



**INSTITUTO DE  
MEDICINA MOLECULAR**  
FACULDADE DE MEDICINA DA  
UNIVERSIDADE DE LISBOA



## **2013 ACTIVITY REPORT**

April 9<sup>th</sup>, 2014



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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.

João Lobo Antunes, MD, PhD (President)  
 Maria Carmo-Fonseca, MD, PhD (Executive Director)  
 Joaquim Alexandre Ribeiro, MD, PhD (Vice-President)

### 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 Committees**

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

***Cell and Developmental Biology Programme – 2013***

John G Gribben, Queen Mary's School of Medicine, University of London, UK

Petra Schwillie, Max-Planck-Institute of Biochemistry, Germany

Phillippe Pierre, Centre d'Immunologie de Marseille-Luminy, France

Fiona Watt, King's College London, UK

***Neurosciences Programme – 2010***

Michael Spyer, University College London, UK

Christine Gall, University of California, USA

Charles Warlow, Western General Hospital, Edinburgh, UK

Reinhard Dengler, Medizinische Hochschule, Hannover, Germany

***Immunology and Infectious Diseases Programme – 2009***

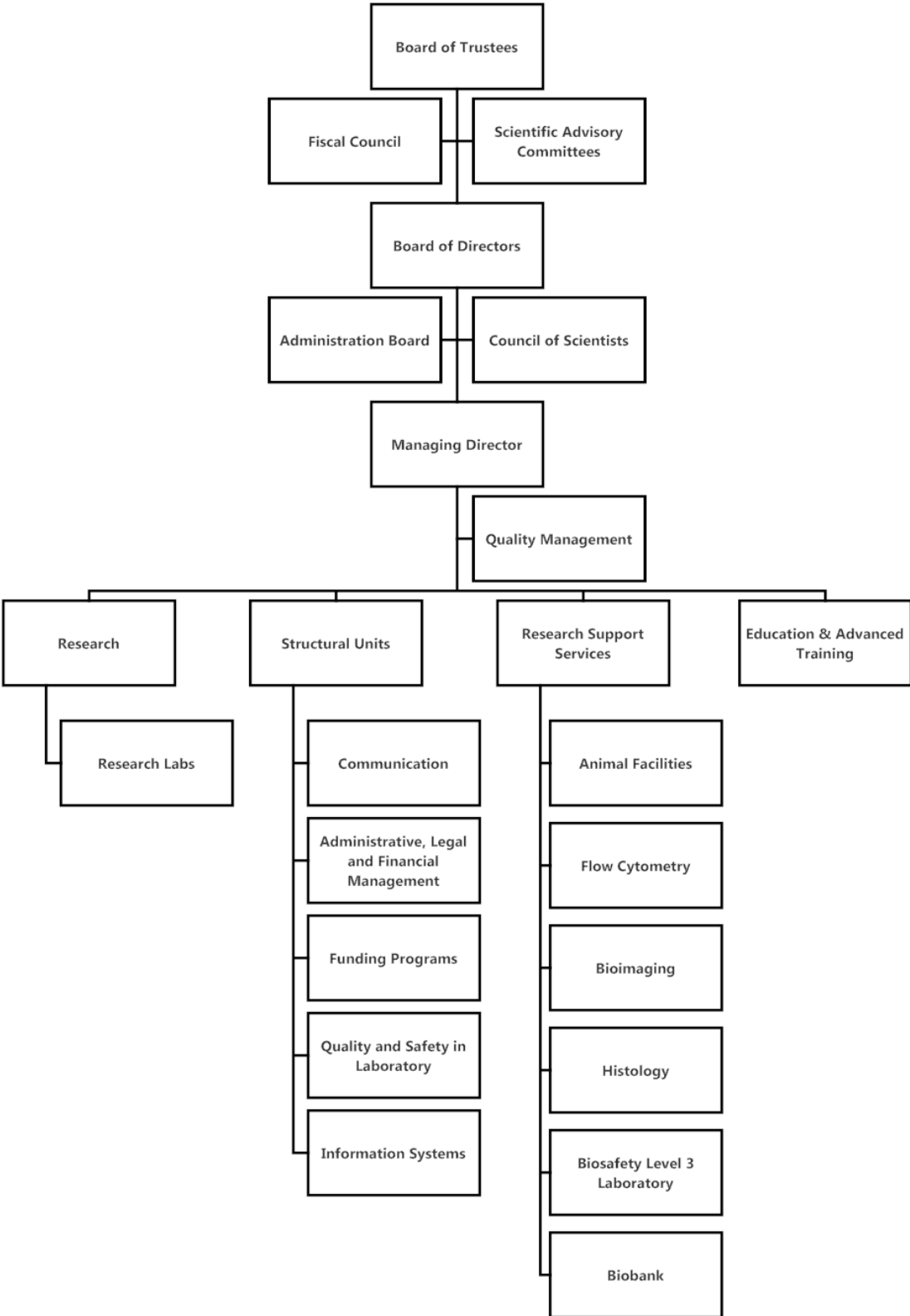
Anne O'Garra, National Institute for Medical Research, UK

Alain Fischer, Hôpital Necker Enfants Malade, Paris, France

William Paul, National Institute of Allergy and Infectious Diseases, NIH, USA

Philippe Sansonetti, Institut Pasteur, France

Antonio Freitas, Institut Pasteur, France



## EVALUATION REPORTS 2013

### Summary of Review Report of the Cell and Developmental Biology Scientific Advisory Committee (SAC) 2013

**Period of evaluation:** 2006-2013

**Scientific Advisory Board members:**

John G Gribben, Queen Mary's School of Medicine, University of London, UK;

Petra Schwille, Max-Planck-Institute of Biochemistry, Germany;

Phillippe Pierre, Centre d'Immunologie de Marseille-Luminy, France;

Fiona Watt, King's College London, UK.

**Summary of the panel's overview:**

The Board were welcomed to the Institute and provided with an overview by the Institute Director. This was followed by presentations by the Heads of Units and PIs. Finally, the SAC were given the opportunity to meet with the post-doctoral fellows and students.

Overall, the SAC were impressed by the work presented. A general comment would be that most presenters exceeded their allocated time slots for presentation, leaving less time for questions and answers, which all of the SAC felt would have been more beneficial.

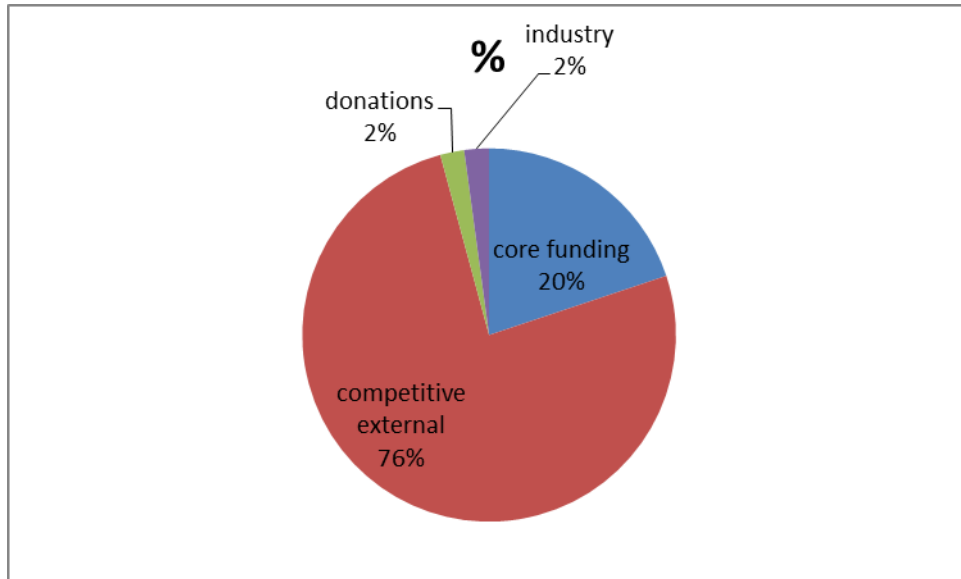
With notable exceptions, there was less evidence of collaborative interactions among the units than we would have liked to see and there was little evidence that the Group Leaders had seen or contributed to each other's talks. The students also commented that they felt they worked for individual labs, rather than as part of a larger unit, thereby missing the opportunity that that whole could be more than its individual parts. There is therefore considerable scope for increasing synergistic activity within the Institute, which would be beneficial to all groups.



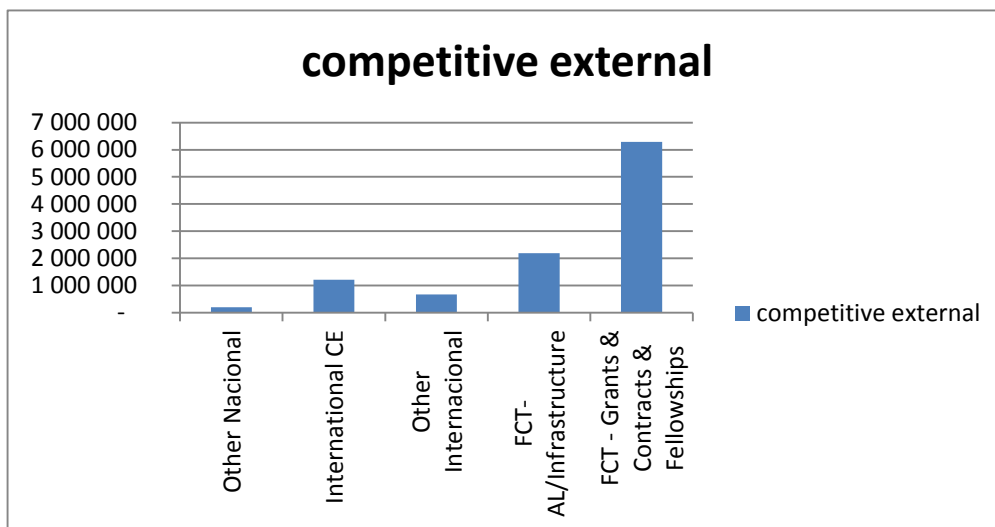
## RESEARCH FUNDING

### Expenditure in 2013 by Funding Source

**Total expenditure:** €13.925.388,00



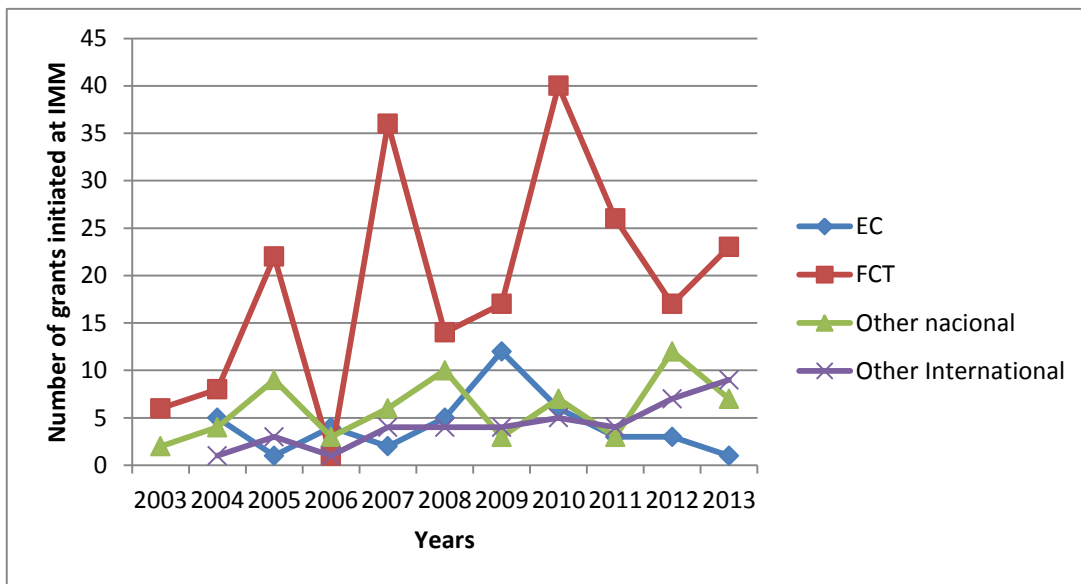
**Competitive external:** €10.573.698,00



### Number of Ongoing Research Grants in 2013

285 Research Grants  
 - 105 Public National FCT  
 - 15 Public Other National  
 - 17 Public European Commission  
 - 0 Public Other International  
 - 111 Private National  
 - 37 Private International

### Number of Research Grants Initiated at IMM from 2003 to 2013



### Research Funding Initiated in 2013

#### Research Grants (39)

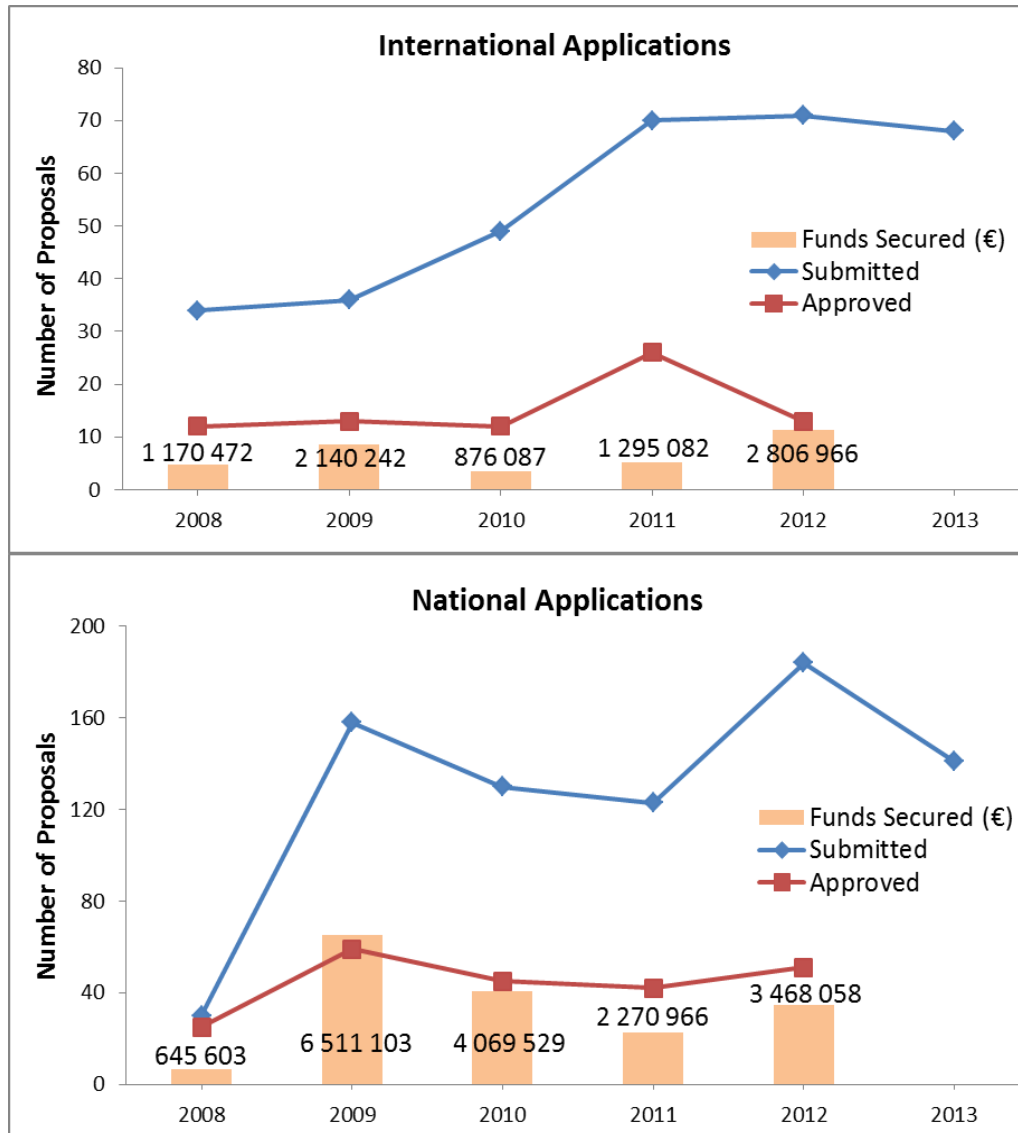
- 1 European Commission
- 9 Other International
- 22 FCT
- 7 Other National

Agency	IMM Budget (euros)	PI - IMM
AXA Research Fund	120 000,00	Luís Figueiredo
Bill and Melinda Gates Foundation	76 260,20	Kirsten Hanson
Bill and Melinda Gates Foundation	890 693,42	Miguel Prudêncio
Cardlane	33 044,00	Ana Maria Sebastião
Congrex Schweiz AG	155 000,00	José Manuel M Cabral Ferro
European Comission	666 969,80	João Rodrigues
Fundação Calouste Gulbenkian	100 000,00	Ana E. Sousa
Fundação para a Ciência e a Tecnologia/Competências	498 665,00	Joana Marques
Fundação para a Ciência e a Tecnologia	11 237,00	Joaquim Ferreira
Fundação para a Ciência e a Tecnologia	12 100,00	Maria Carlota Saldanha Lopes
Fundação para a Ciência e a Tecnologia	26 095,14	Rita Cruz Coelho Ramalho
Fundação para a Ciência e a Tecnologia	33 000,00	Luís Costa
Fundação para a Ciência e a Tecnologia	33 246,00	Ana Sofia Oliveira
Fundação para a Ciência e a Tecnologia/Harvard	35 000,00	Helena Maria Cortez Pinto
Fundação para a Ciência e a Tecnologia	43 804,75	Sérgio Jerónimo Rodrigues Dias
Fundação para a Ciência e a Tecnologia	44 602,72	Sérgio Jerónimo Rodrigues Dias
Fundação para a Ciência e a Tecnologia	49 967,00	Hugo Miguel Vicente Miranda
Fundação para a Ciência e a Tecnologia	50 000,00	Bruno Silva Santos
Fundação para a Ciência e a Tecnologia	73 536,00	Tânia Barão
Fundação para a Ciência e a Tecnologia	125 797,00	Joao Pedro Taborda Barata
Fundação para a Ciência e a Tecnologia	145 001,00	Rui Victorino
Fundação para a Ciência e a Tecnologia	168 637,00	Ghislain Cabal
Fundação para a Ciência e a Tecnologia	171 958,00	Gabriel Miltenyi
Fundação para a Ciência e a Tecnologia	174 533,00	José Augusto G Melo Cristino
Fundação para a Ciência e a Tecnologia	181 199,00	Maria Leonor Tavares Saúde
Fundação para a Ciência e a Tecnologia	184 516,00	Sérgio Almeida
Fundação para a Ciência e a Tecnologia/ANR	250 000,00	Henrique Veiga Fernandes
Fundação para a Ciência e a Tecnologia/Harvard	293 513,00	João Lacerda
Fundação para a Ciência e a Tecnologia/Excelência	331 463,00	Maria Mota
Gilead	14 500,00	Ana E. Sousa
Institut de Recherches Servier	25 000,00	Maria Carmo Fonseca
Kenneth Rainin Foundation	72 632,19	Henrique Veiga Fernandes
Merck Sharp & Dohme	144 350,00	João Eurico Fonseca
Merck, S.A.	24 000,00	Luís Costa
Novartis Farma, S.A.	10 000,00	Sandra Casimiro
Pfizer	60 000,00	João Eurico Fonseca
Pfizer, Bayer, Eisai Farmaceutica, Celgene, Bristol Myers, Glaxosmith, MSD, Astrazeneca, Roche, Fundação para a Ciência e a Tecnologia	69 900,00	Luís Costa
Steris Corporation	12 980,00	Thomas Hanscheid
Tourette Syndrome Association, Inc	56 078,96	Tiago Maia

### Protocols, Donations & Awards (26)

Agency	IMM Budget (euros)	PI - IMM
AMC Medical Research B.V.	750,00	Patrícia Canhão
Angelini Farmacêutica	650,00	Mamede de Carvalho
Astrazeneca	3 750,00	Luís Costa
Banco Espírito Santo	50 000,00	Miguel Prudêncio
BIAL	3 500,00	Ana Verdelho
Celgene Sociedade Unip., Lda.	4 000,00	Luís Costa
Ciência Viva	1 591,01	vários
ECBio, S.A.	111 100,00	Susana Constantino
EMBO	14 500,00	Bruno Silva Santos
Faculdade de Ciências e Tecnologia	2 500,00	Mário Ramirez
FLAD	800,00	Bruno Silva Santos
Fundação para a Ciência e a Tecnologia	4 500,00	Francisco Enguita
Fundação para a Ciência e a Tecnologia	750,00	Miguel Prudêncio
Fundação para a Ciência e a Tecnologia	600,00	Bruno Silva Santos
Fundação para a Ciência e a Tecnologia	5 400,00	Maria Carmo Fonseca
Grunenthal S.A.	10 000,00	Joaquim Ferreira
Hospital Santa Maria	22 500,00	Isabel Pavão Martins
Laço Associação de Solidariedade Social	25 000,00	Sérgio Jerónimo Rodrigues Dias
Linde Portugal	6 000,00	Mamede de Carvalho
L'OREAL	20 000,00	Maria Leonor Tavares Saúde
NEDAI	10 000,00	Ana Sofia Oliveira
Soc. Port. Gastroenterologia	2 500,00	Helena Maria Cortez Pinto
Tecnifar	5 000,00	Carla Bentes
Teva Pharma, Lda.	10 000,00	Joaquim Ferreira
The Board of Trustees of the University of Alabama	4 982,30	Luís Moita
University of Belgrade - Faculty of Chemistry	4 961,00	Miguel Prudêncio

### Number of Applications and Funding Secured from 2008 to 2013



**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 (researchers are not obliged to inform the Office when they submit a grant, thus these data may underestimate the real number of IMM submissions). Funds secured correspond to the sum of the IMM budget of the approved grants in the corresponding year. Note that the national applications graph contains data from one FCT call per year since 2009, despite the 2008 and 2009 deadlines were both in 2009. The total funding secured by the IMM (international and national) was €1.815.000 in 2008, €8.651.000 in 2009, €4.945.000 in 2010, €3.566.000 in 2011, and €6.275.000 in 2012 (still unknown regarding 2013 submissions).

## 2013 IMM ACTIVITIES HIGHLIGHTS

### People at IMM in 2013

Researchers	PhD Researchers	217
	PhD Students	83
	M.Sc Students	43
	Bachelor Students	114
	<b>Total Researchers</b>	<b>457</b>
Technical Staff	PhD Staff	7
	M.Sc Staff	19
	Bachelor Staff	41
	Non-Bachelor Staff	14
	<b>Total Technical Staff</b>	<b>81</b>
Administrative Staff	PhD Staff	2
	M.Sc Staff	2
	Bachelor Staff	21
	Non-Bachelor Staff	5
	<b>Total Administrative Staff</b>	<b>30</b>
People at IMM in 2013		568

### Selection of Prizes and Awards

#### **Prémio D. Antónia Adelaide Ferreira**

*Prize awarded for distinction of a personality by his entrepreneurial spirit, leadership, openness to innovation and creativity, sense of public service and social sensitivity*

Maria Carmo-Fonseca

#### **Prémio Pessoa 2013**

*Prize that aims to highlight personalities of Culture, Arts or Science whose work has achieved featured on national scene*

Maria Manuel Mota

#### **L'Oréal Portugal Award**

*Prize aimed at young researchers (under 35) who completed their doctoral studies and work in Portugal in the health and environmental areas*

Ana Catarina Ribeiro

#### **Prémio Nacional de Inovação BES 2013**

*National Innovation Prize to reward and divulge research, development and innovation projects in application areas linked to the endogenous resources of the country, viewing the improvement of products, processes or services*

Miguel Prudêncio

**Innovator Award of the Kenneth Rainin Foundation (KRF)**

*This award represents a Kenneth Rainin Foundation investment in groundbreaking and collaborative ideas that have the potential to yield transformative discoveries and major new insights into the causes and cures for Inflammatory Bowel Disease.*

Henrique Veiga-Fernandes

**Grant Ciência Sem Fronteiras**

*The Ciência Sem Fronteiras (Science Without Borders) Program is a Brazilian program that seeks to promote the consolidation, expansion and internationalisation of science and technology, innovation and competitiveness through the exchange and international mobility.*

Miguel Castanho

**1<sup>st</sup> Research Grant on Breast Cancer – Laço**

*Laço Associação de Solidariedade Social supports scientists working in Portugal to develop basic science research projects looking into the causes of breast cancer and metastatic breast cancer with an annual grant of 25.000€.*

Sérgio Dias

**Prémio Pfizer 2013**

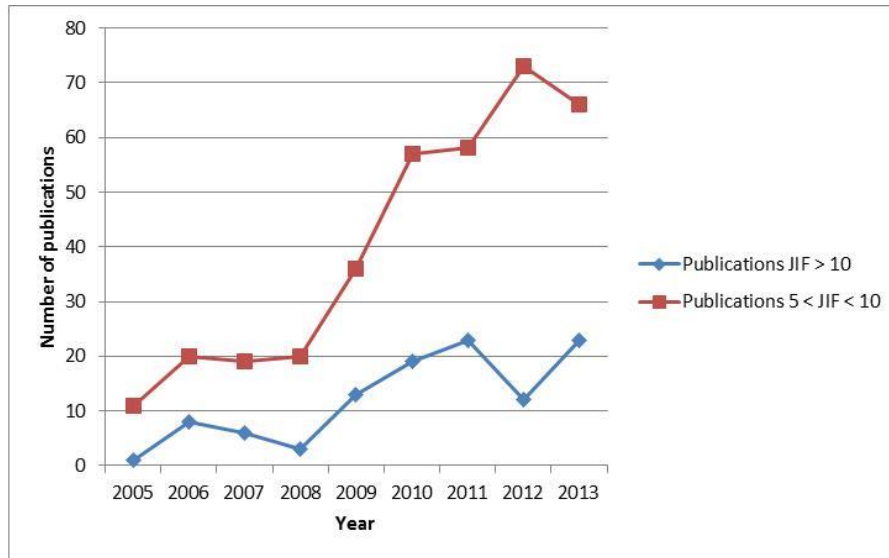
*This Prize aims to stimulate research in Health Sciences in Portugal.*

Luís Moita

**Productivity at a glance**

Publications International Journals	305
...in journals with an impact factor higher than 10	23
...in journals with an impact factor between 5 – 10	66
Book/Book Chapters International	20
Communications in International Conferences	352
Communications in National Conferences	231
Seminars and Invited Lectures	380
Organization of Conferences	64
Prizes	63
PhD Theses	10
Master Theses	50

### IMM Publications in International Journals

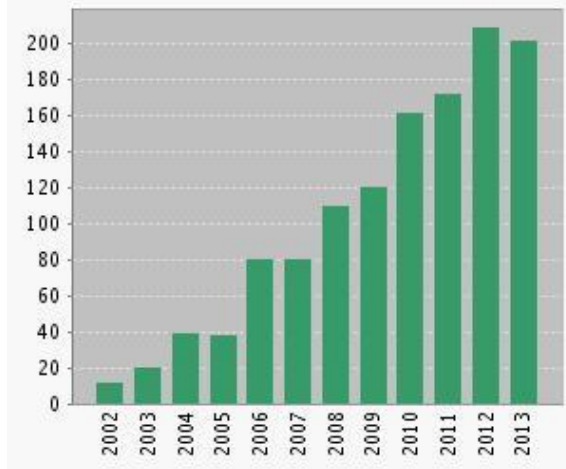


JIF = Journal Impact Factor

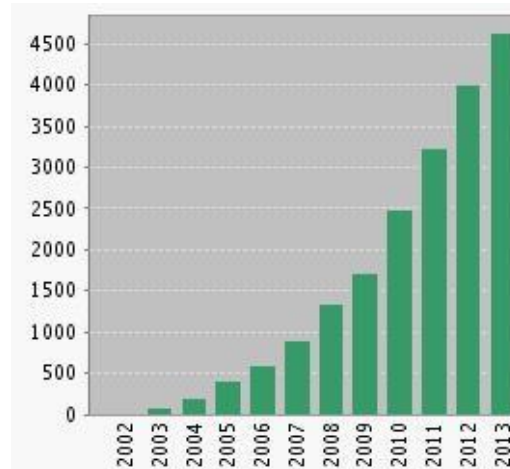
### Citation Report

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

#### Published papers in each year



#### Citations in each year



**202** papers in 2013

**1251** since 2002

Sum of the Times Cited: **20233**

Average Citations per Item: **16.17**

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: Document Type=( ARTICLE OR REVIEW)

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



**Most Relevant papers 2013 (Journal IF > 10)**

Melo-Cristino J., C. Resina, V. Manuel, L. Lito, M. Ramirez. (2013) First case of infection with vancomycin-resistant *Staphylococcus aureus* in Europe. *The Lancet*. **382**,205. <http://www.ncbi.nlm.nih.gov/pubmed/23791472>. (Journal IF: 39.060, Citations 1)

Amaral M, Levy C, Heyes DJ, Lafite P, Outeiro TF, Giorgini F, Leys D, Scrutton NS (2013) Structural basis of kynurenine 3-monooxygenase inhibition. *Nature* **496**, (7445), 382-5 (Journal IF: 38.597, Citations: 2)

Plenge RM, Greenberg JD, Mangravite LM, Derry JM, Stahl EA, Coenen MJ, Barton A, Padyukov L, Klareskog L, Gregersen PK, Mariette X, Moreland LW, Bridges SL Jr, de Vries N, Huizinga TW, Guchelaar HJ; International Rheumatoid Arthritis Consortium (INTERACT), Friend SH, Stolovitzky G. Collaborators: Cui J, Stahl EA, Saevarsdottir S, Miceli C, Diogo D, Mirkov, Canhao H, Ikari K, Terao C, Okada Y, Wedri S, Askling J, Yamanaka H, Momohara S, Taniguchi A, Ohmura K, Matsuda F, Mimori T, Gupta N, Kuchroo M, Morgan AW, Isaacs JD, Wilson AG, Hyrich KL, Herenius M, Doorenspleet ME, Tak PP, Crusius JB, van der Horst-Bruinsma IE, Wolbink GJ, van Riel PL, van de Laar M, Guchelaar HJ, Shadick NA, Allaart CF, Huizinga TW, Toes RE, Kimberly RP, Bridges S Jr, Criswell LA, Moreland LW, Fonseca E, de Vries N, Raychaudhuri S, Weinblatt ME, Gregersen PK, Mariette X, Barton A, Alfredsson L, Klareskog L, Padyukov L, Coenen MJ, Karlson EW, Kremer J, Greenberg JD, Plenge RM. (2013) Crowdsourcing genetic prediction of clinical utility in the Rheumatoid Arthritis Responder Challenge. *Nat Genet*. **45**, (5):468-9. (Journal IF: 35.209, Citations: 1)

Stephanie Fanucchi, Youtaro Shibayama, Shaun Burd, Marc S Weinberg, Musa M Mhlanga (2013) Chromosomal Contact Permits Transcription between Coregulated Genes. *Cell* **155**, 505 [www.cell.com](http://www.cell.com). (Journal IF: 34.366, Citations: 1)

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. *Nat Med* **20**(1), 47-53. doi: 10.1038/nm.3424. Epub 2013 Dec 22. PMID: 24362933. (Journal IF: 27.14, Citations: 1)

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 gd T cell subsets. *Nature Immunology*. **14**, 1093. (Journal IF: 26.199, Citations: 0)

Turner MR, Hardiman O, Benatar M, Brooks BR, Chio A, de Carvalho M, Ince PG, Lin C, Miller RG, Mitsumoto H, Nicholson G, Ravits J, Shaw PJ, Swash M, Talbot K, Traynor BJ Van den Berg LH, Veldink JH, Vucic S, Kiernan MC (2013) Controversies and priorities in amyotrophic lateral sclerosis research. *Lancet Neurol* **12**, 310-322. (Journal IF: 23.917, Citations: 34).

Ederle J, Davagnanam I, van der Worp HB, Venables GS, Lyrer PA, Featherstone RL, Brown MM, Jäger HR; ICSS investigators. Effect of white-matter lesions on the risk of periprocedural stroke after carotid artery stenting versus endarterectomy in the International Carotid Stenting Study

(ICSS): a prespecified analysis of data from a randomised trial. *The Lancet Neurology* 2013; **12**, 866-872. (Journal IF: 23.917, Citations: 3)

Nuno Figueiredo, Angelo Chora, Helena Raquel, Nadja Pejanovic, Pedro Pereira, Björn Hartleben, Ana Neves-Costa, Catarina Moita, Dora Pedroso, Andreia Pinto, Sofia Marques, Hafeez Faridi, Paulo Costa, Raffaella Gozzelino, Jimmy L. Zhao, Miguel P. Soares, Margarida Gama-Carvalho, Jennifer Martinez, Qingshuo Zhang, Gerd Döring, Markus Grompe, J. Pedro Simas, Tobias B. Huber, David Baltimore, Vineet Gupta, Douglas R. Green, João A. Ferreira and Luis F. Moita. Anthracyclines induce DNA damage response-mediated protection against severe sepsis. *Immunity* November 14, 2013. **39**(5), 874-84 (Journal IF: 19.795; Citations: 2)

Dalziel, SR , Thompson, JMD, Macias, CG, Fernandes RM.,Johnson, DW, Waisman, Y, Cheng, N, Acworth, J, Chamberlain, JM, Osmond, MH,Group Author(s): Pediat Emergency Res, Networks PERN, (2013) Predictors of severe H1N1 infection in children presenting within Pediatric Emergency Research Networks (PERN): retrospective case-control study. *British Medical Journal* 347Article Number f4836 (Journal IF: 17.215, Citations: 1)

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(Total: 314)

## Seminars and Workshops

### IMM Seminars

07-01-2013

**Margarida Amaral**, FCUL

*Translating post-genomic knowledge into medicine: the model of Cystic Fibrosis*

Host: Domingos Henrique

14-01-2013

**Luis Pereira Almeida**, Center for Neurosciences and Cell Biology

*From mechanism to therapy of Machado-Joseph disease*

Host: Domingos Henrique

28-01-2013

**Arturo Zychlinsky**, Director of Max Planck Institute for Infection Biology, Berlin

*Host-parasite interactions in acute inflammatory intestinal diseases caused by the Gram negative bacterium Shigella*

Host: Maria Mota

04-02-2013

**Georg Schett**, Friedrich-Alexander University Erlangen-Nuremberg

*Bone as a clue to the pathogenesis of rheumatoid arthritis*

Host: João Eurico Fonseca

18-02-2013

**Shalini Oberdoerffer**, National Cancer Institute, NIH, Frederick, USA

*Chromatin Biology & RNA processing*

Host: Luis Moita, Carmo Fonseca, Sérgio de Almeida

25-02-2013

**Ana Luisa Carvalho**, Center for Neurosciences and Cell Biology

*Synaptic molecules & synapse connectivity*

Host: Ana Sebastião

11-03-2013

**Miguel Soares**, IGC Oeiras

*The Gasotransmitter Carbon Monoxide in Health and Disease*

Host: Domingos Henrique

18-03-2013

**Florence Apparilly**, INSERM, Institute Neurosciences Montpellier, University hospital, Montpellier

*Role of Ly6Chigh monocytes in inflammation: microRNAs as novel molecular targets for innovative immuno-intervention in arthritis*

Host: João Eurico Fonseca

25-03-2013

**Christian Machens**, Champ. Neuroscience Program

*Dynamics of the oculomotor integrator revealed by instantaneous optogenetic perturbations*

Host: Luisa Lopes

08-04-2013

**Austin Smith**, Cambridge, UK

*One of the leaders in Stem Cell biology*

Host: Domingos Henrique

15-04-2013

**Jeremy Henley**, Professor of Molecular Neuroscience, MRC Center for synaptic Plasticity, University of Bristol, UK

*Plasticity, death and SUMOylation*

Host: Ana Sebastião

22-04-2013

**Narla Mohandas**, Vice President for Research and Head, Red Cell Physiology Laboratory, NY Blood center, New York, USA

*Red Cell membrane structure and function: new insights into various human hematological and non-hematological disorders*

Host: Carlota Saldanha

29-04-2013

**Professor William Harris**, Head of Department of Physiology, Development and Neuroscience, University of Cambridge, UK

*Development, visual system, genetic disorders, cell determination*

Host: Alexandra Rosa

06-05-2013

**Sarah Teichmann, PhD**, MRC Programme Leader in Genome Evolution, MRC Laboratory of Molecular Biology, Cambridge, UK and Fellow, Trinity College, Cambridge, UK

*Decoding genetic switches in T helper cell differentiation*

Host: Domingos Henrique

13-05-2013

**Wolfgang Huber, PhD**, Group Leader and Senior Scientist, Computational biology and genomics, European Molecular Biology Laboratory, Germany

*I. Tissue dependent alternative exon usage II. Systematic mapping of synthetic genetic interactions with combinatorial RNAi*

Host: Andreia Amaral

27-05-2013

**Christine Van Broeckhoven PhD DSc**, Neurodegenerative Brain Diseases Group Department of Molecular Genetics, VIB Laboratory of Neurogenetics, Institute Born-Bunge, University of Antwerp

*Genetic insights in neurodegeneration identify biological mechanisms for improved therapeutic interventions*

Host: Alexandre Mendonça

03-06-2013

**Ronald N. Germain, MD, PhD**, NIH, Bethesda, USA

*Revealing the unseen: using advanced optical imaging to understand how the immune system works*

Host: Ana Espada de Sousa

17-06-2013

**Cornelia Van Duijn - Marja, PhD**, Professor of Genetic Epidemiology, The Erasmus University Medical Center, Rotterdam, Holland

*From Genomics to Application in complex diseases*

Host: Madalena Martins

01-07-2013

**Ioannis Aifantis**, NYU, New York, USA

*Balance between physiological stem cell differentiation and malignant transformation.*

Host: Henrique Veiga Fernandes

08-07-2013

**David Kimelman, PhD**, Professor of Biochemistry and Adjunct Professor of Biology, Department of Biochemistry, University of Washington

*To divide or not to divide: Integration of proliferation and differentiation in the progenitor cells forming the vertebrate body*

Host: Leonor Saúde

23-09-2013

**Anthony Watts, Professor, Head of Unit, D.Sc.**, University of Oxford

*Resolving nanoscale details of drugs and ligands at their binding sites of membrane-embedded, functionally competent targets*

Host: Miguel Castanho

30-09-2013

**Ton Schumacher, Professor, PhD, Group Leader**, The Netherlands Cancer Institute

*Dissection of antigen-specific T cell responses in mice and men*

Host: Bruno Silva Santos

07-10-2013

**Joaquim Cabral, Professor**, Instituto Superior Técnico, Lisboa

*Stem Cell Engineering: Bioengineering Strategies for Cellular Therapies*

Host: Domingos Henrique

21-10-2013

**Jonathan Howard, Professor**, Director of Instituto Gulbenkian de Ciência, Oeiras  
*Genetic control of a parasitic disease: Toxoplasma gondii and the mouse*  
Host: Maria Mota

28-10-2013

**Miguel G. Ferreira, Head of Group**, Instituto Gulbenkian de Ciência, Oeiras  
*Telomerase is required for Melanoma in Zebrafish*  
Host: Domingos Henrique

04-11-2013

**Carla Oliveira, Affiliated Professor**, Medical Faculty Porto, IPATIMUP  
*Modulation of cell-cell adhesion in cancer and epithelial-mesenchymal-epithelial transition*  
Host: João Barata

11-11-2013

**Peter Jordan, Principal Investigator, PhD**, Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisboa  
*WNK protein kinases: pleiotropic roles in blood pressure control and cancer*  
Host: João Barata

18-11-2013

**Ana Pombo, Professor, Head of Group**, MDC (Max-Delbrück-Centrum für Molekulare Medizin), Berlin, Germany  
*At the cross-roads of gene regulation and genome architecture: Polymerase meets Polycomb*  
Host: Domingos Henrique

25-11-2013

**Asla Pitkänen, Professor, MD, PhD**, Department of Neurobiology, University of Eastern Finland, Kuopio, Finland  
*Onset of epilepsy after a traumatic brain injury: molecular and cellular mechanisms*  
Host: Ana Sebastião

02-12-2013

**Alisson M. Gontijo, Principal Investigator**, CEDOC, Oeiras  
*Molecular physiology and evolution of a new pathway promoting developmental stability*  
Host: Domingos Henrique

09-12-2013

**Antonio Jacinto, Principal Investigator**, CEDOC, Oeiras  
*Control of Tissue Growth During Fin Regeneration*  
Host: Domingos Henrique

16-12-2013

**Teresa Coelho, MD**, Hospital Santo Antonio, Porto  
*Therapeutic developments in a neurodegenerative disease, Transthyretin Amyloidosis*  
Host: Luis Moita

**Pizza Seminars**

08-01-2013

**Ivo Martins**, Post-Doc, Instituto de Medicina Molecular

*Understanding and inhibiting the dengue virus capsid protein function*

22-01-2013

**Pedro Didelet Pereira**, Chromatin Biology Unit

*Effect of cell cycle phase and chromatin structure on DNA repair*

05-02-2013

**Rosângela Frita**, PhD student, Instituto de Medicina Molecular

*Malaria and Tuberculosis co-infection: role for hemozoin induced immunosuppression?*

19-02-2013

**Carolina Moreira**, PhD student, Instituto de Medicina Molecular

*Drosophila integrin adhesion complexes are essential for hemocyte migration in vivo*

**Madalena Martins**, Postdoc, Instituto de Medicina Molecular

*Malaria Human Genetics: inflammation-related genes (IFNAR1 and NOS2A)*

05-03-2013

**Alexandra Rosa**, Instituto de Medicina Molecular

*Understanding cell fate decisions in the embryonic neural retina*

**Augusto Ministro**, MD, Instituto de Medicina Molecular

*A Novel Approach for Therapeutic Angiogenesis: Low Doses of Ionizing Radiation*

19-03-2013

**Ana Ferreira Rodrigues**, Instituto de Medicina Molecular

*Linking Wnt pathway with bone mineralization, mechanical properties and fracture risk in osteoporosis*

02-04-2013

**Catarina Costa**, PhD student, Instituto de Microbiologia, Faculdade de Medicina de Lisboa

*Macrolide resistance in Streptococcus pyogenes in Portugal (2007-2011): diminishing resistance and clonal instability in spite of high macrolide consumption*

**Sandra Vaz**, Post-Doc, Instituto de Medicina Molecular

*BDNF-mediated enhancement of LTP is modulated by astrocytes*

16-04-2013

**André Faustino**, PhD student FCT, Instituto de Medicina Molecular

*Dengue virus capsid protein interaction with host lipid systems: implications for the viral life cycle*

30-04-2013

**Susana Silva**, PhD student, Instituto de Medicina Molecular

*Strategies to preserve the naive CD4 T-cell pool in adults thymectomized early in life*

**Patrícia Silva**, Postdoc, Instituto de Medicina Molecular

*Post-transcriptional gene regulation during Plasmodium transmission*

14-05-2013

**Francisco Aresta Branco**, PhD student, Instituto de Medicina Molecular

*Chromatin and Transcription: always tightly linked?*

28-05-2013

**Diana Carmona-Fernandes**, PhD student, Instituto de Medicina Molecular

*Coupling of atherosclerosis progression and bone disturbances in rheumatoid arthritis*

**Federico Herrera**, Post-Doc, Instituto de Medicina Molecular

*Phosphorylation pathways involved in huntingtin oligomerization, aggregation and toxicity*

11-06-2013

**Andreia Neves Horácio**, PhD student, Instituto de Medicina Molecular

*Serotypes and antimicrobial resistance of pneumococci causing invasive disease in Portuguese adults*

**Rita Mendes de Almeida**, PhD student, Instituto de Medicina Molecular

*Exploring RNA-targeted gene therapy approaches for Hypertrophic Cardiomyopathy*

25-06-2013

**Carolina Marutam** PhD student, Instituto de Medicina Molecular

*Primary Progressive Aphasia: Diagnosis and evolution*

**Robert Martin**, Postdoc, Instituto de Medicina Molecular

*Live cell visualization of pre-mRNA splicing with single molecule sensitivity*

17-09-2013

**Margarida Rei**, PhD student, Instituto de Medicina Molecular

*Major contribution of  $\gamma\delta$  T cells to IL-17A production and ovarian cancer cell growth in vivo*

**Susana Fernandes**, PhD student, Instituto de Medicina Molecular

*HIV impact on Gut associated lymphoid tissue*

01-10-2013

**Nádia Correia**, PhD student, Instituto de Medicina Molecular

*TAL1 targets beyond protein coding genes: identification of TAL1-regulated microRNA genes in T-cell acute lymphoblastic leukemia*

**Ana Ribeiro**, Post-Doc, Instituto de Medicina Molecular

*Swimming our way to spinal cord regeneration: lessons from zebrafish*

29-10-2013

**Vânia Batalha**, PhD student, Instituto de Medicina Molecular

*A single receptor approach to brain aging?*

**Daniel Carapau**, Postdoc, Instituto de Medicina Molecular

*Iron deficiency causes death in an otherwise non-lethal malaria murine model*

12-11-2013

**Rita Aroeira**, PhD Student, Instituto de Medicina Molecular

*Are glycine transporters modulated by BDNF in brain nerve terminals?*

**Miguel Muñoz Ruiz**, PhD Student, JR Regueiro Lab, Universidad Complutense de Madrid

*Altered gamma delta T lymphocytes in CD3 delta gamma double haploinsufficiency (CD3 delta  $\gamma$ -gamma  $\gamma$ -) mice*

26-11-2013

**Jorge Miranda**, PhD student, Instituto de Medicina Molecular

*Production of CbpD, an essential step to understand pneumococcal fratricide*

**Ksenija Slavic**, Post-Doc, Instituto de Medicina Molecular

*Iron transporters in malaria parasites: functional and genetic studies*

10-12-2013

**Catarina Mota**, PhD student, Instituto de Medicina Molecular

*Delta like-1 enhances the in vitro conversion of human memory CD4 cells into FOXP3-expressing Regulatory T Cells*

### Parasitology Series

18-06-2013

**Ghislain Cabal**, Post-Doc, Instituto de Medicina Molecular

*Malaria liver stage development and host cell autophagy*

02-07-2013

**Cristina Afonso**, Post-Doc, Rui Costa Lab, Champalimaud Neuroscience Programme

*Body Snatchers - Parasite infection and host behavior*

16-07-2013

**Kirsten Hanson**, Post-Doc, Instituto de Medicina Molecular

*Screening for late-acting liver stage antimalarials: can causal prophylaxis drive immunity to Plasmodium in endemic areas?*

03-09-2013

**Ana Filipa Ferreira**, PhD student, Instituto de Medicina Molecular

*Does Trypanosoma brucei alter its host circadian rhythm?*

10-09-2013

**Maria Mota**, PhD, Instituto de Medicina Molecular

*"Recent findings on Host-Plasmodium interactions"*

17-09-2013

**Ghislain Cabal**, Post-doc, Instituto de Medicina Molecular

*Malaria liver stage development and host cell autophagy*

24-09-2013

**Jorge Santos**, PhD student, Instituto de Medicina Molecular

*Novel translationally repressed gene products essential for Plasmodium life cycle progression*

01-10-2013

**Ana Margarida Vaz**, MSc student, Instituto de Medicina Molecular



*The reciprocal influence of malaria and sleeping sickness co-infections*

**Carolina Tempera**, MSc student, Instituto de Medicina Molecular

*Novel applications of a flow cytometric sensitivity assay for Plasmodium spp.: compounds screening as well as gametocyte detection*

08-10-2013

**Carolina Matos**, PhD student, CEDOC – Centro de Estudos de Doenças Crónicas, Laboratório “Membrane Traffic in Infection & Disease” (PI-Duarte Barral)

*Host PI(3,5)2 is necessary for Plasmodium berghei growth during liver stage infection*

15-10-2013

**Neuza Duarte**, MSc student, Instituto de Medicina Molecular

*Gene expression during Plasmodium transmission*

**Carla Bejarano**, EMBO summer fellow, Instituto de Medicina Molecular

*In vivo distribution of transmissible stages of Trypanosomes: differences between organs and during time of infection*

22-10-2013

**Luísa Figueiredo**, Group Leader, Instituto de Medicina Molecular

*The temperature is dropping: can a parasite feel it?*

29-10-2013

**Rosângela Frita**, PhD student, Instituto de Medicina Molecular

*Malaria and Tuberculosis co-infection: role for hemozoin-induced immunosuppression?*

05-11-2013

**Iset Vera**, Post-doc, Instituto de Medicina Molecular

*The role of microRNAs during Plasmodium infection*

12-11-2013

**Ana Guerreiro**, Researcher, Instituto de Medicina Molecular

*Is P. berghei Mei2 homologue involved in meiosis?*

19-11-2013

**Francisco Branco**, PhD Student, Instituto de Medicina Molecular

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

26-11-2013

**Ana Pena**, PhD Student, Instituto de Medicina Molecular

*Trypanosoma brucei histone H1 regulates a small set of genes and is important for virulence in vivo*

03-12-2013

**António Mendes**, Post-doc, Instituto de Medicina Molecular

*RoPlaVac: A new vaccination strategy against Malaria*

17-12-2013

**Patrícia Silva**, Post-doc, Instituto de Medicina Molecular

*Post-transcriptional gene regulation during Plasmodium transmission*

**Neurosciences Seminar**

14-01-2013

**Pedro Antas**, Instituto de Medicina Molecular

*The relationship between the gut microbiota and the brain*

21-01-2013

**Joana Coelho**, Instituto de Medicina Molecular

*Microglia dysregulation as trigger for chronic neuroinflammation: impact for ageing and neurodegenerative*

28-01-2013

**Renato Martinho**, Instituto de Medicina Molecular

*SIRT2: in the crossroad of aging, neurodegeneration and autophagy*

**04-02-2013**

**Patrícia Coelho de Velasco**, Univ. Federal Fluminense, Rio de Janeiro, Brasil

*Impact of omega-3 fatty acids nutritional restriction on the development of the rodent visual system*

**25-02-2013**

**Tiago Rodrigues**, Instituto de Medicina Molecular

*Adenosine A2A Receptors (A2ARs): novel upstream regulators of Brain-Derived Neurotrophic Factor (BDNF)-mediated attenuation of hippocampal Long-Term Depression (LTD)*

04-03-2013

**Diogo Rombo**, Instituto de Medicina Molecular

*Hippocampal neuronal inhibition under control: a role for adenosine receptors*

11-03-2013

**Dina Silva**, Instituto de Medicina Molecular

*Neuropsychological predictors of the outcome in non-demented subjects with cognitive complaints*

18-03-2013

**João Covita**, Instituto de Medicina Molecular

*The effect of BDNF on synaptic and extrasynaptic NMDA currents upon aging*

25-03-2013

**Sara Carvalho**, Instituto de Medicina Molecular

*Contribution of neuronal vs non-neuronal adenosine A2A receptors to age-related cognitive deficits*

08-04-2013

**Luisa Lopes**, Instituto de Medicina Molecular

*Journal Club*

15-04-2013

**Noémia Pereira**, Instituto de Medicina Molecular  
*Glycinergic transmission as a potential therapeutic target for epilepsy*

22-04-2013

**Sofia Duarte**, Instituto de Medicina Molecular  
*Synaptic dysfunction in early epileptic encephalopathies*

29-04-2013

**Diana Ferreira**, Instituto de Medicina Molecular  
Adenosine A2A Receptor - a putative player in alpha-synuclein induced synaptic dysfunction

06-05-2013

**Paula Pousinha**, PhD, Institute Pharmacologie Moléculaire et Cellulaire, France  
*Role of APP C-terminal fragment, AICD, in hippocampal function*

13-05-2013

**Alexandre Mendonça**, Instituto de Medicina Molecular  
*Uma afecção peculiar do córtex cerebral*

20-05-2013

**Sara Xapell**, Instituto de Medicina Molecular  
*Hemopressin as a regulator of oligodendrogenesis in subventricular zone stem/progenitor cell cultures*

27-05-2013

**Márcia Oliveira**, Instituto de Medicina Molecular  
*Modulation of  $\alpha$ -Synuclein aggregation and toxicity*

03-06-2013

**Raquel Dias**, Instituto de Medicina Molecular  
*Erythropoietin: setting the tone for homeostatic plasticity?*

17-06-2013

**Tiago Maia**, Instituto de Medicina Molecular  
*The Catecholamines, Signal, and Noise: From Neuronal Processing to Cognition and Attention-Deficit/Hyperactivity Disorder*

24-06-2013

**Rita Aroeira**, Instituto de Medicina Molecular  
Glycine transporters, GlyT1 and GlyT2, in brain astrocytes – recent insights

01-07-2013

**Sandra Vaz**, Instituto de Medicina Molecular

*BDNF-mediated enhanced LTP is modulated by astrocytes*

08-07-2013

**Susana Eusébio**, MD, Instituto de Psicologia Médica, FMUL  
*Attachment and stress response in breast cancer*

15-07-2013

**Karri Lamsa**, PhD, University of Oxford, Oxford, UK  
*Cell type specific plasticity rules in hippocampal interneurons*  
**João Peça**, PhD, Centro de Neurociências e Biologia Celular, UC  
*(Opto)Genetic Dissection of Neuronal Circuits*

09-09-2013

**Filipe Nascimento**, Instituto de Medicina Molecular  
*Neuromuscular transmission modulation by A1 and A2A adenosine receptors in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis*

16-09-2013

**André Santos**, Instituto de Medicina Molecular  
*Amyloid- $\beta$  peptide dysregulates TrkB receptors and BDNF function by a calpain-dependent mechanism*

23-09-2013

**Mariana Rocha**, PhD student, Mitochondrial Research Group, Institute for Ageing and Health, Newcastle University  
*Mitochondrial dysfunction in ageing skeletal muscle*

30-09-2013

**Rui Soares**, Instituto de Medicina Molecular  
*Generation and Characterization of Novel Transgenic Zebrafish Lines to Study Parkinson's Disease*

07-10-2013

**Mariana Oliveira**, Instituto de Medicina Molecular  
*Synaptic modulation by adenosine in an aged-dependent epilepsy model*

14-10-2013

**Federico Herrera**, Instituto de Medicina Molecular  
*N-terminal phosphorylation regulates huntingtin oligomerization, aggregation and toxicity*

21-10-2013

**Sandra Tenreiro**, Instituto de Medicina Molecular  
*Phosphorylation modulates clearance of alpha-synuclein inclusions in a yeast model of Parkinson's disease*

28-10-2013

**João Covita**, Instituto de Medicina Molecular

*BDNF signaling upon aging: effect on NMDA receptor and glutamate transporter function*

04-11-2013

**Rita Ramalho**, Instituto de Medicina Molecular

*Deciphering the mechanisms underlying the loss of BDNF neuroprotection in Alzheimer's disease*

11-11-2013

**Ana Filipa Ribeiro**, Instituto de Medicina Molecular

*Deciphering the role of adenosine A2A receptor during neuronal development*

18-11-2013

**Filipa Ferreira**, Instituto de Medicina Molecular

*Unravelling the role of BDNF on endocannabinoids-modulation of neurogenesis*

25-11-2013

**Miguel Moutinho**, PhD student, Molecular and Cell Biology of Eukaryotic Systems, iMed.Ulisboa, Faculty of Pharmacy, UL

*Cholesterol 24S-hydroxylase overexpression inhibits the LXR pathway by activating sGTPases in neuronal cells*

02-12-2013

**Sara Carvalho**, Instituto de Medicina Molecular

*Subcellular localization of adenosine A2A receptors in hippocampal synapses*

09-12-2013

**Armando Cruz**, Instituto de Medicina Molecular

*The cross-talk mechanism between adenosine A1 and cannabinoid CB1 receptors in the hippocampal synaptic plasticity*

16-12-2013

**Daniela Magalhães**, Instituto de Medicina Molecular

*Deciphering the role of taurine in hyperexcitability*

### Lisbon Area of Neuroscience meetings

14-01-2013

**Ana Sofia Falcão**, Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL/CPM), Faculdade de Farmácia, Universidade de Lisboa

*A new look on gliomas*

18-02-2013

**Cláudia Caldeira**, PhD student, Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon

*Age-dependent changes in microglia reactivity to  $\beta$ -amyloid oligomers"*

**Maria Benedita Fonseca**, PhD student, Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon

*Amyloid  $\beta$  peptides promote autophagy-dependent differentiation of mouse neural stem cells"*

11-03-2013

**Carolina Cunha**, PhD student, Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL) Faculty of Pharmacy, Universidade de Lisboa

*Exploring modulation of ALS-like motor-neurons by a neuroprotective bile acid and activation on microglia*

**Gonçalo Poças**, PhD student, Instituto de Tecnologia Química e Biológica, Oeiras

*Genetic and functional interaction of alpha-synuclein and huntingtin in Drosophila "Amyloid  $\beta$  peptides promote autophagy-dependent differentiation of mouse neural stem cells"*

15-04-2013

**Inês Palmela**, PhD student, Neuron-Glia Biology in Health and Disease Unit Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL) Faculty of Pharmacy, Universidade de Lisboa

*Alterations in the blood-brain barrier dynamics by bilirubin*

**Joana Xavier**, PhD student, Molecular and Cell Biology of Eukaryotic Systems Unit Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL) Faculty of Pharmacy, Universidade de Lisboa

*Mitochondrial translocation of p53 modulates neuronal fate by preventing differentiation-induced mitochondrial stress*

13-05-2013

**Ana Luisa Raposo**, PhD, Assistant researcher, Cognitive Processes and Social Cognition Group, Faculty of Psychology, University of Lisbon

*Making sense of nonsense: an fMRI study on inference during sentence comprehension*

**Claudia Santos**, PhD, Sênior Researcher, Disease and stress biology Group, Instituto de Biologia Experimental e Tecnologia and Instituto de Tecnologia Química e Biológica, Oeiras

*Potential of plant bioactive compounds as neuroprotective agents*

17-06-2013

**Moreno Coco**, Post-Doc, Faculty of Psychology, University of Lisbon

*The role of interactivity on cognitive alignment and decision-making during dialogue*

**Claudia Almeida**, Principal Investigator, CEDOC - Centro de Estudos de Doenças Crónicas

*Intracellular trafficking in Alzheimer's disease*

### **IMM Internal Seminars**

23-01-2013

**Domingos Henrique**, Instituto de Medicina Molecular

*Nanog&Pluripotency:welcome to the machine*

13-02-2013

**Maria Carmo-Fonseca**, Instituto de Medicina Molecular

*When splicing meets cancer*

27-02-2013

**Luís Moita**, Instituto de Medicina Molecular

*Anthracyclines induce autophagy-mediated protection against severe sepsis*

13-03-2013

**Alexandre Mendonça**, Instituto de Medicina Molecular  
*Recent successes and failures of treatments for Alzheimer's disease*

10-04-2013

**Miguel Castanho**, Instituto de Medicina Molecular  
*Unraveling a new actor in Dengue virus-cell fusion*

29-05-2013

**João Lacerda**, Instituto de Medicina Molecular  
*Induction of immune tolerance in allogeneic hematopoietic stem cell transplantation*

19-06-2013

**Francisco J. Enguita**, Instituto de Medicina Molecular  
*The human non-coding transcriptome in cell aging*

25-09-2013

**Luis Graça**, Instituto de Medicina Molecular  
*Immune regulation by specialized T cells*

09-10-2013

**António Diniz**, Director of the National Plan for HIV/AIDS, Ministério da Saúde  
*30 years of HIV/AIDS in Portugal*

23-10-2013

**Tânia Carvalho**, Instituto de Medicina Molecular  
*Histopathology as a research tool: insights from zebrafish, mouse and man*

30-10-2013

**Gonçalo Bernardes**, Instituto de Medicina Molecular  
*Site-specific protein modification methods for bioimaging and therapeutic applications*

06-11-2013

**Leonor Saúde**, Instituto de Medicina Molecular  
*Building A Perfect Body Plan*

20-11-2013

**Edgar Gomes**, Instituto de Medicina Molecular  
*Amphiphysin-2/BIN1 and N-WASP function in skeletal muscle architecture: Implications for centronuclear myopathies and myotonic dystrophies*

04-12-2013

**Luísa Lopes**, Instituto de Medicina Molecular  
*Clues to the 'early-aging' of memory*

18-12-2013

**Tiago Maia**, Instituto de Medicina Molecular  
*The Role of Norepinephrine in Cognition and Attention-Deficit/Hyperactivity Disorder*

### IMM Rheumatology Series

04-02-2013

**Georg Schett, Friedrich-Alexander**, University Erlangen-Nuremberg  
*Bone as a clue to the pathogenesis of rheumatoid arthritis*

12-03-2013

**Lucien Ionescu**, UCB Global  
*An example of a development pipeline*

18-03-2013

**Florence Apparailly**, INSERN - Institut Neurosciences Montpellier, University Hospital, Montpellier  
*Role of Ly6Chigh monocytes in inflammation: microRNAs as novel molecular targets for innovative immuno-intervention in arthritis.*

14-05-2013

**Professor Costantino Pitzalis MD PhD, FRCP**  
*A pathobiology driven approach to stratified medicine in rheumatoid arthritis*

04-06-2013

**Mari Ainola, PhD**, University of Helsinki Faculty of Medicine Institute of Clinical Medicine  
Department of Medicine  
*Apoptosis-induced microparticles and apoptotic bodies as stimuli to plasmacytoid dendritic cell-mediated autoimmunity in Sjögren's syndrome*

19-11-2013

**Maurizio Cutolo, MD**, University of Genova, Italy  
MORNING GLUCOCORTICOIDS VERSUS NIGHT GLUCOCORTICOIDS  
*How chronotherapy may optimize long-term, low dose glucocorticoid use in rheumatoid arthritis*

### IMM Oncology Series

21-03-2013

Chair: **Isabel Fernandes** | Co-chair: **Margarida Ferreira**  
Soft Tissue Sarcomas

Chair: **Pedro Cardoso** | Co-chair: **Hugo Vasques**  
*Kaposi sarcoma – a single center study; Progression free survival under trabectedin – a single center study*



**Immunology Club**

24-01-2013

**Ana Neves Costa, PhD**, Instituto de Medicina Molecular  
*Roles for TET1 in innate immune responses*

14-02-2013

**Carlos Tadokoro**, IGC  
*Liver sequestration of Plasmodium chabaudi-infected red blood cells and tolerance*

28-02-2013

**Manuela Ferreira**, Instituto de Medicina Molecular  
*Cell-autonomous retinoic acid signaling regulates Lymphoid Tissue inducer cell differentiation and lymphoid organ size*

21-03-2013

**Several Speakers**  
*Challenges of a Severe Combined Immunodeficiency*

04-04-2013

**Julie Ribot, PhD**, Instituto de Medicina Molecular  
*Functional differentiation of human  $\gamma\delta$  thymocytes*

18-04-2013

**Leonor Sarmiento, PhD**, Instituto de Medicina Molecular  
*A role for checkpoint-kinase 1 in T-ALL biology.*

02-05-2013

**Frank Schildberg, PhD**, Percy Knolle Lab, Institute of Molecular Medicine (IMMEI) Bonn,  
*Hepatic stellate cells veto CD8 T cell activation by a CD54-dependent mechanism*

09-05-2013

**Kalet Leon, PhD**, Head of Research, Center of Molecular Immunology, Havana, Cuba  
*Cancer immunotherapy: current research strategy at the Center of Molecular Immunology*

20-06-2013

**Raquel Rodrigues, PhD**, Instituto de Medicina Molecular  
*Genome-wide analysis of alternative splicing during dendritic cell response to a bacterial challenge*

04-07-2013

**Susana L.Silva, MD, PhD Student and Adriana Albuquerque, Post-Doc**, Instituto de Medicina Molecular  
*Homeostasis of human naive-like regulatory T cells*

03-10-2013

**Carlos Almeida, Msc Student**, Instituto de Medicina Molecular  
*Regulation of the enteric immune system by retinoic acid signaling*

10-10-2013

**Diana Fontinha, PhD student**, Instituto de Medicina Molecular  
*Herpesvirus modulation of immunological synapses*

24-10-2013

**Russell B. Foxall, Post-Doc and Jorge Andrade, Post-Doc**, Instituto de Medicina Molecular  
*mir34c-5p as a novel regulator of naïve CD4 T cell activation and HIV replication*

31-10-2013

**Ana Pamplona, Principal Investigator**, Instituto de Medicina Molecular  
*Hepatic gamma-delta T cells are critical for the development of experimental cerebral malaria after Plasmodium sporozoites infection*

21-11-2013

**Marta Monteiro, PhD**, Instituto de Medicina Molecular  
*Activation of NKT cells in the context of allergy induced by proteases*

28-11-2013

**Ana Teresa Veríssimo Alves Bento, Master Student**, Instituto de Medicina Molecular  
*Role of RET signals in human hematopoietic stem cell transplantation*

### Computational Biology and Bioinformatics Seminars

30-01-2013

**Ana Rita Grosso**, Instituto de Medicina Molecular  
*RNA-seq data analysis: methods and challenges*

27-02-2013

**Francisco Enguita**, Instituto de Medicina Molecular  
*Integrated analysis of miRNA regulatory effect in cellular pathways*

27-03-2013

**Daniel Sobral**, Instituto Gulbenkian e Ciência  
*The Regulatory Genome: Surviving the ENCODE data flood*

24-04-2013

**Elsa Abranches, Post-Doc**, Instituto de Medicina Molecular  
*Exploring The Pluripotency Landscape*

29-05-2013

**Andreia Amaral, Post-Doc**, Instituto de Medicina Molecular

*RNA-seq analysis: challenges of non-human data and interaction with wet-lab coats*

26-06-2013

**Joana Cardoso, Post-Doc**, Computational Genomics Laboratory, IGC

*The two stemness associated genes CYR61 and TAZ are early markers of Barrett's esophagus malignant progression*

25-09-2013

**Francisco Enguita, PI**, Instituto de Medicina Molecular

*Current tools and cheap strategies for lincRNA analysis*

30-10-2013

**Nuno Barbosa-Morais, Post-Doc**, Instituto de Medicina Molecular

*Analysis of Transcriptional Regulation and RNA Processing from RNA-Seq Data*

27-11-2013

**Francisco Pina Martins, PhD Student**, CoBiG<sup>2</sup>/FCUL

*Variant detection in non model organisms using 454 data with no strain information*

### Career Path Seminar

02-05-2013

**Cristiana Costa, PhD**, Global Chemical Manufacturing Control Project Manager at Astellas Pharma, Japan

**Nuno Silva, PhD**, Senior Pharmacologist at BIAL, Portugal

*A Career in Translational Research and Development*

06-06-2013

**David Braga Malta, PhD**, Co-Founder, President and Executive Vice-President of Cell2B

**Orfeu Flores**, Founder and CEO of STAB VIDA

*Entrepreneurship as a Career Option in Life Sciences & Health*

19-09-2013

**Pedro Silva**, Coordenador de Comercialização de Ciência e tecnologia da TecMinho

**Ana Neves**, Technology Transfer Agent, UL-INOVAR

**Nuno Silva**, Independent Technology Transfer Agent

*Technology Transfer: How to Make It Happen*

21-11-2013

**Maria Hortense Matos**, Eurotrials

**Ana Carla Gordo**, Pfizer

**Patrícia Rosa**, Boehringer Ingelheim  
*A Career in Clinical Trials*

Other

04-02-2013

**Jessica Strid**, Imperial College London  
*Lymphoid Stress-Surveillance: linking tumour immune-surveillance and atopy*  
Host: Bruno Silva-Santos

15-03-2013

**Igor Tsigelny**, San Diego Supercomputer Center & Department of Neurosciences, University of California, San Diego, CA  
*A hierarchical coherent-gene-group model for brain development: advancing drug discovery for autism and schizophrenia*  
Host: Miguel Castanho

25-03-2013

**Françoise Pflumio and Irina Naguibneva**, Institut de Radiobiologie Cellulaire et Moléculaire (IRCM), Fontenay-aux-Roses, France  
*Studying the role of extra- and intra-cellular factors in human T-ALL: a team effort*

02-04-2013

**Tsvee Lapidot, PhD**, Department of Immunology, The Weizmann Institute of Science,  
*Regulation of normal and leukemic human stem cells: stem cell interactions with the bone marrow microenvironment*  
Host: Henrique Veiga-Fernandes

13-04-2013

**Prof Doutor Joaquim Ferreira /Fisioterapeuta Josefa Domingos/Terapeuta da Fala Ana Rita Cardoso**, Instituto de Medicina Molecular / Faculdade de Medicina da Universidade de Lisboa  
*Acção de formação sobre doença de Parkinson para doentes e cuidadores & Dia Aberto Biobanco "Parkinson"*

16-04-2013

**Entrega de Bolsa Laço**  
*Associação Laço & Instituto de Medicina Molecular*

16-04-2013

**Dr. F. Javier Garcia**, Banco Nacional de ADN Carlos III  
*The experience of the National DNA Bank Carlos III (Spain)*  
Host: João Eurico Fonseca

08-05-2013

**Zhijian 'James' Chen, PhD**, Professor, Department of Molecular Biology University of Texas Southwestern Medical Center  
*The danger from within: Innate immune sensing and signaling of cytosolic DNA and RNA*  
Host: Maria Mota

16-05-2013

**Professor Dr Irving Weissman**, Director, Institute For Stem Cell Biology and Regenerative Medicine (ISCBRM), Stanford University School of Medicine, California, USA

*Normal and Neoplastic Stem Cells*

Host: Lisbon Academic Medical Center PhD Program

20-05-2013

**Especialistas Esclarecem Dúvidas sobre Participação em Ensaios Clínicos**

Centro de Investigação Clínica do Centro Académico de Lisboa

04-06-2013

**Daniel Pennington, PhD**, Blizard Institute, Queen Mary University of London

*Role of the T Cell Receptor in thymic T cell development*

Host: Bruno Silva Santos

06-06-2013

**Rune Matthiesen, PhD**, Institute of Molecular Pathology and Immunology of the University of Porto

*Pharmacoproteomics: Global MS based drug profiling*

Host: Maria Carmo Fonseca

07-06-2013

**Jose Rubio, PhD**, Inserm at Institut Pasteur, France

*Antigenic variation in Plasmodium falciparum: From epigenetic regulation to the generation of diversity*

Host: Maria Carmo-Fonseca

25-06-2013

**Joana Rosario, MD, MPH**, Principal at J. Rosario et Al, LLC Research Consultants, Maryland, USA  
*From Scientist to Entrepreneur*

**Larry Chaityn, BS, MBA**, Managing Director of Propero/Health Care Accelerator, New York, USA  
*From Mechanism of Action to Exit, the Necessary Success Factors*

Host: Business Development & Grants Office

26-06-2013

**Ritu Dhand, PhD**, Chief Biological Sciences Editor at Nature

*Nature: The Journal, Review Process and the Publishing Group*

Host: Maria Carmo-Fonseca

10-07-2013

**Prof. Benhur Lee, MD**, David Geffen School of Medicine, University of California at Los Angeles  
*Forging New Paradigms: Broad Spectrum Antivirals against Enveloped Viruses*

Host: Nuno Santos

15-07-2013 - 16-07-2013

**Several Speakers from EMBO**

*Cell biology-Development-Oncobiology-Immunity & Infection-Neuroscience*

Instituto de Medicina Molecular, Lisboa, Portugal

23-08-2013

**Ertugrul Ozbudak, PhD**, Albert Einstein College of Medicine, New York, USA

*Systems-level analysis of the vertebrate segmentation clock*

Host: Leonor Saúde

18-09-2013 - 20-09-2013

**The 3rd Global Cancer Genomics Consortium Symposium**

*From oncogenomics to cancer care*

21-09-2013

**Celebrating IMM's 10th anniversary**

17-10-2013

**1st Postdoctoral Symposium**

11-11-2013

**Francisco Aresta Branco, Mihailo Mirkovic, Ana Luisa Morgado, Alexandra Vitor, Pedro**

**Rosmaninho**, Five laboratories from IMM, IGC and FFUL

*Lisbon Chromatin Club*

13-11-2013

**Biobanco-IMM**

Novas oportunidades de desenvolvimento da investigação médica

*O que foi feito até hoje e quais as repercussões importantes que o Biobanco-IMM está a ter na investigação médica em Portugal*

27-11-2013

**Bertil Fredholm, Professor**, Karolinska Institute, Stockholm

*The huge difference in effects of low and high doses of caffeine*

Host: Alexandre Mendonça

19-12-2013

**Miguel Remondes, Senior Research Scientist**, MIT, Cambridge, MA, USA

*Cortico-hippocampal activity and reactivations in decision-making and learning*

19-12-2013

**Peter Andersen**, Chair of Research Directors Group – EFPIA

*IMI2 – a new ecosystem for European health care?*

Chair: **Isabel Vieira** – IMI Portuguese State Representative

Invited participants: **Beatriz Lima** – IMI Scientific Committee

**Heitor Costa** - Executive Director, APIFARMA

*Round table discussion: Main challenges to successful participation in IMI2*

Workshop

30-10-2013

**Judith A. Swan, PhD**, Associate Director for Writing in Science and Engineering at Princeton University, USA

*Making sense of the science*

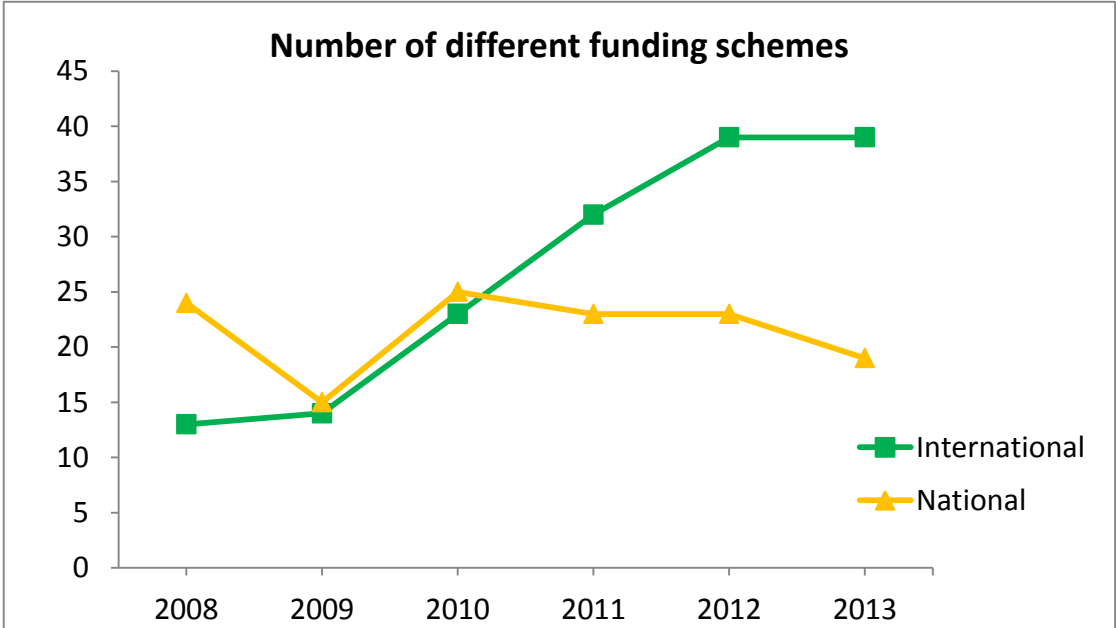
*A Course on Effective Scientific Writing*

## Diversity of Funding Sources of IMM Grant Applications

In 2013, IMM researchers have submitted grants to the following funding schemes:

<b>International</b>	
<b>Public</b>	<b>Private</b>
ERA-Net E-Rare	ALSA
ERA-Net HIVERA	Alzheimer's Drug Discovery Foundation
ERA-Net Infect-ERA	American Institute for Cancer Research
EU Joint Programme – Neurodegenerative Disease Research (JPND)	Axa Research Fund Post-doctoral Fellowship
European Cooperation in Science and Technology (COST)	Bill & Melinda Gates Foundation
European Research Council (ERC) Consolidator	Crohn's & Colitis Foundation of America
European Research Council (ERC) Proof of Concept	European Calcified Tissue Society - ECTS/AMGEN
European Molecular Biology Organization (EMBO) Installation Grant	European Society for Vascular Surgery
European Molecular Biology Organization (EMBO) Young Investigator Grant	Innovation Prize Universal Biotech
FP7 Cooperation Programme - KBBE	International Rett Syndrome Foundation
FP7 People Programme - Career Integration Grants (CIG)	Jérôme Lejeune Foundation
FP7 People Programme - Intra-European Fellowships (IEF)	Leukemia & Lymphoma Society Quest for Cure
FP7 People Programme - Initial Training Networks (ITN)	Mizutani Foundation for Glycoscience
Human Brain Project	National Alliance for Research on Schizophrenia and Depression Young Investigator Grant
Human Frontier Science Program (HFSP) Program Grant	National Multiple Sclerosis Society Pilot Research Grant
Human Frontier Science Program (HFSP) Young Investigators Grant	Parkinson's Disease UK Innovation Grant
Innovative Medicines Initiative (IMI)	Parkinson Research Foundation
Multiple Sclerosis Research Program Idea Development Award	Pfizer Europe Aspire
National Institutes of Health, USA	Samsung Global Research Outreach
Territorial Cooperation Programme (SUDOE)	
<b>National</b>	
<b>Public</b>	<b>Private</b>
Apoio a Atividades Extracurriculares da Universidade de Lisboa	Laço Breast Cancer Grant
FCT Carnegie Mellon Portugal Programme	Bolsa de Estudos em Autoimunidade NEDAI (Núcleo de Estudos de Doenças Auto-Imunes)
FCT European Institute of Technology Preparation Projects	BES Innovation
FCT Exploratory Research Projects in all Scientific Domains	Fundação AstraZeneca Innovate Competition
FCT Harvard Medical School - Portugal Program	Programa Gilead GÉNESE
FCT Investigator Programme	Luso-American Foundation US@PT Grants
FCT PhD Programme	Associação Portuguesa Contra a Leucemia
FCT Protocol of Collaboration with Agence Nationale de la Recherche (ANR)	Building Global Innovator's Venture Competition
FCT Research Infrastructures Roadmap	
FCT Scientific Community Support Fund	
Santa Casa da Misericórdia - Prémio Neurociências	





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

## 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, PhD

*PhD Training Director:* Ana Espada de Sousa, MD, PhD

*LisbonBioMed Program Director:* Maria Mota, PhD

*Postdoctoral Training Director:* Bruno Silva-Santos, PhD

*Career Development Director:* Henrique Veiga Fernandes, PhD

Together with Faculdade de Medicina da Universidade de Lisboa (FMUL) and with Hospital de Santa Maria (HSM), IMM is part of the Lisbon Academic Medical Center (Lisbon AMC), a consortium that provides a completely integrated form of education and training in Biomedicine and Clinical Research, combining multisectorality 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). Therefore, from January 2014, IMM will also count with 10 LisbonBioMed PhD students per year, during 4 years. Furthermore, IMM will be hosting PhD students from two other new multi-institutional FCT PhD Programs: the Bioengineering - Cell Therapies and Regenerative Medicine (CTRM), and the Medical Biochemistry and Biophysics (M2B) PhD Programs.

