogueira da Silva, Abreu A, Laranjo S, Tavares C, Branco L, Alves S, Rocha I, Ferreira R., Arterial baroreflex function in heart failure patients candidates to cardiac resynchronization therapy.XXXV Congresso Português de Cardiologia, Vilamoura, Abril/2014. (Oral presentation)

Laranjo S, Tavares C, Oliveira M, Rocha I. The predictive value of a multivariate model of autonomic and baroreflex function applied to patients with reflex syncope.Congresso Português de Cardiologia, Vilamoura, April 2014 (Oral presentation)

Fernandes M, Oliveira M, Primo J, Reis H, Nicola P.PORTLink Study - Portuguese Research on Telemonitoring with CareLink: Data of the Pilot Phase.Summer Meeting 2014, CCB, Lisboa, Julho/2014. (Oral presentation)

Cunha P, Oliveira M, Nogueira da Silva, Pimenta R, Alves S, Santos S, Ferreira RC.Failure of technical communication in remote monitoring of cardiac implantable electronic devices: a long-term study.Summer Meeting 2014, CCB, Lisboa, Julho/2014. (Oral presentation)

Cunha P, Oliveira M, Nogueira da Silva, Feliciano J, Alves S, Pimenta R, Santos S, Ferreira RC.Frequency and characteristics of remote monitoring event notifications in a population with cardiac implantable electronic devices.Summer Meeting 2014, CCB, Lisboa, Julho/2014. (Oral presentation)

Feliciano J, Oliveira M, Soares R, Nogueira da Silva, Cunha P, Silva T, Branco L, Alves S, Pimenta R, Ferreira RC.Influence of long-term remote monitoring in heart failure patients with implantable devices.Summer Meeting 2014, CCB, Lisboa, Julho/2014. (Oral presentation)

Damásio A, Oliveira M, Cunha P, Mesquita D, Neves D, Lousinha A, Valente B, Osório P, Conceição JM, Nogueira da Silva, Ferreira R.Hematomas com necessidade de drenagem cirúrgica em doentes com dispositivos cardíacos implantáveis: prevalência e fatores de risco.XXIX Jornadas de Cardiologia do Sul e Regiões Autónomas, Évora, Outubro/2014. (Oral presentation)

Brum M, Castro J, Conceição I.Polineuropatia amiloide familiar: eficácia do transplante hepático versus tafamidis na função nervosa periférica.Fórum de Neurologia de 2014. Coimbra, 15 a 17 de Maio 2014. (Oral presentation)

Francisco AR; Cortez Dias N, Menezes MM, Silva GL, Placido R, Ramalho AR, Magalhães A, Guimaraes T, Paixao A, Conceicao I, Diogo AN, Azevedo Coutinho C.Polineuropatia

Amiloidotica Familiar precoce e tardia: dois fenótipos clínicos distintos do ponto de vista disrítmico. XXXV Congresso Portugues de Cardiologia. Palácio de Congressos do Algarve, 27-29 Abril 2014. (Poster presentation)

Coelho T, O Suhr, David A, Conceicao I, Waddington-Cruz M, Hartmut Schmidt, Buades J, Campistol J, Pouget J, Berk J, Falzone R, Harrop J, De Frutos R, Bettencourt B, Cehelsky J, Nochur S, Vaishnav A and Gollob J. Phase 2 Open-Label Extension Study of Patisiran, an RNAi Therapeutic for the Treatment of Familial Amyloidotic Polyneuropathy. Congresso de Neurologia 2014, 12-15 Novembro Lisboa. (Oral presentation)

Forte, D; Sagarribay, A; Nabais, A; Novais, G; Gonçalves, V. Hemanigioma Capilar Lobular – Complicação Cirúrgica? 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014. (Oral presentation)

Forte, D; Sagarribay, A; Nabais, A; Fonseca, L; Gonçalves, V. Tumor Desmóide Dorsal Pós-Cirúrgico – Um Caso Clínico. 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014. (Oral presentation)

Fonseca, L; Forte, D; Sagarribay, A; Mateus, L; Laia, M; Nabais, A; Gonçalves, V. Cavernoma Gigante: A Propósito de 2 Casos Clínicos e Revisão da Literatura. 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014. (Oral presentation)

Novais, G; Joaquim, A; Nabais, A; Laia, M; Gonçalves, V. Alterações Hemodinâmicas Induzidas por Lesões na Úvula Cerebelosa ou Decorrentes da sua Manipulação Cirúrgica. 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014. (Oral presentation)

Sagarribay, A; Forte, D; Fonseca, L; Branco, P; Novais, G; Correia, I; Laia, M; Mateus, L; Nabais, A; Sousa, V; Gonçalves, V. Abordagem Endoscópica Endonasal. A Experiência do Início da Técnica. 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014. (Oral presentation)

Forte, D; A; Nabais, A; Novais, G; Laia, M; Correia, I; Pinto, M; Sousa, V; Gonçalves, V. Paragangliomas Jugulo-Timpânicos: Um Desafio Cirúrgico Multidisciplinar. 30º Congresso Nacional da Sociedade Portuguesa de Neurocirurgia. Lisboa, 30-31 Maio 2014.

Costa J. Portuguese Branch of the Iberoamerican Cochrane Network. Congresso de Neurologia 2014. Lisboa, Nov 2014. (Oral presentation)

Caldeira D, Barra M, Pinto FJ, Ferreira JJ, Costa J. Risco de hemorragia intracraniana com os novos anticoagulantes orais: revisão sistemática e meta-análise. 15º Congresso do NEDVC. Porto Nov 2014. (Oral presentation)

Gouveia M, Borges M, Augusto M, Caldeira D, Alarcão J, Pinheiro L, Sousa R, Fareleira F, Ascensão R, Costa J, Laires P, Fiuza M, Dias NC, Martins S, Belo A, Vaz Carneiro A. The cost of hypercholesterolemia in Portugal. XV Congresso Português Endocrinologia. Vilamoura, Jan 2014. (Poster presentation)

Pinto A. REUNIÃO DA SOCIEDADE PORTUGUESA DE MFR, ELA e MFR/Investigação aplicada, Coimbra, Novembro 2014 (Oral presentation)

### **Organisation of Conferences**

de Carvalho M. Membro do Organizing Committee Vestibular Diagnosis, Treatment and Rehabilitation Course. Lisboa, Janeiro 2014.

de Carvalho M. Membro do International Teaching Program Committee do International Congress of Clinical Neurophysiology. Berlim, Março 2014.

de Carvalho M., Membro do International Advisory Board do International Congress of Clinical Neurophysiology. Berlim, Março de 2014.

de Carvalho M. , Membro do International Program Committee of HEALTHINF 2014 (International Conference on Health Informatics). Angers, Março de 2014.

Maia T.V., Co-Chair, Computational Psychiatry Workshop, Computational and Systems Neuroscience (Cosyne) Meeting, Snowbird, UT, USA.

Maia T.V., Co-Organizer, Symposium on Neurodevelopmental Disorders: From Neuroscience to the Clinic, Champalimaud Centre for the Unknown, Lisbon, Portugal.

Costa J., Vestibular Diagnosis, Treatment and Rehabilitation Course. Hospital de Santa Maria and Clinical Physiology Translational Unit IMM. Lisbon, 27–29 January 2014

Costa J., Inauguração da Portuguese Branch of the Iberoamerican Cochrane Network, 28-29 June 2014.

Costa J., Vestibular Diagnosis, Treatment and Rehabilitation Course (2nd edition). Hospital de Santa Maria and Clinical Physiology Translational Unit IMM. Lisbon, 15-17 September 2014.

Domingos F., Curso Revisões Sistemáticas como Projecto de Investigação Clínica. Faculdade de Medicina da Universidade de Lisboa. 11-12 Setembro 2014.

Domingos F., Editorial Board Member do International Journal of Diabetes & Clinical Diagnosis. Conceição I., (Membro do comité científico) ARIA III SYMPOSIUM : advances and research in TTR - improving diagnosis, improving outcomes". Povia do Varzim, Portugal. Feb 7-8th, 2014.

Conceição I., Presidente e membro do comité científico do V Congresso Nacional de Doenças Neuromusculares, 25-27 de Outubro Aveiro, Portugal

Conceição I., Organizador da Reunião da Primavera da SPEDNM, Hotel M'AR De AR Muralhas, Évora 5 de Abril de 2014

#### **Prizes, honours and awards**

Arterial baroreflex evaluation in Heart Failure Patients Submitted to Cardiac Resynchronization Therapy, Best Clinical Oral Presentation, 5th AIMS meeting (Annual International Medical Students Meeting), Faculdade de Medicina de Lisboa, Março/2014 (João Serôdio, Mário Oliveira, Pedro Silva Cunha, Nogueira da Silva, Ana Abreu, Sérgio Laranjo, Cristiano Tavares, Luisa Branco, Sandra Alves, Isabel Rocha, Rui Ferreira)

Clinical Sciences Prize of XXXV Portuguese Cardiology Meeting 2014 - The Predictive Value of a Multivariate Model Of Autonomic and Baroreflex Function Applied to Patients with Reflex Syncope, Prémio Jovem Investigador – Investigação Clínica, Sociedade Portuguesa de Cardiologia, Abril/2014 (Sérgio Laranjo, Cristiano Tavares, Mário Oliveira, Isabel Rocha)

Mechanistic exploration of molecular changes underlying autonomic-induced atrial remodeling: a new step in the comprehension of arrhythmogenic vulnerability? Best Paper Presentation (MENÇÃO HONROSA), ARRITMIAS 2014, Cascais, Fevereiro/2014 (Mário Oliveira, Mafalda Carvalho, Gabriela Postolache, Vera Galdes, João Paulo Gomes, Cristiano Tavares, Sérgio Laranjo, Isabel Rocha)

#### **Advanced teaching**

de Carvalho M., Professor Associado Convidado e Regente de Fisiologia da Faculdade de Medicina da universidade de Lisboa

de Carvalho M., Professor Catedrático Convidado de Fisiologia, desde Outubro 2011.

de Carvalho M., Member of the Council of the Neurosciences Master/Doctoral Thesis Program.

de Carvalho M., Professor of Biomechanics – Biomedical Engineering – IST-FML

Conceição I. , Seminar and Lessons in Master Degree and Doctoral Program on Neurosciences 2014

Conceição I.Seminar and Lessons in Master Degree and Doctoral Program on Pain, 2014

Conceição I.Lessons in Biomechanics - Biomedical Engineering integrated master degree, 2014

Luís L., Vertigo and dizziness course, Hangzhou, China, 2014 (course main speaker- Leonel Luís)

Luís L., Vertigo and dizziness course, Xi'an, China, 2014 (course main speaker- Leonel Luís)

Luís L., 1st international Vestibular Diagnosis, Treatment and Rehabilitation Course, Lisbon, Portugal, 2014 (course main speaker)

Luís L., 2nd International Vestibular Diagnosis, Treatment and Rehabilitation Course, Lisbon, Portugal, 2014 (course main speaker)

Costa J., Formador no curso pós-graduado para médicos: “Da epidemiologia do medicamento à Farmacoterapia e à decisão clínica”. Promotor: Comissão de Costa J., Farmácia e Terapêutica ARSLVT 201

Costa J., Docente do Mestrado de Neurociências da FMUL

Costa J., Responsável pelo Módulo de Market Access da Pós-graduação “Leading Pharma”. Programa de Gestão para a Indústria Farmacêutica. Católica Executive Education Lisbon.

Costa J., Coordenador do Módulo de Epidemiologia Clínica do Programa Educacional MANAGE - Modelos Aplicados de Economia, Epidemiologia, Gestão e Direito em Saúde. Escola Nacional Superior de Saúde. Universidade Nova de Lisboa.

Costa J., Docente do módulo Módulo XII - Terapêutica Farmacológica Das Doenças Respiratórias na Criança no Curso de Especialização Doenças Respiratórias e do Sono na Criança. Faculdade de Medicina da Universidade de Lisboa. 3-5 Abril de 2014.

Pinto A. Seminário de Reabilitação e VNI nas DNM no Curso de Pós-Graduação em VNI da Universidade de Évora, Março 2014.

Pronto-Laborinho A.C. Hipoxia - Conceitos Gerais e Moleculares, Pós Graduação de Medicina Hiperbárica e Subaquática da Faculdade de Medicina da Universidade de Lisboa

Pinto, S., 2014: Invited Assistant of PRM (undergraduate medical training), FM, UL;

Pinto, S., 2014: Invited Assistant of PRM (undergraduate medical training), FM, UL;2014: Participation in Biomechanics (undergraduate training), Instituto Superior Técnico, Lisbon (lesson on Gait analyses);

Pinto, S., 2014: Invited Assistant of PRM (undergraduate medical training), FM, UL;2014: Invited Assistant of Physiology, FM, UL;



Costa, J., Formador no curso pós-graduado para médicos: “Da epidemiologia do medicamento à Farmacoterapia e à decisão clínica”. Promotor: Comissão de Costa, J., Farmácia e Terapêutica ARSLVT 201

Costa, J., Docente do Mestrado de Neurociências da FMUL

Costa, J., Responsável pelo Módulo de Market Access da Pós-graduação “Leading Pharma”. Programa de Gestão para a Indústria Farmacêutica. Católica Executive Education Lisbon.

Costa, J., Coordenador do Módulo de Epidemiologia Clínica do Programa Educacional MANAGE - Modelos Aplicados de Economia, Epidemiologia, Gestão e Direito em Saúde. Escola Nacional Superior de Saúde. Universidade Nova de Lisboa.

Costa, J., Docente do módulo Módulo XII - Terapêutica Farmacológica Das Doenças Respiratórias na Criança no Curso de Especialização Doenças Respiratórias e do Sono na Criança. Faculdade de Medicina da Universidade de Lisboa. 3-5 Abril de 2014.

Domingos F., Curso Revisões Sistemáticas como Projecto de Investigação Clínica. Faculdade de Medicina da Universidade de Lisboa. 11-12 Setembro 2014. Domingos F., Editorial Board Member do International Journal of Diabetes & Clinical Diagnosis (Fernando Domingos)

#### **Science and society**

Costa J., Inauguração da Portuguese Branch of the Iberoamerican Cochrane Network, 28-29 June 2014

#### **PhD thesis completed**

Pedro Álvaro Chagas 01/01/2014 In Vivo Muscle: Analysis of Functionality-related Patterns Mestrado Integrado de Engenharia Biomédica Ana Fred Mamede de Carvalho

### Msc thesis completed

Ângelo Dias 11/10/2014 Mechanistic characterization of reinforcement learning in healthy humans using computational models School of Medicine, University of Lisbon, and Instituto Superior Técnico (Portugal) Tiago Vaz Maia

Catarina Farinha 21/10/2014 A behavioral investigation of the algorithms underlying reinforcement learning in humans School of Medicine, University of Lisbon, and Instituto Superior Técnico (Portugal) Tiago Vaz Maia

Vasco Conceição 05/05/2014 Study of habit learning impairments in Tourette syndrome and obsessive-compulsive disorder using reinforcement learning models Biomedical Engineering, School of Medicine, University of Lisbon, and Instituto Superior Técnico Tiago Vaz Maia

Licenciado João Serôdio 16/09/2014 Avaliação do Reflexo Baroreceptor em Doentes com Insuficiência Cardíaca Submetidos a Terapêutica de Ressincronização Cardíaca Mestrado Integrado em Medicina 2014. FMUL. Isabel Rocha Mário Oliveira

Mariana Carrondo 15/10/2014 Autonomic Changes Evoked By Head-Up Tilt On Paroxysmal Atrial Fibrillation. (Mestrado em Tecnologia de Diagnóstico e Intervenção - Escola Superior de Tecnologia da Saúde de Lisboa/Faculdade de Medicina de Lisboa) Mário Oliveira

Maria Catarina Tenazinha 03/09/2014 s Inibidores Orais do Fator Xa na Prevenção de Eventos Cerebrovasculares em Doentes com Fibrilhação Auricular Não-reumática Mestrado Integrado em Medicina 2014. FMUL. João Costa

## Maria Carmo-Fonseca Lab

### Major Interests / Objectives

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

### Head of Unit

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

### Research Team

Ana Catarina de Jesus	Master	Technician
Ana Paula Santos Botelho Oliveira Leite	PhD	Post doctoral Investigator, (left March)
André Daniel Faustino Mesquita	Undergraduate	Trainee
Bruno Miguel Bernardes de Jesus	PhD	Post doctoral Investigator
Catarina Alves do Vale	Undergraduate	Trainee
Catarina Pereira Santos	Graduate	MSc Student, (left August)
Célia Carvalho	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Diana Margarida de Almeida Arteiro	Graduate	MSc Student, (started September)
Dinora Levy	Graduate	Administrative, Faculdade Medicina da Universidade de Lisboa

Evguenia Pavlovna Bekman	PhD	Investigator, ISCSEM , Assistant Professor , (started July)
Francisco Javier Enguita	PhD	Senior Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Joana Desterro	MD/PhD	Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Joana Patrícia Moreira Tavares	Graduate	Trainee, (started September)
Jorge Gabriel Palma da Luz	Graduate	MSc Student
José António Branco de Albuquerque	Master	Technician, (started November)
Marina Célia Nunes Ferreira C. H. Silva	PhD	Post doctoral Investigator
Marisa Cabrita	Graduate	Lab manager, Faculdade Medicina da Universidade de Lisboa , Assistant Professor , (left April)
Noélia Maria Fernandes Custódio	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Nuno Luís Barbosa Morais	PhD	Post doctoral Investigator, University of Oxford , (left June)
Paula Sofia Faria Oliveira	Graduate	PhD Student
Prasoon Kumar Thakur	Master	Trainee, (started October)
Rita Catarina Vaz Drago	Master	PhD Student
Rita Mingot de Almeida Mendes de Almeida	Master	PhD Student
Robert M. Martin	PhD	Post doctoral Investigator
Sandra Martins	PhD	Senior Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Sara Filipa Azevedo Barros	Graduate	MSc Student, (started September)
Sérgio Manuel Pires Marinho	Graduate	Technician, Faculdade Medicina da Universidade de Lisboa
Soraia Vanessa Guerreiro da Silva	Graduate	MSc Student, (started October)

Teresa Carvalho	PhD	Investigator, Faculdade Medicina da Universidade de Lisboa , Assistant Professor
Tomás Pires de Carvalho Gomes	Master	MSc Student, (started December)
Vanessa Borges Pires	Graduate	MSc Student, (started September)

#### Keywords / Research Areas

Cell and Molecular Biology, RNA biology, RNA in disease

#### Major scientific achievements

We have developed a methodology that permits direct measurement, in living cells, of the time it takes to synthesize and excise an intron from individual pre-mRNA molecules. We integrated a single reporter gene in the genome of human cells. The fluorescence associated with a single transcription site in the nucleus was detected as a diffraction-limited object and its intensity was determined as a function of time. Increments in fluorescence intensity were due to de novo transcription, while reductions reflected intron excision followed by degradation or diffusion. These fluorescence intensity fluctuations were used to obtain, for the first time, a direct measure of the intron lifetime. We found a splicing rate much faster than previously reported. We believe the reason for this discrepancy derives from the higher resolution of our single-molecule analysis. We expect this experimental approach will prove valuable to further reveal the kinetic properties of gene expression.

#### Selected Publications

Martin, RM, Rino, J, Carvalho, C, Kirchhausen, T, Carmo-Fonseca, M (2013) Live-cell visualization of pre-mRNA splicing with single-molecule sensitivity. *Cell Reports* **4**, 1144-1155. (Journal IF: 7.2, Citations: 8)

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* **18**, 977-983. (Journal IF: 11.6, Citations: 69)

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.* **18**, 1115-1123. (Journal IF: 11.6, Citations: 37)

Grosso, A.R., Gomes, A.Q., Barbosa-Morais, N.L., Caldeira, S., Thorne, N.P., Grech, G., von Lindern, M., and Carmo-Fonseca, M (2008) Tissue-specific splicing factor gene expression signatures. *Nucleic Acids Research* **36**, 4823-32. (Journal IF: 8.8, Citations: 57)

Braga J, Desterro JM, Carmo-Fonseca M (2004) Intracellular macromolecular mobility measured by fluorescence recovery after photobleaching with confocal laser scanning microscopes. *Mol. Biol. Cell* **15**, 4749-4760. (Journal IF: 4.5, Citations: 118)

### Ongoing Research Projects

2011/2014 Title: Survey of tissue-specific alternative splicing in vertebrates by highthroughput sequencing: finding the elements of an evolutionary 'splicing predictor' - PEOF-GA-2010-274037. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Comissão Europeia. Reference: Evoaltplice - PEOF-GA-2010-274037. Amount: 210,566.32€.

2011/2015 Title: RNPnet – RNP structure, function and mechanism of action - PITN-GA-2011-289007. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Comissão Europeia. Reference: RNPnet\_ ITN289007. Amount: 212,892.1€.

2012/2015 Title: Splicing and stochasticity in programmed cell death decisions. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-GMG/118180/2010. Amount: 169,755€.

2012/2015 Title: Identification and manipulation of molecular pathways relevant for age-dependent tissue regeneration. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: AXA SA. Reference: AXA Research Fund - UBCE. Amount: 173,500€.

2012/2016 Title: The role of non-coding RNA in human health and disease - PIRSES-GA-2012-318981. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Comissão Europeia. Reference: RNA\_Regulomics\_GA318981. Amount: 67,200€.

2013/2015 Title: Sino-Portuguese Programme of Cooperation in Science & Technology . Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Fundação Ciência e Tecnologia. Reference: FCT/China. Amount: 9,600€.

2014/2014 Title: Exploring new therapeutic approaches for Hypertrophic Cardiomyopathy. Coordinator: Sandra Martins. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BIM-MEC/0201/2013. Amount: 49,500€.

2014/2017 Title: Epigenética e splicing alternativo: papel na diferenciação de células imunitárias T e na leucemia. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: FCT-ANR/BIM-ONC/0009/2013.

Amount: 200,000€.

2014/2015 Title: Prémio Gulbenkian - Best Plenary Presentation . Coordinator: Catarina Alves do Vale. Agency: AIDFM. Reference: Prémio Gulbenkian - Best Plenary Presentation . Amount: 2,000€.

#### Other Projects

2013/2014 GAPIC-FML/IGC-2012 - Terapia da Distrofia Muscular de Duchenne por modulação do splicing: teste da eficiência de oligonucleótidos LNA na indução de “exon skipping” e na reversão do fenótipo em modelos de DMD. Coordinator: M. Carmo-Fonseca & Célia Carvalho.

#### Publications in peer review Journals

Rino, J, Martin, RM, Carvalho, T, Carmo-Fonseca M. (2014) Imaging dynamic interactions between spliceosomal proteins and pre-mRNA in living cells. *Methods* **65**(3): 359-366. (Journal IF:3.21 Citation:1)

Carmo-Fonseca M. and Kirchhausen T (2014) The timing of pre-mRNA splicing visualized in real time. *Nucleus* **5**(1): 11-14.(Journal IF:3.14 Citation: 0)

De Almeida S.F., and Carmo-Fonseca M. (2014) Reciprocal regulatory links between cotranscriptional splicing and chromatin. *Semin Cell Dev Biol* **32**, 2-10.(Journal IF:5.91 Citation: 1)

Carvalho S, Vítor AC, Sridhara SC, Martins FB, Raposo AC, Desterro JMP, Ferreira J, de Almeida SF. (2014) SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint. *Elife*. May **6**; 3:.(Journal IF: 8.51Citation:0)

Enguita, F.J. and Leitão, A.L. (2014) Fungal extrolites as a new source for therapeutic compounds and as building blocks for applications in synthetic biology. *Microbiol Res.*, **9-10**: 652-665.(Journal IF:1.93 Citation:0 )

Enguita, F.J.. and Leitão, A.L. (2014) The art of unwinding: RNA helicases at the crossroads of cell biology and human disease. *J. Biochem. Pharmacol. Res.*, **2**, (3): 144-158. (Journal IF:4.72 Citation:0)

Leitão, A.L., Costa, M.C. and Enguita, F.J. (2014). A guide for miRNA target prediction and analysis using web-based applications. *Methods Mol. Biol.*, **1182**, 265-277.(Journal IF:1.29

Citation:0 )

Costa, M.C., Leitão, A.L., and Enguita, F.J. (2014). MicroRNA profiling in plasma or serum using quantitative RT-PCR. *Methods Mol. Biol.*, **1182**, 121-129.(Journal IF:1.29 Citation:0 )

Pereira, P., Enguita, F.J., Ferreira, J., and Leitão, A.L. (2014). DNA damage induced by hydroquinone can be prevented by fungal detoxification. *Toxicol. Rep.*, **1**, 1096-1105. (Journal IF:3.84 Citation:0 )

Faustino, A.F., Guerra, G.M., Huber R.G., Hollmann, A., Domingues, M.M., Barbosa, G.M., Enguita, F.J., Bond PJ, Castanho MA, Poian AT, Almeida FC, Santos NC, and Martins IC. (2014) Understanding Dengue Virus Capsid Protein Disordered N-Terminus and pep14-23-Based Inhibition. *ACS Chem Biol.*, **Advanced online publication**, DOI: 10.1021/cb500640t (Journal IF:4.71 Citation:0 )

#### **Other publications International**

Grosso, AR, Carmo-Fonseca, M (2014) The potential of targeting splicing for cancer therapy. R. Kumar (ed.), Nuclear Signalling Pathways and Targeting Transcription in Cancer, Cancer Drug Discovery and Development, DOI 10.1007/978-1-4614-8039-6\_13, © Springer Science+Business Media New York 2014

Alves-Vale C. (2014) A Nobel Day in Lisbon, Portugal – A Unique Experience for Someone who Loves Science. *International Journal of Medical Students*. Mar- Jun;2(2):71-2.

#### **Invited lectures and seminars**

Carmo-Fonseca, M. Cardiologia Molecular. Faculdade de Medicina, Universidade de Coimbra, 20 Janeiro 2014.

Carmo-Fonseca, M. Splicing kinetics. University of Stockholm, Sweden, 18 February 2014.

Carmo-Fonseca, M. Symposium: Internal Medicine - the power of faith and science in the age of wonder. Leaping Forward – International Clinical Congress. Lisboa, 19 February 2014.

Carmo-Fonseca, M. The emergence of RNAs as biomarkers and therapeutic targets. 34th European Workshop for Rheumatology Research. Lisboa, 20-22 February 2014.



Carmo-Fonseca, M. Combining mathematical modeling and live cell microscopy to track gene expression in real time. Departamento de BioEngenharia do Instituto Superior Técnico, Lisboa, 12 May 2014.

Carmo-Fonseca, M. Imaging RNA splicing in live cells. Società Italiana di Biofisica e Biologia Molecolare. Trento, 11-13 June 2014.

Carmo-Fonseca, M. The timing of pre-mRNA splicing. NordForsk ncRNA meeting. Helsinki, 20-22 August 2014.

Carmo-Fonseca, M. The timing of pre-mRNA splicing. FEBS-EMBO meeting, Paris, 30 August-4 September 2014.

Carmo-Fonseca, M. Splicing kinetics in live cells. Workshop “Regulation of gene expression”. University of Lausanne, 10 September 2014.

Carmo-Fonseca, M. The importance of timing for nuclear RNA processing. Universidade do Algarve, Faro, 28 November 2014.

Martins S. Scientific investigation and rare genetic diseases in Portugal. Workshop “Science and Innovation: closer than rare”, European Parliament, Brussels 17 February 2014.

Martins S. Discussion board for new therapeutic approaches in lysosomal diseases. 8th B4B Workshop and InNerMeD Information Network and 1st Open Conference, Frankfurt, Germany. 7-9 March 2014

Enguita, F.J. MiRNAs in human health: new opportunities for diagnosis and therapeutics. BioSys/BioFIG Research seminars. Faculty of Sciences, University of Lisbon, 3 March 2014.

Enguita, F.J. Masters of unwinding: RNA helicases in cell biology and disease. CIMA, University of Navarra, Pamplona, Spain, 31th July 2014.

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

Carmo-Fonseca, M. Five seconds to splice. Talk presented at the “ISMB 2014 conference and Integrative RNA Biology meeting”, Boston, USA, 11 July 2014. (Oral presentation)

Martins S. . From point-to-care to genomics research: how a new research center will unleash the full potential of personalized medicine in rare diseases. Talk presented at MEMBS, 1st Middle East Molecular Biology Congress and Exhibition, Dubai World Trade Center, United

Arab Emirates, 14-17 September 2014.(Oral presentation)

Bernardes de Jesus, B. Role of the lncRNA Zeb2Nat in stemness. Poster presented at the “Cold Spring Harbor meeting on Regulatory and noncoding RNAs”, NY, USA, 26-30 August 2014.  
(Poster presentation)

Vaz-Drago, R. RNA quality control in human genetic diseases. Poster presented at the EMBO Symposium The Complex Life of mRNA, Heidelberg, Germany, October 5-8, 2014.  
(Poster presentation)

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

Mendes de Almeida, R. “Exploring New Therapeutic Approaches for Hypertrophic Cardiomyopathy” Poster presented in Heart without borders: International conference on cardiovascular development, disease and repair. Porto, 28-29 November 2014.

Enguita, F.J. New insights to acute myocardial infarction prognosis by circulating miRNAs. Presentation in Heart without borders, International conference on cardiovascular development, disease and repair. Porto, Portugal, 28-29 November, 2014.

Alves-Vale, C. Avoiding the production of disease-causing proteins at the nuclear level. Presentation in Plenary Session at the 5th Annual International Medical Students Meeting (AIMS Meeting), Lisboa, 7-9 March 2014.

Alves-Vale, C. Quality control of mRNA in the nucleus: safeguarding cells from disease-causing proteins. Presentation in Plenary Session at the 9th Young European Scientist Meeting (YES Meeting), Porto, 19-21 September 2014.

Alves-Vale, C. RNA quality control: a mechanism to avoid disease. Presentation in Plenary Session at the iMed Conference 6.0 (Fundação AstraZeneca Innovate Competition), Lisboa, 12 October 2014.

#### **Prizes, honours and awards**

C. Alves-Vale was awarded the Gulbenkian Prize, for the Best Plenary Presentation. 5th AIMS Meeting, Lisboa, March 2014.

C. Alves-Vale was awarded the Best Poster of Basic Research. iMed Conference 6.0 (Fundação

AstraZeneca Innovate Competition). Lisboa, October 2014.