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

## Advanced Training in numbers

**In 2013, 85 PhD students conducted research at IMM: 73 Lisbon AMC PhD students plus 12 PhD students from other Programs/ Institutions**

**73 LisbonBioMed PhD students conducted research at IMM**

*69 out of 73 have individual fellowships*

- 57 FCT PhD fellowships;
- 2 FCT MD-PhD/ Resident-PhD;
- 3 Marie Curie Initial Training Network- INT;
- 3 *Programa de Formação Médica Avançada- FCG/FCT/Min Saúde*;
- 1 MIT-Portugal;
- 3 IMM (1 through ERC Grant).

Besides Lisbon AMC PhD students, IMM hosted 12 PhD students from other PhD Programs/ Institutions: 2 GABBA PhD Program, 2 BEB PhD Program, 2 Budapest University, 1 *Karmanos Cancer Institute*, 2 UNESP- Brazil, 1 *Instituto Carlos Chagas Filho*-Brazil, 1 supported by Sonangol EP and 1 supported by IMM.

**10 other Lisbon AMC PhD Students are training abroad, with IMM co-supervision:**

10 Lisbon AMC PhD students who are conducting research mainly abroad benefit from co-supervision from IMM Faculty: 6 FCT PhD Fellowships; 1 FCT MD-PhD/ Resident-PhD.

**New PhD Students in 2013:**

**12 IMM /Lisbon AMC PhD Students**, within a total of 19 new Lisbon AMC PhD Students

*Helder Horta Pereira, Armando Dulcideo da Silva Cruz, Joana Margarida Branco dos Santos, Joana Cabrita Afonso, Nataniel João Gonçalves Cleto Rosa, Ângela Raquel Amaro Leal, Josefa Domingos, Filipa Gil Marques, Sandra Pinheiro Garcês Gama, Inês Sofia Alvarez Martins, Ana Paula Martins do Nascimento, Frederico Miguel Bento do Rosário, Inês Maria Vaz Duarte Luís, Tiago Alexandre Mestre, Mónica Sofia Inácio Duarte Inês, Fernando Manuel Magalhães Martins, Pedro Miguel Zuzarte Luís, Carlos Alberto Costa Noronha Ferreira and Tiago dos Reis Matos.*

## Advanced Courses

*A total of 10 Advanced Courses were organized*

Courses organized under the CAML PhD Programme

### **Nanomedicine**

*Organizers: Nuno C. Santos and Ivo Martins, IMM/FMUL*

*Date: Feb 18-20 (1 ECTS)*

*Nº of Participants: 12*

The course focused on: i) nanotechnology-based diagnostics; ii) nanotechnology-

based imaging; iii) targeted drug delivery and release; and, iv) regenerative medicine. Plus, practical sessions on atomic force microscopy (AFM) and “force spectroscopy”.

**Laboratory Animal Science**

*Organizer: Joana Marques, IMM*

*Date: Feb 13- Mar14 (1 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.

**Applied Biostatistics**

*Organizer: Ruy Ribeiro*

*Date: Feb 26 –Mar 22 (4 ECTS)*

*Nº of Participants: 12*

The objective of the course was to teach basic statistical skills that must be part of researcher's culture, and at the same time to sow the seeds allowing for further exploration. Emphasis was given to practical examples to understand statistics, not to ready-made recipes to analyze specific datasets.

**Biosafety**

*Organizer: Miguel Prudêncio, IMM*

*Date: Feb 28 – Mar 1 (0.5 ECTS)*

*Nº of Participants: 9*

The course was aimed at training researchers for use of the IMM BSL3 Facility.

**Protein expression and purification: tips and tricks**

*Organizer: Francisco Enguita, IMM/FMUL*

*Date: Mar 14-15 (1 ECTS)*

*Nº of Participants: 12*

The students were trained in theoretical and practical topics related with heterologous protein expression in several hosts.

**Introduction to Clinical Research**

*Organizers: António Vaz Carneiro and José Ferro(IMM/FMUL/HSM)*

*Date: Mar 15- June 29 (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.

***Flow Cytometry: from basic concepts to multicolor analysis***

*Organizer: Maria Soares, IMM*

*Date: June 17-21(1 ECST)*

*Nº of Participants: 14*

This course introduced participants to the basic concepts of flow cytometry and addressed potential applications. The course had a strong component addressing instrument set-up and calibration, including “hands-on” calibration of FACSalibur and FACSCanto.

***Challenges in Immunology***

*Organizer: Bruno Silva-Santos, IMM/FMUL*

*Date: June 3-5 (5 ECTS)*

*Nº of Participants: 28*

This course exposed participants to some of the hottest topics in Immunology, including challenges in: in T Cell development, response and regulation; in Innate Lymphoid Cells; in TB research, in HIV research and in Cancer immunotherapy.

***miRNAs and non-coding RNAs in cell biology and human***

***disease*** *Organizer: Francisco Enguita, IMM/FMUL*

*Date: July 11-12 (1 ECTS)*

*Nº of Participants: 23*

In this course, the students were introduced to the biology of non-coding RNAs with special focus on miRNAs by comprehensive lectures and bioinformatic tutorials, and also to their role within cell physiology and human disease.

Complementary skills courses:

***Scientific Career Development 101***

*Organizer: Joana do Rosário, MD, MDH*

*Date: Jun26*

*Nº Participants: 15*

Participants were led to expand their professional horizons by actively discussing scientific careers in academic and non-academic milieus including, industry, non-profit, government, multilateral organizations, etc. To explore and put into practice the information gained and the targeted concepts participants took part in several role play activities, such as situational sketches and mock interviews.

**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”.

**2013 PhD Students commission**

Rita Aroeira, Bethania Cassani, Rita Domingues, André Faustino, Susana M Fernandes, João Freire, Ana Filipa Guedes, Ana Marisa Guedes, Andreia Horácio, Sílvia Arroz-Madeira, Anna Carline Marques, Patrícia Meireles, Catarina Mota, Catarina Pato, Ana Pena, Inês Perpétuo, Margarida Rei, Sérgio Ribeiro, André Santos and Nina Schmolka,

**2013 PhD Students representatives**

Alice Melão and Jorge Santos

**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.

**VI IMM/CAML PhD Students Retreat**

*Date: May 3-5*

*Place: Pousada da Areia Branca, Lourinhã*

*Participants: Total 42; PhD students (27), post-docs (3), master students (5), lab managers (2) technicians (3), it-support (1) and UEFA executive manager (1).*

Programme:

1) Sniper Adventure Park; 2) Breaking the ice quiz- testing participants' knowledge on general issues regarding IMM (history, areas of research, facts & figures etc); 3) Walk along the "Dinosaur road trip"; 4) Scientific discussion - Round table.

**VII PhD Students Meeting IMM/CAML**

*Date: December 5-6*

*Place: IMM/FMUL*

*Participants: 61 PhD students presenting their research work (33 posters and 28 oral presentations), 4 Guest Speakers (2 Keynote Lectures and 2 Science Outreach Lectures), 12 Chairs, 6 Members of Jury (3 for oral presentations and 3 for poster sessions). Total: 83 participants; plus other attendants from IMM/FMUL/HSM community.*

**December 5**

**Opening Session**

Carmo Fonseca (Executive Director, IMM), João Lobo Antunes (President, IMM) and José Fernandes e Fernandes (Director, FMUL).

**Keynote Lecture**

Prof. Art Horowich (Yale School of Medicine, Lasker Award 2011)

**Oral Presentation Session I**

Chairs: Diana Cunha-Reis (UFCT, IMM; Fisiologia FMUL) and Helena Cabaço (AE Sousa Lab).

Speakers:

L. Lucas-Neto: The human nucleus accumbens – from anatomy to imaging and clinic

F. Rijo-Ferreira (L Figueiredo Lab): *Trypanosoma brucei* interferes with the mouse circadian rhythm

I.P. Perpétuo (E Fonseca Lab): RANK expression is reduced in circulating monocytes from ankylosing spondylitis patients

M. Gonçalves: A systematic review on wais-III in ebscohost database: a special focus on acquired brain injury.

V.L. Batalha (L Lopes Lab and A Sebastião Lab): Glucocorticoid receptors and memory impairments: modulation by adenosine A2A receptors

C.G.A. Moreira (A Jacinto Lab): *Drosophila* integrin adhesion complexes are essential for hemocyte migration *in vivo*

### **Poster Session I**

A. Amaro Leal, R Mendes de Almeida, D Carmona-Rodrigues, I Vaz-Luis, SA Cerqueira, ST Ribeiro, R Drago, A Ministro, B Vidal, S Arroz-Madeira, SF Fernandes, ST Duarte, AR Maceiras, AF Faustino, I Alvarez-Martins and SL Silva.

### **Oral Presentation Session II**

Chairs: Robert Martin (Maria Carmo-FonsecaLab) and Ana Ribeiro (L Saúde Lab)

E.F. Marques: Efficacy, safety and cost utility of a dual-optic accommodating intraocular lens for surgical correction of presbyopia in patients with senile cataracts

R.I. Aroeira (A Sebastião Lab): Glycine-mediated neurotransmission in rat brain – recent insights

D. Ribeiro (J Barata Lab): IL-7 activates the JAK/STAT5/PIM1 kinase axis thereby mediating viability and growth of T-cell acute lymphoblastic leukemia cells

T. Pereira: Physical exercise and the capacity to form, consolidate and inhibit new motor memories

P. Meireles (M Prudêncio Lab): The role of D-glucose uptake by glucose transporter 1 during the liver stage of *Plasmodium* infection

### **Oral Presentation Session III**

Chairs: Ana de Barros (S Dias Lab) and Diogo Fonseca-Pereira (HV Fernandes Lab)

J.M. Santos (G Mair Lab): IPET: a translationally repressed gene product essential for host cell invasion and transmission of malaria parasites

D.M.Rombo (A Sebastião Lab): Hippocampal network disinhibition of parvalbumin expressing interneurons by adenosine A2A receptors

S.M. Fernandes (AE Sousa Lab): Recovery of enteric mucosa integrity in the presence of preserved innate IL-22 compartment in HIV-1 treated individuals

N. Schmolka (B Silva-Santos Lab): Epigenetic and transcriptional signatures of stable versus plastic differentiation of proinflammatory gamma delta T cell subsets

## **December 6**

### **Outreach Science Lecture I**

Professor Sílvia Conde (CEDOC, FCM/UNL)

### **Oral Presentation Session IV**

Chairs: Federico Herrera (T Outeiro Lab) and Ivo Martins (N Santos Lab)

A.P. Barbosa: VFA: a pioneer technique in hyperthyroidism

T. Pereira (A Jacinto Lab): The cell's cycle around the wound

A. Melão (J Barata Lab): CK2 activity regulates IL-7 pro-oncogenic signaling pathways in T-cell acute lymphoblastic leukemia

F.F. Ribeiro (A Sebastião Lab): The adenosine A2A receptor and microtubule dynamics during axon elongation

#### **Oral Presentation Session V**

Chairs: Rita Fragoso (J Barata Lab) and Sandra Aguiar (M Ramirez Lab)

A. Jerónimo-Santos (A Sebastião Lab) Dysregulation of TrkB receptors and BDNF function by amyloid- $\beta$  peptide is mediated by calpain

J.M. Freire (M Castanho Lab): Intracellular nucleic acid delivery by the supercharged dengue virus capsid protein: putative role during viral infection

C. Mota (AE Sousa Lab): Delta like-1 enhances the *in vitro* conversion of human memory CD4 cells into FOXP3-expressing regulatory T cells

I. Henriques: Hydrogen sulphide reduces infarct size and enhances recovery in a rat model: protection mechanism includes NOX-4 downregulation

#### **Keynote Lecture**

**Professor Maria Leptin** (EMBO Director, EMBL)

#### **Poster Presentation Session II**

N Gonçalves-Rosa, AF Guedes, M Figueiredo, MRebello, AP Nascimento, A Cruz, AN Horácio, AS Silva Herdade, J Diamantino –Miranda, F Mouro, C Pato, RA Pinto, P de Oliveira, RG Domingues, R Vaz and BG Cassani.

#### **Outreach Science Lecture II**

Professor Elvira Fortunato (CENIMAT/I3N, FCT/UNL)

#### **Oral Presentation Session VI**

Chair: Madalena Martins(S Oliveira Lab) and Axel Hollmann (N Santos Lab)

V. Geraldes (M Carvalho Lab): Chronic depression of central neuronal activity produces sustained hypotension in hypertensive rats

M. Rei (B Silva-Santos Lab): Major contribution of  $\gamma\delta$  T cells to IL-17A production and ovarian cancer cell growth *in vivo*

M. Neto: Temporal aspects and interrelationships of psychosocial health determinants in workplace settings

A.C. Pena (L Figueiredo Lab): Histone H1 regulates a small set of genes but is important for virulence of African trypanosomes

M.C. Oliveira: Synaptic modulation by adenosine on an age-dependent epilepsy model

#### **Awards Ceremony and Closing Remarks**

Alice Melão, Jorge Santos and Alexandra Manaia

#### **PhD Meeting Dinner**



## PhD theses

### 10 Lisbon AMC theses: 9 of which were from IMM/Lisbon AMC PhD Students

Telma Sofia Martins Lança (February 4, 2013).  $\alpha\alpha$  Cell Responses to Tumors: recruitment, recognition and functions. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Bruno Silva Santos.

Vanda Lúcia de Carvalho Vitorino de Almeida (Março 25, 2013). The role of Fibrinogen in the mechanism of microvascular inflammatory. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria Carlota Saldanha.

Diogo Fonseca Pereira (April 2, 2013). The role of Neurotrophic Factor Receptor Ret in hematopoiesis. Supervisor: José Henrique Veiga Fernandes.

Mariana Guedes Simões (July 21, 2013). Zebrafish fin regeneration: what has nerve to do with it? Faculdade de Medicina da Universidade de Lisboa. Supervisor: António Jacinto.

Pedro Miguel Baptista de Matos (July 10, 2013). Shedding light on enveloped viruses entry and its inhibition using optical techniques. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Nuno Correia dos Santos.

Marta Ribeiro Lopes Caridade (September 13, 2013). Amyloid  $\beta$  peptide and P63: two prime triggers of neural apoptosis and differentiation. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luís Graça.

Marta Isabel Magalhães Mota do Amara (December 2, 2013). Structure and mechanism of kynurenine 3-monooxygenase, a candidate Huntington's disease drug target. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Tiago Outeiro.

Irina Margarida Pereira Machado Alho Duarte (December 19, 2013). The importance of low molecular weight protein Tyrosine Phosphatase in the progression of metastatic bone disease and therapeutic response. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luís Costa.

Joana Gonçalves de Gouveia Maia Xavier (December 20, 2013). Identification of risk factors for Behçet's. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Sofia Oliveira.

(Total 9 PhD IMM/ Lisbon AMC Thesis)

André Laboreiro Ferreira Mendes Graça (December 20, 2013). Contribuição da Ecografia Cerebral Transfontanelar para a avaliação do crescimento cerebral do recém-nascido pré-termo. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Lopes and José Cabral Campos.

(Total 10 Lisbon AMC PhD Theses)

## Ongoing Partnerships

**Centro Académico de Medicina de Lisboa:** IMM is associated with the Faculdade de Medicina da Universidade de Lisboa and with the Santa Maria teaching hospital through the Medical Academic Centre of Lisbon (CAML). CAML is consortium that represents an infrastructure aiming to promote the academic dimension in clinical practice, renewing the teaching hospital concept.

IMM is also a partner of the **Harvard Medical School – Portugal programme**, sponsored by Fundação para a Ciência e Tecnologia. This programme, directed by M. Carmo-Fonseca (IMM/FMUL), results from a Memorandum of Understanding between Portuguese Ministry of Science, Technology and Higher Education and Harvard Medical School to encourage internationalization and cooperation between Portuguese schools of medicine and major national research centers working in biomedical and health sciences.

Furthermore, IMM is associated with the **Doctoral Programme for Physicians, PFMA**, supported by the Gulbenkian and Champalimaud Foundations, the Ministry of Health and the Foundation for Science and Technology.

Besides education IMM also fosters scientific ideas to turn into products and technologies that make difference in health care. To achieve this goal IMM develops ties and strategic plans with companies, namely companies incubated at IMM: **Genomed, Technophage, Lymphact** and **TcLab** (see companies). In addition, IMM is one of the leading founders of the **Health Cluster Portugal**. This consortium promotes initiatives and research projects that increase the national competitiveness, innovation and technology and also encourages cooperation between companies, organizations, universities and public entities, seeking to expand economic areas related to health and to the improvement of health care.

## RESEARCH

In 2013, IMM hosted 36 research Labs.

Of these:

- 33 are located at Edifício Egas Moniz (IMM-FMUL)
- 1 at Hospital Santa Maria (Joaquim Ferreira Lab)
- 2 at the Faculdade de Farmácia da Universidade de Lisboa (Elsa Anes Lab and João Gonçalves Lab)

**JOÃO BARATA LAB****Major Interests / Objectives**

We aim to understand the role of cell-autonomous alterations and microenvironmental cues in the development of cancer, in particular lymphoid leukemias. We focus on the dissection of signaling pathways activated by cell-intrinsic events and extra-cellular factors to characterize the mechanisms implicated in the acquisition of a selective advantage by malignant cells. To do so, we integrate different biochemical, cellular and molecular biology techniques with appropriate in vitro and in vivo models. The basic and pre-clinical research performed in the lab is translation-oriented and complemented by ongoing collaborations with clinicians. Ultimately, our research aims 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	Post-doctoral Investigator (started May)
Ana Sofia Gírio Veloso	PhD	Post-doctoral Investigator (left March)
Daniel Ribeiro	Master	PhD Student
Ines Lopes Antunes	PhD	Investigator (left May)
Joana Filipa Pereira de Matos	Graduate	MSc Student (started May)
João Paulo Tavanez da Silva Fernandes	PhD	Post-doctoral Investigator (left September)
Leila Raquel Galveias Casquinha Pires Martins	PhD	Post-doctoral Investigator
Maria Leonor Saraiva de Carvalho Morais Sarmiento	PhD	Post-doctoral Investigator
Mariana Lobato de Oliveira	Graduate	MSc Student (started October)
Nádia G. Cavaleiro Sousa Correia	Master	Investigator
Vanda Cristina Barroso Póvoa	Master	Investigator

### Keywords / Research Areas

Oncobiology, Leukemia, Signal transduction, Cellular and molecular biology.

### Major scientific achievements

Previously, we showed that PI3K/Akt signaling is hyperactivated in T-ALL and CLL due to CK2 overexpression. We now demonstrated that clinical-grade inhibitors of CK2 or PI3K delay tumor progression in vivo in pre-clinical models of T-ALL and CLL (Martins et al, *Oncotarget* 2013; Martins et al, *Leukemia* 2013; Lonetti, Antunes et al, *Leukemia* 2013; Buontempo et al, *Leukemia* 2013). These observations should contribute to the integration of CK2 and PI3K specific inhibitors in the therapeutic arsenal against these malignancies.

We identified several microRNA genes (e.g. miR-223, miR-146b-5p) that are regulated by SCL/TAL1, a transcription factor which is aberrantly expressed in T-ALL (Correia et al, *Leukemia* 2013). This is the first contribution to the understanding of the network of microRNA genes modulated by TAL1 that may contribute to its oncogenic potential.

We received a distinction from the Ministry of Health for our contributions to Biomedical research.

### Recent Most Relevant 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. Sarmiento, 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: 35.209, Citations: 40)

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: 12.812, Citations: 110)

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: 13.214, Citations: 103)

### Ongoing Research Projects

2011/2013 Identificação de novos reguladores de CK2 com impacto na função de PTEN em leucemia. Coordinator: João Pedro Taborda Barata. Agency: FCT. Amount: €186.127,00

2012/2015 Dissecando o impacto de mutações ganho-de-função do gene IL7R em leucemia T.

Coordinator: João Pedro Taborda Barata. Agency: FCT. Amount: €165.000,00

2013/2015 Conversas cruzadas entre miRNAs e TAL1? Novas perspectivas sobre a regulação e função de um dos principais oncogenes de células T. Coordinator: João Pedro Taborda Barata. Agency: FCT. Amount: €125.797,00

### Publications in peer review Journals

L.R. Martins, Y. Perera, P. Lúcio, S.E. Perea, M.G. Silva, J.T. Barata (2013). Targeting chronic lymphocytic leukemia using CIGB-300, a clinical-stage CK2-specific cell-permeable peptide inhibitor. *Oncotarget*. (advance online publication). (Journal IF: 6.636)

J.T. Barata (2013). IL-7R $\alpha$ : Mr Hyde's twists and turns. *Blood*. **122**, (26):4151-4152. (commissioned review/commentary) (Journal IF: 9.060)

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\*\* (2013). Activity of the pan-class I phosphoinositide 3-kinase inhibitor NVP-BKM120 in T-cell acute lymphoblastic leukemia. *Leukemia* 2013 Dec 6. doi: 10.1038/leu.2013.369. [Epub ahead of print] \*co-first authors; \*\* co-corresponding authors (Journal IF: 10.164)

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. (2013). Cytotoxic activity of the casein kinase 2 inhibitor CX-4945 against T-cell acute lymphoblastic leukemia: targeting the unfolded protein response signaling. *Leukemia*. 2013 Nov 20. doi: 10.1038/leu.2013.349. [Epub ahead of print] (Journal IF: 10.164)

N.C. Correia, A. Gírio, I. Antunes, L.R. Martins, J.T. Barata (2013). The multiple layers of non-genetic regulation of PTEN tumor suppressor activity. *European Journal of Cancer*. **50**, (1):216-225. doi: 10.1016/j.ejca.2013.08.017. Epub 2013 Sep 19. (review) (Journal IF: 5.061)

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 (2013). Activity of the clinical-stage CK2-specific inhibitor CX-4945 against chronic lymphocytic leukemia. *Leukemia* 2013 Aug 8. doi: 10.1038/leu.2013.232. [Epub ahead of print] (Journal IF: 10.164)

N. Correia, K. Durinck, A.P. Leite, M. Ongenaert, P. Rondou, F. Speleman, F.J. Enguita, J.T. Barata (2013). Novel TAL1 targets beyond protein-coding genes: identification of TAL1-regulated microRNAs in T-cell acute lymphoblastic leukemia. *Leukemia* . **27**, (7):1603-1606. (Journal IF: 10.164)

O. Martinho, R. Silva-Oliveira, V. Miranda-Gonçalves, C. Clara, J.R. Almeida, A.L. Carvalho, J.T. Barata, R.M. Reis (2013). In Vitro and In Vivo Analysis of RTK Inhibitor Efficacy and Identification of Its Novel Targets in Glioblastomas. *Translational Oncology*. **6**, (2):187-96. (Journal IF: 2.943)

D. Ribeiro, A. Melão, J.T. Barata (2013). IL-7R-mediated signaling in T-cell acute lymphoblastic leukemia. *Advances in Biological Regulation*. **53**, (2):211-222. (commissioned review)

### Invited lectures and seminars

J.T. Barata. IL-7 and T-cell Leukemia: How Interleukins can Shape Cancer Behaviour, 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal, August 18-20, 2013.

J.T. Barata. Too much of a good thing: IL-7 and IL-7R in T-cell leukemia, 3rd International Symposium on Translational Oncology, Barretos, SP, Brazil, August 29-30, 2013.

J.T. Barata. The role of IL7R in childhood T-cell acute lymphoblastic leukemia, European Human Genetics Conference 2013, Paris, France, June 8-11, 2013.

J.T. Barata. Signals from the outside, signals from within: IL-7 and IL-7R in acute T-cell leukemia, 8th Annual Helsinki Biomedical Graduate Program Symposium, Biomedicum Helsinki, Finland, May 16-17, 2013.

J.T. Barata. IL-7 and IL-7R-mediated signaling in T-ALL, Second ESH-EHA Scientific Workshop on T-cell Acute Lymphoblastic Leukemia, Lisbon, Portugal, March 22-24, 2013.

J.T. Barata. Good things gone bad: IL-7 and IL-7R in T-cell leukemia. XXXIX Annual Meeting of The Portuguese Society of Immunology, Coimbra, Portugal, November 13-15, 2013.

J.T. Barata. O lado obscuro da lua: IL-7 e IL-7R em leucemia de células T [The dark side of the moon: IL-7 and IL-7R in T-cell leukemia]. IV Science and Medicine Meeting, University of Minho, Braga, Portugal, April 20, 2013.

### Communications in International Conferences

A. Melão, A. Gírio, J.T. Barata (2013). CK2 Activity Regulates IL-7 Pro-Oncogenic Signaling Pathways in T-Cell Acute Lymphoblastic Leukemia. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal, September 18-20, 2013 (Poster presentation)

L.M. Sarmiento, V. Póvoa, R. Nascimento, G. Real, I. Antunes, L.R. Martins, J. Meijerink, J.T. Barata (2013). CHK1 is essential for the growth and survival of T-cell acute lymphoblastic leukemia cells. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal, September 18-20, 2013. (Poster presentation)

D. Ribeiro, A. Melão, R. van Boxtel, C.I. Santos, M.C. Silva, A. Silva, B.A. Cardoso, L.F. Moita, P.J. Coffey, J.T. Barata (2013). IL-7 Activates the JAK/STAT5/PIM1 Kinase Axis Thereby Mediating Viability and Growth of T-Cell Acute Lymphoblastic Leukemia Cells. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal, September 18-20, 2013 (Poster presentation)

N.C. Correia, F.J. Enguita, F. Speleman, J.T. Barata (2013). Novel TAL1 targets beyond protein coding genes: identification of TAL1-regulated microRNA genes in T-cell acute lymphoblastic

leukemia. RNA 2013 – The 18th Annual Meeting of the RNA Society, Davos, Switzerland, June 11-16, 2013. (Poster presentation)

A. Melão, A. Gírio, J.T. Barata (2013). CK2 Basal Activity Regulates IL-7-Mediated JAK/STAT and PI3K/Akt Pathway Activation and Pro-Survival Effects in T-Cell Acute Lymphoblastic Leukemia Cells. Second ESH-EHA Scientific Workshop on T-cell Acute Lymphoblastic Leukemia, Lisbon, Portugal, March 22-24, 2013 (Poster presentation)

D. Ribeiro, A. Melão, R. van Boxtel, C.I. Santos, M.C. Silva, A. Silva, B.A. Cardoso, L.F. Moita, P.J. Coffey, J.T. Barata (2013). IL-7-Mediated Viability and Growth of T-Cell Acute Lymphoblastic Leukemia Cells Relies on a JAK/STAT5/PIM1 Kinase Axis. Second ESH-EHA Scientific Workshop on T-cell Acute Lymphoblastic Leukemia, Lisbon, Portugal, March 22-24, 2013 (Poster presentation)

N.C. Correia, F. Speleman, F.J. Enguita, J.T. Barata (2013). Identification of TAL1-regulated microRNA genes in T-cell acute lymphoblastic leukemia. Second ESH-EHA Scientific Workshop on T-cell Acute Lymphoblastic Leukemia, Lisbon, Portugal, March 22-24, 2013 (Poster presentation)

### **Communications in National Conferences**

L.M. Sarmiento, V. Póvoa, R. Nascimento, G. Real, C. Moita, I. Antunes, L. Martins, P.M. Alves, M. Parkhouse, L. Moita, J. Meijerink, J.T. Barata (2013). CHK1 is essential for the growth and survival of T-cell acute lymphoblastic leukemia. SINAL 2013 – 7th National Meeting on Cell Signalling, University of Aveiro, Portugal, December 6-7, 2013 (Oral communication)

M.T. Fernandes, M.N. Ghezzi, V. Póvoa, A.R. Ribeiro, N.L. Alves, J.T. Barata, N.R. dos Santos (2013). Lymphotoxin-beta Receptor Signalling in Microenvironmental Cells Supports T-Cell Leukemogenesis. SINAL 2013 – 7th National Meeting on Cell Signalling, University of Aveiro, Portugal, December 6-7, 2013 (Oral communication)

### **Organisation of Conferences**

J.T. Barata was a member of the evaluation panel, Poster Session II; Research Day for Medical Students / 16th Workshop “Education through Science”, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 11, 2013.

R. Fragoso was Chair of the Oral session V of the VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013.

J.T. Barata was a member of the Scientific Committee and co-Chair of Session V, SINAL 2013 – 7th National Meeting on Cell Signalling, University of Aveiro, Portugal, December 6-7, 2013.

J.T. Barata was Co-Chair of Sessions II and V, Second ESH-EHA Scientific Workshop on T-cell Acute Lymphoblastic Leukemia, Lisbon, Portugal, March 22-24, 2013.

### **Internationalisation**



All our projects involve some degree of collaborative work with international research groups in Europe, US and Brazil. Our publication track record illustrates this extensively. Our FCT funded projects systematically include foreign researchers as consultants or participants.

Current international collaborators include: 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), Silvio Perea (CIGB, Havana, Cuba) and Alberto Martelli (University of Bologna, Italy).

The lab head, Dr. J.T. Barata, is regularly invited to give talks at research institutes abroad and at international meetings (see Invited Lectures and Seminars section for examples regarding 2013). Furthermore, in 2013 Dr. Barata was asked to act as referee for prestigious international journals (including Nature Medicine, EMBO Molecular Medicine, Blood, Leukemia and PLoS One). He is Associate Editor of the American Journal of Cancer Research since October 2011 and Ad Hoc Section Editor for Leukemia.

We welcome regularly foreign students. In 2013, we hosted a visiting post doc from Cuba and a visiting MSc student from Spain.

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

J.T. Barata was awarded the Silver Medal for Distinct Services from the Portuguese Ministry of Health.

### **Advanced teaching**

J.T. Barata lectured the topic “Signaling in Cancer”, Advanced Course on “Fundamentals of Genetics, Development and Neoplasia”, 5th Edition, International Postgraduate Programme, Instituto de Investigação em Ciências da Vida e Saúde (ICVS), School of Health Sciences, University of Minho, Braga, Portugal, October 15, 2013.

J.T. Barata lectured the topic “Signaling in Cancer and Leukemia”, Masters in Biomedical Sciences, University of Algarve, Faro, Portugal, April 24, 2013.

J.T. Barata lectured the topic “Basic Concepts on Signaling in Cancer”, Advanced Course on Oncobiology, BEB PhD Program of the Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Coimbra, Portugal, February 26, 2013.

J.T. Barata lectured the topic “Signaling in Cancer”, Advanced Course on “Fundamentals of Genetics, Development and Neoplasia”, 4th Edition, International Postgraduate Programme, Instituto de Investigação em Ciências da Vida e Saúde (ICVS), School of Health Sciences, University of Minho, Braga, Portugal, January 21, 2013.

### **Science and society**

J.T. Barata was interviewed on public broadcast TV for the “Maratona da Saúde” fundraising for science effort.

Several members of the lab were involved in IMM laboratories’ showcase for medical students during the FMUL students’ day.

I. Lopes and J.T. Barata wrote perspective articles for the news@FMUL – the institutional Newsletter from Faculdade de Medicina da Universidade de Lisboa.

## GONÇALO BERNARDES LAB

### Major Interests / Objectives

Our research programme lies under the broader field of Chemical Biology. In particular, we are interested in the development of site-selective and rapid protein modification methods in aqueous systems as a means to understand key biological processes and to generate targeted therapeutics.

### Head of Unit

Gonçalo José Lopes Bernardes, PhD, Assistant Professor, Department of Chemistry, University of Cambridge.

### Research Team

João Alexandre Guarita da Silva Rodrigues	PhD	Principal Investigator (started October)
Miguel Correia Botelho Chaves Ferreira	PhD	Technician (started October)

### Keywords / Research Areas

Site-selective protein modification, Protein therapeutics, Targeted cancer therapeutics, Carbohydrate-based vaccines, Small molecule drug discovery, Bioorthogonal labelling strategies.

### Major scientific achievements

The Lab has made strong contributions in the fields of protein chemistry and protein therapeutics. Just recently, the antibody drug conjugate the PI developed while at the ETH Zürich has reached clinical development.

The PI has published 4 papers in 2013, published 1 patent and filled 1 patent application.  
Funding: Marie Curie CIG, Marie Curie ITN, Investigador FCT 2012, Hovione PhD studentship (start 2014).

The PI won the European Federation of Medicinal Chemistry – Young Investigator Award in Academia and the 2013 Royal Society of Chemistry/BMOS Young Investigator Award. For his efforts in translational research, Gonçalo was distinguished by the Portuguese Ministry of Health (MH) of Portugal for relevant services to Public Health and Medicine.

### Recent Most Relevant Publications

Bernardes, G.J.L.; Steiner, M.; Hartmann, I.; Neri, D.; Casi, G. (2013) Site-specific Chemical Modification of Antibody Fragments with Traceless Cleavable Linkers. *Nature Protocols* **8**, 2079 (Journal IF: 7.96, Citations: 1)

Bernardes, G.J.L.; Casi, G.; Trüssel, S.; Hartmann, I.; Schwager, K.; Scheuermann, J.; Neri, D. (2012) A Traceless Vascular Targeting Antibody-Drug Conjugate for Cancer Therapy. *Angew. Chem. Int. Ed.* **51**, 941 (Journal IF: 13.734, Citations: 23) Selected as a Very Important Paper (VIP).

Santos-Silva, T.; Mukhopadkyay, A.; Seixas, J.D.; Bernardes, G.J.L.\*; Romão, C.R.; Romão, M.J. (2011) CORM-3 Reactivity Towards Proteins: The Crystal Structure of a Ru(II) Dicarbonyl-Lysosyme Complex. *J. Am. Chem. Soc.* **133**, 1192 (Journal IF: 10.677, Citations: 33)

Bernardes, G.J.L.; Chalker, J.M.; Errey, J.C.; Davis, B.G. (2008) Facile Conversion of Cysteine and AlkylCysteines to Dehydroalanine: Versatile and Switchable Access to Functionalized Proteins. *J. Am. Chem. Soc.* 130:5052. (Journal IF: 10.677, Citations: 104) Article highlighted in: *Nature Chemical Biology*. **4**, 527-528 and Chemical&Engineering News, March 31, 2008.

Bernardes, G.J.L.; Grayson, E.J.; Thompson, S.; Chalker, J.M.; Errey, J.C.; Oualid, F.E.; Claridge, T.D.W.; Davis, B.G. (2008) From Disulfide- to Thioether-linked Glycoproteins. *Angew. Chem. Int. Ed.* **47**, 2244 (Journal IF: 13.734, Citations: 58)

### Other Projects

2013/2017 Marie Curie Career Installation Grant. Coordinator: Gonçalo Bernardes. Amount: €100.000,00

2013/2017 Marie Curie Initial Training Network. Coordinator: João Rodrigues. Amount: €670.000,00 Total amount: €3.500.000,00

### Publications in peer review Journals

GJL Bernardes, M Steiner, I Hartmann, D Neri, G Casi (2013) Site-specific chemical modification of antibody fragments using traceless cleavable linkers. *Nature protocols*. **8**, (11):2079-2089 (Journal IF: 7.96, Citations: 1)

R Adamo, A Nilo, B Castagner, O Boutureira, F Berti, GJL Bernardes (2013) Synthetically defined glycoprotein vaccines: Current status & future directions. *Chemical Science*. **4**, 2995-3008 (Journal IF: 8.314, Citations: 5)

GJL Bernardes (2013) Highlights from the 48<sup>th</sup> EUCHEM conference on stereochemistry, Bürgenstock, Switzerland. *Chemical Communications*. **49**,(77):8578-8582 (Journal IF: 6.378)

M Steiner, I Hartmann, E Perrino, G Casi, S Brighton, I Jelesarov, GJL Bernardes (2013) Spacer length shapes drug release and therapeutic efficacy of traceless disulfide-linked ADCs targeting the tumor neovasculature. *Chemical Science*. **4**, (1):297-302 (Journal IF: 8.314, Citations: 4)

#### Invited lectures and seminars

Site-selective protein modification for bioimaging and protein therapeutics. Memorial Sloan-Kettering Cancer Center (MSKCC), New York (US), 2013

Site-selective protein modification for bioimaging and protein therapeutics. 15th Brazilian Meeting in Organic Synthesis (BMOS), Campos do Jordão (Brazil), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Department of Chemistry, Technische Universität München, München (Germany), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Institut Curie, Paris (France), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Sanofi Aventis, Frankfurt (Germany), 2013

Site-selective protein modification for bioimaging and protein therapeutics. European Biophysics Congress, EBSA2013, Lisbon (Portugal), 2013

Site-selective protein modification for bioimaging and protein therapeutics. EMBO fellows meeting, Heidelberg (Germany), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Chemistry for Life Sciences, 5th European Conference, Barcelona (Spain), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Advances in Synthetic and Medicinal Chemistry, Moscow (Russia), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Stereochemistry @ Bürgenstock (Switzerland), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Portugal and the Royal Society, Imperial College London (UK), 2013

Site-selective protein modification for bioimaging and protein therapeutics. Department of Chemistry, University of Zürich (Switzerland), 2013

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

Royal Society of Chemistry and Brazilian Meeting in Organic Synthesis Young Investigator Award - 2013

EFMC Prize for a Young Medicinal Chemist in Academia - 2013

Silver Medal - Portuguese Ministry of Health (MH) of Portugal for relevant services to Public Health and Medicine - 2013

Selected for The Lindau Nobel Laureate Meeting – sponsored by AKB Stiftung - 2013

Journals Grant for International Authors, Royal Society of Chemistry - 2013

### **Patents/prototypes**

“Ruthenium carbon monoxide releasing compounds and uses thereof for treatment of inflammatory conditions” Pamplona, A.; Bernardes, G.J.L.; Mota, M.M.; Romão, C.C.; PCT Int. Appl. (2013), WO 2013013179 A1 20130124.

“Chemical modification of protein with metal carbonyl reagents and uses thereof for the treatment of inflammatory conditions and cancer” Bernardes, G.J.L.; Application filled and submitted.

### **Industry contract research**

Novartis Vaccines - development of glycoproteins as vaccine candidates. From October 2013 onwards – PhD Studentship in partnership.

**MARIA ERMELINDA CAMILO LAB**

**Major Interests / Objectives**

Clinical and translational biomedical/nutritional research in nutrition/metabolism in tune with investigators’ interests. Disease management, nutrition/life-style related risk factors prevail, e.g. nutrition & cancer, nutrition & Quality of Life, metabolic dysfunction, body composition & genetic predisposition for cachexia, nutrients and disease modulation/therapy/prognosis, obesity, fatty liver & insulin resistance. Investigate interconnections with basic science, thus genetic polymorphisms studies of inflammatory /immuno-modulatory cytokines, as pathogenic mechanisms of lesion, nutritional deterioration or metabolic implications; the role of nutrigenetics in cancer and inflammatory diseases, as well as apoptosis in alcoholic/non-alcoholic liver disease.

**Head of Unit**

Maria Ermelinda Camilo, MD/PhD.

**Research Team**

Ana Isabel Paulos Ramos de Almeida	Master	PhD Student, Teaching Assistant
Catarina Ferreira Murinello de Sousa Guerreiro	PhD	Investigator, Teaching Assistant
Catarina João Monteiro Ferreira	Graduate	Investigator
Dina Raquel Fernandes João	Master	PhD Student, Teaching Assistant
Helena Maria Ramos Marques Coelho Cortez Pinto	MD/PhD	Investigator, Clinical Specialist, Associate Professor
Inês Vaz Bravo Carretero	Graduate	MSc Student
Maria Isabel de Freitas Ferreira Queimado Monteiro Grillo	MD/PhD	Principal Investigator, Clinical Department Director
Mariana Verdelho Machado	Graduate	PhD Student, MD
Paula Ravasco	MD, PHD	Principal Investigator, Assistant Professor
Sofia Catarina Carvalhana	Master	Investigator

### Keywords / Research Areas

Hepatology, steatohepatitis, obesity, insulin resistance, Oncology /radiotherapy, sarcopenia, cachexia.

### Major scientific achievements

Still the only Research Nutrition and Metabolism Lab in Portugal, its high quality of Advanced Education and Research are widely recognized. Both achievements are highlighted by Publications in Journals with high impact factors and in the internationalization with relevant roles in international bodies, lectures in major international Congresses and advanced teaching.

A small multidisciplinary team has reached international recognition via cutting edge research of excellence in two main areas:

- Cortez-Pinto H focus on liver fat metabolism, from clinical to translational research, is an internationally recognized expert in steatohepatitis.
- Ravasco P is a prized speaker in international meetings as expert in Nutrition and Cancer.

The Lab is increasingly requested for advanced teaching: to guide and/or supervise future professionals in their research projects: e.g. integrated Master Degree in Medicine, Nutrition Master Programs.

### Recent Most Relevant Publications

Mathurin P, Hadengue A, Bataller R, Addolorato G, Burra P, Burt A, Caballeria J, Cortez-Pinto H, Day CP, Forrest EH, Gual A, Leon DA, Lligona A, Jepsen P, Mueller S, Pageaux GP, Roskams T, Seitz HK, Stickel F, Thursz, Naveau S, Morgan T, Nevens F. (2012) European Association for the Study of Liver. EASL Practical guidelines: management of alcoholic liver disease. *Journal of Hepatology* **57**, 399-420. (Journal IF: 9.858, Citations: 10)

Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo ME, Ravasco P. (2011) Teaching nutrition integration: MUST screening in cancer. *The Oncologist* **16**, 239-245. (Journal IF: 4.095, Citations: 3)

Ratzu V, Bellentani S, Cortez-Pinto H, Day C, Marchesini G ( 2010) A position statement on NAFLD/NASH based on the EASL 2009 special conference. *Journal of Hepatology* **53**, 372-384. (Journal IF: 9.858, Citations: 131)

Machado MV, Oliveira AG, Cortez-Pinto H. (2010) Hepatic Steatosis in Patients Coinfected with Human Immunodeficiency Virus/Hepatitis C Virus: A Meta-Analysis of the Risk Factors. *Hepatology* **52**, 71-78. (Journal IF: 12.003, Citations: 12)



Ravasco P. (2009) Cancer and nutrition: key determinants of Quality of Life. *European Journal of Cancer* **45**(supl1):409. (Journal IF: 5.061, Citations: 3)

### Ongoing Research Projects

2012/2014 Estimativa da prevalência de esteatose hepática na população portuguesa. Coordinator: Helena Cortez Pinto. Agency: Roche. Reference: FPJ000633. Amount: €4.000,00

2012/2014 Estimativa da prevalência de esteatose hepática na população portuguesa. Coordinator: Helena Cortez Pinto. Agency: Gilead. Amount: €36.500,00

2013/2016 Treat liver diseases by targeting hepatocyte necroptosis. Coordinator: Helena Cortez-Pinto. Agency: FCT. Amount: €35.000,00 Total amount: €526.947.000,00

2012/2016 Eicosapentaenoic acid in Cancer: does it affect inflammation, body composition, treatment? toxicity, Quality of Life and prognosis? A randomized, prospective controlled trial. Coordinator: Paula Ravasco. Agency: FCGulbenkian. Amount: €120,000,00 (in negotiation)

### Other projects

2011/2014 How to evaluate body composition in cancer: validation of 3 methods for clinical use. Coordinator: Paula Ravasco Agency: FCT.

2013/2015 Cancer: body composition and phase angle, metabolic pattern, and nutrition. Coordinator: Paula Ravasco. Agency: FCT.

2012/2016 Cancer cachexia: Evaluation of body composition using CT scans and identification of genetic markers. Multicentre study supported by Trondheim - Norway, Department of Surgery - Edinburgh University, UK and CIHR Cachexia Research Network.

2012/2016 Watercress in Cancer: a new therapeutic adjuvant in cancer treatment? A randomized longitudinal trial. Coordinator: Paula Ravasco. Amount: €10.000,00

### Publications in peer review Journals

Pimenta NM, Santa-Clara H, Cortez-Pinto H, Silva-Nunes J, da Lapa Rosado M, Sousa PJ, Calé R, Melo X, Sardinha LB, Fernhall B. Body composition and body fat distribution are related to cardiac autonomic control in non-alcoholic fatty liver disease patients. *Eur J Clin Nutr*, 2013, (Journal IF: 2.756) <http://www.ncbi.nlm.nih.gov/pubmed/24300906>

Machado MV, Cortez-Pinto H. Non-Invasive Diagnosis of Non-Alcoholic Fatty Liver Disease - A Critical Appraisal. *J Hepatol*. 2013, **58**, 1007-19 (Journal : 9.858)

Carvalhana S, Leitão J, Alves AC, Bourbon M, Cortez-Pinto H. How good is controlled attenuation parameter and fatty liver index for assessing liver steatosis in general population: correlation with ultrasound. *Liver International*, 2013 (Journal IF: 3.870) <http://www.ncbi.nlm.nih.gov/pubmed/24034415>

Machado M, Cortez-Pinto H. Leptin in the treatment of lipodystrophy-associated nonalcoholic fatty liver disease: are we there already? *Expert Review of Gastroenterology and Hepatology* 2013. **7**(6),513-5 (Journal IF: 2.221)

Castro RE, Ferreira DM, Afonso MB, Borralho PM, Machado MV, Cortez-Pinto H, Rodrigues CM. miR-34a/SIRT1/p53 is suppressed by Ursodeoxycholic acid in rat liver and activated by disease severity in human non-alcoholic fatty liver disease. *J Hepatol.* 2013, **58**(1), 119-25 (Journal IF: 9.858, Citations:3)

Ana Luisa Vasconcelos, Beatriz Nunes, Catarina Duarte, Vera Mendonça, Joana Ribeiro, Marília Jorge, Isabel Monteiro Grillo “ Tamoxifen in breast cancer ipse dixit in uterine malignant mixed Müllerian tumor and sarcoma – A report of 8 cases and review of the literature”. *Reports of Practical Oncology & Radiotherapy* 2013, **18** (5), 251-260. (Journal IF: no IF)

Almeida AI, João DR, Rolão A, Monteiro Grillo I, Camilo M, Ravasco P. “What is the nutritional pattern and lifestyles of cancer patients? *Nutrición Hospitalaria* 2013; **28**, 1468-1474.(Journal IF: 1.305)

Ravasco P, Monteiro-Grillo I, Camilo M. Reply to AG Longhi. *American Journal Clinical Nutrition* 2013, **98**, 246-247. (Journal IF: 6.504)

Mealha V, Ferreira C, Guerra I, Ravasco P. "Students of dietetics and nutrition: a high risk group for eating disorders?" *Nutrición Hospitalaria* 2013, **28**, 1558-1566. (Journal IF: 1.305)

### Other publications International

Machado M, Cortez-Pinto H, Evaluating the NAFLD patient: putting in perspective non-invasive and invasive methods. p. 63-70. In: Therapy in Liver Diseases. Editors: Ginés P, Forns X, Fernandez J, Crespo G, Rodes J, Arroyo V. *Elsevier Publications*, Barcelona, Spain, 2013.

Alan Dal Pra, Isabel Monteiro Grillo. Chapter nº 36: Complicações Tardias em Radioterapia. Book: *Radioterapia em Oncologia* 2nd Edition. (Edts) João Salvajoli, Luís Souhami, Sérgio Faria, Atheneu, Brasil, 2013.

### Invited lectures and seminars

Cortez-Pinto H. How to manage patients with metabolic syndrome and fatty liver on Ultrasound. Lunch Session. UEG Week, Berlin, Germany, October 12-16, 2013.

Cortez-Pinto H. The burden of alcohol worldwide. UEG Week, Berlin, Germany, October 12-16, 2013.

Cortez-Pinto H. Impact of NAFLD on cardiovascular disease. UEG Week, Berlin, Germany, October 12-16, 2013.

Steatosis: how to identify the patients who progress into steatohepatitis. Congresso Brasileiro de Hepatologia, Rio de Janeiro, Brazil, October 2-5, 2013.

Cortez-Pinto H. NASH and microbiota - Mini-Conferência. Congresso Brasileiro de Hepatologia, Rio de Janeiro, Brasil, Rio de Janeiro, Brazil, October 2-5, 2013.

Cortez-Pinto H. Evaluating the NAFLD patient: putting in perspective non-invasive and invasive methods. Curso: "Therapy on liver diseases", Barcelona, Spain, September 17-20, 2013.

Cortez-Pinto H. The obese alcoholic: NASH/ASH interactions. 14th ESBRA Meeting, Varsow, Poland, September 8-11, 2013.

Epidemiology and importance of alcoholic liver disease from a public health point of view. The International Liver Congress, EASL, Amsterdam, Holland, April 24-27, 2013.

Cortez-Pinto H. Diagnostic Work Up of ALD: Biopsy or Non-Invasive Assessment. The International Liver Congress, EASL, Rio de Janeiro, Brazil, October 2-5, 2013.

Cortez-Pinto H. Importância e custos das doenças associadas ao álcool. Fórum Nacional Álcool e Saúde. Lisbon, Portugal, April 4, 2013.

Monteiro-Grillo I. Interação da radioterapia com a terapêutica sistémica no tumor da mama. 12º Reunião Internacional de Cirurgia, FML, Lisbon, Portugal, February 18-20, 2013

Monteiro-Grillo I. Nutrição adjuvante em oncologia: perspectiva de um serviço de radioterapia de referência, XV Congresso Annual da APNEP, Matosinhos, Portugal, April 10-13, 2013.

Monteiro-Grillo I. Nutrición en pacientes con cáncer de cabeza y cuello. IV Congresso ALATRO, Asociacion Latino Americana de Terapia Radiante Oncologica, Cartagena de Índias, Colombia. July 28-31, 2013.

Monteiro-Grillo I. Chairman: Estado nutricional no doente oncológico: novas perspectivas", XV Congresso Anual da APNEP, Matosinhos, Portugal, April 10-13, 2013.

Monteiro-Grillo I. Chairman: Are we the same radiation oncologists? trends and visions of the future. 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013.

Ravasco P. Nutritional in hematological and oncological patients. OeGHO Congress on Nutrition and Oncology, Linz, Austria, April 20, 2013.

Ravasco P. Nutritional intervention and prevention of cancer: update. 55th Congress of SEEN (Spanish Society of Endocrinology and Nutrition), Granada, Spain, May 17, 2013.

Ravasco P. Nutritional diagnosis in cancer: mechanisms and clinical features. Educational Dietetics Session – 35th Annual Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, September 1, 2013.

Ravasco P. Effect of nutrition counseling in cancer patients. Annual Meeting of the Norwegian Society of Clinical Nutrition and Oncology. Rigshospitalet, Oslo, Norway, December 5, 2013.

Ravasco P. Nutrition in cancer. Encontros de Primavera 2013, Évora, Portugal, April 18, 2013.

Ravasco P. The importance of a regular gastrointestinal transit. XV Annual Congress of APNEP (Portuguese Association of Parenteral and Enteral Nutrition) 2013, Oporto, Portugal, April 23, 2013.

Ravasco P. Phase angle, body composition, cancer histology and stage: what is the relation?. XV Annual Congress of APNEP (Portuguese Association of Parenteral and Enteral Nutrition) 2013, Oporto, Portugal, April 23, 2013.

Ravasco P. Mediterranean diet and oncologic disease. Seminars on Mediterranean Diet: life styles, food and health promotion, University of Algarve, Faro, Portugal, October 25, 2013.

Ravasco P. The role of nutrition in disease: Oncology. Academy of Clinical Nutrition promoted by NESTLE Portugal, Lisbon, Portugal, October 29, 2013.

Guerreiro, CS. Nutrigenómica. I Encontro Nacional de Estudantes de Dietética e Nutrição, Leiria, Portugal, September 5, 2013.

Guerreiro, CS. Nutrição e Genes. VI fórum de projetos de prevenção da obesidade. Faculdade Medicina de Lisboa, Lisbon, Portugal, June 22, 2013.

Guerreiro, CS. FODMAPS – Quando e como a sua utilização. XV Congresso da APNEP, Oporto, Portugal, April 22, 2013.

### **Communications in International Conferences**

Carvalhana S, Leitão J, Alves AC, Bourbon M, Cortez-Pinto H. Controlled attenuation parameter (CAP) for non-invasive assessment of liver steatosis in the general population: correlation with ultrasound (US) and fatty liver index (FLI). 48th annual meeting of the European Association for the Study of Liver (EASL), Amsterdam, Netherlands, April 24-28, 2013. (Poster presentation)

Carvalhana S, Marinho R, Cortez-Pinto H, Velosa J. Wilson's Disease: Long-term outcome seems to be influenced by presentation form. 21st United European Gastroenterology (UEGW), Berlin, Germany, October 12-16, 2013. (Poster presentation)

Carvalhana S, Marinho R, Cortez-Pinto H, Velosa J. Wilson's Disease: Long-term outcome seems to be influenced by presentation form. 21st United European Gastroenterology (UEGW), Berlin, Germany, October 12-16, 2013. (Poster presentation)

Ferreira D, Borralho P, Machado M, Cortez-Pinto H, Rodrigues C, Castro R. Skeletal muscle mirnas in non-alcoholic fatty liver disease and targeting by tauroursodeoxycholic acid in vitro. 21st United European Gastroenterology (UEGW), Berlin, Germany, October 12-16, 2013. (Oral communication)

Afonso M, Ferreira D, Cortez-Pinto, Castro R, Rodrigues C. Necroptosis in primary rat hepatocytes and in patients with chronic liver disease. 21st United European Gastroenterology (UEGW), Berlin, Germany, October 12-16, 2013. (Poster presentation)

Duarte M. Ferreira, Pedro M. Borralho, Mariana V. Machado, Helena Cortez-Pinto, Cecília M. Rodrigues, Rui E. Castro. miRNAs are Differentially Expressed in Skeletal Muscle from Non-Alcoholic Fatty Liver Disease Patients and Targeted by Tauroursodeoxycholic Acid in vitro. The Liver Meeting 2013, AASLD, Washington DC, USA, November 1-5, 2013. (Poster presentation)

Marta B. Afonso, Duarte M. Ferreira, Helena Cortez-Pinto, Rui E. Castro, Cecília M. Rodrigues. Necroptosis in liver disease patients and in primary rat hepatocytes. The Liver Meeting 2013, AASLD, Washington DC, USA, November 1-5, 2013. (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Ravasco P. Phase angle in cancer predicts Quality of Life and prognosis. EXPERIMENTAL BIOLOGY 2013, Boston, USA, April 19-24, 2013. (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Ravasco P. Bioelectrical impedance analysis (BIA) and phase angle: how relevant in cancer?. EXPERIMENTAL BIOLOGY 2013, Boston, USA, April 19-24, 2013. (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Ravasco P. Bioelectrical impedance phase angle: predictor of cell disturbance, metabolism and priority for nutritional intervention?. Experimental Biology 2013, Boston, USA, April 19-24, 2013. (Poster presentation)

Orell-Kotikangas H, Schwab U, Saari-Lahti K, Österlund P, Ravasco P, Mäkitie A. Locally advanced head and neck cancer: the effect of intensive nutrition counseling. 35th Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, August 31-September 3, 2013. Clinical Nutrition 2013; 7 (suppl 1): 165. (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Johns N, Fearon K, Ravasco P. Dietary intake, sarcopenia and phase angle in cancer: new insights. 35th Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, August 31-September 3, 2013. Clinical Nutrition 2013; 7 (suppl 1): 179. (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Johns N, Fearon K, Ravasco P. Computed tomography and bioelectrical impedance: relevance for body composition assessment in Oncology. 35th Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, August 31-September 3, 2013. Clinical Nutrition 2013; 7 (suppl 1): 182. Travel Award for abstracts classified among the 20 best of the congress. (Poster presentation)

Ferreira C, Russo A, Mariano A, Ravasco P. The diet of university students in Portugal: what are the food habits? 35th Congress of ESPEN (European Society for Clinical Nutrition and

Metabolism), Leipzig, Germany, August 31-September 3, 2013. *Clinical Nutrition* 2013; 7 (suppl 1): 203. (Poster presentation)

Ferreira C, Russo A, Ravasco P, Azevedo S, Lopes AI. Inflammatory bowel disease in paediatrics: the impact of nutritional status and intake. 35th Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, August 31-September 3, 2013. *Clinical Nutrition* 2013; 7 (suppl 1): 56. (Poster presentation)

### Communications in National Conferences

Carvalhana S, Marinho R, Cortez-Pinto H, Velosa J. Doença de Wilson: prognóstico e correlação com a forma de apresentação. 16ª Reunião da APEF, Coimbra, Portugal, April 2013.

Carvalhana S, Cortez-Pinto H, Velosa J. Síndrome de sobreposição de hepatite autoimune e hepatite C: dificuldades nas decisões terapêuticas. 16ª Reunião da APEF, Coimbra, Portugal, April 2013.

Noronha Ferreira C, Rodrigues T, Cortez-Pinto H, Serejo F, Ramalho F, Alexandrino P, Velosa J. Avaliação Crítica da nova definição de disfunção renal aguda pelo working party em doentes cirróticos. Semana Digestiva, Vilamoura, Portugal, June 12-15, 2013. (Oral communication)

S. Carvalhana, L. Ribeiro, F. Silva, J. Leitão, C. Alves, M. Bourbon, H. Cortez-Pinto. Prevalência da esteatose hepática na população geral Portuguesa: A importância do álcool e da obesidade. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Oral communication)

H. Cortez-Pinto, P. Borralho, J. Machado, M.T. Lopes, A.M. Santos, A.S. Guerreiro. Sinbiótico retarda a progressão de fibrose modulando a microbiota num modelo de EHNA induzida por dieta gorda e deficiente em colina. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Oral communication)

S. Carvalhana, J. Leitão, C. Alves, M. Bourbon, H. Cortez-Pinto. Utilidade do controlled attenuation parameter (CAP) na avaliação de esteatose hepática na população: correlação com a ecografia e FLI. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Oral communication)

S. Carvalhana, A. Costa, R. Murta, J. Coutinho, H. Proença, H. Cortez-Pinto. Fragmento de citoqueratina-18 (CCK-18) como biomarcador não invasivo de esteatohepatite não alcoólica na obesidade mórbida. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Oral communication)

M.B. Afonso, D.M.S. Ferreira, H. Cortez-Pinto, R.E. Castro, C.M.P. Rodrigues. Necroptose em hepatócitos primários de rato e em doentes com hepatite crónica. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Oral communication)

S.R. Fernandes, L. Araújo Correia, H. Cortez-Pinto, R. Esteves, A. Gonçalves, C. Ferreira, J. Velosa. Neoplasia mucinóide papilar intradutal como causa de pancreatite crónica. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Poster presentation)

C. Noronha Ferreira, T. Rodrigues, H. Cortez-Pinto, F. Serejo, F. Ramalho, P. Alexandrino, J. Velosa. Primeira descompensação de cirrose: a rotura de varizes associa-se a doença hepática menos avançada e melhor prognóstico. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Poster presentation)

S. Carvalhana, M. Machado, J. Velosa, H. Cortez-Pinto. Consumo de álcool sem efeito na gravidade ou na progressão da cirrose biliar primária. Semana Digestiva, Vilamoura, Portugal, June 12–15, 2013. (Poster presentation)

Beatriz Matos Nunes, Laurentiu Bujor, Catarina Duarte, José Miguens, Isabel Monteiro Grillo. (Re)descobrimo a Radioterapia em Doença Benigna – O Papel no Craniofaringioma. 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013. (Oral communication)

Beatriz Matos, Catarina Duarte, Ana Amado, Laurentiu Bujor, Isabel Monteiro Grillo. O Papel da Radiocirurgia no Glomus Jugulare – Revisão de 15 Casos . 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Oral communication)

Catarina Duarte, Laurentiu Bujor, Ana Amado, Isabel Monteiro Grillo. Linfoma da Glândula Lacrimal Tratado com RT de Baixa Dose. 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Oral communication)

Beatriz Matos Nunes, Isabel Monteiro Grillo, Marília Jorge, Vera Mendonça. “15 Anos de Follow up após Terapêutica Conservadora em Carcinoma da Mama” 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Poster presentation)

Catarina Duarte, Beatriz Nunes, Laurentiu Bujor, Isabel Monteiro Grillo. BT-HDR Intersticial Perioperatória no Tumor da Língua Localizado. 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Poster presentation)

Virgínia Mareco, Filomena Pina, Isabel Monteiro Grillo. Tratamento do Cancro do Esófago – resultados de um Serviço 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Poster presentation)

André Abrunhosa-Branquinho, Filomena Pina, Isabel Monteiro Grillo. Radioterapia na consolidação de tratamento de osteossarcoma extra-ósseo recidivado localmente avançado. 5º Congresso da Sociedade Portuguesa de Radioterapia Oncologia, Coimbra, Portugal, March 7-9, 2013 (Poster presentation)

Virginia Mareco, Filomena Pina, Isabel Monteiro Grillo. Braquiterapia de Alta Taxa de Dose de Resgate após Radioterapia num Doente com Carcinoma da Próstata: Caso Clínico. XVIII Workshop de Urologia Oncológica, Braga, Portugal, April, 12-14, 2013 (Poster presentation)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Ravasco P. Ingestão alimentar, ângulo de fase e sarcopénia em Oncologia: que relação? XV Congresso Anual da Associação Portuguesa de

Nutrição Entérica e Parentérica (APNEP), Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VII, Nº1: 100. (Oral communication)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Ravasco P. Tomografia Computorizada e Bioimpedância Eléctrica: a validade na avaliação da composição corporal em oncologia. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VII, Nº1: 102. (Oral communication)

Russo A, Ferreira C, Mariano A, Ravasco P. Hábitos alimentares dos estudantes universitários. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VII, Nº1: 106. (Oral communication)

Ravasco P, Azevedo S, Lopes AI. Dyskeratosis congenita: a paradigm for multidisciplinary intervention in paediatric gastroenterology. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VII, Nº1: 110. (Poster presentation)

Ferreira C, Russo A, Ravasco P, Azevedo S, Camilo M, Lopes AI. Doença inflamatória intestinal em pediatria: qual o estado nutricional e que terapêutica nutricional? XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VII, Nº1: 115. (Poster presentation)

Ravasco P, Azevedo S, Lopes AI. Dyskeratosis congenita: a paradigm for multidisciplinary intervention in paediatric gastroenterology. Semana Digestiva 2013, Vilamoura, Portugal, June 12-15, 2013. Jornal Português de Gastreenterologia 2013; 23, Nº4: 48. (Oral communication) Prize NUTRIBÉN 2013 distinguished as the best clinical work presented at congress.

Ferreira C, Russo A, Ravasco P, Azevedo S, Camilo M, Lopes AI. Doença inflamatória intestinal em pediatria: qual o estado nutricional e que terapêutica nutricional? Semana Digestiva 2013, Vilamoura, Portugal, June 12-15, 2013. Jornal Português de Gastreenterologia 2013; 23, Nº4: 100. (Oral communication)

Silva T, Guerreiro C, Wakeling L, Escolme S, Alatawi F, Ford D. Effect of resveratrol and SIRT1 on the expression of ATF4 in Caco-2 cells. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica, Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VI, Nº1: 79 (Oral communication)

Silva T, Goncalves E, Sousa Guerreiro C, Rosas M, Mendes L, Garrett C. Doença de Parkinson e dieta mediterrânica. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica, Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VI, Nº1: 108 (Poster presentation)

Coelho V, Guerreiro C, Alexandre D, Dias P, Cravo M, Mendes L. Adesão dos doentes de Crohn à dieta mediterrânica. XV Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica, Oporto, Portugal, April 22-23, 2013. Revista da APNEP 2013; vol. VI, Nº1: 87 (Oral communication)



### **Organisation of Conferences**

Cortez-Pinto H. Member of the Organizing Committee of the XXlth United European Gastroenterological Week (UEGW) 2013, held in Berlin.

Isabel Monteiro Grillo, co-organizer, member of the scientific committee of the IV Congresso ALATRO, Asociacion Latino Americana de Terapia Radiante Oncologica, Cartagena de Índias, Colombia, July 2013.

Ravasco P. Member of the Scientific and Organizing Committee of the XV Annual Congress of APNEP (Portuguese Association of Parenteral and Enteral Nutrition) 2013, Oporto, Portugal.

Ravasco P. Member of the Organizing Committee of the 37th Annual Congress on Clinical Nutrition and Metabolism by ESPEN (European Society of Clinical Nutrition and Metabolism) to be held in 2015 in Lisbon, Portugal.

Guerreiro CS. Member of the Scientific Committee of the XV Congress of Portuguese Association of Enteral and Parenteral Nutrition, Oporto, Portugal, April 22-23, 2013.

### **Internationalisation**

Cortez-Pinto H. Member of the Scientific Committee of the United European Gastroenterologic Federation (UEGF), as a representative of the European Association for the Study of the Liver (EASL).

Monteiro-Grillo I.: Co-Editor and Editorial Board of Reports of Practical Oncology and Radiotherapy, Poland; Editorial Board of the Journal of Contemporary Brachytherapy, Journal of the Polish Brachytherapy Society, Poland; Board member (European representant) of the Asociación Latinoamericana de Terapia Radiante Oncológica.

Ravasco P.: member of the ESPEN Faculty (European Society for Clinical Nutrition and Metabolism), Associated Editor of Clinical Nutrition, official journal of ESPEN; Portuguese representative at the Educational and Clinical Practice Committee of ESPEN; member of the Scientific Committee of the International Research Group of EORTC (European Organisation for Research and Treatment of cancer); Scientific consultant in the area of clinical nutrition in the Program Harvard Medical School-Portugal; member of the Scientific Committee of the Focus Group on Nutrition in Foregut Cancers - Nutrition, Function, Patient Centered Care, promoted by ESPEN and University of Alberta, Canada; member of the nutrition section of the Editorial Advisory Board of the EJSO - European Journal of Surgical Oncology, official journal of Association for Cancer Surgery and European Society of Surgical Oncology.

Guerreiro CS.: Partner of the European Project: “Equity creating equality in health through capacity building in Europe between health care workers” inscribed in a Lifelong Learning Program, Leonardo Da Vinci financed by the European Commission; external revisor for nutrition projects at European Clinical Research Infrastructures Network.

### Prizes, honours and awards

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo M, Johns N, Fearon K, Ravasco P. Travel Award for the original research work entitled: Computed tomography and bioelectrical impedance: relevance for body composition assessment in Oncology, classified among the 20 best abstracts of the 35th Congress of ESPEN (European Society for Clinical Nutrition and Metabolism), Leipzig, Germany, August 31-September 3, 2013.

Cortez-Pinto H. Editor-in-chief of *Jornal Português de Gastrenterologia* (GE)

Cortez-Pinto H. President of the Portuguese Association of the liver (APEF), since June 2013

Cortez-Pinto H. Director of the Liver Programme of the Post-graduate Course of the United European Week in Berlin, Germany, October 2013

Ravasco P, Azevedo S, Lopes AI. Prize NUTRIBÉN 2013: Dyskeratosis congenita: a paradigm for multidisciplinary intervention in paediatric gastroenterology, distinguished as the best clinical work presented at the XXVI Meeting of the Portuguese Society of Paediatric Gastroenterology and Nutrition., Vilamoura, Portugal, June 12-13, 2013.

### Advanced teaching

Cortez-Pinto H, President of the Scientific board of a Master Course in Clinical Nutrition (2011/2013; 2012-2014; 2013-2015), collaboration between the Faculty of Medicine of the University of Lisbon and the “Escola Superior de Tecnologia da Saúde de Lisboa do Instituto Politécnico de Lisboa”, with the collaboration of the Faculty of Pharmacy of the University of Lisbon.

Cortez-Pinto H. Director of the Liver Programme of the Post-graduate Course of the United European Week in Berlin, Germany, October 2013.

Monteiro Grillo I. Master in Palliative Care, FMU, Tratamento Sintomático I em Cuidados Paliativos. Lecture: O Contributo da Radioterapia nos Cuidados Paliativos do Doente Oncológico. 10th Edition, 2013

Monteiro Grillo I. Organizer and lecture in Advanced Training Seminar. Nutrición y Cáncer. IV Congreso ALATRO, Asociación Latino Americana de Terapia Radiante Oncologica, Cartagena de Índias, Colombia, July 30, 2013.

Monteiro Grillo I. Nutrición y Oncología. Terapéutica anti-neoplásica. Seminario Universidad de Salamanca, Spain, November 27, 2013.

Ravasco P. Mechanisms and clinical features of cancer cachexia. Advanced Teaching Course for Creditation in Medical Education (CME): Educational Long Life Learning on Nutritional support in cancer at the 35th Annual Congress of ESPEN (European Society for Clinical Nutrition and Metabolism). Leipzig, Germany, August 30-September 30, 2013.

Ravasco P. Lecture: Nutrition in Cancer. Moderator: interactive problem based clinical case session at the Advanced Teaching Course for Creditation in Medical Education (CME) promoted by Nestle Nutrition Institute, New Dehli, India, October 13-18, 2013.

Ravasco P. Mechanisms and clinical features of cancer cachexia. Advanced Teaching Course for Creditation in Medical Education (CME): Educational Long Life Learning on Nutritional support in cancer promoted by ESPEN (European Society for Clinical Nutrition and Metabolism), Cairo, Egipt, November 15-17, 2013.

Ravasco P. Nutrition in oncology. Clinical Session and Advanced Teaching for clinicians involved in cancer management at Unidade Local Saúde de Matosinhos - Hospital Pedro Hispano, Portugal, March 8, 2013.

Ravasco P, Costa V. Nutrition in oncology. Clinical Session and Advanced Teaching for clinicians involved in cancer management at Hospital do Espírito Santo em Évora, Portugal, March 14, 2013.

Ravasco P. Nutrition in oncology. Clinical Session and Advanced Teaching for clinicians involved in cancer management at Centro Hospitalar de Vila Nova de Gaia, Portugal, March 20, 2013.

Ravasco P. Nutrition in oncology. Clinical Session and Advanced Teaching for clinicians involved in cancer management at Centro Hospitalar do Alto Minho, Viana do Castelo, Portugal, October 11, 2013.

Ravasco P, Gracês R. Nutrition in oncology. Clinical Session and Advanced Teaching for clinicians involved in cancer management at Hospital Fernando da Fonseca, Lisbon, Portugal, October 31, 2013.

2012/2013: Ravasco P. supervisor of the training and research project for the conclusion of the Degree in Nutritional Sciences of Inês Bravo Carretero of Universidade Atlântica. Classification: 19/20 (Excellent).

2012/2013: Ravasco P. supervisor of the Original Monograph for the conclusion of the Degree in Biomedical Sciences of the Universidade do Algarve of Cláudia Patrícia da Silva Queirós: What is the relevance of body composition in cancer. Classification: 19/20 (Excellent).

2012/2013: Ravasco P. teacher and coordinator of the Module of Oncology and Nutrição at the Master Course in Clinical Nutrition (collaboration project between FMUL and ESTES-L: Prof. Helena Cortez Pinto, Prof. Marília Cravo, Prof. Catarina Guerreiro, MSc Lino Mendes); course started in 2011/2012.

2012/2013 Guerreiro CS. Coordinator and Teacher of the Modules: "Nutrição, Avaliação Nutricional, e Tecnologias de informação e Comunicação" and "Nutrição e Doença Gastroenterológica e Seminários" at the Master degree in Clinical Nutrition FMUL, Lisbon, Portugal.

2013 Guerreiro CS. Voluntary Auxiliary Professor at the Unidade Curricular de Nutrição e Metabolismo of the integrated Master Degree of Medicine of the Faculdade de Ciências

Médicas, Lisbon, Portugal.

### **Science and society**

Ravasco P.: Supervisor of the research training in the area of nutrition and oncology of 3 high-school students: Pedro Mendonça (10th grade), Inês Pires (12th grade) and Inês Grazina (12th grade). These trainings were integrated in the program “Ciência Viva no Laboratório - Ocupação Científica de Jovens nas Férias (OCJF)”, to provide opportunities to students to have a proximity to the reality of scientific research, July 2013.

Ferreira C, Almeida AI, Ravasco P. Everything you should know about sports supplementation. Expert article for the magazine Mens's Health (Public Perception of Science). July 27 2013.

Ferreira C, Almeida AI, Carretero I, Ravasco P. The best whey for you. Expert article for the magazine Mens's Health (Public Perception of Science), August 10 2013.

Miranda I, Ravasco P. Healthy menu of the week. Expert article for Public Perception of Science: <http://saude.pt.msn.com/vidasaudavel/nutricao/item/3248-ementasaudaveldasemanadeinesmirandaepaularavasco>. MSN Health and Well-Being – portal of Microsoft specialized in health and well-being, October 20, 2013.

Guerreiro CS. Member of the board of the Portuguese Association of Dietitians.

Guerreiro CS. Member of the general Council of the Ordem of Nutricionists.

Guerreiro CS. President of the Commission which oversees the preparation of Dietitians before admission to the Ordem of Nutricionists.

Guerreiro CS. Scientific Revisor of Revista Saúde e Tecnologia. ISSN:1646-9704.

### **PhD theses completed**

Margarida Maria Eiras (2013) Avaliação da Cultura de Segurança do Doente e meio hospitalar: Investigação acção numa Unidade de Radioterapia. Escola de Saude Pública, Universidade Nova de Lisboa. Supervisor: Isabel Monteiro-Grillo

### **Msc theses completed**

Filipa Isabel Campos Costa (2013) O carcinoma não de pequenas células. Descrição de um caso clínico e Revisão de Literatura. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Monteiro-Grillo.

Alda Delgado Ribas (2013) Life styles, adiposity, hormones and inflammation: influence on the incidence and progression of cancer of the breast, prostate and colorectal. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paula Ravasco.

**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.

**Research Team**

Alexandra Coitos Vítor	Graduate	MSc Student (left May)
Ana Catarina de Jesus	Master	Technician
Ana Paula Santos Botelho Oliveira Leite	PhD	Post-doctoral Investigator
André Daniel Faustino Mesquita	Undergraduate	Undergraduate (started March)
Bruno Miguel Bernardes de Jesus	PhD	Post-doctoral Investigator (started August)
Catarina Alves do Vale	Undergraduate	Undergraduate (started March)
Catarina Pereira Santos	Graduate	MSc Student (started September)
Célia Carvalho	PhD	Investigator, Assistant Professor
Dinora Levy	Graduate	Administrative
Francisco Javier Enguita	PhD	Principal Investigator, Assistant Professor
Joana Desterro	MD/PhD	Post-doctoral Investigator, Assistant Professor
Jorge Gabriel Palma da Luz	Graduate	MSc Student (started September)
Marina Célia Nunes Ferreira C. H.	PhD	Post-doctoral Investigator

Silva		
Marisa Cabrita	Graduate	Lab manager, Assistant Professor
Miguel Maria das Neves Sousa Pereira	Graduate	MSc Student (left October)
Noélia Maria Fernandes Custódio	PhD	Investigator, Assistant Professor
Nuno Luís Barbosa Morais	PhD	Post-doctoral Investigator (started June)
Paula Sofia Faria Oliveira	Graduate	PhD Student
Rita Catarina Vaz Drago	Master	PhD Student (started March)
Rita Mingot de Almeida Mendes de Almeida	Master	PhD Student
Robert M. Martin	PhD	Post-doctoral Investigator
Sandra Martins	PhD	Post-doctoral Investigator, Assistant Professor
Sérgio Alexandre Fernandes de Almeida	PhD	Principal Investigator, Assistant Professor (left June)
Sérgio Manuel Pires Marinho	Graduate	Technician
Silvia Filipa Camoëira Gonçalves de Carvalho	Master	Technician (left May)
Teresa Carvalho	PhD	Investigator, Assistant Professor
Tomás Pires de Carvalho Gomes	Graduate	MSc Student (started May)

### Keywords / Research Areas

Cell and Molecular Biology, RNA biology, Non coding RNA, RNA in disease, Cancer, Aging.

### Major scientific achievements

How human cells control more than 100,000 alternative splicing decisions remains incompletely understood. To decipher how transcription and splicing occur in real time in the nucleus of living human cells, we combined genomic integration of a single reporter gene, intron labelling with the MS2 technique and spinning disk confocal microscopy. The results show that splicing of

beta-globin transcripts is accomplished in 20-30 s. We further show that replacing the weak polypyrimidine tract in mouse IgM pre-mRNA by a U-rich Py decreases the intron lifetime, thus providing direct evidence that splice site strength influences splicing kinetics. We also found that RNA polymerase II transcribes at elongation rates ranging between 3 and 6 kb per minute, and that transcription is rate limiting for splicing. These results have important implications for mechanistic understanding of co-transcriptional splicing regulation in the live-cell context. (Martin, Rino, Carvalho et al. *Cell Rep*, 2013).

### Recent Most Relevant Publications

de Almeida SF, Grosso AR, Koch F, Fenouil R, Carvalho S, Andrade J, Levezinho H, Gut M, Eick D, Gut I, Andrau JC, Ferrier P, Carmo-Fonseca M (2011) Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36. *Nature Structural & Molecular Biology* **18**, 977-983. (Journal IF: 12.7, Citations: 57)

Martins SB, Rino J, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M. (2011) Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. *Nature Structural & Molecular Biology* **18**, 1115-1123. (Journal IF: 12.7, Citations: 28)

de Almeida SF, García-Sacristan A, Custódio N, Carmo-Fonseca M. (2010) A link between nuclear RNA surveillance, the human exosome and RNA polymerase II transcriptional termination. *Nucleic Acids Research* **38**, 8015-26. (Journal IF: 8.0, Citations: 22)

Grosso AR, Gomes AQ, Barbosa-Morais NL, Caldeira S, Thorne NP, 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: 8.0, Citations: 69)

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: 4.9, Citations: 145)

### Ongoing Research Projects

2012/2016 PIRSES-GA-2012-318981. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: European Commission. Amount: €67.200,00 Total amount: €155.400,00

2011/2013 The role of RNA polymerase II in splicing regulation. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: Amount: €170.000,00

2011/2014 PIOF-GA-2010-274037. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: European Commission. Amount: €210.446,00

2011/2015 PITN-GA-2011-289007. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: FP7. Amount: €212.892,11 Total amount: €4.246.947,34

2012/2015 Splicing and stochasticity in programmed cell death decisions. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: FCT. Amount: €169.755,00

2012/2015 Identification and manipulation of molecular pathways relevant for age-dependent tissue regeneration. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: AXA Research Fund. Amount: €173.500,00 Total amount €700.000,00

2011/2014 Splicing-coupled mechanisms of chromatin remodeling and their global role in transcription. Coordinator: Sérgio Alexandre Fernandes de Almeida. Agency: FCT. Amount: €141.967,00

2011/2014 Oncobiologia: novas ferramentas educativas para as futuras gerações de investigadores clínicos Coordinator: Joana Desterro. Agency: FCT. Amount: €99.000,00

2013/2014 FCT/CAPES – RNA. Coordinator: Francisco Javier Enguita. Agency: FCT. Amount: €4.500,00

2013/2014 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. Amount: €25.000,00

2013/2015 Programme of Cooperation in Science and Technology between China and Portugal. Coordinator: Maria do Carmo Salazar Velez Roque da Fonseca. Agency: FCT. Amount: €5.400,00

### Other Projects

2012/2013 GAPIC-FML-2011 - Terapia génica da Distrofia Muscular de Duchenne: avaliação da eficácia de pequenos oligonucleótidos LNA . Coordinator: M. Carmo-Fonseca & Célia Carvalho.

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

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. *Nuc. Acids Res.* **41**(5), 2881-2893. (Journal IF: 8.27, Citations: 7)

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. (Journal IF: - , Citations: 0)



Rino, J, Martin, RM, Carvalho, T, Carmo-Fonseca M. (2013) Imaging dynamic interactions between spliceosomal proteins and pre-mRNA in living cells. *Methods* pii:S1046-2023(13)00315-0. doi: 10.1016/j.ymeth.2013.08.010. (Journal IF: 3.641, Citations: 0)

Repici M, Straatman KR, Balduccio N, Enguita FJ, Outeiro TF, Giorgini F (2013). Parkinson's disease-associated mutations in DJ-1 modulate its dimerization in living cells. *J Mol Med (Berl)* **91**(5). 599-611. doi: 10.1007/s00109-012-0976-y. (Journal IF: 4.469, Citations: 0 )

Correia NC, Durinck K, Leite AP, Ongenaert M, Rondou P, Speleman F, Enguita FJ, Barata JT (2013). Novel TAL1 targets beyond protein-coding genes: identification of TAL1-regulated microRNAs in T-cell acute lymphoblastic leukemia. *Leukemia* **27**(7). 1603-6. doi: 10.1038/leu.2013.63.(Journal IF: 10.164, Citations: 0 )

### Invited lectures and seminars

Carmo-Fonseca, M. Splicing factors: a novel class of anticancer targets? Institut de Recherche Servier, Paris, France, January 15, 2013.

Carmo-Fonseca, M. Imaging pre-mRNA splicing in living cells Talk presented at the Titisee Conference on RNA transport, Titisee, Germany, March 6-10, 2013.

Carmo-Fonseca, M. Fidelity of gene expression Talk presented at the Department of Cell Biology, Harvard Medical School, Boston, USA March 28, 2013.

Carmo-Fonseca, M. Driving RNA Polymerase II through chromatin on the many roads to splicing regulation. Talk presented at the National Cancer Institute's Symposium on Chromosome Biology: Epigenetics in Development, Bethesda, MD, USA, April 4-5, 2013.

Carmo-Fonseca, M. Nuclear checkpoints. Talk presented at the 38th FEBS Congress, Saint Petersburg, Russia, July 6-11, 2013.

Carmo-Fonseca, M. Checkpoints in gene expression. Talk presented at the EMBO Young Scientists' Forum, Lisboa, July 15-16, 2013.

Carmo-Fonseca, M. Imaging transcription and splicing in real time. Talk presented at the meeting "Molecular Biology in Portugal and EMBL", Lisbon, 18 July 2013.

Carmo-Fonseca, M. Splicing as a target for cancer therapy. Talk presented at the Third Global Cancer Genomics Consortium Symposium "From oncogenomics to cancer care", Lisbon, September 19-20, 2013.

Carmo-Fonseca, M. Genome-wide analysis of gene looping. Talk presented at the EMBO Workshop on "RNA 3' ends", Oxford, UK, September 25-29, 2013.

Carmo-Fonseca, M. Kinetic coupling between transcription and pre-mRNA splicing. Talk presented at the EMBO Conference Series "Nuclear Structure and Dynamics", L'Isle sur la Sorgue, France, October 2-6, 2013

Enguita, FJ. ncRNAs and aging. Talk presented at the XIII Workshop Internacional de Genética, UNESP, Botucatu, Brazil, May 16-18, 2013.

### **Communications in International Conferences**

Carmo-Fonseca, M. Real-time kinetics of human pre-mRNA splicing. Poster presented at the Annual meeting of the RNA Society – RNA 2013, Davos, Switzerland, June 11-16, 2013. (Poster presentation)

Carmo-Fonseca, M. Imaging pre-mRNA splicing with single-molecule sensitivity. Talk presented at the Cold Spring Harbor Laboratory meeting on “Eukaryotic mRNA processing”, New York, USA, August 20-24, 2013. (Oral communication)

Carmo-Fonseca, M. Imaging splicing in real time with single-molecule sensitivity. Talk presented at the ICGEB Symposium on “RNA alternative splicing”, Trieste, Italy, November 18-20, 2013. (Oral communication)

Enguita, FJ. Integrative analysis and functional implications of the aging-related changes in the human non-coding transcriptome. Talk presented at the Current Trends in Biomedicine workshop on “The regulatory roles of ncRNA”, Baeza, Spain, November 18-20, 2013. (Oral communication)

Martin, R. Real-time kinetics of human pre-mRNA splicing. Poster presented at the EMBO Young Scientists Forum, Lisbon, Portugal, July 15-16 2013. (Poster presentation)

Martin, R. Real-time kinetics of human pre-mRNA splicing. Poster presented at The 5th EMBO Meeting 2013, Amsterdam, Netherlands, September 21-24, 2013. (Poster presentation)

Martin, R. Live cell visualization of pre-mRNA splicing with single molecule sensitivity. Poster presented at Single Cell Genomics Conference, Weizmann Institute of Science, Rehovot/Tel Aviv, Israel, October 1-3, 2013. (Poster presentation)

### **Communications in National Conferences**

Carmo-Fonseca, M. Qualidade da publicação científica e factores de impacto. II Simpósio Acta Médica Portuguesa, Lisboa, November 23, 2013.

### **Organisation of Conferences**

M. Carmo-Fonseca co-organized the Third Global Cancer Genomics Consortium Symposium “From oncogenomics to cancer care”, Lisbon. September 19-20, 2013.

M. Carmo-Fonseca co-organized the EMBO Conference Series “Nuclear Structure and Dynamics”, L'Isle sur la Sorgue, France. October 2-6, 2013.

### **Internationalisation**

Participation in an EC-funded Initial Training Network (FP7, People) entitled “RNPnet: RNP structure, function and mechanism of action”.

Collaboration with Prof T. Kirchhausen at Harvard Medical School on a project entitled “Real-time imaging of splicing in living cells”.

Collaboration with Dr. Asifa Akhtar at the Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany on a project to explore the alternative splicing events during sex determination in the model organism *Drosophila melanogaster*.

Within the framework of the scientific cooperation project FCT/CAPES 4.4.1.00, the laboratory hosted Junya Singulani, Ph.D. student, and Fernanda Gullo, Ph.D. student, from UNESP, Araraquara, Brazil, for a scientific training period of 4 months.

Host lab for the following international fellows: Sreerama Chaitanya Sridhara (Indian PhD student) and Robert Martin (German post-doc).

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

M. Carmo-Fonseca was awarded the Prémio D. Antónia Ferreira.

Astra-Zeneca Innovate Competition prize awarded to Inês Figueiredo, with the project “Chronic Myeloid Leukemia Gene Therapy Targeting the BCR/ABL Fusion Gene. Peptide-mediated gene delivery: siRNA and editing tools”, supervised by Dr. Miguel Castanho and Dr. Francisco J. Enguita.

Robert Martin, Poster prize award, 2nd place at EMBO Young Scientists Forum, Lisbon 2013.

### **Advanced teaching**

Carmo-Fonseca, M. Avanços da biologia molecular e projecto genoma humano. Mestrado em Medicina Legal e Ciências Forenses, Lisboa. January 11, 2013.

Carmo-Fonseca, M. RNA e regulação da expressão genética. Jornadas Nacionais de Ciências Biomédicas, Universidade de Aveiro. March 15, 2013.

Enguita, FJ. miRNAs as masters regulators in cell biology and human disease. Doctoral Programme in Experimental Biology and Medicine, CNC, Coimbra, January 8, 2013.

Enguita FJ. The dark (and funniest) side of the genome. Doctoral Programme in Experimental Biology and Medicine, CNC, Coimbra, January 8, 2013.

Enguita F.J. miRNAs and aging. Master Programme in Cellular and Molecular Biology, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, Coimbra, April 22, 2013.

Enguita, F.J. Advanced tools for miRNA functional analysis. Master Programme in Cellular and Molecular Biology, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, Coimbra, 22 April 2013

Enguita, FJ. Application of genomics and transcriptomics in human nutrition. Master in Food Safety and Technology, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Caparica. May 3, 2013.

Enguita, FJ. Advanced course on protein expression and purification: tips and tricks (2013 Edition). Course on CAML Ph.D. Programme, Faculdade de Medicina da Universidade de Lisboa. March 14-15, 2013.

Enguita, FJ. miRNAs and non-coding RNAs in cell biology and human disease. Course on CAML Ph.D. Programme, Faculdade de Medicina da Universidade de Lisboa. July 11-12, 2013.

Enguita, FJ. Non-coding RNAs in cell biology. Course of the post-graduate research programme on Biological Sciences, Instituto de Biociências, UNESP, Botucatu, Brazil. May 13-17, 2013.

Enguita, FJ. New approaches in post-genomic era: the relevance of non-coding RNAs. Course of the post-graduate research programme on Pharmaceutical Biotechnology and Biosciences, Faculdade de Farmácia, UNESP, Araraquara, Brazil. May 7-10, 2013.

Martins, S.B. When nuclear structure meets disease: the laminopathies. Programa Doutoral do IGC (Instituto Gulbenkian de Ciência), February 12, 2013.

### **Science and society**

Carmo-Fonseca, M. “Saúde e Ciências da Vida: investigação reconhecida globalmente. Seminário Diplomático ‘Projectar Portugal’”, Lisbon. January 3, 2013.

Carmo-Fonseca, M. Comment to Maria da Graça Carvalho presentation untitled: Designing research for Europe in a changing world-Horizon 2020. IX Pharmaceutical Industry Conference “A global perspective on science and technology”, Lisbon. January 17, 2013.

Carmo-Fonseca, M. “A importância do conhecimento científico no desenvolvimento da Sociedade.” Fundação Eugénio de Almeida, Évora. April 20, 2013.

### **Msc theses completed**

Marta Alexandra Pereira da Silva (2013) Detection of circulating miRNAs using microfluidics: a diagnosis method for cardiovascular diseases. Master theses in Biotechnology. Instituto Superior Técnico da Universidade de Lisboa. Supervisors: João Pedro Conde and Francisco J. Enguita.

## 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 epithelial or innate immune defense. Some of these may be inspiring to develop new innovative therapeutic 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, antimicrobial, and anticancer agents. We are interested 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.

### Head of Unit

Miguel Castanho, PhD, Full Professor, Faculdade de Medicina da Universidade de Lisboa.

### Research Team

Ana Salomé Rocha do Nascimento Veiga	PhD	Investigator
Antónia Rosa Trindade Pinto	Master	Technician
Diana Maria Diez Gaspar	PhD	Post-doctoral Investigator
Isa Domingues Serrano	PhD	Post-doctoral Investigator (left June)
João Miguel Calado da Silva Freire	Master	PhD Student
Luís Rafael Pereira do Carmo Flores	Graduate	MSc Student, (started March)
Rodrigo Lucarini	Undergraduate	PhD Student (left February)
Sandra Cristina Nunes Trigo Pinto	PhD	Technician (started September)
Sónia Adelaide Queirós de Sá Santos Rocha	PhD	Post-doctoral Investigator
Tiago Nascimento Figueira	Master	MSc Student
Vera Luisa Santos Neves	PhD	Post-doctoral Investigator

### Keywords / Research Areas

Drug discovery, Peptide, Antimicrobials, HIV, Dengue, Blood-brain barrier

### Major scientific achievements

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 without the severe side effect of opioids;
- Kyotorphin was found in the cerebro spinal fluid (CSF) of humans and its level is decreased in Alzheimers' patients. kyotorphin may be the molecular link between pain and neurodegeneration. Moreover, Kyotorphin is a candidate biomarker for pain. In a parallel study it was demonstrated that Alzheimers' patients underreport the pain they feel, which leads to undertreatment;
- Discovering that viral proteins are sources of peptide-based drug delivery system;
- Elucidation of the role of electrostatics in Blood-brain Barrier translocation of small molecules.

### Recent Most Relevant Publications

Sinthuvanich C, Veiga AS, Gupta K, Gaspar D, Blumenthal R, Schneider JP. (2012) Anticancer Beta-hairpin peptides: membrane-induced folding triggers activity. *J Am Chem Soc* DOI:10.1021/ja210569f. **14**, 6210. (Journal IF: 9.907, Citations: 16)

Santos MS, 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. *Frontiers in Ageing Neurosciences* **5**(68), 1-6. doi: 10.3389/fnagi.2013.00068. <http://www.frontiersin.org/Journal/10.3389/fnagi.2013.00068/abstract>. (Journal IF: 5.2, Citations: 0)

Franquelim, HG, Chiantia, S, Veiga, AS, Santos, NC, Schwille, P, Castanho, MARB. (2011) Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes. *AIDS* DOI:10.1097/QAD.0b013e328342ff11 **25**, 419. (Journal IF: 6.2, Citations: 13)

Ribeiro, MMB ; Melo, MN ; Serrano, ID ; Santos, NC ; Castanho, MARB (2011) Drug-lipid interaction evaluation: why a 19th century solution? *Trends in Pharm Sciences* DOI:10.1016/j.tips.2010.06.007, **31** (Journal IF: 10.927, Citations: 18)

M. N. Melo, R. ferre and M. Castanho. (2009) Antimicrobial peptides: linking partition, activity and high membrane bound concentrations. *Nature Rev. Microbiology* DOI:10.1038/nrmicro2095, **7**, 245. (Journal IF: 21.182, Citations: 141)

### Ongoing Research Projects

2009/2013 Selected peptides as drug candidates directed to pain neurodegeneration. Coordinator: Miguel Castanho. Agency: FP7. Amount: €248.037,01 Total amount: €660.000,00

2011/2014 The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies. Coordinator: Miguel Castanho. Agency: FCT. Amount: €130000,00 Total amount: €130.000,00

2011/2014 Membrane fusion mechanism of Influenza Hemagglutinin: a simulation and biophysical approach. Coordinator: Miguel Castanho. Agency: FCT. Coordinator Institution: ITQB-UNL. Coordinator PI: Cláudio Soares. Amount: €44.186,00

2010/2013 Inherent antibacterial activity in peptide-based hydrogels for tissue regeneration. Coordinator: Ana Salomé Rocha do Nascimento Veiga. Agency: FCT. Amount: €199.350,00 Total amount: €199.350,00

2011/2015 Do IT - Desenvolvimento e Operacionalização da Investigação de Translação. Coordinator: Miguel Castanho. Agency: Agência de Inovação, SA. Coordinator Institution: Têxtil Manuel Gonçalves, S.A.. Amount: €218.820,85 Total amount: €7.823.454,06

### 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). Agency: Marie Curie International Research Staff Exchange Scheme (IRSES) Coordinator: Miguel Castanho. Coordinator Institution: IMM. Coordinator PI: Nuno C. Santos. Amount: €131.400,00 Total amount: €181.800,00

### Publications in peer review Journals

Santos S., Castanho M. (2013) The Use of Visual Analog Scales to Compare Pain Between Patients With Alzheimer's Disease and Patients Without Any Known Neurodegenerative Disease and Their Caregivers. *Am. J. Alzheimers Dis Other Demen* **28**(8) doi: 10.1177/1533317513517046 (Journal IF: 1.518, Citations: 0)

Freire JM, Veiga AS, Conceição TM, Kowalczyk W, Mohana-Borges R, Andreu D, Santos NC, Da Poian AT, Castanho MARB. (2013) Intracellular nucleic acid delivery by the supercharged Dengue virus capsid protein. *Plos one* **12**(8) doi: 10.1371/journal.pone.0081450 (Journal IF:3.730, Citations: 0)

Freire JM, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MA. (2013). Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein: design and mechanism of action. *FEBS J.* **281**(1), 191-215 doi: 10.1111/febs.12587 (Journal IF: 4.25, Citations: 0)

Veiga A.S., Schneider J.P. (2013) Antimicrobial hydrogels for the treatment of infection. *Biopolymers* **100**, 637-644. (Journal IF: 2.879; Citations: 0)

Domingos MM, Silva PM, Franquelim HG, Carvalho FA, Castanho MA, Santos NC. (2013) Antimicrobial protein rBPI21-induced surface changes on Gram-negative and Gram-positive bacteria. *Nanomedicine* doi:10.1016/j.nano.2013.11.002 (Journal IF: 6.930; Citations: 0)

Santos MS, Garcia-Nimo L, Sá Santos S, Tavares I, Cocho JA, Castanho MA. (2013) Neuropeptide Kytorphin (Tyrosyl-Arginine) has Decreased Levels in the Cerebro-Spinal Fluid of Alzheimer's Disease Patients: Potential Diagnostic and Pharmacological Implications. *Front Aging Neurosci* **5**(68) doi: 10.3389/fnagi.2013.00068 (Journal IF: 5.2; Citations: 0)

Gaspar D, Veiga AS, Castanho MARB. (2013) From antimicrobial to anticancer peptides. A review. *Front. Microbiol.* **4**, 294, doi: 10.3389/fmicb.2013.00294 (Citations:0)

Torcatto IM, Huang YH, Franquelim HG, Gaspar D, Craik DJ, Castanho MA, Henriques ST, (2013) The antimicrobial activity of Sub3 is dependent on membrane binding and cell-penetrating ability. *ChemBioChem* **14**, 2013-2022. <http://dx.doi.org/10.1002/cbic.201300274>. (Journal IF: 3.740, Citations: 0)

Freire J.M., Veiga A.S., de la Torre B.G., Santos N.C., Andreu D., Da Poian A.T., Castanho M.A.R.B. (2013) Peptides as models for the structure and function of viral capsid proteins: insight on dengue virus capsid. *Biopolymers* **100**, 325-336. (Journal IF: 2.879; Citations: 1)

Faustino AF, Carvalho FA, Martins IC, Castanho MA, Mohana-Borges R, Almeida FC, Da Poian AT, Santos NC, (2013) Dengue virus capsid protein interacts specifically with very low-density lipoproteins. *Nanomedicine* **10**(1), 247-255, doi: 10.1016/j.nano.2013.06.004 (Journal IF: 6.930; Citations: 3)

Domingos MM., Bianconi ML., Barbosa LR., Santiago PS, Tabak M, Castanho MA, Itri R, Santos NC, (2013) rBPI21 interact with negative membranes endothermically promoting for formation of rigid. *Biochim Biophys Acta* **1828**(11), 2419-2427. doi:10.1016/j.bbamem.2013.06.009, (Journal IF: 3.389, Citations: 0)

Palomares-Jerez MF, Nemesio H., Franquelim HG, Castanho MA, Villalaín J. (2013) N-terminal AH2segment of protein NS4B from hepatitis C virus. Binding to and interaction with biomembranes, *Biochim Biophys Acta* **1828**(8), 1938-1952. doi: 10.1016/j.bbamem.2013.04.020 (Journal IF: 3.389, Citations: 1)

Vigant F, Lee J, Hollmann A, Tanner LB, Akyol Ataman Z, Yun T, Shui G, Aguilar HC, Zhang D, Meriwether D, Roman-Sosa G, Robinson LR, Juelich TL, Buczkowski H, Chou S, Castanho MA, Wolf MC, Smith JK, Banyard A, Kielian M, Reddy S, Wenk MR, Selke M, Santos NC, Freiberg AN, Jung ME, Lee B. (2013) A mechanistic paradigm for broad-spectrum antivirals that target virus-cell fusion, *PLoS Pathog* **9**(4) doi: 10.1371/journal.ppat.1003297. (Journal IF: 8.14, Citations: 4)

Hollmann A, Matos PM, Augusto MT, Castanho MARB and Santos NC. (2013) Conjugation of cholesterol to HIV-1 fusion inhibitor C34 increase peptide membrane interactions potentiating



its action, *PLoS ONE* **8**(4), e60302. doi: 10.1371/journal.pone.0060302 (Journal IF: 3.730 Citations: 0)

Franquelim H. G., Gaspar D., Veiga, A. S., Santos, N. C., Castanho, M. A.R.B. (2013) Decoding distinct membrane interactions of HIV-1 fusion inhibitors using a combined atomic force and fluorescence microscopy approach. *Biochimica Biophysica Acta* **1828**, 1777-1785. <http://dx.doi.org/10.1016/j.bbamem.2013.03.006> (Journal IF: 3.389, Citations: 1)

Ribeiro MM, Santos SS, Sousa DS, Oliveira M, Santos SM, Heras M, Bardaji E, Tavares I, Castanho MA (2013) Side-effects of analgesic kyotorphin derivatives: advantages over clinical opioid drugs. *Amino Acids* **45**(1), 171-178, doi: 10.1007/s00726-013-1484-2. (Journal IF: 3.94 Citations: 0)

Freire J.M., Veiga A.S., de la Torre B.G., Andreu D., Castanho M.A.R.B. (2013) Quantifying molecular partition of cell-penetrating peptides-cargo supramolecular complexes into lipid membranes: optimizing peptide-based drug delivery systems. *J. Pep. Sci.* **19**, 182-189. (Journal IF: 2.071; Citations: 2)

Torcatto I. M., Huang Y. H., Franquelim H. G., Gaspar D., Craik D. J., Castanho M. A.R.B., Troeira S. T. (2013) Design and characterization of novel antimicrobial peptides, R-BP100 and RW-BP100, with activity against Gram-negative and Gram-positive bacteria. *Biochimica et Biophysica Acta* **1828**, 944-955. <http://dx.doi.org/10.1016/j.bbamem.2012.12.002> (Journal IF: 3.389; Citations: 4)

#### Invited lectures and seminars

J Freire, AS Veiga, T Conceição, W Kowalczyk, R Mohana-Borges, D Andreu, N. Santos, AT Da Poian, MARB Castanho. Dengue virus capsid protein translocates nucleic acids across lipid membranes. Potential role in viral entry. XLII Annual Meeting of the SBBq, Foz do Uguaiçu, Brazil, May 18-21, 2013.

HG Franquelim, NC Santos, MARB Castanho, P Schwill. AFM: May the Force be with you! Ludwig-Maximilian University, Munich, Germany, May 17, 2013.

M. Castanho. The Physical Chemistry of Dengue virus entry into cells revisited. XXIII Encontro Nacional SPQ (Sociedade Portuguesa de Química), Aveiro, Portugal, June 2013.

J Freire, AS Veiga, T Conceição, W Kowalczyk, R Mohana-Borges, D Andreu, N. Santos, AT Da Poian, MARB Castanho. Unraveling a new actor in dengue virus-cell fusion. EBSA 2013 – 9th European Biophysics Congress, Lisboa, Portugal, July 13-17, 2013. Abstract published on *Eur. Biophys. J.*, **42**, S163, 2013.

FA Carvalho, IC Martins, AF Faustino, FA Carneiro, I Assunção-Miranda, R Mohana-Borges, MARB Castanho, F Almeida, AT Da Poian, NC Santos. AFM-based force spectroscopy probing of dengue virus capsid protein binding to lipid droplets and lipoproteins. Towards a new drug target. VIII Iberoamerican Congress of Biophysics, Valparaíso, Chile, October 1-4, 2013.

FA Carvalho, IC Martins, FA Carneiro, I Assunção-Miranda, AF Faustino, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos. Dengue virus capsid protein binding to lipid droplets and its inhibition. Towards a new drug target. 3rd International Conference on Dengue and Dengue Haemorrhagic Fever, Bangkok, Thailand, October 21-23, 2013.

M. Castanho (Keynote speaker). Rethinking Dengue virus entry into cells. 14th Conference IUBMB, Marrakech, Morocco, November 16-20, 2013.

M. Castanho. Infectious natural cell-penetrating peptides: the lessons from Dengue virus. Invited lecture at the Chalmers University of Technology, Physical Chemistry Department, Sweden, December 2013.

M. Castanho. O que pode o vírus da Dengue revelar-nos? Santarém, Conferência pública a convite da Câmara Municipal de Santarém, Santarém, Portugal, February 2013.

M. Castanho. Beating the blood-brain barrier: (S)low (but effective) throughput screening in the quest for a new analgesic drug. IBB-CMBE invited seminar, University of Algarve, Faro, Portugal, April 2013

#### Communications in International Conferences

JM Freire, AS Veiga, NC Santos, D Andreu, AT Da Poian and MARB Castanho. Viral Capsid proteins as potent scaffolds for nucleic acid delivery vectors: Cell Penetrating Peptides and Supercharged Proteins. 4th Protein and Peptide Science Groups Early Stage Researcher Meeting, Durham, UK, November 11<sup>th</sup>, 2013. (Oral communication)

I Figueiredo, JM Freire, F Enguita, M Cost., S Marinho, MARB Castanho. Peptide-mediated siRNA delivery: Chronic myeloid leukemia therapy targeting the BCR/ABL fusion gene. 17th ECCO – 38th ESMO – 32nd ESTRO European Cancer Congress, Amsterdam, Netherlands, September 27th–October 1<sup>st</sup>, 2013. (Poster presentation)

JM Freire, AS Veiga, NC Santos, D Andreu, AT Da Poian and MARB Castanho. Nucleic acid delivery vectors derived from viral proteins: Cell Penetrating Peptides vs. Supercharged Proteins. (Semi-finalist on Young Investigator Poster Award). 23rd American Peptide Symposium & 6th International Peptide Symposium, Big Island of Hawai'i, USA, June 22-27th, 2013. (Poster presentation)

AF Faustino, V Artilheiro, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, The dengue virus capsid protein inhibitor peptide pep14-23 becomes alpha-helical upon binding to negative lipids, Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published *Biophys. J.*, 104, 536<sup>a</sup>, 2013. (Oral communication)

FA Carvalho, IC Martins, FA Carneiro, I Assunção-Miranda, AF Faustino, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos, Dengue virus capsid protein binding to lipid droplets and its inhibition. Towards a new drug target, Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published on *Biophys. J.* 2013, 104, 415a. (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, Dengue virus capsid protein inhibitor peptide pep14-23: towards a novel drug target, 30th Anniversary Symposium of the Boehringer Ingelheim Fonds, Mainz, Germany, March 16, 2013. (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, Dengue virus capsid protein inhibitor peptide, pep14-23, becomes alpha-helical upon binding to negatively-charged lipids, Biophysical Society Meeting Membrane Protein Folding, Seoul, South Korea, May 19-22, 2013. (Poster presentation )

A Hollmann, PM Matos, MT Augusto, MARB Castanho, NC Santos, Conjugation of cholesterol to HIV-1 fusion inhibitor C34 increases peptide-membrane interactions potentiating its action, 23rd American Peptide Symposium, Waikoloa (Hawaii), USA. June 22-27, 2013. Abstract published on 2013 Biopolymers (Pept. Sci.), 100, 299. (Poster presentation)

A Hollmann, F Vigant, MARB Castanho, B Lee, NC Santos, Singlet oxygen effects on lipid membranes: implication on viral fusion inhibitors mechanism of action, 38th FEBS (Federation of European Biochemical Societies) Congress – Mechanisms in Biology, San Petersburg, Russia, July 6-11, 2013. Abstract published on 2013 FEBS J., 280, 358. (Poster presentation)

AF Faustino, FA Carvalho, IC Martins, MARB Castanho, R Mohana-Borges, FCL Almeida, AT da Poian, NC Santos, Dengue virus capsid protein interacts specifically with very low-density lipoproteins, Modern Biophysical Methods for Protein Ligand Interactions – EMBO (European Molecular Biology Organization) Practical Course, Oulu, Finland, October 21-25, 2013. (Poster presentation)

JM Freire, AS Veiga, I Rego de Figueiredo, BG de la Torre, NC Santos, D Andreu, AT Da Poian and MARB Castanho. Design and mechanism of dengue virus capsid-cell penetrating peptides for nucleic acid delivery. 9th European Biophysics Congress (EBSA), Lisbon, Portugal, July 13-17th, 2013. (Poster presentation)

JM Freire, I Serrano, MN Melo and MARB Castanho. Permeability Revisited – From Fick's Law to Membrane Partition. Examining Single-Cell Permeability. Beating the Blood-Brain & Other Blood Barriers, Lisbon, Portugal, February 6-8th, 2013. (Poster presentation)

AF Faustino, FA Carvalho, IC Martins, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos, Dengue virus capsid protein interacts specifically with very low density lipoproteins, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S196. (Poster presentation)

A Hollmann, F Vigant, MARB Castanho, B Lee, NC Santos, New HIV fusion inhibitors LJ001 and JL103 act by modifying viral lipid membrane properties, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S123. (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, FCL Almeida, AT Da Poian, NC Santos, IC Martins, pep14-23, a peptide drug lead against dengue virus, binds anionic lipids becoming alpha-helical, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013.

Abstract published on 2013 Eur. Biophys. J., 42, S64.(Poster presentation)

MT Augusto, A Hollmann, MARB Castanho, A Pessi, NC Santos, Improvement of the HIV fusion inhibitor C34 activity by membrane anchoring and enhanced exposure. EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S165. (Poster presentation)

### Communications in National Conferences

I Rego de Figueiredo, JM Freire, F Enguita and MARB Castanho. Peptide-Mediated siRNA Delivery. Chronic Myeloid Leukemia Therapy Targeting the BCR/ABL Fusion Gene. 1st reSEARCH Coimbra in Health Sciences, Coimbra, Portugal, April 19-21, 2013. (Oral communication)

I Rego de Figueiredo, JM Freire, F Enguita and MARB Castanho. Chronic Myeloid Leukemia Gene Therapy Targeting the BCR/ABL Fusion Gene. Peptide-mediated gene delivery: siRNA and editing tools. iMed Conference 5.0, Lisbon, Portugal, October 11-13, 2013. (Oral communication)

JM Freire, AS Veiga, I Rego de Figueiredo, BG de la Torre, NC Santos, D Andreu, A T. Da Poian and MARB Castanho. Design and mechanism of dengue virus capsid-cell penetrating peptides for nucleic acid delivery. Molecular Biology in Portugal and EMBL, Lisbon, Portugal, July 18th, 2013. (Poster presentation)

I Serrano, JM Freire and MARB Castanho. Translocation of Kyotorphin-derived peptides across an artificial blood-brain barrier model. Beating the Blood-Brain & Other Blood Barriers, Lisbon, Portugal, February 6-8th, 2013. (Poster presentation)

MT Augusto, A Hollmann, MARB Castanho, M Porotto, A Pessi, NC Santos. Improvement of the HIV fusion inhibitor C34 efficacy by membrane anchoring and enhanced exposure. iMed Conference 5.0 – Innovating Medicine, Lisbon, Portugal, October 11-13, 2013. (Poster presentation)

V Artilheiro, AF Faustino, FCL Almeida, MARB Castanho, AT Da Poian, NC Santos, IC Martins, Understanding the mode of action of pep14-23, a novel Flavivirus drug candidate, 7th YES (Young European Scientist) Meeting, Oporto, Portugal, November 14-16, 2013. (Poster presentation)

V Artilheiro, AF Faustino, GM Guerra, FCL Almeida, MARB Castanho, AT Da Poian, NC Santos, IC Martins, Structure-function study of the dengue virus capsid protein and its the new designed inhibitor peptide, pep14-23, iMed Conference 5.0 – Innovating Medicine, Lisbon, Portugal, October 11-13, 2013. (Poster presentation)

M. Castanho. O que podemos aprender de Bioquímica com o vírus da Dengue. VI ENEBIOQ (Encontro Nacional de Estudantes de Bioquímica), Aveiro, Portugal, March 2013 (Oral communication)

### **Organisation of Conferences**

M. Castanho, International Advisory Committee, Host-pathogen interaction. 14th IUBMB Conference, Marrakech, Morocco, November 16-20, 2013.

M. Castanho, Session chair: Biophysics in Europe (teaching, career and funding), 9th Eur Biophysics Congress, Lisbon, Portugal, July 13-17, 2013.

Miguel Castanho, Chairman of the Beating the Blood-Brain and other Blood Barriers Workshop, IMM, Lisbon, Portugal, February 6-8, 2013.

Isa Serrano, Member of organizing committee of Beating the Blood-Brain and other Blood Barriers Workshop, IMM, Lisbon, Portugal, February 6-8, 2013.

Salomé Veiga, Member of organizing committee of Beating the Blood-Brain and other Blood Barriers Workshop, IMM, Lisbon, Portugal, February 6-8, 2013.

Sónia Sá Santos, Member of organizing committee of Beating the Blood-Brain and other Blood Barriers Workshop, IMM, Lisbon, Portugal, February 6-8, 2013.

Sónia Sá Santos, Chair in Oral Presentations Session II of VII PhD Students Meeting IMM/CAML, Portugal, Lisbon, Portugal, December 4-6, 2013.

M. Castanho, session chair: Biomedical applications of new microscopy techniques, Encontro de Engenharia Biomédica 2013, Lisbon, Portugal, November 6, 2013.

### **Internationalisation**

Our team was recently involved in three projects involving international consortia, from which many collaborative research papers have been published (see reference list).

International collaborations with joint published papers in the last five years:

- David Geffen School of Medicine, UCLA, USA, Prof Benhur Lee;
- Federal University Rio de Janeiro, Brazil, Prof Andrea T. Da Poian;
- National Cancers Institute, Frederick, USA, Prof Jöel Schneider;
- University of Queensland, Australia, Prof David Craik;
- University of Girona, Spain, Prof. Eduard Bardají;
- University Hospital of Santiago de Compostela, Spain, Prof José Cocho;
- University Miguel Henandez, Elche, Spain, Prof José Villalain;
- University Pompeu Fabra, Barcelona, Spain, Prof David Andreu.

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

Inês Rego de Figueiredo was awarded the 2013 iMed5.0 Fundação AstraZeneca Innovate Competition with the project: Chronic Myeloid Leukemia Gene Therapy Targeting the BCR/ABL Fusion Gene. Peptide-mediated gene delivery: siRNA and editing tools. 16th Gulbenkian/GAPIC

Scholarship (€3.000,00). School of Medicine – Fluorescent Labeling of DENV for the Dynamic Analysis of the Viral Infection Cycle using Spinning Disk Confocal Microscopy and Flow Cytometry (ID:20130028/PEC/BG) Journal Cover: Biopolymers 100. Picture from original article Freire, J. M. et al. Biopolymers 100, 325–336 (2013).

### **Advanced teaching**

M. Castanho, Invited Chair of the one-week post-graduate course on Medical Biochemistry of the Federal University of Rio de Janeiro, "Peptide drugs discovery and development", Rio de Janeiro, Brazil, August 2013

M. Castanho, Chairman of the Beating the Blood-Brain and other Blood Barriers Workshop, IMM, Lisbon, Portugal, February 6-8, 2013.

M. Castanho, Chairman of the session "What's in H2020 for me? A focused session on health sciences in academia and clinics", IMM, Lisbon, Portugal, December 20, 2013.

M. Castanho. Host of Prof Anthony Watts (Oxford University, UK) for the seminar "Resolving nanoscale details of drugs and ligands at their binding sites of membrane-embedded, functionally competent targets", Oxford, UK, September 22, 2013.

### **Science and society**

M. Castanho. Invited speaker for a panel discussion - Tertúlias FNACiência "Efemérides Bioquímicas em 2013 - dos enzimas ao DNA", Braga, Portugal, October 17, 2013.

"Miguel Botas Castanho fala sobre o vírus da dengue em Santarém". Newspaper article published on O Mirante, March 7, 2013.

### **Msc theses completed**

Tiago Nascimento Figueira (2013) Blocking HIV at cell entry: innovative exploitation of the interaction between membranes and next generation drugs - single domain antibodies, peptides and photoactivatable oxidants. Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal. Supervisors: Miguel Castanho, Ana Salomé Veiga.

## SUSANA CONSTANTINO LAB

### Major Interests / Objectives

The Angiogenesis Group 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 tumour 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.

### Head of Unit

Susana Constantino Rosa Santos, PhD.

### Research Team

Adriana de Fátima Dias Lisboa Correia	Graduate	MSc Student
Ana Rita Duarte Simões Pereira	Graduate	MSc Student (started October)
Augusto Manuel Almeida Ministro	Graduate	PhD Student
Carolina Isabel Garcia Cardina	Graduate	MSc Student (started September)
Filipa Gil Marques	Master	PhD Student
Paula Alexandra Gomes de Oliveira	Master	PhD Student
Raquel João Santos Ferreira Nunes	PhD	Post-doctoral Investigator
Tiago Filipe Ribeiro Ruas Maçarico	Graduate	MSc Student (started September)

### Keywords / Research Areas

Angiogenesis, Ionizing radiation, Ischemia, Vasculature.

### Major scientific achievements

- 1) Establishment of a clinical protocol to collect and analyse human irradiated and unirradiated samples from rectal cancer patients aiming the validation of the enhancement of angiogenesis by low doses of IR during radiotherapy;
- 2) In the setting of experimentally induced hindlimb ischemia, low doses of ionizing radiation could stimulate angiogenesis and collateral development and thereby improve blood perfusion in the ischemic limb. The outcome of these in vivo experiments performed in a mice model suggests that low doses of IR may have clinical use in the treatment of lower limb vascular insufficiency;
- 3) Transthyretin proteins regulate angiogenesis by conferring different molecular identities to endothelial cells. This work has critical implications in the prevention of early hepatic artery thrombosis in familial amyloidotic polyneuropathy patients after liver transplantation.

### Recent Most Relevant Publications

Nunes RJ, de Oliveira P, Lages A, Becker JD, Marcelino P, Barroso E, Perdigoto R, Kelly JW, Quintas A. and Constantino Rosa Santos S. (2013) Transthyretin proteins regulate angiogenesis by conferring different molecular identities to endothelial cells. *J Biol Chem* **288**, 31752-60. <http://www.jbc.org/content/early/2013/09/12/jbc.M113.469858.full.html#ref-list-1>. (Journal IF: 5.023, Citations: 0)

Domingues I, Rino J, Demmers JAA, de Lanerolle P, Constantino Rosa Santos S. (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: 4.244, Citations: 11)

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: 4.244, Citations: 16)

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: 5.023, Citations: 25)

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: 9.338, Citations: 109)



### **Ongoing Research Projects**

2011/2016. A Novel Approach For Therapeutic Angiogenesis: Low Doses of Ionizing Radiation. Coordinator: Susana Constantino Rosa Santos. Agency: Novartis Farma, SA; Medtronic Portugal, Lda.; Laboratórios Pfizer, Lda. Amount: €19.000,00

2008/2015. Low doses of Ionizing Radiation Induce Angiogenesis: Therapeutic Implications. Coordinator: Susana Constantino Rosa Santos. Agency: Hospital Curry Cabral, Roche, Novartis Farma, Wyeth, Astellas Farma, Merck Sharp & Dohme. Amount: €90.000,00

### **Invited lectures and seminars**

S. Constantino. Tumor angiogenesis. Department of Neurology, Centro Hospitalar Lisboa Norte, Lisbon, Portugal. March 21, 2013.

S. Constantino. Angiogenesis regulation and therapeutic implications. Vascular Department, Centro Hospitalar Lisboa Norte, Lisbon, Portugal. May 23, 2013.

S.Constantino. Transthyretin proteins regulate angiogenesis by conferring different molecular identities to endothelial cells. Liver Transplant Center, Hospital Curry Cabral, Lisbon, Portugal. September 17, 2013.

### **Communications in International Conferences**

Ministro A., Nunes J. R., de Oliveira P., Rocha A., Grillo M. I. and Constantino Rosa Santos S. Low doses of ionizing radiation promote therapeutic revascularization in ischemic tissues. ATVB. Lake Buena Vista, Florida. May 1-3, 2013. (Oral communication)

Marques G.F., Sousa S. J., Malaquias J., Castelo B. H., Grillo M. I., Poli E. and Constantino Rosa Santos S. Low doses of ionizing radiation induce angiogenesis: therapeutic implications. EMBO Young Scientists's Forum. Lisbon, Portugal. July 15-16, 2013. (Poster presentation)

Nunes J. R., de Oliveira P., Ministro A., A., Rocha A., Correia A., Grillo M. I. and Constantino Rosa Santos S. A novel approach for therapeutic angiogenesis: low doses of ionizing radiation. EMBO Young Scientists's Forum. Lisbon, Portugal. July 15-16, 2013. (Poster presentation)

### **Communications in National Conferences**

Marques G.F., Sousa S. J., Malaquias J., Castelo B. H., Grillo M. I., Poli E. and Constantino Rosa Santos S. Low doses of ionizing radiation induce angiogenesis: therapeutic implications. Porto Cancer Meeting. Lisbon, Portugal. April 11-12, 2013. (Poster presentation)

Ministro A., Nunes J. R., de Oliveira P., Rocha A., Grillo M. I. and Constantino Rosa Santos S. Are there new developments on angiogenesis? A new perspective. 4th International Forum on

Vascular Diseases. Lisbon, Portugal. December 13-14, 2013. (Oral communication)

### Internationalisation

#### Collaborative Research:

- Curzio Ruegg, Department of Medicine, Faculty of Sciences, Fribourg, Switzerland. Research Project: Molecular mechanisms and relevance of angiogenesis induced by low-dose ionizing radiation.
- Marc Mareel, Ghent University Hospital, Ghent, Belgium. Research Project: Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis.
- Jeffery W. Kelly, Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, California, USA. Research Project: The differential effect of WT and V30M Transthyretin in the hepatic microenvironment and vasculature response.

#### Collaborative Publication:

- Nunes RJ, de Oliveira P, Lages A, Becker JD, Marcelino P, Barroso E, Perdigoto R, Kelly JW, Quintas A. and Constantino Rosa Santos S. (2013) Transthyretin proteins regulate angiogenesis by conferring different molecular identities to endothelial cells. *J Biol Chem* **288**, 31752-60.

### Advanced teaching

Constantino, S. Tumoral Angiogenesis lecture for the Master in Neurosciences - Pathology of the Nervous System, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. February 7, 2013.

Constantino, S. Radiobiology lecture for the Master in Oncobiology, Instituto de Medicina Molecular –Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. May 8, 2013.

Constantino, S. Angiogenesis and radiotherapy lecture for the PhD programme Metabolismo - Clínica e Experimentação, Faculdade de Medicina da Universidade do Porto, Porto, Portugal. June 4, 2013.

## 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 are reflected the tumor-target organ/host interactions. Our major interests are: (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 how tumors modulate the sensitivity to antineoplastic agents; and (IV) to identify new therapeutic strategies by studying the role of tumor-associated ECM in cancer progression.

### Head of Unit

Luis António Marques da Costa, MD, PhD - Director of the Oncology Department, HSM-CHLN; Assistant Professor, FMUL.

### Research Team

Afonso Camilo Rodrigues Fernandes	PhD	Consultant
Arlindo Júlio Rebelo da Silva Ferreira	Master	Investigator, MD (started October)
Carolina Coimbra Brandão Alves	Master	Investigator (left July)
Diana Domingos de Matos	Graduate	MSc Student (started September)
Inês Maria Duarte Vaz Luis	Graduate	Investigator, Teaching Assistant
Irina Margarida Pereira Machado Alho Duarte	PhD	Technician
Isabel Cristina Ferreira Fernandes Borges da Costa	Master	Investigator, Clinical Specialist, Assistant Professor
Joana Maria Tato Ribeiro Costa	Graduate	Technician
Margarida Caracol Castanho Lopes Matias Ghesquiere	Graduate	Investigator, Clinical Specialist
Maria José Palma Bettencourt	Undergraduate	Undergraduate (left August)

Mário Alberto Ferreira Maia Matos	Graduate	MSc Student (started September)
Ricardo Castanheira Pires	Graduate	Technician
Sandra Cristina Cana de Anjo Casimiro	PhD	Post-doctoral Investigator
Sandra Sofia Chorão Lavajo Lucas	Graduate	Administrative (started November)
Sara Santos Henriques	Graduate	MSc Student (started September)
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 2013 we highlight our participation in the Global Cancer Genomics Consortium. In the scope of GCGC we hosted the The 3rd Global Cancer Genomics Consortium Symposium, at IMM. Our cooperative research originated two publications in 2013, and revealed an essential modifying role of the physiologic level of MTA1 in supporting pulmonary metastasis of breast cancer, and illustrated for the first time the power of RNA-sequencing in revealing the variation landscape of breast transcriptome, exemplifying the analytical strategies to search regulatory interactions among cancer relevant molecules.

We continued to dissect the importance of RANKL-RANK pathway in bone metastases and found that the use of the IAP antagonist AT-406 in the context of bone metastatic disease needs to be carefully monitored for the induction of increased bone resorption, but its combination with anti-RANKL directed therapies could have a beneficial effect, especially in RANK-positive tumors.

### Recent Most Relevant Publications

Casimiro S, Mohammad KS., Pires R, Tato-Costa J, Alho I, Teixeira R, Carvalho A, Ribeiro S, Lipton A, Guise TA, Costa L. (2013) RANKL/RANK/MMP-1 Molecular Triad Contributes to the Metastatic Phenotype of Breast and Prostate Cancer Cells In Vitro. *Plos One* **8**, e63153. (Journal IF: 3.730, Citations: 1)

Casimiro S, Luis I, Fernandes A, Pires R, Pinto A, Gouveia AG, Francisco AF, Portela J, Correia L, and Costa L (2012) Analysis of a bone metastasis gene expression signature in patients with bone metastasis from solid tumors. *Clin Exp Metastasis* **29**, 155. (Journal IF: 3.524, Citations: 2)

Pakala SB, Rayala SK, Wang RA, Ohshiro K, Mudvari P, Reddy SDN, Zheng Y, Pires R, Casimiro S,

Pillai MR, Costa L, Kumar R. (2013) MTA1 Promotes STAT3 Transcription and Pulmonary Metastasis in Breast Cancer. *Cancer Research* **73**(12), 3761-3770 (Journal IF: 8.650; Citations: 0)

Vaz-Luis I, Winer E, and Lin NU. (2012) Human epidermal growth factor receptor-2 positive Breast Cancer: Does Estrogen Receptor status define two distinct subtypes? *Annals of Oncology* **24**(2), 283. (Journal IF: 6.425, Citations: 0)

Horvath A, Pakala SB, Mudvari P, Reddy SDN, Ohshiro K, Casimiro S, Pires R, Fuqua SAW, Polyak K, Costa L, Toi M, Nair S, Sukumar S, Kumar R (2013) Novel Insights into Breast Cancer Genetic Variance through RNA Sequencing. *Scientific Reports* **3**, 2256. (Journal IF: 2.927, Citations: 0)

### Ongoing Research Projects

2011/2014 Multi-Functional Bone Seeking Agents for the Treatment of Skeletal Metastatic Disease. Coordinator: Luis António Marques da Costa. Agency: FCT. Coordinator Institution: ITN. Coordinator PI: Isabel Rego dos Santos. Amount: €50.064,00 (global €147.000).

2012/2013 Educational Program in Oncobiology. Coordinator: Sandra Cristina Cara de Anjo Casimiro. Agency: Fundação Calouste Gulbenkian. Amount: €14.960,00

2013/2013. Luminal-type breast cancer: prognostic value of RANK-positive lymphatic nodes. Coordinator: Sandra Casimiro. Agency: Astrazeneca. Amount: €3.750,00

2013/2013 Global Cancer Genomic Consortium Coordinator: Luis António Marques da Costa. Agency: Astrazeneca. Amount: € 3.000,00

2013/2014 Densidade Mamária e Colagénio: representatividade do colagénio tipo I e tipo III no tecido mamário não neoplásico e neoplásico em doentes com cancro da mama Coordinator: Luis António Marques da Costa. Agency: Celgene Sociedade Unip., Lda.. Amount: €4.000,00

2013/2015 Metal-based Multimodal Probes for Breast Cancer Imaging Targeting Y1-NPY Receptors: Synthesis, Characterization and Pre-clinical Evaluation Coordinator: Luis António Marques da Costa. Agency: FCT. Amount: €33.000,00 Total amount: €500.000,00

2013/2014 c-Met, p-c-Met, and HGF IHC in Bone Metastases. Coordinator: Sandra Casimiro. Agency: Merck, S.A.. Amount: €21.000,00

2011/2014 Molecular markers in multiple myeloma. Coordinator: Inês Luis. Agency: Grupo Hematológico Português. Amount: €5.000,00

2011/2014 Mechanisms of invasion and progression in metastatic bone disease and outcomes in HER2 positive metastatic breast cancer. Coordinator: Inês Vaz Luis. Agency: Harvard Medical School. Amount: €400.000,00

2013/2017 Advanced breast cancer: prognosis and therapeutics. Coordinator: Sandra Casimiro. Agency: Novartis. Amount: €10.000,00

2008/2014 Senescence in rectal cancer. Coordinator: Luís Costa. Agency: Merck, SA. Amount: €45.740,00

2008/2014 Oncology Series. Coordinator: Luís Costa. Agency: Novartis, Pfizer. Amount: €54.130,97

2012/2013 Long Term Bisphosphonates Coordinator: Luís Costa. Agency: Novartis. Amount: €4.040,00

2012/2016 Global Cancer Genomics Consorci. Coordinator: Luís Costa. Private Funding. Amount: €11.440,00

2012/2013 Cachexia in pancreatic cancer Coordinator: Luís Costa. Agency: Pfizer. Amount: €6.000,00

2013 GCGC Meeting Coordinator: Luís Costa. Agency: FCT-FACC. Amount: €3.000,00

### Other Projects

2011/2013 MTDH Activation by 8q22 Genomic Gain and MTDH Overexpression in Advanced Colorectal Cancer – Correlation with Poor Prognosis and Chemoresistance. Coordinator: Sandra Casimiro. No funding

2012/2013 In vitro analysis of the effect of the IAPs inhibitor AT-406 in bone metastases. Coordinator: Sandra Casimiro. No funding

2012/2014 In vitro evaluation of the anti-tumoral and anti-osteoclastogenic effect of combined therapy with zoledronic acid and saracatinib in breast cancer. Coordinator: Sandra Casimiro. No funding

2012/2014 Activation of mTOR pathway in breast cancer: analysis of primary and metastasis tumor samples. Coordinator: Luís Costa. No funding

2013/2014 Clinical significance of the AKT/mTOR pathway activation in KRAS-wt metastatic colorectal cancer response to EGFR-targeted therapy. Coordinator: Luís Costa. No funding

### Publications in peer review Journals

Alho I, Costa L, Bicho M, Coelho C. (2013) The role of low-molecular-weight protein tyrosine phosphatase (LMW-PTP ACP1) in oncogenesis. *Tumour Biology* **34**(4), 1979-89 (Journal IF: 2.518; Citations: 0)

Alho I, Costa L, Bicho M, Coelho C. (2013) Characterization of low molecular weight protein tyrosine phosphatase isoforms in human breast cancer epithelial cell lines. *Anticancer Research* 2013 May **33**(5), 1983-7. (Journal IF: 1.713; Citations: 1)

Casimiro S, Alho I, Bettencourt M, Pires R, Lipton A, Costa L. (2013) RANKL enhances the effect of an antagonist of inhibitor of apoptosis proteins (IAPs) in RANK-positive breast cancer cells. *Journal of Bone Oncology* **2**(3), 116-122. (Journal IF: pending; Citations: 0)

Alho I, Costa L, Bicho M, Coelho C. (2013) Low Molecular Weight Protein Tyrosine Phosphatase Isoforms Regulate Breast Cancer Cells Migration through a RhoA Dependent Mechanism. *PLoS One* **8**(9), e76307. (Journal IF: 3.730; Citations: 0)

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*. 2013 Oct 26. [Epub ahead of print]. (Journal IF: 2.649; Citations: 0)

Vaz-Luis I, Winer E, Lin NU (2013) Human epidermal growth factor receptor-2 positive Breast Cancer: Does Estrogen Receptor status define two distinct subtypes? *Annals of Oncology* **24**(2) (Journal IF: 7.38; Citations: 5)

Vaz-Luis I, Seah D, Olson E, Wagle N, Metzger-Filho O, Sohl J, Litsas G, Burstein HJ, Krop IE, Winer EP, Lin NU (2013) Clinicopathological features among patients with advanced human epidermal growth factor-2-positive breast cancer with prolonged clinical benefit to first line trastuzumab based therapy: A retrospective cohort study. *Clinical Breast Cancer* **13** (4), 254-63. IF: 2.42. (Journal IF: 2.422; Citations: 0)

Vaz-Luis I, Zeghibe CA, Frank E, Sohl J, Washington K, Silverman S, Erica L. Mayer EL, Overmoyer B, Richardson A, Krop I, Winer EP, Lin NU (2013) Prospective clinical experience with research biopsies in breast cancer patients. *Breast Cancer Research and Treatment* 2013 **142**(1), 203-9. IF: 4.47. (Journal IF: 4.47; Citations: 0)

#### Invited lectures and seminars

Luís Costa, Management of Bone Metastases. St. Vincent's University Hospital, Dublin, Ireland, March 7, 2013.

Luis Costa, Improving the medical management of bone metastases, Challenging Metastatic Cancer: Remodelling Management- Evolution or Revolution? London, United Kingdom, April 17, 2013.

Luis Costa, Oncologic treatment of tumors with disorders of the ALK gene. European Congress of Pathology. Lisbon, Portugal, September 2, 2013.

Luis Costa, Difficulties in Pharmacogenomics Clinical Studies in Cancer. 3rd ESPT Pharmacogenomics Advanced Training Course, Lisbon, Portugal, September 25, 2013.

Sandra Casimiro, Identification of prognostic factors and therapeutic targets in breast and colon cancer. Lançamento da Rede Nacional de Bancos de Tumores, Auditório do IPO Lisboa, Lisbon, Portugal, December 12, 2013.

Vaz-Luis I. Teaching Medicine and Teaching Science- Is There a Difference? Celebrating IMM's 10th anniversary, Lisbon, Portugal, September 21, 2013.

Vaz-Luis, I. Being and MD and a researcher. Research Day Medical School University of Lisbon, Lisbon, Portugal. December 11, 2013.

Vaz-Luis, I. How to improve pathways in an Oncology Department- Strategy of organization of clinical research. Oncology Department, Centro Hospitalar Lisboa Norte, Lisbon, Portugal, December, 2013.

Vaz-Luis, I. Practical Implications of Cancer Biology in Treatment Strategy: end-points in the different stages of cancer. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal May 2013.

### **Communications in International Conferences**

Luís Costa, How to Accelerate Drug Development in Cancer Care, The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Oral communication)

Sandra Casimiro, Biobanking in Oncology: Experience from IMM-HSM, The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Oral communication)

Sandra Casimiro, Bone Metastases: Searching for New Targets, The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Oral communication)

Joana Tato-costa, Sandra Casimiro and Luis Costa, Cellular senescence in rectal cancer: friend or foe?, The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Lisbon, September 18-20<sup>th</sup>, 2013 (Poster Presentation)

Ricardo Pires, Sandra Casimiro, Afonso Fernandes, Joana Tato-Costa, Irina Alho, Irina Alho, Emilia Vieira, Cristina Ferreira, Paulo Costa, Henrique Bicha-Castelo, Luis Costa, Colorectal cancer biobanking for genomic and transcriptomic profiling of disease progression. The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Poster presentation)

Irina Alho, Constança Coelho, Manuel Bicho, Luis Costa. The role of low molecular weight protein tyrosine phosphatase isoforms in tumor progression in bone. The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Poster presentation)

Ana C. R. Martins, F.G. Freitas, P.R. Gonçalves, R. Prada, M.I. Crisóstomo, Luis Costa, M. Carmo-Fonseca, J. M.P. Desterro. From cancer research to oncobiology teaching: Development of an oncobiology serious game for medical education. The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20<sup>th</sup>, 2013 (Poster presentation)



C. Fernandes, S. Monteiro, P. Mendes, L. Gano, F. Marques, J. D. G. Correia, L. Costa, S. Casimiro, I. Santos. Bisphosphonate-Containing M(CO)<sub>3</sub>-Complexes (M = <sup>99m</sup>Tc/Re) as Bone-Seeking Agents. The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20th, 2013 (Poster presentation)

C. Fernandes, S. Monteiro, P. Mendes, L. Gano, F. Marques, S. Casimiro, L. Costa, I. Santos. Novel <sup>99m</sup>Tc(I)-labeled bone-seeking molecules for bone imaging. CIBD 2014, Miami, FL, USA, November 6-9<sup>th</sup>, 2013 (Poster presentation)

Vaz-Luis I, Ottesen RA, Hughes ME et al: Time trends in the use of adjuvant chemotherapy and outcomes in patients with T1N0 breast cancer in National Comprehensive Cancer Network (NCCN). 2013 ASCO meeting, Chicago, USA, May 31-June 4, 2013 (Oral communication)

Freedman R, Vaz-Luis I, Lin N et al. Completion of adjuvant trastuzumab for older patients with early breast cancer. 2013 ASCO meeting, Chicago, USA, May 31-June 4, 2013 (Poster presentation)

Meier C, Vaz-Luis I, Seah. D et al. Impact of tumor subtype on clinical features, treatment, and clinical outcomes among breast cancer patients with central nervous system disease. SABC2013, San Antonio, USA, December 10-14, 2013 (Poster presentation)

### **Communications in National Conferences**

Maria Madalena Rosário, Sara Dâmaso, Teresa Pacheco. Development and characterization of a cellular model of acquired resistance to cetuximab derived from human colorectal cancer cells KRAS- and BRAF-wt. 16<sup>o</sup> workshop "Educação pela Ciência". November 16<sup>th</sup>, 2013.

### **Organisation of Conferences**

Luis Costa and Sandra Casimiro organized The 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20, 2013.

Isabel Fernandes organized the Oncology Series. Soft Tissue Sarcomas, Lisbon, Portugal, March 21, 2013.

### **Internationalisation**

During 2013 we continue to participate in the Global Cancer Genomics Consortium whose partners are: George Washington University; Tata Memorial Centre and Rajiv Gandhi Center of Biotechnology; Oxford University; Institute of Molecular Medicine; Graduate School of Medicine Kyoto University.

GCGC aligns a multidisciplinary team to address specific shared global cancer research challenges through the application of high-throughput technologies using human cancer specimens from its network. GCGC aims to facilitate student and faculty academic exchanges and research collaborations in the areas of breast and other cancers through the application of

high-through-put genomic, proteomic, structural and bioinformatic technologies to human cancer specimens. This collaboration leads to the publication of two papers in 2013.

In the scope of GCGC in 2013 we organized the The 3rd Global Cancer Genomics Consortium Symposium, that took place at IMM in September.

### **Advanced teaching**

In 2013, L. Costa (Director) and S. Casimiro, I. Luis, and I. Fernandes (Invited Professors), participated in the development, accreditation and implementation of the first edition of the Master of Science Course in Oncobiology of the FML. This educational program is targeted for bachelors, researchers, medical doctors, and other professionals in health or related areas, who want to gain an in-depth understanding of the biology and clinical behavior. The course will provide participants with a multidisciplinary view of oncology, focusing on the molecular and cellular mechanisms working in cancer, and their impact for patient care – both for diagnosis and therapeutics.

In 2013, L. Costa (Chairman) and S. Casimiro, I. Luis, J. Ribeiro, I. Fernandes, M. Semedo (Invited Professors), participated in the organization and lecturing of Oncobiology, a mandatory course for the 3rd year Medical students from FML. The main goal of this course is to highlight the clinical impact of understanding molecular and cellular mechanisms operating in cancer, and to learn on cancer diagnosis, prognosis and therapeutics, always connecting with the biological viewpoints.

### **PhD theses completed**

Irina Alho (2013) The importance of Low Molecular Weight Protein Tyrosine Phosphatase in the progression of metastatic bone disease and therapeutic response. Universidade de Lisboa. Supervisor: Luis Costa, Constança Coelho.

## SÉRGIO DE ALMEIDA LAB

### Major Interests / Objectives

Our research focuses on the mechanisms that control chromatin dynamics during transcription and DNA damage repair 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, pre-mRNA processing, chromatin modification and DNA damage response are linked to the development of human diseases such as cancer.

### Head of Unit

Sérgio Alexandre Fernandes de Almeida, PhD, - Assistant Professor, FMUL

### Research Team

Alexandra Coitos Vítor	Graduate	Technician (started June)
Ana Filipa Batalha Martins	Master	Technician (left September)
Ana Rita Fialho Grosso	PhD	Post-doctoral Investigator (started November)
Ioana Posa	Graduate	MSc Student (started September)
Joana Patrícia Moreira Tavares	Graduate	MSc Student (started September)
S R CHAITANYA. SRIDHARA	Master	PhD Student
Silvia Filipa Camoëira Gonçalves de Carvalho	Master	Technician (started June)

### Keywords / Research Areas

Chromatin dynamics, Epigenetics, Cancer Biology, DNA damage response.

### Major scientific achievements

In 2013 the members of our Lab have:

- Published an original manuscript in the international journal "Nucleic Acids Research" (Carvalho et al. 2013);
- Been elected Associate Members of the European network of excellence "EpiGeneSys";
- Started a new research project funded by FCT;
- Presented our research work in 7 national and international conferences;
- Been awarded the "Best Poster Award" at the IMM PhD students meeting;
- Participated in advanced teaching in PhD and MSc programs;
- Completed one MSc thesis.

### Recent Most Relevant Publications

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**, 2881-93. (Journal IF: 8.3, Citations: 7)

de Almeida SF, Carmo-Fonseca M (2012) Design principles of interconnections between chromatin and pre-mRNA splicing. *Trends in Biochemical Sciences* **37**, 248-53. (Journal IF: 13.1 (2012 IF), Citations: 14)

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 lysine 36. *Nature Structural and Molecular Biology* **18**, 977-83. (Journal IF: 12.7 (2011 IF), Citations: 47)

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**, 8015-26. (Journal IF: 7.8 (2010 IF), Citations: 19)

### Ongoing Research Projects

2011/2014 Splicing-coupled mechanisms of chromatin remodeling and their global role in transcription. Coordinator: Sérgio Alexandre Fernandes de Almeida. Agency: Fundação Ciência e Tecnologia. Amount: €141.967,00

2013/2015 SETD2 mediates a novel tumor suppressor mechanism that is misregulated in clear cell renal carcinoma. Coordinator: Sérgio Alexandre Fernandes de Almeida. Agency: Fundação Ciência e Tecnologia. Amount: €184.516,00

### **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: Amount: €21.2892, 10

### **Invited lectures and seminars**

de Almeida SF. “Chromatin dynamics during transcription by RNA polymerase II”, GABBA PhD program, Porto, May 13, 2013.

### **Communications in International Conferences**

Carvalho S, Raposo AC, et al. “SETD2 coordinates nucleosome dynamics during transcription” EMBO Conference Series: Chromatin and Epigenetics, Heidelberg, Germany May 8-12, 2013.

Carvalho S, Raposo AC, et al. “SETD2 coordinates nucleosome dynamics during transcription” Chromatin replication and chromosomal stability, Copenhagen, Denmark. June 17-19, 2013.

Grosso AR, Leite AP, et al. "RNA chimeras are widespread in the transcriptome of cells with aberrant chromatin structure" EpiGeneSys Annual Meeting, Cambridge, UK, December 4-6, 2013.

### **Communications in National Conferences**

Carvalho S, Raposo AC, et al. “SETD2 coordinates nucleosome dynamics during transcription”, EMBO Young Scientists' Forum, Lisbon, July 15-16, 2013

Vítor A, Carvalho S, et al. "Methylation of histone H3 is necessary for scheduled repair of DNA double strand breaks" 3rd Global Cancer Genomics Consortium Symposium, Lisbon, September 18-20, 2013.