#### **Industry contract research**

2013/2014 Title: Determining the effect of CLK inhibitors on cancer-associated alternative splicing . Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Institut de Recherches Servier. Reference: Servier - CLK inhibitors. Amount: 25,000€. Amount (total): 25,000€

#### **Advanced teaching**

Carmo-Fonseca, M. The timing of splicing. LisbonBioMed PhD Program, Lisboa, 9 January 2014.

Martins, S. Supervisor of the laboratory training of Catarina Filipe Santos Ribeiro, 17<sup>o</sup> GAPIC Program "Educação pela Ciência", Faculdade de Medicina, Universidade de Lisboa.

Martins, S. Instructor in the Practical Workshop "Stem Cell Biology", 5th AIMS Meeting, Universidade de Lisboa, 7-9 March 2014.

Carvalho, T. Instructor in the Practical Workshop "Stem Cell Biology", 5th AIMS Meeting, Universidade de Lisboa, 7-9 March 2014.

Enguita, F.J. Protein structure and drug design. Lisbon Biomed Ph.D. Programme Research Seminars, Nanomedicine and Biochemistry module, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa. 7 January 2014.

Enguita, F.J.. MicroRNA-mediated regulation of protein levels in heart disease. Ph.D. Programme in Health Sciences, Faculdade de Medicina & IBILI, Universidade de Coimbra, 18 February 2014.

Enguita F.J. Non-coding RNAs and ageing. Master Programme in Cellular and Molecular Biology, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, 22 April 2014.

Enguita F.J. Bioinformatic tools to analyse miRNA sequence, their targets and potential function. Master Programme in Cellular and Molecular Biology, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, 22 April 2014.

Enguita, F.J. Regulation of gene expression. Ph.D. Programme in Health Sciences, Faculdade de Medicina & IBILI, Coimbra, 7 October 2014.

### **Science and society**

Carmo-Fonseca, M., Conferência “Novo rumo para Portugal”. Lisboa, 1 Fevereiro 2014.

Carmo-Fonseca, M. Os Legados do 25 de Abril: a Sociedade e a Ciência. Conferência “25 de Abril 40 anos depois”, Lisboa, 14 Abril 2014.

### **Msc thesis completed**

Catarina Santos 03/12/2014 Exploring RNA-targeted gene therapy approaches for Hypertrophic Cardiomyopathy Master Program in Human Biology and Environment, Faculdade de Ciências da Universidade de Lisboa Sandra Martins

Tomás Gomes. 05/12/2014 Genome-wide profiling of RNA polymerase II and associated cotranscriptional processes using advanced NET-seq data Master Program in Bioinformatics and Computacional Biology, Faculdade de Ciências da Universidade de Lisboa Ana Rita Grosso  
M. Carmo-Fonseca

Rui Miguel Raposo Pinto 27/06/2014 Electrokinetic and optical detection of nucleic acids for biomedical diagnosis in microfluidics Master Program in Biomedical Engineering. Instituto Superior Técnico João Pedro Conde Francisco J. Enguita.

## Maria M. Mota Lab

### Major Interests / Objectives

Malaria is one of the most serious parasitic infectious diseases, with a toll of up to 600,000 deaths every year. It is now consensual that malaria control or elimination will never be feasible until we gain a better understanding of the complex interactions occurring between its main players: Plasmodium, the causative agent of disease, and its hosts. Yet, important gaps subsist in our knowledge of the processes that occur at the parasite-host interface. Thus, the overall goal of our laboratory is to identify key host factors and host-Plasmodium interactions that contribute to: (i) the establishment of a malaria infection during the initial steps of Plasmodium replication inside liver hepatocytes and (ii) the onset of malaria pathology while Plasmodium infects red blood cells.

### Head of Unit

Maria Manuel Mota, PhD

### Research Team

Ana Filipa Caetano Parreira	Graduate	Insectary Manager
Ana Margarida Aires Alves Vigário	PhD	Visiting Researcher
Ana Margarida Ferreira Góis	Master	Technician
Ângelo António Ferreira Chaves do Rosário Chora	PhD	Post doctoral Investigator, (started February)
Aparajita Lahree	Graduate	MSc Student, (started June)
Daniel José Martins Carapau	PhD	Project Manager
Debanjan Mukherjee	Master	PhD Student, (started July)
Sonali Setua	PhD	Post doctoral Investigator, (started August)
Eliana Real	PhD	Post doctoral Investigator
Gabriela Stephanie Peres Cristo	Master	MSc Student

Inês Fernandes Bento	PhD	Investigator, (started July)
Iset Medina Vera	PhD	Post doctoral Investigator
João Tiago Carvalho Jordão de Mello Vieira	Master	PhD Student
Kirsten Hanson	PhD	Post doctoral Investigator ( left October)
Ksenija Slavic	PhD	Post doctoral Investigator
Lénia Marisa Pereira Rodrigues	PhD	Post doctoral Investigator
Liliana Mancio Silva	PhD	Post doctoral Investigator
Márcia Melo Medeiros	MD/PhD	Post doctoral Investigator
Margarida Maria Teles Grilo Ruivo	Master	Technician
Maurice Ayamba Itoe	PhD	Post doctoral Investigator
Sofia Pinto Guia Marques	PhD	Lab manager
Vanessa Alexandra Zuzarte Luís	PhD	Post doctoral Investigator
Viriato M'Bana	Master	PhD Student (started September)

#### **Keywords / Research Areas**

Host-Plasmodium interactions, Nutrient acquisition, Innate immune response against Plasmodium infection, Iron metabolism during Plasmodium infection, Using transgenic parasites as malaria vaccines

#### **Major scientific achievements**

The main achievement of the Mota Laboratory in 2014 was the publication in Nature Medicine of the manuscript "Host-cell sensors for Plasmodium activate innate immunity against liver-stage infection" (Liehl et al. Nat. Med. 20:47-53). Contrary to what was common belief among Malaria researchers, the Lab discovered that the host is capable of detecting the few parasites that reach the liver and infect hepatocytes, leading to the asymptomatic liver stage of infection. Not only are infected cells detected, but also the host tries to actively eliminate them using the type 1 Interferon pathway (IFN- $\gamma$ ) of the innate immune system, which until now was only known to detect viruses. Furthermore, the detection of Plasmodium-infected cells is likely to be initiated by Plasmodium RNA.

Overall in 2014 the Mota Lab was involved in 7 publications in peer-reviewed International Journals, and members of the Lab attended 4 of the main International Conferences in Malaria

research in Europe and the USA.

### Selected Publications

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** (1), 47-53. (Journal IF: 28.05, Citations: 7)

Hanson KK, Ressurreição AS, Buchholz K, Prudêncio M, Herman-Ornelas JD, Rebelo M, Beatty WL, Wirth DF, Hänscheid T, Moreira R, Marti M, Mota MM. (2013) Torins are potent antimalarials that block replenishment of Plasmodium liver stage parasitophorous vacuole membrane proteins. *Proc Natl Acad Sci U S A* **110**(30), E2838-E2847. (Journal IF: 9.81, Citations: 5)

Derbyshire ER, Prudêncio M, Mota MM, Clardy J. (2012) Liver-stage malaria parasites vulnerable to diverse chemical scaffolds. *Proc Natl Acad Sci* **109**, 8511-6. (Journal IF: 9.68, Citations: 25)

Portugal S, Carret C, Recker M, Armitage AE, Gonçalves LA, Epiphanyo S, Sullivan D, Roy C, Newbold CI, Drakesmith H, Mota MM. (2011) Host-mediated regulation of superinfection in malaria. *Nature Medicine* **17**(6), 732-7. (Journal IF: 22.46, Citations: 74)

Epiphanyo S, Campos MG, Pamplona A, Carapau D, Pena AC, Ataíde R, Monteiro CA, Félix N, Costa-Silva A, Marinho CR, Dias S, Mota MM. (2010) VEGF promotes malaria-associated acute lung injury in mice. *PLoS Pathogens* **6**(5), e1000916. (Journal IF: 9.13, Citations: 28)

### Ongoing Research Projects

2009/2014 Title: Towards the establishment of a permanent European Virtual Institute dedicated to Malaria Research (Evimalar). GA242095. Coordinator: Maria Manuel Mota. Agency: University of Glasgow. Reference: EVIMalaR. Amount: 92,846€.

2011/2014 Title: Mechanisms of Plasmodium liver infection: Subverting the host ubiquitin-proteasome pathway towards an immune evasion strategy. Coordinator: Vanessa Alexandra Zuzarte Luís. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-MIC/113697/2009. Amount: 160,162€.

2011/2014 Title: EVIMalaR - fellowship award. Coordinator: Liliana Mancio Silva. Agency: University of Glasgow. Reference: EVIMalaR - fellowship award - Liliana Mancio. Amount: 210,005.11€.

2012/2014 Title: Mechanisms of nutrient-sensing by the malaria parasite. Coordinator: Liliana Mancio Silva. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-MET/118199/2010. Amount: 123,410€.

2012/2017 Title: ParasiteNutriSensing: Nutrient sensing by parasites - 311502 ParasiteNutriSensing. Coordinator: Maria Manuel Mota. Agency: Comissão Europeia. Reference: ParasiteNutriSensing - 311502. Amount: 1,500,000€.

2013/2014 Title: Grand Challenges Explorations Grant Number: OPP1086189 - Liver Stage Antimalarials to Drive Sterile Immunity. Coordinator: Kirsten Hanson. Agency: Bill & Melinda Gates Foundatio. Reference: GATES - Grant n OPP1086189. Amount: 76,260.2€.

2013/2015 Title: Regulation of host cell metabolism during malaria liver stage. Coordinator: Ghislain Guillaume Nicolas Cabal. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/IMI-MIC/1568/2012. Amount: 168,637€.

2013/2015 Title: Host-Plasmodium interactions: a tale of sensing and being sensed. Coordinator: Maria Manuel Mota. Agency: Fundação Ciência e Tecnologia. Reference: EXCL/IMI-MIC/0056/2012. Amount: 331,463€.

2014/2014 Title: The role of Iron in Plasmodium life cycle and disease. Coordinator: Daniel José Martins Carapau. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BIM-MET/0753/2013. Amount: 50,000€.

2014/2014 Title: Differentially chemically attenuated liver stage parasites to elucidate the determinants of unnatural acquired immunity to Plasmodium. Coordinator: Kirsten Hanson. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/IMI-MIC/0866/2013. Amount: 50,000€.

2014/2014 Title: A chemical proteomics approach to identify the P. falciparum target of the Torins. Coordinator: Ana Filipa Pintéus da Cruz. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: EXPL/BBB-BEP/0746/2013. Amount: 50,000€.

2013/2015 Title: Engineered liver platforms to study regulation of host microRNA in Plasmodium liv. Coordinator: Iset Medina Vera. Agency: National Institute of Allergy and Infectious Disea. Reference: GRANT NUMBER: 1F32AI104252-01X1. Amount: 12,379.94€.



### Publications in peer review Journals

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 and Mota MM (2014) Host-cell sensors for Plasmodium activate innate immunity against liver-stage infection. *Nat. Med.* **20**(1), 47-53. (Journal IF: 28.05, Citations: 7)

Zuzarte-Luis V, Sales-Dias J and Mota MM (2014) Simple, sensitive and quantitative bioluminescence assay for determination of malaria pre-patent period. *Malar J.* **13**, 15. (Journal IF: 3.49, Citations: 1)

Ng S, March S, Galstian A, Hanson K, Carvalho T, Mota MM and Bhatia SN (2014) Hypoxia promotes liver-stage malaria infection in primary human hepatocytes in vitro. *Dis Model Mech.* **7**(2), 215-224. (Journal IF: 5.54, Citations: 1)

Zuzarte-Luis V, Mota MM and Vigário AM (2014) Malaria infections: What and how can mice teach us. *J Immunol Methods* **410**, 113-22. (Journal IF: 2.01, Citations: 0)

Carballeira NM, Bwalya AG, Itoe MA, Andricopulo AD, Cordero-Maldonado ML, Kaiser M, Mota MM, Crawford AD, Guido RV and Tasdemir D (2014) 2-Octadecynoic acid as a dual life stage inhibitor of Plasmodium infections and plasmodial FAS-II enzymes. *Bioorg Med Chem Lett.* **24** (17), 4151-4157. (Journal IF: 2.33, Citations: 0)

Derbyshire ER, Zuzarte-Luís V, Magalhães AD, Kato N, Sanschagrín PC, Wang J, Zhou W, Miduturu CV, Mazitschek R, Sliz P, Mota MM, Gray NS and Clardy J (2014) Chemical interrogation of the malaria kinome. *ChemBiochem* **15** (13), 1920-30. (Journal IF: 3.06, Citations: 0)

Hanson KK, March S, Ng S, Bhatia S and Mota MM (2014) In vitro alterations do not reflect a requirement for host cell cycle progression during Plasmodium liver stage infection. *Eukaryot Cell.* Nov 21. pii: EC.00166-14 (Journal IF: 3.18, Citations: 0)

### Invited lectures and seminars

Mota, Maria M. . "Host-Plasmodium interactions". Harvard School of Public Health (invited seminar). January 8, 2014.

Mota, Maria M. "Plasmodium Ability to Sense Changes in the Host". Gordon Research

Conference on Biology of Host-Parasite Interactions, Salve Regina, RI, USA. June 9, 2014.

Mota, Maria M. "Interacções Plasmodium-Hospedeiro: detectar e ser detectado". Congresso Português de Parasitologia. Coimbra, Portugal. November 20, 2014.

Mota, Maria M. "Host-Plasmodium interactions: a continuous tale of sensing and being sensed". Congresso da Sociedade Portuguesa de Bioquímica. Coimbra, Portugal. December 20, 2014.

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

Peter Liehl. Innate Immunity to Malaria Liver Infection. 10th Annual BioMalPar I EVIMalaR Conference - Biology and Pathology of the Malaria Parasite, EMBL Heidelberg, Germany, May 2014 (Oral Presentation)

Patricia Meireles, Joana Sales-Dias, Liliana Mancio-Silva, Maria Mota and Miguel Prudencio. The role of D-Glucose uptake by Glucose Transporter 1 during liver stage of Plasmodium infection. 10th Annual BioMalPar I EVIMalaR Conference - Biology and Pathology of the Malaria Parasite, EMBL Heidelberg, Germany, May 2014 (Poster presentation)

Vanessa Zuzarte-Luís, Peter Liehl, João T. Vieira, Maurice Itoe, Céline Carrét and Maria M. Mota. Administration of a lipid-rich diet abrogates Plasmodium liver infection, 25th Annual Molecular Parasitology Meeting, Woods Hole, USA. September 2014 (Poster presentation)

Ksenija Slavic, Sanjeev Krishna, Guillaume Boyer, Kirsten Hanson, Iset Vera, Jon Pittman, Henry M. Staines and Maria M. Mota. Iron transport in malaria parasites: functional characterization of a novel transporter, 25th Annual Molecular Parasitology Meeting, Woods Hole, USA. September 2014 (Poster presentation)

Liliana Mancio-Silva and Maria M. Mota. Malaria parasitemia and virulence regulated by nutrient sensing. 1st Biannual PARAFRAP Conference. September 2014. Les Embiez Islands, Marseille, France. (Oral presentation)

Liliana Mancio-Silva, Katarzyna Modrzynska, Cameron MacPerson, Ana Rita Grosso, Joana Sales-Dias, Agnieszka Religa, Andrew Waters, Oliver Billker and Maria Mota. Plasmodium senses and adapts to host nutritional status. 63rd ASTMH Annual Meeting, New Orleans, LA, USA, November 2014 (Oral presentation)

#### **Patents/prototypes**

"COMPOSITIONS FOR THE TREATMENT OF MALARIA" provisional patent application nr. PT107692

"COMPOSITIONS FOR THE TREATMENT OF MALARIA" provisional patent application nr.PT107693

**Msc thesis completed**

Gabriela Cristo 12/12/2014 Uncovering the role of host Cullin 3 during Plasmodium berghei liver stage infection Faculdade de Ciencias da Universidade de Lisboa Vanessa Zuzarte-Luis

## Mário Ramirez Lab

### Major Interests / Objectives

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations. Investigations are also exploring the relationships between commensal and disease causing populations of the same bacterial pathogen with the aim of identifying particularly successful clones at causing disease as well as successful colonizers for further characterization. A strong bioinformatics effort in the area of bacterial population simulation, 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 Unit

Mário Nuno Ramos d'Almeida Ramirez, PhD

### Research Team

Adriana Domingos Policarpo	Graduate	MSc Student
Ana Catarina Martins Lameiras	Undergraduate	Technician
Ana Isabel Aquino Friães	PhD	Senior Investigator
Andreia das Neves Horácio	Master	PhD Student
Andreia Sofia Agostinho Gravata	Master	Trainee
Andreia Sofia Monteiro Teixeira	Master	Investigator, (started February) (left June)
Anne JAMET	MD/PhD	Post doctoral Investigator, (started November)
Bruno Filipe Ribeiro Gonçalves	Graduate	MSc Student
Carolina Isabel Glória Tempera	Master	Investigator
Catarina Costa	PhD	Senior Investigator, (started March)

Catarina Teresa Condinho Pato	Master	PhD Student
Cristiano Miguel Pedroso Roussado	Graduate	MSc Student, (started September)
Elisabete Martins	PhD	Post doctoral Investigator
Fábio Filipe dos Santos Luz	Graduate	MSc Student, NA , (started July)
Joana Alexandra Pimento Lopes	Graduate	Technician
Joana Gomes Martins Lopes	Graduate	MSc Student
João André Nogueira Custódio Carriço	PhD	Senior Investigator
Jorge Miguel Diamantino Miranda	Master	PhD Student
José Augusto Gamito Melo Cristino	MD/PhD	Senior Investigator
Liliana Sofia Cardoso	No degree	Investigator
Marcos Pinho	Master	Investigator
Maria João Rua Frias	PhD	Post doctoral Investigator
Maria Sousa Rebelo	Master	PhD Student
Mickael Santos da Silva	Master	MSc Student, (left September)
Nuno Miguel Santos Rodrigues	Graduate	MSc Student
Raquel Baptista Arinto Garcia	Graduate	MSc Student
Rosangela Maria Rodrigues Carvalho Frita	Master	PhD Student
Rui Manuel São Martinho de Oliveira	Master	Investigator, (left January)
Sandra Isabel Rodrigues de Aguiar	PhD	Post doctoral Investigator
Sérgio Miguel Cardoso Marcelino dos Santos	Master	Investigator, (left September)
Thomas Hanscheid	MD/PhD	Senior Investigator

### Keywords / Research Areas

Population biology and epidemiology, Interactions of malaria and other infectious diseases, Bioinformatics, Molecular epidemiology, Diagnostic tools, Antibiotic resistance

### Major scientific achievements

Identification of clones of *S. pyogenes* with particular propensity to cause scarlet fever and documentation of the changes in invasive disease and its correlation with clonal properties.

Development of an ontology for typing methods to facilitate machine-readable information extraction and integration from disparate databases.

Identification of the role played by pherotypes of *S. pneumoniae* in conditioning biofilm formation and recombination within biofilms.

Documentation of continuing changes in *S. pneumoniae* causing invasive infections with vaccination and its consequences for future potential vaccines.

Development and field testing in Gabon of a novel flow cytometry assay for antimalarial drug sensitivity testing, using detection of haemozoin without any further reagents.

Development of a novel and easy haemozoin inhibition assay to screen for haemozoin inhibiting antimalarial drugs.

### Selected Publications

Rebelo, M., C. Sousa, H. M. Shapiro, M. M. Mota, M. P. Grobusch, and T. Häscheid (2013) A novel flow cytometric hemozoin detection assay for real-time sensitivity testing of *Plasmodium falciparum*. *PLoS ONE* **8**, e61606 e61606. (Journal IF: 3.534, Citations: 4)

Francisco, A. P., C. Vaz, P. T. Monteiro, J. Melo-Cristino, M. Ramirez, and J. A. Carriço (2012) Phylogenetic inference and data visualization for sequence based typing methods. *BMC bioinformatics* **13**, 87. (Journal IF: 2.672, Citations: 48)

C. Silva-Costa, A. Friães, M. Ramirez, J. Melo-Cristino, The Portuguese Group for the Study of Streptococcal Infections (2012) Differences between macrolide resistant and susceptible *Streptococcus pyogenes*: the importance of clonal properties in addition to antibiotic consumption. *Antimicrob Agents Chemother* **56**, 5661–5666. (Journal IF: 4.451, Citations: 5)

Horácio AN, Diamantino-Miranda J, Aguiar SI, Ramirez M, Melo-Cristino J, the Portuguese Group for the Study of Streptococcal Infections (2012) Serotype changes in adult invasive pneumococcal infections in Portugal did not reduce the high fraction of potentially vaccine preventable infections. *Vaccine* **30**, 218–224. (Journal IF: 3.485, Citations: 13)

Martins E. R., A. Andreu, P. Correia, T. Juncosa, J. Bosch, M. Ramirez, and J. Melo-Cristino on

behalf of the Microbiologist Group for the Study of Vertical Transmission Infections from the Catalan Society for Clinical Microbiology and Infectious Diseases (2011) Group B streptococci causing neonatal infections in Barcelona are a stable clonal population: 18-year surveillance. *J Clin Microbiol* **49**, 2911-2918. (Journal IF: 4.232, Citations: 14)

#### **Ongoing Research Projects**

2012/2014 Besieged by conjugate vaccination: changes of the pneumococcal population and their genomic consequences. Coordinator: José Augusto Gamito Melo Cristino. Agency: FCT. Amount: €174.533.00

2013/2014 IFDO Research Coordinator: Thomas Hanscheid. Agency: Steris Corporation. Amount: €12.980.00

#### **Publications in peer review Journals**

Magalhães R, Ferreira V, Santos I, Almeida G, Teixeira P, Research Team. 2014. Genetic and phenotypic characterization of *Listeria monocytogenes* from human clinical cases that occurred in Portugal between 2008 and 2012. *Foodborne Pathog. Dis.* **11**, 907–916. (Journal IF:2.092, Citation: 0)

Earnshaw S, Mancarella G, Mendez A, Todorova B, Magiorakos AP, Possenti E, Stryk M, Gilbro S, Goossens H, Albiger B, Monnet DL, European Antibiotic Awareness Day Technical Advisory Committee, European Antibiotic Awareness Day Collaborative Group. 2014. European Antibiotic Awareness Day: a five-year perspective of Europe-wide actions to promote prudent use of antibiotics. *Euro Surveill.* **19**. (Journal IF:4.659, Citation: 0)

Vaz C, Francisco AP, Silva M, Jolley KA, Bray JE, Pouseele H, Rothganger J, Ramirez M, Carriço JA. 2014. TypOn: the microbial typing ontology. *J Biomed Semantics* **5**, 43. (Journal IF:NA, Citation: NA)

Hänscheid T, Rebelo M, Grobusch MP. 2014. Point-of-care tests: where is the point? *Lancet Infect Dis* **14**, 922. (Journal IF:19.446, Citation: 0)

Branquinho R, Meirinhos-Soares L, Carriço JA, Pintado M, Peixe LV. 2014 Phylogenetic and clonality analysis of *Bacillus pumilus* isolates uncovered a highly heterogeneous population of different closely related species and clones. *FEMS Microbiol Ecol.* **2014** **90**:689–698. (Journal

IF:3.875, Citation: 1)

Branquinho R, Sousa C, Osório H, Meirinhos-Soares L, Lopes J, Carriço J, Busse H-J, Abdulmawjood A, Klein G, Kämpfer P, Pintado ME, Peixe L. 2014. *Bacillus invictae* sp. nov., isolated from health products in Portugal. *Int. J. Syst. Evol. Microbiol.* 64:3867–3876. (Journal IF:2.796, Citation: 0)

Neumann A, Völlger L, Berends ETM, Molhoek EM, Stapels DAC, Midon M, Friães A, Pingoud A, Rooijackers SHM, Gallo RL, Mörgelin M, Nizet V, Naim HY, von Köckritz-Blickwede M. 2014. Novel role of the antimicrobial peptide LL-37 in the protection of neutrophil extracellular traps against degradation by bacterial nucleases. *J Innate Immun* 6:860–868. (Journal IF:4.557, Citation: 0)

Horácio, AN, Lopes JP, Ramirez M, Melo-Cristino J, Portuguese Group for the Study of Streptococcal Infections. 2014. Non-invasive pneumococcal pneumonia in Portugal - serotype distribution and antimicrobial resistance. *PLoS ONE* 9:e103092. (Journal IF: 3.534, Citation: 0)

Hänscheid T, Gresnigt T, Löhr S, Flamen A, Zoller T, Melo-Cristino J, Grobusch MP. 2014. Methaemoglobin and COHb in patients with malaria. *Malar. J.* 13:285. (Journal IF: 3.489, Citation: 0)

Friães A., C. Resina, V. Manuel, L. Lito, M. Ramirez, and Melo-Cristino J. 2014. Epidemiological survey of the first case of vancomycin-resistant *Staphylococcus aureus* infection in Europe. *Epidemiol. Infect.* In press (Journal IF: 2.491, Citation: 0)

Mendes JJ, Leandro C, Mottola C, Barbosa R, Silva FA, Oliveira M, Vilela CL, Melo-Cristino J, Górski A, Pimentel M, São-José C, Cavaco-Silva P, Garcia M. 2014. In vitro design of a novel lytic bacteriophage cocktail with therapeutic potential against organisms causing diabetic foot infections. *J. Med. Microbiol.* 63:1055–1065. (Journal IF: 2.266, Citation: 0)

Orbán, A., Á. Butykai, A. Molnár, Z. Pröhle, G. Fülöp, T. Zelles, W. Forsyth, D. Hill, I. Müller, L. Schofield, M. Rebelo, T. Hänscheid, S. Karl, and I. Kézsmárki. 2014. Evaluation of a novel magneto-optical method for the detection of malaria parasites. *PLoS ONE* 9:e96981. (Journal IF: 3.534, Citation: 0)

Olafsdottir, L., H. Erlendsdottir, J. Melo-Cristino, D. Weinberger, M. Ramirez, K. Kristinsson, and M. Gottfredsson. 2014. Invasive infections due to *Streptococcus pyogenes*: seasonal variation of severity and clinical characteristics, Iceland, 1975 to 2012. *Euro Surveill.* 19:pil: 20784 (Journal IF: 4.659, Citation: 0)



Carrasco, M. P., A. S. Newton, L. Gonçalves, A. Góis, M. Machado, J. Gut, F. Nogueira, T. Hänscheid, R. C. Guedes, D. J. V. A. Dos Santos, P. J. Rosenthal, and R. Moreira. 2014. Probing the aurone scaffold against *Plasmodium falciparum*: Design, synthesis and antimalarial activity. *Eur J Med Chem* 80:523–534. (Journal IF: 3.432, Citation: 0)

Prezioso, S., M. D. Pinho, A. R. Attili, J. Melo-Cristino, E. Acke, A. C. Midwinter, V. Cuteri, and M. Ramirez. 2014. PCR based differentiation between *Streptococcus dysgalactiae* subsp. *equisimilis* strains isolated from humans and horses. *Comp. Immunol. Microbiol. Infect. Dis.* 37(3): 169-72. (Journal IF: 2.107, Citation: 0)

Sanderson-Smith M, De Oliveira DMP, Guglielmini J, McMillan DJ, Vu T, Holien JK, Henningham A, Steer AC, Bessen DE, Dale JB, Curtis N, Beall BW, Walker MJ, Parker MW, Carapetis JR, Van Melder L, Sriprakash KS, Smeesters PR, The M Protein Study Group. 2014. A systematic and functional classification of *Streptococcus pyogenes* that serves as a new tool for molecular typing and vaccine development. *J Infect Dis* 210:1325–1338. (Journal IF: 5.778, Citation: 0)

López, E., A. Domenech, M.-J. Ferrándiz, M. J. Frias, C. Ardanuy, M. Ramirez, E. García, J. Liñares, and A. G. de la Campa. 2014. Induction of prophages by fluoroquinolones in *Streptococcus pneumoniae*: implications for emergence of resistance in genetically-related clones. *PLoS ONE* 9:e94358. (Journal IF: 3.534, Citation: 0)

Aguiar, S.I., M. Brito, Horácio, A. N., J. Lopes, M. Ramirez, J. Melo-Cristino, 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. (Journal IF: 4.659, Citation: 1)

Carrolo, M., F. R. Pinto, J. Melo-Cristino, and M. Ramirez. 2014. Pherotype influences biofilm growth and recombination in *Streptococcus pneumoniae*. *PLoS ONE* 9:e92138. (PMID: 24646937) [IF=3.534, Times cited 0]

Cardoso, L. S., C. E. Suissas, M. Ramirez, M. Antunes, and F. R. Pinto. 2014. Comparison of alternative mixture model methods to analyze bacterial CGH experiments with multi-genome arrays. *BMC Res Notes* 7:148. (Journal IF: NA, Citation: 0)

Moreira, A. S., C. P. Coutinho, P. Avezedo, L. Lito, J. Melo-Cristino, and I. Sá-Correia. 2014. *Burkholderia dolosa* phenotypic variation during the decline in lung function of a cystic fibrosis patient along 5.5 years of chronic colonization. *J. Med. Microbiol.* 63:594–601. (Journal IF: 2.266, Citation: 0)

Silva-Costa, C. , J. A. Carriço, M. Ramirez, and J. Melo-Cristino. 2014. Scarlet fever is caused by a limited number of *Streptococcus pyogenes* lineages and is associated with the exotoxin genes *ssa*, *speA* and *speC*. *Pediatr Infect Dis J.* 33(3):306-10. (Journal IF: 3.135, Citation: 1)

#### **Other publications International**

Ramirez M. 2014. *Streptococcus pneumoniae*, p. 1529–1546. In Tang, Y-W, Sussman, M, Liu, D, Poxton, I, Schwartzman, J (eds.), *Molecular Medical Microbiology*, 2nd ed. Academic Press, Elsevier. (DOI: 10.1016/B978-0-12-397169-2.00086-X)

Carriço JA, Ramirez M. 2014. Analysis of typing results, p. 85–112. In Oyarzabal, OA, Kathariou, S (eds.), *DNA Methods in Food Safety: Molecular Typing of Foodborne and Waterborne Bacterial Pathogens*. John Wiley & Sons, Ltd. (DOI: 10.1002/9781118278666.ch5)

#### **Invited lectures and seminars**

J. Melo Cristino. 2014. The first case of VRSA infection in Europe: A cautionary tale. 19th Infection and Sepsis Symposium, Porto, Portugal, 26-28th February.