Grosso AR, Martins F, et al. "Epigenetic Misregulation and Transcriptome Alterations in Renal Carcinoma" 3rd Global Cancer Genomics Consortium Symposium, Lisbon, September 18-20, 2013.

Sridhara SC, Carvalho S, Carmo-Fonseca M and de Almeida SF. "The role of Serine-Arginine Protein Kinases as mediators of cancer-related signaling pathways" VII PhD Students Meeting CAML, Lisbon, December 5-6, 2013.

### **Internationalisation**

In the year 2013 we have been elected Associate Members of the European network of excellence "EpiGeneSys". This Network gathers some of the most productive and influential European labs working on the epigenetics field.

During this year, we published one original research paper in the international journal "Nucleic Acids Research" and our team members presented our research work in 3 international conferences.

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

2013 - Elected Associated Member of "EpiGeneSys Network of Excellence"

2013 - Best Poster Award. IMM PhD Students Meeting (Sridhara Chaitanya).

#### **Advanced teaching**

de Almeida SF. Lecturer on the Gene Expression module of the GABBA PhD program, Universidade do Porto, May 13, 2013.

Grosso AR. Lecturer on the Computational Biology in Biomedicine module of the Masters in Bioinformatics and Computational Biology, Faculdade de Ciências da Universidade de Lisboa, July 22-23, 2013.

#### Opponent to PhD theses defense:

de Almeida SF. Main Examiner of the dissertation of Hugo Noronha de Almeida, Instituto Gulbenkian de Ciência. Thesis supervised by Dr Miguel Godinho Ferreira. June 28, 2013.

de Almeida SF. Member of the jury of the dissertation of Mariluz Gomez, Instituto Gulbenkian de Ciência. Thesis supervised by Dr Lars Jansen. November 18, 2013.

#### Opponent to MSc thesis defense:

de Almeida SF. Main Examiner of the dissertation of Dulce Cordeiro dos Santos, Masters student of Biologia Molecular e Genética from Faculdade de Ciências da Universidade de Lisboa. July 31, 2013.

#### **Msc theses completed**

Alexandra Coitos Vítor (2013) Methylation of histone H3 is necessary for scheduled repair of DNA double strand breaks. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Sérgio de Almeida.

## MAMEDE DE CARVALHO LAB

### Major Interests / Objectives

Our unit focuses on basic, translational, and clinical research on the central, peripheral, and autonomic nervous systems. We address multiple disorders that span these various levels of the nervous system: amyotrophic lateral sclerosis (ALS), familial amyloid neuropathy (FAP), disorders of autonomic regulation, Tourette syndrome, and neuropsychiatric disorders. We use a variety of methodologies, including brain imaging, neurophysiological techniques including transcranial magnetic stimulation, clinical cardio-respiratory evaluation, animal models, histochemistry, molecular biomarkers and computational modeling. We aim to explore the physiology and pathophysiology, but ultimately we are committed to improve the lives of patients.

### 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 Rita Mendes Londral Gamboa	Master	PhD Student
Anabela Leuschner Fernandes Cardoso Pinto Noronha Sanches	MD, PhD	Principal Investigator, Consultant, Associate Professor
Andreia da Silva Borges Carapinha	Graduate	Technician
Andrés Díaz Campos	Graduate MD	Investigator
Ângela Raquel Amaro Leal	Graduate	MSc Student
Ângelo Rodrigo Neto Dias	Graduate	MSc Student
Anna Caroline Marques dos Anjos Braga	Master	PhD Student
Bruno Miguel Gil Rosa	Graduate	PhD Student (left September)
Cristiano Torres Tavares dos Santos	Master	Investigator
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 Casanova	Graduate	MSc Student
Isabel Conceição	MD	Investigator
Isabel Maria Teixeira Máxima Graça	Undergraduate	Administrative
João Nuno Marques Parracho Guerra da Costa	MD/PhD	Investigator, Assistant Professor
José Pedro Almeida	Graduate	PhD Student
José Castro	Graduate	Investigator
Leonel Almeida Luis	MD	PhD Student
Maria do Amparo Barros	Graduate	Technician
Maria Isabel de Sousa Rocha	PhD	Principal Investigator
Mariana Santos Bento	MD	Investigator
Mario Joao Martins Oliveira	MD/PhD	Investigator, Assistant Professor
Marisa Brum	MD	MSc Student
Michael Swash	MD/PhD	Investigator, Invited Full Professor
Nataniel João Gonçalves Cleto Rosa	Master	PhD student
Nuno Miguel Prata Gomes	Master	MSc Student
Pedro Jorge Filipe Pereira	Master	PhD Student
Pedro Miguel Tojais Rodrigues Alves	Graduate	PhD student
Raquel de Sá da Silva Laires Rua	Graduate	Technician
Rita Alexandra Figueira Belo	Graduate	MSc Student
Sofia Batalha Reis de Almeida Santos	Graduate	MSc Student
Sofia Xavier	Graduate	MSc Student
Susana Cristina Da Costa Pinto	MD/PhD	Investigator, Assistant Professor
Tiago Maia	PhD	Principal Investigator
Victor César Ferreira de Moura Gonçalves	MD/PhD	Investigator, Assistant Professor

### Keywords / Research Areas

Amyotrophic lateral sclerosis (ALS), Autonomic Nervous System, Neurophysiology, Neuroimaging computational models, Tourette syndrome.



### Major scientific achievements

Autonomic nervous system (ANS): we have detailed the mechanisms of paroxysmic atrial fibrillation and its interplay with ANS dysfunction; novel methods for investigating heart rate variability were developed; the role of sweat tests, laser evoked potentials and sympathetic skin response to detect early changes in familial amyloid polyneuropathy were described.

Neurophysiology: fasciculation potentials were set as a very early marker of motor neuron dysfunction in ALS.

Neuroimaging computational models: Unknown alterations of frontosatrial circuits and amygdalar activation in psychopathology, including in Tourette's syndrome and in attention-deficit/hyperactivity disorder (ADHD) were reported.

Amyotrophic lateral sclerosis (ALS): the impact of non-invasive ventilation and exercise on survival and disease progression was studied, in addition advanced telemetry methods were implemented to control home-ventilation; the influence of ventilation-exercise on VEGF expression were explored.

### Recent Most Relevant Publications

Turner MR, Hardiman O, Benatar M, Brooks BR, Chio A, de Carvalho M, Ince PG, Lin C, Miller RG, Mitsumoto H, Nicholson G, Ravits J, Shaw PJ, Swash M, Talbot K, Traynor BJ, Van den Berg LH, Veldink JH, Vucic S, Kiernan MC (2013) Controversies and priorities in amyotrophic lateral sclerosis research. *Lancet Neurol* **12**, 310-322. (Journal IF: 23.917, Citations: 34).

Posner J, Marsh R, Maia TV, Peterson BS, Gruber A, Simpson HB (in press) Reduced functional connectivity within the limbic cortico-striato-thalamo-cortical loop in unmedicated adults with obsessive-compulsive disorder. *Human Brain Mapping*. *Human Brain Mapping* DOI: 10.1002/hbm.22371 (Journal IF: 6.878, Citations: 1).

Coelho T, Maia LF, da Silva AM, Cruz MW, Planté-Bordeneuve V, Suhr OB, Conceição I, Schmidt HH, Trigo P, Kelly JW, Labaudinière R, Chan J, Packman J, Grogan DR (2013) Long-term effects of tafamidis for the treatment of transthyretin familial amyloid polyneuropathy. *Neurology* **260**, 2802-14. (Journal IF: 8.250, Citations: 3)

de Carvalho M, Swash M (2013) Origin of fasciculations in ALS and benign fasciculation syndrome. *JAMA Neuro*, **70**(12), 1562-1565. (Journal IF: 6.310., Citations: 1)

Couch Y, Anthony, DC, Dolgov O, Revischin A, Festoff B, Santos AI, Steinbusch HW, Strekalova T (2013) Microglial activation, increased TNF and SERT expression in the prefrontal cortex define stress-altered behavior in mice susceptible to anhedonia. *Brain Behav Immun* **29**, 136-46. (Journal IF: 5.612, Citations: 10)

### Ongoing Research Projects

2010/2013 On the role of VIP receptors in hippocampal dependent cognition and synaptic plasticity: evaluation of the therapeutic potential of VPAC1 receptor antagonists to ameliorate the cognitive deficits in TLE'. Coordinator: Diana Lina Jerónimo da Cunha Reis. Agency: FCT. Amount: €120.000,00

2012/2015 Early Markers in Familial Amyloid Polyneuropathy. Coordinator: Isabel Conceição and Mamede de Carvalho. Coordinator: Mamede de Carvalho. Agency: FCT. Amount: €60.000,00

2012/2013 Threshold tracking in FAP patients. Coordinator: Mamede de Carvalho. Agency: Laboratórios Pfizer, Lda. Amount: €1.350,00

2010/2013 Construção de um Pacemaker Diafragmático a ser testado em rato com vista a ser aplicado no ser humano com insuficiência respiratória. Coordinator: Isabel Rocha Amount: €147.456,00

2012/2015 Sampling and Biomarker Optimization and Harmonization in ALS and other Motor Neuron Diseases (SOPHIA). Coordinator: Mamede Carvalho. Amount: €60.000

2013/2014 Reinforcement learning and motor biases in children with Tourette syndrome. Coordinator: Tiago Vaz Maia. Amount: \$75.000,00

2010/2013 Genetic modification of the paraventricular nucleus of the hypothalamus (PVN) and rostroventrolateral medulla (RVLM) cells to control hypertension chronically' (PTDC/SAU-OSM/109081/2008). Coordinator: Diana Cunha Reis. Coordinator Institution: IMM/FMUL. Coordinator PI: Isabel Rocha.

2013/2016 RSE FISIO – necessidades, requisitos e barreiras de adoção de registo de saúde electrónico em fisioterapia. Coordinator: Gabriela Postolache. Coordinator Institution: RSE FISIO.

2011/2013 Doenças neuromusculares. Coordinator: Mamede de Carvalho. Agency: Linde Portugal. Amount: €6.000,00

2012/2014 Early disease markers in early symptomatic carriers of TTR V30M mutation. Coordinator: Mamede de Carvalho. Agency: Laboratórios Pfizer. Amount: €40.000,00

2011/2014 NEUROCLINOMICS - Compreendendo as doenças neurodegenerativas através da integração de dados clínicos e genómicos. Coordinator: Mamede de Carvalho and Alexandre Mendonça. Coordinator PI: Sara Madeira. Agency: FCT. Amount: €39.067,00 Total amount: €130.472,00

2013/2014 TSA Research Award Program - Reinforcement learning and motor biases in children with Tourette Syndrome. Coordinator: Tiago Maia. Agency: Tourette Syndrome Association, Inc. Amount: \$75.000,00

2010/2013 Genetic modification of the paraventricular nucleus of the hypothalamus (PVN) and rostromedial medulla (RVL) cells to control hypertension chronically. Coordinator: Maria Isabel Rocha. Agency: FCT. Amount: €126.034,00

2010/2013 Construction of a Diaphragmatic Pacing system to be tested on rat with future development for human with insufficient respiration. Coordinator: Maria Isabel Rocha. Agency: FCT. Amount: €147.456,00

2011/2013 Autoregulation in acute stroke. Coordinator: Maria Isabel Rocha. Invited institution: Faculdade de Medicina da Universidade do Porto. Agency: FCT. Amount: €54.982,00 Total amount: €140.000,00

2010/2013 On the role of VIP receptors in hippocampal dependent cognition and synaptic plasticity: evaluation of the therapeutic potential of VPAC1 receptor antagonists to ameliorate the cognitive deficits in TLE. Coordinator: Diana Reis. Agency: FCT. Amount: €120.000,00

2013 Apoio reunião. Coordinator: Mamede de Carvalho. Agency: Angelini. Amount: €650,00

### Other Projects

2010/2013 Mechanical control of respiration in a rat model of respiratory failure- development of a rat diaphragmatic pacemaker. Coordinator: Isabel Rocha.

2011/2013 Autorregulation in acute stroke. Coordinator: Isabel Rocha.

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: Isabel Rocha.

2011/2014 Understanding Neurodegenerative Diseases Through Clinical and OMICS data Integration- Neuroclinomics. Coordinator: Sara Madeira collaboration with Mamede de Carvalho PI: Coordinator: Sara Madeira. (PTDC/EIA-EIA/111239/2009) Amount: €130.572,00

2010/2013 Wi-CardioResp, Sistema Integrado para Monitorização em Ambulatório de Parâmetros Cardio-Respiratórios. Coordinator: Hugo Gamboa. Consultants: Mamede de Carvalho & Anabela Pinto.

2008/2018 Transthyretin-associated amyloidosis outcomes survey (THAOS). A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidosis (Fold Rx Pharmaceuticals, Inc.). Coordinator: Isabel Conceição.

2013/2015. Fx1A303. Open Label Safety and Efficacy Evaluation of Fx?1006A in Patients with Transthyretin Amyloidosis. (Pfizer/FoldRx Pharmaceuticals, Inc.). Coordinator: Isabel Conceição.

### Publications in peer review Journals

Guarino MP, Santos AI, Mota-Carmo M, Costa PF (2013) Effects of anaesthesia on insulin sensitivity and metabolic parameters in Wistar rats. *In Vivo* **27**, 127-32. (Journal IF: 1.264, Citations: 2)

Dombrowski, PA, Maia TV, Boschen SL, Bortolanza M, Wendler E, Schwarting RKW, Brandão ML, Winn P, Blaha CD, Da Cunha C (2013) Evidence that conditioned avoidance responses are reinforced by positive prediction errors signaled by striatal dopamine. *Behavioural Brain Research* **241**, 112-19. (Journal IF: 3.327, Citations: 6)

Luis L, Costa J, Vaz Garcia F, Valls-Solé J, Brandt T, Schneider E (2013) Spontaneous Plugging of the Horizontal Semicircular Canal With Reversible Canal Dysfunction and Recovery of Vestibular Evoked Myogenic Potentials. *Otol Neurotol* **34**, 743-7. (Journal IF: 2.014, Citations: 3)

Conceição I, Costa J, Castro J, de Carvalho M (2013) Neurophysiological techniques to detect early small-fiber dysfunction in transthyretin amyloid polyneuropathy. *Muscle Nerve* doi:10.1002/mus.23901. (Journal IF: 2.314)

Nzwalo H, Conceição I, Pereira P, Santos R, Evangelista T (2013) A Family with 2 Different Hereditary Diseases Leading to Early Cardiac Involvement. *J Clin Neuromuscul Dis* **14**, 204-8. (Journal IF: 0,00, Citations: 0)

Teodoro T, Neutel D, Lobo P, Geraldo A, Conceição I, Rosa MM, Albuquerque L, Ferreira J.J.. Recovery after copper-deficiency myeloneuropathy in Wilson's disease (2013) *J Neurol* **260**, 1917-8. (Journal IF: 3.578)

Coutinho MC, Cortez-Dias N, Cantinho G, Conceição I, Oliveira A, Bordalo e Sá A, Gonçalves S, Almeida AG, de Carvalho M, Diogo AN (2013) Reduced myocardial 123-iodine metaiodobenzylguanidine uptake: a prognostic marker in familial amyloid polyneuropathy. *Circ Cardiovasc Imaging* **6**, 627-36. (Journal IF: 5.941, Citations: 1)

Pinto S, Swash M, de Carvalho M. Does surgery accelerate progression of amyotrophic lateral sclerosis? *J Neurol Neurosurg Psychiatry*. doi:10.1136/jnnp-2013-305770 (Journal IF: 4.924, Citations: 1)

Carilho R, de Carvalho M, Swash M, Pinto S, Pinto A, Costa J. Vascular Endothelial Growth Factor and Amyotrophic Lateral Sclerosis: the interplay with exercise and non-invasive ventilation. *Muscle Nerve* (Journal IF: 2.367)

Lobo PP, Pinto S, Rocha L, Reimão S, de Carvalho M (2013). Oro-facial apraxia in motor neuron disease. *Case Reports in Neurology* **5**, 47-51. (Journal IF: 0,00, Citations: 0)

Ingre C, Pinto S, Birve A, Press R, Danielsson O, de Carvalho M, Gudmundsson G, Andersen PM (2013) No association between VAPB mutations and familial or sporadic ALS in Sweden, Portugal and Iceland. *Amyotr Lat Scler Frontotemporal Degener* **14**, 620-7. (Journal IF: 2.369, Citations: 1)

Pinto S, de Carvalho M (2013) Dropped head presentation in ALS. *Amyotr Lat Scler Frontotemporal Degener* **14**, 235 (Journal IF: 2.369)

Pinto S, de Carvalho M (2013) Can inspiratory muscle training increase survival in early-affected Amyotrophic Lateral Sclerosis patients? *Amyotr Lat Scler Frontotemporal Degener* **14**, 124-6 (Journal IF: 2.369)

Almeida V, de Carvalho M, Scotto M, Pinto P, Pinto A, Ohana B, Swash M (2013) Primary lateral sclerosis: predicting functional outcome. *Amyotr Lat Scler Frontotemporal Degener* **14**, 141-5. (Journal IF: 2.369)

Postolache G, Postolache O, Girão PS (2013) Methods for unobtrusive measurement of indoor air effects on the cardio-respiratory function. *Environmental Engineering and Management Journal* **12**, 1967-81. (Journal IF: 0.970, Citations:0)

Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L (2013) Myogenic oscillations in rabbit ocular vasculature are very low frequency. *Ophthalmic Res* **50**, 123-8. (Journal IF: 0,00, Citations: 0)

Lamberts RJ, Laranjo S, Kalitzin SN, Velis DN, Rocha I, Sander JW, Thijs RD (2013) Postictal generalized EEG suppression is not associated with periictal cardiac autonomic instability in people with convulsive seizures. *Epilepsia* **54**, 523-9. (Journal IF: 3.909, Citations: 6)

Londral A, Silva H, Nunes N, de Carvalho M, Azevedo L (2013) A wireless user-computer interface to explore various sources of biosignals and visual biofeedback for severe motor impairment. *Journal of Accessibility and Design for All (JACCESS)* **3**, 110-26. (Journal IF: 3.909, Citations: 6)

Chester C, de Carvalho M, Miltenberger G, Pereira S, Dillen L, van der Zee J, Broeckhoven CV, de Mendonça A (2013) Rapidly progressive frontotemporal dementia and bulbar amyotrophic lateral sclerosis in Portuguese patients with C9orf72 mutation. *Amyotr Lat Scler Frontotemporal Degener* **14**, 70-2. (Journal IF: 2.369)

de Carvalho M (2013) Split-had to diagnosis shot. *Clin Neurophysiol* (editorial) **124**, 219-20. (Journal IF: 3.144)

de Carvalho M, Swash M (2013) Fasciculation potentials and earliest changes in motor unit physiology in ALS. *J Neurol Neurosurg Psychiatry* **84**, 963-8. (Journal IF: 4.924, Citations: 11)

de Carvalho M (2013) Nerve excitability and fasciculations. *Clin Neurophysiol* (editorial) **124**, 1925. (Journal IF: 3.144)

#### Other publications International

Lip GYH, Laroche C, Dan G-A, Santini M, Kalarus Z, Rasmussen LH, Oliveira MM, Mairesse G, Crijns H, Simantirakis E, Atar D, Kirchhof P, Vardas P, Tavazzi L, Maggioni AP (2013) A prospective

survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of Euro Observational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *EP Europace*. (Journal IF: 2.765)

Oliveira MM, Fernandes M, Primo J, Reis H, Nicola P. Remote monitoring versus conventional follow-up for implantable cardiac devices: Rationale and design of the PORTLink (PORTuguese Research on Telemonitoring with CareLink) trial. *Rev Port Cardiol*. (Journal IF: 0.599)

Oliveira MM, Cunha PS, Silva N (2013) Remote monitoring for follow-up of patients with implantable cardiac devices. *Rev Port Cardiol* **32**, 185-90. (Journal IF: 0.599)

Piçarra BC, Cunha PS, Oliveira MM, Valente, Silva MN, Santos S, Ferreira (2013) Syncope and intermittent Brugada ECG pattern. *Rev Port Cardiol* **32**, 411-4. (Journal IF: 0.599)

de Carvalho M, Pinto S (2013) Patologia neuromuscular e distúrbios do sono. in Paiva T, Andersen ML, Tufik S. *O Sono e a Medicina do Sono*. Ed Manole 486-498.(Book Chapter)

Santos M. (2013) Alterações disautonómicas em Doença de Parkinson, Manuel Prático.2013;176-184. Ed Lidel. (Book Chapter)

### Invited lectures and seminars

#### Tiago Maia

- Reinforcement Learning in Avoidance, Habits, and Tics, Institut d'Investigacions Biomediques August Pi i Sunyer, University of Barcelona, Spain, December 19, 2013;
- The Role of Norepinephrine in Inhibitory Control and Attention-Deficit/Hyperactivity Disorder, Inaugural Alumnus Colloquium, Department of Psychology, Carnegie Mellon University, Pittsburgh, PA, USA, October 28, 2013;
- Norepinephrine and ADHD: Neurocomputation, Brain, and Behavior, Computational Psychiatry 2013, Miami, FL, USA, October 23, 2013;
- Noradrenergic Disturbances and Attention-Deficit/Hyperactivity Disorder, Symposium on Computational Psychopharmacology, British Association for Psychopharmacology Summer Meeting, Harrogate, UK, July 30, 2013;
- Reinforcement Learning in Avoidance, Habits, and Tics, XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal, May 31, 2013;
- Reinforcement Learning in Avoidance, Habits, and Tics, Fundação Champalimaud, Lisbon, Portugal, May 21, 2013;
- Integrated Neuroimaging and Neurocomputational Approaches to Cognition and Psychiatric Disorders, Instituto de Biofísica e Engenharia Biomédica, Lisbon, Portugal, April 26, 2013;
- Reinforcement Learning in Avoidance, Habits, and Tics, Guest Lecture Series, Bernstein Computational Neuroscience Center (BCCN) Berlin, Germany, April 16, 2013;
- The Role of Dopamine in Avoidance Learning, 11th International Basal Ganglia Society Meeting, Eilat, Israel, March 5, 2013.

**Leonel Luís**

- vHIT as a Diagnostic Tool, International Masterclass, American Balance Society, Scottsdale, EUA (international guest), March 6-7, 2013;
- Central or Peripheral Vertigo? New Insights from Video Head Impulse Test, 10th Annual Middle East Update in Otolaryngology Conference, Dubai. April 21-23, 2013;
- BPPV Diagnosis and Treatment – Current concepts, 10th Annual Middle East Update in Otolaryngology Conference, Dubai, April 21-23, 2013;
- Meniere’s disease: A controversial diagnosis of exclusion, 10th Annual Middle East Update in Otolaryngology Conference, Dubai, April 21-23, 2013;
- Benign Positional Vertigo, 10th Annual Middle East Update in Otolaryngology Conference, Dubai, April 21-23, 2013;
- Vestibular Evaluation Update, 10th Annual Middle East Update in Otolaryngology Conference, Dubai, April 21-23, 2013;
- Diagnostic Approach to Vertigo and Dizziness in Children, 10th Annual Middle East Update in Otolaryngology Conference, Dubai, April 21-23, 2013;
- Electrophysiology course (vHIT, VNG and VEMP module), University of Barcelona, Barcelona, Spain May, 2013;
- Video Head Impulse Test, Masterclass, Iberia Otoneurology Congress, Madrid, Spain, May, 2013;
- Video Head Impulse Test, Instruction course, Portuguese National ENT Congress, Porto, Portugal, May 15, 2013;
- Vertigo and Dizziness Course, Guanzhou, China., May, 2013;
- New Technologies in Vestibular Testing, IFOS-world ENT conference, Seoul, June, 2013
- vHIT in Spinocerebellar Ataxias, European Neurology Society meeting, Barcelona, Spain, June 8-9, 2013;
- Acute Vestibular Syndrome, Masterclass, National ENT conference, Romania. June 28, 2013;
- Diagnóstico Clínico del Balance y Vértigo y su Rehabilitación, Curso de actualización, Santiago, Chile. September 2-4, 2013;
- vHIT, American Academy of Otolaryngology-Head and Neck surgery., Canada, Vancouver, September 29 - October 2, 2013;
- Video Head Impulse test como instrumento de exploración vestibular, Congresso nacional SEORL, Madrid, Spain, October 26-28, 2013;
- Topodiagnostico en Síndrome vestibular agudo, Congresso nacional SEORL, Madrid, Spain, October 26-28, 2013.

**Mariana Santos**

- Abordagem do doente diabético com disautonomia – Introdução e diagnóstico, III Jornadas de Diabetes do Hospital de Santarém, Portugal, May 10, de 2013.

**Isabel Conceição**

- Diagnosis of polyneuropathies and related symptoms, ARIA II SYMPOSIUM: advances and research in TTR - improving diagnosis, improving outcomes -, Barcelona, Spain, February 1-2, 2013;
- Early diagnosis of TTR-FAP, ARIA III SYMPOSIUM: advances and research in TTR –, 2013 Berlin, Germany, February 3-4, 2013;

- Polineuropatia Amiloidotica Familiar: aspectos clínicos, XVII Jornadas Nacionais Patient Care. Symposium Pfizer – Lisbon, Portugal, February 21-22, 2013
- HRQoL. Health related quality of life in patients in the transthyretin amyloidosis outcomes survey (THAOS), THAOS Investigator Meeting Prague. Check Republic, April 20-21, 2013;
- FAP - Neurological manifestations and evaluations. European Advanced Postgraduate Course on Transthyretin Associated Amyloidosis- Porto, Portugal ;
- Early Markers of the Disease. The Ideal Moment to Treat, Neurological Markers . ISFAP 2013, Rio de Janeiro, Brasil, November 10-14, de 2013,
- Abordagem do doente neuromuscular em idade adulta: Polineuropatias, Curso de Doenças Neuromusculares –Aveiro, Portugal, 2013;
- FAP - Neurological manifestations and evaluations, European Advanced Postgraduate Course on Transthyretin Associated Amyloidosis – 13-17 May 2013. Porto. Portugal;
- Early Markers of the Disease. The Ideal Moment to Treat, Neurological Markers- ISFAP 2013, November 10 -14, 2013, Rio de Janeiro. Brazil;
- Potenciais Evocados e Monitorização Intra-Operatória. Curso de Neurofisiologia Clínica: Electromiografia e Potenciais Evocados. Forum de Neurologia 2013, May 9-11, Hotel Vila Galé, Coimbra, Portugal.

#### **Susana Pinto**

- Avaliação funcional respiratória na doença do neurónio motor – parâmetros a monitorizar, Reunião de Primavera da SPEDNM, Monte Real, April, 2013

#### **Gabriela Postalache**

- (palestra) Pedro Silva Girão; Gabriela Postolache. Registo de Saúde Electrónico em Portugal, 1st Workshop RSE FISIO, Lisboa, ISCTE-IUL, Portugal;
- (apresentação de trabalho na sessão poster) Sónia Barcia, Lia Jacobsohn, Claudia Maia Moura, Raul Oliveira, Gabriela Postolache. Revolução Digital em Fisioterapia, Conferencia Hospital Cuf Saúde Mobile Health, Centro de Congressos de Estoril, Portugal, January , 2013;
- (palestra) Gabriela Postolache, Pedro Silva Girão - Requisitos e barreiras para adopção do Registo de Saúde Electrónico, Seminário 'Comunidade como Cliente de Enfermagem' Escola Superior de Saúde Ribeiro Sanches, Lisbon, Portugal, January, 2013.
- (palestra) Gabriela Postolache, Pedro Silva Girão. Registo de Saúde Electrónico. Como? Porque? Seminário a 'Multidimensionalidade da Comunicação', Escola Superior de Saúde Ribeiro Sanches, Lisbon, Portugal, January, 2013.

#### **Mamede de Carvalho**

- Electrophysiological Monitoring of the Disease Courses in ALS, 57th Annual Congress of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN) – Leipzig, 3-5 March, 2013;
- Doença do Neurónio Motor: esclerose lateral amiotrófica e amiotrofia muscular espinhal, Fórum de Neurologia – Coimbra, Portugal, 3 May, 2013;
- Electrophysiological Study of Peripheral Neuropathy, 5TH Asian and Oceanian Congress of Clinical Neurophysiology –Bali, August, .2013;



- Fasciculation Potentials: benign observation versus a marker of ALS. Monitoring Disease Progression, 5TH Asian and Oceanian Congress of Clinical Neurophysiology – Bali, August, 2013;
- Polineuropatias Desmielinizantes Crónicas Autoimunes, V Congresso de Neuromusculares –Aveiro, Portugal, September 2013;
- Complicações Neurológicas na Gravidez: doenças neuromusculares, Congresso de Neurologia. Lisbon, Portugal, October, 2013

#### **Isabel Rocha**

- Autonomic Activity in Heart Failure, Sorin HF Board - Amsterdam.2013

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

Pinto S, Swash M, de Carvalho M. Surgical interventions aggravate progression of Amyotrophic Lateral Sclerosis. 11th annual congress of the European network for the cure of ALS (ENCALS), Birmingham, UK, June 2013 (Poster presentation)

Jorge S. de Carvalho M, Batista J, Gomes A, Carilho R, Pinto S, Pinto A, Costa J. Protein Glycosylation in Amyotrophic Lateral Sclerosis. 11th annual congress of the European network for the cure of ALS (ENCALS), Birmingham, UK, June 2013 (Poster presentation)

Luís L. Anticompensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmu. 9th Meeting of the British Society of Neuro-otology, London, UK (Oral communication), 11 October 2013

Amaro-Leal A, Rocha I, Cunha-Reis D. Preventing epileptogenesis, cognitive decline and sudden death in a rat model of TLE: training in novelty exploration tasks. VII PhD Students Meeting CAML, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Amaro-Leal A., Rocha I., Cunha-Reis D. Cognitive impact of repeated exposure to novel spatial arrangement of objects. SPE: 10º Congresso Nacional de Etiologia, Centro Champalimaud, October 24-25, 2013. Lisboa, Portugal.(Poster presentation)

Amaro-Leal A, Carmo AJS, Rocha I, Cunha-Reis D. Repeated exposure to novel spatial arrangement of objects: impact on hippocampal-dependent learning and synaptic plasticity. Communication PCD118 to the XXXVII International Congress of Physiological Sciences – IUPS 2013, Birmingham, UK, July 21-26, 2013. (Oral communication)

Cunha-Reis D. Contribution of endogenous VIP VPAC1 receptor activation during hypoxia and interictal-like activity induced in vitro by 0-Mg<sup>2+</sup> to subsequent changes in LTP expression in the rat hippocampus. Communication PCB102 to the XXXVII International Congress of Physiological Sciences – IUPS 2013, Birmingham, UK, July 21-26, 2013. (Oral communication)

Isabel Conceição, Ana Franco, João Ferreira, Vanda Freitas, Carla Bentes. Central nervous system manifestations in long survival FAP TTR V30M patients. ISFAP 2013, Rio de Janeiro, Brazil, November 10–14, 2013. (Oral communication)

Andrés Diaz, José Castro, Isabel Conceição. Detection of early abnormalities in Familial Amyloidotic Polyneuropathy by quantitative sensory testing. ISFAP 2013, Rio de Janeiro, Brazil, November 10–14, 2013. (Oral communication)

Isabel Conceição, Pedro Pereira, José Castro. Transthyretin familial amyloid polyneuropathy – disease progression over 12 months on Tafamidis: the Lisbon center experience. ISFAP 2013, Rio de Janeiro, Brazil, November 10–14, 2013. (Oral communication)

Jose Alvir, Isabel Conceicao, Mat Maurer, Michelle Stewart. TTR Phenotypes Using Patient Reported Symptoms: A Latent Class Analysis-. THAOS Investigator Meeting, Prague, Czech Republic, April 20-21, 2103 (Oral communication).

Santos S, Oliveira M, Laranjo S, Tavares C, Oliveira E, Alves S, Rocha I, Ferreira R. Autonomic and haemodynamic changes associated to tilt training response in recurrent reflex syncope. ECAS, Paris, France, April 2013. (Oral communication)

Santos S, Oliveira M, Laranjo S, Tavares C, Rocha I, Ferreira R. Baroreflex effectiveness index and improvement in symptoms after tilt training in patients with recurrent syncope ECAS, Paris, France, April 2013. (Oral communication)

Laranjo S, Tavares C, Gomes J, Oliveira M, Silva S, Santos E, Ferreira R, Rocha I. Independent role of reduced arterial baroreflex sensitivity in predicting reflex syncope during head-up tilt. ECAS, Paris, France, April 2013. (Oral communication)

Gonçalves-Rosa N, Geraldes V, Laires R, Lopes-Gonçalves R, Paton JFR, Rocha I. Decreased rostroventrolateral medulla neurons excitability maintains normotensive values of blood pressure in spontaneously hypertensive rats. 37th Congress of the International Union of Physiological Sciences, Birmingham, UK, July 2013. (Poster presentation)

Geraldes V, Gonçalves-Rosa N, Laires R, Lopes-Gonçalves R, Paton JFR, Rocha I. Chronic suppression of paraventricular nucleus of the hypothalamus neuronal activity produces sustained hypotension in spontaneously hypertensive rats 37th Congress of the International Union of Physiological Sciences, Birmingham UK, July 2013. (Poster presentation)

Amaro-Leal A, Carmo AJ, Rocha I, Cunha-Reis D. Repeated exposure to novel spatial arrangements of objects: impact on hippocampal-dependent learning and synaptic plasticity. 37th Congress of the International Union of Physiological Sciences, Birmingham, UK, July 2013. (Poster presentation)

S. Laranjo, C. Tavares, J. Gomes, E. Oliveira, S. Silva, M.M. Oliveira, R.C. Ferreira, I. Rocha "The role of reduced arterial baroreflex sensitivity in predicting reflex syncope during head-up tilt testing", EHRA, European Heart Rhythm Association, Athens, Greece, Jun 23-26, 2013. (Oral communication)

Campos AD, Conceição I, Castro J, de Carvalho M. Uso del Test de Cuantificación Sensitiva para el Estudio de la Neuropatía de Fibra Pequeña de Origen Genético. XI Congreso Colombiano de Neurología, Cartagena, Colombia, August 2013. (Poster presentation)

Campos AD, Casanova I, Brum M, de Carvalho M. Resultados del Estudio de Excitabilidad Axonal en una Poblacion Control por la Tecnica de Threshold Tracking. XI Congreso Colombiano de Neurologia. Cartagena, Colombia, August 2013. (Poster presentation)

Geraldo AF, Pereira J, Nunes P, Reimão S, Sousa R, Castelo-Branco M, Pinto S, Campos JG, de Carvalho M. Beyond Fractional Anisotropy: the value of axial diffusivity and radial diffusivity and its correlation with neurophysiological changes in ALS patients. II Reunião Ibérica de Neuroradiologia. Lisbon, Portugal, October 2013. (Oral communication)

de Carvalho M, Swash M. Origin of Fasciculations in ALS and Benign Fasciculation Syndrome. 24th INTERNATIONAL SYMPOSIUM on ALS/MND. Milan, Italy, December 2013. (Poster presentation)

Pinto A, Braga AC, Almeida JP, de Carvalho M. Can NIV Parameters Settings and Changes Overtime Predict Functional and Survival Outcome in ALS Patients? 24<sup>th</sup> International Symposium on ALS/MND, Milan, Italy, December 2013. (Oral communication)

Luis L, Costa J, Munoz E, Lehnen N, de Carvalho M, Valls-Sole J. Rapid Eye-Movements Triggered During Head Impulses Differentiate Peripheral and Central Patients with Spontaneous Nystagmus. 23<sup>rd</sup> Meeting of the European Neurological Society. Barcelona, Spain, June 2013. (Oral communication)

### **Communications in National Conferences**

Pedro Pereira, José Castro, Isabel Conceição. FAPS: uma nova escala para a Polineuropatia Amilóide Familiar? Sociedade Portuguesa Estudo das Doenças Neuromusculares, 12 September 2013 (Oral communication)

Marisa Brum; Andrés Diaz; José Castro; Ana Rita Silvestre; Teresinha Evangelista; Isabel Conceição. Sociedade Portuguesa Estudo das Doenças Neuromusculares, 12 September 2013 (Oral communication)

Castro J, Costa J, Pinto S, de Carvalho M. Avaliação da progressão de doentes com ELA através de uma técnica de estimativa do número de unidade motoras – MUNIX. Congresso da SPDNM Aveiro, Portugal, 2013 (Oral communication);

Pinto S, Swash M, de Carvalho M. Cirurgia na Esclerose lateral Amiotrófica – o risco de progressão clínica. Congresso de Neurologia 2013, Repercussões Neurológicas das Doenças Sistémicas. Lisbon, Portugal, 2013 (Oral communication)

Victor Gonçalves. Cavernous Malformation Of The Optical Nerve As Cause Of Migraine: Operative Removal And Result. International Microneurosurgical Meeting, Faculdade de Medicina -Hospital de S. João, Oporto, Portugal, April 2013. (Oral communication)

Victor Gonçalves. Facial Reanimation With Nerve Anastomosis Without Tongue Atrophy After Removal Of A Cerebellar Pontine Angle Arteriovenous Malformation. International Microneurosurgical Meeting, Faculdade de Medicina -Hospital de S. João, Oporto, April 2013.

(Oral communication)

Castro J, Costa J, Pinto S, de Carvalho M. Avaliação da progressão de doentes com ELA através de uma técnica de estimativa do número de unidade motoras – MUNIX. Congresso da SPDNM Aveiro, Portugal, 2013. (Oral communication)

Pinto S, Swash M, de Carvalho M. Cirurgia na Esclerose lateral Amiotrófica – o risco de progressão clínica. Congresso de Neurologia 2013, Repercussões Neurológicas das Doenças Sistémicas. Lisbon, Portugal, November, 6-9, 2013. (Oral communication)

Oliveira M, Carvalho M, Laranjo S, Rocha I, ARRITMIAS, Cascais, Portugal, February 2013. (Oral communication)

Viana, P; Castro-Caldas, A; Moldovan, O; de Carvalho, M; Geraldes, R. Miotonia Congénita Autossómica Recessiva: dificuldade diagnósticas e terapêuticas. V CONGRESSO de NEUROMUSCULARES. Aveiro, Portugal, October 2013. (Oral communication)

Pereira P, de Carvalho M. Parésia Flácida e Aguda do Membro Superior, por Grave Lesão Axonal: podemos prever o prognóstico? V Congresso de Neuromusculares. Aveiro, Portugal, October 2013. (Oral communication)

Pereira, P; de Carvalho, M. Adalimumab: um novo mundo de complicações para a patologia neuromuscular V Congresso de Neuromusculares. Aveiro, Portugal, October 2013. (Poster presentation)

Ohana, B; Cordeiro, C; de Carvalho, M. Experiência com o uso de imunoglobulina-subcutânea nas neuropatias motoras desmielinizantes. V Congresso de Neuromusculares. Aveiro, Portugal, October 2013. (Poster presentation).

de Carvalho, M; Swash, M. Estudo sobre as Alterações Electromiográficas Precoces na Esclerose Lateral Amiotrófica. Congresso de Neurologia 2013. Lisbon, Portugal, November 2013. (Oral communication)

Luis, L; de Carvalho, M. Vestibular-ocular reflex dynamics with head-impulses discriminates hereditary cerebellar ataxias. Congresso de Neurologia 2013. Lisbon, Portugal, November 2013. (Oral communication)

### **Organisation of Conferences**

Member of the Steering Committee of ARIA II SYMPOSIUM: advances and research in TTR amyloidosis. Barcelona, Spain, February 1-2, 2013. (Dr. Isabel Conceição)

Member of the Scientific Board Committee of International Symposium on Familial Amyloid Polyneuropathy. ISFAP 2013, Rio de Janeiro, Brazil, November 10–14, 2013. (Dr. Isabel Conceição)

President and Member of the Scientific Board Committee V Congresso Nacional de Doenças

Neuromusculares, Aveiro, Portugal, October 25-27, 2013. (Dr. Isabel Conceição)

Member of International Programm Committee of NEURORECHNIX 2013 (International Congress on Neurotechnology, Electronics and Informatics). Vilamoura, Portugal, September 2013. (Mamede de Carvalho)

Member of International Advisory Committee do 5th Asian and Oceanian Congress of Clinical Neurophysiology. Bali, Indonesia, August 2013. (Mamede de Carvalho)

Co-chairman Session “Amyotrophie Lateralsklerose – aktueller Stand und Funktionsdiagnostik”, do Deutsche Gesellschaft fur Klinische Neurophysiologie und Funktionelle Bildgebung (DGKN) Leipzig, Germani, 2013. (Mamede de Carvalho)

Chairman da Sessão “Temas Neuromusculares” do Fórum de Neurologia 2013, Coimbra, Portugal, 2013. (Mamede de Carvalho)

Chairman do “Curso de Neurofisiologia Clínica” promovido pela Sociedade Portuguesa de Neurologia, Coimbra, Portugal, 2013. (Mamede de Carvalho)

Co-chairman Session “Nerve Conduction Study and EMG Workshop” do 5th Asian and Oceanian Congress of Clinical Neurophysiology, Bali, Indonesia, 2013. (Mamede de Carvalho)

Chairman da Sessão “Doenças Neuromusculares Autoimunes” do V Congresso de Neuromusculares, Aveiro, Portugal, 2013. (Mamede de Carvalho)

Co-chairman Session “Disease Progression” no 24th International Symposium on ALS/MND, Milan, Italy, 2013. (Mamede de Carvalho)

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

“Rising Star”, Association for Psychological Science, 2013 (Tiago Maia)

2º prémio apresentações livres Congresso da Sociedade Portuguesa de Otoneurologia (Leonel Luís)

### **Industry contract research**

Fx1A-303 - Open-Label Safety and Efficacy Evaluation of Fx-1006A in Patients with Transthyretin Amyloidosis. (Pfizer/FoldRx Pharmaceuticals, Inc.)- - (Dr. Isabel Conceição - Principal Investigator. Clinical Trial)

Transthyretin-associated amyloidoses outcomes survey (THAOS) A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidosis (Pfizer/FoldRx Pharmaceuticals, Inc.) – (Dr. Isabel Conceição Scientific Board Member)

A Phase 2, Open-Label, Multi-Dose, Dose Escalation Trial to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Intravenous Infusions of ALN-TTR02 in Patients with TTR Amyloidosis (Alynlam Pharmaceuticals) - (Dr. Isabel Conceição -Principal Investigator-Clinical Trial)

A Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of ISIS 420915 in Patients with Familial Amyloid Polyneuropathy. (ISIS Pharmaceuticals, Inc.) - (Dr. Isabel Conceição - Principal Investigator-Clinical Trial)

### **Science and society**

Member-at-Large da International Federation of Clinical Neurophysiology and Liaison-Member of IFCN to the European Chapter (Mamede de Carvalho)

President International Clinical Neurophysiology Society (Mamede de Carvalho)

### **PhD theses completed**

Susana Pinto (2013) “Estudos Clínicos e Neurofisiológicos para a Compreensão e a Reabilitação da Fraqueza e da Fadiga Respiratórias na Esclerose Lateral Amiotrófica. University of Lisbon, Lisbon, Portugal. Supervisor: Mamede de Carvalho.

### **Msc theses completed**

Adriana Soares (2013) Diagnóstico Patológico de Doenças Musculares em Idade Pediátrica. University of Lisbon, Lisbon, Portugal. Supervisor: Mamede de Carvalho.

## 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, Associate Professor, Faculdade de Medicina da Universidade de Lisboa.

### Research Team

Ana Cláudia Dourado Clemente	Graduate	MSc Student (started July)
Ana Luísa Ferro Espadanal Torres Magalhães	PhD	Post-doctoral Investigator
Ana Maria Matias de Barros	PhD	Post-doctoral Investigator
Ana Raquel Machado Duarte	Graduate	MSc Student (left September)
Andreia Cristina Martins Silva	Graduate	MSc Student (left September)
Celina Maria dos Reis Parreira	Graduate	MSc Student (left September)
Germana Andreia Taipa Leandro Domingues	Master	PhD Student
Inês Mendes Matias	Graduate	Technician
Inês Sofia Alvarez Martins	Graduate	PhD Student
Joana Cabrita Afonso	Master	PhD Student
Sandrina Nóbrega Pereira	PhD	Post-doctoral Investigator (started August)

### Keywords / Research Areas

Angiogenesis, Tumor spread, Metabolism.

### Major scientific achievements

2013 was our first Year at IMM. As major achievements, we would like to highlight the "Laço" Award for Breast Cancer Research (the first Grant to be awarded by Laço) and the publication of the following papers:

- Costa A, Afonso J, Osório C, Gomes AL, Caiado F, Valente J, Aguiar SI, Pinto F, Ramirez M, Dias S. miR-363-5p regulates endothelial cell properties and their communication with hematopoietic precursor cells. *J Hematol Oncol*. 2013 Nov 21;6(1):87 (2013)  
This paper exploited the role of microRNAs in the regulation of bone marrow endothelial cell properties.
- Caiado F, et al and Dias S. Bone marrow-derived CD11b+Jagged2+ cells promote epithelial to mesenchymal transition and metastization in colorectal cancer. *Cancer Research*, 73(14):4233-46 (2013)  
This paper identified a population of bone marrow derived cells (CD11b+jagged2+) that induces EMT in colorectal cancer, starting the metastatic process.

The Team also started fruitful collaborations with several Units at IMM.

### Recent Most Relevant Publications

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: 14)

Real C, Remedio L, Caiado F, Igreja C, Borges C, Trindade A, Pinto-do-Ó P, Hyagita H, Duarte A, Dias S. (2011) Bone marrow-derived Endothelial Progenitors expressing Delta-like 4 (Dll4) regulate tumor angiogenesis. *PlosOne* **6**(4), e18323. (Journal IF: 4.1, Citations: 19)

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: 24)

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: 76)

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: 8.65, Citations: 3)



### Ongoing Research Projects

2013/2014 Explorando a base molecular dos nichos vasculares aberrantes em mieloma múltiplo. Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: FCT. Amount: €43.804,75 Total Amount: € 160.000,00

2013/2014 Colesterol promove a angiogénese e a formação de metástases? Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: FCT. Amount: €44.602,72 Total amount: €166.720,00.

2013/2014 Bolsa Laço para o Cancro da Mama. Coordinator: Sérgio Jerónimo Rodrigues Dias. Agency: Laço Associação de Solidariedade Social. Amount: €25.000,00

### Publications in peer review Journals

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. *J Hematol Oncol*. 2013 Nov 21 **6**(1), 87 (Journal IF: 4.46, Citations: 0)

### Invited lectures and seminars

Sérgio Dias. "Metabolic selection of metastatic potential". Oncogenomics to Cancer Care International Conference. IMM, September 2013.

### Communications in International Conferences

Inês Matias, Haakan Norell, Bruno Silva-Santos and Sérgio Dias. "LDL-cholesterol favors leukemia Immune Evasion through modulation of genes associated with susceptibility and resistance to gamma delta T cells." Cell Symposia: "Immunometabolism: From Mechanisms to Therapy". Sheraton Hotel, Toronto, Canada, June 2013.

Inês Matias, Haakan Norell, Bruno Silva-Santos and Sérgio Dias. "LDL-cholesterol favors leukemia Immune Evasion through modulation of genes associated with susceptibility and resistance to gamma delta T cells." EMBO Young Scientist´ Forum. Instituto de Medicina Molecular, Lisbon, Portugal. 15-16 July 2013.

Ana de Barros, Inês Matias, Haakan Norell, Bruno Silva-Santos and Sérgio Dias. "LDL-cholesterol affects human Vg9Vd2 T cell activation and tumor cell killing" EMBO Young Scientists´ Forum. Instituto de Medicina Molecular, Lisbon, Portugal 15-16 July 2013.

Ana de Barros, Inês Matias, Haakan Norell, Bruno Silva-Santos and Sérgio Dias. "LDL-cholesterol affects human Vg9Vd2 T cell activation and tumor cell killing" Cell Symposia: "Immunometabolism: From Mechanisms to Therapy". Sheraton Hotel, Toronto, Canada June 2013.

Ana Magalhães, Inês Matias, Sérgio Dias. “How systemic cholesterol affects endothelial barrier function” EMBO Young Scientists´ Forum. Instituto de Medicina Molecular, Lisbon, Portugal. July 15-16, 2013.

Germana Domingues, Catarina Rodrigues dos Santos, Lénia Rodrigues, Jacinta Serpa, Sérgio Dias. "Vascular Heterogeneity in breast cancer". EMBO Young Scientists´ Forum, Instituto de Medicina Molecular, Lisbon, Portugal. 15-16 July 2013.

Ana Magalhães, Inês Matias, Sérgio Dias. “How does systemic cholesterol affect endothelial cell barrier function?” Beating the Blood-Brain & Other Blood Barriers. Lisbon 6th-8th, 2013

Delta-like 4 in the bone marrow vascular niche affects bone marrow recovery and function. Inês Alvarez-Martins, António Duarte, Sérgio Dias. Symposium: The Bone Marrow Niche, Stem Cells, and Leukemia: Impact of Drugs, Chemicals, and the Environment. New York Academy of Sciences, New York. May 29 - 31, 2013.

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

Laço Award for Breast Cancer Research.

#### **Advanced teaching**

Master Course in Development and Cancer: Master in Oncobiology. Instituto de Medicina Molecular – Faculdade de Medicina da Universidade de Lisboa, 2013.

Module on Hematology: MSc Course on Biological Sciences. Universidade do Algarve, May 2013.

Lecture on Angiogenesis and Metastasis. CNC PhD Program. Universidade de Coimbra, February 2013.

Lecture on Tumor Angiogenesis. Nova University Biomedical PhD Program. Faculdade de Ciências Médicas da Universidade de Lisboa, May 2013.

#### **Science and society**

Sergio Dias is Evaluator of National Grants and Fellowships for the Portuguese Foundation for Science and Technology (FCT) and has also served as evaluator of grants and fellowships for the European Commission.

#### **PhD theses completed**

Leonor Remédio (2013) Modulating the Bone marrow microenvironment: the role of DLL4:Notch signaling and hypoxia. Faculdade de Ciências Médicas da Universidade de Lisboa. Lisbon. Supervisor: Sérgio Dias.

**Msc theses completed**

Celina Parreira (2013) The role of miR21 in the bone marrow microenvironment. Faculdade de Ciências e Tecnologia da Universidade de Coimbra. Coimbra. Supervisor: Sérgio Dias.

Ana Raquel Duarte (2013) Study of the factors that regulate the expression of Jagged-2. Faculdade de Ciências da Universidade de Lisboa. Lisbon. Supervisor: Sérgio Dias.

**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 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, HSM, Associate Professor, Faculdade de Medicina da Universidade de Lisboa.

**Research Team**

Ana Cláudia Marques Salgueiro	Graduate	MSc Student (started September)
Ana Margarida Faisca do Carmo Pires de Noronha	Graduate	Administrative (left January)
Ana Marta Teixeira Anes	Master	Investigator
Ana Patrícia Silva Pita Lobo	Graduate	Investigator
Ana Rita Simões Cardoso	Graduate	MSc Student
Ana Teresa Martins Sousa Santos	Graduate	Manager
Anabela Ferreira Valadas		Investigator, MD
André Filipe da Silva Lopes Cardoso	Graduate	MSc Student (started September)
Catarina Afonso Godinho	PhD	Investigator, Assistant Professor (started September)
Claudio Virgilio Antunes David	Graduate	Investigator, MD
Cristina Sampaio	MD/PhD	Investigator

Daisy Andreína Vieira De Abreu	Graduate	Investigator
Daniel Gomes Caldeira	Graduate	Investigator
Ema Roque	Graduate	Administrative
Isabel Boaventura	Graduate	Investigator
João Costa	MD/PhD	Investigator, Assistant Professor
João Franco		Investigator
Josefa Domingos	Master	Investigator
Leonor Correia Guedes	Graduate	Investigator
Márcio Correia Barra	Graduate	MSc Student (started September)
Margarida Borges	Graduate	Investigator
Margherita Fabbri	Graduate	Investigator
Maria Dulce dos Santos Neutel	Graduate	Investigator
Maria Finisterra	Graduate	Administrative
Mário Miguel Coelho da Silva Rosa	MD/PhD	Investigator, MD, Associate Professor
Miguel Coelho	Graduate	Investigator
Nádia Espada	Graduate	Investigator
Nilza Karina Cabral Gonçalves	Graduate	Investigator (started October)
Ricardo Miguel Ribeiro Marques Cunha Fernandes	Graduate	Investigator, MD
Rita Cardoso	Graduate	Investigator
Sofia Cristina Pereira Coutinho Reimao	Graduate	Investigator
Tiago Mestre	Master	Investigator
Tiago Rodrigues Teodoro	Graduate	Investigator
Tiago Soares	Graduate	Investigator
Vanda Filipa Viseu Cândido Freitas Castro	Graduate	Investigator

### 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). In these first months 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.

The Lab also supported the process for the creation of The Clinical Research Centre of the Lisbon Medical Academic Centre (CIC-CAML). A Biostatistics and Methodological Sub-Unit was developed. Funding for the next 3 years was guaranteed with the success in three international research grants.

### Recent Most Relevant Publications

Vellas, B, Carrillo, MC,, Sampaio C, Brashear, HR, Siemers, E, Hampel, H, Schneider, LS, Weiner, M, Doody, R, Khachaturian, Z, Cedarbaum, J, Grundman, M, Broich, K, Giacobini, E, Dubois, B, Sperling, R, Wilcock, GK, Fox, N, Scheltens, P, Touchon, J, Hendrix, S, Andrieu, S, Aisen, P, EU US CTAD Task Force Members (2013) Designing drug trials for Alzheimer's disease: What we have learned from the release of the phase III antibody trials: A report from the EU/US/CTAD Task Force. *Alzheimers & Dementia* **4**, 438-444. (Journal IF: 14.483, Citations: 6)

Maetzler W, Domingos, J., Sruļijes K, Ferreira JJ, Bloem BR (2013) Quantitative wearable sensors for objective assessment of Parkinson's disease. *Movement Disorders* **12**, 1628-37. (Journal IF: 4.505, Citations: 0)

Ferreira JJ, Katzenschlager R, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Schuepbach M, Tolosa E, Trenkwalder C, Schapira A, Berardelli A, Oertel W H, (2013) Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management of Parkinson's disease. *European Journal of Neurology* **1**, 5 (Journal IF: 3.692, Citations: 2)

Caldeira D, Martins C, Alves LB, Pereira H, Ferreira JJ, Costa J (2013) Caffeine does not increase the risk of atrial fibrillation: a systematic review and meta-analysis of observational studies. *Heart* **9**, 1383-1389. (Journal IF: 5.014, Citations: 1)

Caldeira D, Fernandes R, David C, Costa J, Ferreira JJ (2013) Warfarin, acetylsalicylic acid and risk of incident atrial fibrillation in patients with heart failure and sinus rhythm: A meta-analysis.

*International Journal of Cardiology* **168**, 4842-4843. (Journal IF: 5.509, Citations: 0)

### 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.

2012/2014 FP7 funded project SENSE-PARK: Supporting and Empowering Parkinson patients in their home environment using a Novel Sensory information system that monitors daily life-relevant parameters of Parkinson disease and their change. Coordinator: Joaquim Ferreira. Coordinator Institution: Eberhard Karls Universitaet Tuebingen. Coordinator PI: Walter Maetzler.

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. Ammount: € 172.000,00

### Publications in peer review Journals

Neutel D, Biscoito L, Campos J, E Melo TP, Albuquerque L. Giant cell arteritis with symptomatic intracranial stenosis and endovascular treatment. *Neurol Sci.* 2013 Dec 10. (Journal IF: 1.412, Citations: 0)

Elble, R, Bain, P, Forjaz, MJ, Haubenberger, D, Testa, C, Goetz, CG, Leentjens, AFG, Martinez-Martin, P, Traon, AL, Post, B, Sampaio C, Stebbins, GT, Weintraub, D, Schrag, A, (2013) Task Force Report: Scales for Screening and Evaluating Tremor Critique and Recommendations. *Movement disorders* **28**, 1793-1800 (Journal IF: 4.505, Citations 0)

Caldeira D, Vaz-Carneiro A, Costa J (2013). Cochrane Corner: Evaluation of the Cochrane systematic review "Antiplatelet agents for chronic kidney disease". *Rev Port Cardiol* **32**,(issue 11):917-918. (Journal IF: 0.592, Citations: 0)

Neutel D, Galdes R, Pereira P, Gomes da Costa A, Pimentel J, Melo TP (2013) Recurrent Ischemic Stroke in an Adult with Cystinosis: A Clinical-Pathological Case. *J Stroke Cerebrovasc Dis.* **22**,(8):E674-E675 (Journal IF: 1.984, Citations 0)

Domingos, J, Coelho, M, Ferreira, JJ, (2013), Referral to rehabilitation in Parkinson's disease: who, when and to what end? *Arquivos de Neuropsiquiatria* **71**(12): 967-972. (Journal IF: 0.827. Citations: 0)

Ferreira JJ, Neutel D, Mestre T, Galitzky M, Santos AT, Sampaio C, Rascol O (2013) Usefulness of OSLER test in Parkinson's disease. *Sleep Medicine* **3**, 297-298. (Citations: 0)

Pita Lobo, P, Pinto S, Rocha L, Reimão S, Mamede de Carvalho, (2013), Orofacial apraxia in motor neuron disease, *Case Rep Neurol* **5**, 47–51 (Journal IF: not indexed, Citations:0)

Metzger S, Walter C, Riess O, Roos RA, Nielsen JE, Craufurd D, (2013) REGISTRY Investigators of the European Huntington's Disease Network, Nguyen HP. The V471A polymorphism in autophagy-related gene ATG7 modifies age at onset specifically in Italian Huntington disease patients. *PLoS One*. **8**, e68951 (Journal IF: 3.713, Citations:0)

Sidiropoulos C, Hutchinson W, Mestre T, et al. (2013), Bilateral pallidal stimulation for Wilson's disease. *Mov Disord* **28**(9):1292-1294 (Journal IF: 4.505; Citations:1)

Mestre TA, Zurowski M, Fox SH, (2013), 5-Hydroxytryptamine 2A receptor antagonists as potential treatment for psychiatric disorders. *Expert Opinion on Investigational Drugs* **22**, (4):411-421 (Journal IF: 4.744, Citations:1)

Mestre TA, Thomsen T, Voon V, Strafella AP, Miyasaki J. (2013) Diagnosis and treatment of impulse control disorders in patients with movement disorders. *Therapeutic Advances in Neurological Disorders* **6**, (3): 175-188 (Journal IF: not indexed, Citations:0)

Hubers AA, van Duijn E, Roos RA, Craufurd D, Rickards H, Bernhard Landwehrmeyer G, van der Mast RC, Giltay EJ (2013) REGISTRY investigators of the European Huntington's Disease Network. Suicidal ideation in a European Huntington's disease population. *J Affect Disord*. **151**, (1):248-58. (Journal IF: 3.295, Citations:0)

Leonel L, Costa J, Garcia FV, Valls-Sole J, Brandt T, Schneider E, Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials. *Otology & Neurotology* **34**, (4):743-747. (Journal IF: 2.014, Citations:0)

Caeiro L, Ferro JM, Costa J, Apathy secondary to stroke: a Systematic Review and Meta-Analysis, (2013) *Cerebrovascular Diseases* **35**, (1):23-39 (Journal IF: 2.814, Citations: 2)

Caldeira D, Fernandes RM, Costa J, David C, Sampaio C, Ferreira JJ, Branded versus Generic Clopidogrel in Cardiovascular diseases: a Systematic Review. *Journal of Cardiovascular Pharmacology* **61**, (4):277-282 (Journal IF: 2.383, Citations: 0)

Vellas B, Carrillo MC, Sampaio C, Brashear H R, Siemers E, Hampel H, Schneider Lon, Weiner M, Doody R, Khachaturian Z, Cedarbaum J, Grundman M, Broich K, Giacobin E, Dubois B, Sperling R, Wilcock GK, Fox N, Scheltens P, Touchon J, Hendrix S, Andrieu S, Aisen P, (2013) Adverse event assessment, analysis, and reporting in recent published analgesic clinical trials: ACTION systematic review and recommendations. *Pain* **154**, (7):997-1008 (Journal IF: 5.644, Citations: 1)

Ratilal BO, Pappamikail, Costa J, Sampaio C, (2013), Anticonvulsants for preventing seizures in patients with chronic subdural haematoma. *Cochrane Database of Systematic Reviews* **6**, CD004893 (Journal IF: 5.912, Citations:0)



Borowsky B, Warner J, Leavitt BR, Tabrizi SJ, Roos RAC, Durr A, Becker C, Sampaio C, Tobin AJ, Schulman H, (2013) 8OHdG is not a biomarker for Huntington disease state or progression. *Neurology* **80**, (21):1934-1941 (Journal IF: 8.312, Citations: 0)

Sampaio C, Konopka AE (2013), Memory for non-native language: The role of lexical processing in the retention of surface form. *Memory* **21**, 4): 537-544 (Journal IF: not indexed, Citations: 0)

Lobo PP, Coelho M, Mestre TA, Rosa MM, Ferreira JJ, (2013) Wearing-off phenomena and levodopa-induced dyskinesias in posttraumatic hemiparkinsonism. *Movement Disorders* **28**, 1212-U17 (Journal IF: 4.505, Citations: 0)

Teodoro T, Neutel D, Lobo P, Geraldo AF, Conceição I, Rosa MM, Albuquerque L, (2013) Recovery after copper-deficiency myeloneuropathy in Wilson's disease. *Journal of Neurology* **260**, 1917-1918 (Journal IF: 3.578, Citations: 0)

Caldeira D, Vaz-Carneiro A, Costa J (2013). What is the benefit of salt reduction on blood pressure? Assessment of the Cochrane Review: Effect of longer-term modest salt reduction on blood pressure. He FJ, Li J, Macgregor GA. *Cochrane Database Syst Rev*. Apr 30;4:CD004937]. *Acta Med Port*. 2013, **26**, (issue 5):490-2. (Journal IF: 0.151, Citations: 0)

Ferreira JJ, Colosimo C, Bhidayasiri R, Marti MJ, Maisonoble P, Om S, (2013) Assessment of factors influencing secondary non response to botulinum toxin A treatment in cervical dystonia. *Journal of Neural Transmission* **120**, 1142-1143 (Journal IF: 2.730, Citations: 0)

Mestre TA, Thomsen T, Voon V, Strafella AP, Miyasaki J, (2013) Diagnosis and treatment of impulse control disorders in patients with movement disorders. *Therapeutic Advances in Neurological Disorders* **6**, (3):175-188 (Journal IF: 4.505, Citations: 0)

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Dalziel, SR , Thompson, JMD, Macias, CG, Fernandes RM.,Johnson, DW, Waisman, Y, Cheng, N, Acworth, J, Chamberlain, JM, Osmond, MH,Group Author(s): Pediat Emergency Res, Networks PERN, (2013) Predictors of severe H1N1 infection in children presenting within Pediatric Emergency Research Networks (PERN): retrospective case-control study. *British Medical Journal* 347Article Number f4836 (Journal IF: 17.215, Citations: 1)

#### Other publications National

Freire, RA, Ferreira JJ, Epidemiologia da Doença de Parkinson, Incidência e prevalência, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: pg 2-7.

Valadas A, Costa J, Ferreira JJ, Epidemiologia da Doença de Parkinson, História Natural, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: pg 8-28.

Neutel D, Ferreira JJ, Epidemiologia da Doença de Parkinson, Alterações do Sono, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: pg 185-201.

Ferreira JJ, Rosa MM, Coelho MH. Doenças do Movimento, In *Neurologia fundamental, Princípios, diagnóstico e Tratamento*, capítulo IX, 2ª edição, Lidel, 2013, pg 159-188.

Coelho M, Epidemiologia da Doença de Parkinson, Tremor essencial, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: pg 121 - 131

Coelho M, Epidemiologia da Doença de Parkinson, Parkinsonismo Iatrogénico, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: pg 113-120

Guedes LC, Rosa MM, Epidemiologia da Doença de Parkinson, Flutuações motoras e discinésias. In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: 238-253.

Sampaio C, Epidemiologia da Doença de Parkinson, Tratamento do doente Parkinsoniano de Novo, In *Doença de Parkinson – Manual Prático*. Lidel, Lisboa 2013: 222-237

Carneiro AV, Costa J, Marinho RT, Acta Médica Portuguesa and the Cochrane Collaboration. *Acta Médica Portuguesa* **26**(4):295. (Journal IF: 0.151)

Domingos, J. Estratégias para o dia-a-dia na Doença de Parkinson. *Revista PARKINSON*, Associação Portuguesa de doentes de Parkinson, Dezembro, 2013.

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

Ferreira JJ, Progression of PD from premotor to late stages, Design, Conduct and Interpretation of Clinical trials in Movement Disorders, Toulouse, France, 29-31 October, 2013.

Ferreira JJ, Critical appraisal of a clinical trial, Design, Conduct and Interpretation of Clinical trials in Movement Disorders, Toulouse, France, 29-31 October, 2013.

Ferreira JJ, Systematic review of RCT and meta-analysis, Design, Conduct and Interpretation of Clinical trials in Movement Disorders, Toulouse, France, 29-31 October, 2013.

Ferreira JJ, Strengthening capacities for clinical trial, Orphan Drug Rare disease seminar, Marselha, October 17-18, 2013.

Ferreira JJ, Update on the non-Huntington disease choreas, Uncommon Causes of Movement Disorders, Rome , Italy, October 11-12, 2013.

Domingos, J. Actividade Física e doença de Parkinson, Conferência “3.ª Idade: Um Novo Olhar, um Novo Caminho”, Torres Vedras, Portugal, October 7-11, 2013.

Ferreira JJ, Current definitions and diagnostic criteria: reasons for redefining the disorder, 3rd World Parkinson Congress, Montreal, Canadá, October 1-4, 2013

Domingos, J. Actividade Física e doenças neurodegenerativas. Seminar Alzheimer a nossa realidade. Torres Vedras, Portugal, September 21st, 2013.

Ferreira J, Um enfoque baseado em evidências para o tratamento da Doença de Huntington, 2013 World Congress in Huntington's disease, Rio de Janeiro, Brasil, September 15-18, 2013.

Ferreira JJ, What is the future for clinical trials in orphan diseases? PSP Association International Medical Workshop, London, UK. July 25, 2013

Ferreira JJ, Parkinson's disease and related disorders, 5th Regional Teaching Course in Sub-Saharan Africa, Dakar, Senegal, July 11-13, 2013.

Domingos, J. Complex Case Studies. MDS Allied Health Professional Summer School: Physiotherapy for people with Parkinson's disease. Nijmegen, Netherlands, July 4-6, 2013.

Ferreira JJ, What if it's not Huntington's disease? 17th International Congress of Parkinson's Disease and Movement Disorders, Sydney, Australia, June 16-20, 2013

Ferreira JJ, O valor da inovação: da investigação ao doente, Lisbon, Ciclo Conferência Apifarma 2013, Lisbon, Portugal, June 28 2013.

Ferreira JJ, Investigação clínica no internato médico, Sessão de Boas vindas aos novos internos, Centro hospitalar Lisboa Norte, Lisbon, Portugal, June 5, 2013.

Ferreira JJ, Late-stage Parkinson disease. How is changing the landscape of PD's later stage? Beyond advanced phase of PD. Update focusing on dementia and gait/balance problems in the late stage of PD, Open issues in Parkinson's Disease: questions and answers, Cuglieri, May 30-31, 2013.

Mestre T, Enroll-HD a hub for biomarker development, 2013 HD Therapeutics Conference, Venice, Italia, April 2013.

Mestre T, Brain and Behavior, a clinical neuroscience course for first-year medical students, University of Toronto. March 2013.

Mestre T, Movement disorders full-day course, American Academy of Neurology Annual Meeting, San Diego, USA, March 2013.

Ferreira JJ, Pharmacological treatment of Parkinson's disease, Winter School of young neurologists, Tartu, Estonia, March 1, 2013.

### **Communications in International Conferences**

Daniel Caldeira, Rita Calé, Cristina Martins, et al. Quantification and prognosis of incomplete coronary revascularization after percutaneous coronary intervention in octogenarians. ESC Congress 2013, Amsterdam, Netherlands, 2013. (Oral communication)

Ana Almeida, Liliana Lopes, Maria Loureiro, Carlos Cotrim, Inês Cruz, Bruno Stuart, Daniel Caldeira, Helder Pereira. Echocardiographic assessment of right ventricular contractile reserve in patients with pulmonary hypertension. 5th World Symposium on Pulmonary Hypertension, Nice, France, 2013. (Poster presentation)

Daniel Caldeira, Inês Cruz, Bruno Stuart, Cristina Martins, Helder Pereira, On Behalf of Investigators of the Registry of Acute Coronary Syndromes. Heart failure is a determinant of painless acute coronary syndrome. Heart Failure 2013, Lisbon, Portugal, 2013. (Poster presentation)

Domingos, J., Godinho, C., Ferreira, JJ. Which treatments are in the pipeline for the management of falls in Parkinson disease? 3rd World Parkinson Congress, Montréal, Canada, October 1st to 4th, 2013 (Poster presentation)

Mestre T, Shah PS, Marras C, Lang AE. The lessebo effect in Parkinson's disease. *Movement Disorders*, 2013, 28(Suppl. 1), S170-171 (Poster presentation)

Mestre T, Teodoro T, Graf J, Reginold W, Sale J, Zurowski M, Miyasaki J, Ferreira JJ, Marras C. Reluctance to start medication in Parkinson's disease from the patient perspective: Results from an international observational study. *Movement Disorders*, 2013, 28(Suppl. 1), S427-428. (Poster presentation)

Pondal M, Marras C, Walsh R, Mestre T, Lang AE. Challenges in establishing reliability of transcranial sonography (TCS) of the substantia nigra (SN) in parkinsonism. *Movement Disorders*, 2013, 28(Suppl. 1), S51-S52 (Poster presentation)

Daniel Caldeira, Rita Calé, Cristina Martins, et al. Quantification and prognosis of incomplete coronary revascularization after percutaneous coronary intervention in octogenarians. ESC Congress 2013, Amsterdam, Netherlands, 2013. (Oral communication)

Daniel Caldeira, Inês Cruz, Bruno Stuart, Cristina Martins, Helder Pereira, On Behalf of Investigators of the Registry of Acute Coronary Syndromes. Heart failure is a determinant of painless acute coronary syndrome. Heart Failure 2013, Lisbon, Portugal, 2013. (Poster presentation)

Daniel Caldeira, Cristina Martins, Helder Pereira, Joaquim J Ferreira, João Costa. Caffeine does not increase the risk of atrial fibrillation: a systematic review and meta-analysis of observational studies, ESC Congress 2013, Amesterdam, Netherlands, 2013. (Oral communication)

Domingos, J., Graziano, M., Jones, D., Ramaswamy, B. Making the most of expert practice - The Association of Physiotherapists in Parkinson's Disease Europe Case Study Project" 3rd World Parkinson Congress, Montréal, Canada, October 1st to 4th, 2013 (Poster presentation)

Domingos, J., Cardoso, R., Ferreira, JJ. Josefa Domingos, Rita & Joaquim J Ferreira. What if you had it all in one setting? An Innovative Parkinson Intensive Multi-Program Rehabilitation Approach (PIMPRA)" 3rd World Parkinson Congress, Montréal, Canada, October 1st to 4th, 2013. (Poster presentation)

Neutel D, Karachi C, Welter ML, et al. Worldwide Record of REM Sleep Time In a Patient with Pedunculopontine Nucleus Area (PPNa) stimulation. World Congress of Neurology – Vienna, Austria, 21st - 26th September 2013 (Poster presentation)

Neutel D, Karachi C, Welter ML, et al. Worldwide Record of REM Sleep Time In a Patient with Pedunculopontine Nucleus Area (PPNa) stimulation. 17th International Congress of Parkinson's Disease and Movement Disorders, Sidney, Australia, 16Th- 20Th June 2013 (Poster presentation)

Reimão S, Pita Lobo P, Neutel D, Nunes R, Ferreira J, Campos J, Ferreira JJ, (2013) Locus ceruleus and substantia nigra neuromelanin magnetic resonance imaging in patients with early Parkinson's disease, *Neuroradiology* 55:1464. (Oral communication)

Tavares JB, Rodrigues D, Casimiro C, Reimão S, Sá Nunes G, Campos JG, (2013) Imaging signs in pediatric neuroradiology, *Neuroradiology*, 55:1470. (Oral communication)

Tavares J, Leite E, Matoso T, Teixeira Gomes AS, Neto L, Reimão S, Campos JG, (2013) Radiation exposure in imaging professionals - a 2-year retrospective study in North Lisbon Hospital Centre, *Neuroradiology*, 55:1463 (Oral communication)

Geraldo AF, Pereira J, Nunes P, Reimão S, Sousa R, Castelo-Branco M, Pinto S, Guedes Campos J, Mamede de Carvalho, (2013) Beyond fractional anisotropy: the value of axial diffusivity and radial diffusivity and its correlation with neurophysiological changes in ALS patients, *Neuroradiology*, 55:1466. (Oral communication)

Caldeira I, Lavrador J, Reimão S, Geraldo A, Sousa R, Campos J, (2013) Remote cerebellar haemorrhage after placement of external ventricular drainage for acute hydrocephalus: case report and short review of literature, *Neuroradiology*, 55:1475. (Oral communication)

Aguiar de Sousa D, Tavares J, Geraldo AF, Reimão S, Albuquerque L, (2013), Multiphasic disseminated encephalomyelitis associated with *Campylobacter jejuni* infection, *Neuroradiology*, 55:1491. (Poster presentation)

Tavares J, Basílio G, Sousa D, Casimiro C, Reimão, S, Campos J, (2013), Selection of region of interest and technical parameters in singlevoxel spectroscopy in MELAS, *Neuroradiology*, 55:1497. (Poster presentation)

### **Communications in National Conferences**

Ferreira JJ, O que os cuidadores e familiares devem saber sobre a Doença de Parkinson, Conversas no Campus sobre saúde, Torres Vedras, Portugal, December 15. (Oral communication)

Guedes LC, Projecto BIOBANCO IMM – Doença de Parkinson, Conversas no Campus sobre saúde, Torres Vedras, Portugal, December 15. (Oral communication)

Domingos, J. Exercício físico na Doença de Parkinson. 1st Ciclo de Conferências “Conversas no Campus”- Conversas sobre Doença de Parkinson para familiares e cuidadores, Torres Vedras,

Portugal December 14th, 2013 (Oral Presentation).