J. Melo Cristino. 2014. Evolução da Resistência aos antibioticos em *Staphylococcus aureus* em Portugal. Ciclo de conferências de Infeciologia, Hospital de Santa Maria, 16th.

J Melo Cristino. 2014. Mecanismos de resistência e avaliação da susceptibilidade aos antibióticos. IV Curso de Antimicrobianos, Sociedade de Infeciologia Pediátrica, Coimbra, Portugal, 29-30th May.

J Melo Cristino. 2014. Testes de identificação e susceptibilidade aos antimicrobianos: Interpretação clínica dos resultados. Jornadas do Médico Interno de Patologia Clínica. Lisboa, Portugal, 25th-26th September.

J Melo Cristino. 2014. A tuberculose na ópera. Congresso Nacional VIH, Doenças Infecciosas e Microbiologia Clínica. Lisboa, Portugal, 1st-3rd December.

Ramirez M. 2014. Principais grupos farmacológicos e mecanismos de acção. IV Curso de Antimicrobianos, Sociedade de Infeccologia Pediátrica, Coimbra, Portugal, 29-30th May.

M. Ramirez. 2014. New diagnostic tests in infection. 19th Infection and Sepsis Symposium, Porto, Portugal, 26-28th February.

T. Hanscheid. 2014. Malária diagnóstico e tratamento, nos nossos dias. Sessão Clínica no Hospital SAMS, Lisboa, Portugal, 12/03/2014.

T. Hanscheid. 2014. Malária o que há de novo? Sessão Clínica no Hospital da Luz. Lisboa, Portugal, 04/06/2014.

T. Hanscheid. 2014. Shedding new light on old diseases: optical methods for the investigation and diagnosis of tuberculosis or malaria. Seminar Medical Cell Biophysics, Faculty of Science and Technology, Twente University, Enschede, The Netherland, 26/06/2014

T. Hanscheid. 2014. Malária o que há de novo? Sessão Clínica no Hospital Agostino Neto (HAN). Cidade da Praia, Cabo Verde, 09/07/2014.

T. Hanscheid. 2014. Malaria and flow cytometry: current applications and future perspectives. ESCCA 2014. Congress of the European Society for Clinical Cell Analysis. Lisbon, Portugal, 14-17th Sep.

T. Hanscheid. 2014. Diagnóstico de malária em Portugal. X Congresso Nacional de VIH/SIDA e o XII Congresso Nacional de Doenças Infecciosas e Microbiologia Clínica. 1-3 Dec 2014.

T. Hanscheid. 2014. Times of emergent artemisinin resistance - importance of drug sensitivity testing. Seminar. Global Health & Tropical Medicine, Instituto de Higiene e Medicina Tropical. 9/12/2014.

Carricho JA . 2014. Integrating phylogenetic inference and metadata visualization for NGS data: PHYLOViZ (WS20-Typing of Bacterial Pathogens in 2014: Expanding Scope of NGS).114th American Society of Microbiology General Meeting (ASM2014), Boston, USA, 17-20 May

Carriço JA . 2014. How to compare Typing Techniques: Do's and Don't's (WS20-Typing of Bacterial Pathogens in 2014: Expanding Scope of NGS).114th American Society of Microbiology General Meeting (ASM2014), Boston, USA, 17-20 May.

#### Communications in International Conferences

Silva-Costa, C, Aguiar, S, Pinho, M, Ramirez, M, Melo-Cristino, J, The Portuguese Group for the Study of Streptococcal Infections. 2014. The role of conventional and real-time PCR in determining the pneumococcal etiology of complicated pneumonia cases (22.042). International Meeting on Emerging Diseases and Surveillance. Viena, Austria, 31st October–3rd November.

Melo-Cristino, J, Friães, A, Resina, C, Manuel, V, Lito, L, Ramirez, M. 2014. Emergence of vancomycin resistant *Staphylococcus aureus* (VRSA) in Portugal (23.003). International Meeting on Emerging Diseases and Surveillance. Viena, Austria, 31st October–3rd November.

Melo Cristino J, Friães A, Resina C, Manuel V, Lito L M, Ramirez M. 2014. Detection, evolution and outcome of the first case of Vancomycin Resistant *Staphylococcus aureus* (VRSA) infection in Europe (P271). ID Week 2014, Philadelphia, PA, USA, 8-12th October.

Horácio A, Lopes J, Ramirez M, Melo Cristino J, the Portuguese Group for the Study of Streptococcal Infections. Non-invasive pneumococcal pneumonia has its own and distinct serotype distribution in Portugal (P774). ID Week 2014, Philadelphia, PA, USA, 8-12th October.

Carriço JA, Friães A, Prior K, Harmsen D, Ramirez M, Melo-Cristino J. 2014.

Whole Genome Analysis of the first Vancomycin resistant *Staphylococcus aureus* (VRSA) isolated in Europe . (O112). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Santos Costa S, Viveiros M, Melo-Cristino J, Couto I. 2014. Impact of active efflux in the development of M phenotypes in *Staphylococcus aureus*. (P1559). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Semedo-Lemsaddek T, Barroco C, Mottola C, Mendes JJ, Melo-Cristino J, Cavaco-Silva P, Tavares L, Oliveira M. 2014. (P1592). Haemolytic multidrug-resistant enterococci from diabetic foot ulcers. 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Mottola C, Mendes JJ, Melo-Cristino J, Cavaco-Silva P, Tavares L, Oliveira M. 2014. Polymicrobial biofilms by diabetic foot clinical isolates. (eP295). 24th European Congress of

Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

R. Arinto-Garcia, M. D. Pinho, M. Ramirez and J. Melo-Cristino. 2014. Comparison between phenotypic and genotypic methods for the identification of the *Streptococcus anginosus* group (P0593). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

E.S. Björnsdóttir, E.R. Martins, H. Erlendsdóttir, G. Haraldsson, J. Melo-Cristino, M. Ramirez, K.G. Kristinsson. 2014. Comparative analysis of *Streptococcus agalactiae* isolates causing infections in cattle and humans in Iceland (P1505). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

E.S. Björnsdóttir, E.R. Martins, H. Erlendsdóttir, G. Haraldsson, J. Melo-Cristino, M. Ramirez, K.G. Kristinsson. 2014. Group B streptococcal infections among adults in Iceland: 1978-2012 surveillance (P0592). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

J. Diamantino-Miranda, S.I. Aguiar, J. Melo-Cristino, M. Ramirez. 2014. Pherotype diversity is not affected by conjugate vaccine induced serotype changes (eP158). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Aguiar, S.I., Brito, M.J.; Horácio, A.; Lopes, J.P.; Ramirez, M.; Melo-Cristino, J.. 2014. Invasive pneumococcal disease in children and adolescents: incidence of infection and serotype coverage of conjugate vaccines in Portugal (eP154). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Horácio, A. N., Lopes, J.P., Ramirez, M., Melo-Cristino, J. on behalf of the Portuguese Group for the Study of Streptococcal Infections and the Portuguese study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society. 2014. Differences in serotype distribution and dynamics of non-invasive pneumococcal pneumonia and invasive pneumococcal disease (R711). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

Carrico J.A., A. Friães, K. Prior, D. Harmsen, M. Ramirez, J. Melo-Cristino. 2014. Whole genome analysis of the first vancomycin-resistant *Staphylococcus aureus* (VRSA) isolated in Europe (O112). 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Barcelona, Spain, 10-13th May.

S.I. Aguiar, M.J. Brito, A.N. Horácio, J.P. Lopes, M. Ramirez, J. Melo-Cristino. 2014. Declining incidence and changing serotypes in pediatric invasive infections accompany the introduction

of expanded valency pneumococcal conjugate vaccines in Portugal (P-252). 9th International Symposium on pneumococci and pneumococcal diseases - ISPPD9, Hyderabad, India, 9-13th March. (Published in *Pneumonia* 3:193)

A.N. Horácio, M. Ramirez, J. Melo-Cristino. 2014. The serotype distribution of adult non-invasive pneumococcal pneumonia changed in the era of childhood vaccination (P-469). 9th International Symposium on pneumococci and pneumococcal diseases - ISPPD9, Hyderabad, India, 9-13th March. (Published in *Pneumonia* 3:271)

M. Rebelo. 2014. Flow Cytometric Detection of Light Depolarization: A Novel Assay to Detect Antimalarial Drug Effects. At CYTO2014 - XXIX Congress of the International Society for Advancement of Cytometry, Fort Lauderdale, USA, 20 May 2014.

M. Rebelo, J. Fernandes, P.G. Kremsner, T. Hanscheid and M. P. Grobusch. Hemozoin Detection Assay: A Novel Ex Vivo Assay To Detect Antimalarial Drug Resistance. At the the 7th European & Developing Countries Clinical Trials Partnership (EDCTP) Forum, Berlin, Germany, 30 June – 2 July 2014.

#### **Organisation of Conferences**

J. Melo Cristino. Congresso Nacional VIH, Doenças Infecciosas e Microbiologia Clínica. Lisboa, Portugal, 1-3 December 2014. President of the Congress and chairman of the organizing committee.

#### **Prizes, honours and awards**

Maria Rebelo. 2014. Exceptional Student Award, awarded by the International Society for Advancement of Cytometry during the CYTO2014 meeting in Fort Lauderdale, USA.

#### **Advanced teaching**

J. Carriço and M. Ramirez. Lisbon BioMed PhD program , Centro Académico de Medicina de Lisboa, 2014-2015, Faculty of Medicine of Lisbon . Responsible for the Microbes & Host course.

J. Carriço. Post graduation in Oncobiology , Centro Académico de Medicina de Lisboa, 2013-2014, Faculty of Medicine of Lisbon . Responsible for the Biostatistics course.

J. Carriço. Participation on the second cycle course of Computational Biology for Master and PhD programmes of Instituto Superior Técnico, Universidade Técnica de Lisboa in collaboration with the Faculty of Medicine of Lisbon. Responsible for a module on Molecular Phylogenetics.

T. Hanscheid. Lisbon BioMed PhD program , Centro Académico de Medicina de Lisboa, 2014-2015, Faculty of Medicine of Lisbon. Responsible for Clinical Case Presentation in the Host and Pathogens course.

T. Hanscheid, M. Rebelo. PGCD –Postgraduate Program for Science and Development, 2014, Universidade de Cabo Verde, Instituto Calouste Gulbenkian. Responsible for module on Clinical Microbiology.

#### **Science and society**

J. Melo Cristino. 2014. Grande Reportagem SIC. Antibióticos – Alerta Vermelho. 8th May.

#### **PhD thesis completed**

João João Duarte Alves Mendes 04/11/2014 Topical bacteriophage therapy of the infected diabetic foot Faculdade de Medicina, Universidade de Lisboa José Melo Cristino Patrícia Cavaco Silva, Andrzej Górski

Rosangela Maria Rodrigues Carvalho Frita 19/05/2014 Malaria and Tuberculosis co-infection: role for Hemozoin immunosuppression? Faculdade de Medicina, Universidade de Lisboa Thomas Hanscheid

Marcos Daniel Caetano Borges de Pinho 23/05/2014 Lancefield group C and G streptococci in human infection: Molecular typing, virulence and antimicrobial susceptibility Faculdade de Medicina, Universidade de Lisboa Mario Ramirez

Ana Catarina Silva Costa 03/03/2014 Characterization of Streptococcus pyogenes associated with tonsillo-pharyngitis in Portugal with particular emphasis on macrolide resistance Faculdade de Medicina, Universidade de Lisboa José Melo Cristino Mario Ramirez

#### **Msc thesis completed**

Bruno Filipe Ribeiro Gonçalves 29/12/2014 ProGenViz: a novel interactive tool for prokaryotic genome visualization and comparison Faculdade de Ciências, Universidade de Lisboa João André Carriço Octávio Paulo

Mickael Santos Silva 29/06/2014 NGSOnto - Proposta de uma ontologia para descrever o processo de Sequenciação de Alto Desempenho Faculdade de Ciências, Universidade de Lisboa  
João André Carriço Francisco Couto

Raquel Arinto Garcia 28/04/2014 Streptococcus anginosus como agentes de infeção em Humanos: um estudo epidemiológico numa taxonomia em mudança Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa Mário Ramirez Ilda Sanches



## Miguel Castanho Lab

### Major Interests / Objectives

There are many biological processes that depend on the interaction between peptides/proteins and membrane lipids, such as viral fusion, translocation across epithelia or innate immune defence. Some of these may be inspiring to develop new innovative therapeutical tools. The goal of the Physical Biochemistry Unit 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 antimicrobials. We are interest not only in drug targets and drug discovery itself, but also in the molecular-level mechanism of action of drugs that are known for their therapeutic efficacy and safety. We are particularly interested on the central nervous system and translocation of the blood-brain barrier.

### Head of Unit

Miguel Castanho, PhD, Full Professor

### Research Team

Ana Salomé Rocha do Nascimento Veiga	PhD	Investigator
Antónia Rosa Trindade Pinto	Master	Technician, (left July)
Carla Iris Cadima Couto	PhD	Post doctoral Investigator, (started May)
Diana Maria Diez Gaspar	PhD	Post doctoral Investigator
Inês Filipa de Oliveira Almeida	Graduate	MSc Student, (started July)
João Miguel Calado da Silva Freire	Master	PhD Student
Juliana Rodrigues Perazzo	Master	PhD Student
Luís Rafael Pereira do Carmo Flores	Graduate	MSc Student, (left July)
Margarida Filipe Dias Rodrigues	PhD	Investigator, (started June)
Nuno Rebello de Andrade Bustorff Silva	Graduate	Technician, (started March) (left July)
Sandra Cristina Nunes Trigo Pinto	PhD	Post doctoral Investigator, (started

		April)
Sónia Adelaide Queirós de Sá Santos Rocha	PhD	Post doctoral Investigator
Susana Filipa Almeida Dias	Master	Trainee, (started July)
Tânia Sofia Ferreira Morais	PhD	Post doctoral Investigator, (started April)
Tiago Nascimento Figueira	Master	PhD Student, (started April)
Vera Luisa Santos Neves	PhD	Post doctoral Investigator

#### Keywords / Research Areas

Drug discovery, Peptide, Antimicrobials, HIV, Dengue, Blood-brain barrier

#### Major scientific achievements

Our goal is to apply physical principles to study lipid-peptide interactions, aiming to discover not only drugs and targets, but also the mechanism of action at to determine therapeutic efficacy. The main recent achievements were:

**Demonstration** that T20, T1249 and sifuvirtide are anti-HIV molecules that make interactions with lipids as part of their mechanism of action.

**Amidated Kyotorphin** and ibuprofen-amidated Kyotorphin exhibit powerful analgesic properties together with promising opioids alternatives. Furthermore they could lead to neuroprotection compounds. (Ribeiro et al & Santos et al)

**Discovering** that viral proteins are sources of peptide-based drug delivery system (Freire et al)

**Elucidation** of the role of electrostatics in Blood-brain Barrier translocation of small molecules (Ribeiro et al & Serrano et al)

#### Selected Publications

Freire JM, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MA. (2014) Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein: design and mechanism of action. *FEBS J.* DOI: 10.1111/febs.12587, 281, 191-215. <http://onlinelibrary.wiley.com/doi/10.1111/febs.12587/abstract>. (Journal IF: 3.986, Citations: 4)

Santos SM, Garcia-Nimo L, Sá Santos S, Tavares I, Cocho JA, Castanho MA (2013) Neuropeptide

kyotorphin (tyrosyl-arginine) has decreased levels in the cerebro-spinal fluid of Alzheimer's disease patients: potential diagnostic and pharmacological implications. *Front Aging Neurosci.* doi: 10.3389/fnagi.2013.00068, 5, 1. (Journal IF: 2.843, Citations: 2)

Veiga AS, Sinthuvanich C, Gaspar D, Franquelim HG, Castanho MA, Schneider JPB (2012) Arginine-rich self-assembling peptides as potent antibacterial gels. *Biomaterials* doi: 10.1016/j.biomaterials.2012.08.046, 33, 8907–8916. (Journal IF: 8.312, Citations: 39)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MA (2011) Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes. *AIDS* doi: 10.1097/QAD.0b013e328342ff11, 25, 419-28. (Journal IF: 6.557, Citations: 18)

### Ongoing Research Projects

2011/2014 Title: LIPIDENGUE: The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies.. Coordinator: Miguel Castanho. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/QUI-BIQ/112929/2009. Amount: 130,531.17€.

2011/2014 Title: Membrane fusion mechanism of Influenza Hemagglutinin: a simulation and biophysical approach. Coordinator: Miguel Castanho. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/QUI-BIQ/114774/2009. Amount: 46,946€.

2011/2015 Title: Sistema de Incentivos à Investigação & Desenvolvimento Tecnológico do Programa Operacional do QREN - nº 2011/013853 - DO IT. Coordinator: Miguel Castanho. Agency: Agência de Inovação, SA. Reference: QREN - Do It. Amount: 291,962.67€.

2014/2016 Title: Uma estratégia inovadora para distribuição e entrega de inibidores de entrada do HIV multi-alvo usando lipossomas catiónicos. Coordinator: Miguel Castanho. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: HIVERA/0002/2013. Amount: 99,000€.

2014/2016 Title: Multi-target HIV entry inhibitors delivery by cationic liposomes. Coordinator: Ana Salomé Rocha do Nascimento Veiga. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: VIH/SAU/0047/2011. Amount: 129,209€.

2014/2015 Title: 2nd Laço Breast Cancer Grant: Research to Make a Difference – 2014 - The role of cell-cell and cell-extracellular matrix interactions on breast cancer development and dissemination into the brain unravelled by Atomic Force Microscopy. . Coordinator: Miguel Castanho. Agency: Laço Associação de Solidariedade Social . Reference: Bolsa Laço - Diana Gaspar. Amount: 25,000€.

2014/2014 Title: Neuropore Therapies. Coordinator: Miguel Castanho. Agency: Neuropore

Therapies, Inc.. Reference: Neuropore Therapies. Amount: 20,000€.

### Other Projects

2010/2014 Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration (MEMPEPACROSS). Marie Curie International Research Staff Exchange Scheme (IRSES) Call: FP7-PEOPLE-2009-IRSES. Coordinator Institution: IMM. Coordinator PI: Nuno Santos.

### Publications in peer review Journals

Marcelo G, Pinto S, Cañeque T, Mariz I F A, Cuadro A M, Vaquero J J, Martinho J M G and Maçôas E M S (2014) Nonlinear Emission of Quinolizinium Based Dyes With Application in Fluorescence Lifetime Imaging, (in press in *The Journal of Physical Chemistry A*). (Journal IF: 2.775, Citations: 0)

Silva J, Vandermeulen G, Oliveira V, Pinto S N, Rodrigues C, Afonso C, Salgado A, Viana A S, Jerome C, Silva L C, Graça L, Videira M, Prát V and Florindo H F (2014) Development of Functionalized Nanoparticles for Vaccine Delivery to Dendritic Cells: a Mechanistic Approach. *Nanomedicine* **9** (17), 2639-2656. (Journal IF: 5.82, Citations: 1)

Mil-Homens D, Leça M I, Fernandes F, Pinto S N and Fialho A (2014) Characterization of BCAM0224, a multifunctional trimeric autotransporter from the human pathogen *Burkholderia cenocepacia*. *Journal of Bacteriology* **196**, 1968-79. (Journal IF: 2.69, Citations: 2)

Pinto S N, Laviad E L, Stiban J, Merrill A H, Prieto M, Futerman A H and Silva L C (2014) Changes in membrane biophysical properties induced by sphingomyelinase depend on the sphingolipid N-acyl chain. *Journal of Lipid Research* **55**, 53-61. (Journal IF: 4.73, Citations: 5)

Figueira TN, Veiga AS, Castanho MARB (2014) The interaction of antibodies with lipid membranes unraveled by fluorescence methodologies, *J Mol Struct* **1077**, 114–120. (Journal IF: 1.599, Citations: 0)

Serrano ID, Ramu VG, Pinto ART, Freire JM, Tavares I, Heras M, Bardaji ER, and Castanho MARB (2014) Correlation between membrane translocation and analgesic efficacy in kyotorphin derivatives. *Biopolymers* **104**, 1-10. (Journal IF: 2.879, Citations: 0)

de Figueiredo IR, Freire JM, Flores L, Veiga AS & Castanho MARB (2014) Cell-penetrating peptides: A tool for effective delivery in gene-targeted therapies. *IUBMB Life* doi:10.1002/iub.1257. (Journal IF: 2.79, Citations: 4)

Serrano ID, Freire JM, Melo MN, Carvalho MV, Neves M, and Castanho MARB (2014) The Mechanisms and Quantification of the Selective Permeability in Transport Across Biological Barriers: The Example of Kyotorphin. *Mini Rev Med Chem* **14**, 99-110. (Journal IF: 3.19, Citations: 1)

Derniame S, Perazzo J, Lee F, Domogala A, Escobedo-Cousin M, Alnabham R, Luevano M, Pedroza-Pacheco I, Cooper N, Madrigal A and Saudemont A (2014) Differential effects of mycophenolate mofetil and cyclosporine A on peripheral blood and cord blood natural killer cells activated with interleukin-2. *Cytotherapy* **16**, 1409-1418 (Journal IF: 3.1, Citations: 0)

Faustino A, Guerra G, Huber R, Hollmann A, Domingues M, Barbosa G, Enguita F, Bond P, Castanho M, Da Poian A, Almeida F, Santos N and Martins I (2014) Understanding dengue virus capsid protein disordered N-terminus and pep14-23-based inhibition. *ACS Chem Biol*. [Epub ahead of print] (Journal IF: 5.356, Citations: 0)

Domingues M, Silva P, Franquelim H, Carvalho F, Castanho M and Santos N (2014) Antimicrobial protein rBPI21-induced surface changes on Gram-negative and Gram-positive bacteria. *Nanomedicine* **10**, 543-551. (Journal IF: 5.978, Citations: 4)

Faustino A, Carvalho F, Martins I, Castanho M, Mohana-Borges R, Almeida F, Da Poian A, Santos N (2014) Dengue virus capsid protein interacts specifically with very low-density lipoproteins. *Nanomedicine* **10**, 247-255. (Journal IF: 5.978, Citations: 2)

JM Freire, AS Veiga, I Rego de Figueiredo, BG Torre, NC Santos, D Andreu, AT Dapoian, MARB Castanho, 2014, Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein: design and mechanism of action. *FEBS Journal* **281** (1), 191-215. (Journal IF: 3.986, Citations: 2)

#### Invited lectures and seminars

Sá Santos, S. Types of Tissue Culture: primary cultures versus cell lines, in Fundamentos de Cultura Celular 2nd Course, at Escola de Ciências e Tecnologias da Saúde- Universidade Lusófona de Humanidades e Tecnologias, Lisboa, Portugal, February 22, 2014

Sá Santos, S. Beating the Blood-Brain Barrier: targeting the analgesic drug Kyotorphin to the Brain, in LisbonBioMed PhD Program: Towards a Creative and Critical Mind, IMM-FMUL,

Lisboa, Portugal, January 6, 2014

Varela A R, Ventura A E, Carreira A C, Pinto S N, de Almeida R F M, Futerman A H, Prieto M and Silva L C, "Tackling sphingolipids' biophysical properties to decipher their biological roles", Symposium Sphingolipids in Health and Disease, Porto, Portugal, February, 2014.

Varela A R, Ventura A E, Santos A G, Pinto S N, Futerman A H, Prieto M and Silva L C, "Lipid-lipid and lipid-drug interplay in biological membranes: from membrane lipid organization to membrane physiology", Université Catholique de Louvain & Louvain Drug Research Institute, Brussels, Belgium, 2014.

Pinto S N, Varela A R, Ventura A E, Futerman A H, Prieto M and Silva L C. Imaging Ceramide platforms in model and cell membranes. EMBO Workshop on "Lipid Imaging", Naples, Italy, June 2014.

M. Castanho, Peptide-lipid duets in viruses, bacteria, and humans. A physical biochemistry approach. Física Química (h)à descoberta – Cinquentenário da licenciatura em Física e licenciatura em Química da FCUL, Lisbon, October 24th, 2014 (invited speaker)

M. Castanho, How to make my article publishable, Annual International Medical Students Meeting – AIMS Meeting, Lisbon, March 7th-9th, 2014

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

M. Castanho, Peptide-lipid duets in viruses, bacteria, and humans: new views, new avenues, Opening Lecture of the 33rd European Peptide Symposium, European Peptide Society, Sofia, Bulgaria, August 31st, 2014. (Key note speaker)

M. Castanho, Peptide-lipid duets in viruses, humans, and bacteria. 4th Austrian Peptide Symposium, Austrian Peptide Symposium, Salzburg, Austria, December 4th, 2014. (Key note speaker)

Ventura A E, Santos A G, Pinto S N, Prieto M, Futerman A H and Silva L C. Characterization of ceramide-induced changes on the biophysical properties of cellular membranes, 2nd International Workshop on Molecular Medicine of Sphingolipids, Kloster Banz, Germany, October 2014 (Oral presentation).

Pinto S N, Varela A R, Ventura A E, Laviad E L, Merrill A H, Futerman A H, Prieto M and Silva L C. Ceramide-platforms@the endolysosomal pathway: a novel mechanism by which ceramide activates intracellular targets?, International Conference on the Bioscience of Lipids, Aberdeen, UK, June 2014 (Oral presentation).

Pinto S N, Varela A R, Laviad E L, Merrill A H, Futerman A H, Prieto M and Silva L C. Ceramide-

platforms@the endo/lysosomal pathway: a novel mechanism by which ceramide activates intracellular targets?, Gordon Research Conference on Glycolipid and Sphingolipid Biology, Ventura, CA, USA, January 2014 (Selected as a "HOT TOPICS presentation by young investigators") (Oral presentation).

Sá Santos, S., Santos, SM., Pinto, ART., Ramu, VG., Heras, M., Bardaji, E., Tavares, I. and Castanho, MARB. Neuroprotective effects of kyotorphin derivatives in a rat model of dementia, 18th Congress of the Portuguese Biochemical Society, Coimbra, Portugal. December 2014 (Poster Presentation)

Gaspar D, Freire JM, Pacheco TR, Barata JT and Castanho MARB. Evaluation of tumor cells' biomechanical properties for assessing the chemotherapy efficacy of anticancer peptides, 1st ASPIC International Congress, Lisboa, Portugal. November 2014 (Poster Presentation)

Sousa T, Coutinho A, Castro R E, Lucas S D, Moreira R, Rodrigues C M P, Pinto S N, Prieto M P and Fernandes F. The cytotoxic bile acid DCA modulates apoptotic signalling through alteration of mitochondrial membrane properties, Membrane, Morphology and Function, FEBS/Biochemical Society Focused Meeting, Fara San Martino, Abruzzo, Italy, May 2014. (Poster Presentation).

Sousa T, Pinto S N, Lucas S D, Moreira R, Coutinho A, Castro R E, Rodrigues C M P, Prieto M and Fernandes F. Interaction of apoptotic and cytoprotective bile acids with biomembranes, International Liver Congress TM, 49th Annual Meeting of the European Association for the Study of the Liver (EASL), London, United Kingdom, April 2014 (Poster Presentation).

Freire JM, de Figueiredo IR, Veiga AS, Enguita F & Castanho MARB. FEBS-EMBO meeting 2014, Paris, France, August 30-September 4 (2012). siRNA-Bioportide conjugates as a Chronic Myeloid Leukemia gene therapy targeting the BCR/ABL Fusion Gene. (Poster Presentation)

Freire JM, Veiga AS and Castanho MARB 58th Annual Meeting of the Biophysical Society, February 15th-19th, 2014, San Francisco, USA. Dengue virus Capsid protein delivers nucleic acids intracellularly. (Poster Presentation)

## Internationalisation

All projects coordinated by the MCastanho lab are international. The projects reveal the impact that the MCastanho lab has in Peptide Science, mainly in the field of membrane-active peptides.

M. Castanho is the PI of an international consortium, INPACT, funded by H2020 that involves ten different teams from four continents. This consortium combines teams from industry, academia, and media. They all join efforts to produce and disseminate new knowledge on the development of new high impact antibiotics and anticancer drugs.

DELIN is an on-going project that consists in a joint effort of three teams in different European countries to study innovative molecular targeting against HIV.

One other international project having M. Castanho as PI, PEP2BRAIN, ended in 2014. Five different teams from industry and academia, from three different countries were funded by FP7 to develop derivatives of neuropeptides as analgesic and neuroprotective drugs.

M. Castanho was selected in 2012 for invited researcher at the Medical Biochemistry Institute of the Federal University of Rio de Janeiro under the Science Without Borders Program. This position involves the implementation of a scientific, advanced training, and outreach program. The fusion between Dengue Virus and host cells is the main theme of the project.

MCastanho has provided research contract services for a US company in 2014.

Most of the papers published by MCastanho lab have international co-authors, albeit most of them have corresponding authors from the lab.



### **Prizes, honours and awards**

Leonidas Zervas Award to M. Castanho, European Peptide Society, 2014.

2nd edition of the Associação Laço Research Grant 2014 to Diana Gaspar.

FEBS-EMBO meeting 2014 Molecular Oncology journal Poster Prize to João Miguel Freire.

FEBS bursary to attend FEBS-EMBO meeting 2014 to João Miguel Freire.

IUBMB Wood-Whelan Fellowship to João Miguel Freire.

### **Industry contract research**

MCastanho Lab partnered with Neuropore (Berkeley, USA).

### **Advanced teaching**

Castanho, M. External international examiner for PhD theses in the University of Rome and University of Cagliari.

Figueira TN participated as a PhD student in the international course organized by the European Biophysics Societies' Association entitled "EBSA Biophysics Course on: Membranes and Lipid-Protein Interactions" and contributed with an oral presentation entitled "Evaluating the protein-lipid interactions of F63, a broad and potent anti-HIV single domain antibody, through fluorescence spectroscopy methodologies", Le Grand Motte, Presqu'île du Ponant, Hérault, France, September 8-12, 2014

### **Msc thesis completed**

Luís Rafael Carmo Flores 17/03/2014 Membrane-active Peptides from structural viral proteins: identifying novel delivery vectors for gene therapy Universidade Católica Portuguesa Miguel Castanho Salomé Veiga

Inês Rego de Figueiredo 29/04/2014 Chronic Myeloid Leukemia Gene Therapy Delivered by Cell Penetrating Peptides – from bench to clinic University of Lisbon Miguel Castanho Salomé Veiga

## Miguel Prudêncio Lab

### Major Interests / Objectives

Our interests span a wide range of topics within the malaria field, with particular emphasis on the hepatic stage of infection. We are interested in elucidating novel aspects of the biology of Plasmodium infection, 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
- Novel compounds against Plasmodium liver stages
- Malaria vaccines
- The reciprocal influence of Plasmodium and Trypanosoma co-infections

### Head of Unit

Miguel Prudêncio, PhD

### Research Team

Ana Filipa Gonçalves Teixeira	Master	Investigator, (started March)
Ana Margarida Roque Sanches Vaz	Master	Investigator
António Manuel Barbeiro Mendes	PhD	Post doctoral Investigator
Carolina Morgado de Andrade	Graduate	MSc Student, (started July)
Cláudia B. Rodrigues Sá e Cunha Mesquita Gabriel	PhD	Post doctoral Investigator
Inês Isabel Fernandes Gomes	PhD	Post doctoral Investigator
Joana da Silva Pissarra	Master	Investigator, (started April)

Jorge Manuel Santos	PhD	Post doctoral Investigator, (started December)
Maria Inês Sousa de Albuquerque	Master	Technician, (left May)
Marija Markovic	PhD	Post doctoral Investigator, (started March)
Marta Monteiro Maia Machado	Graduate	Technician
Miguel Filipe Duarte	Graduate	MSc Student, (left November)
Patrícia dos Santos Meireles	Master	PhD Student
Pedro Gil Gameiro Eloy Sena Rego	Undergraduate	Trainee, (started April)

#### **Keywords / Research Areas**

Malaria, Parasitology, Vaccines, Host-pathogen interactions, Liver-stage Plasmodium infection, Plasmodium

#### **Major scientific achievements**

During 2014, the Prudêncio lab has:

- published several collaborative papers in peer-reviewed, international journals
- been awarded a supplement of a Phase II Grand Challenges Explorations award by the Bill & Melinda Gates Foundation
- filed one international patent application (Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine)
- been a finalist in the “Everis Foundation Entrepreneurs” award
- been a finalist in the “6th Universal Biotech Innovation Prize”
- participated in several International and National conferences and meetings
- had several media appearances in relation to its scientific activities

In this period the lab has also expanded from 8 to the present 11 researchers, and established or furthered collaborations with several National and International research groups.

#### **Selected Publications**

J. Lin, P. Meireles, M. Prudêncio, S. Engelmann, T. Annoura, M. Sajid, S. Chevalley?Maurel, J. Ramesar, C. Nahar, C.M.C. Avramut, A.J. Koster, K. Matuschewski, A.P. Waters, C.J. Janse, G.R.

Mair, S.M. Khan (2013) Loss-of-Function Analyses Defines Vital and Redundant Functions of the Plasmodium Rhomboid Protease Family. *Mol. Microbiol* **88**, 318-338. (Journal IF: 5.0, Citations: 3)

F.P. da Cruz, C. Martin, K. Buchholz K, M.J. Lafuente-Monasterio, T. Rodrigues, B. Sönnichsen, R. Moreira, F.J. Gamo, M. Marti, M.M. Mota, M. Hannus, M. Prudêncio (2012) Drug Screen Targeted at Plasmodium Liver Stages Identifies a Potent Multi-Stage Anti-Malarial Drug. *J. Inf. Dis.* **205**, 1278-1286. (Journal IF: 5.8, Citations: 18)

M. Prudêncio, M.M. Mota, A.M. Mendes (2011) A toolbox to study liver stage malaria. *Trends Parasitol* **27**, 565-574. (Journal IF: 5.3, Citations: 19)

M. Prudêncio, C.D. Rodrigues, M. Hannus, C. Martin, E. Real, L .A. Gonçalves, C. Carret, R. Dorkin, I. Röhl, K. Jahn-Hoffmann, A.J.F. Luty, R. Sauerwein, C.J. Echeverri, M.M. Mota (2008) Kinome-Wide RNAi Screen Implicates at Least 5 Host Hepatocyte Kinases in Plasmodium Sporozoite Infection. *PLoS Pathogens* **4**, 1-15. (Journal IF: 8.92, Citations: 42)

M. Prudêncio, A. Rodriguez, M.M. Mota (2006) The silent path to thousands of merozoites: the Plasmodium liver stage. *Nat. Rev. Microbiol* **4**, 849-856. (Journal IF: 23.3, Citations: 143)

#### Ongoing Research Projects

2012/2014 Title: Utilization of host cell resources by the malaria parasite in the liver. Coordinator: Miguel Prudêncio. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-MIC/117060/2010. Amount: 154,755€.

2012/2015 Title: Towards malaria eradication. A novel approach for multi-targeting the parasite's life cycle. Coordinator: Miguel Prudêncio. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-FAR/118459/2010. Amount: 36,741€.

2013/2014 Title: DO88. Coordinator: Miguel Prudêncio. Agency: University of Belgrade - Faculty of Chemistry. Reference: DO88. Amount: 4,961€.

2013/2014 Title: Global Health Grant Number: OPP1086130 - A New whole-organism vaccine against malaria. Coordinator: Miguel Prudêncio. Agency: Bill & Melinda Gates Foundation. Reference: Bill & Melinda - Vaccine. Amount: 566,161.21€.

2013/2014 Title: Prémio Inovação BES categoria Saúde. Coordinator: Miguel Prudêncio. Agency: Banco Espírito Santo. Reference: Prémio Inovação BES categoria Saúde. Amount: 50,000€.

### Publications in peer review Journals

C. Ramalhete, F.P. da Cruz, I.J. Sousa, S. Mulhovo, M.X. Fernandes, M. Prudêncio, M.-J.U. Ferreira (2014), "Dual-stage triterpenoids from an African medicinal plant targeting the malaria parasite", *Bioorganic & Medicinal Chemistry*, **22**, 3887-3890 (Journal IF: 3.2, Citations: 0)

R. Oliveira, R.C. Guedes, P. Meireles, I.S. Albuquerque, L.M. Gonçalves, E. Pires, M.R. Bronze, J. Gut, P.J. Rosenthal, M. Prudêncio, R. Moreira, P.M. O'Neill, F. Lopes (2014), "Tetraoxane-Pyrimidine Nitrile Hybrids as Dual Stage Antimalarials", *J. Med. Chem.*, **57**, 4916-4923 (Journal IF: 5.5, Citations: 0)

D. Miranda, R. Capela, I.S. Albuquerque, P. Meireles, I. Paiva, F. Nogueira, R. Amewu, J. Gut, P.J. Rosenthal, R. Oliveira, M.M. Mota, R. Moreira, F. Marti, M. Prudêncio, P.M. O'Neill, F. Lopes (2014) "Novel Endoperoxide-Based Transmission-Blocking Antimalarials with Liver- and Blood-Schizontocidal Activities", *ACS Med. Chem. Lett.*, **5**, 108-112 (Journal IF: 3.1, Citations: 0)

A. Gomes, B. Pérez, I. Albuquerque, M. Machado, M. Prudêncio, F. Nogueira, C. Teixeira, P. Gomes (2014) "N-cinnamoylation of antimalarial classics: new quinacrine analogues with reduced toxicity and dual-stage activity", *ChemMedChem*, **9**, 305-310 (Journal IF: 3.1, Citations: 0)

P. Liehl, V. Zuzarte-Luís, J. Chan, T. Zillinger, F. Baptista, D.I Carapau, M. Konert, K. Hanson, C. Carret, C. Lassnig, M. Müller, U. Kalinke, M. Saeed, A.F. Chora, D.T. Golenbock, B. Strobl, M. Prudêncio, L.P. Coelho, S.H. Kappe, G. Superti-Furga, A. Pichlmair, A.M. Vigário, C.M. Rice, K.A. Fitzgerald, W. Barchet, M.M. Mota (2014) "Host cell sensors for Plasmodium activate innate immunity against liver stage infection", *Nature Medicine*, **20**, 47-53 (Journal IF: 24.7, Citations: 7)

### Invited lectures and seminars

MP, "Whole-organism pre-erythrocytic malaria vaccines - Development of a new strategy to vaccinate against malaria", EU FP7 Marie Curie Initial Training Network, GlycoPar, 1st Training Workshop, 1 October 2014, Instituto de Medicina Molecular, Lisbon, Portugal

AM, "RoPlaVac – Revolutionizing malaria vaccination", September 2014, Innovations teams of MIT Portugal, Fundação Luso-Americana (FLAD), Lisbon, Portugal

AM, "The BioMalPar PhD programme: the highs and the lows", May 2014, 10th Annual BioMalPAR/EVIMalPar conference on the Biology and Pathology of the Malaria Parasite, EMBL, Heidelberg, Germany

MP, "Malária: situação atual, necessidades e desafios", 11 April 2014, 6th REVIVE Workshop, INSA - Centro de Estudos de Vetores e Doenças Infecciosas, Águas de Moura, Portugal

MP, "Uma nova estratégia de vacinação contra a malária", 7 April 2014, V Seminário Educação

pelos Pares - Small Creatures, Big Threat, Coimbra Health School, Coimbra, Portugal

MP, "Malária: situação atual e desenvolvimento duma nova estratégia de vacinação", 2 April 2014, Semana das Ciências e Tecnologias, Universidade de Évora, Évora, Portugal

AM, "A new vaccination strategy against malaria", 4<sup>o</sup> Encontro de Biologia Molecular em Saúde, March 2014, Escola Superior de Saúde Egas Moniz, Monte da Caparica, Portugal

MP, "Malaria vaccine", AstraZeneca ACS Scientific Meeting, 15 March 2014, Fundação Champalimaud, 15 March 2014, Lisboa, Portugal

MP, "Thinking outside the species: a new vaccine against malaria", IMM Seminar, 12 March 2014, Instituto de Medicina Molecular, Lisboa, Portugal

MP, "Design and development of a project for a new vaccination strategy against malaria", DQB Seminars, 27 February 2014, Faculdade de Ciências, Universidade de Lisboa, Portugal

MP, "Vacina contra a malária: uma abordagem diferente para uma necessidade urgente", Sessão Clínica, 13 February 2014, Hospital Santa Maria, Lisbon, Portugal

MP, "Development of a vaccine against malaria", I Jornadas FCUL/CESAM, 12 February 2014, Faculdade de Ciências, Universidade de Lisboa, Portugal

MP, "Exploiting a new strategy for vaccination against malaria", Jornadas Tecnológicas da FCT, 10 February 2014, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal

MP, "Plasmodium liver stages and anti-malarial strategies: development of a new vaccination approach against malaria", Institutional Seminar, 23 January 2014, Biochemical Colloquium, Institut fur Biochemie, University of Freiburg, Germany. Hosted by Dr. Susana Andrade and Prof. Oliver Einsle

MP, "Thinking outside the species: a rodent Plasmodium-based strategy for vaccination against human malaria", Institutional Seminar, 21 January 2014, Instituto de Higiene e Medicina Tropical, Lisboa, Portugal.

### Communications in International Conferences

Miguel Prudêncio, "Thinking outside the species: development of a new approach to vaccination against malaria", iMed Conference 6.0, 10-12 October 2014, Universidade Nova, Lisbon, Portugal. (Oral presentation)

Miguel Prudêncio, "Of mice and men: A rodent Plasmodium platform for immunization against human malaria", NIH/NIAID workshop: Exploring Immunological Mechanisms of Whole Sporozoite Vaccination against Plasmodium falciparum Malaria, 2-3 September 2014, Rockville, MD, USA. (Oral presentation)

António M. Mendes, Inês S. Albuquerque, Marta Machado, Ahmed Salman, Belen Jimenez-Diaz, Iñigo Angulo-Barturem, Rob Hermsen, Merije Behet, Nataniel Gonçalves-Rosa, Isabel Rocha, Sangeeta Bhatia, Alexis Kaushansky, Stefan Kappe, Lander Foquet, Geert Leroux-Roels, Philip Meuleman, Anne-Marie Zeeman, Ed Remarque, Clemens Kocken, Shahid Khan, Chris J. Janse, Maria M. Mota, Robert W. Sauerwein, Miguel Prudêncio, "Towards a rodent Plasmodium-based vaccine against human malaria", Grand Challenges 2014 Annual Meeting, 5-8 October 2014, Seattle, Washington, USA. (Poster presentation)

Peter Liehl, Patrícia Meireles, Inês S. Albuquerque, Mykola Pinkevych, Fernanda Baptista, Maria M. Mota, Miles P. Davenport, Miguel Prudêncio, "Innate immunity induced by Plasmodium liver infection inhibits malaria reinfections", 2014 (25th) Annual Molecular Parasitology Meeting, 14-18 September 2014, MBL, Woods Hole, MA, USA. (Poster presentation)

T.A.F. Cardote, R.A. Guedes, S.D. Lucas, M. Prudêncio, R. Moreira, R.C. Guedes, "Targeting the Qi binding site of cytochrome bc1 complex to design new antimalarials", ISMC 2014 - XXIII International Symposium on Medicinal Chemistry, 7-11 September 2014, Lisbon, Portugal. (Poster presentation)

Rudi Oliveira, Rita C. Guedes, Patrícia Meireles, Inês S. Albuquerque, Lídia M. Gonçalves, Elisabete Pires, Maria R. Bronze, Jiri Gut, Philip J. Rosenthal, Miguel Prudêncio, Paul M. O'Neill, Francisca Lopes, Rui Moreira, "Tetraoxane – Pyrimidine Nitrile Hybrids, Combination of Dual Mechanism of Action with Dual Stage Antimalarial Activity", ISMC 2014 - XXIII International Symposium on Medicinal Chemistry, 7-11 September 2014, Lisbon, Portugal. (Poster presentation)

D. Miranda, J. Magalhães, M.J. Perry, I. Albuquerque, M. Monteiro, P.J. Rosenthal, J. Gut, R. Moreira, M. Prudêncio and F. Lopes, "SAR and stability studies of hybrid compounds with multistage antimalarial activity", ISMC 2014 - XXIII International Symposium on Medicinal Chemistry, 7-11 September 2014, Lisbon, Portugal. (Poster presentation)

Patrícia Meireles, Joana Sales-Dias, Liliana Mâncio, Maria M. Mota, Miguel Prudêncio, "The Role of D-Glucose Uptake by Glucose Transporter 1 during the liver stage of Plasmodium

Infection", 10th Annual BioMalPar | EVIMalaR Conference, 12-15 May 2014, EMBL Heidelberg, Germany. (Poster presentation)

Cláudia Sá e Cunha, Britta Nyboer, Maria M. Mota, Miguel Prudêncio, Ann-Kristin Mueller, "Unveiling a novel host-parasite interaction during the liver stage of malaria infection, 10th Annual BioMalPar | EVIMalaR Conference, 12-15 May 2014, EMBL Heidelberg, Germany. (Poster presentation)

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

Mariana Romão, Inês Gomes, Miguel Peixoto, Cláudia S. Cunha, Miguel Prudêncio, Eulália Pereira, Ricardo Franco, "Nanoimmunoassays for malaria antigen detection in clinical samples using gold nanoparticles-antibody conjugates", VII Encontro Nacional de Estudantes de Bioquímica (ENEBIOQ), 11-14 April 2014, FCT-UNL, Campus da Caparica, Portugal. (Poster presentation)

Carlos Caro, Ana Góis, Carolina Tempera, Vânia André, Peter Eaton, Peter Burke, M. Teresa Duarte, Miguel Prudêncio, Thomas Hänscheid, Ricardo Franco, "Molecular structure of hemozoin-like crystals and their interaction with chloroquine", 10th Inorganic Chemistry Conference of SPQ, 11-12 April, 2014, Costa da Caparica, Portugal. (Poster presentation)

Inês Gomes, Cláudia S. Cunha, Eulália Pereira, Nuno C. Santos, Diane W. Taylor, Maria M. Mota, Miguel Prudêncio, Ricardo Franco, "Development of a rapid diagnostic test for malaria antigens detection using gold nanoparticles-antibody conjugates", Nanoscience and Nanotechnology International Conference, nanoPortugal 2014, February 12-14, Porto, Portugal. (Poster presentation)

#### **Prizes, honours and awards**

Grand finalist "Everis Foundation Entrepreneurs" award

Grand finalist "6th Universal Biotech Innovation Prize"

#### **Patents/prototypes**

"Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine", *"Entering National/Regional Phase"*



### **Advanced teaching**

#### Advanced Training Courses

"O Método Científico e a publicação científica", Academic training for researchers of the Centro de Investigação em Saúde (CISA), January 2014, Caxito, Angola (AM)

"Host-Plasmodium interactions and anti-malarial vaccination", 17 March 2014, BioSys/BioFIG Research Seminar, Faculdade de Ciências, Universidade de Lisboa, Portugal (MP)

#### Master's Courses

Master's in clinical biochemistry, Universidade Nova de Lisboa, June 2014 (MP)

Master's in Evolutionary and development biology, Universidade de Lisboa, November 2014 (MP)

Master's in Molecular Biology and Genetics, Universidade de Lisboa, November 2014 (MP)

#### PhD Courses

Glycopar, 1st TRAINING WORKSHOP 29th September to 3rd October, 2014 Instituto de Medicina Molecular, Lisbon, Portugal (MP)

### **Science and society**

MP, "O impacto da ciência e dos cientistas na sociedade atual", 25 March 2014, Dialogue Café, Fundação Calouste Gulbenkian, Lisboa, Portugal

MP, "Malária em Portugal: uma ameaça real?", 10 April 2014, Comemorações do Dia Mundial da Saúde: Doenças associadas a vetores - Small bite, big threat", INSA Ricardo Jorge, Lisboa, Portugal

MP, "Aquecimento global e a possibilidade de reaparecimento de malária em Portugal: uma ameaça real?", 19 May 2014, iMED6.0 opening ceremony, Faculdade de Ciências Médicas Univ. Nova Lisboa, Portugal

MP, "Refletir para além da espécie: uma nova vacina contra a malária", 20 June 2014, TEDx FCT-UNL, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal

### **Msc thesis completed**

Miguel Filipe Duarte 14/11/2014 Characterization of a new malaria vaccine candidate against Plasmodium vivax using genetically modified rodent Plasmodium parasites Fac. Ciências Univ. Lisboa António Mendes Miguel Prudêncio

Pedro Gil Gameiro Eloy Sena Rego 19/11/2014 Paving a freezing way to defeat malaria Instituto Superior Técnico Miguel Prudêncio Miguel Rodrigues

## **Miguel Remondes Lab**

### **Major Interests / Objectives**

Explaining how billions of neurons connected trillions of times generate mental functions remains one of the greatest tasks science faces today. One such function, declarative memory, involves the association and storage of information from distinct brain regions, orchestrated by a medial temporal structure called the hippocampus, through a mechanism called activity-dependent neural plasticity. Disruption of such mechanism leads to socially pervasive mental dysfunctions. Scientists have investigated the physiology of memory circuits, but less so the way these circuits integrate incoming sensory information, or govern the use of memory for other brain functions. In addition, until recently we lacked the technology to adequately address causality between physiology and behavior.

### **Head of Unit**

Armando Miguel Caseiro Pires Remondes, PhD

### **Keywords / Research Areas**

Neurophysiology, Behavior, Optogenetics and Chemogenetics

### **Major scientific achievements**

While the space and infrastructural resources were being setup, this lab has been purchasing and assembling technology to achieve the main research goals, hiring lab members, and started to train the first lab member in the techniques necessary for such research. In addition, we have been gathering institutional support from other institutes in providing advice in the neurophysiology and manipulation techniques. We have also presented our work and research plans in scientific sessions at IMM and in other venues.

### **Ongoing Research Projects**

2014/2019 Title: Exploratório - IFCT. Coordinator: Armando Miguel Caseiro Pires Remondes.  
Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: Exploratório Miguel Remondes.  
Amount: 50,000€.

## Nuno Santos Lab

### Major Interests / Objectives

Biochemical and biophysical processes occurring in membranes of human cells, as well as of their viral and bacterial pathogens. Study of two steps of the enveloped viruses life cycle (mainly HIV-1 and dengue virus) that involve biomembranes – the entrance of the virus or its content into the target cell and the assembly of new virions. Study of the binding of fibrinogen to the erythrocyte membrane and its relevance as cardiovascular risk factor. Pre-clinical evaluation of the membrane activity and mechanism of action of antimicrobial peptides (AMP) and cell-penetrating peptides (CPP). On the Nanomedicine area, work on the development of innovative protein-ligand interactions biosensor systems, with improved selectivity and sensitivity (nanoparticles and amyloid-based biosensors).

### Head of Unit

Nuno Fernando Duarte Cordeiro Correia dos Santos, PhD Agregação, Associate Professor

### Research Team

Ana Filipa Barata Duarte Guedes	Master	PhD Student
Ana S. Martins	Graduate	MSc Student
André F. Faustino	Master	PhD Student
Axel Hollmann	PhD	Post doctoral Investigator
Bárbara Sofia Lopes Gomes	Master	PhD Student, (started April)
Filomena A. Carvalho	PhD	Investigator, Assistant Professor
Gabriela Maria Pereira Carvalho Guerra	Master	Technician
Ivo Cristiano da Rocha Martins	PhD	FCT Investigator
Joana Maria de Almeida Monteiro	Graduate	MSc Student, (started March)
Marcelo Alexandre da Costa Tavares Augusto	Master	PhD Student

Margarida Filipe Dias Rodrigues	PhD	PhD Student, (left May)
Mário R. Felício	Master	Investigator, (started April)
Patrícia Maria de Oliveira e Silva	Master	Investigator, (left March)
Sónia Gonçalves Abreu	PhD	Investigator
Susana dos Reis Gregório	Graduate	MSc Student
Virgínia Sara Grancieri do Amaral	Master	PhD Student, Instituto de Biofísica Carlos Chagas Filho , (left January)

#### Keywords / Research Areas

Membranes, HIV and Dengue Virus, Peptide-based therapies (CPPs, AMPs, pep14-23), Atomic Force Microscopy (AFM), Fibrinogen, Nanomedicine

#### Major scientific achievements

Singlet oxygen produced by the new broad-spectrum antiviral LJ001 and related compounds, namely JL103 and dUY11, induce changes on the viral membrane resulting in the inhibition of the virus-cell membrane fusion necessary for cell infection by HIV and other enveloped viruses. The enhanced interaction with membranes of HIV fusion inhibitor peptides conjugated with cholesterol, concomitant with an enhanced exposure of the pocked binding domain, due the addition of a PEG linker, result in a more efficient blocking of HIV entry.

Dengue virus capsid protein (DENV C) interacts with lipid droplets and very low-density lipoproteins (VLDL), requiring K<sup>+</sup> and being inhibited by a new drug lead, pep14-23. Human proteins and anionic phospholipids are also involved in these processes, essential for dengue virus replication.

The quantification of fibrinogen-erythrocyte binding forces may be used as a new prognostic marker of the risk of hospitalization on heart failure patients.

#### Selected Publications

Augusto MT, Hollmann A, Castanho MARB, Porotto M, Pessi A, Santos NC (2014) Improvement of the HIV fusion inhibitor C34 efficacy by membrane anchoring and enhanced exposure. *J. Antimicrob. Chemother.* **69**, 1286-1297. (Journal IF: 5.439, Citations: 2)

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 lowdensity

lipoproteins. *Nanomedicine: NBM* **10**, 247-255. (Journal IF: 5.978, Citations: 2)

Padilla-Parra S, Matos PM, Kondo N, Marin M, Santos NC, Melikyan GB (2012) Quantitative imaging of endosome acidification and single retrovirus fusion with distinct pools of early endosomes. *Proc. Natl. Acad. Sci. U. S. A* **109**, 17627-17632. (Journal IF: 9.809, Citations: 13)

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. (Journal IF: 12.033, Citations: 36)

Hauser CA, Maurer-Stroh S, Martins IC (2004) Amyloid-Based Nanosensors and Nanodevices. *Chem. Soc. Rev.* **43**, 5326-5345. (Journal IF: 30.425, Citations: 5)

### Ongoing Research Projects

2010/2014 Title: Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration.. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Agency: Comissão Europeia. Reference: Mempepacross. Amount: 133,200€.

2012/2015 Title: Molecular characterization of the fibrinogen-erythrocyte interaction and its influence on Cardiovascular pathologies. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/QUI-BIQ/119509/2010. Amount: 175,000€.

2012/2015 Title: AMYLOID DETECTORS: Employing amyloid fibrils as biosensors of the interaction of peptides with phospholipids and/or protein domains. Coordinator: Ivo Cristiano da Rocha Martins. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-ENB/117013/2010. Amount: 144,010€.

2012/2015 Title: Adhesion, Differentiation and Invasion: different processes, common cadherin players. Coordinator: Nuno Fernando Duarte Cordeiro Correia dos Santos. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-GMG/120049/2010. Amount: 49,500€.

### Other Projects

2014/2017 Análises moleculares comparativas de peptídeos cíclicos e lineares com atividades imunomodulatórias e antimicrobianas. Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) Ciência sem Fronteiras Project 300965/2014, Brazil.. Coordinator: N.C. Santos.

2010/2016 The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation, FCG, Calouste Gulbenkian Foundation Frontiers in Life Sciences Research Prize, €50 000. Coordinator: I.C. Martins.

2011/2014 LIPIDENGUE: The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies, FCT, FCT - PTDC/QUI-BIQ/112929/2009, €130 000. Coordinator: N.C. Santos. Coordinator PI: M. Castanho.

2012/2015 Multi-target HIV entry inhibitors delivery by cationic liposomes, FCT, FCT - VIH/SAU/0047/2011, €129 209. Coordinator: N.C. Santos.

2013/2014 Studying the interaction with biological membranes of pep14-23, a novel dengue virus capsid protein inhibitor, Calouste Gulbenkian Foundation (FCG) & Lisbon Medical Faculty (FMUL) project 20130008/PEC/BG, € 3000. Coordinator: I.C. Martins,.

2014/2016 DELIN: An innovative approach to deliver dual targeting HIV entry inhibitors using cationic liposomes, FCT/ HIVERA (União Europeia). . Coordinator: N.C. Santos.

2012/2014 Do IT - Desenvolvimento e Operacionalização da Investigação de Translação.. Coordinator: N.C. Santos. Coordinator Institution: Quadro de Referência Estratégico Nacional (QREN).

2013/2018 The Role of Fibrin Clot Structure in Thrombosis.. Coordinator: N.C. Santos. Coordinator Institution: Project of the British Heart Foundation.

2010/2015 Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease. Calouste Gulbenkian Foundation Prize Stimulus to Research.. Coordinator: N.C. Santos.

2014/2015 Flavivirus capsid protein structure-function relationship. Supervisor of Mafalda Vasconcelos, Biochemistry trainee, Faculty of Medicine, University of Lisbon, Lisbon, Portugal.. Coordinator: I.C. Martins.

2014/2015 Assessment of the changes on fibrinogen-induced erythrocyte-erythrocyte adhesion on different cardiovascular pathologies by AFM-based force spectroscopy. Supervisor of Eduardo Bento, Biochemistry trainee, Faculty of Medicine, University of Lisbon, Lisbon, Portugal. . Coordinator: F.A. Carvalho.

2013/2016 DELIN: An innovative approach to deliver dual targeting HIV entry inhibitors using cationic liposomes, 99 000 €. Coordinator: N.C. Santos. Coordinator Institution: FCT/ HIVERA (European Union). Coordinator PI: M.Castanho.

### Publications in peer review Journals

Faustino AF, Guerra GM, Huber RG, Hollmann A, Domingues MM, Barbosa GM, Enguita FJ, Bond PJ, Castanho MARB, Da Poian AT, Almeida FCL, Santos NC, Martins IC (2014) Understanding Dengue virus capsid protein disordered N-terminus and pep14-23 based inhibition, *ACS Chem. Biol.*, in press. (Journal IF: 5.356, citations: 0)

Gomes B, Loureiro JA, Coelho M, Pereira MC. (2014) The potential effect of fluorine in the treatment of Alzheimer's disease. *Curr. Pharm. Des.*, in press. (Journal IF: 3.288, citations: 0)

Rodrigues M, Andreu D, Santos NC (2014) Uptake and cellular distribution of nucleolar targeting peptides (NrTPs) in different cell types, *Biopolymers (Pept. Sci.)*, in press. (Journal IF: 2.288, citations: 0)

Hauser CA, Maurer-Stroh S, Martins IC (2014) Amyloid-Based Nanosensors and Nanodevices. *Chem. Soc. Rev.*, **43**, 5326-5345. (Journal IF: 30.425, citations: 5)

Santos C, Gomes B, Gonçalves L, Oliveira J, Rocha S, Coelho M, Rodrigues J, Freitas V, Aguilar H. (2014) Pyranoflavylum derivatives extracted from wine grapes as photosensitizers in solar cells. *J. Braz. Chem. Soc.* **25**, 1029-1035. (Journal IF: 1.253, citations: 0)

Morinha F, Travassos P, Seixas F, Martins A, Bastos R, Carvalho D, Magalhães P, Santos M, Bastos E, Cabral JÁ. (2014) Differential mortality of birds killed at wind farms in Northern Portugal, *Bird Study.* **61**, 255-259. (Journal IF: 1.033, citations: 1)

Felício MR, Nunes TG, Vaz PM, Botas AMP, Ribeiro-Claro P, Ferreira RAS, Freire RO, Vaz PD, Carlos LD, Nunes CD, Nolasco MM. (2014) Modelling the luminescence of extended solids: the example of highly luminescent MCM-41 impregnated with Eu<sup>3+</sup>  $\beta$ -diketonate complex. *J. Mater. Chem. C.* **2**, 9701-9711. (Journal IF: 6.626, citations: 0)

Gomes B, Loureiro JA, Coelho M, Pereira MC, Rocha S. (2014) Targeting nanoparticles across the blood brain barrier with monoclonal antibodies. *Nanomedicine* **9**, 709-709 (Journal IF: 5.824, citations: 1)

Augusto MT, Hollmann A, Castanho MARB, Porotto M, Pessi A, Santos NC (2014) Improvement of the HIV fusion inhibitor C34 efficacy by membrane anchoring and enhanced exposure. *J. Antimicrob. Chemother.* **69**, 1286-1297. (Journal IF: 5.439, citations: 2)



Domingues MM, Silva PM, Franquelim HG, Carvalho FA, Castanho MARB, Santos NC (2014) Antimicrobial protein rBPI21 induced surface changes on Gramnegative and Grampositive bacteria, *Nanomedicine: NBM* **10**, 543-551. (Journal IF: 5.978, citations: 2)

Hollmann A, Castanho MARB, Lee B, Santos NC (2014) Singlet oxygen effects on lipid membranes: implications for the mechanism of action of broadspectrum viral fusion inhibitors, *Biochem. J.* **459**, 161-170. (Journal IF: 4.779, citations: 0)

Silva PM, Gonçalves S, Santos NC (2014) Defensins: antifungal lessons from eukaryotes. *Front. Microbiol.* **5**, 97. (Journal IF: 3.941, citations: 3)

Matos PM, Andreu D, Santos NC, Gutiérrez-Gallego R (2014) Structural requirements of glycosaminoglycans for their interaction with HIV1 envelope glycoprotein gp120, *Arch. Virol.* **159**, 555-560. (Journal IF: 2.282, citations: 1)

Vigant F, Hollmann A, Lee J, Santos NC, Jung ME, Lee B (2014) The rigid amphipathic fusion inhibitor dUY11 acts through photosensitization of viruses, *J. Virol.*, **88**, 1849-1853. (Journal IF: 4.648, citations: 2)

Bouchet AM, Iannucci NB, Pastrian MB, Cascone O, Santos NC, Disalvo EA, Hollmann A (2014) Biological activity of antibacterial peptides matches synergism between electrostatic and non-electrostatic forces, *Colloids Surf. B Biointerfaces*, **114**, 363-371. (Journal IF: 4.287, citations: 2).