Ferreira JJ, Especialidades médicas – Uma escolha para o futuro, XXIII Encontro Nacional de Estudantes de Medicina, Peniche, 23-25 November, 2013. (Oral communication)

Domingos, J. Actividade Física e doença de Parkinson, Conferência “3.ª Idade: Um Novo Olhar, um Novo Caminho”, Torres Vedras, Portugal, October 7th-11th, 2013 (Oral Presentation)

Rosa MM, Multi-system atrophy, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013. (Oral communication)

Rosa MM, Wilson’s Disease, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013. (Oral communication)

Guedes LC, Huntington Disease, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013. (Oral communication)

Valadas A, Psychogenic Movement Disorders, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013. (Oral communication)

Daniel Caldeira, Inês Cruz, Bruno Stuart, Cristina Martins, Hélder Pereira, em nome dos Investigadores do Registo Nacional dos Síndrome Coronários Agudos. Síndrome coronária aguda indolor: determinantes e prognóstico, XXXIV Congresso Português de Cardiologia, Vilamoura, 2013. (Poster presentation)

Daniel Caldeira, Rita Calé, Cristina Martins, Ingrid do Rosário; Carina Machado, Pedro Galvão Santos, João Brito, Ricardo Esteves, Ernesto Pereira, Manuel Almeida, Miguel Mendes, Hélder Pereira. Quantificação e impacto da revascularização coronária incompleta após intervenção percutânea em octagenários, XXXIV Congresso Português de Cardiologia, 2013. (Poster presentation)

Daniel Caldeira, Inês Cruz, Bruno Stuart, Cristina Martins, Hélder Pereira, em nome dos Investigadores do Registo Nacional dos Síndrome Coronários Agudos Síndrome coronário agudo indolor e fibrilhação auricular, Arritmias 2013, Portugal. (Poster presentation)

Ferreira JJ, Early Parkinson’s Disease vs Essential Tremor, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013 (Oral communication)

Ferreira JJ, Restless Legs Syndrome, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013 (Oral communication)

Ferreira JJ, Tourette's Syndrome, V Teaching Course in Movement Disorders of the Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, June 29, 2013 (Oral communication)

Ferreira JJ, Doença de Parkinson – Viver com Parkinson, III Jornadas: Viver com Parkinson, Biblioteca do Hospital Dr. Nélio Mendonça, 10-11 Maio 2013 (Oral communication)

Batista A, Casimiro C, Neto L, Reimão S, Campos J, Hipersinal lesional em ressonância magnética ponderada em difusão – diagnóstico diferencial Neurorradiológico, III Jornadas Ibéricas de Radiologia, Coimbra, Novembro 7-8, 2013 (Poster presentation)

Tavares JB, Basílio G, Geraldo A, Reimão S, Campos J. Cerebral and Supra-Aortic Branches Angio-CT, European Joint Congress of Clinical Anatomy, Lisbon, June 26-29, 2013. (Oral communication)

Tavares JB, Caldeira I, Sousa D, Reimão S, Campos J. Guillain-Mollaret Triangle's Disruption on DTI European Joint Congress of Clinical Anatomy, Lisbon, June 26-29, 2013. (Oral communication)

Ferreira S, Reimão S, Nunes R, Simulation study comparing algorithms for estimation of T2\* relaxation maps, 5th Workshop on Biomedical Engineering, Lisbon, April 20, 2013. (Poster presentation)

Cordeiro I, Coelho M, Guedes LC, Lobo PP, FERREIRA JJ, Rosa MM, Efeito distinto da estimulação do núcleo Vim do tálamo no tremor distónico e no tremor de acção num doente com tremor essencial, Reunião da Sociedade Portuguesa de Doenças do Movimento, Vimeiro, 22-24 March 2013. (Poster presentation)

Guedes LC, Zhang L, Quadri M, Coelho M, Valadas A, Mestre T, Lobo PP, Rosa MM, Simons E, Oostra BA, FERREIRA JJ, Bonifati V, Comprehensive LRRK2 screening in Portuguese patients with Parkinson's disease: a new family segregating the p. Arg1441His mutation and novel variants, Reunião da Sociedade Portuguesa de Doenças do Movimento, Vimeiro, 22-24 March 2013. (Poster presentation)

Miltenberger-Miltenyi G, Guedes LC, Mendes T, Pinho R, Coelho M, Mestre T, Valadas A, Lobo PP, Neutel D, Rosa MM, FERREIRA JJ, Outeiro T, Slow versus Rapid Progression Parkinson's Disease: Molecular Determinants and Biomarkers, Reunião da Sociedade Portuguesa de Doenças do Movimento, Vimeiro, 22-24 March 2013. (Poster presentation)

Teodoro T, Agostinho S, Lobo PP, Coelho M, FERREIRA JJ, Ataxia progressiva com tremor do palato, Reunião da Sociedade Portuguesa de Doenças do Movimento, Vimeiro, 22-24 March 2013. (Poster presentation)

### **Organisation of Conferences**

Domingos, J. Co-organized 1st Ciclo de Conferências “Conversas no Campus”- Conversas sobre Doença de Parkinson para familiares e cuidadores, December 14th, 2013, Torres Vedras,

Portugal.

Ferreira JJ, Director do IV Curso Botulinum Toxin Training Course, Instituto de Medicina Molecular, Lisboa, Lisbon, Portugal, October 19th 2013.

Ferreira JJ, Director do Curso Revisões sistemáticas como Projecto de Investigação Clínica, Faculdade de Medicina de Lisboa, Lisbon, Portugal, September 11-12, 2013.

Ferreira JJ, Membro da Comissão organizadora da MDS/ParkinsonNet Allied Health Professionals Summer School, Nijmegen (NL), July 4-6 2013.

Ferreira JJ, Director do V Teaching Course in Movement Disorders, Instituto de Medicina Molecular, Lisbon, Portugal, June 29, 2013.

Ferreira JJ, Co-Director do I Curso Pós-Graduado de Actualização em Boas Práticas Clínicas do Centro de Investigação Clínica do Centro Académico de Medicina de Lisboa, Lisbon, Portugal, May 22-23, 2013.

Rosa MM, Co-Director do I Curso Pós-Graduado de Actualização em Boas Práticas Clínicas do Centro de Investigação Clínica do Centro Académico de Medicina de Lisboa, Lisbon, Portugal, May 22-23, 2013.

Caldeira D, Member of the Organizing committee the X Course of Echocardiography of Hospital Garcia de Orta, Almada, Portugal, May 2013.

Ferreira JJ, Second Annual Winter School for Young Neurologists, The Movement Society's European section, Tartu, Estonia, March 1-3, 2013.

### **Internationalisation**

Chair of The Education Committee, International Parkinson's Disease and Movement Disorders Society.

Elected-President MDS-ES, International Parkinson's Disease and Movement Disorders Society.

Representative of the Portuguese Neurology Society at the European Board of Neurological of European Union of Medical Specialists (UEMS/EBN).

Co-Chair of the Clinical Working Partie, COST Action BM1101 European network for the study of dystonia syndromes.

Lead facilitator of The Neuroprotective Therapy Working Group, European Huntington Disease Network.

Member of the Executive Committee, European Huntington Disease Network.



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

Honor mention to Sofia Reimão for the Oral Communication - Locus coeruleus and substantia nigra neuromelanin magnetic resonance imaging in patients with early Parkinson's disease, Congresso Ibérico de Neuroradiologia, Lisbon, 2013.

### **Advanced teaching**

Reimão S, Masters Degree Program in Biomedical Engineering, IBEB – Faculdade de Ciências da Universidade de Lisboa, co-orientation of three projects.

Ferreira JJ, Introdução à metodologia da investigação clínica, Certificado Nível 1, Sub-investigador médico e staff não médico, Clinical Investigator Certification, Universidade de Aveiro.

Ferreira JJ, Training Programme in Pharmaceutical Medicine, Director of the module Systematic review and meta-analysis: Clinical Data Management and Analysis, Universidade de Aveiro, 2013-2014.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, Faculdade Medicina de Lisboa, Lisbon, December 18, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, USF Marginal, S. João do Estoril, November 21, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, USF Linda-a-Velha, Carnaxide, November 14, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, ACES Lisboa Central - USF Loios, Lisbon, November 13, 2013.

Fernandes RF, Desenvolvimento de medicamentos: novos paradigmas e investigação clínica em Portugal, Programa Educacional Manage, Modelos Aplicados de Economia, Epidemiologia, Gestão e Direito em Saúde, Lisboa, Escola Nacional de Saúde Pública, November 8, 2013.

Costa J, Efetividade relativa de novos medicamentos, Programa Educacional Manage, Modelos Aplicados de Economia, Epidemiologia, Gestão e Direito em Saúde, Lisboa, Escola Nacional de Saúde Pública, November 8, 2013.

Ferreira JJ, Farmacologia Clínica e Prescrição Racional, Programa Educacional Manage, Modelos Aplicados de Economia, Epidemiologia, Gestão e Direito em Saúde, Lisboa, Escola Nacional de Saúde Pública, November 8, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, ACES Arrábida - Centro de Saúde S. Sebastião, Setúbal, October 25, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting - practical session, Intensive

Course in Pharmacovigilance, Faculdade de Medicina de Lisboa, Lisbon, October 24, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, Intensive Course in Pharmacovigilance, Faculdade de Medicina de Lisboa, Lisbon, October 22, 2013.

Ferreira JJ, Overview on botulinum toxin: clinical uses, formulations, injection techniques and identification of best muscle targets, 4th IMM Teaching Course on Botulinum Toxin of the Clinical Pharmacology Unit, Lisbon, Portugal, October 19, 2013.

Ferreira JJ, Hands on: preparation of botulinum toxin, 4th IMM Teaching Course on Botulinum Toxin of the Clinical Pharmacology Unit, Lisbon, Portugal, October 19, 2013.

Ferreira JJ, Preparation of botulinum toxin (flash presentation), 4th IMM Teaching Course on Botulinum Toxin of the Clinical Pharmacology Unit, Lisbon, Portugal, October 19, 2013.

Ferreira JJ, Hands on: writer's cramp, 4th IMM Teaching Course on Botulinum Toxin of the Clinical Pharmacology Unit, Lisbon, Portugal, October 19, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, UCSP Lumiar, Lisbon, October 17, 2013.

Ferreira JJ, Update on the non-Huntington disease choreas, Uncommon causes of Movement disorders, Rome, Italy, October 11-12, 2013.

Anes, AM, Safety and Adverse Event Reporting in Clinical Trials, 1st Course in Good Clinical Practice, Faculdade de Medicina de Lisboa, Lisbon, May 23, 2013.

Ferreira JJ, Estrutura de um centro de investigação clínica, I Curso Pós-graduado de actualização em Boas Práticas Clínicas, Faculdade de Medicina de Lisboa, 22-23 de Maio de 2013.

Ferreira JJ, Responsabilidades do investigador, I Curso Pós-graduado de actualização em Boas Práticas Clínicas, Faculdade de Medicina de Lisboa, 22-23 de Maio de 2013.

Ferreira JJ, Introdução e princípios de Boas Práticas Clínicas, I Curso Pós-graduado de actualização em Boas Práticas Clínicas, Faculdade de Medicina de Lisboa, 22-23 de Maio de 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting - practical session, Intensive Course in Pharmacovigilance, Faculdade de Medicina de Lisboa, Lisbon, May 16, 2013.

Rosa MM, Reacções adversas neuropsiquiátricas, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

Rosa MM, Mecanismos e reacções adversas medicamentosas e factores de risco, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

Rosa MM, Avaliação risco-benefício, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

Rosa MM, Estudos em Farmacoepidemiologia, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

Rosa MM, Métodos de monitorização de segurança de medicamentos, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

David C, Reações adversas cardiovasculares, Curso intensivo de Farmacovigilância, Faculdade de Medicina de Lisboa, May 13-16, 2013.

Domingos J, 1.º Curso da Sociedade Portuguesa de doenças do Movimento (SPDMov). Doenças do movimento em doenças médicas. Vimeiro, March 22, 2013.

Ferreira JJ, Video Diagnosis of Movement Disorders, 4th Aims Meeting, University of Lisbon, Faculty of Medicine, March 15-17, 2013

Ferreira JJ, Clinical aspects of Parkinson's disease, Neurobiology and Disease, The Doctoral Programme in Health Sciences, Faculty of Medicine, University of Coimbra, February 26, 2013

Ferreira JJ, Module Clinical Trials, Introduction to clinical research: a practical course, Clinical Research course of the Lisbon Academic Medical Center PhD Program, Faculty of Medicine, University of Lisbon, 2013

Ferreira JJ, Clinical Trials in Portugal, Training Program in Pharmaceutical Medicine, Clinical Development, Infarmed, Lisbon, January 10-12, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, Hospital CUF Descobertas, Lisbon, January 30, 2013.

Anes, AM, Pharmacovigilance and ADR spontaneous reporting, ACES Lx Oriental/Marvila-Chelas, Lisbon, January 29, 2013.

### **Science and society**

Interview to Daniel Caldeira (October 2013) in Visão: “Café não faz mal ao coração”.

Interview to Daniel Caldeira in Portuguese Cardiology Society Website in November 2013. Available in [http://www.spc.pt/DL/Home/fm/Cafe\\_Coracao\\_PortalSPC\\_22.10.2013.pdf](http://www.spc.pt/DL/Home/fm/Cafe_Coracao_PortalSPC_22.10.2013.pdf)

Domingos, J. Co-organized 1st Ciclo de Conferências “Conversas no Campus”- Conversas sobre Doença de Parkinson para familiares e cuidadores, December 14th, 2013, Torres Vedras, Portugal.

Ferreira JJ, O que os cuidadores e familiares devem saber sobre a Doença de Parkinson, Conversas no Campus sobre saúde, Torres Vedras, December 15, 2013.

Guedes LC, Projecto BIOBANCO IMM – Doença de Parkinson, Conversas no Campus sobre saúde, Torres Vedras, December 15, 2013.

Domingos, J. Exercício físico na Doença de Parkinson. 1st Ciclo de Conferências “Conversas no

Campus”- Conversas sobre Doença de Parkinson para familiares e cuidadores, Torres Vedras, Portugal Decembre 14th, 2013 (Oral Presentation).

Domingos, J. Actividade Física e doença de Parkinson, Conferência “3.ªIdade: Um Novo Olhar, um Novo Caminho”, Torres vedras, Portugal, October 7th-11th, 2013 (Oral Presentation).

## JOSÉ FERRO LAB

### Major Interests / Objectives

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. Main advantage of the lab: strong collaboration among the experienced Principal Investigators, and the development of multiple collaborations, both at IMM and at other national and international major research centers and networks, in the areas of basic neurosciences, clinical genetics, advanced statistical methods, biological engineering, and neuroimaging.

We share common facilities and know-how that have allowed the conduction of many clinical trials as well as the assessment of the clinical impact of different interventions in a multinational effort 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	Principal Investigator
Ana Catarina Gaspar Fonseca	Master	PhD Student
Ana Isabel Figueira Verdelho	MD/PhD	Investigator
Bruno André e Silva Miranda	Master	PhD Student
Carolina Pires Maruta	Master	PhD Student
Catarina Carapeto da Silva Chester	Graduate	MSc Student
Dina Lúcia Gomes da Silva	PhD	PhD Student
Elisabete Mendes Lopes	No degree	Investigator
Fátima Soares	No degree	Investigator
Frederico Simões do Couto	No degree	Investigator
Helena Sofia Garrido Bárrios	Master	Investigator, MD

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
Mafalda Alexandra Ramos de Matos	Master	Technician
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 Geraledes Ramos Dias	Master	Investigator
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, Alzheimer's disease, Cognitive decline, Complex diseases, Genetics, Clinical trials.

### Major scientific achievements

The researchers of José Ferro Lab made in 2013 significant scientific contributions expressed in full papers published in international peer-reviewed journals. Important results were obtained regarding treatment of cerebral venous thrombosis, 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

### Recent Most Relevant Publications

Caeiro L, Ferro JM, Pinho E Melo T, Canhão P, Figueira ML. (2013) Post-stroke apathy: an exploratory longitudinal study. *Cerebrovascular Diseases* **35**, 507-513. (Journal IF: 2.814, Citations: 0)

Canhão P, Abreu LF, Ferro JM, Stam J, Bousser MG, Barinagarrementeria F, Fukujima MM; for the ISCVT Investigators. (2013) Safety of lumbar puncture in patients with cerebral venous thrombosis. *European Journal of Neurology* **20**, 1075-1080 (Journal IF: 4.162, Citations: 0)

Martins IP, Leal G, Fonseca I, Farrajota L, Aguiar M, Fonseca J, Lauterbach M, Gonçalves L, Cary MC, Ferreira JJ, Ferro JM. (2013) A randomized, rater-blinded, parallel trial of intensive speech therapy in sub-acute post-stroke aphasia: the SP-I-R-IT study. *International Journal of Language & Communication Disorders* **48**, 421-431 (Journal IF: 1.441, Citations: 1)

Pires C, Coelho M, Valadas A, Barroso C, Pimentel J, Martins M, Duyckaerts C, de Mendonça A, Verdelho A, Miltenberger-Miltenyi G. (2013) Phenotypic variability of familial and sporadic Progranulin p.Gln257Profs\*27 mutation. *Journal of Alzheimer's Disease* **37**, 335-342 (Journal IF: 4.174, Citations: 0)

Verdelho A, Madureira S, Moleiro C, Ferro JM, O'Brien JT, Poggesi A, Pantoni L, Fazekas F, Scheltens P, Waldemar G, Wallin A, Erkinjuntti T, Inzitari D; LADIS Study. (2013) Depressive symptoms predict cognitive decline and dementia in older people independently of cerebral white matter changes: the LADIS study. *Journal of neurology, neurosurgery, and psychiatry* **84**, 1250-1254 (Journal IF: 4.924, Citations: 3)

### Publications in peer review Journals

Aguiar de Sousa D, Geraldés R, Gil-Gouveia R, de Sá JC. (2013) New daily persistent headache and radiologically isolated syndrome. *Journal of Neurology* **260**, 2179-2181. (Journal IF: 3.578, Citations: 0)

Bárrios H, Narciso S, Guerreiro M, Maroco J, Logsdon R, de Mendonça A. (2013) Quality of life in patients with Mild Cognitive Impairment. *Aging Ment Health* **17**, 287-292. (Journal IF: 1.978, Citations: 1)

Bárrios H, Verdelho A, Narciso S, Gonçalves-Pereira M, Logsdon R, de Mendonça A. (2013) Quality of life in patients with cognitive impairment: validation of the Quality of Life-Alzheimer's Disease scale in Portugal. *International Psychogeriatrics* **25**, 1085-1096. (Journal IF: 2.504, Citations: 0)

Caeiro L, Ferro JM, Costa J. (2013) Apathy secondary to stroke: a systematic review and meta-analysis. *Cerebrovascular Diseases* **2013**; **35**, 23-39. (Journal IF: 2.814, Citations: 2)

Chester C, de Carvalho M, Miltenberger G, Pereira S, Dillen L, van der Zee J, Van Broeckhoven C, de Mendonça A. (2013) Rapidly progressive frontotemporal dementia and bulbar amyotrophic lateral sclerosis in Portuguese patients with C9orf72 mutation. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration* **14**, 70–72. (Journal IF: 2.369, Citations: 1)

Coutinho JM, Ferro JM, Zuurbier SM, Mink MS, Canhão P, Crassard I, Majoie CB, Reekers JA, Houdart E, de Haan RJ, Bousser MG, Stam J. (2013) Thrombolysis or anticoagulation for cerebral venous thrombosis: rationale and design of the TO-ACT trial. *International Journal of Stroke* **8**, 135-140. (Journal IF: 2.748, Citations: 0)

Duarte S, Roche A, Armstrong J, Ortez C, Gerontina E, Pérez A, O'Callaghan M, Pereira A, Sanmarti F, Molero M, Artuch R, Pineda M, García-Cazorla A. (2013) Abnormal expression of cation chloride cotransporters in Rett syndrome patients. *PLoS ONE* **8**, e68851. (Journal IF: 3.730, Citations: 1)

Dunkler D, Dehghan M, Teo KK, Heinze G, Gao P, Kohl M, Clase CM, Mann JF, Yusuf S, Oberbauer R; ONTARGET Investigators. Diet and kidney disease in high-risk individuals with type 2 diabetes mellitus. *JAMA Internal Medicine* **2013**; **173**, 1682-1692. (Journal IF: 10.58, Citations: 2)

Ederle J, Davagnanam I, van der Worp HB, Venables GS, Lyrer PA, Featherstone RL, Brown MM, Jäger HR; ICSS investigators. Effect of white-matter lesions on the risk of periprocedural stroke after carotid artery stenting versus endarterectomy in the International Carotid Stenting Study (ICSS): a prespecified analysis of data from a randomised trial. *The Lancet Neurology* **2013**; **12**, 866-872. (Journal IF: 23.917, Citations: 3)

Ferro JM, Canhão P. Evidence basis for anticoagulants for cerebral sinus venous thrombosis? Reply to david k. Cundiff. *Stroke* **2013**; **44**, e150. (Journal IF: 6.158, Citations: 0)

Fonseca AC, Ferro JM. Drug abuse and stroke. *Current neurology and neuroscience reports* **2013**; **13**, 325. (Journal IF: 3.783, Citations: 0)

Fonseca AC, Matias JS, E Melo TP, Pires C, Geraldés R, Canhão P, Brito D, Ferro JM. Time course of NT-proBNP levels after acute ischemic stroke. *Acta Neurologica Scandinavica* **2013**; **128**, 235-240. (Journal IF: 2.474, Citations: 0)



Fonseca AC, Pinho E, Melo T, Ferro JM. Cotard delusion after stroke. *European Journal of Neurology* 2013; **20**, e98-99. (Journal IF: 4.162, Citations: 0)

Gil-Gouveia R. Treatment Orthostatic Headache without intracranial hipotension A case report. *Cephalalgia* 2013; **33**, 948-950. (Journal IF: 3.485, Citations: 0)

Gil-Gouveia R, Fonseca A. Cluster headache after cataract surgery. *The Clinical Journal of Pain* 2013; **29**, 19-21. (Journal IF: 2.552, Citations: 0)

Jokinen H, Schmidt R, Ropele S, Fazekas F, Gouw AA, Barkhof F, Scheltens P, Madureira S, Verdelho A, Ferro JM, Wallin A, Poggesi A, Inzitari D, Pantoni L, Erkinjuntti T; LADIS Study Group. Diffusion changes predict cognitive and functional outcome: the LADIS study. *Annals of Neurology* 2013; **73**, 576-583. (Journal IF: 11.193, Citations: 1)

Kharitonova TV, Melo TP, Andersen G, Egado JA, Castillo J, Wahlgren N; SITS investigators. Importance of cerebral artery recanalization in patients with stroke with and without neurological improvement after intravenous thrombolysis. *Stroke* 2013; **44**, 2513-2518. (Journal IF: 6.158, Citations: 0)

Kreisel SH, Blahak C, Bänzner H, Inzitari D, Pantoni L, Poggesi A, Chabriat H, Erkinjuntti T, Fazekas F, Ferro JM, Langhorne P, O'Brien J, Scheltens P, Visser MC, Wahlgren LO, Waldemar G, Wallin A, Hennerici MG. Deterioration of gait and balance over time: the effects of age-related white matter change--the LADIS study. *Cerebrovascular Diseases* 2013; **35**, 544-553. (Journal IF: 2.814, Citations: 0)

Lobo S, Ferro JM, Barinagarrementeria F, Bousser MG, Canhão P, Stam J. Shunting in Acute Cerebral Venous Thrombosis: A Systematic Review. *Cerebrovascular Diseases* 2013; **37**, 38-42. (Journal IF: 2.814, Citations: 0)

Machet A, Fonseca AC, Oppenheim C, Touzé E, Meder JF, Mas JL, Naggara O. Does anticoagulation promote mural hematoma growth or delayed occlusion in spontaneous cervical artery dissections?. *Cerebrovascular Diseases* 2013; **35**, 175-181. (Journal IF: 2.814, Citations: 0)

Marques JF, Mares I, Martins ME, Martins IP. The hierarchical organization of semantic knowledge in stroke aphasia: The role of feature sharedness and executive function. *Journal of Neurolinguistics* 2013; **26**, 552-556. (Journal IF: 1.115, Citations: 0)

Martins IP, Maruta C, Freitas V, Mares I. Executive performance in older Portuguese adults with low education. *Clinical Neuropsychology* 2013; **27**, 410-425. (Journal IF: 1.678, Citations: 0)

Menezes Cordeiro I, Tavares JB, Reimão S, Geraldes R, Ferro JM. Hypertrophic olivary degeneration after pontine hemorrhage: a cause of delayed neurological deterioration. *Cerebrovascular Diseases* 2013; **36**, 153-154. (Journal IF: 2.814, Citations: 0)

Moleiro C, Madureira S, Verdelho A, Ferro JM, Poggesi A, Chabriat H, Erkinjuntti T, Fazekas F, Hennerici M, O'Brien J, Pantoni L, Salvadori E, Scheltens P, Visser MC, Wahlgren LO, Waldemar G, Wallin A, Inzitari D. Confirmatory factor analysis of the Neuropsychological Assessment Battery of the LADIS study: A longitudinal analysis. *Journal of Clinical and Experimental Neuropsychology*

2013; **35**, 269-278. (Journal IF: 2.116, Citations: 0)

Neutel D, Geraldes R, Pereira P, Gomes da Costa A, Pimentel J, e Melo TP. Recurrent ischemic stroke in an adult with cystinosis: a clinical-pathological case. *J Stroke Cerebrovasc Dis* 2013; **22**, e674-675. (Journal IF: 1.984, Citations: 0)

Poggesi A, Gouw A, van der Flier W, Pracucci G, Chabriat H, Erkinjuntti T, Fazekas F, Ferro JM, Hennerici M, Langhorne P, O'Brien JT, Visser MC, Wahlund LO, Waldemar G, Wallin A, Scheltens P, Inzitari D, Pantoni L. Cerebral white matter changes are associated with abnormalities on neurological examination in non-disabled elderly: the LADIS study. *Journal of Neurology* 2013; **260**, 1014-1021. (Journal IF: 3.578, Citations: 1)

Rodrigues IT, Leal MG. Tradução Portuguesa e análise de aspectos psicométricos da escala "Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39)". *Audiol Comm Res* 2013; **18**, 341-346.

Silva D, Albers U, Santana I, Vicente M, Martins IP, Verdelho A, Guerreiro M, de-Mendonça A. Do MCI patients with vitamin B12 deficiency have distinctive cognitive deficits? *BMC Research Notes* 2013; **6**, 357.

Silva D, Guerreiro M, Santana I, Rodrigues A, Cardoso S, Maroco J, de Mendonça A. Prediction of long-term (5 years) conversion to dementia using neuropsychological tests in a memory clinic setting. *Journal of Alzheimer's Disease* 2013; **34**, 681-689. (Journal IF: 4.174, Citations: 0)

Sousa DA, Geraldes R, Gil-Gouveia R, Sá JC. New daily persistent headache and radiologically isolated syndrome. *Journal of Neurology* 2013; **260**, 2179-2181. (Journal IF: 3.578, Citations: 0)

Teodoro T, Ferreira J, Franco A, Almeida V, Coelho M, Ferro JM, Albuquerque L, Casimiro C. Vertebral artery dissection mimicking status migrainosus. *Am J Emerg Med* 2013; **31**, 1721.e3-5.

Teodoro T, Neutel D, Lobo P, Geraldo AF, Conceição I, Rosa MM, Albuquerque L, Ferreira JJ. Recovery after copper-deficiency myeloneuropathy in Wilson's disease. *Journal of Neurology* 2013; **260**, 1917-1918.

Van der Zee J, Gijselinck I, Dillen L, Van Langenhove T, Jessie Theuns J, Engelborghs S, Philtjens S, Vandenbulcke M, Sleegers K, Sieben A, Bäumer V, Maes G, Corsmit E, Borroni B, Padovani A, Archetti S, Pernecky R, Diehl-Schmid J, de Mendonça A, Miltenberger-Miltenyi G, Pereira S, Pimentel J, Nacmias B, Bagnoli S, Sorbi S, Graff C, Chiang H-H, Westerlund M, Sanchez-Valle R, Llado A, Gelpi E, Santana I, Almeida MR, Santiago B, Frisoni G, Zanetti O, Bonvicini C, Synofzik M, Maetzler W, vom Hagen JM, Schöls L, Heneka MT, Jessen F, Matej R, Parobkova E, Kovacs GG, Ströbel T, Sarafov S, Tournev I, Jordanova A, Danek A, Arzberger T, Fabrizi GM, Testi S, Salmon E, Santens P, Martin J-J, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Van Broeckhoven C on behalf of the European Early-Onset Dementia (EOD) Consortium. A Pan-European study of the C9orf72 repeat associated with FTL: geographic prevalence, genomic instability and intermediate repeats. *Human Mutation* 2013; **34**, 363-373.

Viegas LD, Stolz E, Canhão P, Ferro JM. Systemic Thrombolysis for Cerebral Venous and Dural Sinus Thrombosis: A Systematic Review. *Cerebrovascular Diseases* 2013; **37**, 43-50. (Journal IF: 2.814, Citations: 0)

### Other publications International

Martins IP, Caeiro L, Ferro J. Cognitive and behavioral disorders according to stroke site and side. *The Behavioral and Cognitive Neurology of Stroke*, 2nd Edition, Eds: Godefroy O. 2013:32-42.

Martins IP, Caeiro L, Ferro J. Right versus left hemisphere syndrome. *The Behavioral and Cognitive Neurology of Stroke*, 2nd Edition. Eds Godefroy, O., Bogousslavsky, J. 2013:617-636.

Abad A, Pompili A, Costa A, Trancoso I, Fonseca J, Leal G, Farrajota L, Martins IP. Automatic word naming recognition for an on-line aphasia treatment system. Eds. McCoy KF, John L, Ferres L, Fried-Oken M, and Roark B. *Computer Speech & Language, Special Issue on Speech and Language Processing for Assistive Technology* 2013; **27**, 1235–1248.

Neuropsychiatric symptoms of cerebrovascular diseases. Ferro JM Ed. Springer, London, 2013.  
Santos CO, Caeiro L, Ferro JM. Mania. Ferro JM Ed. *Neuropsychiatric symptoms of cerebrovascular diseases*. Springer, London, 2013: 65-80.

Caeiro L, Ferro JM. Apathy. Ferro JM Ed. *Neuropsychiatric symptoms of cerebrovascular diseases*. Springer, London, 2013: 109-130.

### Other publications National

Martins IP. Admissão ao Internato Complementar em Portugal: Análise dos Resultados do Exame Nacional de Seriação entre 2006 e 2011. *Acta Médica Portuguesa* 2013; **265**, 569-577. IF 0.151  
Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013.

Pavão I. Funções cognitivas. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013: 1-24.

Ferro JM. Perturbações da consciência. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013: 25-34.

Pavão I, Gouveia RG. Cefaleias. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013:57-70.

Ferro JM. Acidentes vasculares cerebrais. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013:101-112.

Mendonça A, Verdelho A. Declínio cognitivo e demência. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013:207-222.

Pimentel J, Ferro JM. Infecções do sistema nervoso central. Neurologia fundamental. Princípios e diagnóstico e tratamento. Coordenação Ferro JM, Pimentel J. *Lidel*, Lisbon, 2013:223-232.

### Invited lectures and seminars

Canhão P. Acidente isquémico transitório: Como abordar? 7º Congresso Português do AVC, Oporto, Portugal, January 31-February 2, 2013.

Canhão P. Complicações neurológicas da Gravidez. Congresso de Neurologia 2013, Lisbon, Portugal, November 6-9, 2013.

Canhão P. Prevenção secundário do AVC com os novos anticoagulantes orais. Que evidência existe?, 7º Congresso Português do AVC, Oporto, Portugal, January 31- February 2, 2013.

Ferro JM. Acute care management of ischemic stroke. EFNS Regional teaching course. Dakar, Senegal, July 11, 2013.

Ferro JM. Anticoagulation in CVT, which type and for how long. 8th National Conference of the Indian Stroke Association. Ludhiana, India, March 1-3, 2013.

Ferro JM. Approach to a patient with stroke in the young. 8th National Conference of the Indian Stroke Association. Ludhiana, India, March 1-3, 2013.

Ferro JM. Can Biomarkers help in detecting stroke etiology. Heart and Stroke 2013. New Dehli, India, November 8, 2013.

Ferro JM. Cerebral venous thrombosis. Stroke symposium 2013. Bern, Switzerland, March 14, 2013.

Ferro JM. Cerebral venous thrombosis. XXI World Congress of Neurology. Vienna, Austria, September 22, 2013.

Ferro JM. CVT trials: TO-ACT trial; DECOMPRESS registry; EXCOA study. 8th National Conference of the Indian Stroke Association. Ludhiana, India, March 1-3, 2013.

Ferro JM. En prévention. Actualités en neurologie vasculaire. 18èmes Journées de la SFNV. Paris, France, November 21, 2013.

Ferro JM. How far have we come? How far do we need to go? How can NOACS change stroke epidemics? II Thrombosis Forum Portugal 2013. Oporto, Portugal, November 2, 2013.

Ferro JM. Practical issues of the management of NOACS in AF patients - Neurologist' perspective. II Thrombosis Forum Portugal 2013. Oporto, Portugal, November 2, 2013.

Ferro JM. Repercussões neurológicas das doenças sistémicas. Congresso de Neurologia 2013. Lisbon, Portugal, November 6-9, 2013.

Ferro JM. Secondary prevention after cerebral infarction among young adults. Stroke in the Young. Bergen, Norway, April 26, 2013.

Ferro JM. Stroke related to pregnancy. XXI World Congress of Neurology. Vienna, Austria, September 23, 2013.

Ferro JM. The burden of AF and stroke. Heart and Stroke 2013. New Dehli, India, November 8, 2013.

Geraldes R. Potenciando a investigação nacional. Oportunidades de desenvolvimento da investigação médica. Biobanco-IMM, Lisbon, Portugal, November 13, 2013.

Martins IP. Porque é diferente a Neurologia. Fórum de Neurologia 2013, Coimbra, Portugal, May 9-11, 2013.

Martins IP. Cefaleias breves, pouco frequentes. Reunião de Primavera da Sociedade Portuguesa de Cefaleias. Lisbon, Portugal, April 19-20, 2013.

Martins IP. Classificação de outras cefaleias primárias. Reunião de Outono da Sociedade Portuguesa de Cefaleias. Coimbra, Portugal, October 18-19, 2013.

Martins IP. Perturbações específicas da linguagem e afasias adquiridas. VIII Congresso de Neuro-pediatria – Dilemas em epilepsia. Lisbon, Portugal, January 25, 2013.

Martins IP. Preparação de casos clínicos para publicação. Comunicar Ciência em Medicina. Centro Academico de Medicina de Lisboa. Gabinete de Apoio à Investigação Científica, Tecnológico e Inovação-GAPIC. Lisbon, Portugal, September 23, 2013.

Martins IP. Processamento cerebral da linguagem. Uma viagem interdisciplinar. XI Encontro Engenharia Biomédica FMUL/IST. Aula Magna da Faculdade de Medicina de Lisboa, Lisbon, Portugal, November 6, 2013.

Maruta C, Farrajota L, Maroco J, Martins IP, Guerreiro M, De Mendonça A. Speech Therapy in Primary Progressive Aphasia: A pilot study. Dementia Research Centre Lunchtime Meetings, UCL Institute of Neurology, London, UK, May 23, 2013.

Melo TP. Desafios comuns no tratamento do AVC agudo em doentes anticoagulados. 7º Congresso Português do AVC, Porto, Portugal, 31-2 January - February 2013 27. Verdelho A. Vascular risk factors and dementia. 23rd Meeting of the European Neurological Society. Barcelona, Spain, June 8-11, 2013.

### **Communications in International Conferences**

Aguiar de Sousa D, Ferro JM, Canhão P, Barinagarrementeria F, Boussier M-G, Stam J on behalf of the International Study on Cerebral Vein and Dural Sinus Thrombosis investigators. No association between severe thrombophilia and cerebral venous thrombosis severity. 23rd Meeting of the European Neurological Society. Barcelona, Spain, June 8-11, 2013. (Oral presentation)

Aguiar de Sousa D, Geraldés R, Almeida A, Canhão P. Carney complex in a young patient with ischemic stroke. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Aguiar de Sousa D, Pita Lobo P, Castro Caldas A, Coelho M, Albuquerque L. Pure ataxia associated with N-methyl-D-aspartate receptor antibodies. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Canhão P, Ferro JM, Barinagarrementeria F, Bousser M-G, Stam J, ISCVT investigators. Cerebral venous thrombosis associated with medications and medical procedures (iatrogenic CVT): ISCVT experience. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Carioca F, Canhão P. Blood biomarkers and recurrence of stroke in patients with transient ischaemic attack – a systematic review. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Carrasco G, Rybarczyk Y, Cardoso T, Martins IP. A Serious Game For Multimodal Training Of Physician Novices. ICERI 2013 Conference. Seville, Spain, November 18-20, 2013. (Poster presentation)

Castro Caldas A, Machado S, Fonseca AC, Evangelista T, Correia Guedes L, Albuquerque L, Coelho M. Spinocerebellar ataxia 7 associated with myopathy of tubular aggregates. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Coutinho J, Ferro JM, Zuurbier SM, Canhão P, Crassard I, Majoie CB, Reekers JA, Houdart E, de Haan RJ, Bousser M-G, Stam J. Thrombolysis or anticoagulation for cerebral venous thrombosis (TO-ACT TRIAL). XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Ferreira J, Franco A, Agostinho S, Santos C, Teodoro T, Coelho M, Albuquerque L. Vernet syndrome as a presentation of varicella-zoster virus infection. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Ferro JM, Canhão P, Coutinho J, Stam J, Bousser MG for the DECOMPRESS – 2 Steering Committee. Prospective registry of decompressive surgery for CVT patients - DECOMPRESS-2. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Fonseca AV, Brito D, Sampaio Matias J, Pinho e Melo T, Geraldés R, Canhão P, Caplan LR, Ferro JM. NT proBNP shows diagnostic accuracy for atrial fibrillation. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Franco AC, Ferreira J, Antunes AP, Peralta AR, Coelho M, Albuquerque L. Hail Mary prayer – an ictal manifestation of non-convulsive status epilepticus. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Geraldes R, Castro Caldas AC, Sousa D, Canhão P, Melo TP. Subachnoid hemorrhage with aneurysmal pattern and negative angiography: evaluation of long-term rebleeding. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Oral presentation)

Geraldes R, Silva C, Pita Lobo P, Soares F, Palha A. Giant cell arteritis as a cause of vertebrobasilar territory transient ischemic attacks in an elderly patient. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Gil-Gouveia R, Martins IP, Oliveira AG. Cognitive Dysfunction during a Migraine Attack – A Study on Migraine without Aura. International Headache Society Conference, Boston, USA, June 27-30, 2013. (Oral presentation)

Henriques I Gutiérrez-Fernández M, Rodriguez-Frutos B, Ramos J, Ferro J, Díez-Tejedor E. Hydrogen sulphide reduces infarct size and enhances recovery in a rat model: protection mechanism includes nox 4 downregulation. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Melo TP, Carvalho M, Cruz VT, Fernandes C, Silva FA, Ferreira C, Lopes G, Leitão A, Pinto AAN, Guerreiro R, Gabriel JP, Calado S, Rodrigues M, Ferro JM. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Miranda B , Ferro JM, Canhão P, Stam J, Boussier MG, Crassard I, Barinagarrementeria F, Massaro AR, on behalf of the EXCOA-CVT investigators. The benefit of Extending oral antiCOAgulant treatment after acute Cerebral Vein Thrombosis (EXCOA-CVT): a cluster observational study. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Rybarczyk Y, Fonseca J, Martins R. Lisling 3D: a serious game for the treatment of Portuguese aphasic patients. 12th AAATE, Vilamoura, Portugal, September 11-22, 2013. (Oral presentation)  
Santos AC, Ferro JM. Profile of anger in acute stroke. A multifactorial model of anger determinants. 22th European Stroke Conference. London, United Kingdom, May 28-31, 2013. (Poster presentation)

Teodoro T, Ferreira J, Franco A, Almeida V, Casimiro C, Coelho M, Ferro J, Albuquerque L. Vertebral artery dissection mimicking satus migarinous. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Teodoro T, Geraldes R, Batista P, Pimentel J, Albuquerque L, Peralta R. Giant cell arteritis and varicella zoster infection: Concomitant causes of temporal headache. XXI World Congress of Neurology, Vienna, Austria, September 21-26, 2013. (Poster presentation)

Verdelho A , Madureira S, Moleiro C, Ferro JM, Fazekas F, Barkhof F, Scheltens P, Schmidt R, Poggesi A, Inzitari D, Pantoni L on behalf of the LADIS study group. White matter changes and migraine in elderly subjects. Results of the LADIS study. 23rd Meeting of the European Neurological Society. Barcelona, Spain, June 8-11, 2013. (Oral presentation)

### Communications in National Conferences

Aguiar de Sousa D, Barata Tavares J, Pereira P, Teixeira J, Cattoni MB, Miguéns J, Pimentel J. Glioma centrado ao véu medular superior com extensão à região pineal. Congresso de Neurologia 2013. Lisbon, Portugal, November 6-9, 2013, (Poster presentation)

Carioca F, Canhão P. Biomarcadores sanguíneos e a recorrência de acidentes vasculares cerebrais em doentes com acidentes isquémicos transitórios: revisão sistemática da literatura. 7º Congresso Português do AVC. Oporto, January 31-February 2, 2013. (Poster presentation)

Castro Caldas A, Machado S, Fonseca A, Evangelista T, Guedes L, Albuquerque L, Coelho M. Ataxia espinocerebelosa tipo 7 associada a miopatia com agregados tubulares. Fórum de Neurologia, Coimbra, May 9-11, 2013. (Poster presentation)

Ferreira J, Franco A, Teodoro T, Santos C, Coelho M, Albuquerque L. Síndrome de Vernet pelo VEB na ausência de mononucleose infecciosa. Fórum de Neurologia, Coimbra, May 9-11, 2013. (Poster presentation)

Fonseca AC, Brito AC, Melo TP, Geraldes R, Canhão P, Ferro JM. NT-proBNP como biomarcador para detecção de fibrilhação auricular paroxística em doentes com AVC criptogénico. 7º Congresso Português do AVC. Oporto, January 31-February 2, 2013. (Oral presentation)

Fonseca AC, Geraldes R, Mas JL, Ferro JM. Investigação etiológica de AVC jovem em duas unidades de acidente vascular cerebral europeias. 7º Congresso Português do AVC. Oporto, January 31-February 2, 2013. (Oral presentation)

Fonseca J. Adaptação da Bateria Montreal de Avaliação da Comunicação (MAC) ao PE: resultados preliminares. VI Congresso Nacional da Associação Portuguesa dos Terapeutas da Fala. Instituto Superior de Ciências Sociais e Políticas. Lisbon, May 11, 2013. (Oral presentation)

Fonseca J. Avaliação online da linguagem na cirurgia cerebral. Escola Superior de Saúde do Instituto Politécnico de Setúbal. Setúbal, March 8, 2013. (Oral presentation)

Fonseca J. VITHEA – Sistema Virtual de Terapia de Afasia. III Conferência - Práticas Clínicas em Terapia da Fala. Auditório Casa de Saúde da Boavista. Oporto, March 23, 2013. (Oral presentation)

Fonseca J. VITHEA – Terapia Online da Afasia. VI Congresso Nacional da Associação Portuguesa dos Terapeutas da Fala. Instituto Superior de Ciências Sociais e Políticas. Lisbon, May 11, 2013. (Oral presentation)

Franco A, Teodoro T, Ferreira J, Viana P, Antunes P, Lobo P, Guedes L, Albuquerque L. Encefalite límbica anti-Ma2, miastenia gravis e timoma. Congresso de Neurologia 2013. Lisbon, November 6-9, 2013. (Poster presentation)

Geraldes R, Rego Sousa P, Fonseca AC, Canhão P, Melo TP. Hemorragia subaracnoideia não traumática da alta convexidade: prognóstico a longo prazo. 7º Congresso Português do AVC. Oporto, January 31, February 2, 2013. (Oral presentation)



Gil-Gouveia R. Utilidade Clínica do Mig-SCog. Reunião de Outono da Sociedade Portuguesa de Cefaleias. Coimbra, October 18-19, 2013. (Oral presentation)

Gil-Gouveia R, Oliveira AG, Martins IP. Uma curta bateria para avaliar a discunção cognitiva na enxaqueca. Reunião de Primavera da Sociedade Portuguesa de Cefaleias. Lisbon, April 19-20, 2013. (Oral presentation)

Gil-Gouveia R, Oliveira AG, Martins IP. Uma bateria para avaliar a disfunção cognitiva na Enxaqueca. Fórum de Neurologia 2013. Coimbra, May 9-11, 2013. (Poster presentation)

Pereira A, Antunes AP, Peralta R, Guedes L, Albuquerque L. Freezing como manifestação inicial de IFF e CJD. Fórum de Neurologia 2013. Coimbra, May 9-11, 2013. (Poster presentation)

Sousa D, Tavares J, Pimentel J, Albuquerque L. Pseudotumor inflamatório intracraniano. Fórum de Neurologia 2013. Coimbra, May 9-11, 2013. (Poster presentation)

Teodoro T, Ferreira J, Franco A, Almeida V, Casimiro C, Coelho M, Ferro JM, Albuquerque L. Dissecção da artéria vertebral mimetizando um estado de mal migranhoso. Congresso de Neurologia 2013. Lisbon, November 6-9, 2013. (Poster presentation)

Teodoro T, Geraldes R, Batista P, Pimentel J, Albuquerque L, Peralta R. Arterite de células gigantes "mascarada" por herpes zoster oftálmico. Congresso de Neurologia 2013. Lisbon, November 6-9, 2013. (Poster presentation)

Viana-Baptista M, Melo TP, Carvalho M, Tedim Cruz V, Fernandes C, Alves Silva F, Ferreira C, Lopes G, Leitão A, Nogueira Pinto AA, Guerreiro R, Gabriel JP, Calado S, Rodrigues M, Ferro JM, Investigadores PORTYSTROKE. Congresso de Neurologia 2013. Lisbon, November 6-9, 2013. (Oral presentation)

### **Organisation of Conferences**

Albuquerque L. organized the VI Congresso Nacional Associação Portuguesa de Neuro-Oncologia, in Hotel Melia Capuchos, Almada, November 15-16, 2013.

Canhão P. organized the 7º Congresso Português do AVC. Oporto, January 31-February 2, 2013.

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

Abad, A., Pompilia, A., Trancoso, I., Fonseca, J., Martins, I.P. (2013) VITHEA – Terapeuta Virtual para o tratamento de afasia. Conferencias Saúde CUF 2013. Leiria, Portugal.

Abad, A., Pompilia, A., Trancoso, I., Fonseca, J., Leal, G., Farrajota, L., Martins, I.P. (2013) VITHEA - Virtual Therapist for Aphasia treatment. Galardão da Inclusão na área da Investigação Aplicada do Centro de Recursos para a Inclusão Digital (CRID) da Escola Superior de Educação e Ciências Sociais - Instituto Politécnico de Leiria (IPL). Leiria, Portugal.

Menção Honrosa Comunicação Oral to Ana Catarina Fonseca. 7º Congresso do AVC, Oporto, Portugal, in 2013.

2º Prémio Cartaz to Filipa Carioca and Patrícia Canhão. 7º Congresso do AVC, Oporto, Portugal, in 2013.

### **Industry contract research**

2009/2013 - Ensaio multicêntrico internacional AVAGLIO. Promotor Hoffman-LaRoche – A randomized, double blind, placebo controlled, multicenter Phase III trial of bevacizumab, temozolomide and radiotherapy, followed by bevacizumab and temozolomide versus placebo, temozolomide and radiotherapy followed by placebo and temozolomide in patients with newly diagnosed glioblastoma – Luisa Albuquerque, Conceição Lourenço e Mónica Semedo – Serviço de Oncologia, HSM.

2013/ - Ensaio multicêntrico internacional 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 – Albuquerque, L., Sousa, D., Macedo, D., Abreu, C.- Serviço de Oncologia, HSM.

2013/ - 24 week international, multi-centre, randomized, double-blind, placebo controlled phase II b study. Efficacy and safety of 3 doses of s 38093 versus placebo, in patients with moderate Alzheimer's disease. Alexandre de Mendonça, Manuela Guerreiro, Vanda Freitas e Carolina Maruta (Servier).

2013/ - Multicenter, randomized, double-blind, placebo-controlled, parallel-group two year study to evaluate the effect of subcutaneous RO4909832 on cognition and function in prodromal Alzheimer's disease Alexandre de Mendonça, Manuela Guerreiro, Ana Verdelho, Frederico Couto, Vanda Freitas e Carolina Maruta (Roche).

### **Advanced teaching**

Caeiro L. Description of cases. Case-series. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 18, 2013.

Caeiro L. Diagnostic traps in post stroke dementia, depression, apathy etc. European Master in Stroke Medicine, Krems, Austria, October 24, 2013.

Caeiro L. How to evaluate cognition in the follow-up of stroke patients? European Master in Stroke Medicine, Krems, Austria, October 24, 2013.

Canhão P. Basic tools of clinical research in neurosciences: defining the research question and the study protocol. Study designs. Random and systematic errors. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 11, 2013.

Canhão P. Cohort studies. Prognosis. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 9, 2013.

Canhão P. Desenho e análise de estudos de prognóstico. Análise crítica. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML. Lisbon, Portugal, June 14, 2013.

Canhão P. Exemplos práticos. Aplicação e impacto de modelos de prognóstico no processo de decisão clínica. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 15, 2013.

Canhão P. Exercício prático: desenvolver um modelo de prognóstico numa coorte prospectiva. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 15, 2013.

Canhão P. Introdução e apresentação do módulo. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 14, 2013.

Canhão P. Limitações actuais da investigação em prognóstico. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 15, 2013.

Canhão P. Module Coordinator: Research in Clinical Neurosciences. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, 2013.

Ferro JM. Anxiety and disorders of emotional control. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Ferro JM. Case-control studies. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 16, 2013.

Ferro JM. Delirium and related disorders. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Ferro JM. Executive deficits. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Ferro JM. Mood disorders. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Ferro JM. Vegetative state. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, December 18, 2013.

Ferro JM. Visual agnosias. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Ferro JM. Acute and long-term prevention of cardioembolic stroke. ESO Stroke Summer School. Perugia, Italy, September 12, 2013.

Ferro JM. Causation studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, May 3, 2013.

Fonseca AC. Validação de modelos de prognóstico. Exercício prático: análise crítica de estudos de validação de modelos de prognóstico. Prognostic studies, Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 15, 2013.

Fonseca J. “Metodologias de avaliação linguística na afasia”. 3ª Pós-Graduação em Perturbação Neurológicas da Comunicação no Adulto – 3ª Edição. CRIAP, Oporto, Portugal, November 16, 2013.

Guerreiro M. “Cognitive Rehabilitation”. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 21, 2013.

Guerreiro M. “Episodic memory”. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 14, 2013.

Martins .P. “Neglect”. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Martins IP. "Como preparar um caso clínico para publicação". Módulo de Introdução do Curso de Investigação Clínica do CAML, Lisbon, Portugal, March 16, 2013.

Martins IP. “Aphasia, recovery of language and brain reorganization after brain lesions”. Master in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, March 5, 2013.

Martins IP. “General Introduction Aphasia”. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Martins IP. “Memory disorders”. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Martins IP. “Neuroimagiologia”. Mestrado em Engenharia Biomédica, Instituto Superior Técnico. Lisbon, Portugal, December 4, 2013.

Martins IP. “Reading and Writing Disorders”. European Master in Stroke Medicine, Krems, Austria, October 23, 2013.

Santos AC. Individualizar o prognóstico: factores de prognóstico e modelos de prognóstico. Análise multivariada. Calibração e discriminação. Prognostic studies. Introduction to Clinical Research: a practical course. Programa Doutoral do CAML, Lisbon, Portugal, June 14, 2013.

Santos C. How to develop, validate and apply questionnaires. Master in Neurosciences. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, April 23, 2013.

### **Science and society**

Fonseca J. O treinador das palavras. Plataforma VITHEA, Portugal faz bem, Revista Exame Informática, January, 2013.

Fonseca J. O treinador das palavras. Plataforma VITHEA, Exame Informática TV, SIC Notícias, January 10, 2013.

Martins IP. Maruta C, Fonseca J. Dia da Investigação na FMUL. Visita ao Laboratório de Estudos de Linguagem, inserido nas visitas às Unidade de Investigação, December 11, 2013.

Canhão P. Organização das comemorações do dia Nacional do Doente com AVC, March 31, 2013.

### **PhD theses completed**

Ana Isabel Figueira Verdelho (2013) Clinical implications of cerebral age-related white matter cerebral changes. Faculdade de Medicina da Universidade de Lisboa. Supervisor: José M. Ferro.

Lara Isabel Pires de Melo Caeiro (29/11/2013) Apatia na fase aguda do AVC e alteração da personalidade após AVC. Faculdade de Medicina da Universidade de Lisboa. Supervisor: José M. Ferro.

### **Msc theses completed**

Helena Bárrios (2013) Quality of life in patients with Mild Cognitive Impairment. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Alexandre Mendonça.

Sandra Cardoso (2013) Non-literal language in Mild Cognitive Impairment. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Alexandre Mendonça.

## LUÍSA FIGUEIREDO LAB

### Major Interests / Objectives

*Trypanosoma brucei* is a unicellular parasite that, in humans, causes a fatal disease called African sleeping sickness. While in the bloodstream, the parasite evades its host immune system through antigenic variation; specifically, it periodically switches from one dense, uniform coat of variant surface glycoprotein (VSG) to an antigenically distinct one.

Although the *T. brucei* genome contains hundreds of VSG genes, all but one are transcriptionally silenced. Such transcriptional changes do not involve alterations in the DNA sequence but are inherited nevertheless, which indicates that VSG transcription is under epigenetic control. Our goal is to identify and characterize the factors involved in the epigenetic control of VSG gene expression.

### 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	MSc Student
Carla Andrea Sequeira Bejarano	Undergraduate	Undergraduate (started August)
Daniel Pinto de Oliveira Gonçalves Neves	Graduate	MSc Student
Diogo Maia e Silva	Undergraduate	Undergraduate (started April)
Fabien Marc Guegan	PhD	Post-doctoral Investigator
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	Graduate	MSc Student (started July)
Leonor Duarte Pinho	Master	Lab manager (started July)
Mafalda Ramos de Melo Pimentel	Master	MSc Student
Sandra Isabel Gonçalves Trindade	PhD	Post-doctoral Investigator

### Keywords / Research Areas

Antigenic variation, chromatin, gene expression, parasitology, infection, chromatin.

### Major scientific achievements

Co-organizer of EMBO Young Scientists' Forum. IMM, Lisboa, Portugal.

Session chairman at Kinetoplastid Molecular Cell Biology meeting, Woods Hole, MA, USA.

AXA post-doctoral fellowship awarded to Fabien Guegan, a fellow in my group.

### Recent Most Relevant Publications

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: 3.395, Citations: 15)

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: 32.406, Citations: 30)

Siegel TN, Hekstra DR, Kemp LE, Figueiredo LM, Lowell JE, Fenyo D, Wang X, Dewell S, Cross GAM (2009) Four histone variants mark the boundaries of polycistronic transcription units in *Trypanosoma brucei*. *Genes Dev* **23**, 1063-1076. (Journal IF: 12.889, Citations: 88)

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: 20.686, Citations: 41)

Figueiredo LM, Janzen CJ, Cross GAM (2008) A histone methyltransferase modulates antigenic variation in African trypanosomes. *PLoS Biol* **6**, e161. (Journal IF: 12.472, Citations: 45)

### Ongoing Research Projects

2010/2014 HistoneH1Tryp. Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes. Coordinator: Luisa Miranda Figueiredo. Agency: FP7. Amount: €100.000,00

2011/2015 Embo Instalation Grant. Coordinator: Luisa Miranda Figueiredo. Agency: PRIV-UE. Amount: €250.000,00

2011/2013 Prémio Crioestaminal. Coordinator: Luisa Miranda Figueiredo. Agency: PRIV-NAC. Amount: €20.000.00

2011/2014 The role of histone H1 in antigenic variation of African trypanosomes. Coordinator: Luisa Miranda Figueiredo. Agency: FCT. Amount: €189.828,00

2011/2014 Screening of chromatin factors involved in antigenic variation in *Trypanosoma brucei*. Coordinator: Luisa Miranda Figueiredo. Agency: FCT. Amount: 113.407,00

2012/2014 Embo Small Grant. Coordinator: Luisa Miranda Figueiredo. Agency: PRIV-UE. Amount: €5.000,00

2012/2017 Howard Hughes Medical Institute. Coordinator: Luisa Miranda Figueiredo. Agency: Howard Hughes Medical Insti. Amount: €560.000,00

2013/2015 Postdoctoral Sponsorship Agreement – Fellow Fabien Guegan. Estudo do papel dos long non-coding RNA na infecção e transmissão de *Trypanosoma brucei*. Coordinator: Luisa Miranda Figueiredo. Agency: AXA SA. Amount: €120.000,00

### Other publications International

Figueiredo LM and Horn D (2013). *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. Functions of lncRNA and histone H1 in *T. brucei*. Centre for Genomic Regulation. Barcelona, Spain, March, 2013.

### Communications in International Conferences

Pena A, Figueiredo LM. Histone H1 regulates a specific set of genes and is important for virulence in *Trypanosoma brucei*. 30th Annual Swiss Trypanosomatid Meeting. Leysin, Swiss. January, 2013 (Oral communication)

Figueiredo LM. Chromatin and antigenic variation in *T. brucei*. 30th Annual Swiss Trypanosomatid Meeting. Leysin, Swiss. January, 2013 (Oral communication)

Pena A, Pimentel M, Manso H, Ferreira AF, Neves D, Aresta-Branco F, Guegan F, Coelho LP, Figueiredo LM. Histone H1: a linker between chromatin, gene expression and virulence in *T. brucei*. Kinetoplastid Molecular Cell Biology Meeting. Marine Biological Laboratory, Woods Hole, MA, USA. April, 2013 (Oral communication)

Aresta-Branco F, Pimentel M, Figueiredo LM. Open chromatin of the VSG Expression Site is maintained independently of transcription in *Trypanosoma brucei*. Kinetoplastid Molecular Cell Biology Meeting. Woods Hole, Massachusetts, United States of America. April, 2013 (Poster presentation)

Figueiredo LM. Chromatin dynamics and VSG gene regulation in African trypanosomes. EMBO Young Scientists' Forum. IMM, Lisbon, Portugal. July 2013 (Oral communication)



Maia-Silva D, Guegan F, Figueiredo LM. Do long noncoding RNAs regulate *T. brucei* differentiation? Annual International Medical Students (AIMS) meeting. Lisbon, Portugal, December, 2013 (Awarded second best poster presentation)

Aresta-Branco F, Pimentel M, Figueiredo LM. Open chromatin of the VSG Expression Site is maintained independently of transcription in *Trypanosoma brucei*. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Guegan F, Kedra DA, Notredame C, Figueiredo LM. Long non-coding RNA in *Trypanosoma brucei* parasites. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Trindade S, Carvalho T, Ferreira AF, Itoe MA, Figueiredo LM. Tissue tropism of *Trypanosoma brucei*: causes and consequences. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Ferreira AF, Carvalho T, Trindade S; Takahashi JS, Figueiredo LM. A mouse model to study circadian rhythm changes during an infection by *Trypanosoma brucei*. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Vaz MS, Mendes AM, Figueiredo LM, Prudêncio M. Trypanosomes inhibit Plasmodium liver stage. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Pena AC, Pimentel M, Manso H, Ferreira AF, Neves D, Aresta-Branco F, Guegan F, Coelho LP, Figueiredo LM. Histone H1 controls the expression of a specific set of genes and it is important for virulence of African trypanosomes. EMBO Young Scientists' Forum, Instituto de Medicina Molecular, Lisbon, Portugal, July, 2013 (Poster presentation)

Ferreira AF, Carvalho T, Trindade S; Takahashi JS, Figueiredo LM. A mouse model to study circadian rhythm changes during an infection by *Trypanosoma brucei*. European Biological Rhythms Society, Ludwig-Maximilians-University, Munich, Germany, August, 2013 (Poster presentation)

Ferreira AF, Carvalho T, Trindade S; Takahashi JS, Figueiredo LM. A mouse model to study circadian rhythm changes during an infection by *Trypanosoma brucei*. HHMI Science meeting 2013. Janelia Farm Research Campus, Ashburn, Virginia, United States of America, September, 2013 (Poster presentation)

Manso H, Neves D, Pimentel M, Pena AC, Figueiredo LM. Histone H1 depletion controls trans-splicing in *Trypanosoma brucei*. EMBO Practical Course Analysis of High-Throughput Sequencing Data. European Bioinformatics Institute, Cambridge, United Kingdom, October, 2013 (Poster presentation)

Aresta-Branco F and Figueiredo LM. Formaldehyde-assisted isolation of regulatory elements (FAIRE): where is "open chromatin"? EMBO Young Investigator PhD Course 2013. EMBL campus. Heidelberg, Germany, December, 2013 (Poster presentation)

### Communications in National Conferences

Vaz MS, Mendes AM, Prudêncio M, Figueiredo LM. African trypanosomes inhibit Plasmodium liver stage infection. Fighting NTDs in Portuguese-speaking African countries, Fundação Calouste Gulbenkian, Lisbon, Portugal. October, 2013. (Oral Communication)

Ferreira AF, Takahashi JS, Figueiredo LM. *Trypanosoma brucei* interferes with the mouse circadian rhythm. IMM PhD Meeting 2013. Instituto de Medicina Molecular, Lisbon, Portugal, December, 2013 (Oral communication)

Pena AC, Pimentel M, Manso H, Neves D, Aresta-Branco F, Ferreira AF, Guegan F, Coelho LP, Figueiredo LM. Histone H1 regulates a small set of genes but is important for virulence of African trypanosomes. IMM PhD Meeting 2013. Instituto de Medicina Molecular, Lisbon, Portugal, December, 2013 (Oral communication)

Ferreira AF, Takahashi JS, Figueiredo LM. *Trypanosoma brucei* accelerates mouse circadian rhythm. GABBA PhD program. Universidade do Porto, Oporto, Portugal, December, 2013. (Oral communication)

### 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.

Co-organizer of the EMBO Young Scientists' forum, Lisbon, July, 2013.

The EMBO Young Scientists' Forum aimed to bring together young European researchers in order to motivate and inspire students to pursue their career and education in life sciences. The meeting provided the opportunity to European and Portuguese Ph.D. students, post-docs and junior investigators to interact with Europe's most promising young scientists, members of the EMBO Young Investigator Programme. Younger scientists (students and post-docs) had the possibility to present their work as short talks and as posters. Poster sessions and a social event provided friendly environment for informal discussions of the policies and practices for doing world-class science.

### Internationalisation

Our research group acts internationally at several levels. First, by presenting our work and acting as chairman in international meetings (EMBO Young Scientists' Forum - Lisboa and Kinetoplastid Molecular Cell Biology Meeting - USA); second by establishing and maintaining collaborations (Gerald Spaeth, Institut Pasteur, France; Cedric Notredame, Center for Genomic Regulation,

Spain; Nicolai Siegel, University of Wuerzburg, Germany); third by acting as reviewer for several international journals including Nucleic Acids Research, Journal of Cell Science and Eukaryotic Cell; finally by hosting a summer undergraduate from an EMBO-sponsored partnership with Cabo Verde.

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

AXA post-doctoral fellowship awarded to Fabien Guegan, a fellow in my group. The mission of AXA Research Fund is to boost scientific progress and discoveries that contribute to understand and better prepare against environmental, life and socio-economic risks. The 30 grantees were assessed by well-recognized referees and an independent scientific board composed of world class experts with robust and transparent selection processes. Fabien Guegan, a fellow in my group, was the only AXA-awardee in a Portuguese research institute.

### **Advanced teaching**

Main examiner in PhD juri of Raquel de Sá da Silva Lares. Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa. “*Trypanosoma brucei* peptidase inhibitors. Immunolocalization, secretion and potential use as targets for therapy” January 2013.

Figueiredo LM. 2 hour lecture for students of Masters in Biomedical Sciences, IHMT, Lisbon, Portugal. “What can the post-genomic era teach us about chromatin structure and gene regulation?” February 2013

Figueiredo LM. 3 hour lecture for students of Masters in Evolution and Development Biology, FCUL, Lisbon, Portugal. “Mouse model to study circadian rhythm and understand how trypanosomes cause sleeping sickness” November 2013

### **Science and society**

Figueiredo LM. Casos que nos inspiram: investigadores de sucesso em Portugal. Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa. Lisbon, Portugal, January 2013.

### **Msc theses completed**

Ana Margarida Vaz (2013) The reciprocal influence of Malaria and Sleeping Sickness co-infection. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Luisa Figueiredo and Miguel Prudêncio.

**JOÃO EURICO FONSECA LAB****Major Interests / Objectives**

The João Eurico Fonseca Lab results from a partnership between the IMM/FML and the Rheumatology Department of the Santa Maria Hospital. Is devoted to the translational study of the early burden of inflammatory rheumatic diseases on bone and vessel, seeking prognostic markers, predictors of treatment response and new treatment targets. We have created a network of biologists, biomedical engineers and physicians, sharing a common mission, goals and values, which allow the ongoing pattern of a highly interactive work that is leading the translational research in the field of Rheumatology in Portugal. The long-term objective of the Lab is to achieve recognition as an European League Against Rheumatism Centre of Excellence in Rheumatology.

**Head of Unit**

João Eurico Fonseca, MD/PhD/ Professor FMUL.

**Research Team**

Ana Catarina Coimbra do Vale	No degree	PhD Student
Ana Filipa Mourão	No degree	Investigator
Ana Filipa Rodrigues Lopes	Master	Lab manager
Ana Henrique Baptista Daniel	Graduate	MSc Student (started September)
Ana Maria Ferreira Rodrigues	Graduate	PhD Student
Ana Rita Cascão Rodrigues	PhD	PhD Student
Ana Rita Fernandes Vieira	Graduate	MSc Student (started March)
António José Nicolau Marques Fernandes	Graduate	MSc Student (started November)
Bruno Miguel Costa Vidal	Graduate	PhD Student
Cláudia Cristina Valente Quaresma	Graduate	Investigator (started April)
Diana de Almeida Carmona Fernandes	Master	PhD Student
Elsa Cristina Vieira de Sousa	Graduate	Investigator

Filipe Carlos Pereira dos Reis Cortes Figueiredo	No degree	MSc Student (started November)
Helena Cristina de Matos Canhão	MD/PhD	Principal Investigator
Inês Pedro Perpétuo	Master	PhD Student
Joana Ribeiro Caetano Lopes	PhD	Post-doctoral Investigator
Joaquim Miguel Polido Pereira	No degree	Investigator
Luísa Sofia Campos Magalhães Garcia	Graduate	MSc Student (started October)
Marco Aurélio Carmelino Cardoso Sarmento	Graduate	Investigator
Maria Helena Regalo da Fonseca	MD/PhD	Principal Investigator (started March)
Maria João Gonçalves	Master	Investigator, MD (started March)
Maria José Parreira dos Santos	MD/PhD	Investigator, Associate Professor
Mónica Cristina Medina Lopes	Graduate	MSc Student (left November)
Rita Alexandra Pedra Aguiar de Moura	PhD	Post-doctoral Investigator
Rita Maria Mendes Raposeiro	Graduate	MSc Student (started September)
Saba Abdulghani Oliveira da Silva	PhD	Post-doctoral Investigator
Tânia da Cunha Branco dos Santos	Graduate	Investigator
Vanessa Sofia de Oliveira Artilheiro	Undergraduate	MSc Student
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;
- 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.

### Recent Most Relevant Publications

Visser K, Katchamart W, Loza E, Martinez-Lopez JA, Salliot C, Trudeau J, Bombardier C, Carmona L, van der Heijde D, Bijlsma JW, Boumpas DT, Canhao H, et al. (2009) Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. *Ann Rheum Dis.* **68**, 1086-1093. (Journal IF: 9.111, Citations: 128)

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: 7.975, Citations: 104)

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: 9.111, Citations: 38)

Fonseca JE, Cortez-Dias N, Francisco A, Sobral M, Canhão H, Resende C, Castelão W, Macieira C, Sequeira G, Saraiva F, da Silva JA, Carmo-Fonseca M, Viana Queiroz M. (2005) Inflammatory cell infiltrate and RANKL/OPG expression in rheumatoid synovium: Comparison with other

inflammatory arthropathies and correlation with outcome. *Clin Exp Rheumatol.* **23**, (2):185-192. (Journal IF: 2.655, Citations: 29)

Cascão R, Vidal B, Raquel H, Neves-Costa A, Figueiredo N, Gupta V, Fonseca JE, Moita LF (2012) Effective treatment of rat adjuvant-induced arthritis by celastrol. *Autoimmun Rev.* **11**, 856-62. (Journal IF: 7.975, Citations: 7)

### Ongoing Research Projects

2012/2015 How inflammation early affects bone's nano-properties at arthritis onset. Coordinator: João Eurico Fonseca. Agency: UCB Celltech. Amount: €50.000,00

2012/2015 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: PRIV-NAC. Amount: €85.000,00

2011/2013 Clinical, serological and genetic predictors of evolution, outcome and response to treatment in Portuguese patients with Juvenile Idiopathic Arthritis. Coordinator: Ana Filipa Mourão. Agency: PRIV-NAC. Amount: €108.000,00

2012/2014 Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis. Coordinator: João Eurico Fonseca. Agency: MSD. Amount: €30.000,00

2011/2013 Fabry and Gaucher diseases investigation in Juvenile Idiopathic Arthritis patients. Coordinator: Helena Cristina de Matos Canhão. Agency: Shire Pharmaceuticals Portugal. Amount: €19.000,00

2010/2013 Response to anti-TNF treatment biomarkers in Rheumatoid Arthritis . Coordinator: Helena Cristina de Matos Canhão. Agency: FCT. Amount: €398.618,00

2011/2013 Collaboration in “A National Genome Wide Association Study to Predict the Response to Anti-TNF Treatment in Rheumatoid Arthritis”. Coordinator: Helena Cristina de Matos Canhão. Agency: Abbott Laboratorios, Lda. Amount: €100.000,00

2012/2014 Linking biomechanics and the immune system in early Psoriatic Arthritis – a translational approach. Coordinator: Elsa Sousa. Agency: Laboratórios Pfizer, Lda. Amount: €51.800,00

2012/2016 Predictors of atherosclerosis progression in patients with rheumatoid arthritis over a period of 5 years: focus on adipose tissue and inflammation . Coordinator: Maria José Santos. Agency: Fundação AstraZeneca. Amount: €15.000,00

2013/2014 Inhibition of bone and cartilage degradation in rat induced arthritis treated with tofacitinib. Coordinator: João Eurico Fonseca. Agency: Laboratórios Pfizer, Lda. Amount: €50.000,00

2012/2014 Golimumab as first line DMARD therapy in MTX naive psoriatic arthritis - a 24 weeks

efficacy and safety study focusing on dactylitis and enthesitis. Coordinator: Elsa Sousa. Agency: Merck Sharp & Dohme. Amount: €114.350, 00.

### Other Projects

2011/2014 Portuguese Epidemiologic Study of Rheumatic Diseases – EpiReumaPt. Coordinator: Helena Canhão.

2006/2013 National and International Guidelines for the diagnosis and treatment of rheumatic diseases, Portuguese Society of Rheumatology. Coordinator: João Eurico Fonseca, Helena Canhão, Maria José Santos.

2006/2013 Research Projects involving National and International Databases and Registries. Cooperation with Institutional Health Organizations. Coordinator: Helena Canhão.