Freire JM, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MARB. (2014) Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein: design and mechanism of action, *FEBS J.*, **281**, 191-215. (Journal IF: 3.986, citations: 2).

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 lowdensity lipoproteins, *Nanomedicine: NBM*, **10**, 247-255. (Journal IF: 5.978, citations: 2)

### Invited lectures and seminars

Carvalho, F.A., Faustino, A.F., Martins, I.C., Carneiro, F.A., Assunção-Miranda, I., Mohana-Borges, R., Castanho, M., Almeida, F., Da Poian, A.T., Santos, N.C. Dengue virus capsid protein binding to lipid droplets and lipoproteins. A new drug target revealed by AFM-based force spectroscopy. XVIII Congress of the Portuguese Biochemical Society (SPB). Coimbra, Portugal, December 17-20, 2014.

Santos, N.C. Novas estratégias antivirais para HIV e vírus da dengue. Universidade Federal de Mato Grosso do Sul, Campo Grande, Brazil, September 26, 2014.

Santos, N.C. Novas estratégias antivirais para HIV e vírus da dengue. Universidade Católica Dom Bosco, Campo Grande, Brazil, September 26, 2014.

Santos, N.C. Novas estratégias antivirais para HIV e vírus da dengue. Instituto de Biologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, June 25, 2014.

Santos, N.C. New antiviral strategies against HIV and dengue virus. Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, June 18, 2014.

Santos, N.C. Atomic force microscopy and AFM-based force spectroscopy on the study of peptides against dengue virus and bacterial infections. 14th Naples Workshop on Bioactive Peptides, Naples, Italy, June 12-14, 2014.

### Communications in International Conferences

Guedes, A.F., Carvalho, F.A., Santos, N.C. Fibrinogen-dependent cell-cell adhesion of erythrocytes assessment by AFM-based force spectroscopy. 6th AFM BioMed Conference International Meeting on AFM in Life Sciences and Medicine. San Diego, USA, December 13-17, 2014. (Oral presentation)

Guedes, A.F., Carvalho, F.A., Sargento, L., Lousada, N., Moreira, C., Nogueira J.B., Santos, N.C. Fibrinogen-erythrocyte binding as biomarker of increased cardiovascular risk. An atomic force microscopy study. 6th AFM BioMed Conference International Meeting on AFM in Life Sciences and Medicine. San Diego, USA, December 13-17, 2014. (Oral presentation)

Hollmann, A., Augusto, M.T., Gregório, S., Matos, P.M., Porotto, M., Pessi, A., Castanho, M.A.R.B., Santos, N.C. Membrane role in the rational design of HIV fusion inhibitors. SAB2014 XLIII Reunión de la Sociedad Argentina de Biofísica. Sierra de la Ventana, Argentina, December 35, 2014. (Oral presentation)

Monteiro, J., Ribeiro, A.S., Carvalho, F.A., Guedes, A.F., Santos, N.C., Paredes, J. Bioimaging P-cadherin represses cell-cell adhesion mediated by E-cadherin in breast cancer cells: an AFM analysis. 2014 – 3rd International Symposium in Applied Bioimaging – Capturing Life in a Pixel. Oporto, Portugal, October 15-17, 2014. (Oral presentation)

Guedes, A.F., Carvalho, F.A., Lousada, N., Sargento, L., Santos, N.C. High fibrinogen concentrations promote erythrocyte-erythrocyte adhesion through fibrinogen-erythrocyte binding. An atomic force microscopy study. Bioimaging 2014 – 3rd International Symposium in Applied Bioimaging – Capturing Life in a Pixel. Oporto, Portugal, October 15-17, 2014. (Oral presentation)

Gomes, B., Hollmann, A., Santos, N.C. Characterization of HIV1 inhibition by 25-hydroxycholesterol at the membrane level. EBSA Biophysics Course on Membranes and Lipid-Protein Interactions, La Grand-Motte, France, September 8-12, 2014. (Oral presentation)

Felício, M.R., Silva, P.M., de Medeiros, L.N., Kurtenbach, E., Santos, N.C., Gonçalves, S. Glucosylceramides as a target for Psd1 antimicrobial peptide interaction with fungal membrane. EBSA Biophysics Course on Membranes and Lipid-Protein Interactions, La Grand-Motte, France, September 8-12, 2014. (Oral presentation)

Augusto, M.T., Hollmann, A., Castanho, M.A.R.B., Porotto, M., Pessi, A., Santos, N.C. Higher exposure of the pocket binding domain of C34 HIV fusion inhibitor derivatives leads to enhanced efficacy. EBSA Biophysics Course on Membranes and Lipid-Protein Interactions, La Grand-Motte, France, September 8-12, 2014. (Oral presentation)

Guedes, A.F., Carvalho, F.A., Lousada, N., Sargento, L., Santos, N.C. Fibrinogen-erythrocyte interactions and hemorheological parameters: association with cardiovascular risk on heart failure patients. 33rd International Fibrinogen Workshop, Marseille, France, July 9-11, 2014. (Oral presentation)

Carvalho, F.A., Guedes, A.F., Duval, C., Swithenbank, L., Ariëns, R.A.S., Santos, N.C. Different mutations on fibrinogen influence the binding to its receptor on erythrocytes. 33rd International Fibrinogen Workshop, Marseille, France, July 9-11, 2014. (Oral presentation)

Augusto, M.T., Hollmann, A., Castanho, M.A.R.B., Porotto, M., Pessi, A., Santos, N.C. Higher exposure of the pocket binding domain of C34 HIV fusion inhibitor derivatives leads to enhanced efficacy. EPI 2014 – XIV Iberian Peptide Meeting, Bilbao, Spain, February 56, 2014. (Oral presentation)

Grancieri, V.S.A., Felício, M.R., Gonçalves, S., Santos, N.C., Kurtenbach, E. The Psd2 defensin interacts with cardiolipin, an anionic lipid present in bacteria and mitochondria membranes. VII Latin American Postgraduate Program of Biophysics (POSLATAM) Course 2014, Caxambú, Brazil, August 26-27, 2014. (Poster presentation)

Guedes, A.F., Carvalho, F.A., Lousada, N., Sargento, L., Santos, N.C. Atomic force microscopy-

based force spectroscopy study of fibrinogen-erythrocyte interactions: association with cardiovascular risk on heart failure patients. European Summit for Clinical Nanomedicine and Targeted Medicine (CLINAM), Basel, Switzerland, June 23-25, 2014. (Poster presentation)

Hollmann, A., Augusto, M.T., Gonçalves, S., Vigant, F., Castanho, M.A.R.B., Lee, B., Santos, N.C. New broad-spectrum viral fusion inhibitors act by deleterious effect on the viral membrane through the production singlet oxygen molecules. Biophysical Society's 58th Annual Meeting, San Francisco, USA, February 15-19, 2014. Abstract published in (2014) *Biophys. J.*, 106, 708a. (Poster presentation)

Faustino, A.F., Carvalho, F. A., Martins, I.C, Castanho, M.A.R.B., Mohana-Borges, R., Almeida, F.C.L., Da Poian, A.T., Santos, N.C.. Dengue virus capsid protein interacts specifically with very low-density lipoproteins. Biophysical Society's 58th Annual Meeting, San Francisco, USA, February 15-19, 2014. Abstract published in (2014) *Biophys. J.*, 106, 388a. (Poster presentation)

Castanho, M.A., Freire, J., Veiga, A.S., Conceição, T., Kowalczyk, W., Borges, R., Andreu, D., Santos, N., Da Poian, A. Dengue virus capsid protein delivers nucleic acids intracellularly. Biophysical Society's 58th Annual Meeting, San Francisco, USA, February 15-19, 2014. Abstract published in (2014) *Biophys. J.*, 106, 296a. (Poster presentation)

Gomes, I., Cunha, C.S., Pereira, E., Santos, N.C., Taylor, D.W., Mota, M.M., Prudêncio, M., Franco, R. Development of a rapid diagnostic test for malaria antigens detection using gold nanoparticles antibody conjugates. Nanoscience and Nanotechnology International Conference – nanoPortugal 2014, Oporto, Portugal, February 12-14, 2014. (Poster presentation)

Gomes I., Cunha C.S., Pereira E., Santos N.C., Taylor D.W., Mota M.M., Prudêncio M., Franco R.. Gold nanoparticles based fluorescence immunoassay for malaria antigens detection. 1st International Symposium on Nanoparticles/Nanomaterials and Applications, Monte da Caparica, Portugal, January 20-22, 2014. (Poster presentation)

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

Vasconcelos, M., Artilheiro, V., Martins, A., Faustino, A.F., Santos, N.C., Martins, I.C. Improving dengue virus inhibitor peptide pep14-23 by understanding the Flavivirus capsid protein N-terminus function. iMed Conference 6.0, Lisbon, Portugal, October 10-12, 2014. (Oral presentation)

Gregório, S., Hollmann, A., Augusto, M.T., Porotto, M., Santos, N.C. Improvement of viral fusion inhibitors efficacy by conjugation with membrane anchoring lipids. iMed Conference 6.0, Lisbon, Portugal, October 10-12, 2014. (Poster presentation)

Martins, A., Faustino, A.F., Carvalho, F.A., Martins, I.C., Santos, N.C. West-Nile virus inhibition by targeting its capsid protein. iMed Conference 6.0, Lisbon, Portugal, October 10-12, 2014. (Poster presentation)

Carvalho, F.A., Guedes, A.F., Lousada, N., Sargento, L., Santos, N.C. Erythrocyte deformability and blood viscosity changes in systolic heart failure patients. XXXV Congresso Português de Cardiologia, Albufeira, Portugal, April 27-29, 2014. (Poster presentation)

### **Organisation of Conferences**

Carvalho FA, Hollmann A and Martins IC co-organized and lectured of the networking event “Protein-Ligand Interactions”, Lisbon Academic Medical Center PhD program, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal. Supported partially by the Biophysical Society (BPS), USA. Lisbon. September 15-18, 2014.

### **Internationalisation**

Collaborative publications and/or funded projects with groups from the University of California at Los Angeles (USA), Mount Sinai Medical Center (New York, USA), Cornell University (New York, USA), Federal University of Rio de Janeiro (Brazil), Pompeu Fabra University (Barcelona, Spain), Federal University of Ceará (Fortaleza, Brazil), University of Leeds (UK), Emory University (Atlanta, USA), Catholic University of Brasília (Brazil), Oswaldo Cruz Foundation (Rio de Janeiro, Brazil), Agency for Science, Technology and Research (Singapore), University of Santiago del Estero (Argentina), University of Quilmes (Argentina), and PeptiPharma (Rome, Italy).

Nuno C. Santos coordinates a Marie Curie International Research Staff Exchange Scheme (IRSES) Project, funded by the European Commission through the 7th Framework Program.

Nuno C. Santos received and oriented one PhD student (Virginia Amaral) from the Federal University of Rio de Janeiro (Brazil).

### **Prizes, honours and awards**

Honor Prize Subscription to the American Association for the Advancement of Science (AAAS) awarded by the scientific journal "Science" to M. Vasconcelos (Medical Master Student) on the 6th iMed Conference, October 10-12, 2014, Lisboa, Portugal.

Young Investigator Travel Award to A.F. Guedes by the International Fibrinogen Research Society, July 10, 2014.

YSP Fellowship Award to A.F. Guedes to participate on the SBBq & IUBMB meeting, 2015.

Biophysical Society 59th annual meeting Travel Award to M.T. Augusto to further support the participation at the meeting, 2015.

### **Patents/prototypes**

Faustino AF, Martins IC, Almeida FCL, Da Poian AT, Santos NC (2014) Understanding dengue virus capsid protein disordered Nterminus and pep14-23based inhibition. Instituto Nacional de Propriedade Industrial (INPI), provisional patent application nr. 108040.

### **Advanced teaching**

Santos, N.C. lecturer on Curso de Nanobiotecnologia, Programa de Pós-Graduação (MSc and PhD) em Biotecnologia, Universidade Católica Don Bosco, Campo Grande, Brzsil. November 17-21, 2014.

Carvalho, F.A. lecturer on the Workshop Nano2014 - Shaping the Future, on "AFM measurement of cell-cell interactions on cardiovascular and cancer research". Academia das Ciências, Lisbon. October 10, 2014.

Carvalho, F.A. lecturer and practical classes on the academic teaching for Lisbon Academic Medical Center (CAML) PhD Program nanocourse on "Force Spectroscopy. Biological and Biomedical Applications". Faculdade de Medicina da Universidade de Lisboa, Lisbon. September 15-18, 2014.

Martins, I.C. lecturer and practical classes on the academic teaching for Lisbon Academic Medical Center (CAML) PhD Program nanocourse on "Studying proteins/peptides structure via Fourier tranformed infra-red (FTIR) and circular dichroism (CD) spectroscopy". Faculdade de Medicina da Universidade de Lisboa, Lisbon. September 15-18, 2014

Hollmann, A. practical course on the academic teaching for Lisbon Academic Medical Center (CAML) PhD Program nanocourse “Protein ligand interactions”. Faculdade de Medicina da Universidade de Lisboa, Lisbon. September 15-18, 2014

Santos, N.C. lecturer on Programa Doutoral em Bioengenharia MIT Portugal, Lisboa, Portugal – Using the force at the nanoscale: from cardiovascular risk to dengue. May 14, 2014.

Santos, N.C. lecturer on Programa Doutoral do Instituto de Higiene e Medicina Tropical, Lisboa, Portugal – Estudos biofísicos para seleção de novos alvos terapêuticos para o vírus da dengue May 13, 2014.

Santos, N.C. lecturer on Mestrados em Biologia Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Portugal – Force Spectroscopy. April 28, 2014.

Carvalho, F.A. lecturer on the academic teaching for REQUIMTE BIO-AFM Hands-on Workshop “Force Spectroscopy. Biological and Biomedical Applications.” Faculdade Ciências, Universidade do Porto, Porto. April 14-17, 2014.

Santos, N.C. lecturer on Mestrados em Bioquímica e Biotecnologia, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal – AFM de força. Sistemas coloidais e sua caracterização por técnicas de dispersão de luz. April 4, 2014.

Santos, N.C. lecturer on Programa de Pós-Graduação Ciência para o Desenvolvimento (Programa Doutoral para alunos de Angola, Cabo Verde, Guiné-Bissau, Moçambique, São Tomé e Príncipe, e Timor Lorosae), Praia, Cabo Verde – Várias apresentações e outras actividades ao longo de uma semana de aulas. February 10-14, 2014.

Martins, I.C. lecturer of the IMM doctoral program funded by FCT “Lisbon Biomedical and Clinical Research PhD Program (LisbonBioMed)”. January 6, 2014.

### **Science and society**

Santos, N.C. Novas estratégias contra infeções virais e bacterianas. Semana da Ciência e Tecnologia 2014, Escola Secundária Ferreira Dias, Agualva-Cacém, Portugal, December 1, 2014.

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 the Unit’s Research work.

#### **PhD thesis completed**

Margarida Rodrigues 03/04/2014 Molecular Determinants of the Cellular Internalization of Crotonamine-Derived Peptides Faculdade de Medicina da Universidade de Lisboa Nuno C. Santos

#### **Msc thesis completed**

Ana de Souto Martins 30/10/2014 Interaction of West-Nile virus capsid protein with lipid systems Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa Nuno C. Santos Ivo C. Martins

Susana dos Reis Gregório 10/11/2014 Improvement of viral fusion inhibitor enfuvirtide efficacy by conjugation with membrane anchoring lipids Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa Nuno C. Santos Axel Hollmann



## Paulo Filipe Lab

### Major Interests / Objectives

We devote our efforts to the search of clinically useful markers and drug targets in common skin diseases afflicting humans such as psoriasis and superficial mycosis. Psoriasis is a common (~2% in western populations), chronic immune-mediated inflammatory disease associated with lowered quality of life and relevant co-morbidities, namely an increased risk of cardiovascular disease and mortality. We aim at elucidating the earliest molecular signatures in the skin of psoriatic patients for a better selection of biologic therapeutic agents and prevention of relapse. We are particularly interested in elucidating the role of cells such as keratinocytes, neutrophils, cross-talk between Th9 and Th17 cells in the initiation and maintenance of the inflammatory process associated with psoriasis.

### Head of Unit

Paulo Manuel Leal Filipe, MD/PhD, Assistant Professor

### Research Team

João António Augusto Ferreira	MD/PhD	Investigator, Ass. Professors
João Borges da Costa	PhD	Investigator, Assistant Professor
João Nuno Maia Rodrigues Silva	MD/PhD	Investigator, Assistant Professor
Luis Mguel dos Santos Reis Soares de Almeida	PhD	Senior Investigator
Maria Clara Gomes da Fonseca Pedro Bicho	MD/PhD	Investigator

### Keywords / Research Areas

Human Th9 and Tc9 cells, Human Th17 and Tc17 cells, Keratinocyte, Neutrophil, Psoriasis, Pityriasis versicolor

### Major scientific achievements

1. We show that, in both lesional and non-lesional skin, the epidermal profiles of Fe contents showed a peak at the basal layer and that Fe concentration along the basal layer was not uniformly distributed. Typically, Fe levels were significantly higher in epidermal ridges relative to regions above dermal papillae. Lesional skin displayed excess Fe over extended regions above basal layer.
2. Regarding ferritin in psoriatic skin, we verified that this iron storing protein is mainly distributed in epidermal basal layer of both perilesional and lesional skin
3. We began the identification and characterization of *Malassezia* species from subjects with Malassezia dermatitis by cultures and PCR and performed the in vitro sensitivity tests to imidazole antifungal agents and with a polypeptide extracted from the *Lupinus albus* plant, as new possible topical antifungal agent (studies conducted in collaboration with Laboratório de Micologia of FM/UL, Converde, SA and Instituto Superior Agronomia

### Selected Publications

Morlière P, Hug GL, Patterson LK, Mazière JC, Ausseil J, Dupas JL, Ducroix JP, Santus R, Filipe P. *Biochim Biophys Acta*. 2014 Oct; 1840 (10): 3190-7. doi: 10.1016/j.bbagen.2014.07.002. Epub 2014 Jul 10. (2014) Chemistry of free radicals produced by oxidation of endogenous  $\alpha$ -aminoketones. A study of 5 aminolevulinic acid and  $\alpha$ -aminoacetone by fast kinetics spectroscopy.. *Biochim Biophys Acta*, **1840** 2014 Oct; (10): 3190-7. doi: 10.1016/j.bbagen.2014.07.002. Epub 2014 Jul 10. 1840, 3190-7. (Journal IF: 4.554, Citations: 1)

Pinheiro T, Silva R, Fleming R, Gonçalves A, Barreiros MA, Silva JN, Morlière P, Santus R, Filipe P. *Acta Derm Venereol*. 2014 Jan; 94 (1): 14-9. doi: 10.2340/00015555-1601. (2014) Distribution and quantitation of skin iron in primary haemochromatosis: correlation with total body iron stores in patients undergoing phlebotomy. *Acta Derm Venereol*. 2014 Jan; **94** (1): 14-9. doi: 10.2340/00015555-1601. 94, 14-9. (Journal IF: 4.244, Citations: 3)

Carvalho S, Vítor AC, Sridhara SC, Martins FB, Raposo AC, Desterro JMP, Ferreira J, de Almeida SF. *ELife*, 2014; 3:e02482. doi: 10.7554/eLife.02482 (2014) SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint. . *ELife*, 2014; **3**, e02482. doi: 10.7554/eLife.02482 (Journal IF: 8.519, Citations: 4)

Figueiredo N, Chora A, Raquel H, Pejanovic N, Pereira P, Hartleben B, Neves-Costa A, Moita C, Pedroso D, Pinto A, Marques S, Faridi H, Costa P, Gozzelino R, Zhao JL, Soares MP, Gama Carvalho M, Martinez J, Zhang Q, Döring G, Grompe M, Simas JP, Huber TB, Baltimore D, Gupta G, Green DR, Ferreira J, Moita LF. *Immunity* 2013; 39: 874-84. PMID: 24184056 (2013) Anthracyclines induce DNA damage response-mediated protection against severe sepsis. *Immunity* 2013; **39**: 874-84. PMID: 24184056 39, 874-84. (Journal IF: 19.748, Citations: 15)

Silva JN, Galmiche A, Tomé JP, Boullier A, Neves MG, Silva EM, Capiod JC, Cavaleiro JA, Santus R, Mazière JC, Filipe P, Morlière P. *Biochem Pharmacol.* 2010 Nov 1; 80 (9): 1373-85. doi: 10.1016/j.bcp.2010.07.033. Epub 2010 Aug 4. (2010) Chain-dependent photocytotoxicity of tricationic porphyrin conjugates and related mechanisms of cell death in proliferating human skin keratinocytes.. *Biochem Pharmacol.* 2010 Nov 1; 80 (9): 1373-85. doi: 10.1016/j.bcp.2010.07.033. Epub 2010 Aug 4. 80, 1373-85. (Journal IF: 4.65, Citations: 15)

#### Publications in peer review Journals

Transition to ustekinumab in patients with moderate-to-severe psoriasis and inadequate response to methotrexate: a randomized clinical trial (TRANSIT). Paul C, Puig L, Kragballe K, Luger T, Lambert J, Chimenti S, Girolomoni G, Nicolas JF, Rizova E, Lavie F, Mistry S, Bergmans P, Barker J, Reich K; TRANSIT Investigators. *Br J Dermatol.* 2014 Feb; **170** (2): 425-34. doi: 10.1111/bjd.12646. (Journal IF:4.11 Citations: 1)

One-year safety and efficacy of ustekinumab and results of dose adjustment after switching from inadequate methotrexate treatment: the TRANSIT randomized trial in moderate-to-severe plaque psoriasis. Reich K, Puig L, Paul C, Kragballe K, Luger T, Lambert J, Chimenti S, Girolomoni G, Nicolas JF, Rizova E, Brunori M, Mistry S, Bergmans P, Barker J; *TRANSIT Investigators.* *Br J Dermatol.* 2014 Feb; **170** (2): 435-44. doi: 10.1111/bjd.12643. (Journal IF:4.11 Citations: 2)

Bacillary Angiomatosis in a HIV-positive Patient with Poor Adherence to Antiretroviral Therapy. Lopes L, Borges-Costa J, Janeiro N, Neves D, Soares Almeida L, Filipe P. *Acta Dermatovenerol Croat.* 2014 Dec; **22** (4): 294-7. (Journal IF: 0.58 Citations: 0)

Nicolau syndrome after benzathine penicillin treated with hyperbaric oxygen therapy. Lopes L, Pires S, Alves A, Guerreiro F, Filipe P. *Int J Dermatol.* 2014 Dec 29. doi: 10.1111/ijd.12751. [Epub ahead of print] (Journal IF: 1.27 Citations: 0)

Subungual ectopic hair studied by scanning electron microscopy. de Vasconcelos P, Goyri-O'Neill J, Soares-Almeida L, Ferreira J, Filipe P. *J Eur Acad Dermatol Venereol.* 2014 Nov 20. doi: 10.1111/jdv.12855. [Epub ahead of print] (Journal IF: 2.69 Citations: 0)

Appearance of de novo dysplastic spitzoid compound naevus in an adalimumab-treated psoriatic patient: case report and review of the possible causal relationship with TNF- $\alpha$  blockers. Sousa M, Freitas JP, Antunes J, Soares-de-Almeida L, Filipe PL. *Australas J Dermatol.* 2014 May; **55** (2): 156-7. doi: 10.1111/ajd.12170. (Journal IF: 0.98 Citations: 0)

Desferrioxamine treatment of porphyria cutanea tarda in a patient with HIV and chronic renal failure. Vasconcelos P, Luz-Rodrigues H, Santos C, Filipe P. *Dermatol Ther.* 2014 Jan-Feb; **27** (1): 16-8. doi: 10.1111/dth.12024. Epub 2013 Jun 6.(Journal IF: 1.48 Citations: 0)

Sweet syndrome-like neutrophilic infiltrate as initial presentation of acute myelogenous leukemia. Travassos AR, Soares-de-Almeida L, Kutzner H, Guerra L, Alves do Carmo J, Filipe P, Marques MS. *Am J Dermatopathol.* 2014 Oct; **36** (10): e167-70. doi: 10.1097/DAD.0b013e3182897b0a. (Journal IF: 1.42 Citations: 0)

#### **Other publications National**

Impact of biosimilars in psoriasis treatment. Torres T, Filipe P, Selores M. *Acta Med Port.* 2013 Nov Dec; **26** (6): 646-8. Epub 2013 Dec 20. (Journal IF: 0.28 Citations: 1)

#### **Invited lectures and seminars**

Dermatological Disorders and ocular Disease  
International Conference on Clinical and Experimental Ophthalmology  
July 14-16, 2014, Baltimore, USA

#### **Organisation of Conferences**

Workshop on the International Conference on Clinical and Experimental Ophthalmology  
"repercussions in Eye Microcirculation of Patients with Systemic Vascular Disease"  
July 14-16, 2014, Baltimore, USA

#### **Internationalisation**

Vollaboration with the University of Amiens - Biochemistry Department: project entitled "mechanisms of vemurafenib phototoxicity".

Collaboration with University Paris VII - Laboratoire de Cytogénétique: project entitled "Clastogenicity of serum ultrafiltrates from psoriatic patients submitted to phototherapies"

### **Industry contract research**

Clastogenic Plasma Factors in psoriatic patients submitted to narrow-band UVB phototherapies Period: 2013-2016 Budget : 15000 Euros Financial support: Associação para o Desenvolvimento da Dermatologia e Université Paris VI

Influence of Etanercept® in the Serum Proteome of Psoriatic Patients. A SELDI Approach format Period: 2012-2016 Budget : 37000 Euros Financial Support: Pfizer Inc.

### **Government/Organisation contract research**

P. Filipe: Coordinator of the Sub-Committee for Technical Advisory on Dressings and Similar Devices of the Hospital Center Lisbon North, 2014- Member of the Commission for Drug Evaluation of INFARMED since July 2010-present President of the eDermatology Portal Committee of Fondation René Touraine Member of the Scientific Board of Fondation René Touraine

João Ferreira: Member of the Pedagogical Council, Fac. of Medicine, Lisbon (2012-present) Member of the Scientific Council, Fac. of Medicine, Lisbon (2012-present) Consultant, Gulbenkian Program for Advanced Medical Education/PFMA (2013-present) Associate professor, Molecular Biology of the Cell, Faculty of Medicine, Lisbon (2008-present) Coordinator of GAPIC (a Faculty department for promotion of research by under-graduate students (2011-present)

### **Advanced teaching**

Internships in our Lab - Specialiaty in Dermatology- Ana Teixeira (Dermatology resident from Serviço de Dermatologia, Centro Hospitalar Lisboa Norte, Hospital Santa Maria)

### **Science and society**

Screening of skin cancer in the Lisbon area in collaboration with “Programa Saúde mais Próxima da Santa Casa da Misericórdia de Lisboa” 2013 and 2014

Screening of superficial mycosis in university students from the Lisbon area in collaboration with “Programa Saúde mais Próxima da Santa Casa da Misericórdia de Lisboa” 2014-ongoing

## Pedro Simas Lab

### Major Interests / Objectives

We utilize murine 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 Unit

João Pedro Monteiro e Louro Machado de Simas, PhD

### Research Team

Cristina Sofia Godinho da Silva	No degree	Investigator, (left May)
Diana Marisa Pinto Freire Fontinha	Master	PhD Student
Inês Marques Basto	Graduate	MSc Student
Maria Leonor dos Santos Diniz Orge	PhD	Investigator
Marta Pires de Miranda	PhD	Post doctoral Investigator
Sofia Isabel Arriaga Mimoso Cerqueira	Master	PhD Student

### Keywords / Research Areas

herpes virus, B lymphocytes, E3 ubiquitin ligase, Kaposi sarcoma herpesvirus (KSHV), B cell and Lymphomas, MuHV-4 and animal model of infection

### Major scientific achievements

(1) Persistent infections are subject to constant surveillance by CD8+ cytotoxic T cells (CTL). Their control should therefore depend on MHC class I-restricted epitope presentation. Many epitopes are described for  $\gamma$ -herpesviruses and form a basis for prospective immunotherapies and vaccines. However the quantitative requirements of in vivo immune control for epitope presentation and recognition remain poorly defined. Using MuHV-4 we could define critical engagement thresholds for the in vivo immune control of virus-driven B cell proliferation.

(2) MuHV-4 promotes polyclonal B cell activation and establishes latency in memory B cells via unclear mechanisms. We aimed at exploring whether B cell receptor specificity plays a role in B cell susceptibility to viral latency. Our data support a model in which the establishment of latency in B cells by  $\gamma$ -herpesviruses is not stochastic in terms of BCR specificity and is tightly linked to the formation of GCs.

### Selected Publications

Jérémie Decalf, Cristina Godinho-Silva, Diana Fontinha, Sofia Marques, J. Pedro Simas (2014) Establishment of Murine Gammaherpesvirus Latency in B Cells Is Not a Stochastic Event. PLoS Pathogens 10(7), e1004269. (Journal IF: 8.06, Citations: 0)

Godinho-Silva, C., Marques, S., Fontinho, D., Stevenson, P.G., Simas, J.P (2014) Defining Immune Engagement Thresholds for in vivo Control of virus-driven Lymphoproliferation. PLoS Pathogens 10(6):, e1004220. (Journal IF: 8.06, Citations: 1)

Pires de Miranda M, Lopes FB, McVey CE, Bustelo XR, Simas JP. (2013) Role of Src-homology domain binding in signaling complexes assembled by the murid gammaherpesvirus M2 protein. Journal of Biological Chemistry 288, 3858. (Journal IF: 4.773, Citations: 5)

Correia, B., Cerqueira, S.A., Beauchemin, C., Pires de Miranda, M., Li S., Ponnusamy, R., Rodrigues, L., Schneider, T.R., Carrondo, M.A., Kaye, K.M., Simas, J.P., McVey C.E. (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. (Journal IF: 8.06, Citations: 2)

Lénia Rodrigues, Nikita Popov, Kenneth M. Kaye and J. Pedro Simas (2013) Stabilization of Myc Through Heterotypic Poly-Ubiquitination by mLANA is Critical for  $\gamma$ -Herpesvirus Lymphoproliferation. PLoS Pathogens 9(8), e1003554. (Journal IF: 8.02, Citations: 2)

#### **Ongoing Research Projects**

2011/2014 Title: Pathogenesis of Kaposi's sarcoma herpesvirus LANA. Coordinator: João Pedro Monteiro e Louro Machado de Simas. Agency: Fundação Ciência e Tecnologia. Reference: HMSP-ICT/0021/2010. Amount: 294,892€.

#### **Internationalisation**

We have a formal collaboration with Kenneth Kaye at Harvard Medical School and Hidde Ploegh at MIT.

#### **PhD thesis completed**

Cristina Godinho-Silva 24/09/2014 Immune engagement thresholds for CD8+ T cell control of gamma-herpesvirus-driven B cell proliferation Faculdade de Medicina/Universidade de Lisboa Pedro Simas



## Sérgio Almeida Lab

### 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 molecular aspects of the different stages of the transcription cycle, focusing on pre-mRNA processing and chromatin modification events; 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 Unit

Sérgio Alexandre Fernandes de Almeida, PhD, Assistant Professor

### Research Team

Alexandra Coitos Vítor	Master	PhD Student
Ioana Posa	Graduate	MSc Student
Joana Patrícia Moreira Tavares	Graduate	MSc Student
Luís Carlos Pereira Simões	Graduate	MSc Student, (started September)
Mafalda Alexandra Ramos de Matos	Master	PhD Student, (started March)
S R CHAITANYA. SRIDHARA	Master	PhD Student
Silvia Camoëira Carvalho	Master	Technician

### Keywords / Research Areas

Epigenetics, Chromatin Biology, Cancer Biology, Gene expression, DNA repair

### Major scientific achievements

In 2014 the members of our lab have:

- . published three original research papers in international peer reviewed journals
- . received a FCT Investigator award (Ana Grosso)
- . received a FCT individual PhD fellowship (Mafalda Matos)
- . presented our work on nine national and international meetings
- . participated in advanced teaching activities on five PhD and three MSc programs
- . supervised two MSc thesis

### Selected Publications

Carvalho S, Vitor A, Sridhara SC, Martins FB, Raposo AC, Desterro JM, Ferreira J, de Almeida SF (2014) SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint. *eLife* **3**, <http://elifesciences.org/content/3/e02482>. (Journal IF: 8.5, Citations: 3)

Carvalho S, Raposo AC, Martins FB, Grosso AR, Sridhara SC, Rino J, Carmo-Fonseca M, de Almeida SF (2013) Histone methyltransferase SETD2 coordinates FACT recruitment with nucleosome dynamics during transcription. *Nucleic Acids Research* **41**, 2881. <http://nar.oxfordjournals.org/content/early/2013/01/15/nar.gks1472.full-text-lowres.pdf>. (Journal IF: 8.8, Citations: 17)

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* **18**,977.[http://www.genomicregulationlab.com/Genomic\\_Regulation\\_Lab/Publications\\_files/deAlmeidaSF%20NSMB%202011.pdf](http://www.genomicregulationlab.com/Genomic_Regulation_Lab/Publications_files/deAlmeidaSF%20NSMB%202011.pdf). (Journal IF: 12.7, Citations: 71)

de Almeida SF, Garcia-Sacristan S, Custodio N and Carmo-Fonseca M (2010) A link between nuclear RNA surveillance, the human exosome and RNA polymerase II transcriptional termination. *Nucleic Acids Research* **38**, 8015. (Journal IF: 8.8, Citations: 30)

### Ongoing Research Projects

2013/2015 Title: SETD2 mediates a novel tumor suppressor mechanism that is misregulated in clear cell renal carcinom. Coordinator: Sérgio Alexandre Fernandes de Almeida. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/BIM-ONC/0384/2012. Amount: 184,516€.

### Other Projects

2012/2015 RNA\_REGULOMICS: Role of non-coding RNA in human health and disease. Coordinator: EU. FP7–PEOPLE–2012–IRSES, MARIE CURIE ACTIONS.

2012/2015 RNPnet - Marie Curie Initial Training Network. Coordinator: Coordinator: Institution: EU MARIE CURIE ACTIONS .

### Publications in peer review Journals

da Glória VG, Martins de Araújo M, Mafalda Santos A, Leal R, de Almeida SF, Carmo AM, Moreira A. (2014) T cell activation regulates CD6 alternative splicing by transcription dynamics and SRSF1. *Journal of Immunology* , **193**, 391. (Journal IF: 6.2, Citations: 1)

Carvalho S, Vitor A, Sridhara SC, Martins FB, Raposo AC, Desterro JM, Ferreira J, de Almeida SF (2014) SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint. *eLife* **3**, <http://elifesciences.org/content/3/e02482>. (Journal IF: 8.5, Citations: 3)

de Almeida SF & Carmo-Fonseca M (2014) Reciprocal regulatory links between cotranscriptional splicing and chromatin. *Seminars in Cell & Development Biology* **32**, <http://www.sciencedirect.com/science/article/pii/S108495211400038X>. (Journal IF: 6.2, Citations: 1)

### Invited lectures and seminars

. de Almeida SF, “How to preserve the integrity of the genetic information?” Symposium “From gene to genius”. Instituto de Biologia Molecular e Celular, Porto, Nov 17, 2014.

. de Almeida SF, “Chromatin dynamics & Transcriptional regulation” Instituto Gulbenkian de Ciência, Oeiras, Portugal, Feb 19, 2014.

. de Almeida SF, “The role of chromatin in the regulation of genome integrity” BioFig seminar, Lisboa, February 19, 2014.

. de Almeida SF, “The chromatin landscape of a cancer cell” JORTEC conferences, Universidade Nova de Lisboa, Portugal, February 19, 2014.

### **Communications in International Conferences**

de Almeida SF & Grosso AR, "Widespread transcription read-through in SETD2 mutant renal carcinoma" EpiGeneSys Annual Meeting, Barcelona, Spain, 26-28 November 2014.(Poster presentation)

de Almeida SF "SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint" Workshop RNA meets DNA, Baeza, Spain, 2-5 November 2014. (Poster presentation)

Vitor A, "The role of SETD2 on DNA damage repair and checkpoint activation". Copenhagen Bioscience Conference: PTMs in Cell Signaling. The Novo Nordisk Foundation, Denmark. 14-18 Sept, 2014. (Poster presentation)

Sridhara SC, "The novel role of Serine-Arginine Protein Kinases (SRPKs) in splicing." RNP: Structure meets function symposium, Biology Centre, Czech Academy of Sciences in ?eské Bud?jovice (Budweis), Czech Republic. 4-5 Sept 2014. (Oral presentation)

Sridhara SC, "Analysis of SRPK1/2 genome wide distribution using CHIP-seq" Centre for Genomic Regulation, Barcelona, Spain. 21-25 July, 2014. (Oral presentation)

Sridhara SC, "The role of SR protein kinases as mediators of cancer-related signaling pathways that control alternative splicing". RNPnet 3rd report meeting, La grande Motte, France. 28-29 June, 2014 (Oral presentation)

Grosso AR, "RNA chimeras are widespread in the transcriptome of cells with aberrant chromatin structure", Integrative and Computational Biology Joint symposium, CRG, Barcelona. 26-28 March, 2014 (Poster presentation)

### **Communications in National Conferences**

Vitor A, "Chromatin dynamics in the regulatory network of DNA repair". VIII IMM/CAML PhD students meeting, Instituto de Medicina Molecular, Lisbon. 28th March, 2014.

Matos MR, "Novel Mechanisms of Genomic and Epigenomic stability". VIII IMM/CAML PhD students meeting, Instituto de Medicina Molecular. 28th March, 2014.

### **Internationalisation**

Our unit is an associate member of the European Network of Excellence "EpiGeneSys". This research network gathers some of the most productive and influential European labs working in epigenetics. Our lab participated with two members on the Epigenesys annual meeting that took place in Barcelona last December.

We are also part of RNPnet, a Marie Curie Initial Training network, which includes labs across Europe that work on RNA biogenesis and processing.

During this year, the members of our unit presented their work on several international meetings, visited foreign institutions and established collaborations with groups in Spain (CNAG, Barcelona), France (Paris), Scotland (Wellcome Trust, Edinburgh), Switzerland (ETH, Zurich) and England (Babraham Institute, Cambridge).

### **Prizes, honours and awards**

2014 FCT Investigator Award to Ana Rita Grosso

### **Advanced teaching**

de Almeida SF, (Lecturer). Oncobiology MSc Program (Faculdade de Medicina da Universidade de Lisboa) class of 2014.

de Almeida SF, (Lecturer). Metabolism PhD Program, University of Porto, class of 2014.

de Almeida SF, (Lecturer). BioSys PhD program, Faculty of Sciences, University of Lisbon, class of 2014

de Almeida SF, (Coordinator of the "Epigenetics" classes). Lisbon BioMed PhD Program, University of Lisbon, class of 2014

de Almeida SF, (Lecturer). IBB PhD program, Instituto Gulbenkian de Ciência, class of 2014.

Grosso AR, (Lecturer). 2014 Computational Biology in Biomedicine course for Masters in Bioinformatics and Computational Biology (FCUL)

Grosso AR, (Lecturer). 2014 Bioinformatics course for Master in Oncobiology (FMUL)

Grosso AR, (Lecturer). 2014 Biostatistics seminar for Master in Biostatistics (FCUL)

#### **Msc thesis completed**

Miguel Pereira 03/11/2014 Intragenic Initiation in SETD2 deficient cells Faculdade de Ciências da Universidade de Lisboa Ana Rita Grosso

Tomás Gomes 15/12/2014 Genome-wide profiling of RNA polymerase II and associated cotranscriptional processes using advanced NET-seq data Faculdade de Ciências da Universidade de Lisboa Ana Rita Grosso

## Sérgio Dias Lab

### Major Interests / Objectives

We study the role of blood vessels, and of endothelial cells, in regulating normal organ function and in disease.

In detail, we study cancer (solid and hematologic) as a systemic disease that involves (and requires) blood vessels for its onset and progression.

In addition to the role of blood vessels, we also study the involvement of bone marrow-derived cells and of metabolic systemic signals in cancer onset and progression.

### Head of Unit

Sérgio Jerónimo Rodrigues Dias, PhD

### Research Team

Ana Cláudia Dourado Clemente	Graduate	MSc Student
Ana Luísa Ferro Espadanal Torres Magalhães	PhD	Post doctoral Investigator
Ana Maria Matias de Barros	PhD	Post doctoral Investigator
Filipa Duarte Baptista	Master	Trainee, (started November)
Filipe Manuel Pereira Seguro de Oliveira Paula	Master	Investigator, (started April)
Germana Andreia Taipa Leandro Domingues	Master	PhD Student
Inês Mendes Matias	Graduate	Technician
Inês Sofia Alvarez Martins	Graduate	PhD Student
Joana de Sousa Grácio Fernandes Rodrigues	Graduate	MSc Student, (started September)
Marta Sofia Carvalho Teles de Figueiredo	Master	PhD Student

Marta Zegre Graça Oliveira Costa de Amorim	Graduate	PhD Student, Centro Hospitalar Lisboa Central , Clinical Specialist
Neidy Varela Rodrigues	Master	PhD Student, (started October)
Sandrina Nóbrega Pereira	PhD	Post doctoral Investigator
Vanessa Carina Silva Cesário	Graduate	MSc Student, (started September)

#### Keywords / Research Areas

Angiogenesis, Tumor spread, Metabolism

#### Selected Publications

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. (Journal IF: 4.93, Citations: 4)

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. (Journal IF: 9.3, Citations: 7)

Caiado F, Carvalho T, Silva F, Castro C, Clode N, Dye JF and Dias S. (2011) Fibrin E modulates endothelial progenitors adhesion, differentiation and angiogenic growth factor production and promotes wound healing. *Biomaterials* **32**, (29), 7096-105. (Journal IF: 7.404, Citations: 24)

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. (Journal IF: 9.9, Citations: 55)

Fragoso R, Pereira T, Wu Y, Zhu Z, Cabeçadas J and Dias S. (2006) VEGFR-1 (FLT-1) activation modulates acute lymphoblastic leukemia localization and survival within the bone marrow, determining the onset of extramedullary disease. *Blood* **107**, (4), 1608-16. (Journal IF: 9.9, Citations: 92)



### **Ongoing Research Projects**

2013/2014 Title: Exploiting the molecular basis underlying an aberrant vascular niche in Multiple myeloma. Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-ORG/113617/2009. Amount: 43,804.75€.

2013/2014 Title: Does Cholesterol promote tumor angiogenesis and metastasis formation Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/SAU-ONC/114080/2009. Amount: 44,605.73€.

2013/2014 Title: Bolsa Laço para o Cancro da Mama. Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: Laço Associação de Solidariedade Social. Reference: Laço - Cancro da Mama. Amount: 25,000€.

### **Publications in peer review Journals**

Dos Santos CR, Domingues G, Matias I, Matos J, Fonseca I, de Almeida JM, Dias S. LDL-cholesterol signaling induces breast cancer proliferation and invasion. *Lipids Health Disease*. 13(1):16 (2014) (Journal IF: NA Citation: NA)

Rodrigues Dos Santos C, Fonseca I, Dias S, Mendes de Almeida J. Plasma level of LDL-cholesterol at diagnosis is a predictor factor of breast tumor progression. *BMC Cancer*. 14(1):132 (2014) (Journal IF: 3.319 Citation: 0)

Afonso Â, Pereira JP, Dias S. Biobanco-IMM, Lisbon Academic Medical Centre. *Biopreserv Biobank*. 2014 Dec;12(6):433-4. (Journal IF: 1.578 Citation: 0)

Rodrigues Dos Santos C, Fonseca I, Dias S, Mendes de Almeida J. Plasma level of LDL-cholesterol at diagnosis is a predictor factor of breast tumor progression. *BMC Cancer*. 14(1):132 (2014) (Journal IF: 3.319 Citation: 0)

### **Other publications International**

Caiado F and Dias SJR (2013). Vasculogenese na Angiogénese. *Tratado de Oncologia*. Editora Atheneu (Brasil). Vol 1, Chapter 29. Pgs 395-401.

### **Other publications National**

Domingues G and Dias S (2013). Angiogénese no Melanoma. Melanoma 2013. Editado pelo Intergrupo Português de Melanoma. Pgs 107-113.

### **Invited lectures and seminars**

Dias S. Cancer metabolism... a simplified approach. PhD Program (Invited Lecture). ITQB. 6th February 2014.

Dias S. Metabolic selection of Metastatic Potential. PhD Program (Invited Lecture). CNC (Univ. Coimbra) 15th July 2014.

Dias S. Cancer as a systemic disease. Invited Seminar. ICVS (Minho University). 28th April 2014.

Dias S. Fat Feeds Cancer. MDAnderson Visit to Portugal. Invited Lecture. 21st November 2014.

Dias S. Cancer Metabolism, our simplified approaches. Invited Lecture. Instituto Portugues de Oncologia Francisco Gentil Centro de Coimbra. 14th November 2014.

Dias S. Fat Feeds Cancer or How Lipids promote tumor progression. Invited Lecture. University of Algarve. 12th December 2014.

### **Communications in National Conferences**

Ana Magalhaes and Sérgio Dias. First Congress of the Portuguese Association Against Cancer (ASPIC). Lisboa, 25-26 November 2014. (Poster Presentation)

### **Organisation of Conferences**

Dias S. Scientific Coordinator of the First Congress of the Portuguese Association Against Cancer (ASPIC). Lisboa, 25-26 November 2014.

### **Advanced teaching**

Dias S. Developmental Biology and Cancer. Masters in Oncobiology. IMM, Lisbon, January 22-25, 2014.

Dias S, Barata JT and Bernardes G. Oncobiology. LisbonBiomed PhD Program. IMM, Lisbon. January 2014.

### **Science and society**

Sérgio Dias. Campanha Revista Máxima. "100 Homens sem Preconceitos". Máxima (magazine) campaign. "100 Men without Prejudice". To Raise Public awareness on the discrimination of women. 2014.

### **PhD thesis completed**

Germana Andreia Taipa Domingues 19/12/2014 Specific Features of Endothelial Cells in Primary Tumors Universidade Nova de Lisboa Sérgio Dias

### **Msc thesis completed**

Andreia Cristina Martins Silva 19/02/2014 Contribution of the intracellular cholesterol levels for the expression of VEGF-C and VEGFR-3 in acute myeloid leukemia Universidade do Algarve Sérgio Dias Ana Magalhães

## Sofia Oliveira Lab

### Major Interests / Objectives

Our research focuses on understanding the genetic architecture of complex diseases such as Stroke, Behçet's Disease, Primary Spontaneous Pneumothorax, and Intracranial Aneurysms. Common diseases result from the interaction of environmental and genetic factors, and an in-depth evaluation of their genetic underpinnings will not only unravel complex inheritance patterns but will also enable a better understanding of the environmental risks. We use both traditional and new approaches to identify novel susceptibility genes. We believe that studies with a multifaceted and multidisciplinary framework will have the greatest success in dissecting the complex etiology of common disorders and that they will ultimately lead to the development of novel prevention strategies and targeted therapies.

### Head of Unit

Ana Sofia Simões Domingues de Almeida Oliveira, PhD

### Research Team

Catarina Beatriz Silva Ferreira	Graduate	MSc Student, (left June)
David Miguel Ferreira Francisco	Graduate	MSc Student, (started September)
Inês Girão Meireles de Sousa	PhD	Post doctoral Investigator, (started April)
Madalena Cristina Rocha Martins	PhD	Post doctoral Investigator, (left September)
Patrícia Alexandra Silva Santos	Graduate	MSc Student
Patricia Carla Simões Abrantes	PhD	Post doctoral Investigator
Vânia Patrícia Ferreira Francisco	Master	Technician

### Keywords / Research Areas

Genetics, Genomics, Complex traits

### Major scientific achievements

In 2014, genome-wide association studies (GWAS) in Portuguese led to the identification of:

- 4 variants associated for the first time with intracranial aneurysms and the replication of the known 9p21 locus;
- the association of SLC6A1 and an intergenic region at 8q24.21 with Primary Spontaneous Pneumothorax risk.

Furthermore, we characterized in more detail the association of the MHC locus and of the IL10 gene with Behçet's disease in Iranian.

### Selected Publications

Xavier JM, Shahram F, Sousa I, Davatchi F, Matos M, Abdollahi BS, Sobral J, Nadji A, Oliveira M, Ghaderibarim F, Shafiee NM, Oliveira SA. (2013) FUT2: filling the gap between genes and environment in Behçet's disease?. *Annals of the Rheumatic Diseases*, doi: 10.1136/annrheumdis-2013-204475. (Journal IF: 9.082, Citations: 0) .

Krug T, Gabriel JP, Taipa R, Fonseca BV, Domingues-Montanari S, Fernandez-Cadenas I, Manso H, Gouveia L, Sobral J, Albergaria I, Gaspar G, Jiménez-Conde J, Rabionet R, Ferro JM, Montaner J, Vicente AM, Silva MR, Matos I, Lopes G, Oliveira SA. (2012) Tetratricopeptide repeat domain 7B emerges as a novel risk factor for ischemic stroke through the convergence of several genome-wide approaches. *Journal of Cerebral Blood Flow and Metabolism* , **32**, 1061-1072. . (Journal IF: 5.398, Citations: 5) .

Xavier JM, Shahram F, Davatchi F, Rosa A, Crespo J, Abdollahi BS, Nadji A, Jesus G, Barcelos F, Patto JV, Shafiee NM, Ghaderibarim F, Oliveira SA. (2012) Association study of IL10 and IL23R-IL12RB2 in Iranian Behçet's disease patients. *Arthritis & Rheumatism* , **64**, 2761-2772. . (Journal IF: 7.477, Citations: 20) .

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; The 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; on behalf of the 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*

*Neurology* , **11**, 951-962. . (Journal IF: 23.917, Citations: 63) .

Xavier JM, Shafiee NM, Ghaderi F, Rosa A, Abdollahi BS, Nadji A, Shahram F, Davatchi F, Oliveira SA. (2011) Association of mitochondrial polymorphism m.709G>A with Behçet's disease (BD). *Annals of the Rheumatic Diseases* , **70**, 1514-16. . (Journal IF: 9.111, Citations: 1) .

#### **Ongoing Research Projects**

2013/2015 Title: Patients as Health Care Innovators: An Empirical Investigation of Treatment, Therapies and Medical Devices (TT&MD) developed by Patients of Chronic Diseases. Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: Fundação Ciência e Tecnologia. Reference: PTDC/IIM-GES/5015/2012. Amount: 33,246€.

2013/2014 Title: Prémio NEDAI 2012. Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: NEDAI. Reference: Prémio NEDAI 2012. Amount: 8,506.39€.

2014/2018 Title: Technology, Entrepreneurship and Innovation Policy Lab. Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: Fundação para a Ciência e a Tecnologia, IP. Reference: CMUP-ERI/TPE/0028/2013. Amount: 89,300€.

#### **Other Projects**

2012/2014 L'ORÉAL Award for Women in Science 2012 . Coordinator: Sousa I.

2014/2015 Prémio Robalo Cordeiro SPP/GSK 2013. Coordinator: Feijó S.

2013/2015 Prémio Robalo Cordeiro SPP/GSK 2013. Coordinator: Feijó S.

#### **Publications in peer review Journals**

Matos M, Xavier JM, Abrantes P, Sousa I, Rei N, Davatchi F, Shahram F, Jesus G, Barcelos F, Vedes J, Salgado M, Abdollahi BS, Nadji A, Moraes-Fontes MF, Shafiee NM, Ghaderibarmi F, Vaz Patto J, Crespo J, Oliveira SA. IL10 low-frequency variants in Behçet's disease patients. *International Journal of the Rheumatic Diseases* 2014 Apr 8. doi: 10.1111/1756-185X.12369.

### **Communications in International Conferences**

Crespo J, Xavier JM, Davatchi F, Abade O, Shahram F, Francisco V, Abdollahi BS, Trindade H, Nadjji A, Shafiee NM, Ghaderibarmi F, Ligeiro D, Oliveira SA. Characterization of the MHC locus association with Behçet's disease in Iran. Poster presentation at the 16th International Conference on Behçet's Disease, Paris, 18-20 Sep. 2014.(Poster presentation)

Abrantes PCS, Santos MM, Xavier JM, Sousa I, Francisco V, Krug T, Sobral J, Matos M, Jacinto A, Coiteiro D, Oliveira SA. Identification of 4 novel susceptibility loci for intracranial aneurysms in Portuguese using a pooling-based GWAS. Poster presentation at the ASHG 64th Annual Meeting, San Diego, USA, 18-22 Oct. 2014.(Poster presentation)

Sousa I, Abrantes P, Francisco V, Teixeira G, Monteiro M, Neves J, Norte A, Robalo Cordeiro C, Moura e Sá J, Santos P, Oliveira M, Sousa S, Fradinho M, Malheiro F, Reis E, Negrão L, Feijó S, Oliveira SA. Genome-wide association study implicates LEKR1 at 3q25.31 and an intergenic region at 8q24.21 in Primary Spontaneous Pneumothorax risk. Poster presentation at the ASHG 64th Annual Meeting, San Diego, USA, 18-22 Oct. 2014.(Poster presentation)

Francisco V, Oliveira R, Oliveira P, Zejnilović L, Oliveira SA. Patients and caregivers as sources of innovative ideas and solutions: A multiple case study approach. Poster presentation at the ASHG 64th Annual Meeting, San Diego, USA, 18-22 Oct. 2014.(Poster presentation)

Oliveira SA, Fidelis T, Zejnilović L, Oliveira P. Diffusion as a validation process: Learning from patient innovators. Poster presentation at the ASHG 64th Annual Meeting, San Diego, USA, 18-22 Oct. 2014.(Poster presentation)

### **Communications in National Conferences**

Santos P, Sousa I, Francisco V, Xavier J, Patto JV, Barcelos F, Oliveira SA. Genetics of Familial Paget's Disease of Bone. Poster presentation at the 18ª Reunião Anual da Sociedade Portuguesa de Genética Humana, Lisboa, Portugal, 19-21 Nov. 2014.(Poster presentation)

Abrantes P, Santos MM, Xavier J, Sousa I, Francisco V, Krug T, Sobral J, Matos M, Jacinto A, Coiteiro D, Oliveira SA. Genome-wide association study identifies 4 variants for intracranial aneurysms in the Portuguese population. Oral communication (Abrantes P) at the 18ª Reunião Anual da Sociedade Portuguesa de Genética Humana, Lisboa, Portugal, 19-21 Nov. 2014. (Oral presentation)

Sousa I, Abrantes P, Francisco V, Teixeira G, Monteiro M, Neves J, Norte A, Robalo Cordeiro C,

Moura e Sá J, Reis E, Roquette J, Santos P, Oliveira M, Sousa S, Fradinho M, Malheiro F, Negrão L, Feijó S, Oliveira SA. Genome-wide association study implicates SLC6A1 and an intergenic region at 8q24.21 in Primary Spontaneous Pneumothorax risk. Poster presentation at the 18ª Reunião Anual da Sociedade Portuguesa de Genética Humana, Lisboa, Portugal, 19-21 Nov. 2014.(Poster presentation)

#### **Internationalisation**

Our research depends critically on the establishment effective collaborations with clinical groups for study design, sample ascertainment and collection, and clinical input. We have been able to establish these fruitful interactions with several teams nationwide and internationally, as demonstrated by the large and well-curated biobanks we have set-up in the past ten years and the ensuing research, grants, prizes and publications. The BD biobank was mostly assembled by Iranian collaborators, while the PSP and IA samples were collected throughout Portugal.

We are also part of the METASTROKE international collaboration in the field of ischemic stroke genetics and are currently involved in the sequencing efforts of stroke patients and controls.

#### **Advanced teaching**

Oliveira SA. Lecturer in the Mestrado em Doenças Metabólicas e do Comportamento Alimentar, FML, 11 January 2014.

Oliveira SA. Lecturer in the 4th module (Causation) of the Course in Clinical Research for the FMUL/CAML PhD Students, FML, 16 May 2014.

Oliveira SA. Lecturer in the Mestrado de Neurociências, FML, 21 May 2014.



## Susana Constantino Lab

### Major Interests / Objectives

The Angiogenesis Unit studies molecular and cellular mechanisms that regulate the angiogenic process. Our aim is to interfere with vasculature formation, preventing diseases related with excessive vessel growth or proposing innovative approaches for revascularization in ischemic tissues.

We are particular interested in:

- a) Addressing a clinically relevant issue of radiotherapy and investigating the effects of low doses of ionizing radiation on the vasculature that surrounds the tumor area and their contribution to metastasis formation.
- b) Evaluating the potential use of low doses of ionizing radiation as a novel approach to improve blood flow in vascular occlusive disease.
- c) Understanding why FAP patients have more hepatic artery thrombosis incidence after liver transplantation.

### Head of Unit

Susana Constantino Rosa Santos, PhD (Left July)

### Research Team

Adriana de Fátima Dias Lisboa Correia	Graduate	MSc Student, (left July)
Ana Rita Duarte Simões Pereira	Graduate	MSc Student, (left July)
Augusto Manuel Almeida Ministro	Graduate	PhD Student, (left July)
Carolina Isabel Garcia Cardina	Graduate	MSc Student, (left July)
Filipa Gil Marques	Master	PhD Student, (left July)
Paula Alexandra Gomes de Oliveira	Master	PhD Student, (left July)
Raquel João Santos Ferreira Nunes	PhD	Post doctoral Investigator
Tiago Filipe Ribeiro Ruas Maçarico	Graduate	MSc Student, (left July)

### Keywords / Research Areas

Angiogenesis, Ionizing radiation, Ischemia, Vasculature

### Selected Publications

Domingues I, Rino J, Demmers JAA, de Lanerolle P, Santos SCR (2011) VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. *PLoS ONE* **6**, e25668. <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0025668>. (Journal IF: 4.4, Citations: 4)

Vala I, Martins L, Imaizumi N, Nunes R, Rino J, Kuonen F, Carvalho LM, Rüegg C, Grillo IM, Barata JT, Mareel M and Constantino Rosa Santos S (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *PLoS ONE* **5**, e11222. <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0011222>. (Journal IF: 4.4, Citations: 12)

Constantino Rosa Santos S, Vala I, Miguel C, Barata J, Garção P, Agostinho P, Mendes M, Coelho A, Oliveira C, Martins e Silva J and Saldanha C (2007) Expression and subcellular localization of a novel nuclear Acetylcholinesterase protein. *J Biol Chem* **282**, 25597-603. <http://www.jbc.org/content/282/35/25597.long>. (Journal IF: 5.4, Citations: 23)

Constantino Rosa Santos S, Miguel C, Domingues I, Calado A, Zhu Z, Wu Y and Dias S (2007) VEGF and VEGFR-2 (KDR) internalization is required for endothelial recovery during wound healing. *Exp Cell Res* **313**, 1561-1574. (Journal IF: 3.7, Citations: 41)

Constantino Rosa Santos S and Dias S (2004) Internal and external autocrine VEGF/KDR loops regulate survival of subsets of acute leukemia through distinct signaling pathways. *Blood* **103**, 3883-3889. <http://bloodjournal.hematologylibrary.org/content/103/10/3883.long>. (Journal IF: 10.6, Citations: 99)

### Ongoing Research Projects

2011/2016 Title: LDIR. Coordinator: Susana Constantino Rosa Santos. Agency: Novartis Farma, S.A.. Reference: LDIR. Amount: 19,000€.