### Publications in peer review Journals

Carmona-Fernandes D, Santos MJ, Canhão H, Fonseca JE.(2013) Anti-ribosomal P protein IgG autoantibodies in patients with systemic lupus erythematosus: diagnostic performance and clinical profile.*BMC Med.* **4**, (11):98. (Journal IF: 6.679, Citations: 1)

Cui J Stahl EA Saevarsdottir S Miceli C Diogo D Trynka G Raj T Mirkov MU Canhao H Ikari K Terao C Okada Y Wedrén S Askling J Yamanaka H Momohara S Taniguchi A Ohmura K Matsuda F Mimori T Gupta N Kuchroo M Morgan AW Isaacs JD Wilson AG Hyrich KL Herenius M Doorenspleet ME Tak PP Crusius JB van der Horst-Bruinsma IE Wolbink GJ van Riel PL van de Laar M Guchelaar HJ Shadick NA Allaart CF Huizinga TW Toes RE Kimberly RP Bridges SL Jr Criswell LA Moreland LW Fonseca JE de Vries N Stranger BE De Jager PL Raychaudhuri S Weinblatt ME Gregersen PK Mariette X Barton A Padyukov L Coenen MJ Karlson EW Plenge RM. (2013) Genome-Wide Association Study and Gene Expression Analysis Identifies CD84 as a Predictor of Response to Etanercept Therapy in Rheumatoid Arthritis. *PLoS Genet.* **9**, (3):e1003394. (Journal IF: 8.517, Citations: 0)

Caetano-Lopes J, Rodrigues A, Lopes A, Vale AC, Pitts-Kiefer MA, Vidal B, Perpétuo IP, Monteiro J, Kontinen YT, Vaz MF, Nazarian A, Canhão H, Fonseca JE.(2013) Rheumatoid Arthritis Bone Fragility Is Associated With Upregulation of IL17 and DKK1 Gene Expression. *Clin Rev Allergy Immunol.* 2013 Apr 2. (<http://link.springer.com/article/10.1007%2Fs12016-013-8366-y>) (Journal IF: 5.590, Citations: 0)

Romão VC, Canhão H, Fonseca JE. (2013) Old drugs old problems: where do we stand in prediction of rheumatoid arthritis responsiveness to methotrexate and other synthetic DMARDs? *BMC Med.* **23**, 11:17. (Journal IF: 6.679, Citations: 0)

Vale A, Pereira M, Maurício A, Vidal B, Rodrigues A, Caetano-Lopes J, Nazarian A, Fonseca J, Canhão H, Vaz M.(2013) Micro-computed tomography assessment of human femoral trabecular bone for two disease groups (fragility fracture and coxarthrosis): age and gender related effects



on the microstructure. *Journal of Biomedical Science and Engineering* **6**, 175-184. (Journal IF: 0.27, Citations: 0)

Costa N, Pires AE, Gabriel AM, Goulart LF, Pereira C, Leal B, Queiros AC, Chaara W, Moraes-Fontes MF, Vasconcelos C, Ferreira C, Martins J, Bastos M, Santos MJ, Pereira MA, Martins B, Lima M, João C, Six A, Demengeot J, Fesel C. (2013) Broadened T-cell repertoire diversity in Ivlg-treated SLE patients is also related to the individual status of regulatory T-cells. *J Clin Immunol.* **33**, (2):349-60. (Journal IF: 3.382, Citations: 1)

Moura RA, Canhão H, Polido-Pereira J, Rodrigues AM, Navalho M, Mourão AF, Resende C, Campanilho-Marques R, Dias JM, da Silva JA, Graca L, Fonseca JE. (2013) BAFF and TACI Gene Expression Are Increased in Patients with Untreated Very Early Rheumatoid Arthritis. *J Rheumatol.* **40**, 1293-302. (Journal IF: 3.258, Citations: 1)

Navalho M, Resende C, Rodrigues AM, Pereira da Silva JA, Fonseca JE, Campos J, Canhão H. (2013) Bilateral evaluation of the hand and wrist in untreated early inflammatory arthritis: a comparative study of ultrasonography and magnetic resonance imaging. *J Rheumatol.* **40**, 1282-92. (Journal IF:3.258, Citations: 0)

Plenge RM, Greenberg JD, Mangravite LM, Derry JM, Stahl EA, Coenen MJ, Barton A, Padyukov L, Klareskog L, Gregersen PK, Mariette X, Moreland LW, Bridges SL Jr, de Vries N, Huizinga TW, Guchelaar HJ; International Rheumatoid Arthritis Consortium (INTERACT), Friend SH, Stolovitzky G. Collaborators: Cui J, Stahl EA, Saevarsdottir S, Miceli C, Diogo D, Mirkov, Canhao H, Ikari K, Terao C, Okada Y, Wedri S, Askling J, Yamanaka H, Momohara S, Taniguchi A, Ohmura K, Matsuda F, Mimori T, Gupta N, Kuchroo M, Morgan AW, Isaacs JD, Wilson AG, Hyrich KL, Herenius M, Doorenspleet ME, Tak PP, Crusius JB, van der Horst-Bruinsma IE, Wolbink GJ, van Riel PL, van de Laar M, Guchelaar HJ, Shadick NA, Allaart CF, Huizinga TW, Toes RE, Kimberly RP, Bridges S Jr, Criswell LA, Moreland LW, Fonseca E, de Vries N, Raychaudhuri S, Weinblatt ME, Gregersen PK, Mariette X, Barton A, Alfredsson L, Klareskog L, Padyukov L, Coenen MJ, Karlson EW, Kremer J, Greenberg JD, Plenge RM. (2013) Crowdsourcing genetic prediction of clinical utility in the Rheumatoid Arthritis Responder Challenge. *Nat Genet.* **45**, (5):468-9. (Journal IF:35.209, Citations: 1)

Vale AC, Faustino J, Reis L, Lopes A, Vidal B, Monteiro J, Fonseca JE, Canhao H, Vaz MF. (2013) Effects of the Shear Strain Rate on the Torsion of Human Trabecular Bone. *J Biomech Eng.* Sep 1 (Waiting IF, Citations: 0)

Lin C, Karlson EW, Canhao H, Miller TA, Dligach D, Chen PJ, Perez RN, Shen Y, Weinblatt ME, Shadick NA, Plenge RM, Savova GK. (2013) Automatic prediction of rheumatoid arthritis disease activity from the electronic medical records. *PLoS One.* **16**, 8(8):e69932. (Journal IF: 3.730, Citations: 0)

Vale AC, Aleixo IP, Lúcio M, Saraiva A, Caetano-Lopes J, Rodrigues A, Amaral PM, Rosa LG, Monteiro J, Fonseca JE, Vaz MF, Canhão H. (2013) At the moment of occurrence of a fragility hip fracture, men have higher mechanical properties values in comparison with women. *BMC Musculoskelet Disord.* **16**, 14:295 (Journal IF: 1.875)

Cáliz R, Canet LM, Lupiañez CB, Canhãõ H, Escudero A, Filipescu I, Segura-Catena J, Soto-Pino MJ, Expósito-Ruiz M, Ferrer MÁ, García A, Romani L, González-Utrilla A, Vallejo T, Pérez-Pampin E, Hemminki K, Försti A, Collantes E, Fonseca JE, Sainz J. Gender-Specific Effects of Genetic Variants within Th1 and Th17 Cell-Mediated Immune Response Genes on the Risk of Developing Rheumatoid Arthritis. *PLoS One*. **30**, 8(8):e72732. (Journal IF: 3.730, Citations: 0)

Laires PA, Mesquita R, Veloso L, Martins AP, Cernadas R, Fonseca JE.(2013)Patient's access to healthcare and treatment in rheumatoid arthritis: the views of stakeholders in Portugal. *BMC Musculoskelet Disord*. **25**, 279 (Journal IF: 1.875)

Bettencourt BF, Rocha FL, Alves H, Amorim R, Caetano-Lopes J, Vieira-Sousa E, Pimentel-Santos F, Lima M, Porto G, Branco JC, Fonseca JE, Bruges-Armas J. (2013) Protective effect of an ERAP1 haplotype in ankylosing spondylitis: investigating non-MHC genes in HLA-B27-positive individuals. *Rheumatology* **52**, 2168-76 (Journal IF: 4.212)

Gonçalves MJ, Rodrigues AM, Canhãõ H, Fonseca JE.(2013) Osteoporosis: From Bone Biology to Individual Treatment Decision. *Acta Med Port*. **26**, (4):445-455. (Journal IF: 0.695, Citations: 0)

Fonseca JE. (2013) Biobanco-IMM, Lisbon Academic Medical Centre: A Case Study. *Acta Med Port*. **26**, (4):312-4. (Journal IF: 0.695, Citations: 0)

Reis C, Mestre C, Canhãõ H. (2013) Prevalence of fatigue in a group of airline pilots. *Aviat Space Environ Med*. **84**, (8):828-33. (Journal IF: 0.782, Citations: 0)

Marques A, Mota A, Canhãõ H, Romeu JC, Machado P, Ruano A, Barbosa AP, Dias AA, Silva D, Araújo D, Simões E, Aguas F, Rosendo I, Silva I, Crespo J, Alves JD, Costa L, Mascarenhas M, Lourenço O, Ferreira PL, Lucas R, Roque R, Branco JC, Tavares V, Johansson H, Kanis J, Pereira da Silva JA. A FRAX model for the estimation of osteoporotic fracture probability in Portugal. *Acta Reumatol Port*. **38**, 104-112 (Journal IF: 0.695, Citations: 0)

Santos MJ (2013) Systemic rheumatic diseases: beyond classification criteria. *Acta Reumatol Port*. **38**, 7-8. (Journal IF: 0.695, Citations: 0)

C. Ponte, E. Vieira-Sousa, F. Saraiva, R. Sousa, A. Francisco, S. Livraghi, J.C. Romeu, J.A. Pereira da Silva.(2013) Acute Low Back Pain - A Clinical and Imaging Challenge. *Acta Reumatol Port*. **2**, 133-135. (Journal IF: 0.695, Citations: 0)

### Other publications International

Aleixo I, Vale AC, Lucio M, Amaral PM, Rosa LG, Caetano-Lopes J, Rodrigues A, Canhãõ H, Fonseca JE, Vaz MF. (2013) A method for the evaluation of femoral head trabecular compressive properties. *Materials Science Forum*. 730-732: 3-8.

### Other publications National

Helena Canhão, João Eurico Fonseca. Investigação translacional em doenças reumáticas. *Observatório Nacional das Doenças Reumáticas*.

Canhão H, Faustino A, Fonseca JE. Registo Nacional de Doentes Reumáticos, Reuma.pt, in: Doenças Reumáticas em Portugal: da Investigação às Políticas de Saúde. *Observatório Nacional das Doenças Reumáticas*, Ed. 2013.

Fonseca JE, Canhão H e Viana Queiroz M – *Reumatologia Fundamental*. Lidel, 2013.

### Invited lectures and seminars

Canhão U. Mitochondrial genetics on RA susceptibility, Sociedade Portuguesa de Reumatologia, Lisbon, Portugal, April 23, 2013

Canhão H. Speaker in session Update Registos; Fonseca JE. Chairman in lecture Jak Pathways - Clinical Implications; Sousa E. Speaker in session "What's New ACR 2012"; Santos MJ. Chairman in lecture Rastreo e Monitorização da Tuberculose. Pfizer Summit Inflamação, Vilamoura, Portugal, February 2-3, 2013

Fonseca JE. Doenças inflamatórias musculares- update; Santos MJ. Vasculites associadas a ANCA- Estratégias para alcançar e manter a remissão; Vieira-Sousa E. Estágio Internacional: bring home messages. Temas de relevo na Reumatologia: o ano de 2012, Batalha, Portugal, February 22-23, 2013

Fonseca JE. Chairman in round table Arthritis and bone: two faces of the same coin; Fonseca JE. Bone and Cartilage interaction?; Perpétuo IP. Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis; Caetano-Lopes J. Effects of inflammation on bone biological structural and mechanical behavior. 11th Medinterna International Meeting, Porto, Portugal, February 6-9, 2013.

Vieira-Sousa E. Terapêutica com "Biológicos" em Diversas Especialidades. 5as Jornadas de Dermatologia e Dermocosmética em Medicina Familiar, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Mar 8-9, 2013

Sarmento M. Chairmain in lecture Módulo 1: Fracturas da extremidade proximal do úmero. AO Trauma Shoulder Course, Lisbon, Portugal, March 7-9, 2013

Cascão R. Inflamasoma: Doenças Auto-Inflamatórias e Artrites Microcristalinas; Santos MJ. B-cell depletion in autoimmunity. A Look Across Registries; Simpósio - Satélite Roche; Santos MJ and Fonseca C. Screening do VHB no Contexto das Terapêuticas Imunossupressoras; Sousa Vieira S. O que Devemos Mudar no Registo Clínico das Espondilartrites; Canhão H and Oliveira M. Artrite Reumatóide - Onde Estamos e Até Onde Podemos Ir, Simpósio - Satélite AbbVie; Fonseca JE. Novos DMARDs Orais na Era das Terapêuticas Biotecnológicas, Simpósio - Satélite Pfizer; Fonseca JE. Chairman in lecture Inflamação - Mecanismos Intracelulares e Extracelulares; Fonseca JE. Chairman in round table Lacunas no Diagnóstico, Referenciação e Tratamento dos

Doentes com Artrite Reumatóide em Portugal. Simpósio - Satélite MSD, Hot Topics In Rheumatology. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013

Canhão H. The Challenges and opportunities of patient registries “Reuma.pt”. Connecting for the future – Inflammatory Immunomediated Disease, Fundação Champalimaud, Lisbon, Portugal, May 11, 2013

Canhão H. Chair of the Local Organising Committee ECTS 2013; Canhão H. Welcome to Lisbon from the Chair of the Local Organising Committee; Abdulghani S. 2010 ECTS / SERVIER FELLOWSHIP, Previous Grant Winner Presentation; Caetano-Lopes J. Chair in session Bone quality and fracture repair - animal models; Fonseca JE. Chairman in Workshop 1: Fat and bone; Rodrigues AM. Chair in session Osteoporosis pathophysiology and genetics; Perpétuo IP. Chair in session Oral Posters 2: Pre-clinical Perpétuo IP. Invited speaker - New Investigator workshop 3 - How to get started as a post-doc?; Perpétuo IP. Chair in session Workshop 4 - Pre-clinical - Osteoclast activity and hematopoiesis; Rodrigues AM. Chair in session Treatment of osteoporosis; Fonseca JE. Chairman in session Meet the Professor Sessions- Arthritis, inflammation and bone: from bench to bedside; Abdulghani S. Chair in session Meet the Professor Sessions State-of-the-Art techniques in Bone research. ECTS Lisbon, Portugal, May 18-21, 2013.

Fonseca JE. Chairman in lecture AIJ sistémica: outros conceitos; Santos MJ. Chairman in lecture Casos Clínicos; Canhão H. Chairman in lecture Casos Clínicos; Ramos F. Chairman in Lombalgias: do funcional ao estrutural; Mourão AF. Chairman in lecture Discussão de Posters. 5ª Reunião de Casos Clínicos da Secção de Reumatologia Pediátrica da SPP, Centro de Investigação Médica da Universidade do Porto, Porto, Portugal, June 7, 2013.

Fonseca JE. Artrite Reumatoide e espondilite anquilosante. 1ª Reunião de Medicamentos Biológicos, Leiria, Portugal, June 28-29, 2013.

Fonseca JE. Miosites: da patogenia à terapêutica; Canhão H. Reuma.pt; MJ Santos Lúpus Eritematoso Sistémico - desafios na era de novas terapêuticas. Rheumatology Expert Update Meeting (REUM 2013), Lisbon, Portugal, June 28-29, 2013.

Canhão H. Osteoarthritis biomarker analysis to enable patient stratification and disease modifying experimental medicine clinical trials. IMI Consultation Workshop Brussels, Belgium, July 8, 2013.

Fonseca JE. A Visão do Clínico. Conferência da APIFARMA “Inovação Biofarmacêutica e Biossimilares – A Identidade dos Biológicos”, Lisbon, Portugal, September 18, 2013.

Fonseca JE. O biobanco como fulcro no desenvolvimento da investigação médica na pediatria. 14º Congresso Nacional de Pediatria, Porto, Portugal, October 3-5, 2013

Fonseca JE. Fisiopatologia da AR: aceitar a complexidade; Canhão H. Repensar os ensaios clínicos em Portugal. Colóquio da ANDAR - Explorando o futuro na AR: a contribuição Portuguesa, Lisbon, Portugal, October 11, 2013.

Fonseca JE. Biobanco-IMM:Uma Oportunidade Para Todos? XIII Reunião Científica Sociedade Portuguesa de Menopausa, Lisbon, Portugal, October 18-19, 2013.

Sousa E. Qual o papel dos anti-TNF na Espondilartrite axial não radiográfica; Fonseca JE. Prevenir a reativação da Hepatite B em doentes medicados com anti-TNF: está na altura de rever as guidelines?; Santos MJ. Doença Cardiovascular e Malignidade nos doentes tratados com anti-TNF – ponto da situação. VI Forum das Espondilartrites, Batalha, Portugal, November 8-9, 2013.

Fonseca JE and Santos MJ. Mesa redonda - Neurologia / reumatologia. Congresso de Neurologia 2013 - "Repercussões Neurológicas das Doenças Sistemáticas, Lisbon, Portugal, November 6-9, 2013.

Canhão H. O tempo de Manter ou Parar. Vieira-Sousa E. Prevenção de Fraturas. XXI Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 28-29, 2013.

### **Communications in International Conferences**

Moura RA, De la Torre I, Leandro MJ, Cambridge G. Effect of Rituximab on B Cell Subpopulations Expressing the 9G Idiotype in Patients with Rheumatoid Arthritis. 33rd European Workshop for Rheumatology Research in Czech Republic, Prague, February 28-March 2, 2013 (Poster Presentation)

Canhão H, Rodrigues A, Santos MJ, Carmona-Fernandes D, Costa J, Santos H, Branco J, Plenge R, Solomon D, Armas J, Silva JA, Fonseca JE, Karlson E. Lack of Replication of PTPRC Gene as a Predictor of Response to Anti-Tumour Necrosis Factor Therapy in Patients with Rheumatoid Arthritis. 33rd European Workshop for Rheumatology Research in Czech Republic, Prague February 8 - March 2, 2013 (Poster Presentation)

Perpétuo IP, Marques R, Ponte C, Canhão H, Fonseca JE. Rankl Expression is Lower on T and B Lymphocytes and Rankl+ Cells Tend to Accumulate in Circulation of Rheumatoid Arthritis Patients Treated with TNF Blockers. 33rd European Workshop for Rheumatology Research in Czech Republic, Prague, February 28-March 2, 2013 (Poster Presentation)

Romão VC, Santos MJ, Canas da Silva J, Polido Pereira J, Pereira da Silva JA, Duarte C, Pereira da Silva J, Silva C, Teixeira AA, Costa JA, Araújo D, Pimentel Santos F, Branco J, Melo Gomes JA, Faustino A, Fonseca JE, Canhão H. Comparative Effectiveness of Biological Therapies in Rheumatoid Arthritis is Influenced by Response Measures and Disease Activity State. 33rd European Workshop for Rheumatology Research in Czech Republic, Prague, February 28-March 2, 2013 (Poster Presentation)

Castro A, Carmona-Fernandes D, Santos MJ, Mendes-Pedro L, Canhão H, Fonseca JE. Ultrasonographic Carotid Plaque Morphology in Women with Rheumatoid Arthritis without Previous Cardiovascular Events. ECTS Lisbon, Portugal, May 18-21, 2013 (Poster presentation)

Canhao H, Gouveia N, REgo T, Rodrigues AM, Branco J. BMA assessment standard curves for wrist and ankle in both sexes – data from EpiReumaPt. ECTS Lisbon, Portugal, May 18-21, 2013

(Poster presentation)

Abdulghani S, Santos L, Vidal B, Cascão R, Fonseca JE. Bone mineral density distribution in early osteoporotic bone. ECTS Lisbon, Portugal, May 18-21, 2013 (Poster presentation)

Gonçalves MJ, Rodrigues AM, Caetano-Lopes J, Raquel E, Lopes A, Vidal B, Vale AC, Sarmiento M, Vaz MF, Monteiro J, Fonseca JE, Canhão H. Estimated glomerular filtration rate is associated with bone fragility in the elderly. ECTS Lisbon, Portugal, May 18-21, 2013 (Poster presentation)

Gouveia N, Canhão H, Rego T, Sousa S, Branco J. Portuguese and Spanish FRAX® tool versions: a comparative analysis from EpiReumaPt. ECTS Lisbon, Portugal, May 18-21, 2013 (Poster presentation)

Vieira-Sousa E, Rodrigues A, Caetano Lopes J, Capela S, Ramos F, Figueira R, Polido-Pereira J, Ponte C, Campanilho-Marques R, Barros R, Romeu JC, Pereira da Silva JA. Zoledronate Efficacy and Safety in active Paget's Disease Long-term follow-up and retreatment in clinical practice. ECTS Lisbon, Portugal, May 18-21, 2013 (Poster presentation)

Gouveia N, Canhão H, Rego T, Sousa S, Branco J. Portuguese and Spanish FRAX® tool versions: a comparative analysis from EpiReumaPt. 39º Congresso Nacional de la SER, Tenerife, Spain, May 21-23, 2013 (Poster presentation)

Campanilho-Marques R, Ramos F, Mourão AF, Martins F, Canhão H, Fonseca JE, Pereira da Silva JA. Disease activity in a Juvenile idiopathic arthritis population after 5 years follow-up. Annual European Congress of Rheumatology EULAR congress, Madrid, Spain, June 12 -15, 2013 (Poster Presentation)

Kearsley-Fleet L, Zavada J, Lunt Hetland M, Nordström DC, Aaltonen KJ, Iannone F, Gremese E, Kievit W, Van Riel P, Lie E, Kvien TK, Canhão H, Fonseca JE, Rotar Z, Loza E, Carmona L, Askling J, Johansson K, Finckh A and Dixon WG, Hyrich KL on behalf of the EULAR Study Group on Registers and Observational Drug Studies. The EULAR Study Group for Biologic Registers: Initiating a Combined Approach to the Analysis of Rare Outcomes. Annual European Congress of Rheumatology EULAR congress, Madrid, Spain, June 12 -15, 2013 (Poster Presentation)

Sousa SI, Gonçalves MJ, Roque R, Vinagre F, Cordeiro A, Godinho F, Saavedra MJ, Ramos F, Macieira C, Canhao H, Fonseca JE, da Silva C, Pereira da Silva JA, Santos MJ. Reuma.PT/LES: The experience of two central hospitals in Lisbon. Annual European Congress of Rheumatology EULAR congress, Madrid, Spain, June 12 -15, 2013 (Poster Presentation)

Gonçalves MJ, Rodrigues AM, Caetano-Lopes J, Lopes A, Vidal B, Raquel E, Sarmiento M, Canhão H, Fonseca JE, Vaz F, Monteiro J. Estimated glomerular filtration rate is associated with bone fragility in the elderly Annual European Congress of Rheumatology EULAR congress, Madrid, Spain, June 12 -15, 2013 (Poster Presentation)

Mourão AF, Ramos F, Santos MJ, Martins F, Oliveira M, Costa J, Brito I, Figueira R, Duarte C, Salgado M, Sousa M, Furtado C, Figueiredo G, Melo Gomes J, Branco J, Fonseca JE, Canhão H. JADAS-CRP instead of JADAS-ESR...Results from Reuma.PT Annual European Congress of Rheumatology EULAR congress, Madrid, Spain, June 12 -15, 2013 (Poster Presentation)

Saldanha C, Santos MJ, Mendes Pedro L, Canhão H, Fernandes e Fernandes, Canas da Silva J, Fonseca JE. Erythrocyte Nitric Oxide Association with Low Grade Inflammation. 17th Conference of the European Society for Clinical Hemorheology and Microcirculation, Pécs, Hungary, July 6-9, 2013 (Oral communication)

Moura RA, Canhão H, Polido-Pereira J, Rodrigues AM, Navalho M, Mourão AF, Rosa CM, Resende C, Campanilho-Marques R, Madruga Dias J, da Silva JR, Bexiga M, Pereira da Silva JA, Graça L, Fonseca JE. BAFF and TACI gene expression are increased in untreated very early Rheumatoid Arthritis patients. EMBO Young Scientists' Forum. Lisbon, Portugal, July 15-16, 2013 (Poster presentation)

Torre C, Guerreiro J, Mende Z, Miranda M, Canhão C, Branco J, Machado M, Ferreira I, Feudjo-Tepie M, Joaquim M, Cristino J. Low Persistence with Oral Bisphosphonate Treatment in Portuguese Women with Postmenopausal Osteoporosis. 29th International Conference on Pharmacoepidemiology & Therapeutic Risk Management. Montreal, Canada. August 25-28, 2013 (Oral communication)

Torre C, Guerreiro J, Mende Z, Miranda M, Canhão C, Branco J, Machado M, Ferreira I, Feudjo-Tepie M, Joaquim M, Cristino J. Persistence to oral bisphosphonates in portuguese women with posmenopausal osteoporosis (PMO) : 18-month results. 17th Annual Meeting of European Symposium on PATient COMpliance and Persistence (ESPACOMP), Budapest, Hungary, November 15-16, 2013.

Campanilho-Marques R, Ramos F, Perpétuo I, Fernandes S, Furtado AC, Mourão AF, Martins F, Canhão H, Fonseca JE, Pereira da Silva JA. Older age predicts poor response o 6-months methotrexate therapy in a juvenile idiopathic Arthritis cohort of patients. European Pediatric Rheumatology 20th Congress, Ljubljana, Slovenia, September 25-29, 2013 (Poster Presentation)

Campanilho-Marques R, Ramos F, Mourão AF, Martins F, Canhão H, Fonseca JE, Pereira da Silva JA. Disease activity in a Juvenile idiopathic arthritis population after 5 years follow-up. European Pediatric Rheumatology 20th Congress, Ljubljana, Slovenia, September 25-29, 2013 (Poster Presentation)

Mourão AF, Santos MJ, Melo Gomes J, Martins F, Oliveira M, Costa J, Ramos F, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues AM, Salgado M, Sousa M, Branco J, Fonseca JE, Canhão H. JADAS-CRP instead of JADAS-ESR...Results from Reuma.PT European Pediatric Rheumatology 20th Congress, Ljubljana, Slovenia, September 25-29, 2013 (Poster Presentation)

Lin C, Wood Karlson E, Canhao H, Miller T, Dligach D, Chen PJ, Perez R, Cai T, Weinblatt ME, Shadick NA, Plenge RM, Savova G. Automatic Prediction of Rheumatoid Arthritis Disease Activity from the Electronic Medical Records. AMIA 2013 annual Symposium, Washington DC, November 16- 20, 2013 (Oral communication)

Finckh A, Iannone F, Gomez Reino J, Neto D, Lie E, Van Riel P, Hetland ML, Pavelka K, Canhão H, Turesson C, Mariette X, Gottenberg JE. The Impact Of Inadequate Response To Prior Biologic Agents On Abatacept Drug Retention In Rheumatoid Arthritis (RA) Patients. A Pan-European

Analysis Of RA Registries. 2013 ACR/ARHP Annual Meeting, San Diego, CA, October 25-30, 2013 (Poster Presentation)

Neto D, Finckh A, Iannone F, Loza A, Lie E, Van Riel P, Hetland ML, Pavelka K, Gottenberg JE, Canhão H, Mariette X, Turesson C. Differences In Abatacept Use In Rheumatoid Arthritis Patients Across Europe: A Pan-European Database Analysis Of Abatacept In European RA Registries. 2013 ACR/ARHP Annual Meeting, San Diego, CA , October 25-30, 2013 (Oral communication)

### Communications in National Conferences

Gonçalves MJ, Fonseca VR, Luís P, Lopez D, Oliveira ME, Vilas AP. Doença de Kikuchi num jovem com quadro consumptivo e trombocitopenia. 19º Congresso nacional de Medicina Interna, Vilamoura, Portugal, May 22-25, 2013. (Poster presentation)

Sarmiento M. Chair Exercício prático 1 - Osteossíntese com placa philosAO Trauma Shoulder Course, Lisbon, Portugal, March 7-9, 2013 (Oral communication)

Di Sarno A, Gonçalves MJ, Vilas AP. Neuropatia sensitive pura, um desafio diagnóstico. 19º Congresso nacional de Medicina Interna, Vilamoura, Portugal, May 22-25, 2013 (Poster presentation)

Medina-Lopes MC , Perpétuo IP , Fonseca JE. Osteoclast activity in patients with rheumatoid arthritis treated with TNF blocking therapies. iMed 5.0 – Innovating Medicine Conference, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

Vieira AR, Moura RA, Fonseca JE. B Cell gene expression in rheumatoid arthritis: effect of immunosuppressive treatment. iMed 5.0 – Innovating Medicine Conference, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

Oliveira Santos P, Carmona-Fernandes D, Barreira S, Fernandes AN, Mendes Pedro L, Castro A, Fonseca JE, Canhao H, Santos M. Vitamin D – A link between atherogenesis and bone mass? iMed 5.0 – Innovating Medicine Conference, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

Barreira S, Carmona-Fernandes D, Castro A, Santos P, Nicolau Fernandes A, Pedro LM, Canhão H, Fonseca JE, Santos MJ. Osteoporosis in patients with severe carotid atherosclerosis. iMed 5.0 – Innovating Medicine Conference, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

Artilheiro V. Estudo da via de sinalização Wnt e relação com mineralização óssea, propriedades mecânicas e risco de fractura em osteoporose. Fórum das Bolsas Universidade de Lisboa / Fundação Amadeu Dias (UL/FAD), Lisbon, Portugal, Outubro 9, 2013 (Oral communication)

Madruza Dias J, Balogh E, Mullan R, Harty L, Szekanecz Z, Gallagher P, Molloy M, O’Flynn E, O’Kelly A, O’Neill M, Moore L, Murray M, FitzGerald O, Fearon U, Veale D J. A Comparison of DAS 28(4v)-CRP and ACR/EULAR Remission Criteria in an Anti-TNF-treated Rheumatoid Arthritis Patient Cohor. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Oral



communication)

Sousa SI Gonçalves MJ, Roque R, Vinagre F, Cordeiro A, Godinho F, Saavedra MJ, Ramos F, Macieira C, Canhao H, Fonseca JE, da Silva C, Pereira da Silva JA. Santos MJ Reuma.Pt/LES: The Experience of Two Central Hospitals in Lisbon 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Oral communication)

Castro A, Carmona-Fernandes D, Santos MJ, Mendes-Pedro L, Canhão H, Fonseca JE, Pereira da Silva JA. Ultrasonografic Carotid Plaque Morphology in Women with Rheumatoid Arthritis without Previous Cardiovascular Events. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Oral communication)

Romão VC, Saavedra MJ, Vieira-Sousa E, Costa M, Polido-Pereira J, Rodrigues AM, Ramos F, Macieira C Capela S, Resende C, Madruga-Dias J, Ponte C, Campanilho-Marques R, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Tuberculosis in rheumatic patients treated with biological therapies- is screening enough? 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Castro A, Resende C, Ramos F, Canhão H, Navalho M, Mascarenhas V, Gaspar A, Pereira da Silva JA. Factores preditivos de RMN positiva no diagnóstico de sacroiliite. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Castro A, Vieira de Sousa E, Resende C, Miranda Rosa C, Pereira da Silva JA. Uveíte anterior como primeira manifestação da doença reumática: casuística da consulta de Uveítes do Hospital de Santa Maria. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Ponte C, Campanilho-Marques R, Morais F, Resende C, Pereira da Silva JA Systemic sclerosis: demographic clinical features and treatment in 9 patients. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Furtado C, Madruga Dias J, Costa M, Fernandes S, Resende C, Capela S, Pereira da Silva JA Grávida com hipertensão arterial pulmonar grave como manifestação inagural do Lupus Erirematoso Sistémico. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Ponte C, Morais F, Campanilho-Marques R, Resende C, Pereira da Silva JA. High-resolution computed tomographic findings in patients with systemic sclerosis and their clinical correlations. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Fernandes J, Romão VC, Pereira JG, Castro-Lopes A, Meneses J, Victorino R. Febre, confusão e tosse como expressão clínica da arterite de células gigantes. 19º Congresso de Nacional de Medicina Interna, Vilamoura, Portugal, May 22-25, 2013 (Poster presentation)

Pereira e Silva R, Rodrigues T, Oliveira S, Brites J, Romão VC, Neves M, Garcia R, Palma dos Reis J, Lopes T. Resultados do overactive bladder questionnaire em doentes de cuidados de saúde primaries. Congresso da Associação Portuguesa de Urologia, Vilamoura, Portugal, October 10-13, 2013 (Poster Presentation)

Romão VC, Gonçalves MJ, Saraiva F, Canhão H, Romeu JC, Pereira da Silva JA. Poliartrite, papulose, diarreia e emagrecimento: expressões da mesma doença? Sessão Clínica Conjunta Gastroenterologia, Dermatologia, Reumatologia, Hospital de Santa Maria, Lisbon Portugal, November 13, 2013 (Oral presentation)

Gonçalves MJ, Fernandes S, Freira S, Romão VC, Romeu JC, Fonseca JE, Pereira da Silva JA. A diversidade clínica de uma mesma entidade: a propósito de 3 casos. Sessão Clínica da Faculdade de Medicina da Universidade de Lisboa, Hospital de Santa Maria, Lisbon, Portugal, November 14, 2013 (Oral communication)

Romão VC, Conceição I, Pereira da Silva JA, Fonseca JE. Miosite e mononeuropatia secundária a infecção viral por Coxsackie. XXI Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 28-29, 2013 (Poster Presentation)

Romão VC, Gonçalves MJ, Freira S, Fonseca H, Ramos F, Fonseca JE. Adolescente com SAPHO refractário – implicações bio-psico-sociais. XXI Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 28-29, 2013 (Poster Presentation)

Campanilho-Marques R, Ramos F, Mourão AF, Martins F, Canhão H, Fonseca JE, Pereira da Silva JA. Disease activity in a Juvenile idiopathic arthritis population after 5 years follow-up. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Mourão AF, Ramos F, Santos MJ, Martins F, Rodrigues AM, Oliveira M, Costa J, Brito I, Figueira R, Duarte C, Salgado M, Sousa M, Furtado C, Figueiredo G, Melo Gomes J, Branco J, Fonseca JE, Canhão H. JADAS-CRP instead of JADAS-ESR...Results from Reuma.PT. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Campanilho-Marques R, Ramos F, Perpétuo I, Fernandes S, Furtado AC, Mourão AF, Martins F, Canhão H, Fonseca JE, Pereira da Silva JA. Older age predicts poor response to 6-months methotrexate therapy in a juvenile idiopathic Arthritis cohort of patients. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Marques A, Mota A, Canhão H, Romeu J.C, Silva D, Ruano A, Barbosa A.P, Dias A.A, Araújo D, Simões E, Águas F, Silva I.R, Silva I, Crespo J, Alves J.D, Costa L, Mascarenhas M, Lourenço OL, Ferreira P, Lucas R, Roque R, Branco J, Tavares V, Kanis J, P. da Silva JA. Validação do algoritmo FRAX para a população Portuguesa. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Barreira S, Carmona-Fernandes D, Castro A, Santos P, Silvestre L, Fernandes RF, Pedro LM, Canhão H, Fonseca JE, Santos MJ. Será a densidade mineral óssea mais baixa nos doentes com aterosclerose carotídea? 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Gonçalves MJ, Rodrigues AM, Caetano-Lopes J, Raquel E, Lopes A, Vidal B, Vale AC, Sarmiento M, Vaz MF, Monteiro J, Fonseca JE, Canhão H. Estimated glomerular filtration rate is associated with bone fragility in the elderly. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Romão VC, Saavedra MJ, Vieira-Sousa E, Costa M, Polido-Pereira J, Rodrigues AM, Ramos F, Macieira C Capela S, Resende C, Madruga-Dias J, Ponte C, Campanilho-Marques R, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Tuberculosis in Rheumatic patients treated with biological therapies- is screening. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Romão VC, Saavedra MJ, Vieira-Sousa E, Costa M, Polido-Pereira J, Rodrigues AM, Ramos F, Macieira C Capela S, Resende C, Madruga-Dias J, Ponte C, Campanilho-Marques R, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Can we safely start biological therapy in rheumatic patients with prior history of active tuberculosis? 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Gouveia N, Canhão H, Ramiro S, Mourão AF, Silva I, Machado P, Laires P, Branco JC. Comparação da frequência das patologias reumáticas auto-reportadas com as confirmadas pelo reumatologista – resultados do EpiReumaPt após 1 ano no terreno. 3º Simpósio SPR Inflamação e Dor so, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Gonçalves MJ, Sousa S, Saavedra MJ, Ramos F, Fonseca JE, Pereira da Silva JA, da Silva C, Macieira C, Santos MJ, Canhão H. Rituximab use in systemic lupus erythematosus patients: The experience of two central hospitals in Lisbon. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Furtado C, Fernandes S, Castro A, Saavedra MJ, Ramos F, Tortosa F, Ortiz S, Gonçalves AR, Romeu JC, Pereira da Silva JA. Dermatomiosite do adulto rapidamente progressiva com envolvimento gastrointestinal grave. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Fernandes S, Furtado C, Castro A, Resende C, Romeu JC, Pereira da Silva JA. Pneumonite na doença de still do adulto. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Furtado C, Fernandes S, Marques R, Macieira C, Pereira da Silva JA. Vasculites: experiencia de um ano de consulta. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Furtado C, Fernandes S, Gomes L, Navalho M, Capela S, Pereira da Silva JA. Brucelose osteoarticular por transmissão sexual. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Romão VC, Furtado C, Fernandes S, Saraiva F, Barros R, Ramos F, Canhão H, Fonseca JE, Romeu JC, Pereira da Silva JA. Dois casos de artrite infecciosa com procalcitonina negativa. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Madruga Dias J, Balogh E, Harty L, Mullan R, Costa MM, Veale DJ. The role of arthroscopy in rheumatology: review of the training experience in an Irish centre 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Gouveia N, Canhão H, Ramiro S, Mourão AF, Silva I, Machado P, Laires P, Branco JC. Estado de

saúde e capacidade funcional em diversas doenças reumáticas – resultados de uma sub-amostra do EpiReumaPt. 3º Simpósio SPR Inflamação e Dor, Espinho, Portugal, May 2-4, 2013 (Poster presentation)

Laires PA, Canhão H, Gouveia N, Branco J. Health Resource Consumption Associated with Rheumatic Diseases in Portugal? Preliminary Results from the Portuguese Epidemiology Study on Rheumatic Diseases (EpiReumaPt) 13th Portuguese Conference on Health Economics, Braga, Portugal, Octobre 10-12, 2013 (Poster presentation)

Perpétuo IP , Campanilho-Marques R, Caetano-Lopes J, Fonseca JE, Canhão H, Osteoclast in ankylosing spondylitis: The role of systemic inflammation. ECTS PhD course, Hamburg, German, September 15-18, 2013 (Poster presentation)

### **Organisation of Conferences**

Fonseca JE was a member of the International advisory board, 33rd European Workshop for Rheumatology Research in Czech Republic, Prague, February 28-March 2, 2013

Fonseca JE, Canhão H, Caetano-Lopes J and Perpétuo IP were members of the ECTS Lisbon, Portugal, May 18-21, 2013.

### **Internationalisation**

2012-2013 CERRERA and TOCERRA collaboration. Coordinator: Helena Canhão. Funding Roche, €5.000€

2011-2013 Comparative patient outcome measures study in Dutch and Portuguese rheumatoid arthritis patients – data from Meteor Project. Coordinator: Helena Canhão. Funding Meteor, €25.000€

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

Prize for best poster communication in Simpósio Inflamação & Dor Espinho Portugal May 2-4 2013. Romão VC, Saavedra MJ, Vieira-Sousa E, Costa M, Polido-Pereira J, Rodrigues AM, Ramos F, Macieira C, Capela S, Resende C, Madruga Dias J, Ponte C, Campanilho-Marques R, Castro A, Furtado C, Fernandes S, Gonçalves MJ, Pereira da Silva JA, Canhão H, Fonseca JE. Can we safely start biological therapy in rheumatic patients with prior history of active tuberculosis?

Romão VC, Canhão H and Fonseca JE. Bolsa de Investigação do Centro Hospitalar Lisboa Norte. Tuberculosis prevention in patients with immune- mediated inflammatory diseases treated with biological therapy.

2013 ASPIRE EU Inflammation Pfizer Research Awards. Inhibition of bone and cartilage degradation in rat induced arthritis treated with tofacitinib.

Third prize for best Image in the Clinical Images Competition in XXI Jornadas Internacionais do Instituto Português de Reumatologia, Lisbon, Portugal, November 28-29. Gonçalves MJ, Romão VC, Fernandes S, Barros R, Romeu JC, Pereira da Silva JA. Sabre tibia in Paget's Bone Disease.

### **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**

Romão VC. Artrite Psoriática de difícil controlo – de anti-TNF em anti-TNF. Rheumatology in Practice, Monte Real, Portugal, November 16th 2013 (Oral Presentation, Clinical Case and Literature Review)

Caetano Lopes J supervisor of the laboratory module of the medical degree from University of Algarve (A. Correia and J. Fernandes), Algarve, Portugal, 2013.

Canhao H. Masters in Biomedical Sciences – University of Algarve Module: Biology of Bone and Cartilage, March, 2013.

Sarmiento M. Exercício prático 1 - Osteossíntese com placa philos. Rigidez do cotovelo. Rigidez do ombro pós-traumática. AO Trauma Shoulder Course, Lisbon, Portugal, March 7-9, 2013.

Canhao H. I Curso pós-graduado de atualização de boas práticas clínicas. Centro de Investigação Clínica do Centro Académico de Medicina de Lisboa, Lisbon, Portugal, May 22-23, 2013.

Canhao H. Curso para internos de Reumatologia. Doenças ósseas metabólicas. Metabolismo ósseo e fosfocálcio, Sociedade Portuguesa de Reumatologia, Lisbon, Portugal, June 22, 2013.

Canhão H. Moderadora na Mesa. Uma visão actual sobre a artrite Reumatoide; Mourão AF. Moderadora na Mesa. Doenças reumáticas infantis e juvenis; Gonçalves MJ. “Uma Visão Actual sobre a Artrite Reumatóide”; Romão VC, Ramos F, Mourão AF. Nem todas as dores na criança são dores de crescimento...quanto mais precoce o diagnóstico, melhor o prognóstico. 6º Curso de Reumatologia Prática em Cuidados Primários, Lisbon, Portugal, September 18-19, 2013.

Perpétuo IP , Campanilho-Marques R, Caetano-Lopes J, Fonseca JE, Canhão H; Osteoclasts in ankylosing spondylitis: the role of systemic inflammation; ECTS PhD training course, Hamburg, Germany September 15-18, 2013 (Poster Presentation)

### **Science and society**

RRU has participated in "Ciência Viva" in July and August, receiving a total of 4 students.

RRU received students from Escola Secundária de São Brás do Alportel in a visit to IMM.

Helena Canhão participated, in October 2013, in TV programs, Saúde em Jogo - Bola TV and Especial Saúde - RTP1 to talk about Osteoporosis.

João Eurico Fonseca participated, in October 2013, in TV program, to talk about two points: "O que é um biobanco" and "Tratamento com biológicos".

### **Msc theses completed**

Patrícia de Navais Paiva de Mourão Gamelas (2013) Aplicação do "Reuma-pt " na caracterização de uma população pediátrica na consulta de Reumatologia Pediátrica. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Filipa Ramos

Maria Emília da Conceição Moura Pereira (2013) Consulta biodisciplinar de artrite psoriática. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Elsa Sousa.

Emília Raquel Francisco (2013) Factores de risco na fractura de fragilidade da anca no género masculino. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Maria Rodrigues.

Sara Marques Batista (2013) Relação entre adipocinas, composição corporal e actividade inflamatória em mulheres com Lupus eriematoso sistémico. Faculdade de Medicina da Universidade de Lisboa Supervisor: Maria José Santos.

## 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 required 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

Telma Cristina Lourenço Carrilho	Master	Technician (started September)
Tiago Maria de Carvalho da Costa Amado	Master	Technician (started September)

### Keywords / Research Areas

Cell Biology, Cytoskeleton, Cell Migration, Skeletal Muscle.

### Major scientific achievements

Last year we established that the position of the nucleus in skeletal muscle cells is important for muscle physiology. This year we focused our efforts in understanding why nuclear positioning is important for cell migration. We developed new systems and engineer novel reagents able to address this question.

Furthermore, we were awarded with the following grants:

- ERC Consolidator Grant 2013 - "Positioning the nucleus for cell migration and muscle fiber function".
- EMBO Installation Grant 2014 - "Positioning the cell nucleus".
- Investigador FCT to Edgar Gomes.

### Recent Most Relevant Publications

Metzger, T., Gache, V., Xu, M., Cadot, B., Folker, E., Richardson, B., Gomes, E.R., Baylies, M.K. (2012) MAP and Kinesin dependent nuclear positioning is required for skeletal muscle function. *Nature* **484**, 120 (Journal IF: 38.6, Citations: 23)

Luxton GW, Gomes ER, Folker ES, Vintinner E, Gundersen GG (2010) Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement. *Science* **125**,1099. (Journal IF: 31.03, Citations: 83)

### Publications in peer review Journals

Osorio, D. S. Gomes, E. R. (2013) The contemporary nucleus: A trip down memory lane. *Biology of the Cell*. **105**(9), 430–441 (Journal IF: 3.488, Citations: 1)

### Invited lectures and seminars

Edgar Gomes, Daniel Osorio. Mechanisms of nuclear positioning in migrating cells, CEA, France, February 2013.

### Communications in International Conferences

Edgar Gomes, Daniel Osorio. Mechanisms of nuclear positioning in migrating cells. Society for Experimental Biology, Valencia, Spain, July 2013.

### Organisation of Conferences

Scientific and organising committee. Club Muscle, Montpellier, France, November 2013.

### Internationalisation

Our research projects involve multiple collaborations with teams in Europe, United States, Canada and Australia. We are involved in the organisation of international meetings and workshops and most of our funding is provided by non-Portuguese funding agencies.

### PhD theses completed

Daniel Osorio (2013) Identification of Nuclear Envelope proteins involved in actin-dependent nuclear movement. Universidade do Porto. Supervisor: Edgar Gomes.



## LUÍS GRAÇA LAB

### Major Interests / Objectives

Our Lab 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 at FMUL.

### Research Team

Alexandre Varela Santos Costa	Graduate	Lab manager
Ana Água-Doce	PhD	Post-doctoral Investigator
Ana Raquel Maceiras Oliveira	Master	PhD Student
Joana Catarina Mendão Azeitão da Silva	Master	PhD Student
JORGE IVAN RAMIREZ SEPULVEDA	Master	Investigator (left June)
Marta Isabel de Carvalho Ferreira Gomes	Graduate	MSc Student (left November)
Marta Ribeiro Lopes Caridade	Master	PhD Student
Marta Sofia Ferreira Monteiro Coelho Antunes	PhD	Post-doctoral Investigator
Raquel Filipa Reis de Freitas	Master	Technician (started August)
Ruy Miguel Sousa Soeiro de Figueiredo Ribeiro	PhD	Principal Investigator
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 cells, Natural Killer T cells (NKT), Transplantation, Autoimmunity, Allergy.

### Major scientific achievements

Our data on the induction of Foxp3 expression by peripheral iNKT cells challenges the idea that iNKT cells exit the thymus as functionally committed effectors. We found that iNKT cells respond to environmental cues acquiring different types of effector responses, namely IL-17 production. (J. Immunol 2013)

Our studies on tolerance induction with non-depleting anti-CD4 monoclonal antibodies led us to find evidence that an adjuvant may be necessary to allow efficient antigen presentation for tolerance induction to factor VIII in hemophilic mice. Surprisingly, tolerance, in this situation, appears to be Foxp3-independent (Blood 2013). Instead, we found that the molecular mechanism for tolerance induction that is Foxp3-independent relies on IL-10.

### Recent Most Relevant Publications

Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira V, Faro J, Graca L (2011) Regulation of germinal centre reaction by Foxp3+ follicular regulatory T cells. *J. Immunol* **187**, 4553. (Journal IF: 5.745, Citations: 41)

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**, 1249-1255. (Journal IF: 5.179, Citations: 17)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Agua-Doce A, Wollenberg I, Silva-Santos B, Graca L. (2010) J Immunol. 185: 2157-2163. (2010) Identification of Regulatory Foxp3+ Invariant NKT Cells Induced by TGF- $\beta$ . *J Immunol* **185**, 2157.2163. (Journal IF: 5.646, Citations: 30)

Curotto de Lafaille MA, Lafaille JJ, Graca L (2010) Mechanisms of tolerance and allergic sensitization in the airways and the lungs. *Curr Opin Immunol* **22**, 616. (Journal IF: 10.881, Citations: 7)

Graca L, Cobbold SP, Waldmann H (2002) Identification of regulatory T cells in tolerated allografts. *J Exp Med* **195**, 1641-1646. (Journal IF: 15.837, Citations: 340)

### Ongoing Research Projects

2011/2013. Cellular therapy for liver-specific immune suppression. Coordinator: Luis Graça. Agency: FCT. Amount: €173.000,00

2012/2013. Cellular therapy to induce local immune suppression in islet transplantation. Coordinator: Luis Graça. Agency: PRIV-UE. Amount: €100.000,00

2012/2014 . Regulation of germinal centre reaction by Foxp3+ follicular T cells. Coordinator: Luis Graça. Agency: FCT. Amount: 124.555,00

### Other Projects

2009/2013 Tolerance induction to recombinant clotting factors in a murine model of hemophilia. Coordinator: Vanessa Oliveira. Agency: FCT. Amount: €200.000.

2011/2014 Boosting dendritic cell function to facilitate tolerance induction to recombinant clotting factors. Coordinator: Vanessa Oliveira. Agency: Bayer. Amount: \$170.000.

### Publications in peer review Journals

Caridade M, Graca L, Ribeiro RM. (2013) The mechanisms underlying immune regulation in the adult: from experiments to models, *Front Immunol* **4**, 378. (<http://www.ncbi.nlm.nih.gov/pubmed/?term=The+mechanisms+underlying+immune+regulation+in+the+adult%3A+from+experiments+to+models>) (Journal IF: -, Citations: 0)

Caridade M, Oliveira VG, Agua-Doce A, Graca L, Ribeiro RM. (2013) The fate of CD4+ T cells under tolerance-inducing stimulation: a modeling perspective, *Immunol Cell Biol* **91**, 652. (Journal IF: 3.661, Citations: 0)

Monteiro M, Graca L. (2013) Letter to the Editor: Induced IL-17-producing invariant Natural Killer T cells require activation in presence of TGF- $\beta$ , *J Immunol* **190**, 5910. (Journal IF: 5.742, Citations: 0)

Oliveira VG, Agua-Doce A, Curotto de Lafaille M, Lafaille JJ, Graca L. (2013) Adjuvant facilitates anti-CD4 mediated immune tolerance to recombinant factor VIII in hemophilia through a Foxp3-independent mechanism that relies on IL-10, *Blood* **121**, 3938. (Journal IF: 10.555, Citations: 0)

Moura RA, Canhão H, Polido-Pereira J, Rodrigues AM, Navalho M, Mourão AF, Resende C, Campanilho-Marques R, Dias JM, Pereira da Silva JA, Graca L, Fonseca JE. (2013) BAFF and TACI gene expression are increased in untreated very early rheumatoid arthritis patients, *J Rheumatol* **40**, 1293. (Journal IF: 3.69, Citations: 0)

Monteiro M, Almeida CF, Agua-Doce A, Graca L. (2013) Induced IL-17-producing invariant Natural Killer T cells require activation in presence of TGF- $\beta$ , *J Immunol* **190**, 805. (Journal IF: 5.745, Citations: 4)

Santos JM, Bárcia RN, Simões SI, Gaspar MM, Calado S, Agua-Doce A, Almeida SCP, Almeida J, Filipe M, Teixeira M, Martins JP, Graca L, Cruz MEM, Cruz P, Cruz H. (2013) The role of human umbilical cord tissue-derived mesenchymal stromal cells (UCX(R)) in the treatment of

inflammatory arthritis, *J Translational Medicine* **11**, 18. (Journal IF: 3.47, Citations: 0)

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

Graca L, Regulatory T cells. 2nd European Midwinter Workshop on Immunology, Angerer Alm, Austria, January 28-30, 2013.

Graca L, Controlo da resposta imunitária através de linfócitos reguladores. IV Jornadas Nacionais de Ciências Biológicas, Aveiro, Portugal, March 14, 2013.

Graca L, Células T reguladoras em doenças alérgicas. Congresso Nacional de Autoimunidade, Vilamoura, Portugal, April 11, 2013.

Graca L, Follicular regulatory T cells. Gordon Conference on Tfh cells, Hong Kong, China, July 21-26, 2013.

Graca L, Control of immune-mediated inflammatory diseases by regulatory T cell subsets. Departmental seminar, University of Macau, Macau, China, July 29, 2013.

Graca L, Immunological aspects of inhibitor development. Bayer International Hematology Conference 2013, Lisbon, Portugal, October 19, 2013.

Graca L, Indução de tolerância em Artrite Reumatóide. Disclosing the Future in RA. Fundação Calouste Gulbenkian, Lisbon, Portugal, October 11, 2013.

Graca L, Prevention of immune pathology by different regulatory mechanisms. 39th Congress of Portuguese Society for Immunology, Coimbra, Portugal, November 13-15, 2013.

Graca L, Exploiting distinct regulatory mechanisms in transplantation tolerance, Regulatory T lymphocytes and transplantation, Toulouse, France, December 13, 2013.

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

Agua-Doce A, Caridade M, Oliveira VG, Bergman L, Demengeot J, Curotto de Lafaille M, Lafaille JJ, Graca L, Induction of Foxp3-independent dominant tolerance mechanisms that allow long-term transplant acceptance. Cold Spring Harbor Symposium on Quantitative Biology – Immunity Tolerance, Cold Spring Harbor, May 29-June 3, 2013 (Poster presentation)

Maceiras-Oliveira A, Agua-Doce A, Faro J, Graca L, Regulation of germinal centre response and antibody production by Foxp3+ follicular regulatory T cells. Gordon Research Conference on T Follicular Helper Cells, Hong Kong, July 21-26, 2013 (Poster Presentation)

Oliveira RM, Agua-Doce A, Faro J, Graca L, Regulation of germinal centre response and antibody production by Foxp3+ follicular regulatory T cells. 6th Aegean Conference on Autoimmunity: Mechanisms and Novel Treatments, Corfu, Greece, October 2–7, 2013 (Oral communication)

Almeida SCP, Ferreira-Gomes M, Graça L, Distinctive phenotypical features of liver and spleen iNKTs. 7th International Symposium on CD1 and NKT cells, Tours, France, September 13–17, 2013 (Poster presentation)

Monteiro M, Graça L, Cross-talk between NKT cells and basophils in protease-induced allergic Th2 responses. The 7th International Symposiumon CD1/NKT Cells, Tours, France, September 13–17, 2013 (Poster presentation)

Monteiro M, Graça L, Cross-talk between NKT cells and basophils in the context of allergen-induced Th2 responses. EMBO Young Scientists' Forum, Lisbon, Portugal. July 15-16, 2013 (Poster presentation)

### **Communications in National Conferences**

Maceiras AR, Agua-Doce A, Faro J, Graça L, Regulation of germinal center reaction by Foxp3+ follicular regulatory T cells. IMM/CAML PhD Students Meeting, Lisbon, Portugal, December 5-6, 2013. (Poster Presentation)

### **Internationalisation**

Collaborative research with Dr. José Faro (University of Vigo, Spain) – co-supervision of PhD student – Ana Raquel Maceiras.

Collaborative research with Dr. Ruy M. Ribeiro (Los Alamos National Laboratory, NM, USA) – co-supervision of PhD student – Marta Caridade.

Collaborative research with Dr. Kalet Leon (CIM, Havana, Cuba). Exchange of materials and joint experiments involving one PhD student (Tania Carmenate) that spent three months in our laboratory.

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

Monteiro M, SPI Travel Award to attend the 7th International Symposiumon CD1/NKT Cells, Tours, France.

### **Advanced teaching**

Luís Graça, Member of the board of LisbonBioMed PhD Program at IMM. 2013-present

Luís Graça and Marta Monteiro, GABBA PhD Program. Seminar "Regulatory T cells" within the module on Immunology, IBMC, Porto, Portugal, June 6, 2013.

Luís Graça, CEDOC PhD Program. Workshop "Regulatory T cells" integrated in the module on Inflammation, CEDOC, Lisbon, March 26, 2013.

### **Science and society**

Collaboration with artist Herwig Turk in the work "The conversation that never took place", developed during the artist's residency at IMM, and presented at Pavilhão do Conhecimento – Ciência Viva, Lisbon, Portugal, November 24–December 15, 2013.

Collaboration with artist Marta de Menezes / Cultivamos Cultura (as scientific consultant) for the exhibition about art and science "Sul-Sol" that was exhibited in Odemira (18/10 – 24/11/2013) and will be on tour in Spain and France during 2014.

Participation in the National Day of Scientific Culture with the lecture "Artistas no Laboratório: a prespetiva do cientista", part of the symposium ArteFacto, Auditório Municipal de Odemira, Odemira, Portugal, November 24, 2013.

Book Chapter: Menezes, M and Graça L, n-Degrees, In "Field Notes", Erich Berger (Ed.) 2013, Finland.

### **PhD theses completed**

Marta Caridade (2013) Defining the quantitative aspects of dominant tolerance induction and maintenance. Faculdade de Medicina da Universidade de Lisboa. Supervisors: Luis Graça and Ruy M Ribeiro.

Ana Água-Doce (2013) Mechanisms of tolerance induction to foreign proteins. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luis Graça.

### **Msc theses completed**

Marta Isabel Ferreira Gomes (2013) Impact of Foxp3+ regulatory invariant NKT cells in the allergic airways disease. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Luis Graça and Sílvia Almeida.

## 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:

- embryonic stem cells to study the mechanisms underlying their pluripotent state;
- 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 Leonor Heitor Lopes	Graduate	Trainee (left February)
Ana Marisa Mendes Gonçalves Vinhais Guedes	Master	PhD Student
Ana Rita Ponce Álvares de Águeda Pedrosa	Master	PhD Student (started September)
Ana Sofia Temudo Duarte António	Master	PhD Student
Anna Pezzarossa	PhD	Post-doctoral Investigator, (started September)
Catarina Esteves Lopes Ramos	PhD	Post-doctoral Investigator (left March)
Cláudia Sofia Cardoso Gaspar	PhD	Post-doctoral Investigator
Dusan Djokovic	MD/PhD	Post-doctoral Investigator, MD (started October)

Elsa Margarida Cavaco Abranches	PhD	Post-doctoral Investigator
Evguenia Pavlovna Bekman	PhD	Post-doctoral Investigator, Assistant Professor
Pedro Miguel Branco Barbacena	Graduate	MSc Student
Sanja Ivkovic	PhD	Post-doctoral Investigator
Sara Sofia Gasalho Ferreira	Graduate	Technician
Willianne Kaline Alves da Silva	Graduate	MSc Student (left November)

### Keywords / Research Areas

Stem cells, Notch signalling, Pluripotency, Neurogenesis, Gene regulatory networks, Systems biology.

### Major scientific achievements

Our work focused on how cell fate decisions are controlled at the single-cell level, revealing how cell-cell communication functions to coordinate the proper assembly of tissues and organs. In the developing nervous system, our research allowed us to unravel how neuronal differentiation is controlled by the timing of Notch activity. We have also investigated how the pluripotent state is regulated in embryonic stem (ES) cells. By monitoring the activity of the pluripotency gene *Nanog*, combined with mathematical modelling, our work uncovered the existence of significant stochastic gene expression noise in individual ES cells, which we propose allow these cells to explore the pluripotent decision space. This research shall contribute to design more rational strategies to direct the in vitro and in vivo production of specific cell types, required to develop cell-replacement therapies in humans, aimed at regenerating damaged tissues and organs.

### Recent Most Relevant Publications

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: 3)

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*. **4**, (7):e6286. ([www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0006286](http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0006286)) (Journal IF: 4.537, Citations: 39)

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**, 54-65. ([www.sciencedirect.com/science/article/pii/S0012160609000293](http://www.sciencedirect.com/science/article/pii/S0012160609000293)) (Journal IF: 4.407, Citations: 11)

Henrique, D. Bally-Cuif, L. (2010) A cross-disciplinary approach to understanding neural stem cell in development and disease. *Development*. **137**, (12):1933-8. (<http://dev.biologists.org/content/137/12/1933.short>) (Journal IF: 7.,091, Citations: 2)

Fior, R., Henrique, D. (2005) A novel hes5/hes6 circuitry of negative regulation controls Notch activity during neurogenesis. *Developmental Biology*. **281**, 318-333. (Journal IF: 4.407, Citations: 53)

### Ongoing Research Projects

2010/2013 “Células estaminais: dialéctica, biologia e matemática”, Coordinator: Domingos Manuel Pinto Henrique. Agency: FCT. Amount: €140.000, 00.

2012/2015 “O domínio V2 da espinal medula como modelo de estudo de decisões do destino neuronal”, Coordinator: Domingos Manuel Pinto Henrique. Agency: FCT. Amount: €139.755,00

### Publications in peer review Journals

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”, *PLoS One*. 2013; **8**, (3):e59928 <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0059928>

Sanchez-Ripoll Y, Bone HK, Owen T, Guedes AM, Abranches E, Kumpfmüller B, Spriggs RV, Henrique D, Welham MJ. (2013): “Glycogen synthase kinase-3 inhibition enhances translation of pluripotency-associated transcription factors to contribute to maintenance of mouse embryonic stem cell self-renewal”, *PLoS One*. **8**, (4):e60148 <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0060148>

### Invited lectures and seminars

Domingos Henrique, "From ES cells to Neurons", Invited lecture at 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013.

### **Communications in International Conferences**

Elsa Abranches, Ana Guedes, Anna Pezzarossa, Domingos Henrique, "The role of Nanog in pluripotency network regulating Embryonic Stem Cells". 2013 IMB Conference: Chromatin Dynamics & Stem Cells, Mainz, Germany, October 17-20, 2013 (Poster presentation)

Cláudia Gaspar, Alexandra I. Rosa, Sara Ferreira, Catarina Ramos & Domingos Henrique, "Understanding cell fate decisions in the embryonic retina". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Poster presentation)

Aida Costa, S. Juniat, J. Gale, N. Daudet and D. Henrique, "From Embryonic Stem Cells to Sensory Hair Cells: A Cell Reprogramming Approach". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Oral communication)

Pedro Barbacena, Catarina Ramos, Joana Neves & Domingos Henrique "Unravelling the regulation of Dll4 expression and its function during embryonic neurogenesis". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Poster presentation)

Ana Guedes, Elsa Abranches, Domingos Henrique, "Analysis of the dynamic properties of the pluripotency network in Embryonic Stem Cells". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Poster presentation)

Sanja Ivkovic & Domingos Henrique, "EGF and Notch signaling are required for the proper organization of postnatal retina". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Poster presentation)

Willianne K. A. Silva, Domingos Henrique & Elsa Abranches, "Identification of different pluripotent states in cultures of Embryonic Stem Cells, using combinations of cell surface antibodies". 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013 (Poster presentation)

### **Organisation of Conferences**

Organisation of 3<sup>rd</sup> StEmbryo Meeting, international meeting on Stem Cells& Embryos, IMM, Lisbon, Portugal, May 19-20, 2013. Participants: 20.

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

Aida Costa - Best Presentation at 2nd Joint Meeting SPDB/SEBD Meeting, Lisbon, Portugal, October 24-26, 2013.

Sofia Duarte - Best Poster at IMM PhD Meeting 2013, IMM, Lisbon, Portugal, 2013.

### **Advanced teaching**

Domingos Henrique - Lecturer at Mestrado em Biologia Evolutiva e do Desenvolvimento, FCUL, Lisbon, Portugal, 2013.

Domingos Henrique - Lecturer at International Neuroscience Doctoral Programme (INDP), Fundação. Champalimaud, Lisbon, Portugal, 2013.

Domingos Henrique - Lecturer and Organizer of Course on Developmental Biology, GABBA PhD, Universidade do Porto, Porto, Portugal, 2013.

### **Science and society**

Lecture for Students of Escola Salesiana Estoril, on scientific careers, Estoril, Portugal, February 28, 2013.

### **Msc theses completed**

Pedro Miguel Branco Barbacena (2013) Unravelling the regulation of Dll4 expression and its function during embryonic neurogenesis. Universidade Lisboa. Supervisor: Catarina Lopes Ramos, Domingos Henrique.

Willianne Kaline Alves da Silva (2013) Dissecting the Pluripotent state in Embryonic Stem Cells. Universidade Lisboa. Supervisor: Elsa Abranches, Domingos Henrique.

**JOÃO LACERDA LAB****Major Interests / Objectives**

The main research focus of our laboratory is the study of immune reconstitution after hematopoietic stem cell transplantation (HSCT) in humans and the development of strategies that modulate immune responses and tolerance post-transplant. Donor immunity emerging post-transplant plays a pivotal role in the protection against pathogens, such as *Aspergillus*, CMV and EBV, as well as in the development of graft-versus-host disease (GVHD) and graft-versus-leukemia effect. Our laboratory aims to identify immunological risk factors and the mechanisms by which these complications emerge post-transplant. We are particularly interested in developing strategies that may be translated into the clinical setting, such as the use of pathogen-specific T cells, donor regulatory T cells for GVHD and disease-specific T cells, with the aim of improving patient survival. We also maintain research lines investigating the pathogenesis of hematologic malignancies.

**Head of Unit**

João Mascarenhas Forjaz de Lacerda, MD/PhD, Associate Professor, Faculdade de Medicina da Universidade de Lisboa, Clinical Specialist, Hospital de Santa Maria

**Research Team**

António Maria Moura Tavares de Sampaio Soares	Graduate	MScStudent (started June)
António Maria Santa Marta de Soure	Master	PhD Student (started October)
Inês Raquel Antunes Ferreira	Master	Technician
Maria Godinho A.V. Duarte Soares	PhD	Principal Investigator (started December)
Rita Isabel Silva de Azevedo	PhD	Post-doctoral Investigator
Telma Raquel Martins da Palma	PhD	Post-doctoral Investigator (started September)

**Keywords / Research Areas**

Immune reconstitution after hematopoietic stem cell transplantation (HSCT), Homeostasis of regulatory T cells in patients submitted to HSCT, Cytomegalovirus-specific immunity after HSCT,

Development of cellular adoptive immunotherapies under GMP conditions, Genetic susceptibility to invasive fungal and viral infections, Gene expression and signaling pathways of hematologic malignancies.

### Major scientific achievements

Our Lab, officially created in July 2013, has established collaborations with national and international researchers working towards 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 invasive infections after hematopoietic stem cell transplantation (HSCT). We are also developing strategies to modulate immune tolerance after HSCT, such as the treatment of chronic graft versus host disease, by examining regulatory T cell homeostasis in this setting.

Our lab is currently funded by a Collaborative Research Grant of the Harvard Medical School Portugal Program.

### Recent Most Relevant 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**(5), 703-712. <http://www.sciencedirect.com/science/article/pii/S1083879113000530> (Journal IF: 3.940, Citations: 0)

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. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2913090> (Journal IF: 5.935, Citations: 19)

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. <http://bloodjournal.hematologylibrary.org/content/113/13/2999.long>. (Journal IF: 9.06, Citations: 28)

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. (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**(9), 3574-3581. <http://bloodjournal.hematologylibrary.org/content/112/9/3574.long>. (Journal IF: 9.06, Citations: 81)

### Ongoing Research Projects

2013/2016 Indução de Tolerância Imunológica após Transplante Alogénico de Células Estaminais Hematopoiéticas em Humanos, FCT. Coordinator: João Forjaz de Lacerda. Amount: €293.513,00  
Total amount: €563,495.000.

2012/2014 Impact of cellular therapy with CMV-specific CD4+ and CD8+ T cells following unrelated hematopoietic stem cell transplantation, Terry Fox Foundation. Coordinator: João Forjaz de Lacerda. Amount: €15.000,00

### Other Projects

2013/2016 Induction of Immune Tolerance in Human Allogeneic Hematopoietic Stem Cell Transplantation. Harvard Medical School Portugal Collaborative Research Grant: HMSP-ICT/0001/2011; Lacerda (PI); 01/01/2013 - 31/12/2015. Coordinator: João Lacerda.

2012/2013 Impact of cellular therapy with CMV-specific CD4+ and CD8+ T cells following unrelated hematopoietic stem cell transplantation. Terry Fox Grant; Lacerda (PI); 01/01/2012 - 31/12/2013. Coordinator: João Lacerda.

2009/2013 Clinical implications of activation of PI3K/Akt signaling pathway in primary adult acute lymphoblastic leukemia FCT: PIC/IC/83023/2007; Lacerda (PI); 01/03/2009 - 29/02/2013. Coordinator: João Lacerda.

### Publications in peer review Journals

Lacerda JF, Oliveira CM (2013). Diagnosis and treatment of invasive fungal infections focus on liposomal amphotericin B. *Clin Drug Investig.* 33Suppl 1, S5-14. (Journal IF: 1.9)

### Invited lectures and seminars

Lacerda JF. Principles of hematopoietic stem cell transplantation. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, September 2013.

Lacerda JF. Immunology of hematopoietic stem cell transplantation. Instituto Superior Técnico, Lisboa, Lisbon, Portugal, November 18, 2013.

Lacerda JF. Clinical applications of hematopoietic stem cell transplantation. Instituto Superior Técnico, Lisbon, Portugal, November 19, 2013.

Lacerda JF. Cellular immunotherapy in oncology and hematopoietic stem cell transplantation. Instituto Superior Técnico, Lisbon, Portugal, November 21, 2013.

Lacerda JF. The Immune System and Cancer – A Dual Role. In: Cancer and Oncobiology. PhD Program. Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, December 4, 2013.

Alho A, Azevedo RI, Lacerda JF. Immune tolerance after hematopoietic stem cell transplantation. Harvard Medical School Retreat. Lisbon, Portugal, December 7, 2013.

### Communications in International Conferences

Alho A, Espada E, Santos Sousa P, Martins C, Lourenço F, Moreno R, Rodrigues A, Juncal C, Garção A, Ferrão A, Palaré MJ, Morais, Lacerda JF, Carmo JA. Unrelated donor stem cell transplantation in severe aplastic anemia using a fludarabine and thymoglobulin based reduced intensity conditioning regimen. 39th Annual Meeting of the European Group for Marrow Transplantation and 29th Meeting of the Nurses Group. Bone Marrow Transplantation 48; S414, Paris, France, 2013. (Poster presentation)

Esteves G, Neves M, Martins H, Costa MJ, Valle S, Raposo J, Martins C, Guerra L, Lopes C, Mendes S, Alho A, Ferreira R, Viveiros C, Espada E, Conde I, Alves D, Lacerda J, Pólo B, Proença H, Carmo JA. Serum Free Light Chain Ratio (FLCr) Is a Powerful Prognostic Factor For Survival In Newly Diagnosed Multiple Myeloma (MM) In The Era Of New Agents Namely On ISS Stage II Patients. 55th Annual Meeting of the American Society of Hematology. Blood in press. New Orleans, USA, 2013. (Poster presentation)

Esteves G, Neves M, Martins H, Martins C, Costa MJ, Valle S, Lopes C, Raposo J, Guerra L, Pólo B, Alho A, Viveiros C, Mendes S, Ferreira R, Espada E, Conde I, Alves D, Lacerda J, Proença H, Carmo JA. Serum Free Light Chain Ratio (FLCr) Is a Powerful Prognostic Factor For Survival In Newly Diagnosed Multiple Myeloma (MM) Eligible For High Dose Melphalan (HDM). 55th Annual Meeting of the American Society of Hematology. Blood in press. New Orleans, USA, 2013. (Poster presentation)

### Communications in National Conferences

Martins H, Neves M, Esteves G, Martins C, Costa MJ, Valle S, Lopes C, Raposo J, Guerra L, Pólo B, Alho A, Viveiros C, Mendes S, Ferreira R, Espada E, Conde I, Alves D, Lacerda J, Proença H, Carmo JA. A relação das cadeias leves livres séricas (RCLL): poderoso factor prognóstico nos doentes com mieloma múltiplo de novo (MM) elegíveis para tratamento com melfalan alta dose (MAD). Livro de Resumos - Reunião Anual da Sociedade Portuguesa de Hematologia, Oporto, Portugal, 2013. (Oral communication)

Neves M, Martins H, Esteves G, Costa MJ, Valle S, Raposo J, Martins C, Guerra L, Lopes C, Mendes S, Alho A, Ferreira R, Viveiros C, Espada E, Conde I, Alves D, Lacerda J, Pólo B, Proença H, Carmo JA. Relação das cadeias leves livres séricas (RCLL): poderoso factor prognóstico na sobrevivência de doentes com mieloma múltiplo de novo e ISSII na era dos novos agentes terapêuticos. Livro de Resumos - Reunião Anual da Sociedade Portuguesa de Hematologia, Oporto, Portugal, 2013. (Oral communication)

Martins H, Neves M, Esteves G, Martins C, Costa MJ, Valle S, Lopes C, Raposo J, Guerra L, Pólo B, Alho A, Viveiros C, Mendes S, Ferreira R, Espada E, Conde I, Alves D, Lacerda J, Carmo JA. Importância das resposta e terapêuticas pós-transplantação autóloga de progenitores

hematopoiéticos (TAPH): experiência de um centro. Livro de Resumos - Reunião Anual da Sociedade Portuguesa de Hematologia, Oporto, Portugal, 2013. (Poster presentation)

Espada E, Alves D, Conde I, Neves, Valle S, Lopes C, Esteves G, Raposo J, Polo B, Costa MJ, Guerra L, Fajardo J, Moreno R, Lourenço F, Martins C, Lacerda JF, Carmo JA. Quimioterapia específica e transplante alogénico de progenitores hematopoiéticos no tratamento da linfocitose hemofagocítica do adulto – experiência de um centro. Livro de Resumos - Reunião Anual da Sociedade Portuguesa de Hematologia, Oporto, Portugal, 2013. (Poster presentation)

### **Internationalisation**

Our Lab collaborates with Dr Cristina Cunha and Dr Agostinho Carvalho from Professor Luigina Romani's group from University of Perugia, in multi-institutional studies evaluating genetic susceptibility for hematological malignancies and invasive infections by studying patient-donor pairs submitted to allogeneic hematopoietic stem cell transplantation.