### Other Projects

2014/2016 FPJ000758-UCX 111100.00. Coordinator: Susana Constantino.

2014/2016 FPJ000758 111100.00. Coordinator: Susana Constantino.

2014/2016 FPJ000758 111100.00. Coordinator: Susana Constantino.

2014/2016 FPJ000758 111100.00. Coordinator: Susana Constantino.

2014/2016 FPJ000758-UCX 111100. Coordinator: Susana Constantino.

2014/2016 FPJ000758-UCX 111100.00. Coordinator: Susana Constantino.

## FACILITIES AND SUPPORT

Alongside research, IMM has a core of resource units, which complement and maintain the high quality scientific environment. Among these are the Management, the Information Systems, Communication, Funding Programs Office, Quality and safety in Laboratory, Advanced Training. In addition to these transversal units, and in the spirit of shared resources, IMM offers recently equipped state-of-the-art Facilities: Flow Cytometry, Bioimaging, Animal and Fish Facilities, as well as a Biosafety level 3 Laboratory, a Histology Service and a Biobank. All Resource Units have dedicated staff that provides support to IMM community and to develop initiatives that promote research.

Communication Unit	Liliana de Almeida (left October)
Education & Advanced Training	Alexandra Manaia (left July)
Funding Programs Office	Filipa Nunes
Information Systems Unit	José Braga
Management Unit	Margarida Pinto Gago
Quality and Safety in Laboratory	Alexandra Maralhas
Animal Facility	Joana Marques
Bioimaging	José Rino
Biosafety Level Laboratory 3	Miguel Prudêncio
Flow Cytometry	Henrique Veiga-Fernandes
Histology Service	Tânia Carvalho
IMM Biobank	João Eurico Fonseca
Zebrafish Facility	Leonor Saúde

## Animal Facility

### Major Interests / Objectives

The rodent facility of the IMM aims to support state-of-the-art animal research. For that purpose we provide the best housing and care of laboratory rodents and support training and education in Laboratory Animal Science.

### Head of Unit

Joana Margarida da Silva Marques, PhD

### Research Team

Ana Catarina Jorge Mendes	Graduate	Technician
Ana Rafaela Dinis Coelho	Graduate	Technician
Carlos Barata da Silva	Graduate	Technician
Cecília Gonçalves Simão	Undergraduate	Technician
Felícia Maria Augusto Ramos	Undergraduate	Technician
Iolanda Safira Sousa Moreira	Graduate	Technician
José António Vila Chã	No degree	Auxiliary
Márcia Pereira da Silva	Graduate	Trainee, (started April)
Maria Dolores Paulos Bonaparte Figueira	Graduate	Veterinary
MIAELA ELENA MORARI	Undergraduate	Technician, (started August)
Olena Pavlovska Borges de Pinho	Undergraduate	Technician
Pedro Manuel Nogueira dos Santos	Undergraduate	Technician
Pedro Nuno de Moura Baptista	Undergraduate	Technician, (started April) (left September)
Sara Ghirelli	Undergraduate	Technician, (started August)

### **Keywords / Research Areas**

Rodents, Laboratory Animal Science, Animal welfare

### **Major achievements**

During 2014 the major achievements of the rodent facility including major remodeling of the housing and procedures rooms, which allowed a better use and organization of the areas. This remodeling comprised:

- Expansion of the production area by merging the mouse rooms into a single, open space area
- Adding a new procedure room to the BEEM's experimental area
- Expanding mouse housing in the BEEM's experimental area by merging different room into one single open space area
- Expansion of the support areas (clean storage of the BEEM and washing area).

Another important achievement was the organization of the workshop 'Communicating Animal Research', for IMM researchers. This subject is a hot topic which needed to be discussed given the rise in the activity of animal rights associations. Therefore, this workshop was very important to provide basic tools for researchers who need to communicate their work to the general public.

### **Other Projects**

2013/2014 Modelos animais de doenças humanas: Refinamento de estratégias e implementação de novas tecnologias . Coordinator: Joana Marques.

### **Advanced teaching**

Marques, J. M. organized the workshop 'Communicating Animal Research', IMM, January 31, 2014

Marques, J.M. Lecture 'Animal Research - History, Ethics and Scientific validity' in the LisbonBiomed PhD program, IMM, Lisbon, February 26, 2014

Bonaparte, D. Lecture 'Animal research 1.0.1' in the LisbonBiomed PhD Program, IMM, Lisbon, February 26, 2014

Marques, J.M. organized the course 'Laboratory Animal Science', IMM, Lisbon, April 1-21, 2014

Marques, J.M. Lecture 'Animal Research - History, Ethics and Scientific Validity ' in the BioEthics module of the MSc in BioOncology, IMM, Lisbon, November 1, 2014

Marques, J.M. Lecturer in the module 'Laboratory Animal Behaviour and Welfare' in the Postgraduation in Applied Animal Behaviour & Welfare, Instituto Superior de Psicologia Aplicada, Lisboa Mat 24 and 31, 2014

## **Bioimaging**

### **Major Interests / Objectives**

The BioImaging Unit constitutes the core microscopy facility of the IMM, serving as a support structure to carry out and nurture research done with Light Microscopy inside the institute. We aim at providing IMM scientists and visitors with excellence in scientific know-how and expertise in using advanced light microscopy methods for their research. We assist in project planning, experiment design, provide advice and support on sample preparation, image analysis and processing and in writing research papers with microscopy data. Together with continuous training of new users, we organize regular courses and workshops on basic and advanced microscopy techniques.

### **Head of Unit**

José Miguel Rino Henriques, PhD

### **Research 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 achievements

Scientific collaboration with 2 IMM research units and one external research unit resulted in 3 publications in which José Rino is co-author:

- da Silva AS et al, *Org Biomol Chem* (PMID: 24915168, IF: 3.487)
- Tenreiro S et al, *PLoS Genet* (PMID: 24810576, IF: 8.167)
- Fernandes SM et al, *J Infect Dis* (PMID: 24604817, IF: 5.778)

In 2014 the BioImaging Unit services were used by 189 users from 42 different research units, 8 of them from outside the IMM. We trained 75 new users in different microscopy systems during the year.

The Bioimaging Unit became one of the Imaging Nodes of the Portuguese Platform for Bioimaging, a nationwide consortium of 17 nodes with nearly 1.400 registered users that was approved for the second phase of evaluation in the FCT Infraestrutura call and aims to integrate the EuroBioimaging network.

In 2014 the Bioimaging Unit was certified with ISO 9001 Quality Management System by TÜV Rheinland Portugal, as part of IMM Certification.

### Selected Publications

Martin RM\*, Rino J\*, Carvalho C\*, Kirchhausen T, Carmo-Fonseca M (2013) Live-Cell Visualization of Pre-mRNA Splicing with Single-Molecule Sensitivity. *Cell Reports* **4** (6), 1144-1155. <http://www.sciencedirect.com/science/article/pii/S2211124713004373#>. (Journal IF: 7.207, Citations: 8) \* these authors have contributed equally to this work.

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>. (Journal IF: 8.278, Citations: 15)

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. *Nat Struct Mol Biol* **18**, 1115. <http://www.nature.com/nsmb/journal/v18/n10/full/nsmb.2124.html>. (Journal IF: 12.712, Citations: 37) \* these authors have contributed equally to this work.

### Publications in peer review Journals

da Silva AF, Seixas RS, Silva AM, Coimbra J, Fernandes AC, Santos JP, Matos A, Rino J, Santos I, Marques F (2014) Synthesis, characterization and biological evaluation of carboranyl methylbenzo[b]acridones as novel agents for boron neutron capture therapy. *Org Biomol Chem* **12**(28), 5201-11 (Journal IF3.487)

Tenreiro S, Reimão-Pinto MM, Antas P, Rino J, Wawrzycka D, Macedo D, Rosado-Ramos R, Amen T, Waiss M, Magalhães F, Gomes A, Santos CN, Kaganovich D, Outeiro TF (2014) Phosphorylation modulates clearance of alpha-synuclein inclusions in a yeast model of Parkinson's disease. *PLoS Genet* **10**(5), e1004302 (Journal IF: 8.167)

Fernandes SM, Pires AR, Ferreira C, Foxall RB, Rino J, Santos C, Correia L, Poças J, Veiga-Fernandes H, Sousa AE (2014) Enteric mucosa integrity in the presence of a preserved innate interleukin 22 compartment in HIV type 1-treated individuals. *J Infect Dis* **210**(4), 630-40 <http://jid.oxfordjournals.org/content/210/4/630.long> (Journal IF: 5.778)

### Invited lectures and seminars

Rino J, "Imaging proteins at work inside living cells", IBEB Seminar, Lisboa, Portugal, November 14, 2014

### Advanced teaching

Rino J organized and lectured the "Bioimaging Microscopy Nanocourse", IMM, Lisbon, May 15-16, 2014

Rino J lectured (both theoretical lectures and hands-on practicals) at the "Advanced Fluorescence Microscopy Course", Center for Neuroscience and Cell Biology, Coimbra, March 12-14, 2014

Rino J lectured at the "6th Course on Optical Microscopy Imaging for Biosciences", lecture entitled "Molecular Imaging Dynamics", IBMC, Porto, April 9, 2014

## Biosafety Level Laboratory 3

### Major Interests / Objectives

The IMM houses a 70 m<sup>2</sup> BSL3 Facility meeting 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 containment conditions, including research that involves rodent models.

The Facility is available to IMM internal and affiliated researchers, as well as to external researchers from academia, pharma and biotech. All work to be carried out in the BSL3 Lab must follow the established SOPs, as defined in the Facility's Rules and Guidelines Manual.

The IMM's BSL3 Facility comprises two fully equipped tissue culture rooms and one animal experimentation room for rodents. Available equipment includes incubators, benchtop centrifuges, refrigerators and freezers, microscopes, a -80 freezer, and an ultracentrifuge.

### Head of Unit

Miguel Prudêncio, PhD

### Research Team

Inês Antunes Cabral Queiroz de Matos	Graduate	Technician
Maria Dolores Paulos Bonaparte Figueira	Graduate	Veterinary

### Keywords / Research Areas

Biosafety level 3, HIV, Mycobacterium tuberculosis, ABSL3

### Major achievements

In 2014 the Facility continued to provide a high-quality service to users. The Facility officially joined the Lab-PT-BioNet network of the Portuguese laboratory biosafety network (<http://www.labptbionet.ibmc.up.pt/>). Some infrastructural alterations were implemented, in coordination with IMM animal house, to improve the services made available to researchers.

One training course was organized for new users and the head of facility participated in biosafety seminars and workshops.

#### **Invited lectures and seminars**

Miguel Prudêncio, "Malária em Portugal: uma ameaça real?", Comemorações do Dia Mundial da Saúde: Doenças associadas a vetores - Small bite, big threat", INSARJ, Lisbon, Portugal, 10 April 2014

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

Miguel Prudêncio, 4th Workshop "Biossegurança, Saúde e Legislação no laboratório de Microbiologia", INSARJ, Lisbon, Portugal, 31 October 2014

#### **Internationalisation**

The IMM BSL3 facility is a member of the LabPTBioNet network of Portuguese high containment facilities. One of the aims of this network is to apply for membership with EBSA (European Biosafety Association). The facility is actively contributing to this goal, through its participation in network meetings and providing its Guidelines to serve as the basis for a uniform set of procedures to be adopted by BSL3 facilities nationally. Besides, since his appointment as Head of the IMM BSL3 facility, Dr. Miguel Prudêncio has participated in several international biosafety training events.

#### **Advanced teaching**

Prudêncio, M. organized the course "IMM BSL3 Facility", IMM, Lisbon, Portugal, 19 March 2014.

## Flow Cytometry

### Major Interests / Objectives

The Flow Cytometry Unit (UCF) is a core facility that provides support and training to IMM and external researchers who require this technology in their research projects. The Unit is currently equipped with 3 cell analysers (1 FACSCalibur and 2 BD LSR Fortessa) and 2 cell sorters (FACSARIA I and FACSARIA III). One LSR Fortessa is equipped with High Throughput Sampler (HTS), which allows the automated acquisition of samples from 96 and 384 well plates. A substantial part of our work is to provide training in flow cytometry concepts, experiment planning, experimental controls, instrument operation and data analysis. UCF staff further ensures quality control and maintenance procedures on all instruments and the implementation of the Quality Management System, according to ISO 9000.

### Head of Unit

José Henrique Veiga Fernandes, PhD

### Research Team

Ana Isabel da Silva Vieira	Graduate	Technician
Ana Sílvia Pacheco Gonçalves	Master	Technician
Cláudia Marília Ferreira Da Silva	Master	Technician, (started July) (left October)
Filipa Gomes de Almeida Dias	Master	Technician, (started December)

### Keywords / Research Areas

Flow Cytometry, High Speed Cell Sorting, Multiparametric Analysis, Fluorochrome, Fluorescent Protein

### **Major achievements**

In 2014 a total of 26 IMM Units used Flow Cytometry facility, in addition to 3 external units, representing a total of 141 users. From April 2014, we extended our work hours on cell sorters, allowing more hours of sorting per day. In July 2014, to improve the unit's efficiency, we applied new rules and penalties for last minute cancellations and no-shows. Subsequently, last minute cancellations and no-shows have significantly decreased. Since the High Throughput Sampler (HTS) installation in February 2013, 16 users did the induction and they acquire their samples in a rapid and fully automated way from 96- and 384-well plates.

The negotiation for the upgrade of LSR Fortessa cell analysers with two more colors was concluded and the installation will be performed in early 2015, creating a significant upgrade to the Flow Cytometers available at the IMM. Therefore, UCF will be equipped with 2 LSR Fortessa enabling the detection of up to 10 colors simultaneously.

## **Histology and Comparative Pathology Laboratory**

### **Major Interests / Objectives**

The Histology and Comparative Pathology Laboratory aims at providing histology and comparative pathology support to IMM scientists investigating animal models of human disease, and scientists/physicians investigating human disease. Services are also available for extramural investigators.

Services include HISTOLOGY (tissue processing for paraffin-embedding; gelatin/OCT-embedding and cryosectioning; histochemistry), IMMUNOHISTOCHEMISTRY, TRANSMISSION ELECTRON MICROSCOPY and VETERINARY PATHOLOGY. We also provide assistance in study design and procedural training for researchers (necropsy, tissue harvesting).

### **Head of Unit**

Tânia Gilot Mendes de Carvalho, DVM, PhD

### **Research Team**

Ana Margarida Biscaia Fernandes dos Santos	Graduate	Technician
Andreia Lúcia do Nascimento Pinto	Master	Technician

### **Keywords / Research Areas**

Histology, Comparative Pathology, Electron Microscopy, Immunohistochemistry

### **Major achievements**

In 2014 the Histology and Comparative Pathology Laboratory provided Histology, Pathology and Electron Microscopy support to IMM research units, and extramurally to researchers from Hospital de Santa Maria, iMed at Faculdade de Farmácia, Instituto Gulbenkian Ciência, CEDOC, Biocant and others, in a total of up to 700 requests.

Scientific collaboration with 2 IMM research units and one external research unit resulted in 3 publications in which Tânia Carvalho is co-author, in *Journal of Virology*, *Cell Host and Microbe*, and *Pancreas*, with one more publication already accepted (in *Cell Death and Disease*) and three other under revision.

We have expanded the Immunohistochemistry service, with the optimization of several antibodies for mouse tissue - ki67, BrdU, e-cadherin, CD3, myeloperoxidase, CD2, GFAP; human - Ki67, vimentin; and trypanosome - VSG. For Transmission Electron Microscopy we have dedicated histotechnician and re-equipped the service, to further expand the processing and imaging techniques available.

In 2014 the Histology and Comparative Pathology Laboratory was certified with ISO 9001 Quality Management System by TÜV Rheinland Portugal, as part of IMM Certification.

#### **Selected Publications**

F Caiado, T Carvalho, I Rosa, L Remédio, A Costa, J Matos, B Heissig, H Yagita, K Hattori, JP Silva, P Fidalgo, A Dias Pereira, S Dias (2013) Bone marrow-derived CD11b+Jagged-2+ cells promote epithelial to mesenchymal transition and metastization in colorectal cancer. *Cancer Research* (Journal IF: 8.650, Citations: 6)

F Caiado, T Carvalho, F Silva, C Castro, N Clode, JF Dye, S Dias (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* (Journal IF: 8.496, Citations: 25)

AL Gomes, T Carvalho, J Serpa and S Dias (2010) Hypercholesterolemia promotes bone marrow cell mobilization by perturbing the SDF1:CXCR4 axis. *Blood* (Journal IF: 9.898, Citations: 55).

#### **Publications in peer review Journals**

Nunes-Cabaço H, Matoso P, Foxall RB, Tendeiro R, Pires AR, Carvalho T, Pinheiro AI, Soares RS, Sousa AE (2014) Thymic HIV-2 infection uncovers post-transcriptional control of viral replication in human thymocytes. *Journal of Virology* (Journal IF: 4.648, Citations: 0)

S Weis, T Schlaich, F Dehghani, T Carvalho, I Sommerer, S Fricke, F Kahlenberg, J Mössner, A Hoffmeister (2014) Deficiency Causes Siderosis in Spleens and Lymphocyte Apoptosis in Acute Pancreatitis. *Pancreas* (Journal IF: 3.008, Citations: 0)



Shengyong Ng, S March, A Galstian, K Hanson, T Carvalho, M Mota, and S Bhatia (2014)  
Hypoxia Promotes Liver Stage Malaria Infection in Primary Human Hepatocytes In Vitro.  
*Disease Models & Mechanisms* (Journal IF: 5.537, Citations: 1)

#### **Advanced teaching**

Carvalho, T organized and lectured the workshop "Mouse Lab - Necropsy Workshop", IMM, Lisbon. July 24th, 2014

## IMM Biobank

### Major Interests / Objectives

In the early years of Biobanco-IMM CAML several priorities were established, such as communication (through the society and scientific partners), expanding collections, promoting collaborations and standardizing procedures. One of our major goals is promote the collections with added value. Our control collection represents 70% of the samples requested in the last year. Biobanco-IMM CAML aims to achieve sustainable growth, focused on improving quality, not only in samples but also in data management. We are working on several aspects of serum and DNA quality control parameters. Other strategic goals are to promote national biobanking networking with standardized procedures and established synergies as well as international integration of biobanking networks.

### Head of Unit

João Eurico-Fonseca, MD, PhD (Left November)

Sérgio Jerónimo Rodrigues Dias, PhD and Joaquim Polido Valente, MD, PhD (started November)

### Research Team

Ana Filipa Soares Garcia	Graduate	Technician
Ana Rita Cascão Rodrigues	PhD	Technician
Ana Sofia Zhao	Master	Technician
Ângela Maria Cerqueira Coelho Afonso	Master	Technician
Joana Ribeiro Caetano Lopes	PhD	Technician
Telmo Filipe Araújo Catarino	Master	Technician, (started December)
Vanessa Gonçalves Silva	Graduate	MSc Student, (left February)

### Keywords / Research Areas

Biobanks, Human Samples, Clinical Information, Biomedical Research

### **Major achievements**

- Collected 11 thousand donors and 95 thousand samples across 32 collections
- More than 2400 Samples from the Biobanco-IMM CAML have been requested for research projects.
- Organization of meetings in pharmaceutical companies, presentations in several other hospitals, meetings with scientific medical societies and patients associations, presentations in national medical congresses and involvement with the media gave positioned Biobanco-IMM, CAML as the reference biobank in Portugal.
- Used of standard operational procedures (SOPs) in daily activity
- Improved the quality control of samples focusing the serum samples
- Launch of the national biobank concept (Biobanco.pt), based on a network of biobanks with a common information system

### **Selected Publications**

Afonso A, Polido-Pereira J, Dias S. (2014) Biobank Profile: Biobanco-IMM, Lisbon Academic Medical Centre.. *Biopreservation and Biobanking* , **12**, 433-434. (Journal IF: 1.578, Citations: 0)

### **Other Projects**

2013/2014 Collection of samples from young patients with auto-inflammatory diseases. Coordinator: Filipa Ramos.

2013/2014 Collection of samples from patients with Bipolar Disorders. Coordinator: Maria Luisa Figueira.

2013/2014 Collection of samples from transplanted patients.. Coordinator: João Lacerda.

2012/2014 Collection of femoral epiphysis, including bone and cartilage, from hip replacement surgery patients.. Coordinator: Helena Canhão.

2012/2014 Collection of samples from controls, based on a questionnaire and interviewed by a physician.. Coordinator: Biobanco-IMM CAML.

### **Publications in peer review Journals**

Afonso A, Polido-Pereira J, Dias S. (2014) Biobank Profile: Biobanco-IMM, Lisbon Academic Medical Centre. *Biopreservation and Biobanking* **12**, 433-434. (Journal IF: 1.578, Citations: 0)

### **Invited lectures and seminars**

Fonseca JE. "Biobanco-IMM", Curitiba, Brasil. April 2, 2014

### **Communications in National Conferences**

Polido-Pereira. "Importância dos Biobanco", VII Congresso Nacional Associação Portuguesa Neuro Oncologia, Lisboa . November 21, 2014

### **Msc thesis completed**

Ângela Maria Cerqueira Coelho Afonso 18/11/2014 Identification of biomarkers for quality control in human biological serum samples Universidade da Beira Interior Joana Lopes Cândida Tomaz

Vanessa Silva 08/05/2014 Implementação de um método de validação do controlo de qualidade amostras de DNA armazenadas no Biobanco-IMM Escola Superior de Saúde Egas Moniz Joana Lopes

## Zebrafish Facility

### 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 Unit

Maria Leonor Tavares Saúde, PhD, Invited Assistant Professor

### Research Team

Aida Gonçalves Lino Barros	No degree	Technician
Lara Carvalho	Master	Lab manager

### Keywords / Research Areas

zebrafish, development, regeneration & disease

### Major achievements

- Implementation of a New Diet ([www.gemmafish.com](http://www.gemmafish.com))
- Optimization of Zebrafish in vitro Fertilization
- Implementation of a Swimming Track System
- Acquisition of new housing system (Aquatic Blue line from Tecniplast)

### Selected Publications

Fior R., Maxwell A.A., Ma T.P., Vezzano A., Moens C.B., Amacher S.L., Lewis J. and Saúde L. (2012) Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by Mesogenin1. *Development* **139**(24), 4656-65. (Journal IF: 6,273, Citations: 10)

#### **Invited lectures and seminars**

Saúde, L. Cell movement choreographies that shape the vertebrate body plan. Departamento de Ciências Biomédicas e Medicina da Universidade do Algarve, Faro, Portugal, January 16, 2014

Saúde, L. The amazing regenerative capacity of the zebrafish. Encontro ENEBioq FCT-UNL, Monte da Caparica, Portugal, April 12, 2014

Saúde, L. The zebrafish in Biomedical Research. Serviço de Neurologia, Hospital de Santa Maria, Lisboa, Portugal, April 23, 2014

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

Saúde, L. Quaking A, a post-transcriptional regulator of early patterning in zebrafish, The 3rd European PI Meeting, Ein Gedi, Israel. 30 March-3 April (Poster Presentation)

Ribeiro, A & Saúde, L. Foxj1a-positive cells at the center of spinal cord regeneration in zebrafish. Development and Regeneration of the Spinal Cord, EMBO Workshop, Sitges, Spain. 1-4 October (Poster Presentation)

Pinto, R., Almeida-Santos, J. & Saúde, L. Asymmetry versus Symmetry: the role of Dmrt2a in the formation of the vertebrate body plan, X Meeting of the Spanish Society of Developmental Biology, Madrid, Spain. 13-15th October (Poster Presentation)

#### **Science and society**

Carvalho, L. & Barros, A. performed guided visits to the Fish Facility on the following DATES and to the following GROUPS:

20th January- Professional Course

19th February- Primary School "João de Deus - 4ª classe"

20th February – Medical Students, FMUL

6th March - Secondary School "São Brás de Alportel"  
27th March - Secondary School "Coruche"  
3rd April – FMUL Candidate Day  
7th May – Secondary School "Colégio de Santa Maria"  
23rd October - Preparatory School  
4th December - Secondary School Vergilio Ferreira

## **Communication Unit**

### **Major Interests / Objectives**

The Communication Unit 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 advise IMM Direction on Public Affairs issues. With the firm belief that science should inform decisions because it impacts everyone's lives, the communication unit 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 Unit**

Liliana de Almeida, Master (Left October)

### **Research Team**

Andreia Sofia Moita Machado	Graduate	Administrative
Silvana Daniela Fonseca Paules	Graduate	Administrative (Left August)

### **Keywords / Research Areas**

Corporate and Institucional Communication, Science Communication, Public Affairs

### **Major achievements**

Produced media materials to promote the corporate image of IMM (report, folders, videos) and reinforced IMM presence in the social networks and in the national and international press.



A new website is being developed and should be online in 2015. During this year we organized school visits, promoted internal and external seminars, improved our internal communication and organized a first “IMM Christmas Party” to the entire IMM community.

In 2014 we prepared a new strategic plan to the Communication Unit of IMM, where we will partner with LPM as press office and with GBNT as advertising agency.

The Unit also organized official meetings with foreign delegations and also with national and international students.

### **Organisation of Conferences**

- “A Choice of Challenges in Breast Cancer”
- “MDS Awareness Day”
- “LisbonLymph “Aggressive B-Cell Lymphomas”
- Visit to Portugal by Dr. Ronald A.DePinho TBS, 2014 – CAML
- Biobanco-IMM’s 2<sup>nd</sup> anniversary
- “Nutrição em Oncologia” – Paula Ravasco

### **Science and society**

The Communication Unit participated in a series of institutional processes such as the production of annual reports (activity report IMM, Biobanco-IMM CAML), preparation of institutional texts and profiles, the support to the preparation of official visits of foreign delegations.

We have also concluded a series of monitoring processes: IMM presence in the media, consultation of IMM website and social networks, IMM programme of school visits/educational activities.

The Communication Unit gave support to media visits to IMM with an increased regular presence of IMM and IMM researchers in reference general and specialized media, at both national and international level.

There were 24 Press releases disseminated through the media (national and international) and a improvement of the internal communication.

## Education & Advanced Training

### 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 PhD (CAML, LisbonBioMed) and Postdoctoral Programs: Launch Calls; Administrative execution; Managerial Support to PhD and Postdoctoral fellows activities; Support PhD and Postdoctoral Fellows throughout their training. Update UEFA Webpages within new IMM site.
- Run Advanced Courses, scheduled upon CAML & LisbonBioMed Scientific Boards approval; cover all organizational aspects.

New Programs:

- Launch & implementation of Mindthegap- Postdoctoral Training Program approved for funding under Marie Curie Actions;
- Join EMBL- lead international consortium for Horizon 2020 application: outreach as post-graduate training.

### Head of Unit

Domingos Manuel Pinto Henrique, PhD

### Research Team

Ana Rute Côrte-Real Martins	Master	Technician, (left July)
Maria Alexandra Gama Mendonça Simões Manaia	PhD	Director, (left July)
Sónia Silva Arroz	Graduate	Technician

### Keywords / Research Areas

Education, Advanced-Training, PhD-Program, Postdoctoral-Program, Career Development, Advanced Courses

## Major achievements

Transversal Managerial Achievements i) Help desk: Standardized email messages and info packages for regular requests: FCT grant applications, renewals, spontaneous applications, general queries etc ii) Scientific events centralized management. Initiating and maintaining communication with guests; coordinating travel and accommodation bookings; providing travel plan and scientific program; booking rooms and audiovisual support; booking meals; assessing participants feedback.

Specific Achievements i) Support CAML-related applications to FCT Fellowships-2013 Call: BDs (including for medical interns) & BDPs. ii) Launch & administrative execution of LisbonBioMed PhD Program: Internal call for potential PI supervisors; international call launch, info dissemination, applications management, coordination of the selection and admission process, production of overall program metrics and statistics and reporting. Building the 8-week initial training program and its implementation.

## Funding Programs Office

### Major Interests / Objectives

Initially created in 2008 the Funding Programs Office was restructured in February 2013. It facilitates and streamlines every step of the pre-award process, including grant preparation, submission, and contract negotiation, in compliance with institutional, government and sponsor policies and regulations. In addition, the Office acts as liaison with academia, enterprises and other organizations for the development of strategic collaborations. Our specific goals include: i) promote a service of funding opportunities tailor-made for IMM researchers; ii) prepare institutional grant applications; iii) promote academic/entrepreneurial scientific collaborations underpinning the establishment of national/international grant applications; iv) promote partnerships with companies and explore relevant financial opportunities; v) assist obtaining funding for entrepreneurial projects.

### Head of Unit

Ana Filipa Duarte Nunes Almeida, PhD

### Research Team

Joana Catarina da Rocha Lamego	PhD	Manager,
Joana Costa	PhD	Manager
Rudolfo Pais Mendes Ferreira Francisco	Graduate	Facility assistant, (left August)

### Keywords / Research Areas

Competitive research funding, Funding opportunities dissemination and support, Institutional grant applications, Networking, Scientific and entrepreneurial collaborations, Entrepreneurship

### Major achievements

- We provided support to the submission of 107 international and 75 national grant applications.
- We initiated the preparation of institutional project proposals with IMM's Board of Directors

for Horizon 2020 calls of Spreading Excellence and Widening Participation section, including ERA-Chairs and Twinning of research institutions.