Furthermore, the Collaborative Research Grant of the Harvard Medical School Portugal Program established a strong collaboration with Professor Jerome Ritz, at Dana-Farber Cancer Institute (DFCI) and Harvard Medical School (HMS), USA.

We have established further collaborations with Prof 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.



## 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 Lab'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 are now working on the hypothesis that brain adenosine A2A receptors drive age-related synaptic dysfunction.

Major research lines:

- Molecular switches from aging towards neurodegeneration in the hippocampus;
- Therapeutic actions of caffeine and caffeine analogs against memory deficits;
- Epigenetics and glucocorticoid actions in aging;
- Cognitive dysfunction in Alzheimer's mouse models;
- Molecular mechanisms of early cognitive deficits in Parkinson's disease.

### Head of Unit

Luísa Maria Vaqueiro Lopes, PhD.

### Research Team

Diana Gabriela Ribeiro Ferreira	Master	PhD Student (started June)
Joana Fernandes Esteves Soares Coelho	PhD	Post-doctoral Investigator (started June)
Rui Artur Paiva Loureiro Gomes	PhD	Investigator, Assistant Professor (started June)
Sara Alexandra Fernandes Carvalho	Graduate	MSc Student (started June)
Vânia Luisa Neves Batalha	Master	PhD Student (started June)

### Keywords / Research Areas

Aging, cognition, hippocampus, neurodegeneration, Alzheimer's Disease, Stress.

### Major scientific achievements

Using animal models, we found that one common feature in stress and aging is the disruption of the hypothalamic-pituitary- axis (HPA) which in turn compromises hippocampal circuitry. We

have established a link between adenosine A2A receptors (A2AR) upsurge and cognitive deficits. We described for the first time that the therapeutic administration of A2AR blockers reverts hippocampal-related impairments, including HPA imbalance.

Papers published in 2013:

V Flaten, C Laurent, JE Coelho, U Sandau, VL Batalha, S Burnouf, M Hamdane, S Humez, D Boison, LV Lopes, L Buée, D Blum, From epidemiology to pathophysiology: what about caffeine in Alzheimer's disease?. *Biochem. Soc Trans*, **42** doi:10.1042/BST20130229

VL Batalha, JM Pego, B Fontinha, AR Costenla, J Valadas, Y Baqi, CE Müller, AM Sebastião and LV Lopes, Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *Mol. Psychiatry* **18**, 32 (Journal IF: 15.4)

### Recent Most Relevant Publications

Batalha VL, Pego JM, Fontinha B, Costenla AR, Valadas J, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV. (2013) Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *Mol. Psychiatry* **18**, 320-31. (Journal IF: 15.4, Citations: n/a)

Chen JF, Sonsalla PK, Pedata F, Melani A, Domenici MR, Popoli P, Geiger J, Lopes LV, de Mendonça (2007) Adenosine A2A receptors and brain injury: broad spectrum of neuroprotection, multifaceted actions and "fine tuning" modulation. *Progress in Neurobiology* **83**, 310. (Journal IF: 11.8, Citations: 97)

Diógenes MJ, Dias RB, Rombo DM, Miranda HV, Maiolino F, Guerreiro P, Nasstrom T, Franquelim HG, Oliveira LM, Castanho M, Lannfelt L, Bergstrom 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: 7.3, Citations: 7)

Diógenes MJ, Costenla AR, Lopes LV, Jerónimo AS, Sousa VC, Fontinha B, Ribeiro JA, Sebastião AM. (2011) Enhancement of LTP in aged rats is dependent on endogenous BDNF. *Neuropsychopharmacology* **36**, 1823. (Journal IF: 6.9, Citations: 19)

Valadas JS, Batalha VL, Ferreira DG, Gomes R, Coelho JE, Sebastião AM, Diógenes MJ, Lopes LV. (2012) Adenosine A2A receptors mediated neuroprotection is modulated by corticotrophin-releasing factor (CRF) in a model of glutamate induced cell death. *Journal of Neurochemistry* **123**, 1030. (Journal IF: 4.5, Citations: 2)

### Ongoing Research Projects

2008/2013 Coordinator: Luísa Maria Vaqueiro Lopes. Agency: Nestec S.A.. Amount: €159.091,00

2011/2013 Coordinator: Luísa Maria Vaqueiro Lopes. Agency: Fundação Ciência e Tecnologia.

Amount: €6.400,00

### Other Projects

2013 – LisbonLiving+: Innovative strategies for a healthy life and an active ageing in the Region of Lisbon Agency: EU-Horizon2020. Amount: €49. 920,00

2013/2015 “Adenosine A2A receptors and alpha-synuclein: Novel targets for Parkinson´s disease” This projects addresses the in vitro role of A2ARs to to aSyn aggregation and toxicity using cellular models of aSyn aggregation. Coordinators: Tiago Outeiro/Luisa Lopes. Agency: Fritz Thyssen Foundation. Amount: €110.000,00

2011/2015 Molecular determinants of microglial activation and neuronal dysfunction in in vivo models of Parkinson´s disease. Coordinator: Teresa Pais. Coordinator Institution: IMM. Coordinator PI: Teresa Pais. Agency: FCT. Amount: €115.664,00

2011/2014 “Psychological indicators of stress reactivity and disease adaptation“. Coordinators: Luisa Lopes/Silvia Ouakinin. Coordinator Institution: HSM/FML Lisbon. Coordinator PI: Sílvia Ouakinin. Agency: Bial Foundation. Amount: €38.000,00.

### Publications in peer review Journals

Flaten V, Laurent C, Coelho JE, Sandau U, Batalha VL, Burnouf S, Hamdane M, Humez S, Boison D, Lopes LV, Buée L, Blum D. (2013) From epidemiology to pathophysiology: what about caffeine in Alzheimer´s disease?. *Biochem. Soc Trans*, **42** doi:10.1042/BST20130229

### Invited lectures and seminars

Lopes LV. Clues to the ‘early-aging’ of the hippocampus. 2nd Annual MIND Symposium Molecular Mechanisms of Neurodegeneration, Harvard Medical School, Boston, United States of America, June, 2013.

Lopes LV. Caffeine and adenosine receptor controlling stress activated pathway. 24th Biennial Meeting of the International-Society-for-Neurochemistry, Cancun, Mexico, April, 2013.

### Communications in International Conferences

Lopes LV, Ferreira DG, Coelho JE, Miranda HV, Albino-Teixeira A, Outeiro TF. Adenosine A2A receptor - A putative player in alpha-synuclein induced LTP impairment. Society For Neuroscience, San Diego, US, November 2013. (Oral communication)

Batalha V, Hamdane M, Buée L, Blum D, Sadri-Vakili G, Lopes LV. A novel role of adenosine A2A receptor as epigenetic and transcriptional modulator of glucocorticoid receptor. Society For Neuroscience, San Diego, US, November 2013. (Poster presentation)

Blum D, Laurent C, Burnouf S, Ferry B, Marciniak E, Derisbourg M, Eddarkaoui S, Parrot S, Demeyer D, Ledent C, Müller C, Sergeant N, Hamdane M, Humez S, Lopes L, Buee L. Effects of caffeine intake and adenosine A2A receptor deletion in a transgenic model of Alzheimer's Disease-like Tau pathology. Society For Neuroscience, San Diego, US, November 2013. (Poster presentation)

Batalha VL, Ferreira DG, Coelho JE, Buée-Scherrer V, Valadas JS, Gomes R, Outeiro T, Blum D, Lopes LV. Can a single receptor drive age-like hippocampal dysfunction? IBRO international symposium Currents Aspects of Current Aspects in Pathophysiology of Alzheimer's disease: what do we miss?”, Braga, Portugal, October 2013. (Oral communication)

Batalha VL, Valadas JS, Baqi Y, Radjaini H, Müller CE, Sebastião AM and Lopes LV. Adenosine A2AR as the trigger to age-like modifications on adenosine neuromodulation of hippocampal synaptic transmission. International Society of Neurochemistry, Cancun, Mexico, April 2013. (Poster presentation)

Batalha VL, Valadas JS, Ferreira DG, Coelho JE, Muller CE, Outeiro TF, Blum D, Lopes LV. Caffeine and adenosine receptor controlling stress activated pathways: a window for depression. International Society of Neurochemistry, Cancun, Mexico, April 2013. (Oral communication)

Gomes C, Correia AM, Gomes R, Vaz AR, Brites D. An approach to study glia reactivity in Amyotrophic Lateral Sclerosis. Molecular Biology in Portugal and EMBL (and EMBL alumni meeting), Faculdade de Ciências, Universidade de Lisboa, European Molecular Biology Laboratory, July 18<sup>th</sup>, 2013 P.6 page 22 Abstract book (Poster presentation)

Vaz AR, Ferreira A, Barbosa M, Cunha C, Marçal AM, Gomes R., Brites D. Role of inflammatory modulators in ALS models. Champalimaud Neuroscience Symposium CNPS 2013. Abstract n. 31 (Poster presentation)

### **Communications in National Conferences**

Ferreira DG, Coelho JE, Batalha VL, Miranda HV, Albino-Teixeira A, Outeiro TF, Lopes LV. “Adenosine A2A receptor blockade prevents LTP impairment induced by alpha-synuclein”. XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal, May 2013.

Batalha VL, Hamdane M, Buée L, Blum D, Sadri-Vakili G, Lopes LV. Modulation of Glucocorticoid Receptors by adenosine A2A receptor activation: from gene to protein level. XIII Reunião da Sociedade Portuguesa de Neurociências. Luso, Portugal, May 2013.

Nascimento F, Correia A, Gomes R, Pousinha PA, Sebastião A, Ribeiro JA. Neuromuscular transmission modulation by adenosine A2A receptors in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis. Comunicação oral SNIII6, XLII Reunião Anual da Sociedade Portuguesa de Farmacologia, ICBAS-UP, Porto, Portugal, February 2013.

### 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 EMBO. LL is PhD supervisor in the EU Erasmus/Mundus “Ageing Brain” network and frequently chairs symposia and delivers lectures internationally (FENS, SFN, Purines, ICAD). From 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

Award of the Royal Society discussion meeting, Long-term potentiation: enhancing neuroscience for 40 years, to Vânia Batalha, London, UK, December 2013.

ISN travel award for the joint ISN-ASN meeting to Vânia Batalha, Cancun, Mexico, ISN, April 2013.

### Industry contract research

Nestlé Research Center, Lausanne, Switzerland (Nestec/IMM/474/2011) PI: Luísa Lopes “Brain-gut interaction – neurotrophic actions”

### Advanced teaching

#### Luisa Lopes

- Since 2013 - Faculty member of the Lisbon Biomed PhD program (IMM) under the topic Neurosciences (*Lecturer and supervisor*)
- Since 2012 - PhD supervisor within the NEU4EU - European PhD education and training network ‘Ageing Brain’ (Coordinator: Univ. Groningen) (*Lecturer*)
- Since 2011 – Faculty member in the Doctoral Course “Clinical Neurosciences and Neuropsychiatry” - Faculdade de Medicina do Porto, Portugal, Module: Stress and Cognition. (*Lecturer*)
- Since 2008 – Co-coordinator and lecturer of the Neurochemistry course (Medical Biochemistry Master degree) at Faculdade de Ciências, Universidade de Lisboa (Modules: “Neurotransmitters”; “Neurotransmitter receptors”; “Cell signaling”; “Receptor radioligand binding”; “Neurogenesis and stem cell therapy.

Rui Gomes

- Coordinator and lecturer of the Molecular Biology and Genetics course (Doctoral Program in Biology, Faculdade de Ciências, Universidade de Lisboa, Lisbon, Portugal).
- Coordinator and lecturer of the Cell Cycle Regulation course (Master degree in Molecular Biology and Genetics, Faculdade de Ciências, Universidade de Lisboa, Lisbon, Portugal).

**Msc theses completed**

Sara Carvalho (2013) Subcellular Localization of Adenosine A2A Receptors in Hippocampal Synapses. Faculdade de Ciências, Universidade de Lisboa, Lisboa, Portugal. Supervisors: Luísa Lopes, Pedro Lima.

Joana Mafalda Dias Cardoso (2013) Haptoglobina e TNF-  $\alpha$ , dois biomarcadores genéticos e circulantes associados às respostas de fase aguda na Psoríase Master Thesis in Molecular Biology and Genetics. Faculdade de Ciências, Universidade de Lisboa, Lisbon, Portugal. Supervisors: Manuel Bicho, Rui Gomes.

Lígia Marisa Sampaio Pinda (2013) Development of tal effector – Recombinase fusion proteins for genome engineering Master Thesis in Molecular Biology and Genetics. Faculdade de Ciências, Universidade de Lisboa, Lisbon, Portugal. Supervisors: Frank Buchholz, Rui Gomes

Renato Gomes da Silva Martinho (2013) SIRT 2: in the crossroad of aging, neurodegeneration and autophagy. Master Thesis in Molecular Biology and Genetics. Faculdade de Ciências, Universidade de Lisboa, Lisbon, Portugal. Supervisors: Tiago Outeiro, Rui Gomes.

## MUSA MHLANGA LAB

### Major Interests / Objectives

In biology several important processes occur at spatial dimensions currently beyond the reaches of light microscopy. Our lab focuses on biological questions at this scale as they are related to gene expression. We study RNA transcription, metabolism and transport, as well as the development and innovation of technology to study these problems. Dynamic multi-molecular complexes in the eukaryotic cell nucleus remain well outside the resolution of light microscopy. Intrinsic to RNA transcription are modifications to nuclear architecture and the repositioning of chromosomal loci, and the interplay of ribonucleic proteins. These events remain opaque at the single molecule level, and are intensively researched by our research group.

### Head of Unit

Musa Mazibonela Kasiyedwa Mhlanga, PhD, Associate Professor, CSIR- South Africa.

### Research Team

Ana Catarina Fidalgo Barata	Undergraduate	Investigator
JAGDISH PARIHAR	Master	Technician
Joana Rita Gonçalves da Cruz	Graduate	MSc Student (left September)
Luis Pedro Coelho	PhD	Post-doctoral Investigator
Ricardo José dos Santos Duarte Vieira Henriques	No degree	Investigator (left May)
Sílvia Almeida dos Santos Rosa	Master	Investigator

### Keywords / Research Areas

RNA biology, Super-resolution, Nuclear Architecture, Gene Expression, Host-Pathogen, Transcription.

### Major scientific achievements

We published a few important papers this year. We were also a new EPO patent awarded and filed a number of other patents. We participated in a number of international conferences.

#### Publications:

Statin Therapy Reduces the Mycobacterium tuberculosis Burden in Human Macrophages and in

Mice by Enhancing Autophagy and Phagosome Maturation, *Journal of Infectious Diseases*.  
Chromosomal Contact Permits Transcription between Coregulated Genes, *Cell*.

Patents:

Polynucleotide suitable for single cell based reporter assay to monitor gene expression patterns with high spatio-temporal resolution. EP Patent 2,036,989.

Major Conference Participation:

Hong Kong University & Institut Pasteur Hong Kong - Molecular & Cell Biology Course - Speaker and organizer of practical.

EMBO conference : Nuclear Structure & Dynamics – Speaker.

EMBO Practical Course: Imaging Infection & Immunity - Speaker & Organizer.

### Recent Most Relevant Publications

R Henriques, M Lelek, EF Fornasiero, F Valtorta, C Zimmer, MM Mhlanga (2010) QuickPALM: 3D real-time photoactivation nanoscopy image processing in ImageJ. *Nature Methods* **7**, 339. (Journal IF: 23.565, Citations: 83)

Stephanie Fanucchi, Youtaro Shibayama, Shaun Burd, Marc S Weinberg, Musa M Mhlanga (2013) Chromosomal Contact Permits Transcription between Coregulated Genes. *Cell* **155**, 505 www.cell.com. (Journal IF: 34.366, Citations: 1)

MM Mhlanga, DY Vargas, CW Fung, FR Kramer, S Tyagi (2005) tRNA-linked molecular beacons for imaging mRNAs in the cytoplasm of living cells . *Nucleic acids research* **33**, 1902. (Journal IF: 8.026, Citations: 90)

DP Bratu, BJ Cha, MM Mhlanga, FR Kramer, S Tyagi (2004) Visualizing the distribution and transport of mRNAs in living cells. *Proceedings of the National Academy of Sciences* **100**, 13308. (Journal IF: 9.737, Citations: 304)

LG Kostrikis, S Tyagi, MM Mhlanga, DD Ho, FR Kramer (19 (1998) Spectral genotyping of human alleles . *Science* **279**, 1228. (Journal IF: 31.03, Citations: 332)

### Ongoing Research Projects

2011/2013 Coordinator: Musa Mazibonela Kasiyedwa Mhlanga. Agency: FCT. Amount: €185.980,00

### Invited lectures and seminars

Musa Mhlanga, Collaborative meeting between RIKEN & South African Partners. RIKEN - Yokohama, Japan. December 2013 (Oral communication)

Musa Mhlanga, E-Research Conference - Using IT infrastructures in scientific Research. UCT-



Cape Town, South Africa. October 2013. (Oral communication)

Musa Mhlanga, Cheap Diagnostics for the Developing world. Wellcome Trust, New Delhi, India. February 2013. (Oral communication)

### **Communications in International Conferences**

Musa Mhlanga. Super resolution microscopy: PALM/STORM. Hong Kong University & Institut Pasteur Hong Kong - Molecular & Cell Biology Course. Hong Kong, HK. April 14-26, 2013.

Musa Mhlanga. Chromatin contact permits transcription of co-regulated genes. EMBO conference: Nuclear Structure & Dynamics. Ile sur la Sorgue, France. October 2-6, 2013

Musa Mhlanga. Imaging Host-Pathogen Interactions. EMBO Practical Course: Imaging Infection & Immunity. CSIR-Pretoria South Africa. March 20-30th 2013.

### **Organisation of Conferences**

Musa Mhlanga, EMBO Practical Course: Imaging Infection & Immunity, Speaker & Organizer. CSIR-Pretoria South Africa. March 20-30th 2013.

### **Advanced teaching**

Musa Mhlanga, Speaker and organiser of the EMBO Practical Course: Imaging Infection & Immunity. CSIR-Pretoria South Africa. March 20-30, 2013.

Musa Mhlanga, speaker and organiser of practical course, Molecular & Cell Biology Course. Hong Kong University & Institut Pasteur Hong Kong. Hong Kong, HK. April 14-26, 2013.

### **Msc theses completed**

Joana Cruz (2013) Evaluating differential gene expression using RNA-sequencing data: a case study in host-pathogen interaction upon *Listeria monocytogenes* infection. Instituto Superior Técnico de Lisboa. Supervisors: Luis Coelho, Musa Mhlanga.

## Luís Moita Lab

### Major Interests / Objectives

The general unifying goal of our research unit is to use unbiased functional genomic and genetic tools to identify and characterize human and mouse genes and signalling pathways that regulate central processes of an immune response, their targets and role in an in vivo immune response.

### Head of Unit

Luís Filipe Ferreira Moita, MD/PhD - Assistant Professor at FMUL

### Research Team

Ana Roxo Leão Neves Costa	PhD	Post-doctoral Investigator
Ângelo António Ferreira Chaves do Rosário Chora	PhD	Post-doctoral Investigator (left October)
Catarina Susana Ferreira Moita	PhD	Post-doctoral Investigator
Dora Cristina dos Santos Pedroso	PhD	Technician (left in December)
João António Augusto Ferreira	MD, PhD	Principal Investigator (left in December)
Maria Helena Teixeira Raquel Gonçalves	PhD	Post-doctoral Investigator
Nadja Pejanovic	PhD	Post-doctoral Investigator (left in July)
Pedro Martins Didelet Pereira	Master	PhD Student (left in December)
Raquel Ferreira Rodrigues	PhD	Post-doctoral Investigator
Richard Staats	MD	PhD student
Susana de Castro Luís Lopes Moreira	MD	PhD Student
Tiago Rodrigues Velho	Under-graduate	MSc Student

### Keywords / Research Areas

Innate Immunity, Dendritic Cells, Inflammation, Sepsis, RNAi.

### Major scientific achievements

Nuno Figueiredo, Angelo Chora, Helena Raquel, Nadja Pejanovic, Pedro Pereira, Björn Hartleben, Ana Neves-Costa, Catarina Moita, Dora Pedroso, Andreia Pinto, Sofia Marques, Hafeez Faridi, Paulo Costa, Raffaella Gozzelino, Jimmy L. Zhao, Miguel P. Soares, Margarida Gama-Carvalho, Jennifer Martinez, Qingshuo Zhang, Gerd Döring, Markus Grompe, J. Pedro Simas, Tobias B. Huber, David Baltimore, Vineet Gupta, Douglas R. Green, João A. Ferreira and Luis F. Moita. Anthracyclines induce DNA damage, response-mediated protection against severe sepsis. *Immunity* **39**(5), 874-84, November 14, 2013.

2013 Pfizer Award for Basic Research. “Anthracyclines induce DNA damage response-mediated protection against severe sepsis”. Nuno Figueiredo, Angelo Chora, Helena Raquel and Luis Ferreira Moita.

### Recent Most Relevant Publications

Cebrian I, Visentin G, Blanchard N, Jouve M, Bobard A, Moita C, Enninga J, Moita LF, Amigorena S, Savina A. (2011) Sec22b regulates phagosomal maturation and antigen crosspresentation by dendritic cells, *Cell* (<http://www.sciencedirect.com/science/article/pii/S0092867411013596>) (Journal IF: 32.403, Citations: 26)

Robinson MJ, Osorio F, Rosas M, Freitas RP, Schweighoffer E, Gross O, Verbeek JS, Ruland J, Tybulewicz V, Brown GD, Moita LF, Taylor PR, Reis e Sousa C. (2009) Dectin-2 is a Syk-coupled pattern recognition receptor crucial for Th17 responses to fungal infection. *Journal of Experimental Medicine* (<http://jem.rupress.org/content/206/9/2037.long>) (Journal IF: 13.853, Citations: 148)

Ostrowski, M., Carmo, N.B., Krumeich, S., Fanget, I., Raposo, G., Savina, A., Moita, C.F., Schauer, K., Hume, A.N., Freitas, R.P., Goud, B., Benaroch, P., Hacohen, N., Fukuda, M., Desnos, C., Seabra, M.C., Darchen, F., Amigorena, S., Moita, L.F.\*, Thery, C. (2010) Rab27 controls constitutive exosome secretion. *Nat Cell Biol* (<http://www.nature.com/ncb/journal/v12/n1/full/ncb2000.html>) (Journal IF: 19.488, Citations: 139)

Savina, A., Peres, A., Cebrian, I., Carmo, N., Moita, C., Hacohen, N., Moita, L.F., and Amigorena, S. (2009) Rac2 controls phagosomal alkalization and crosspresentation selectively in CD8+ dendritic cells. *Immunity* (<http://www.sciencedirect.com/science/article/pii/S107476130900137X>) (Journal IF: 21.637, Citations: 61)

Oberdoerffer, S., Moita, L.F., Neems, D., Freitas, R.P., Hacohen, N., Rao, A. (2008) Regulation of CD45 alternative splicing by heterogeneous ribonucleoprotein, hnRNPLL. *Science*

(<http://www.sciencemag.org/content/321/5889/686.long>) (Journal IF: 31.201, Citations: 64)

### Ongoing Research Projects

2010/2013 Role of ASF/SF2 and SRp20 in IL-1 $\beta$  secretion. Coordinator: Luís Filipe Ferreira Moita. Agency: FCT. Amount: €198.591,00

2011/2014 Role of newly identified genes in in vivo antigen cross-presentation-dependent generation of CTL responses against tumors. Coordinator: Luís Filipe Ferreira Moita. Agency: FCT. Amount: €136.840,00

2006/2014 FLAD-SHRNA. Coordinator: Luís Filipe Ferreira Moita. Agency: Fundação Luso Americana. Amount: €250.000,00

2013/2014 UAB Center for AIDS Research. Coordinator: Luís Filipe Ferreira Moita. Agency: The Board of Trustees of the University of Alabama. Amount: €10000,00

### Publications in peer review Journals

Nuno Figueiredo, Angelo Chora, Helena Raquel, Nadja Pejanovic, Pedro Pereira, Björn Hartleben, Ana Neves-Costa, Catarina Moita, Dora Pedroso, Andreia Pinto, Sofia Marques, Hafeez Faridi, Paulo Costa, Raffaella Gozzelino, Jimmy L. Zhao, Miguel P. Soares, Margarida Gama-Carvalho, Jennifer Martinez, Qingshuo Zhang, Gerd Döring, Markus Grompe, J. Pedro Simas, Tobias B. Huber, David Baltimore, Vineet Gupta, Douglas R. Green, João A. Ferreira and Luis F. Moita. Anthracyclines induce DNA damage response-mediated protection against severe sepsis, *Immunity* November 14, 2013. **39**(5), 874-84 (Journal IF: 19.795; Citations: 2)

Marina Colombo, Catarina Moita, Guillaume van Niel, Joanna Kowal, James Vigneron, Philippe Benaroch, Nicolas Manel, Luis F. Moita, Clotilde Théry, Graça Raposo. Analysis of ESCRT functions in exosome biogenesis, composition and secretion highlights the heterogeneity of extracellular vesicles released by different cells. *Journal of Cell Science* October 8, 2013. [Epub ahead of print]. (Journal IF: 5.877; Citations: 0)

Rehwinkel J, Maelfait J, Bridgeman A, Rigby R, Hayward B, Liberatore RA, Bieniasz PD, Towers GJ, Moita LF, Crow YJ, Bonthron DT, Reis E Sousa C. SAMHD1-dependent retroviral control and escape in mice. *EMBO J.* **32**(18), 2454-62. (Journal IF: 9.822; Citations: 4) September 11, 2013.

Raquel Rodrigues, Ana Rita Grosso and Luis F. Moita. Genome-Wide Analysis of Alternative Splicing during Dendritic Cell Response to a Bacterial Challenge. *PLoS ONE* April 17, 2013. **8**(4), e61975. (Journal IF: 3.730; Citations: 0)

Ana Neves-Costa, Luis F. Moita. TET1 is a negative transcriptional regulator of IL-1 $\beta$  in the THP-1 cell line *Molecular Immunology*, **54**(3-4), 264-70. (Journal IF: 2.645; Citations: 3)

Moniz S, Martinho O, Pinto F, Sousa B, Loureiro C, Oliveira MJ, Moita LF, Honavar M, Pinheiro C, Pires M, Lopes JM, Jones C, Costello JF, Paredes J, Reis RM, Jordan P. Loss of WNK2 expression

by promoter gene methylation occurs in adult gliomas and triggers Rac1-mediated tumour cell invasiveness. *Hum Mol Genet*, January 1, 2013. **22**(1), 84-95. (Journal IF: 7.692 Citations: 3)

### Invited lectures and seminars

"The Anthracycline Epirubicin Triggers an ATM-Dependent Protective Response to the CLP Mouse Model of Sepsis". Host: Nir Hacohen. Harvard Medical School, Boston, USA, June 4th, 2013.

"The Anthracycline Epirubicin Triggers an ATM-Dependent Protective Response to the CLP Mouse Model of Sepsis". Host: Gerd Döring. University of Tuebingen, Tuebingen, Germany, April 25th, 2013.

"The Anthracycline Epirubicin Triggers an ATM-Dependent Protective Response to the CLP Mouse Model of Sepsis". Seminar at Faculdade de Ciencias, Lisbon, Portugal, Host: Margarida Gama-Carvalho. May 22nd, 2013.

"IMM". Seminário de Biotecnologia Brasil-Portugal. Biocant Park, Cantanhede, Portugal. June 27-28, 2013. (In official representation of IMM).

Basic Biomedical Research: from MD to PhD. CNIAC II. Covilhã, Portugal, September 21st, 2013.

"Effective treatment of rat adjuvant-induced arthritis by celastrol". Disclosing the future in RA: the Portuguese contribution. Meeting sponsored by ANDAR. Calouste Gulbenkian Foundation, Lisbon, Portugal, October 11th, 2013.

### Communications in International Conferences

"The expression of the Per2 clock gene is up-regulated in non-treated OSAS patients and normalises its mRNA levels upon positive pressure treatment". SEPAR, Barcelona, Spain, June 14-17th, 2013. (Oral presentation)

"The expression of the Per2 clock gene is up-regulated in non-treated OSAS patients and normalises its mRNA levels upon positive pressure treatment". World Congress in Sleep Medicine. Valencia, Spain. September 28th – October 2nd, 2013. (Oral presentation)

### Internationalisation

The Innate Immunity and Inflammation Unit has multiple longstanding collaborations with international laboratories from which have emerged several high level publications. The most important are with: (1) Sebastian Amigorena (Institute Curie, Paris, France); (2) Caetano Reis e Sousa (Cancer Research UK London Research Institute, London, UK); (3) Nir Hacohen (Harvard Medical School / Broad Institute of Harvard and MIT, Boston, USA).

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

2013 Pfizer Award for Basic Research. “Anthracyclines induce DNA damage response-mediated protection against severe sepsis” to Nuno Figueiredo, Angelo Chora, Helena Raquel and Luis Ferreira Moita.

Portuguese Pulmonology Society/SEPAR/Vitoria FAES PHARMA 2013 “The expression of the Per2 clock gene is up-regulated in non-treated OSAS patients and normalizes its mRNA levels upon positive pressure treatment” to S. Moreira, J. Valença, A. Bugalho de Almeida, L. Moita

### **Advanced teaching**

GABBA, Immunology Module, organized by Antonio Freitas. IBMC, Porto, Portugal, February 6th, 2013.

### **PhD theses completed**

Nuno L. Figueiredo (28/06/2013) Severe sepsis protective role of epirubicin. University of Lisbon, Lisbon, Portugal. Supervisors: Luis Ferreira Moita, Paulo Costa.

**MARIA MOTA LAB****Major Interests / Objectives**

Despite renewed eradication efforts from the international community, malaria still exerts an enormous disease burden, with nearly half the planet's population at risk of infection. Our overall goal has always been to understand how the disease-causing Plasmodium parasites establish and survive in their host as a way to design efficient and rational strategies to combat malaria.

**Head of Unit**

Maria Manuel Mota, PhD, Harvard School of Public Health.

**Research Team**

Afonso Miguel Nunes Ferreira	Graduate	Trainee
Ana Filipa Caetano Parreira	Graduate	Technician
Ana Filipa Pintéus da Cruz	PhD	Post-doctoral Investigator
Ana Margarida Aires Alves Vigário	PhD	Investigator, Assistant Professor
Ana Margarida Ferreira Góis	Master	Technician
Ana Margarida Roque Sanches Vaz	Master	MSc Student (left June)
António Manuel Barbeiro Mendes	PhD	Post-doctoral Investigator
Carolina Martins Peralta Lopes da Silva	Undergraduate	Technician (left November)
Cláudia B. Rodrigues Sá e Cunha Mesquita Gabriel	PhD	Post-doctoral Investigator
Daniel José Martins Carapau	PhD	Post-doctoral Investigator
Eliana Real	PhD	Post-doctoral Investigator
Fernanda Garcia Guedes Baptista	Master	Lab manager (left November)
Gabriela Stephanie Peres Cristo	Master	MSc Student (started September)
Ghislain Guillaume Nicolas Cabal	PhD	Post-doctoral Investigator

Inês Isabel Fernandes Gomes	PhD	Post-doctoral Investigator
Iset Medina Vera	PhD	Post-doctoral Investigator
Joana Cristina da Silva Sales Dias	Master	Investigator
Kirsten Hanson	PhD	Post-doctoral Investigator
Ksenija Slavic	PhD	Post-doctoral Investigator
Lénia Marisa Pereira Rodrigues	PhD	Post-doctoral Investigator (started September)
Liliana Mancio Silva	PhD	Post-doctoral Investigator
Lisa Alves Azevedo	Undergraduate	Technician
Márcia Melo Medeiros	MD/PhD	Post-doctoral Investigator (started February)
Marco Andre Manso Domingues	PhD	Investigator (started April) (left November)
Margarida Maria Teles Grilo Ruivo	Master	Technician (started September)
Maria Inês Sousa de Albuquerque	Master	Technician (left August)
Maurice Ayamba Itoe	PhD	Post-doctoral Investigator
Miguel Dinis Monteiro dos Santos	Undergraduate	Trainee (started September)
Miguel Prudêncio	PhD	Principal Investigator (left August)
Neide Marina Vieira Pereira	PhD	Post-doctoral Investigator
Patrícia dos Santos Meireles	Master	PhD Student (left August)
Patrícia Irene da Silva Inácio	No degree	PhD Student
Peter Liehl	PhD	Post-doctoral Investigator
Sofia Pinto Guia Marques	PhD	Lab manager (started August)
Vanessa Alexandra Zuzarte Luís	PhD	Post-doctoral Investigator



### Keywords / Research Areas

Host-Plasmodium interactions, Nutrient sensing, Innate immune response against Plasmodium infection, Host metabolism and Plasmodium infection, Effects of dietary habits on malaria, Cell biology of Plasmodium liver stages.

### Major scientific achievements

During 2013 the Mota Laboratory has:

- Shown that torins, developed as ATP-competitive mTOR kinase inhibitors, are fast-acting and highly potent antiplasmodial compounds (PNAS 110:E2838);
- Revealed, in collaboration with R. Moreira and F. Lopes (FFUL, PT), a number of new anti-malarial compounds (*J Med Chem.* **56**, 7679; *Eur J Med Chem.* **69**, 872);
- Established, in collaboration with S. Bhatia (MIT, USA), the liver stages for both human malaria parasites *P. falciparum* and *P. vivax* in a microscale human liver platform (*Cell Host Microbe* **14**, 104);
- Discovered that the host uses a sensor mechanism (until now only known to detect certain type of viruses) to detect Plasmodium parasites during liver stages of infection, ending the long disseminated dogma that this stage progressed invisible to the host defences (*Nat Med.* **20**, 47).

The PI of the team, Maria M. Mota, has received the “Prémio Pessoa”, a highly prestigious Award given yearly to a Portuguese personality of Arts, Literature or Science.

### Recent Most Relevant Publications

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: 9.74, Citations: 14)

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. *Nat Med* **20**(1), 47-53. doi: 10.1038/nm.3424. Epub 2013 Dec 22. PMID: 24362933. (Journal IF: 27.14, Citations: 1)

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 USA* **110**(30), E2838-47. (Journal IF: 9.74, Citations: 3)

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: 27.14, Citations: 55)

Epiphanio 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: 23)

### Ongoing Research Projects

2012/2014 Mechanisms of nutrient-sensing by the malaria parasite. Coordinator: Liliana Mancio Silva. Agency: FCT. Amount: €123.410,00

2011/2014 EVIMalaR award (Establishment of a European Virtual Institute for Malaria Research). Coordinator: Liliana Mancio Silva. Agency: European Commission. Amount: €210.000,00

2010/2013 Respiratory tract infections & malaria: a new case of mutual interactions? Coordinator: Maria Manuel Mota. Agency: FCT. Amount: €190.850,00

2009/2014 Establishment of a European Virtual Institute for Malaria Research. Coordinator: Maria Manuel Mota. Agency: FP7. Amount: €91.837,20

2010/2013 Unravelling the secrets of Plasmodium liver stage: a multi-directional approach. Coordinator: Maria Manuel Mota. Agency: FCT. Amount: €199.943,00

2010/2013 New drugs for treating and eradicating malaria. Coordinator: Maria Manuel Mota. Agency: FCT. Amount: €300.000,00

2010/2013 The influence of bile acids on malaria liver infection. Coordinator: Miguel Prudêncio. Agency: FCT. Amount: €171.482,00

2012/2014 Utilization of host cell resources by the malaria parasite in the liver. Coordinator: Miguel Prudêncio. Agency: FCT. Amount: €154.755,00

2012/2015 Towards malaria eradication. A novel approach for multi-targeting the parasite's life cycle. Coordinator: Miguel Prudêncio. Agency: FCT. Coordinator Institution: Faculdade de Farmácia da Universidade de Lisboa. Coordinator PI: Francisca Conceição Lopes. Amount: €36.741,00 Amount (total): €191.759,00

2011/2013 Mechanisms of Plasmodium liver infection: Subverting the host ubiquitin-proteasome pathway towards an immune evasion strategy. Coordinator: Vanessa Alexandra Zuzarte Luis. Agency: FCT. Amount: €157.162,00

2013/2015 Regulation of host cell metabolism during malaria liver stage. Coordinator: Ghislain Guillaume Nicolas Cabal. Agency: FCT. Amount: €168.637,00

2013/2014 Liver stage antimalarials that drive sterile immunity. Coordinator: Kirsten Hanson. Agency: Bill & Melinda Gates Foundation. Amount: €76.260,20

2013/2015 Host-Plasmodium interactions: a tale of sensing and being sensed. Coordinator: Maria Manuel Mota. Agency: FCT. Amount: €331.463,00

### Publications in peer review Journals

March S, Ng S, Velmurugan S, Galstian A, Shan J, Logan DJ, Carpenter AE, Thomas D, Sim BK, Mota MM, Hoffman SL, Bhatia SN. 2013. A microscale human liver platform that supports the hepatic stages of Plasmodium falciparum and vivax. *Cell Host Microbe*. 17 **14**(1), 104-15. (Journal IF: 13.02; Citations: 1)

Rodrigues T, Ressurreição AS, da Cruz FP, Albuquerque IS, Gut J, Carrasco MP, Gonçalves D, Guedes RC, Dos Santos DJ, Mota MM, Rosenthal PJ, Moreira R, Prudêncio M, Lopes F. 2013. Flavones as isosteres of 4(1H)-quinolones: Discovery of ligand efficient and dual stage antimalarial lead compounds. *Eur J Med Chem*. **69**, 872-80. (Journal IF: 3.50; Citations: 0)

Ressurreição AS, Gonçalves D, Siteo AR, Albuquerque IS, Gut J, Góis A, Gonçalves LM, Bronze MR, Hanscheid T, Biagini GA, Rosenthal PJ, Prudêncio M, O'Neill P, Mota MM, Lopes F, Moreira R. 2013. Structural optimization of Quinolone-4(1H)-imines as dual-stage antimalarials: toward increased potency and metabolic stability. *J Med Chem*. **56**(19), 7679-90. (Journal IF: 5.61; Citations: 1)

Rodrigues T, da Cruz FP, Lafuente-Monasterio MJ, Gonçalves D, Ressurreição AS, Siteo AR, Bronze MR, Gut J, Schneider G, Mota MM, Rosenthal PJ, Prudêncio M, Gamo FJ, Lopes F, Moreira R. 2013. Quinolone-4(1H)-imines are potent antiplasmodial drugs targeting the liver stage of malaria. *J Med Chem*. **56**(11) 4811-5. (Journal IF: 5.61; Citations: 4)

Rebello M, Sousa C, Shapiro HM, Mota MM, Grobusch MP, Hänscheid T. 2013. A novel flow cytometric hemozoin detection assay for real-time sensitivity testing of Plasmodium falciparum. *PLoS One*. **8**(4), e61606. (Journal IF: 3.73; Citations: 2)

Ng S, March S, Galstian A, Hanson K, Carvalho T, Mota MM, Bhatia SN. 2013. Hypoxia promotes liver stage malaria infection in primary human hepatocytes in vitro. *Dis Model Mech*. Nov 28, 2013. PMID: 24291761. (Journal IF: 4.96, Citations: 0)

Spavieri J, Allmendinger A, Kaiser M, Itoe MA, Blunden G, Mota MM, Tasdemir D. 2013. Assessment of dual life stage antiplasmodial activity of british seaweeds. *Mar Drugs* **11**(10):4019-34. (Journal IF: 3.98, Citations: 0)

Prudêncio M, Mota MM. 2013. Targeting host factors to circumvent anti-malarial drug resistance. *Curr Pharm Des*. **19**(2), 290-9. Review. PMID: 22973886. (Journal IF: 4.41; Citations: 1)

Sinnis P, De La Vega P, Coppi A, Krzych U, Mota MM. 2013. Quantification of sporozoite invasion, migration, and development by microscopy and flow cytometry. *Methods Mol Biol*. **923**, 385-400 (Journal IF: 1.29; Citations: 1)

### Invited lectures and seminars

Maria Mota, Meeting of the French Dendritic Cell Society, Paris, France, December 9-10, 2013.

Maria Mota, XXIII Brazilian Conference on Parasitology, Florianopolis, Brazil, October 22-26, 2013.

Maria Mota, Conference "Intracellular Niches of Pathogens", Frankfurt, Germany, September 29-30, 2013.

Maria Mota, 8th European Congress on Tropical Medicine and International Health, Copenhagen, Denmark, September 10-13, 2013.

Maria Mota, Gordon Research Conference on Malaria, Lucca - Italy, August 4-9, 2013.

Maria Mota, Biozentrum (invited seminar), Basel, Switzerland, June 17, 2013.

Maria Mota, The Ninth Elsinore Meeting On Infection Immunity, Elsinore, Denmark, May 29-31, 2013.

Maria Mota, 9th Annual BioMalPar/ I EVIMalaR Meeting - Biology and Pathology of the Malaria Parasite, EMBL-Heidelberg, Germany, May 13-15, 2013.

Maria Mota, International Biolron Society Meeting, London, UK, April 14-18, 2013.

Maria Mota, Rockefeller University (invited seminar), New York, USA, March 18, 2013.

Maria Mota, Keystone Malaria Conference, New Orleans, USA, January 20-24, 2013.

### Communications in International Conferences

Vanessa Zuzarte-Luís. miRNA fingerprinting of individuals with an ongoing *P. falciparum* liver infection. 6th MIM Pan-African Malaria Conference Durban, South Africa, October 6-11, 2013. (Oral communication)

Kirsten Hanson. "Torins are potent antimalarials that block the trafficking and replenishment of Plasmodium parasitophorous vacuole membrane proteins" Gordon Research Seminar - Malaria, Lucca, Italy, August 4-9, 2013. (Oral communication)

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, Mohsan S, Ferreira Chora A, 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. "Host cell sensors for Plasmodium activate innate immunity against liver stage infection". EMBO Young Scientist Forum 2013, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

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. “Torins are potent antimalarials that block the trafficking and replenishment of Plasmodium parasitophorous vacuole membrane proteins” 9th Annual BioMalPar/ EVIMalaR Conference: Biology and Pathology of the Malaria Parasite. Heidelberg, Germany, May 13-15, 2013. (Poster presentation)

Liliana Mancio-Silva, Agnieszka Religa, Joana Sales-Dias, Andrew Waters, Oliver Billker, Maria M. Mota “Nutrient-sensing by Plasmodium parasites” 9th Annual BioMalPar/ I EVIMalaR Conference – Biology and Pathology of the Malaria Parasite. EMBL Heidelberg, Germany, May 13-15, 2013. (Oral communication).

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. “Torins are potent antimalarials that block the trafficking and replenishment of Plasmodium parasitophorous vacuole membrane proteins” Research Advances in Malaria: Malaria transmission from the mosquito midgut to the mammalian liver. Johns Hopkins School of Public Health, Baltimore, USA, April 24-25, 2013. (Poster presentation)

Ksenija Slavic, Jon Pittman, Kirsten Hanson, Iset Vera, Sanjeev Krishna, Henry M Staines, Maria M Mota “Characterization of novel iron transporter in malaria parasites” The International Biolron Society (IBIS) Congress, London, UK, April 14-18, 2013. (Poster presentation)

Vanessa Zuzarte-Luís, Peter Liehl, Kirsten Hanson, Céline Carrét, Maria M. Mota “Dietary Lipids abrogate Plasmodium liver infection via IL-1R signaling”, Keystone Symposia Conference – Metabolic Control of Inflammation and Immunity, Breckenridge, Colorado, USA, January 21-26, 2013. (Poster presentation).

### Internationalisation

The Maria Mota Laboratory of IMM is part of EVIMalaR (European Virtual Institute of Malaria Research), a European Network of Excellence funded by the European Commission. This network includes Laboratories across Europe that work on many aspects of Malaria research: from mosquito stages to the mammalian host, from disease pathogenesis to transmission, from drug development to vaccine discovery. The laboratory participated with 3 researchers in the first EVIMalaR Annual Meeting (also known as “BioMalPar” - Biology and Pathology of the Malaria Parasite meeting) that took place in Heidelberg last May.

The Maria Mota Laboratory has attracted funding from International agencies, including the European Research Council, the Bill & Melinda Gates Foundation, and the Howard Hughes Medical Institute.

The researchers in the Laboratory often present their research at International Meetings, and also make experimental work at the Laboratories of collaborators in foreign Institutions such as EMBL or Leiden University.

Among the many collaborators of the Laboratory across the World are:

- Sangeeta N. Bhatia (MIT, Cambridge, USA);
- Shahid Kahn, Chris Janse (Leiden University, Holand);
- Friedrich Frischknecht (Hygiene Institut Heidelberg, Germany);

- Kate Fitzgerald, Doug Golenbock (UMass, USA);
- Fidel Zavala (JHSPH, Baltimore, USA);
- Mathias Mann (MPI, Martinsried, Germany);
- Júlio Sampaio, Andrej Schevshenko (MPI, Dresden, Germany);
- Oliver Billker (Sanger Institute, Cambridge, UK);
- Arthur Scherf (Institut Pasteur, Paris France);
- Manuel Llinas (Princeton University, New Jersey, USA);
- Jon Clardy (HMS, Boston, USA);
- Mathias Marti (HMS, Boston, USA);
- Robert Sauerwein (Nijmegen University, Holand);
- Ana Rodriguez (NYU, USA);
- Manuela Santos (University of Montreal, Canada).

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

"Prémio Pessoa" awarded to Maria Mota, December 2013.

#### **Patents/prototypes**

“Rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine”, PCT international application WO/2013/156949 submitted 17.04.2013, published 24.10.2013. Authors: Miguel Prudêncio, Maria Mota, António Mendes.

#### **PhD theses completed**

Patricia Irene Silva Inácio (2013) The Liver Endoplasmic Reticulum response in Malaria Liver infection. Universidade Nova de Lisboa. Supervisor: Maria Mota.

## 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 (started September)
Inês Girão Meireles de Sousa	PhD	Post-doctoral Investigator
Joana Gonçalves de Gouveia Maia Xavier	Master	PhD Student (started June) (left July)
Madalena Cristina Rocha Martins	PhD	Post-doctoral Investigator (started June)
Maria João Matos Rocha	Graduate	MSc Student (started August) (left November)
Patrícia Alexandra Silva Santos	Graduate	MSc Student (started August)
Patricia Carla Simões Abrantes	PhD	Post-doctoral Investigator (started June)
Vânia Patrícia Ferreira Francisco	Master	Technician (started June)

### Keywords / Research Areas

Genetics, Genomics, Complex diseases.

### Major scientific achievements

In 2013, we published several papers describing for the first time:

1. The association of the neuroregulin signaling pathway with Behçet's disease (BD);
2. The FUT2 gene as a putative link between genes and environment in BD susceptibility.

These novel findings were achieved through the convergence of several genome-wide approaches (e.g. microarray expression profiling, GWAS-genomewide association studies) and open new avenues for research into BD etiopathogenesis.

Furthermore, we were awarded the Prémio Robalo Cordeiro SPP/GSK 2013 from the Sociedade Portuguesa de Pneumologia in recognition of our pioneering work in the field of the genetic susceptibility to primary spontaneous pneumothorax (PSP). We expect to publish in 2014 the results of the GWAS we conducted in Portuguese PSP patients and controls.

Two post-doctoral fellows of the lab contributed significantly to establish the IMM Post-Doc Association and organized several activities during its first year of existence.

### Recent Most Relevant Publications

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)

Martins M, Rosa A, Guedes LC, Fonseca BV, Violante S, Mestre T, Coelho M, Rosa MM, Martin ER, Vance JM, Outeiro TF, Wang L, Borovecki F, Ferreira JJ, Oliveira SA. (2011) Convergence of microRNA expression profiling,  $\alpha$ -synuclein interacton and GWAS results support the role of the glycosphingolipid biosynthesis and the ubiquitin proteasome system in Parkinson's disease. *PLoS One* **6**, e25443. (Journal IF: 3.730, Citations: 13)

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: 2)

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: 5)

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: 16)

### Ongoing Research Projects

2010/2013 “BEDGET: deciphering BEhçet’s Disease GEneTics” Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: FCT. Amount: €180.708,00

2013/2014 “NEDAI (Study Group for Auto-Immune Diseases)” Coordinator: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: NEDAI. Amount: €10.000,00

2013/2015 “Patients as health care innovators: An empirical investigation of treatment, therapies and medical devices (TT&MD) developed by patients of chronic diseases” Participant: Ana Sofia Simões Domingues de Almeida Oliveira. Agency: FCT. Amount: €180.174,00

### Other Projects

2012/2014 LÓREAL Award for Women in Science 2012. Coordinator: Sousa I. Amount: €20.000,00

2013/2015 Prémio Robalo Cordeiro SPP/GSK 2013. Coordinator: Feijó S. Amount: €5.000,00

### Publications in peer review Journals

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* Dec 10, 2013. doi:10.1136/annrheumdis-2013-204475. (<http://www.ncbi.nlm.nih.gov/pubmed/24326010>) (Journal IF: 9.111, Citations: 0)

Xavier JM, Krug T, Davatchi F, Shahram F, Fonseca BV, 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 (2013). Gene expression profiling and association studies implicate the neuregulin signalling pathway in Behçet's disease susceptibility. *Journal of Molecular Medicine* **91**, 1013-1023. (Journal IF: 4.768, Citations: 0)

### **Invited lectures and seminars**

Sousa I. Pneumotórax: estudo genético. XXIX Congresso de Pneumologia, Albufeira, October 25-27, 2013. (Oral Communication, Keynote speaker).

### **Communications in International Conferences**

Oliveira SA. Identification of FUT2 as a risk factor for Behçet's disease in a genome-wide association study. Joint Conference of HGM 2013/21st International Congress of Genetics, Singapore, April 13-18, 2013. (Oral Communication).

### **Communications in National Conferences**

Xavier JM. Genome-wide association study identifies FUT2 as a novel genetic risk factor for Behçet's disease. XXXVIII Jornadas Portuguesas de Genética, Porto, Portugal. June 4-5, 2013 (Oral Communication).

Oliveira SA. FUT2: filling the gap between genes and environment in Behçet's disease? 17<sup>a</sup> Reunião Anual Sociedade Portuguesa de Genética Humana, Coimbra, Portugal. November 21-23, 2013 (Oral Communication).

### **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.

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

Prémio Robalo Cordeiro SPP/GSK 2013 from the Sociedade Portuguesa de Pneumologia.

### **Advanced teaching**

Oliveira SA. Lecturer in the Mestrado em Doenças Metabólicas e do Comportamento Alimentar, Faculdade de Medicina da Universidade de Lisboa, January 19, 2013.

Oliveira SA. Lecturer in the Farmacogenética Clínica course of Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa, February 22, 2013.

Martins M. Lecturer in the Master/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa, April 3, 2013.

Oliveira SA. Lecturer in the Mestrado de Neurociências, Faculdade de Medicina da Universidade de Lisboa, April 24, 2013.

### **Science and society**

Martins M and Sousa I. Members of the IMM Post-Doc Association (PDA) Committee.

Martins M. Alzheimer's Disease: what do genes tell us? Postdoctoral Day – 10th Anniversary of IMM, School Session, 17 October 2013, Instituto de Medicina Molecular – Faculdade de Medicina da Universidade de Lisboa.

### **PhD theses completed**

Joana Gonçalves de Gouveia Maia Xavier (2013) Identification of genetic risk factors for Behçet's disease. Faculdade de Medicina da Universidade de Lisboa. Doutoramento em Ciências Biomédicas, Especialidade de Genética. Supervisor: Sofia A Oliveira.

## TIAGO OUTEIRO LAB

### Major Interests / Objectives

The Tiago Outeiro's Lab started in June 2007, with the goal of understanding the molecular basis of disorders intimately associated with protein misfolding and aggregation, mostly those which affect the brain, such as Parkinson's, Huntington's, or Alzheimer's disease.

Because the molecular pathways involved in protein homeostasis are highly conserved, we employ a wide variety of model organisms, from the simple but powerful budding yeast to mammalian cell culture and mice.

Our ultimate goal is to develop novel therapeutic approaches for these and other related disorders. We are working closely together with clinicians in order to accelerate drug discovery efforts, translating basic research into clinical applications that will improve the lives of patients.

### Head of Unit

Tiago Outeiro, PhD.

### Research Team

Ana Dulce Correia	PhD	Principal Investigator
David Miguel de Jesus Pedras	Graduate	MSc Student (started September)
Diana Leonor Constantino Macedo	Master	PhD Student
Elisa Basso	Master	PhD Student
Federico Herrera García	PhD	Post-doctoral Investigator
Filipa Magalhães da Silva	Graduate	MSc Student
Hugo Vicente Miranda	PhD	Post-doctoral Investigator
Joana Margarida Marques Branco Santos	Master	PhD Student
João Tiago dos Santos Fernandes	Master	PhD Student
Madalena Reimao Pinto	Graduate	Technician (left May)
Márcia Santos Oliveira	Master	Technician (started November)
Marcos António dos Santos Rodrigues Gomes	Master	Technician (started June)

Maria Leonor Lemos Pereira Miller Fleming	Graduate	PhD Student
Maria Teresa A.S. Faria Pais	PhD	Principal Investigator
Marta Sofia Pereira De Castro Vitorino	Graduate	Technician (started December)
Oldriska Marques	Master	PhD Student
Patricia Isabel da Silva Guerreiro	Master	PhD Student
Pedro Rafael da Costa Antas	Master	Technician (left October)
Rafaela Ferreira Cássio	Graduate	MSc Student (started July)
Renato Gomes da Silva Martinho	Graduate	MSc Student (left November)
Rita João de Oliveira	PhD	Investigator
Rita João Rosado Serranito Ramos	Graduate	Technician (started February)
Rui Manuel da Silva Soares	PhD	Post-doctoral Investigator
Sandra Clara Dias Jacinto Figueiredo	Graduate	PhD Student, MD
Sandra Isabel Nogueira Tenreiro	PhD	Principal Investigator
Susana Alexandra de Barros Gonçalves	Master	PhD Student
Telma Elita Bertolin	MD/PhD	Post-doctoral Investigator (started August)
Tiago Nuno Calado Mendes	Master	Technician
Tomás Ribeiro da Silva Lopes da Fonseca	Master	PhD Student

### Keywords / Research Areas

Protein misfolding and aggregation, Yeast models of neurodegenerative disease, Neurodegeneration and Neuroinflammation, Genetic screens, In vivo imaging, Translational research.

### Major scientific achievements

A major hurdle in the study of posttranslational modifications in alpha-synuclein, a central player in Parkinson's disease, is its purification from relevant biological materials. We developed a simple and effective method (*Journal of Neurochemistry*, 2013) that enabled us to conduct a series of studies demonstrating the contribution of different PTMs to its aggregation and toxicity

(*Mol. Neurobiology*, 2013). In collaboration with colleagues in the UK, we determined the crystal structure of KMO, an important molecule in the context of several neurodegenerative disorders (*Nature*, 2013). In another study, we provided evidence, for the first time, that sirtuin 2 modulates the inflammatory responses of microglia, the resident immune cells in the brain (*The EMBO Journal*, 2013).

In 2013, Tiago Outeiro was awarded the Silver Medal of Merit from the Portuguese Ministry of Health for our contributions in the field of neurodegenerative disorders, a clear sign of recognition for our work.

### Recent Most Relevant Publications

Diógenes, M.J.\*, DiasR.B.\*, Rombo, D.M.\*, Vicente Miranda, H., Maiolino, F., Guerreiro, P., Nasstrom, T., Franquelim, H.G., Oliveira, L.M., Castanho, M.A.R.B., Lannfelt, L., Bergstrom, J., Ingelsson, M., Quintas, A., Sebastião, A.M., Lopes, L.V., Outeiro, T.F. (2012) Extracellular alpha-synuclein oligomers modulate synaptic transmission and impair LTP via NMDA-receptor activation. *Journal of Neuroscience* **32**, (34), 11750-62 (Journal IF: 6.908, Citations: 7)

Sajjad MU, Green EW, Hands S, Miller-Fleming L, Herrera F, Kyriacou CP, Faull R, Morton AJ, Jones L, Outeiro TF, Giorgini F, Wytenbach A (2013) DJ-1 modulates aggregation and pathogenesis in models of Huntington's disease. *Human Molecular Genetics* **23**(3), 755-66 (Journal IF: 7.692, Citations: 0)

Pais TF, Szegő EM, Marques O, Miller-Fleming L, Antas P, Guerreiro P, de Oliveira RM, Kasapoglu B and Outeiro TF (2013) . The NAD-dependent deacetylase sirtuin 2 is a suppressor of microglial activation and brain inflammation. *EMBO Journal* **32**, (19), 2603-16 (Journal IF: 9.822, Citations: 2)

Amaral M, Levy C, Heyes DJ, Lafite P, Outeiro TF, Giorgini F, Leys D, Scrutton NS (2013) Structural basis of kynurenine 3-monooxygenase inhibition. *Nature* **496**, (7445), 382-5 (Journal IF: 38.597, Citations: 2)

Outeiro TF, Kontopoulos E, Altmann SM, Kufareva I, Strathearn KE, Amore AM, Volk CB, Maxwell MM, Rochet JC, McLean PJ, Young AB, Abagyan R, Feany MB, Hyman BT, Kazantsev AG (2007) Sirtuin 2 inhibitors rescue alpha-synuclein-mediated toxicity in models of Parkinson's disease. *Science* **317**, (5837), 516-9 (Journal IF: 31.027, Citations: 337)

### Ongoing Research Projects

2011/2013 Eurostars Park, Coordinator: Ana Dulce Correia. Agency: PRIV-OM. Amount: €200.067,62 Total Amount: €150.395,72

2011/2014 Polyphenols as protective agents in Parkinson's disease models (PTDC/BIA-BCM/111617/2009) Coordinator: Sandra Isabel Nogueira Tenreiro. Agency: FCT. Amount: €58.089,00

2012/2014 The role and regulation of alpha-synuclein phosphorylation in both pathological and

physiological conditions (PTDC/BIA-BCM/117975/2010) Coordinator: Sandra Isabel Nogueira Tenreiro. Agency: FCT. Amount: €119.102,00

2010/2013 Mendelian Forms of Parkinson's Disease (MEFOPA). Coordinator: Tiago Outeiro. Agency: FP7. Amount: €226.800,00

2009/2013 Academic-Industrial Initial Training Network (ITN) on Alpha-Synuclein Related Brain Diseases (NEURASYNC). Coordinator: Tiago Outeiro. Agency: FP7. Amount: 180.687,00

2010/2013 From phosphorylation to cleavage: switching on alpha-synuclein aggregation and toxicity (PTDC/NEU/105215/2008). Coordinator: Tiago Outeiro. Agency: FCT. Amount: €130.000,00

2010/2013 Mitochondrial-dependent impairment of intracellular trafficking in Parkinson's disease (PTDC/SAU-NEU/102710/2008). Coordinator: Tiago Outeiro. Agency: FCT. Amount: €2.6950,00

2010/2013 Deciphering the molecular mechanisms linking alpha-synuclein dysfunction and cytotoxicity in Parkinson's disease - the role of GDNF (PTDC/SAU-NEU/101928/2008) Coordinator: Tiago Outeiro. Agency: FCT. Amount: €25.600,00

2012/2013 European Huntington's Disease Network PJ328 Coordinator: Tiago Outeiro. Agency: PRIV-UE. Amount: € 44.350,00

2011/2014 Molecular determinants of microglial activation and neuronal dysfunction in in vivo models of Parkinson's disease (PTDC/SAU-ORG/114083/2009) Coordinator: Maria Teresa A.S. Faria Pais. Agency: FCT. Amount: €115.664,00

### Other Projects

2013/2014 Alpha-synuclein as a blood biomarker for Parkinson's disease (EXPL/NEU-OSD/0606/2012). Coordinator: Hugo Vicente Miranda. Agency: FCT. Amount: €49,967,00

### Publications in peer review Journals

Basso E, Antas P, Marijanovic Z, Gonçalves S, Tenreiro S, Outeiro TF, (2013) PLK2 modulates  $\alpha$ -synuclein aggregation in yeast and mammalian cells. *Mol Neurobiol.* December 2013 **48**, (3), 854-62. (Journal IF: 5.471)

Tenreiro S, Munder MC, Alberti S, Outeiro TF. (2013). Harnessing the power of yeast to unravel the molecular basis of neurodegeneration. *J Neurochem* November 2013 **127**, 438-52. (Journal IF: 3.973)

Vicente Miranda H, Xiang W, de Oliveira RM, Simões T, Pimentel J, Klucken J, Penque D, Outeiro TF, (2013) Heat-mediated enrichment of  $\alpha$ -synuclein from cells and tissue for assessing post-translational modifications, *J Neurochemistry.* September 2013. **126**, (5), 673-84. PMID:

23534813 (Journal IF: 3.973)

Faria C, Jorge CD, Borges N, Tenreiro S, Outeiro TF, Santos H. (2013) Inhibition of formation of  $\alpha$ -synuclein inclusions by mannosylglycerate in a yeast model of Parkinson's disease. *Biochim Biophys Acta*. August 2013. **1830**, 4065-72. (Journal IF: 3.848)

Goncalves S and Outeiro TF (2013) Assessing the subcellular dynamics of alpha-synuclein using photoactivation microscopy. *Mol Neurobiol*. June 2013. **47**, (3), 1081-92. (Journal IF: 5.471, Citations: 1)

Martín V, Sanchez-Sanchez AM, Herrera F, Gomez-Manzano C, Fueyo J, Alvarez-Vega MA, Antolín I, Rodriguez C (2013). Melatonin-induced methylation of the ABCG2/BCRP promoter as a novel mechanism to overcome multidrug resistance in brain tumour stem cells. *Br J Cancer*. May 28 2013. **108**, (10), 2005-12. doi: 10.1038/bjc.2013.188. (Journal IF: 5.082, Citations: 1)

Guerreiro P, Huang Y, Gysbers A, Cheng D, Gai WP, Outeiro TF, Halliday GM (2013) LRRK2 interactions with  $\alpha$ -synuclein in Parkinson's disease brains and in cell models. *Journal of Molecular Medicine*. April 2013. **91**,(4), 513-22. (Journal IF: 5.471)

Rodriguez C, Martín V, Herrera F, García-Santos G, Rodriguez-Blanco J, Casado-Zapico S, Sánchez-Sánchez AM, Suárez S, Puente-Moncada N, Anítua MJ and Antolín I (2013). Mechanisms involved in the pro-apoptotic effect of melatonin in cancer cells. *Int. J. Mol. Sci*. April 2013, **14**, (4), 6597-613. doi:10.3390/ijms140x000x. Review (Journal IF: 2.464, Citations: 4)

Lopes da Fonseca T, Correia A, Hasselaar W, van der Linde HC, Willemsen R, Outeiro TF (2013) The zebrafish homologue of Parkinson's disease ATP13A2 is essential for embryonic survival. *Brain Res Bull*. January 2013; **90**, 118-26. doi: 10.1016/j.brainresbull.2012.09.017. (Journal IF: 2.935, Citations: 3)

### Other publications International

Herrera F, Gonçalves S, Branco-Santos J, Outeiro TF (2013). Studying the molecular determinants of oligomerization in neurodegenerative disorders by bimolecular fluorescence complementation within living cells. In: *Bio-nanoimaging in protein misfolding and aggregation*. Elsevier Inc. Editors: Vladimir N. Uversky and Yuri L. Lyubchenko. Part 1, Chapter 19

### Invited lectures and seminars

Herrera F. Protein complementation assays: past, present and future. JORTEC, Faculdade de Ciencia e Tecnologia, Universidade Nova de Lisboa, Lisbon, Portugal, February 2013.

Herrera F. Cell-to-cell traffic in neurodegenerative disorders. M.Sc. and PhD Neuroscience Program, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. December 2013.

Teresa F. Pais. Neuroinflammation. Master/Phd in Neurosciences, Faculdade de Medicina da Universidade de Lisboa. Lisbon, Portugal. November 26, 2013.



Tenreiro S. Yeast: a simple model to study the complexity of Parkinson's disease. Jornadas do centro de investigação CB3. Universidade Lusófona, Lisbon, Portugal. May 2013.

Tenreiro S. "Yeast as a model to study the molecular mechanisms of Parkinson's disease" Seminários em Biotecnologia do mestrado de Biotecnologia Aplicada, Escola Superior de Turismo e Tecnologia do Mar, Instituto Politécnico de Leiria, Leiria, Portugal, April 18, 2013.

Tenreiro S. "Yeast: a simple model to answer complex questions in Parkinson's disease" IV Jornadas de Ciências da Saúde, Instituto Superior de Ciências da Saúde Egas Moniz, Lisbon, Portugal, April 18, 2013.

### Communications in International Conferences

Pais TF, Szegő EM, Marques O, Miller-Fleming L, Antas P, Guerreiro P, de Oliveira RM, Kasapoglu B and Outeiro TF. The NAD-dependent deacetylase sirtuin 2 is a suppressor of microglial activation and brain inflammation. Gordon Research Conferences: Glial Biology: Functional Interactions among Glia & Neurons. Ventura, CA, USA. March 3-8, 2013. (Poster Presentation)

Teresa F. Pais. The NAD-dependent deacetylase sirtuin 2 is a suppressor of microglial activation and brain inflammation. 11th World Congress on Inflammation. Natal, Brazil. September 21-25, 2013. (Oral communication)

Tenreiro S., Reimão-Pinto M.M., Antas P., Rino J., Waiss M., Magalhães F., Wawrzycka D., Macedo D., Cunha M.E., Kaganovich D., Outeiro T.F. 2013. Harnessing the power of yeast to decipher the role of alfa-synuclein phosphorylation in Parkinson's disease. 26th International Conference on Yeast Genetics and Molecular Biology, Frankfurt, Germany, August 29–September 3, 2013. Yeast. 30:S79. (Oral communication)

Macedo D., Tavares L., McDougall G.J., Stewart D., Ferreira R.B., Outeiro T.F., Tenreiro S., 2013. Polyphenols protect from alfa-synuclein toxicity by increasing autophagy and reducing reactive oxygen species in a yeast model of Parkinson's disease. 26th International Conference on Yeast Genetics and Molecular Biology, Frankfurt, Germany, August 29–September 3, 2013. Yeast. 30:S204. (Poster Presentation)

Patrícia Guerreiro "Leucine-Rich Repeat Kinase 2 (LRRK2): A central player in Parkinson's disease"; 10 th Meeting of German Neuroscience Society; Goettingen; Germany. March 13-17, 2013 (Oral communication)

Patrícia Guerreiro, Yue Huang, Ellen Gerhardt, Eva Rodrigues, Glenda M. Halliday, and Tiago F. Outeiro; "LRRK2 interacts with  $\beta$ -synuclein and tau and is present in Lewy bodies in Parkinson's disease"; AD/PD; Florence; Italy. March 6-10, 2013 (Poster Presentation)

Tiago Outeiro, Diana Lázaro, Eva Rodrigues, Patricia Guerreiro, Ellen Gerhardt; "Systematic comparison of the effects of alpha-synuclein mutations on oligomerization and aggregation"; AD/PD; Florence; Italy. March 6-10, 2013 (Poster Presentation)

C. Jardim, P. Pinto, D. Macedo, D. Stewart, G.J. McDougall, R.B. Ferreira, C.N. Santos, Disclosing the mechanisms behind the protective effect of A. unedo fruit metabolites against oxidative injury in yeast. 4th Management Committee & Working Groups Meeting of COST Action FA 1005. Izmir, Turkey - Swiss Hotel & Ege University. October 8-10, 2013 (Poster Presentation)

Tavares L, Jardim C, Pimpão RC, Pinto P, Macedo D, Gomes A, Figueira I, Alves M, Ferreira RB, Santos CN. 2013. Berries polyphenols: a multiapproach to disclose human health benefits. Granada, Spain. September 15-20, 2013. (Poster Presentation)

### Communications in National Conferences

Branco-Santos J, Herrera F, Outeiro TF, The role of N-terminal phosphorylation on mutant huntingtin oligomerization, aggregation and toxicity. EMBO Young Scientist Forum, Instituto de Medicina Molecular – Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. July 2013.

Branco-Santos J, Herrera F, Outeiro TF, The role of N-terminal phosphorylation on mutant huntingtin oligomerization, aggregation and toxicity. Portuguese Society for Neurosciences (SPN) meeting 2013, Luso, Portugal. May 30–June 1, 2013

Vicente Miranda H, Xiang W, de Oliveira RM, Simões T, Pimentel J, Klucken J, Penque D, Outeiro TF, Heat-mediated enrichment of  $\alpha$ -synuclein from cells and tissue for assessing post-translational modifications. Portuguese Society for Neurosciences (SPN) meeting 2013, Luso, Portugal. May 30–June 1, 2013

Gonçalves S, Elucidating the effect of modulators of alpha-synuclein aggregation in vesicular trafficking, XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal. May 30-31 and June 1, 2013 (Oral communication and Poster presentation)

Ferreira DG, Coelho JE, Batalha VL, Miranda HV, Albino-Teixeira A, Outeiro TF, Lopes LV 2013 “Adenosine A2A receptor blockade prevents LTP impairment induced by  $\alpha$ -synuclein” XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal. May 30–June 1, 2013 (Oral communication and Poster Presentation)

Tenreiro S., Reimão-Pinto M.M., Antas P., Rino J., Magalhães F., Wawrzycka D., Macedo D., Outeiro T.F. Preventing S129 alpha-synuclein phosphorylation decreases protein turnover in a Parkinson’s disease yeast model. EMBO Young Scientists’ Forum. Lisbon, Portugal, July 15-16. 2013

Claudia N. Santos, Andreia Gomes, Carolina Jardim, Diana Macedo, Inês Figueira, Lucélia Tavares, Marta Alves, Paula Pinto, Rui C. Pimpão, Ricardo B. Ferreira. Potential of berries polyphenols for preventing age-related neurodegeneration. 7th International Workshop on Anthocyanins. Porto, Portugal. September 9-11, 2013. (Poster Presentation)

Diana Macedo, Sandra Tenreiro, Ricardo B. Ferreira, Tiago F. Outeiro and Cláudia N. Santos, Mechanistic insights into polyphenol-mediated protection against alpha-synuclein toxicity, IV

ITQB PhD Student's Meeting, Oeiras, Portugal. October 24-25, 2013. (Poster Presentation)

### **Internationalisation**

Teresa Faria Pais, Visiting Professor, August to November, CAPES, Brazil.

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

Silver Merit Award from the Ministry of Health to Tiago Outeiro, 2013.

FCT Investigator 2013, Fundação para a Ciência e a Tecnologia (IF/00094/2013), Portugal, to Federico Herrera.

### **Advanced teaching**

Herrera F. Cell-to-cell traffic in neurodegenerative disorders (December 2013). M.Sc. and PhD Neuroscience Program, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Teresa F. Pais. Neuroinflammation. November 26. Master/Phd in Neurosciences, Faculdade de Medicina da Universidade de Lisboa.

Vicente Miranda H. (collaboration in CAML Advanced Course organized by Francisco Enguita, PhD) “Advanced Course on protein expression and purification: tips and tricks”, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa.

### **Science and society**

Herrera F. Founding committee member of the Postdoctoral Association at the Instituto de Medicina Molecular - Faculdade de Medicina da Universidade de Lisboa.

Herrera F. Organizer of various scientific and social events at the Instituto de Medicina Molecular - Faculdade de Medicina da Universidade de Lisboa (Lisbon Area of Neuroscience Meeting Series, Beer Hour, Postdoctoral Day, Pizza Seminar Series, Career Path Seminar Series).  
Herrera F. Interview to the Portuguese/Spanish journal “Actualidade. Economia Iberica”. Dec 2013, 198:50-51.

### **PhD theses completed**

Marta Amaral (2013) Structure and Mechanism of Kynurenine 3-monooxygenase, a candidate Huntington’s disease drug target. Faculdade de Medicina, Universidade de Lisboa. Supervisor: Tiago F. Outeiro, Nigel Scrutton.

### Msc theses completed

Renato Martinho (2013) sirt2: in the crossroad of aging, neurodegeneration and autophagy. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Tiago Fleming Outeiro, Rita João Oliveira.

Filipa Magalhães Silva (2013) Alpha-synuclein phosphorylation role on Parkinson's disease. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Tiago Fleming Outeiro, Sandra Tenreiro.

Márcia Oliveira (2013) Modulation of  $\alpha$ -synuclein aggregation and toxicity. Universidade Nova de Lisboa. Supervisors: Tiago Fleming Outeiro, Hugo Vicente Miranda.

Andreia Pereira Gameiro (2013) Microfluidic Systems for Studies in Parkinson Diseases. Instituto Superior Técnico. Supervisors: Tiago Outeiro, João Pedro Conde.

**MIGUEL PRUDÊNCIO LAB****Major Interests / Objectives**Research Interests

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 hitherto obscure aspects of the biology of Plasmodium infection, unveiling novel host-parasite interactions, and developing new drug- and vaccine-based anti-malarial strategies.