- We submitted an institutional grant application to the Horizon 2020 scheme ERA-Chairs (submitted on the 15th October 2014).

#### **Ongoing Research Projects**

2012/2014 Title: Dinamização da Participação Portuguesa no 7PQ:Saúde - Lisboa . Coordinator: Ana Filipa Duarte Nunes Almeida. Agency: Clientes Diversos. Reference: SIAC. Amount: 305,007.13€.

#### **Invited lectures and seminars**

Filipa Nunes, A Indústria Farmacêutica como motor de Ciência e Inovação, Dia da Porta Aberta da Inovação Biofarmacêutica, Comissão Especializada de Biotecnologia da APIFARMA, Taguspark, Lisboa, Portugal, May 21, 2014

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

Joana Lamego, Academic excellence and knowledge transfer to society at Instituto de Medicina Molecular, Hearing on Horizon 2020 and EIT, New tools for transforming Southern Europe and the Mediterranean area in regions of Innovation and Research Excellence, hosted by MEPs Prof. Ioannis A. Tsoukalas and Prof. Maria da Graça Carvalho, European Parliament, Brussels, Belgium, February 19, 2014

#### **Organisation of Conferences**

Filipa Nunes, Innovative Medicines Initiative (IMI) Event, Panel I: What is IMI and how can Portuguese groups participate (Michel Goldman, IMI Executive Director; Irene Norstedt, DG Research & Innovation, European Commission; Maria da Graça Carvalho, Member of the European Parliament; Beatriz Lima, Chair of the IMI Scientific Committee); Panel II: Showcase of Portuguese scientific expertise relevant for IMI; Working Session (restricted): Practical strategies for successful applications to IMI calls, IMM, Lisbon, Portugal, January 17, 2014

### **Advanced teaching**

Filipa Nunes, lectured the seminar “Entrepreneurship and strategies to take scientific ideas into the market”, LisbonBioMed PhD Program, IMM, Lisbon, February 19, 2014

Joana Costa, lectured the information session "ERC Starting and Consolidator Grant", IMM, Lisbon, February 24, 2014

## Information Systems Unit

### 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:

1. Provide state-of-the-art information technology infrastructure and support services.
2. Contribute significantly to improve productivity of researchers and research outcomes.
3. Facilitate and optimize management business processes.

USI intervenes mainly in the following areas:

1. Information Technology (IT) support to IMM users.
2. Planning, implementation and maintenance of the infrastructure to store, process and protect research data.
3. Design, implement and integrate information systems to facilitate scientific and management processes.

### Head of Unit

José Joaquim Carvalho da Costa Braga, PhD

### Research Team

Daniel José Vilhena Guerreiro	Graduate	Technician
Emanuela Simões	Graduate	Technician
Nuno Andrade da Cruz Henriques	Master	Technician
Pedro Miguel Bernardino Eleuterio	Graduate	Technician

### **Keywords / Research Areas**

IT support, Data protection, Information integration, Web Services

### **Major achievements**

This year, to cope with the current support demand, USI implemented remote assistance of domain computers in order to achieve faster response times.

To increase uptime of our services our infrastructure was enhanced by virtualizing more servers. Reliability was improved by the implementation of redundancy and of an automatic monitoring service which issues alerts via email and mobile interfaces. An additional server was created for researchers interested in performing standard bioinformatics and computational biology tasks. A storage server was setup for saving research data and is currently in its final configuration steps.

We laid the groundwork for interoperable Web services and Web applications. Based on this we developed a person data service that is able to feed any other application and service (e.g., future IMM website). We also implemented tools for quality improvement such as source code version control system (software programming tasks) and a project management service.



## Management Unit

### Major Interests / Objectives

IMM legal, Human Resources and general administrative and financial matters:

- Accounts –IMM statutory accounts and tax returns; cost accounting;
- Projects management - from contractual start until final report submission; related support to researchers;
- Human Resources - contracts and salaries; performance assessment
- Legal – Institutional and researchers support: namely on intellectual property and consortium agreements;
- Quality Management System
- General Administrative and financial support

The Management Unit also gives support to the Executive Director and the other Statutory Boards in relation to organizational issues, inter-institutional collaborations, financial and budget management strategy.

### Head of Unit

Maria Margarida Mendonça Correia Pires Pinto Gago, Graduate

### Research Team

André Rebelo da Silva Fialho	Graduate	Lawyer
Andreia Sofia Gonçalves Almeida Vaz Veiga	Graduate	Manager
Annie Cibebe Guerreiro Semião	Graduate	Administrative, (left February)
Cláudia Aurora Mira Soeiro	Graduate	Administrative
Daniela Filipa Ferreira Madeira	Graduate	Administrative
Eduarda Maria Seabra Rosmaninho	Master	Administrative
Isabel Pequenino Roque	Graduate	Administrative
Maria José Flores Marques Antunes	Graduate	Administrative
Mónica Aurora Malheiro Vieira	Graduate	Administrative

Mónica Raquel Carvalho Paquete	Graduate	Administrative, (left January)
Nuno Manuel Barradas da Fonseca	Graduate	Administrative
Patricia Cucio	Undergraduate	Board Secretary
Pedro Gaspar Rebelo Lopes Moura	Master	Administrative, (started April)
Sandra Paula da Silva Duarte	Graduate	Accountant
Sara Sofia de Almeida Nunes	Graduate	Administrative, (started February)
Susana Isabel dos Santos Pedroso	Undergraduate	Administrative
Tânia Cristina Torres Pereira Ascensão	Graduate	Administrative
Teresa Maria Paulo Ferreira da Conceição Saúde Fernandes	Graduate	Lawyer
Vera Cristina Felício Conceição Rego	Undergraduate	Administrative

#### **Keywords / Research Areas**

Continuous improvement, Human Resources, accounts and Budget control, Project Management, Quality Management System, Legal

#### **Major achievements**

Effective response to a continually increasing number of scientific collaboration protocols and HR contracts.

Quality Management System – certification granted.

Publication of IMM Career's framework and Performance Assessment regulations

Appointment of a HR manager and beginning of the reorganization of the service.

## Quality and Safety in Laboratory

### Major Interests / Objectives

The Lab Management Unit is divided in three different areas, each one dedicated to improve the quality of research of the Institute and comply with National and International guidelines and best practices.

The Washing Room is responsible for the cleaning and sterilization of lab material, both common and specific of all research units. The Purchasing Office centralizes all the Institute acquisitions, namely products, services and equipments and provides important information related to prices and ongoing promotions to all research units.

The Lab Management is responsible for the adequate selection and installation of new equipment, the preventive and corrective maintenance of common equipment; design/renewal of laboratory infrastructures; advisory and authority regarding safety with products, equipment and infrastructure.

### Head of Unit

Alexandra Maralhas, Graduate

### Research Team

Alexandre Manuel Raposo de Jesus	Master	Technician
Ana Cristina dos Santos Anunciação Silva	Undergraduate	Technician, (left March)
Ana Rita Fonseca Vicente	Graduate	Technician
André Paiva Antunes	Graduate	Technician, (left April)
Bruno André Baltazar dos Santos Braga	Undergraduate	Technician, (started April) (left July)
Cátia Vanessa Sanches Mesquita	Graduate	Technician, (left April)
Edna neias f. gomes	Graduate	Technician
Rossandro Martins Gomes	Undergraduate	Technician, (started April)
Sandra Isabel Francisco Lopes	Graduate	Technician

Sara Diana Pinheiro dos Santos	Master	Technician, (started October)
Susana Maria Andrade	Undergraduate	Auxiliary
Vânia Isabel Estevens Polido Marques Paula	Graduate	Technician

#### **Keywords / Research Areas**

Infrastructure and equipments maintenance, Health and Safety in Work, Laboratory Design, Purchases, Budgeting, Technical Consulting

#### **Major achievements**

The Unit was actively involved in several re-modeling works of laboratory spaces and research support structures, such as a new histology and bioimaging room, new laboratory spaces for research groups – a Biochemistry lab for Gonçalo Bernardes, a Molecular Biology lab for João Lacerda; a new tissue culture room to be used by the incoming research groups and a new clinical research center named “Centro de Investigação Clínica”, located in Santa Maria Hospital. The equipment management (acquisition, maintenance and repair) was improved with the ongoing inventory of all IMM equipments (in 2014 IMM acquired 254 equipments), required for an excellent level of support to over 300 equipments with maintenance contracts. 2014 was also marked by the progressive implementation of health and safety in work policies, development of risk assessment procedures and monthly training sessions with lab managers, focused on the work developed in the laboratories.

## COMPANIES

### GENOMED

#### 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 over 385 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 of Unit

Teresa Porta Nova, MSc

#### Team

Gabriel Miltenberger-Miltenyi	MD/PhD	Coordinator
Ana Coutinho	PhD	Technician
André Janeiro	Graduate	Technician
Catarina Silveira	MSc	Technician
Inês Silva	MSc	Technician
Hélia Guerreiro	Graduate	Technician
Vânia Martins	Graduate	Technician (started in November 2014)
Sónia Santos	PhD	Coordinator
Paula Costa	Graduate	Technician
Ana Carla Sousa	Graduate	Technician
Sónia Matos	MSc	Coordinator
Sara Malveiro	Graduate	Technician

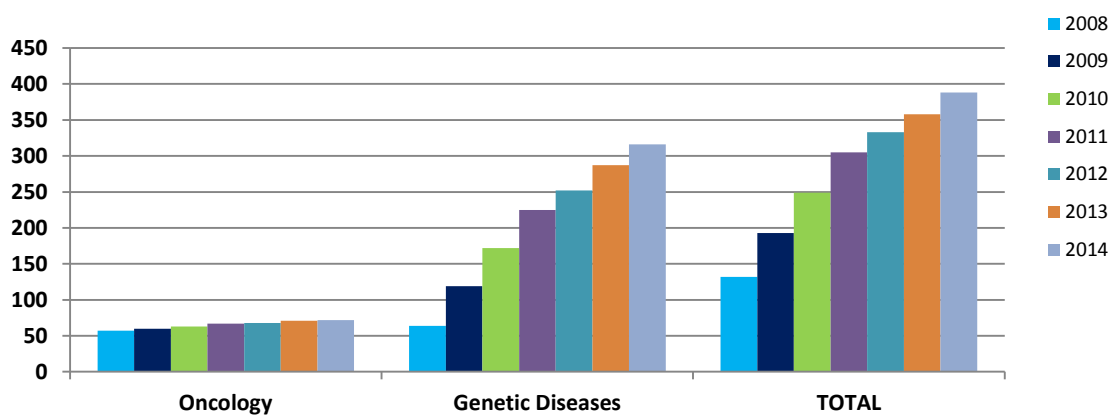
Paula Mimoso	Graduate	Technician, Quality Manager
Fabíola Rosa	Undergraduate	Direction Assistant
Ana Flores	Undergraduate	Management Assistant
Sara Malveiro	Graduate	Technician

### Major scientific achievements

Increased number of tests available.

### Graphical Abstract

Total Number of Tests Available



### Selected Publications

van der Zee J, Dillen L, Deschamps W, Van Langenhove T, Engelborghs S, Vandenbulcke M, Dermaut B, Sieben A, Smets K, Van Damme P, Merlin C, Laureys A, Van Den Broeck M, Mattheijssens M, Peeters K, Benussi L, Binetti G, Ghidoni R, Borroni B, Padovani A, Archetti S, Pastor P, Razquin C, Ortega-Cubero S, Hernández I, Boada M, Ruiz A, de Mendonça A, Miltenberger-Miltényi G, do Couto FS, Sorbi S, Nacmias B, Bagnoli S, Graff C, Chiang HH, Thonberg H, Pernecky R, Diehl-Schmid J, Alexopoulos P, Frisoni GB, Bonvicini C, Synofzik M, Maetzler W, Müller vom Hagen J, Schöls L, Haack TB, Strom TM, Prokisch H, Dols-Icardo O,

Clarimón J, Lleó A, Santana I, Almeida MR, Santiago B, Heneka MT, Jessen F, Ramirez A, Sanchez-Valle R, Llado A, Gelpi E, Sarafov S, Tournev I, Jordanova A, Matej R, Parobkova E, Fabrizi GM, Testi S, Salmon E, Kovacs GG, Ströbel T, Santens P, Robberecht W, De Jonghe P, Martin JJ, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Van Broeckhoven C, on behalf of the BELNEU consortium and of the EU EOD consortium (2014) Rare mutations in SQSTM1 modify susceptibility to frontotemporal lobar degeneration. *Acta Neuropathol.* **128**(3):397-410. (citations: 1)

Machado MV, Janeiro A, Miltenberger-Miltenyi G, Cortez-Pinto H (2014) Genetic polymorphisms of proangiogenic factors seem to favor hepatocellular carcinoma development in alcoholic cirrhosis. *Eur J Gastroenterol Hepatol.* **26**(4):438-43.

Madruza Dias J, Rosa R, Perpétuo I, Rodrigues A, Janeiro A, Costa MM, Gaião L, Pereira da Silva J, Fonseca JE, Miltenberger-Miltenyi G (2014) Pachydermoperiostosis in an African patient caused by a Chinese/Japanese SLCO2A1 mutation – case report and review of literature. *Seminars in Arthritis and Rheumatism.* **43**(4):566-9.

#### Ongoing Research Projects

Starting in 2014: From bed to bench in Angelman- and Angelman-like syndromes in Portugal: genotype - phenotype association studies and next generation sequencing for novel mutations. Bolsa Pedro Maria José de Mello Costa Duarte, Fundação Amélia de Mello. Participant: Sandra Jacinto and Gabriel M.-Miltenyi

Starting in 2014: Non-small-cell lung cancer ALK positive incidence study in Portugal. Pfizer. Coordinator: Encarnação Teixeira. Participant: Sónia Santos e Paula Costa

2013/present: Glucocerebrosidase in Parkinson's disease: from risk factor to biomarker. Fundação para a Ciência e Tecnologia. Participant: Gabriel Miltenberger-Miltenyi

2013/present: Analysis of CD34+ peripheral blood cells by FISH as cytogenetic monitoring of MDS. Celgene. Coordinator: Maria João Costa. Participant: Sónia Santos

2013/2014: Randomized, Double-blind, Placebo-controlled Phase 3 Study of Ibrutinib, a Bruton's Tyrosine Kinase (BTK) Inhibitor, in Combination with Bendamustine and Rituximab (BR) in Subjects With Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Janssen-Cilag. Coordinator: João Raposo Participant: Sónia Santos.

2012/present: Diagnosis and monitoring of Chronic Myeloid Leukemia (CML) patients: Molecular and Cytogenetic analysis. Bristol-Myers Squibb. Coordinator: José Alves do Carmo. Participants: Sónia Santos and Sónia Matos

2012/present: From bed to bench in atypical hemolytic uremic syndrome: genotype - phenotype association studies and screening for novel mutations in Portugal. 2011 Investigation grant of the Portuguese Society of Nephrology. Participant: Gabriel Miltenberger-Miltenyi

2012/present: Biomarkers for Alzheimer's disease and Parkinson's disease (BIOMARKADP). European research projects for the optimisation of biomarkers and harmonisation of their use between clinical centres. Joint Programming in Neurodegenerative Disease (JPND). Portuguese coordinator: Alexandre de Mendonça. Participant: Gabriel Miltenberger-Miltenyi

2012/present: Investigação translacional em Alzheimer. Quadro de Referência Estratégico Nacional (QREN). Coordinator: Sofia Corte-Real. Participant: Gabriel Miltenberger-Miltenyi

2011/present: Nephrotic syndrome in childhood - genotype phenotype association studies and screening for novel mutations. 2010 Investigation grant of the Portuguese Society of Nephrology. Coordinator: Gabriel Miltenberger-Miltenyi

2010/present: Phenotype-genotype association studies in medullary cystic kidney disease - searching for new candidate genes. 2009 Investigation grant of the Portuguese Society of Nephrology Coordinator: Gabriel Miltenberger-Miltenyi

2008/present: Genetics of obesity - a study of polymorphisms. FCT Funding. Coordinators: Helena Cortez Pinto and Gabriel Miltenberger-Miltenyi. PTDC/SAU-OSM/100878/2008

2008/2014: Genetics of alcohol - a study of polymorphisms. APEF/Schering-Plough Farma Funding. Coordinators: Helena Cortez Pinto and Gabriel Miltenberger-Miltenyi

#### **Publications in peer review Journals**

van der Zee J, Dillen L, Deschamps W, Van Langenhove T, Engelborghs S, Vandenbulcke M, Dermaut B, Sieben A, Smets K, Van Damme P, Merlin C, Laureys A, Van Den Broeck M, Mattheijssens M, Peeters K, Benussi L, Binetti G, Ghidoni R, Borroni B, Padovani A, Archetti S, Pastor P, Razquin C, Ortega-Cubero S, Hernández I, Boada M, Ruiz A, de Mendonça A, Miltenberger-Miltenyi G, do Couto FS, Sorbi S, Nacmias B, Bagnoli S, Graff C, Chiang HH, Thonberg H, Pernecky R, Diehl-Schmid J, Alexopoulos P, Frisoni GB, Bonvicini C, Synofzik M, Maetzler W, Müller vom Hagen J, Schöls L, Haack TB, Strom TM, Prokisch H, Dols-Icardo O, Clarimón J, Lleó A, Santana I, Almeida MR, Santiago B, Heneka MT, Jessen F, Ramirez A, Sanchez-Valle R, Llado A, Gelpi E, Sarafov S, Tournev I, Jordanova A, Matej R, Parobkova E, Fabrizi GM, Testi S, Salmon E, Kovacs GG, Ströbel T, Santens P, Robberecht W, De Jonghe P, Martin JJ, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Van Broeckhoven C, on behalf of the BELNEU consortium and of the EU EOD consortium (2014) Rare mutations in SQSTM1 modify susceptibility to frontotemporal lobar degeneration. *Acta Neuropathol.* **128**(3):397-410. (citations: 1)



Machado MV, Janeiro A, Miltenberger-Miltenyi G, Cortez-Pinto H (2014) Genetic polymorphisms of proangiogenic factors seem to favor hepatocellular carcinoma development in alcoholic cirrhosis. *Eur J Gastroenterol Hepatol*. **26**(4):438-43.

Madruga Dias J, Rosa R, Perpétuo I, Rodrigues A, Janeiro A, Costa MM, Gaião L, Pereira da Silva J, Fonseca JE, Miltenberger-Miltenyi G (2014) Pachydermoperiostosis in an African patient caused by a Chinese/Japanese SLCO2A1 mutation – case report and review of literature. *Seminars in Arthritis and Rheumatism*. **43**(4):566-9.

#### **Other publications National**

Brito D, Miltenberger-Miltenyi G, Moldovan O, Navarro C, Madeira HC. (2014) Cardiac Anderson-Fabry Disease: lessons from a 25-year follow up of a patient. *Rev Port Cardiol*. **33**(4):247.e1-7

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

Miltenberger-Miltenyi, G. Genética de demências. Mesa redonda “Doença de Alzheimer Prodrómica”. Congresso de Sociedade Portuguesa de Neurologia, Lisbon, Portugal, November 12 - 15, 2014.

Santos S. Citogenética convencional, Síndromes Mielodisplásicas (SMD), Abordagem integrada da patologia. Faculdade de Medicina da Universidade de Lisboa, Edifício Egas Moniz, Lisbon, Portugal, October 25, 2014.

Miltenberger-Miltenyi, G. Caracterização genética do síndrome nefrótico cortico-resistente. Encontro Renal, Congress of the Portuguese Society of Nephrology, Vilamoura, Portugal, April 10, 2014.

Matos S, Ferreira AR, Mimoso P, Malveiro S, Guerra L, Polo B, Neves M, Valle S, Lopes C, Conde I, Espada E, Alves D, Raposo J, Alves do Carmo J. Resposta molecular precoce à terapêutica com Inibidores Tirosina Cinase em doentes com LMC fase crónica *de novo* – experiência de um centro. Reunião Anual da Sociedade Portuguesa de Hematologia, Évora, Portugal, November 20-22, 2014 (Poster presentation)

Oliveira Ramos F, Conde M, Martins FM, Marques JG, Esteves I, Sousa AB, Miltenberger-Miltenyi G, Henriques C, Farela Neves J, Cordeiro-Ferreira G, Pereira da Silva JA, Fonseca JE, Canhão H. Auto-inflammatory diseases register :data from the newest Reuma.pt protocol. XVII Congresso Português de Reumatologia. CS Palácio de Congressos do Algarve, Albufeira, Portugal, May, 07-10, 2014 (Poster presentation)

Martins AF, Martins JM, Vale S, Gomes AR, Miltenberger-Miltenyi G. A new mutation in thyroid hormone resistance. Congresso Português de Endocrinologia, Vilamoura, Portugal, January, 24-26, 2014 (Poster presentation)

Martins AF, Martins JM, Vale S, Gomes AR, Dias T, Miltenberger-Miltenyi G. Atypical presentation of multiple endocrine neoplasia with a new RET gene mutation. Congresso Português de Endocrinologia, Vilamoura, Portugal, January 24-26,2014 (Poster presentation)

#### **Advanced teaching**

Miltenberger-Miltenyi, G. Human genetics and bone diseases. Seminars in Masters in Biomedical Sciences (Formação avançada); University of Algarve, Faro, Portugal, January 29, 2014.

Miltenberger-Miltenyi, G. Cerebrospinal fluid biomarkers. Master/PhD in Neuroscience Symposium: Biomarkers for Alzheimer's disease. Lisbon, April 9, 2014.

## Technophage, SA

### Major interests / Objectives

TechnoPhage, SA ([www.technophage.pt](http://www.technophage.pt)) is a private Portuguese multiplatform biotech company involved in the R&D of new molecules (chemicals and biologicals) in diverse therapeutic areas, such as inflammation, metabolic, musculoskeletal, neurology, infection and rare disorders. TechnoPhage, SA continuously strives to increase the number of proprietary technologies and derived products, through an active R&D program and collaboration agreements with national and international pharmaceutical companies, research centers and academia.

The overall strategy of TechnoPhage, SA is to generate novel therapeutics and diagnostics in early phases of development and later on enter into partnering deal for pre-clinical or clinical development or both.

### Head of Unit

Miguel Garcia, PharmD, PhD, MBA, TechnoPhage, SA

### Team

Ana Raquel Martins Barbosa	MSc	Scientist
Cátia Cascão	Graduate	MSc Student
Clara Isabel Rodrigues Leandro	MSc	Senior Scientist
Daniela Sofia Moreira Proença	MSc	PhD Student
Diana Sofia Chapela Duarte Pires	MSc	Technician
Joana Henriques Ministro	MSc	PhD Student
João João Duarte Alves Mendes	Graduate	PhD Student
João Miguel Sotinho Oliveira	PharmD	Project Coordinator
Mariana Lima de Faria Trigo Pereira	Master	R&D Funding and Financial Manager
Miguel Ângelo da Costa Garcia	PharmD, PhD, MBA	CEO
Nuno Miguel Duarte Afonso	PhD	Corporate Development Director

Patricia Alexandra Norte Ferreira Pinto	No degree	Technician
Pedro Manuel Correia Canhão	MSc	Scientist Trainee
Peter Vanlandschoot	PhD	Chief Scientific Officer
Rita Leitão Landeiro Vaz	MSc	PhD Student
Sara Cristina Mauricio de Sousa	PhD	Senior Scientist
Sara Ferreira Llorente Grancho Lourenço	MSc	Scientist
Sofia Volker Corte-Real	PhD	R&D 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 achievements

In 2014, TechnoPhage, SA has attained a major milestone in Drug Discovery and Development. The company received authorization from U.S. Food and Drug Administration (FDA) for its Investigational New Drug (IND) application for TP-102, a bacteriophage cocktail for the treatment of infected chronic ulcers, namely diabetic foot infections. This authorization created the required regulatory ground to run clinical trials of Phase I.

Also, TechnoPhage has obtained from Portuguese Science Funding Agency (FCT) the highest rank in previous evaluations for PhD students at the company. The company has had during almost 10 years of existence, 4 PhD students with FCT PhD grants, including two who already attained successfully the objectives of their PhD research projects (1 defense in 2014, 1 defense in 2015).

#### Selected Publications

J Oliveira, C Zagalo, P Cavaco-Silva. *Prevention of ventilator-associated pneumonia. Rev Port Pneumol.* 2014; **20**(3): 152-61.

JJ Mendes, C Leando, C Mottola, R Barbosa, FA Silva, M Oliveira, CL Vilela, J Melo-Cristino, A Górski, M Pimentel, C São-José, P Cavaco-Silva, M Garcia. *In vitro design of a novel lytic bacteriophage cocktail with therapeutic potential against organisms causing diabetic foot infections. Journal of Medical Microbiology* (2014), **63**, 1055–65.

D Proença, C Velours, M Garcia, M Pimentel, C São-José. *A two-component, multimeric endolysin encoded by a single gene. Mol Microbiol.* 2015 Mar; **95**(5):739-53. doi: 10.1111/mmi.12857. Epub 2014 Dec 8.

#### **Ongoing Research Projects**

Current projects are focused in inflammatory, metabolic, musculoskeletal, neurological, infectious and rare diseases.

#### **Internationalization**

TechnoPhage, SA and SIMM have signed on 14th May 2014 a new R&D program to develop TA-141, an anti-IL6R antibody, for the treatment of inflammatory and autoimmune diseases.

A Collaboration Agreement relating to the development of new therapeutics directed at ageing-related diseases has subsequently been signed on 18th May 2014 between TechnoPhage, SA and University of Macau.

#### **Patents/prototypes**

2 patents granted in the areas of single domain antibodies and bacteriophages.

#### **Industry contract research**

TechnoPhage, SA has successfully partnered with several pharmaceutical companies including the top Portuguese pharmaceutical companies.

#### **PhD thesis completed**

The first study leading to a PhD in Medicine in bacteriophage therapy field at TechnoPhage, SA was concluded in 2014:

Name: João João Mendes

Date of defense: 4<sup>th</sup> of November

Title: Topical bacteriophage therapy of the infected diabetic foot

University: Faculty of Medicine, University of Lisbon

Supervisor: Professor José Melo Cristino

Co-supervisor: Professor Andrzej Górski and Professor Patrícia Cavaco Silva

## **TCLab – Tecnologias Celulares para Aplicação Médica**

### **Major interests / Objectives**

TCLab is a spin-off biotechnology company of IMM, created in 2012 and headquartered in the Department of Veterinary Medicine from the University of Évora. The company assumes research and development of human induced pluripotent stem cells (hiPSCs) as a primordial aim, as well as rendering specialized consulting services.

Due to their large differentiation potential, hiPSCs may provide access to cellular models of disease either to study the mechanisms of disease or to test drugs for efficacy and safety. Moreover, because hiPSCs contain the genetic makeup of the individual patients, these cells represent a valuable tool for pharmacogenetics and personalized medicine.

### **Head of Unit**

Filipa Nunes, PharmD, PhD – Chief Scientific Officer

### **Team**

Andreia Matos	MSc	Research Technician
Laura Felício	MSc	Lab Technician (left in November 2014)
Alexandra Maralhas	BSc	Consultant Lab Manager

### **Keywords/Research Areas**

Human induced pluripotent stem cells; disease modelling; primary cultures of human fibroblasts

### **Major achievements**

Certification by TÜV Rheinland Portugal, in Research, Development and Innovation NP 4457:2007 - Research, Development and Innovation in Cellular Technologies: Cellular Reprogramming and Human Primary Cultures.

Certification of the Integrated Management Systems (IMS), by TÜV Rheinland Portugal - NP EN ISO 9001:2008, NP EN ISO 14001:2012 and OHSAS 18001:2007 - Specialized services in laboratory techniques and management.

Participation in the PhD Programme entitled “Cell Therapies and Regenerative Medicine”, funded by the Fundação para a Ciência e Tecnologia (FCT), coordinated by IST/IBB, and with the participation of IMM, CEDOC and IBET.

Conclusion of the QREN project aimed at the development of an optimized protocol for the establishment of fibroblast culture from human skin biopsy and subsequent reprogramming into hiPSCs (2012/2014 Núcleo para Investigação e Desenvolvimento de meios de cultura para reprogramação e diferenciação de iPSCs, Sistema de Incentivos à *Investigação e Desenvolvimento Tecnológico Núcleos de I&DT – FEDER/QREN/PORAlentejo*).

Consolidation of a second project funded by QREN dedicated to the exploration of potential markets, and internationalization of the company and its products/services.

Implementation of Laboratory Safety Guidelines and elaboration of risk assessment studies in the Quality laboratories at Siderurgia Nacional, Seixal.

#### **Ongoing Projects**

2013/2015 Plano Estratégico de Valorização, Crescimento e Internacionalização, Sistema de Incentivos à Qualificação e Internacionalização de PME – FEDER/QREN/PORAlentejo.

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

Matos, A. The Portuguese Way to Induced Pluripotency. InTeraQB SunSet Session, ITQB, Oeiras, Portugal, January 20, 2014.

Nunes, F. New tools for disease research: reprogrammed cells in disease modeling. Stem Cells Bioengineering Curricular Unit of the Integrated Master in Biomedical Engineering, IST, Lisbon, Portugal, May 15, 2014.

#### **Advanced teaching**

Nunes, F. lectured a seminar integrated in the Stem Cells Bioengineering Curricular Unit of the Integrated Master in Biomedical Engineering, IST, Lisbon, Portugal, May 15, 2014.

## **Lymphact S.A**

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 of Unit**

Diogo R. Anjos, MBA – CEO, Lymphact S.A.

### **Research Team**

Afonso Almeida	PhD	Senior Scientist
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### **Keywords/Research Areas**

Cellular Therapies, Immunology, Oncology, Immunotherapies, Start-up, Business Development

### **Major achievements**

Successfully completed all agreed project milestones

Hired a Senior Scientist (team increased)

Increased the project management team

Assembled a world class scientific council

### **Ongoing Research Projects**

Proprietary Research



**Patents/prototypes**

Proprietary Patent- PCT IB2012/052545

**Industry contract research**

Pre-clinical and clinical consultancy from Parexel International