Research Areas

- Nutrient and ion transport and homeostasis during Plasmodium development inside hepatic cells;
- Novel host-Plasmodium molecular interactions;
- Bile acid metabolism and nuclear receptor-mediated signaling mechanisms in the context of Plasmodium liver infection;
- 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 Margarida Roque Sanches Vaz	Master	MSc Student (started July)
António Manuel Barbeiro Mendes	PhD	Post-doctoral Investigator (started July)
Cláudia B. Rodrigues Sá e Cunha Mesquita Gabriel	PhD	Post-doctoral Investigator
Inês Isabel Fernandes Gomes	PhD	Post-doctoral Investigator
Maria Inês Sousa de Albuquerque	Master	Technician
Marta Monteiro Maia Machado	Graduate	Technician (started November)
Miguel Filipe Duarte	Graduate	MSc Student (started June)
Patrícia dos Santos Meireles	Master	PhD Student

### Keywords / Research Areas

Malaria, Parasitology, Vaccines, Host-pathogen interactions, Liver-stage Plasmodium infection.

### Major scientific achievements

Since July 2013, when it was created, the Prudêncio Lab has:

- Published 5 collaborative papers in peer-reviewed, international journals;
- Been awarded a Phase II Grand Challenges Explorations award by the Bill & Melinda Gate Foundation;
- Filed one PCT international application (Genetically modified rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine);
- Won the health track and the grand prize of the “BES inovação 2013” award;
- Won a honorary mention in the “Building Global Innovators 2013” contest;
- Participated in several International and National conferences and meetings;
- Organised a symposium on pre-erythrocytic malaria vaccines at the 6th MIM conference on malaria (South Africa);
- Had numerous media appearances in relation to its scientific activities.

In this period the lab has also expanded from its original 6 to the present 8 researchers, and established or furthered collaborations with several National and International research groups.

### Recent Most Relevant 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. *Nat Med* **20**(1), 47-53. doi: 10.1038/nm.3424. Epub 2013 Dec 22. PMID: 24362933. (Impact Factor: 27.14; Citations: 0)

A.S. Ressurreição, D. Gonçalves, A.R. Siteo, I.S. Albuquerque, J. Gut, A. Góis, L.M. Gonçalves, M.R. Bronze, T. Hanscheid, G.A. Biagini, P.J. Rosenthal, M. Prudêncio, P. O'Neill, M.M. Mota, F. Lopes, R. Moreira (2013) Structural optimization of quinolon-4(1H)-imines as dual-stage antimalarials: towards increased potency and metabolic stability. *J. Med. Chem* **56**, 7679-7960. (Journal IF: 5.8, Citations: 0)

T. Rodrigues, A.S. Ressurreição, F.P. da Cruz, I.S. Albuquerque, J. Gut, M. Carrasco, D. Gonçalves, M.M. Mota, P.J. Rosenthal, R. Moreira, M. Prudêncio, F. Lopes (2013). Flavones as isosteres of 4(1H)-quinolones: discovery of ligand efficient and dual stage antimalarial lead compounds. *Eur. J. Med. Chem.* **69**, 872-880. (Journal IF: 3.8, Citations: 0)

### Ongoing Research Projects

2010/2013 “The influence of bile acids on malaria liver infection”. Coordinator: Miguel Prudêncio. Agency: FCT. Amount: €171.482,00

2012/2014 “Utilization of host cell resources by the malaria parasite in the liver”. Coordinator: Miguel Prudêncio. Agency: FCT. Amount: €154.755,00

2012/2015 “Towards malaria eradication. A novel approach for multi-targeting the parasite’s life cycle”. Coordinator: Francisca Lopes. Agency: FCT. Amount: €36.741,00

2013/2014 “Prémio BES Inovação 2013”. Coordinator: Miguel Prudêncio. Agency: Banco Espírito Santo. Amount: €50.000,00

2013/2014 “Evaluation of anti-Plasmodial activity of tetraoxane compounds”. Coordinator: Miguel Prudêncio. Agency: University of Belgrade - Faculty of Chemistry. Amount: €4.961,00

2013/2014 “A new whole-organism vaccine against malaria”. Coordinator: Miguel Prudêncio. Agency: Bill & Melinda Gates Foundation. Amount: €888.939,54

### Invited lectures and seminars

Miguel Prudêncio, "Biomolecular Methods for Malaria Research", Semester at Sea, August 16, 2013, Instituto de Medicina Molecular, Lisbon, Portugal.

Miguel Prudêncio, "Challenges in Clinical Research in Portugal", Apifarma conference 'The value of innovation: from research to patient', June 18, 2013, Lisbon, Portugal.

### Communications in International Conferences

António M. Mendes, Inês Albuquerque, Ahmed Salman, Belen Jimenez-Diaz, Sara Viera-Mollina, Rob Hermsen, Merije Behet, Alexis Kaushansky, Sangeeta Bhatia, Stefan Kappe, Iñigo Angulo-Barturem, Chris J. Janse, Robert W. Sauerwein, Shahid Khan, Maria M. Mota, Miguel Prudêncio, "A rodent Plasmodium-based strategy for vaccination against human malaria", 6th MIM Pan-African Malaria Conference, Durban, South Africa, October 6-11, 2013. (Oral communication)

António M. Mendes, Inês Albuquerque, Ahmed Salman, Belen Jimenez-Diaz, Sara Viera-Mollina, Rob Hermsen, Merije Behet, Alexis Kaushansky, Sangeeta Bhatia, Stefan Kappe, Iñigo Angulo-Barturem, Chris J. Janse, Robert W. Sauerwein, Shahid Khan, Maria M. Mota, Miguel Prudêncio, "Thinking outside the species: Novel approaches to pre-erythrocytic P. falciparum vaccines", 9th Grand Challenges Meeting, , Rio de Janeiro, Brazil, October 27-30, 2013. (Oral communication)

António M. Mendes, Inês Albuquerque, Ahmed Salman, Belen Jimenez-Diaz, Sara Viera-Mollina, Rob Hermsen, Merije Behet, Alexis Kaushansky, Sangeeta Bhatia, Stefan Kappe, Iñigo Angulo-Barturem, Chris J. Janse, Robert W. Sauerwein, Shahid Khan, Maria M. Mota, Miguel Prudêncio, "Towards a rodent Plasmodium-based vaccine against human malaria", 9th Grand Challenges

Meeting, , Rio de Janeiro, Brazil, October 27-30, 2013. (Poster presentation)

Ana M.S. Guerreiro, Jessica Kehrler, Inês S. Albuquerque, Miguel Prudêncio, Leonor Pinho, Freddy Frischknecht, Celine K. Carret, Gunnar R. Mair, "Characterization of the Plasmodium berghei mei2-like gene", Molecular Parasitology Meeting (24th MPM 2013), Woods Hole, MA, September 08-12, 2013. (Poster presentation)

### **Organisation of Conferences**

Miguel Prudêncio, Organizer of Symposium "Whole-organism pre-erythrocytic malaria vaccination strategies", 6th MIM Pan-African Malaria Conference, Durban, South Africa, October 6-11, 2013.

### **Internationalisation**

The lab has an extensive network of collaborations with leading International researchers, including:

- Iñigo Angulo-Barturem - GSK Tres Cantos, Madrid;
- Angus Bell - University of Dublin;
- Peter Eaton - Faculty of Chemistry, Porto;
- Randolph Elble - Southern Illinois University;
- Lesley Ellies - University of California San Diego~;
- Michael Hannus and Christophe Echeverri - Cenix Bioscience, Dresden;
- Thomas Hanscheid - Instituto de Medicina Molecular;
- Hillary Hurd - Keele University;
- Chris Janse and Shahid Khan - Leiden University;
- Stefan H. Kappe - Seattle Biomedical Research Institute;
- Clemens Kocken - Biomedical Primate Research Centre, Rijswijk;
- Ann-Kristin Mueller - University of Heidelberg;
- Robert Sauerwein - University of Nijmegen;
- Bogdan Solaja - Faculty of Chemistry, Belgrade;
- Henry Staines and Sanjeev Krishna - St. George's University London;
- Rita Tewari - University of Nottingham.

These collaborations involve important scientific exchanges with researchers from these International institutions. Besides, lab members regularly participate in International conferences and meetings. Finally the lab is funded, in part, by an International organization (the Bill & Melinda Gates Foundation) with whom it maintains close interactions.



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

“BES Inovação Award 2013”. Winner of Health Track and Winner of Grand Prize.

“Building Global Innovators Contest 2013”. Honorary Mention Health Track.

### **Patents/prototypes**

“Rodent Plasmodium parasites as platforms for a whole-organism malaria vaccine”, PCT international application WO/2013/156949 submitted 17.04.2013, published 24.10.2013  
Authors: Miguel Prudêncio, Maria Mota, António Mendes.

### **Advanced teaching**

PhD Courses - GABBA PhD programme, Universidade do Porto, May 2013.

#### Master's Courses:

Master's in clinical biochemistry, Universidade Nova de Lisboa, May 2013.

Master's in Evolutionary and development biology, Universidade de Lisboa, December 2013.

### **Science and society**

Miguel Prudêncio, "Challenges in Clinical Research in Portugal", Apifarma conference 'The value of innovation: from research to patient', 28 June 2013, Lisbon, Portugal.

### **Msc theses completed**

Ana Margarida Roque Sanches Vaz (2013) The Reciprocal Influence of Malaria and Sleeping Sickness Co-infections. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Miguel Prudêncio and Luísa Figueiredo.

**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 (started October)
Ana Catarina Martins Lameiras	Graduate	Investigator (started December)
Ana Isabel Aquino Friães	Master	PhD Student
Ana Paula da Silva Pereira	Master	Administrative (left July)
Ana Sílvia Soares Mendes Moreira	Undergraduate	Investigator (left May)
Andreia das Neves Horácio	Master	PhD Student
Andreia Sofia Agostinho Gravata	Master	Trainee
Bruno Filipe Ribeiro Gonçalves	Graduate	MSc Student (started May)
Carolina Isabel Glória Tempera	Graduate	Technician
Catarina Costa	Master	PhD Student
Catarina Teresa Condinho Pato	Master	PhD Student
Cláudia Patrícia Machado Lemos e Sousa	Graduate	MSc Student (left May)

Elisabete Martins	PhD	Post-doctoral Investigator
Joana Alexandra Pimento Lopes	Graduate	Technician
Joana Gomes Martins Lopes	Graduate	MSc Student
João André Nogueira Custódio Carriço	PhD	Principal Investigator
Jorge Miguel Diamantino Miranda	Master	PhD Student
José Melo Cristino	MD, PhD	Principal Investigator
Liliana Sofia Cardoso	No degree	Investigator
Márcia Carlos Rocha Boura	Graduate	MSc Student
Marcos Pinho	Master	Investigator
Maria João Rua Frias	PhD	Post-doctoral Investigator
Maria Sousa Rebelo	Master	PhD Student
Mickael Santos da Silva	Graduate	MSc Student
Nuno Miguel Santos Rodrigues	Graduate	MSc Student (started September)
Pedro Tiago Gonçalves Monteiro	PhD	Post-doctoral Investigator (left May)
Raquel Baptista Arinto Garcia	Graduate	MSc Student
Rita Gaspar Cabrita	Undergraduate	Undergraduate (started April) (left May)
Rosangela Maria Rodrigues Carvalho Frita	Master	PhD Student
Rui Manuel São Martinho de Oliveira	Master	Investigator (started April)
Sandra Cristina Machado de Matos	Graduate	Investigator (left March)
Sandra Isabel Rodrigues de Aguiar	PhD	Post-doctoral Investigator
Sérgio Miguel Cardoso Marcelino dos Santos	Master	Investigator (started October)
Thomas Hanscheid	MD, PhD	Principal 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

Characterization of differences in virulence potential of *S. pyogenes* clones and changes in their major virulence factors.

Identification of an unusual secretion mechanism of the lysins of pneumococcal phages.

Development of MLST for *S. canis* and characterization of its zoonotic origin.

Documentation of continuing changes in *S. pneumoniae* causing invasive infections with vaccination and its consequences for future potential vaccines.

Laying the foundations for the development of a typing and a NGS process ontology, with the aim of linking existing sequence based typing databases and novel NGS data.

Development 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.

Interactions of haemozoin with a rodent model of tuberculosis and effects of hemozoin on phagocytosis and killing of *Salmonella typhim*.

### Recent Most Relevant 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. <http://www.ncbi.nlm.nih.gov/pubmed/23637865>. (Journal IF: 3.730, Citations: 0)

Francisco, A. P., C. Vaz, P. T. Monteiro, J. Melo-Cristino, M. Ramirez, and J. A. Carriço. (2012) PHYLOViZ: Phylogenetic inference and data visualization for sequence based typing methods. *BMC bioinformatics* **13**,87. <http://www.ncbi.nlm.nih.gov/pubmed/22568821>. (Journal IF: 3.024, Citations: 21)

Melo-Cristino J., C. Resina, V. Manuel, L. Lito, M. Ramirez. (2013) First case of infection with vancomycin-resistant *Staphylococcus aureus* in Europe. *The Lancet*. **382**,205. <http://www.ncbi.nlm.nih.gov/pubmed/23791472>. (Journal IF: 39.060, Citations 1)

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. <http://www.ncbi.nlm.nih.gov/pubmed/21697333>. (Journal IF: 4.068, Citations: 9)

Aguiar, S. I., M. J. Brito, J. Gonçalo-Marques, J. Melo-Cristino, and M. Ramirez. (2010) Serotypes 1, 7F and 19A became the leading causes of pediatric invasive pneumococcal infections in Portugal after 7 years of heptavalent conjugate vaccine use. *Vaccine* **28**,5167–5173. <http://www.ncbi.nlm.nih.gov/pubmed/20558247>. (Journal IF: 3.492, Citations: 23)

### 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

2010/2013 Characterization and genotyping of portuguese strains of Francisella tularensis, Coordinator: Thomas Hanscheid. Agency: FCT. Amount: €8.100.00

2013/2014 IFDO Research Coordinator: Thomas Hanscheid. Agency: Steris Corporation. Amount: €12.980.00

### Publications in peer review Journals

Costa, A., J. Afonso, C. Osório, A. L. Gomes, F. Caiado, J. Valente, S. I. Aguiar, F. Pinto, M. Ramirez, S. Dias. 2013. miR-363-5p regulates endothelial cell properties and their communication with hematopoietic precursor cells. *J Hematol Oncol* **6**,87. (<http://www.ncbi.nlm.nih.gov/pubmed/24257019>) (Journal IF: 4.458, Citations: 0)

C. Silva-Costa, J. A. Carriço, M. Ramirez, and J. Melo-Cristino. 2013. 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*. In press. Epub 2013 Oct 28 (<http://www.ncbi.nlm.nih.gov/pubmed/24168973>) (Journal IF: 3.569, Citations: 0)

Horácio, A. N., J. Diamantino-Miranda, S. I. Aguiar, M. Ramirez, J. Melo-Cristino, and the Portuguese Group for the Study of Streptococcal Infections. 2013. The majority of adult pneumococcal invasive infections in Portugal are still potentially vaccine preventable in spite of significant declines of serotypes 1 and 5. *PLoS ONE* **8**,e73704. (<http://www.ncbi.nlm.nih.gov/pubmed/24020770>) (Journal IF: 3.730, Citations: 0)

Ressurreição, A. S., D. Gonçalves, A. R. Siteo, I. S. Albuquerque, J. Gut, A. Góis, L. M. Gonçalves, M. R. Bronze, T. Hänscheid, G. A. Biagini, P. J. Rosenthal, M. Prudêncio, P. O'Neill, M. M. Mota, F. Lopes, and R. Moreira. 2013. Structural optimization of Quinolon-4(1H)-imines as dual-stage antimalarials: toward increased potency and metabolic stability. *J Med Chem*. **56**,7679–7690. (<http://www.ncbi.nlm.nih.gov/pubmed/23499920>) (Journal IF: 5.614, Citations: 0)

Boura, M., R. Frita, A. Góis, T. Carvalho, and T. Hänscheid. 2013. The hemozoin conundrum: is malaria pigment immune-activating, inhibiting, or simply a bystander? *Trends Parasitol*. **29**,469–476. (<http://www.ncbi.nlm.nih.gov/pubmed/23937890>) (Journal IF: 5.513, Citations: 0)

Friães A., Lopes J.P., Melo-Cristino J., M. Ramirez, the Portuguese Group for the Study of

Streptococcal Infections. 2013. Changes in *Streptococcus pyogenes* causing invasive disease in Portugal: Evidence for superantigen gene loss and acquisition. *Int J Med Microbiol.* **303**,505-513 (<http://www.ncbi.nlm.nih.gov/pubmed/23932912>) (Journal IF: 4.537, Citations: 0)

Hanson, K. K., A. S. Ressurreição, K. Buchholz, M. Prudêncio, J. D. Herman-Ornelas, M. Rebelo, W. L. Beatty, D. F. Wirth, T. Hänscheid, R. Moreira, M. Marti, and M. M. Mota. 2013. Torins are potent antimalarials that block replenishment of *Plasmodium* liver stage parasitophorous vacuole membrane proteins. *Proc Natl Acad Sci USA.* **110**,E2838–2847. (<http://www.ncbi.nlm.nih.gov/pubmed/23836641>) (Journal IF: 9.737, Citations: 0)

Mendes J.J., C. Leandro, S. Corte-Real, R. Barbosa, P. Cavaco-Silva, J. Melo-Cristino, A. Górski, M. Garcia. 2013. Wound healing potential of topical bacteriophage therapy on diabetic cutaneous wounds. *Wound Repair Regen.* **21**,:595-603. (<http://www.ncbi.nlm.nih.gov/pubmed/23755910>) (Journal IF: 2.757, Citations: 0)

Tavares, A., M. Miragaia, J. Rolo, C. Coelho, H. de Lencastre, and CA-MRSA/MSSA working group. 2013. High prevalence of hospital-associated methicillin-resistant *Staphylococcus aureus* in the community in Portugal: evidence for the blurring of community-hospital boundaries. *Eur. J. Clin. Microbiol. Infect. Dis.* **32**,1269–1283. (<http://www.ncbi.nlm.nih.gov/pubmed/23604782>) (Journal IF: 3.024, Citations: 0)

Espadinha, D., N. A. Faria, M. Miragaia, L. M. Lito, J. Melo-Cristino, and H. de Lencastre. 2013. Extensive dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA) between the hospital and the community in a country with a high prevalence of nosocomial MRSA. *PLoS ONE* **8**,e59960. (<http://www.ncbi.nlm.nih.gov/pubmed/23593155>) (Journal IF: 3.730, Citations: 0)

Gouveia, C., A. Friães, M. Cassiano-Neves, J. Melo-Cristino, and M. Ramirez. 2013. MRSA and PVL positive *Staphylococcus aureus* are rarely found in community-acquired osteoarticular infections in children in Portugal, a country with high MRSA prevalence. *Online Int J of Micr Res* **1**,20–24. (<http://www.onlineresearchjournals.org/OIJMR/abstracts/2013/mar/Gouveia%20et%20al..htm>) (Journal IF: NA, Citations: 0)

Vaz, M., L. Meirinhos-Soares, C. C. S. Sousa, M. Ramirez, J. Melo-Cristino, J. A. Lopes. 2013. Serotype discrimination of encapsulated *Streptococcus pneumoniae* strains by Fourier-transform infrared spectroscopy and chemometrics. *J. Microbiol. Methods* **93**,102–107. (<http://www.ncbi.nlm.nih.gov/pubmed/23499920>) (Journal IF: 2.161, Citations: 1)

Valadas, E., A. Gomes, A. Sutre, S. Brilha, A. Wete, T. Hänscheid, and F. Antunes. 2013. Tuberculosis with malaria or HIV co-infection in a large hospital in Luanda, Angola. *J Infect Dev Ctries* **7**,269–272. (<http://www.ncbi.nlm.nih.gov/pubmed/23493006>) (Journal IF: 0.996, Citations: 0)

McMillan, D. J., P.-A. Drèze, T. Vu, D. E. Bessen, J. Guglielmini, A. C. Steer, J. R. Carapetis, L. Van Melderen, K. S. Sriprakash, P. R. Smeesters and the M protein study group. 2013. Updated model of group A *Streptococcus* M proteins based on a comprehensive worldwide study. *Clin. Microbiol. Infect.* **19**,E222–229. (<http://www.ncbi.nlm.nih.gov/pubmed/23464795>) (Journal IF: 4.578, Citations: 1)

Costa, S. S., C. Mourato, M. Viveiros, J. Melo-Cristino, L. Amaral, and I. Couto. 2013. Description of plasmid pSM52, harbouring the gene for the Smr efflux pump, and its involvement in resistance to biocides in a meticillin-resistant *Staphylococcus aureus* strain. *Int. J. Antimicrob. Agents.* **41**,490–492. (<http://www.ncbi.nlm.nih.gov/pubmed/23434536>) (Journal IF: 4.415, Citations: 0)

Coelho JR, Carriço JA, Knight D, Martínez JL, Morrissey I, Oggioni MR, Freitas AT. 2013 The use of machine learning methodologies to analyse antibiotic and biocide susceptibility in *Staphylococcus aureus*. *PLoS One.* 2013 **8**(2),e55582. doi:10.1371/journal.pone.0055582. Epub 2013 Feb 19. (<http://www.ncbi.nlm.nih.gov/pubmed/23431361>) (Journal IF: 3.730, Citations: 0)

J. A. Carriço, A. Sabat, A. Friederich, M. Ramirez, on behalf of the ESCMID Study Group for Epidemiological Markers (ESGEM). 2013. Bioinformatics in bacterial molecular epidemiology and public health: databases, tools and the next-generation sequencing revolution. *Euro Surveill.* 2013. **18**,pii=20382. (<http://www.ncbi.nlm.nih.gov/pubmed/23369390>) (Journal IF: 5.491, Citations: 3)

Pinho M. D., S. C. Matos, C. Pomba, A. Lübke-Becker, L. H. Wieler, S. Preziuso, J. Melo-Cristino, M. Ramirez. 2013. Multilocus sequence analysis of *Streptococcus canis* confirms the zoonotic origin of human infections and reveals genetic exchange with *Streptococcus dysgalactiae* subsp. *equisimilis*. *J. Clin. Microbiol.* **51**,1099-109. (<http://www.ncbi.nlm.nih.gov/pubmed/23345291>) (Journal IF: 4.068, Citations: 0)

Martins E. R., A. Andreu, J. Melo-Cristino, and M. Ramirez. 2013. Distribution of pilus islands in *Streptococcus agalactiae* causing human infections: insights into evolution and implication for vaccine development. *Clin. Vaccine Immunol.* **20**,313–316. (<http://www.ncbi.nlm.nih.gov/pubmed/23269415>) (Journal IF: 2.598, Citations: 1)

Janssen, S., X. Padanilam, R. Louw, R. Mahanyele, G. Coetzee, T. Hänscheid, T. Leenstra, and M. P. Grobusch. 2013. Sputum culture results to monitor MDR-TB patients during treatment: How many do we need? *J. Clin. Microbiol.* **51**,644-6. (<http://www.ncbi.nlm.nih.gov/pubmed/23224098>) (Journal IF: 4.068, Citations: 0)

Frias, M. J., J. Melo-Cristino, M. Ramirez. 2013. Export of the pneumococcal phage SV1 lysin requires choline-containing teichoic acids and is holin-independent. *Mol Microbiol.* **87**, 430–445. (<http://www.ncbi.nlm.nih.gov/pubmed/23171061>) (Journal IF: 4.961, Citations: 0)

A. Friães, Pinto FR, C. Silva-Costa, M. Ramirez, J. Melo-Cristino 2013. Superantigen gene complement of *Streptococcus pyogenes* - relationship with other typing methods and short-term stability. *Eur. J. Clin. Microbiol. Infect. Dis.* **32**, 115-125. (<http://www.ncbi.nlm.nih.gov/pubmed/22936424>) (Journal IF: 3.024, Citations: 1)

Costa, S. S., E. Junqueira, C. Palma, M. Viveiros, J. Melo-Cristino, L. Amaral, I. Couto. 2013. Resistance to antimicrobials mediated by efflux pumps in *Staphylococcus aureus*. *Antibiotics* **2**, 83-99, 2013. (<http://dx.doi.org/10.3390/antibiotics2010083>) (Journal IF: NA, Citations: 0)

### Other publications International

Shapiro, H. M., S. H. Apte, G. M. Chojnowski, T. Hänscheid, M. Rebelo, and B. T. Grimberg. 2013. Cytometry in malaria—a practical replacement for microscopy? *Curr Protoc Cytom* Chapter 11:Unit 11.20. (<http://www.ncbi.nlm.nih.gov/pubmed/23835802>) (Journal IF: NA, Citations: 0)

### Invited lectures and seminars

Melo-Cristino, J.. 2013. Laboratório e sépsis. O que há de novo? VI Reunião do Departamento de Pediatria. Infeciologia Neonatal. Hospital Prof. Fernando Fonseca EPE, Amadora, Portugal, September 23, 2013.

Melo-Cristino, J.. 2013. Resistência aos antimicrobianos. Round Table – Antimicrobianos na prática clínica. 13º Encontro Nacional de Atualização em Infeciologia. Centro Hospitalar do Porto, Hospital Joaquim Urbano, Porto, Portugal, September 25-27, 2013.

Ramirez, M.. 2013. Qué datos hay nuevos sobre la importancia de la utilización de Prevenar 13 en la evitación de la enfermedad neumocócica invasiva? VI Symposium de Pediatría Grupo Uncibay, Málaga, Spain, January 24-25, 2013.

Thomas Hanscheid. Usefulness of flow cytometry in malaria: DNA stains, hemozoin, GFP and more. Simposia de Microbiologia. Congresso da Sociedade Iberica de Citometria, Aveiro, May 9-11, 2013.

Maria Rebelo. A novel flow cytometric approach to assess antimalarial drug resistance. Simposia de Microbiologia. Congresso da Sociedade Iberica de Citometria, Aveiro, May 9-11, 2013.

Ana Gois. Depolarized Side-Scatter to study immune responses of hemozoin-containing monocytes from malaria patients. Simposia de Microbiologia. Congresso da Sociedade Iberica de Citometria, Aveiro, May 9-11, 2013.

Thomas Hanscheid. Flow Cytometry for diagnosis of Malaria. Official Symposium: Innovative technologies for the diagnosis of parasitic diseases. 23rd European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany, April 27-30, 2013.

### Communications in International Conferences

S.I.Aguiar, A.N. Horácio, J. Lopes, M. Ramirez, J. Melo Cristino, Portuguese Group for the study of Streptococcal Infections. 2013. High coverage 13-valent pneumococcal conjugate vaccine in children after ten years of non-universal vaccination with pneumococcal conjugate vaccines in Portugal (P-264). 8th World Congress on Pediatric Infectious Diseases (WSPID), Cape Town, South Africa, November 19-22, 2013. ( Poster presentation)

S.I. Aguiar, A.N. Horácio, J. Lopes, M. Ramirez, J. Melo Cristino, Portuguese Group for the study of Streptococcal Infections. 2013. Invasive pneumococcal infections in Portuguese older children and in adolescents: Epidemiological data and new tools for prevention (P-265). 8th World



Congress on Pediatric Infectious Diseases (WSPID), Cape Town, South Africa, November 19-22, 2013. (Poster presentation)

Mickael Silva, Cátia Vaz, Alexandre Francisco, Mário Ramirez, Francisco M Couto, João André Carriço. NGSOnto - Keeping track of the NGS pipeline process using an ontology approach and its application on molecular epidemiology. 10th International Meeting on Microbial Epidemiological Markers (IMMEM-10), Paris, France, October 2-5, 2013. (Oral presentation)

Eduardo N. Taboada, Peter Kruczkiewicz, Steven K. Mutschall, Benjamin Hetman, Catherine D. Carrillo, Gary Van Domselaar, and João A. Carriço Avoiding YATM: a generalized framework for assessing analytical approaches for WGS data using an in silico typing approach 10th International Meeting on Microbial Epidemiological Markers (IMMEM-10), Paris, France, October 2-5, 2013. (Poster presentation)

Andreia Sofia Teixeira, Alexandre Francisco, Pedro Monteiro, Rui Oliveira, Mário Ramirez, João André Carriço NetPopSim – a population simulator for microbial allelic profiles for simulating spread and evolution within social networks. 10th International Meeting on Microbial Epidemiological Markers (IMMEM-10), Paris, France. October 2-5, 2013. (Poster presentation)

Alexandre Francisco, Andreia Sofia Teixeira, Pedro Monteiro, Mário Ramirez, João A. Carriço. Not seeing the forest for the trees: Novel metrics for the use of Minimum Spanning Trees in Molecular Epidemiology Studies. 10th International Meeting on Microbial Epidemiological Markers (IMMEM-10), Paris, France, October 2-5, 2013. (Poster presentation)

J. Melo-Cristino, M. Ramirez. 2013. Streptococcus pneumoniae: direct and indirect effects of the conjugate vaccines (Invited talk SP2-1). 28th International Congress of Chemotherapy and Infection (ICC 2013). Yokohama, Japan, 3rd-7th June. (Published in *Int J Antimicrob Agents* **42**(S2):S2) (Oral presentation)

C. Silva-Costa 1, M. Ramirez, J. Melo-Cristino, On behalf of the Portuguese Group for the Study of Streptococcal Infections. 2013. Streptococcus pyogenes in Portugal: decrease of macrolide resistance and clonal instability in spite of sustained macrolide consumption (P76). 28th International Congress of Chemotherapy and Infection (ICC 2013). Yokohama, Japan, June 3-7, 2013. (Published in *Int J Antimicrob Agents* **42**(S2):S65-S66) (Poster presentation)

M.D. Pinho, S.C. Matos, C. Pomba, A. Lübke-Becker, L.H. Wieler, S. Preziuso, J. Melo-Cristino, M. Ramirez, and Portuguese Group for the Study of Streptococcal Infections. 2013. A new multilocus sequence typing scheme for the genotypic characterization of Streptococcus canis isolated from human and animal sources (P163). 28th International Congress of Chemotherapy and Infection (ICC 2013). Yokohama, Japan, June 3-7, 2013. (Published in *Int J Antimicrob Agents* **42**(S2):S93-S94) (Poster presentation)

E.R. Martins, C. Silva-Costa, A. Andreu, J. Melo-Cristino, M. Ramirez 2013. Pilus islands in Streptococcus agalactiae causing human infections: implication for vaccine development (P366). 28th International Congress of Chemotherapy and Infection (ICC 2013). Yokohama, Japan, June 3-7, 2013. (Published in *Int J Antimicrob Agents* **42**(S2):S158) (Poster presentation)

A.N. Horácio, J. Diamantino-Miranda, S.I. Aguiar, M. Ramirez, J. Melo-Cristino and the Portuguese Group for the Study of Streptococcal Infections. 2013. The 13-valent pneumococcal conjugate vaccine could prevent a significant proportion of adult invasive pneumococcal disease and covers the majority of resistant isolates. XI European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo). Madrid, Spain, May 28-31, 2013. (Oral communication)

J. Diamantino-Miranda, S.G. Bartual, J.A. Hermoso, J. Melo-Cristino and M. Ramirez. 2013. Genetic diversity of ComD, the competence-stimulating peptide receptor. XI European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo). Madrid, Spain, May 28-31, 2013. (Poster presentation)

J.A. Carriço, M. Silva, M. Ramirez, A. Francisco, H Pouseele, K. Jolley, J. Bray, J. Rothgaenger, C. Vaz on behalf of the PathoNGenTrace Consortium. 2013. Towards a common language for the exchange of Bacterial Typing and Next Generation Sequencing data. Applied Bioinformatics and Public Health Microbiology, Cambridge, UK, May 15-17, 2013. (Oral presentation)

E.R. Martins, A. Andreu, J. Melo-Cristino, and M. Ramirez. 2013. Distribution of pilus islands in *Streptococcus agalactiae*: insights into evolution (P2417). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Poster presentation)

A. Horácio, S.I. Aguiar, J. Diamantino-Miranda, M. Ramirez, J. Melo-Cristino and the Microbiology and Pediatric pneumococcal working group. 2013. Severe pneumococcal infection in Portugal: serotype distribution and antimicrobial resistance (O395). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Oral presentation)

C.T. Pato, C. Silva-Costa, L. Sancho, C. Portugal, T. Sardinha, M. Ramirez and J. Melo-Cristino. 2013. Decreasing macrolide resistance among pharyngeal group A streptococci recovered in a prospective survey in a Portugal hospital (P1495). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Oral presentation)

S.I. Aguiar, J. Melo-Cristino and M. Ramirez. 2013. Expansion and decline of paediatric pneumococcal clones in response to 7-valent conjugate vaccine (PCV7) use in Portugal (P2169). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Poster presentation)

I. Faria-Ramos, J. Maia, J. Santos Antunes, J. Melo-Cristino, V. Lopes, J. Teixeira et al. Species distribution and in vitro antifungal susceptibility profile of invasive fungal isolates from a Portuguese multicentre prospective survey. (P978). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Oral presentation)

JJ Mendes, C. Leandro, SS Corte-Real, R. Barbosa, P. Cavaco-Silva, J. Melo-Cristino et al. Topical bacteriophage therapy for cutaneous wounds in two animal models of diabetes. (P1124). 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Berlin, Germany, April 27-30, 2013. (Poster presentation)

A. Friães, F. R. Pinto, C. Silva-Costa, M. Ramirez, J. Melo-Cristino. 2013. Superantigen gene complement of group A streptococci: short-term stability and association with invasive infections. GAS Infections 2013, Rome, Italy, March 21-23, 2013. (Oral communication)

C. Silva-Costa, M. Ramirez, J. Melo-Cristino, Portuguese Group for the Study of Streptococcal Infections. 2013. Macrolide resistance in *Streptococcus pyogenes* in Portugal (2007-2011). diminishing resistance and clonal instability in spite of high macrolide consumption (Poster). GAS Infections 2013, Rome, Italy, March 21-23, 2013. (Poster presentation)

C. Silva-Costa, A. Friães, M. Ramirez, J. Melo Cristino, Portuguese Group for the Study of Streptococcal Infections. 2013. Importance of clonal properties in addition to antibiotic consumption in determining the differences between macrolide resistant and susceptible *Streptococcus pyogenes*. International Meeting on Emerging Diseases and Surveillance. 21.002. Vienna, Austria, February 15-18, 2013. (Poster presentation)

Rebelo M, Sousa C, Tempera C, Grobusch MP, Hanscheid T. Detection of Antimalarial Drug Resistance: a novel and simple real-time sensitivity assay for *Plasmodium falciparum*. Poster number PO19.09. 13th Conference of the International Society of Travel Medicine, Maastricht, The Netherlands, May 19-23, 2013. (Poster presentation)

Rebelo M, Fernandes J, Grobusch MP, Hanscheid T. Detection of Antimalarial Drug Resistance: performance of the novel Hemozoin sensitivity assay in Gabon. Poster 318. ASTMH 62nd Annual Meeting, Washington DC, USA, November 13-17, 2013. (Poster presentation)

### Communications in National Conferences

Frita R, Góis A, Gilot T, Mota MM, Hänscheid T. 2013. Co-infecção malaria e tuberculose: o papel da hemozoína. 5º Congresso Pandemias na Era da Globalização. Coimbra, Portugal, May 16-18, 2013.

M. Boura, A. Góis, T. Hänscheid, C. Silva-Costa, A. Friães, M. Ramirez, J. Melo Cristino, 2013. Salmonella sepsis in Malaria patients: what is the role of malaria pigment? 5º Congresso Pandemias na Era da Globalização, Coimbra, Portugal, May 16-18, 2013.

### Internationalisation

- Veterinary Faculty, Freie Universität Berlin, Berlin, Germany and University of Camerino, Matelica, Italy on streptococci infecting animals;
- Dr. Juan Hermoso at CSIC, Madrid, Spain with the aim of crystallizing and characterizing competence related proteins;
- Academic partners on the EU project PathoNGenTrace (<http://patho-ngen-trace.eu/>);
- Collaboration with STERIS, in the development of a novel hemozoin inhibition assay - Dr. Vincent Thomas, Toulouse, France;
- Creation of a working group on malaria cytometry – Howard Shapiro (USA), Brian Grimberg (USA), Grace Chojnowski (Australia);

- Sensitivity testing using flow cytometric principles to detect hemozoin – flow cytometer for measurement in Gabon, in collaboration with Martin Grobusch, head of the Infectious Diseases department, University Hospital Amsterdam, The Netherlands;
- Use of haemozoin to investigate immune response and as possible vaccine adjuvant – Cevayir Coban, Institute for Immunology, Osaka University, Japan;
- Diagnosis of tuberculosis using fluorescent microscopy. Study in collaboration with, Alberts Schweitzer Hospital, Lambaréné, Gabon and Congolese Foundation for Medical Research, Brazzaville, Congo;
- Non-invasive detection of Met-hemoglobin levels to investigate the role of heme-oxygenase in malarious African children in Gabon in collaboration with peter Kremsner, head Tropical diseases Unit, Tuebingen University, Germany.

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

Maria Rebelo. 2013: Scholarship to attend the 7th European & Developing Countries Clinical Trials Partnership (EDCTP) Forum in Dakar, Senegal.

#### **Industry contract research**

Thomas Hanscheid. The use of growing Hemozoin-Like Crystals (HCL) to screen compounds for antimalarial activity. STERIS Company, Ohio. USA.

#### **Advanced teaching**

Melo-Cristino, J.. 2013. Bactérias Gram + patogénicas. I Curso Pós-Graduado de Atualização: Diferenciação em Pediatria - Inovação e Tecnologia. Módulo de Infecçiology Pediátrica. Instituto de Formação Avançada. Faculdade de Medicina da Universidade de Lisboa. March , 2013.

J. Carriço. Post graduation in Oncobiology, Centro Académico de Medicina de Lisboa, 2012-2013, Faculdade de Medicina da Universidade de Lisboa. 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 , Faculdade de Medicina da Universidade de Lisboa. Responsible for a module on Molecular Phylogenetics.

#### **PhD theses completed**

Ana Friães (2013) Molecular characterization of Streptococcus pyogenes isolates associated with invasive infections and pharyngitis in Portugal: evaluation of typing methods and relationship with invasive ability. Faculdade de Medicina da Universidade de Lisboa. Supervisors: José Melo Cristino, Mário Ramirez.

### Msc theses completed

Sandra Matos (2013) Distribuição de exotoxinas em estreptococos dos grupos C e G de Lancefield - Comparação entre estirpes responsáveis por infecções no Homem e em animais. Faculdade de Farmácia da Universidade de Lisboa. Supervisors: Mário Ramirez, Madalena Pimentel.

Joana Lopes (2013) Distribuição e diversidade de elementos genéticos associados à virulência em *Streptococcus pneumoniae*. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Mário Ramirez, Ricardo Dias.

César Vieira (2013) Prevalência de *Staphylococcus aureus* metilino-resistente da comunidade na infecção nosocomial. Faculdade de Medicina da Universidade de Lisboa. Supervisor: José Melo Cristino.

Cláudia Sousa (2013) Detecção de hemozoína em eritrócitos infetados com *Plasmodium falciparum* por citometria de fluxo, para monitorização do efeito de antimaláricos. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Thomas Hanscheid, Ana Tenreiro.

**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 distinct chemoattractants, like 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 and the validation of inflammatory biomarkers in vascular diseases. We expect to translate our findings towards a better understanding and management of inflammatory pathologies (ex: sepsis and cardiovascular diseases).

**Head of Unit**

Maria Carlota Saldanha Lopes, PhD Agregação, Faculdade de Medicina da Universidade de Lisboa.

**Research Team**

Ana Rosa Miranda dos Santos Silva Herdade	Master	PhD Student
Angelo Calado	PhD	Principal Investigator
Catarina Cabrita Ramos	Master	Investigator (started July)
Ekaterina Sergueevna Potapova	Graduate	MSc Student
Henrique Rosário	PhD	Investigator
Mariana Mota Castro Dias	Graduate	Investigator
Marta Filipa Paulino Silvestre	Graduate	PhD Student
Nuno Alexandre Almeida Santos	Graduate	MSc Student (started October)
Patrícia Alexandra Veloso Napoleão	PhD	Post-doctoral Investigator
Pedro Miguel Araújo Guerreiro Teixeira	Graduate	MSc Student
Rita Maria Santos Esteves	Graduate	Investigator (started September)
Sara Louro Moleirinho	Master	Investigator

Sara Maria de Almeida Beijinho	Graduate	MSc Student (started October)
Sofia Ludovina Novais de Oliveira	Graduate	PhD Student
Vanda Lúcia de Carvalho Vitorino de Almeida	Graduate	PhD Student

### Keywords / Research Areas

Inflammation, Microcirculation, Neutrophil, Erythrocyte, Hemorheology.

### Major scientific achievements

Inflammation requires the interplay of distinct mediators, like erythrocytes and neutrophils as well as acetylcholine (ACh), fibrinogen, chemokines and hemodynamic forces. Importantly, it is associated with hemorheological abnormalities and a dysfunctional endothelium. In erythrocytes, we have demonstrated that soluble fibrinogen is able to target the membrane CD47 in an age-dependent way. We have also shown that the erythrocyte nitric oxide (NO) efflux increases under conditions simulating hyperfibrinogenemia in dependence of the induction of band 3 protein phosphorylation but remains unchanged in the presence of ACh. Moreover, erythrocyte NO efflux was shown to be negatively associated with carotid intima-media thickness in systemic lupus erythematosus and rheumatoid arthritis patients presenting a reduced whole blood viscosity and erythrocyte deformability and an increased erythrocyte aggregation tendency. We have also reported that soluble fibrinogen is able to increase neutrophil free radical production and to bind the neutrophil membrane independently of the integrin Mac-1. In fibrinogen-deficient mice, we have further documented compromised leukocyte recruitment in comparison to control animals, that showed a role for fibrinogen in this process.

We have further used the zebrafish model to study the function of the CXC chemokine, CXCL8, in inflammation. Both zebrafish homologs, cxcl8-l1 and cxcl8-l2, were shown to be up-regulated upon wounding. By combining their expression knockdown with the *in vivo* tracking of neutrophils, we have shown that both chemokines are crucial for neutrophil recruitment and inflammation resolution. Cxcl8-l2 was further shown to signal at least through the zebrafish CXC chemokine receptor 2 (Cxc2) for inducing neutrophil recruitment. By analyzing neutrophil migration *in vivo* via the use of the tracking software, PhagoSight, we observed that in the absence of these chemokines, the speed of the neutrophils migrating to the wound was significantly increased in comparison to control ones, although the directionality of the movement was not affected. These results suggest that in the zebrafish, a neutrophil sub-population may be recruited to inflamed areas in Cxcl8-independent mode. The development of numerical simulations based on hemodynamic and hemorheological parameters obtained *in vivo* from animal models allowed us to discriminate the existence of regions with distinct shear stress properties on the surface of leukocytes approaching the endothelium. We have also shown that the hydrodynamic behaviour of a cluster of recruited leukocytes establishes a strong motive for additional leukocyte recruitment. In this situation, we have further observed an increased endothelial shear stress. Finally, we have disclosed a new association between CD3+ T lymphocytes, oxidized low-density lipoprotein, and C-reactive protein in patients with acute

myocardial infarction (AMI), by using a multi-biomarker approach, thus confirming the specificity of the immune response in AMI towards myocardial inflammation and remodelling.

#### Recent Most Relevant Publications

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.* (Epub ahead of print) DOI: 10.3233/CH-121662  
<http://iospress.metapress.com/content/h7348151t0883757/?genre=article&id=doi%3a10.3233%2fCH-121662> (Journal IF: 3.398, Citations: 0)

de Almeida VV, Calado A, Silva-Herdade AS, Rosário HS, Saldanha C. (2012) An in vitro study on the modulation of the neutrophil adhesive behavior by soluble fibrinogen. *Clin Hemorheol Microcirc.* (Epub ahead of print) DOI: 10.3222/CH-121662;  
(<http://iospress.metapress.com/content/h7348151t0883757/?genre=article&id=doi%3a10.3233%2fCH-121662>) (Journal IF: 3.398, Citations: 0)

de Oliveira, S., Reyes-Aldasoro, C.C., Candel, S., Renshaw, S.A., Mulero, V., Calado, A. (2013) Cxcl8 (Interleukin-8) mediates neutrophil recruitment and behavior in the zebrafish inflammatory response. *J.Immunol.* **190**, 4349-59. (Journal IF: 5.673, Citations: 4)

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: 1)

#### Ongoing Research Projects

2012/2013 UBIMI. Coordinator: Maria Carlota Saldanha. Agency: Soc Portuguesa Hemorreologia. Amount: €13.000,00

2013/2016 Modelação Matemática e Computacional da Fisiologia Humana. Coordinator: Maria Carlota Saldanha Lopes. Agency: FCT. Amount: €12.100,00 Total Amount: €238.000,00

#### Other Projects

2012/2015 Evaluation of inflammation profiles in septic patients – contribution to multiple cross prognostic biomarkers. Coordinator: Carlota Saldanha. (no funding)

2011/2013 Functional characterization of the neutrophil in alcoholic and non-alcoholic steatohepatiti. Coordinator: Ângelo Calado. Amount: €5.000,00



### Publications in peer review Journals

Barvitenko, N.N., Aslam, M., Filosa, J., Matteucci, E., Nikinmaa, M., Pantaleo, A., Saldanha, C., Baskurt, O.K. (2013) Tissue oxygen demand in regulation of the behavior of the cells in the vasculature. *Microcirculation* **26** (Epub ahead of print) <http://onlinelibrary.wiley.com/doi/10.1111/micc.12052/pdf> (Journal IF: 2.574, Citations: 0)

Silva-Herdade AS, Saldanha C. (2013) Effects of acetylcholine on an animal model of inflammation. *Clin Hemorheol Microcirc* **53** (1),195-202. (Journal IF: 3.389, Citations: 1)

Saldanha C. (2013) Fibrinogen interaction with the red blood cell membrane. *Clin Hemorheol Microcirc* **53**(1),39-44. (Journal IF: 3.389, Citations: 0)

Napoleão P, Selas M, Freixo C, Mota Carmo M, Viegas-Crespo AM, Ferreira RC, Pinheiro T. (2013) T lymphocytes alterations are associated with oxidized LDL, troponin T, white blood cells and C-reactive protein during acute myocardial infarction. *Clinical Hemorheology and Microcirculation* **55**(3),349-358. (Journal IF: 3.389, Citations: 0)

### Other publications International

Ramos C, Napoleão P, Ferreira RC, Foundinho C, Selas M, , Mota Carmo M, Viegas-Crespo AM, Pinheiro T. Relationship between ox-LDL, immune cells, atheroma dimensions and angiographic measurements assessed by coronary angiography and intravascular ultrasound. Assessed by Coronary Angiography and Intravascular Ultrasound, What Should We Know About Prevented, Diagnostic, and Interventional Therapy in Coronary Artery Disease, Prof. Baskot Branislav (Ed.), ISBN: 978-953-51-1043-9, InTech, 2013, Available from: <http://www.intechopen.com/books/what-should-we-know-about-prevented-diagnostic-and-interventional-therapy-in-coronary-artery-disease/relationship-between-ox-ldl-immune-cells-atheroma-dimensions-and-angiographic-measurements-assessed>

Saldanha C, Teixeira P, Santos-Freitas T, Napoleão P. (2013) Timolol modulates erythrocyte nitric oxide bioavailability. *Journal of Clinical & Experimental Ophthalmology*. **4**, 3 <http://dx.doi.org/10.472/2155-9570.1000285>

### Other publications National

Saldanha C, (2013) "Invitation". *Bulletin of the SPHM* **28**,(1):3.

Saldanha C, (2013). "Microcirculation". *Bulletin of the SPHM* **28**, (2):3-4.

Saldanha C, (2013) "Highlights". *Bulletin of the SPHM* **28**, (3):3-4.

Saldanha C, (2013) "Plasma viscosity" *Bulletin of the SPHM* **28**, (4):3-4.

Saldanha C (2013) "Monóxido de azoto e endotélio" Patient Care, Edição Portuguesa Suplemento 3-7.

### Invited lectures and seminars

Carlota Saldanha, Pedro Teixeira, Teresa Santos-Freitas and Patrícia Napoleão “Modulation of Erythrocyte Nitric Oxide Bioavailability. 3<sup>rd</sup> International Conference on Clinical Experimental Ophthalmology Hilton, Chicago/ Northbrook, USA, April 15 – 17, 2013.

Carlota Saldanha, Freitas T, Lopes de Almeida JP "Signal transduction pathways in erythrocyte nitric oxide metabolism under high fibrinogen levels". 17<sup>th</sup> Conference of the European Society for Clinical Hemorheology and Microcirculation, Pécs, Hungary, July 6-9, 2013.

Carlota Saldanha, Napoleão P, Calado A, Morais A, Faustino P, Coelho A, Lavinha 17<sup>th</sup> Conference of the European Society for Clinical Hemorheology and Microcirculation, Pécs, Hungary, July 6-9, 2013.

Saldanha C, Santos MJ, Mendes Pedro L, Canhão H, Fernandes e Fernandes, Canas da Silva J, Fonseca JE, Erythrocyte Nitric Oxide Association with Low Grade Inflammation, 17<sup>th</sup> Conference of the European Society for Clinical Hemorheology and Microcirculation, Pécs, Hungary, July 6-9, 2013.

### Communications in International Conferences

V. Vitorino de Almeida, A.S.S. Herdade, A. Calado, H. S. Rosário C. Saldanha. Effects of fibrinogen in mice leukocyte recruitment IUPS 2013 Joint Meeting 27<sup>th</sup> European Society for Microcirculation Hosted by British Microcirculation Society and 7<sup>th</sup> European Vascular Biology Organization, Birmingham, UK, July 21-26, 2013 (Poster presentation).

de Oliveira, S., López-Muñoz, A., Candel, S., Calado, A. and Mulero, V. (2013) “Early ATP and calcium signals modulate zebrafish acute inflammatory response via Duox1 activation and hydrogen peroxide release”. ZDM6 – Zebrafish Disease Models 6, Murcia, Spain, July 14-17, 2013 (Awarded prize for Best Oral Presentation in ZDM6) (Oral presentation)

Candel, S., de Oliveira, S., Garcia-Moreno, D., Espin, R., Cayuela, M.L., Tyrkalska, S.D., Renshaw, S.A., Meseguer, J., Sepulcre, M,P. and Mulero, V. (2013) “TNFR2 deficiency triggers skin inflammation in the zebrafish via the production of H<sub>2</sub>O<sub>2</sub> and the Activation of the NF-B signaling pathway.” ZDM6 – Zebrafish Disease Models 6, Murcia, Spain, July 14-17, 2013 (Oral presentation)

de Oliveira, S., López-Muñoz, A., Candel, S., Pelegrin, P., Calado, A. and Mulero, V. (2013) “ATP and calcium signals modulate zebrafish acute inflammatory response via Duox1 activation and hydrogen peroxide release”. Semmelweis Symposium 2013, Budapest, Hungary, 2013 (Awarded prize for Best Oral Presentation) (Oral presentation)

Candel, S., de Oliveira, S., Garcia-Moreno, D., Espin, R., Cayuela, M.L., Tyrkalska, S.D., Renshaw, S.A., Meseguer, J., Sepulcre, M,P. and Mulero, V. (2013) “Identification of new therapeutic targets for the treatment of skin inflammatory diseases using the zebrafish.” Semmelweis Symposium 2013. Budapest, Hungary, 2013 (Poster presentation)

### **Communications in National Conferences**

Carlota Saldanha Erythrocyte Promotes Nitric Oxide Bioavailability 6<sup>th</sup> Workshop Beathing the blood –brain and other blood barriers, Lisbon, Portugal, February 6-8, 2013 (Poster presentation)

### **Organisation of Conferences**

Carlota Saldanha. Organization of the “Biochemistry Module” of the 8<sup>th</sup> Post-Graduate Course in Sports Medicine, Sports Medical Center, Lisbon, Portugal, January 18, 2013

Carlota Saldanha. Co-Organizer of the Symposium S5 “The mechanism of changes in blood cell microrheology and microcirculation: experiments and clinics. 17<sup>th</sup> Conference of the European Society for Clinical Hemorheology and Microcirculation (ESCHM), Pécs, Hungary, July 6-9, 2013.

### **Internationalisation**

De Oliveira, S. PhD fellowship SFRH/BD/62674/2009, FCT. PhD work entitled “In vivo imaging of Inflammation in Zebrafish: the role of chemokine system in the neutrophil and macrophage migration”. Performed under the co-supervision of Dr. Ângelo Calado and Dr. Victor Mulero (Univ. Murcia, Spain) in the two laboratories.

Carlota Saldanha is currently member of the Strategy Committee of the European Society of Microcirculation; member of the International Advisory Board of European Society of Hemorheology and Microcirculation (ESCHM); member of the Editorial Board of the “Clinical Hemorheology and Microcirculation”; President of the Portuguese Society of Hemorheology and Microcirculation. She is nominated the President of the 18<sup>th</sup> European Conference on Clinical Hemorheology and Microcirculation to be held in 2016 at Lisbon.

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

Patrícia Napoleão - “Hemorreologia, Hemostase e Inflamação na Patologia Vasular – Da investigação à prática clínica”, Lisbon, Portugal, Award of SPHM-SPACV/Biosaúde.

de Oliveira, S., López-Muñoz, A., Candel, S., Calado, A. and Mulero, V. (2013) “Early ATP and calcium signals modulate zebrafish acute inflammatory response via Duox1 activation and hydrogen peroxide release”. ZDM6 – Zebrafish Disease Models 6, Murcia, Spain. 14th-17th July. Awarded prize for Best Oral Presentation in ZDM6.

de Oliveira, S., López-Muñoz, A., Candel, S., Pelegrin, P., Calado, A. and Mulero, V. (2013) “ATP and calcium signals modulate zebrafish acute inflammatory response via Duox1 activation and hydrogen peroxide release”. Semmelweis Symposium 2013, Budapest, Hungary, 2013 (Oral presentation). Awarded prize for Best Oral Presentation.

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

Carlota Saldanha Counsel Member of the Quality Assurance of the University of Lisbon from 2007 until June 2013.

### **Advanced teaching**

Carlota Saldanha organized and lectured the “Biochemistry Module” of the 8<sup>th</sup> Post-Graduate Course in Sports Medicine, Sports Medical Center, Lisbon, January 18, 2013

Napoleão P. Inflammation in acute coronary artery disease. Lecture at Mestrado em Genética Molecular e Biomedicina da Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, May 20, 2013.

Napoleão P. Inflammation in acute coronary artery disease. Lecture at Mestrado de Biologia Humana e Ambiente da Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal, May 15, 2013.

Napoleão P. Biomarcadores de inflamação na doença coronária aguda. Lecture at Curso Livre Experimental de Bioquímica da Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, February 20, 2013.

### **PhD theses completed**

Vanda Vitorino de Almeida (2013) The role of fibrinogen in the mechanism of microvascular inflammatory response. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Carlota Saldanha

### **Msc theses completed**

Pedro Teixeira (2013) Modulação da biodisponibilidade do monóxido de azoto no eritrócito- Avaliação do Efluxo de GSNO e do efeito do timolol. Faculdade de Ciências da Universidade de Lisboa, Supervisors: Carlota Saldanha, Deodália Dias.

Sara Louro Moleirinho (2013) Avaliação da explosão oxidativa em neutrófilos de doentes com sepsis- uma abordagem longitudinal. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa. Supervisors: Patricia Napoleão, Paula Gonçalves.

## 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 C. Santos, PhD, Agregação - Associate Professor, Faculdade de Medicina da Universidade de Lisboa.

### Research Team

Ana de Souto Martins	Graduate	MSc Student (started September)
Ana Filipa Guedes	Master	PhD Student (started April)
Ana Isabel Figueiredo Martins	Master	Investigator (left May)
André Faustino	Master	PhD Student
Axel Hollmann	PhD	Post-doctoral Investigator
Filomena Carvalho	PhD	Investigator, Assistant Professor
Gabriela Guerra	Master	Investigator
Ivo C. Martins	PhD	Post-doctoral Investigator
Marcelo T. Augusto	Master	Investigator (started November)
Marco M. Domingues	PhD	PhD Student (left November)
Margarida Rodrigues	Graduate	PhD Student
Maria Inês Malho	Graduate	MSc Student (started February)

Patrícia M. Silva	Graduate	MSc Student
Pedro M. Matos	Graduate	PhD Student (left November)
Saulo Vieira	Master	PhD Student from Universidade Federal do Rio de Janeiro (started March; left September)
Sónia Gonçalves Abreu	PhD	Investigator
Susana dos Reis Gregório	Graduate	MSc Student (started September)
Virgínia Amaral	Master	PhD Student from Universidade Federal do Rio de Janeiro (started October)

### Keywords / Research Areas

Membranes, Nanomedicine, HIV, Dengue Virus, Peptide-based therapies (CPPs, AMPs, pep14-23), Atomic Force Microscopy (AFM), Fibrinogen.

### Major scientific achievements

- Understanding dengue virus (DENV) replication mechanisms is required to identify new therapeutic targets. Using AFM-based force spectroscopy, DLS, NMR and computational studies, we showed that DENV capsid (C) protein binds specifically to very low-density lipoproteins (VLDL). DENV C-VLDL interaction is K<sup>+</sup>-dependent and is inhibited by a new drug lead that we recently developed. ApoE may be the DENV C ligand on VLDL. Thus, lipoviroparticles formation may potentially be targeted for DENV life cycle inhibition.
- Singlet oxygen produced by the new broad-spectrum antiviral LJ001 and related compounds, as well as by dUY11, induces changes on the viral membrane resulting in the inhibition of the fusion pore necessary for cell infection by HIV and other enveloped viruses.
- The enhanced interaction of C34 cholesterol-conjugates with membranes 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.

### Recent Most Relevant Publications

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: 12.062, Citations: 24)

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. USA* **109**, 17627-17632 (Journal IF: 9.737, Citations: 9)

Matos PM, Castanho MARB, Santos NC (2010) HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes. *PLoS ONE* **5**, e9830. (Journal IF: 3.730, Citations: 14)

Ribeiro MM, Melo MN, Serrano I, Santos NC, Castanho MARB (2010) Drug-lipid interaction evaluation: Why a 19th century solution? *Trends Pharmacol. Sci.* **31**, 449-454. (Journal IF: 9.250, Citations: 12)

Carvalho FA, Carneiro FA, Martins IC, Assunção-Miranda I, Faustino AF, Pereira RM, Bozza PT, Castanho MARB, Mohana-Borges R, Da Poian AT, Santos NC (2012) Dengue virus capsid protein binding to hepatic lipid droplets (LD) is potassium ion dependent and is mediated by LD surface proteins. *J. Virol.* **86**, 2096-2108 (Journal IF: 5.076, Citations: 9)

### Ongoing Research Projects

2012/2015 AMYLOIDECTORS: Employing amyloid fibrils as biosensors of the interaction of peptides with phospholipids and/or protein domains. Coordinator: Ivo C. Martins. Agency: FCT. Amount: €144.010,00

2010/2014 MEMPEPACROSS - Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration. Coordinator: Nuno C. Santos. Agency: Marie Curie Actions – IRSES. Amount: € 131.400,00 Total amount: €181.800, 00

2012/2015 Molecular characterization of the fibrinogen-erythrocyte interaction and its influence on cardiovascular pathologies. Coordinator: Joana Paredes (IPATIMUP). IMM Coordinator: Nuno C. Santos. Agency: FCT. Amount: €175.000,00

2012/2015 Adhesion, Differentiation and Invasion: different processes, common cadherin players. Coordinator: Nuno C. Santos. Agency: FCT. Amount: €49.500,00

2010/2014 Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Coordinator: Nuno C. Santos. Agency: Applications in health and disease, FCG, Calouste Gulbenkian Foundation Prize Stimulus to Research. Amount: €12.500,00

2010/2016 The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation. Coordinator: Ivo C. Martins. Agency: FCG, Calouste Gulbenkian Foundation Frontiers in Life Sciences Research Prize. Amount: €50.000,00

2011/2014 LIPIDENGUE: The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies. Coordinator: Miguel Castanho. Agency: FCT. Amount: €130.000,00

2012/2015 Multi-target HIV entry inhibitors delivery by cationic liposomes. Coordinator: A.S. Veiga. Agency: FCT. Amount: €129.209,00

2013/2014 Studying the interaction with biological membranes of pep14-23, a novel dengue virus capsid protein inhibitor. Coordinator: I.C. Martins. Agency: Calouste Gulbenkian Foundation (FCG) & Lisbon Medical Faculty (FMUL). Amount: €3.000,00

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: R. Ariens. Agency: Project of the British Heart Foundation.

2013/2016 DELIN: An innovative approach to deliver dual targeting HIV entry inhibitors using cationic liposomes. Coordinator: Miguel Castanho. Agency: FCT/ HIVERA (European Union). Amount: €99.000,00

#### Other Projects

2010/2013 Membrane fusion mechanism of Influenza Hemagglutinin: a simulation and biophysical approach. Coordinator: N.C. Santos. Agency: FCT. Amount: € 44.186,00

2013/2013 Peptide-based dengue virus therapeutics. Coordinator: I.C. Martins. Agency: IMM “Ciência Viva” project. Amount: €250,00

2013/2013 Amyloid-based nanotechnology. Coordinator: I.C. Martins. Agency: IMM “Ciência Viva” project. Amount: €250,00

#### Publications in peer review Journals

Augusto MT, Hollmann A, Castanho MARB, Porotto M, Pessi A, Santos NC (2013) Improvement of the HIV fusion inhibitor C34 efficacy by membrane anchoring and enhanced exposure. *J. Antimicrob. Chemother.* (Journal IF: 5.338, Citations: 0)

Freire JM, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MARB. (2013) 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. (Journal IF: 4.250, Citations: 0)

Vigant F, Hollmann A, Lee J, Santos NC, Jung ME, Lee B (2013) The rigid amphipathic fusion inhibitor dUY11 acts through photosensitization of viruses. *J. Virol.*, doi: 10.1128/JVI.02907-13. (Journal IF: 5.076, Citations: 0)



Domingues MM, Silva PM, Franquelim HG, Carvalho FA, Castanho MARB, Santos NC (2013) Antimicrobial protein rBPI21-induced surface changes on Gram-negative and Gram-positive bacteria. *Nanomedicine* (NBM), doi: 10.1016/j.nano.2013.11.002. (Journal IF: 6.930, Citations: 0)

Bouchet AM, Iannucci NB, Pastrian MB, Cascone O, Santos NC, Disalvo EA, Hollmann A (2013) Biological activity of antibacterial peptides matches synergism between electrostatic and non electrostatic forces. *Colloids Surf. B - Biointerfaces*, doi: 10.1016/j.colsurfb.2013.10.025. (Journal IF: 3.554, Citations: 0)

Matos PM, Andreu D, Santos NC, Gutiérrez-Gallego R. (2013) Structural requirements of glycosaminoglycans for their interaction with HIV-1 envelope glycoprotein gp120. *Arch. Virol.* (Journal IF: 2.030, Citations: 0)

Faustino AF, Carvalho FA, Martins IC, Castanho MARB, Mohana-Borges R, Almeida FC, Da Poian AT, Santos NC. (2013) Dengue virus capsid protein interacts specifically with very low-density lipoproteins. *Nanomedicine* (NBM) doi: 10.1016/j.nano.2013.06.004. (Journal IF: 6.930, Citations:0)

Pimenta J, Viegas A, Sardinha J, Santos A, Martins IC, Cantante C, Dias F, Soares R, Cabrita E, Gonçalves J, Fontes C, Prates J, Pereira R (2013). Paving the way through prion-like biogenesis. Ovine Doppel co-expression with SUMO fusion technology, and NMR solution structure of its N-terminal sequence (1-30). *Reprod Biol Endocrin* **11**, 25 (Journal IF: 2.14, Citations: 0)

Pimenta J, Viegas A, Sardinha J, Martins IC, Cabrita E, Fontes C, Prates J, Pereira R (2013). NMR Solution Structure and SRP54M predicted interaction of the N-Terminal sequence (1-30) of the ovine Doppel protein. *Peptides* **49**, 32-40, doi: 10.1016/j.peptides.2013.08.013. (Journal IF: 2.522, Citations: 0)

Bravo-Ferrada B, Hollmann A, Delfederico L, Valdés La Hens D, Semorile L (2013) Patagonian red wines: Selection of *Lactobacillus plantarum* isolates as potential starter cultures for malolactic fermentation. *World J Microbiol Biotechnol* **29**(9), 1537-1549 doi: 10.1007/s11274-013-1337-x (Journal IF: 1.262, Citations: 1)

Disalvo EA, Hollmann A, Semorile L, Martini F (2013) Evaluation of the Defay-Prigogine model for the membrane interphase in relation to biological response in membrane-protein interactions. *Biochim. Biophys. Acta* **1828**(8), 1834-1839 doi: 10.1016/j.bbamem.2013.03.026. (Journal IF: 3.389, Citations: 1)

Freire JM, Veiga AS, Conceição TM, Kowalczyk W, Mohana-Borges R, Andreu D, Santos NC, Da Poian AT, Castanho MARB (2013) Intracellular nucleic acid delivery by the supercharged dengue virus capsid protein. *PLoS ONE* **8**, e81450. doi: 10.1371/journal.pone.0081450. (Journal IF: 3.730, Citations: 0)

Domingues MM, Bianconi ML, Barbosa LRS, Santiago PS, Tabak M, Castanho MARB, Itri R., Santos NC (2013) rBPI21 interacts with negative membranes endothermically promoting the formation of rigid multilamellar structures. *Biochim. Biophys. Acta* **1828**, 2419-2427. doi: 10.1016/j.bbamem.2013.06.009. (Journal IF: 3.389, Citations: 0)

Freire JM, Veiga AS, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MARB (2013) Peptides as models for the structure and function of viral capsid proteins: insights on dengue virus capsid. *Biopolymers (Pept. Sci.)* 100:325-336. doi: 10.1002/bip.22266. (Journal IF: 2.879, Citations: 1)

Ascenso A, Cruz M, Euletério C, Carvalho FA, Santos NC, Marques HC, Simões S (2013) Novel tretinoin formulations: a drug-in-cyclodextrin-in-liposome approach. *J. Liposome Res.* **23**, 211-219. doi: 10.3109/08982104.2013.788026 (Journal IF: 1.909, Citations: 0)

Rodrigues M, de la Torre BG, Andreu D, Santos NC (2013) Kinetic uptake profiles of cell penetrating peptides in lymphocytes and monocytes. *Biochim. Biophys. Acta* **1830**, 554-4563. doi: 10.1016/j.bbagen.2013.05.020 (Journal IF: 3.848, Citations: 0)

Matos PM, Marin M, Ahn B, Lam W, Santos NC, Melikyan GB (2013) Anionic lipids are required for Vesicular Stomatitis Virus G protein-mediated single particle fusion with supported lipid bilayers. *J. Biol. Chem.* **288**, 12416-12425. doi: 10.1074/jbc.M113.462028 (Journal IF: 4.651, Citations: 2)

Franquelim HG, Gaspar D, Veiga AS, Santos NC, Castanho MARB (2013) Decoding distinct membrane interactions of HIV-1 fusion inhibitors using a combined atomic force and fluorescence microscopy approach. *Biochim. Biophys. Acta* **1828**, 1777-1785. doi: 10.1016/j.bbamem.2013.03.006 (Journal IF: 3.389, Citations: 1)

Vigant F, Lee J, Hollmann A, Tanner LB, Ataman ZA, Yun T, Shui G, Aguilar HC, Zhang D, Meriwether D, Roman-Sosa G, Robinson LR, Juelich TL, Buczkowski H, Chou S, Castanho MARB, Wolf MC, Smith JK, Banyard A, Kielian M, Reddy S, Wenk MR, Selke M, Santos NC, Freiberg AN, Jung ME, Lee B (2013) A mechanistic paradigm for broad-spectrum antivirals that target virus-cell fusion. *PLoS Pathog.*, **9**, e1003297. doi: 10.1371/journal.ppat.1003297. (Journal IF: 8.136, Citations: 1)

Hollmann A, Matos PM, Augusto MT, Castanho MARB, Santos NC (2013) Conjugation of cholesterol to HIV-1 fusion inhibitor C34 increases peptide-membrane interactions potentiating its action. *PLoS ONE*, **8**, e60302. doi: 10.1371/journal.pone.0060302. (Journal IF: 3.730, Citations: 0)

Carvalho FA, Martins IC, Santos NC (2013) Atomic force microscopy and force spectroscopy on the assessment of protein folding and functionality. *Arch. Biochem. Biophys.*, **531**, 116-127. doi: 10.1016/j.abb.2012.11.007. (Journal IF 3.370, citations: 1)

#### Invited lectures and seminars

NC Santos, Índices Bibliométricos em Biomedicina, Serviço de Pediatria, Hospital de Santa Maria, Lisbon, Portugal, January 17, 2013.

NC Santos, Biomedical applications of atomic force microscopy-based force spectroscopy: cardiovascular risk and dengue virus replication, IV Jornadas de Bioquímica da Universidade do Minho, Braga, Portugal, April 10, 2013.

AF Faustino, GM Guerra, A Hollmann, F Almeida, AT. Da Poian, NC Santos, IC Martins, Dengue virus capsid protein inhibitor peptide, pep14-23, becomes alpha-helical upon binding to negatively-charged lipids, Bioinformatics Institute (BII), A\*STAR, Singapore. May 16, 2013.

HG Franquelim, NC Santos, MARB Castanho, P Schwille, AFM: May the Force be with you!, Ludwig-Maximilian University, Munich, Germany, May 17, 2013.

S Padilla-Parra, PM Matos, R Suter, M Marin, NC Santos, GB Melikian, Sensing extra- and intra-viral pH enables visualization of retrovirus entry into acidic endosomes, measurement of the true kinetics of fusion and detection of nascent fusion pores, Cold Spring Harbor Laboratory Retroviruses Meeting, Cold Spring Harbor (New York), USA, May 20-25, 2013.

NC Santos, Using the force at the nanoscale - From cardiovascular risk to dengue, UL Summer Course Lecture Series – Windows into Health, Science & Technology, Faculdade de Letras da Universidade de Lisboa, Lisbon, Portugal, July 8, 2013.

J Freire, AS Veiga, T Conceição, W Kowalczyk, R Mohana-Borges, D Andreu, N Santos, AT Da Poian, MARB Castanho, Unraveling a new actor in dengue virus-cell fusion, EBSA 2013 – 9th European Biophysics Congress, Lisboa, Portugal, July 13-17, 2013. Abstract published on *Eur. Biophys. J.* (2013), 42, S163.

NC Santos, Microscopia de força atômica e espectroscopia de força. Aplicações biológicas e biomédicas, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, August 22, 2013.

FA Carvalho, IC Martins, AF Faustino, FA Carneiro, I Assunção-Miranda, R Mohana-Borges, MARB Castanho, F Almeida, AT Da Poian, NC Santos, AFM-based force spectroscopy probing of dengue virus capsid protein binding to lipid droplets and lipoproteins. Towards a new drug target, VIII Iberoamerican Congress of Biophysics, Valparaíso, Chile, October 1-4, 2013.

I Siqueira, I Assunção-Miranda, A Faustino, FA Carvalho, IC Martins, N Santos, AT Da Poian, Alterations in hepatic lipid metabolism during dengue virus infection, 3rd International Conference on Dengue and Dengue Haemorrhagic Fever, Bangkok, Thailand, October 21-23, 2013.

FA Carvalho, IC Martins, FA Carneiro, I Assunção-Miranda, AF Faustino, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos, Dengue virus capsid protein binding to lipid droplets and its inhibition. Towards a new drug target, 3rd International Conference on Dengue and Dengue Haemorrhagic Fever, Bangkok, Thailand, October 21-23, 2013.

NC Santos, The search for an inhibitor of dengue virus replication using AFM-based force spectroscopy, XI Encontro de Engenharia Biomédica, Lisboa, Portugal, November 6, 2013.

NC Santos, Biomedical applications of AFM-based force spectroscopy: from cardiovascular risk to dengue virus replication, Departamento de Bioengenharia do Instituto Superior Técnico, Lisboa, Portugal, November 11, 2013.

NC Santos, Force spectroscopy, Innovation in Microscopy Course (Congresso da Sociedade Portuguesa de Microscopia), Monte da Caparica, Portugal, December 11, 2013.

### Communications in International Conferences

AF Faustino, V Artilheiro, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, The dengue virus capsid protein inhibitor peptide pep14-23 becomes alpha-helical upon binding to negative lipids, Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published on (2013) *Biophys. J.*, 104, 536a. (Oral communication)

PM Matos, M Marin, B Ahn, W Lam, NC Santos, GB Melikyan, Single virus imaging reveals dependence on endosome-specific lipid for vesicular stomatitis virus fusion, 5th EMBO (European Molecular Biology Organization) Meeting, Amsterdam, Holland. September 21-24, 2013 (Oral communication)

M Rodrigues, BG de la Torre, D Andreu, NC Santos, Kinetic uptake profiles of cell penetrating peptides in lymphocytes and monocytes, Cell Penetrating Peptides – Joint FEBS (Federation of European Biochemical Societies) / Biochemical Society Lecture Course, London, UK, October 7-10, 2013. (Oral communication)

FA Carvalho, IC Martins, FA Carneiro, I Assunção-Miranda, AF Faustino, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos, Dengue virus capsid protein binding to lipid droplets and its inhibition. Towards a new drug target. Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published on *Biophys. J.* (2013) 104, 415a. (Poster presentation)

S Padilla-Parra, PM Matos, N Kondo, M Marin, NC Santos, GB Melikyan, Time-resolved imaging of endosome acidification and single retrovirus fusion with endosomes, Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published on *Biophys. J.* (2013) 104, 87a (Poster presentation)

A Bouchet, NB Iannucci, MB PASTRIAN, O Cascone, NC Santos, EA Disalvo, A Hollmann, Balance between additional van Der Waals and electrostatic components of 107-115 hLZ synergistically increase peptide-membrane interactions potentiating its antimicrobial activity, Biophysical Society's 57th Annual Meeting, Philadelphia, USA, February 2-6, 2013. Abstract published on *Biophys. J.* (2013) 104, 601a (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, Dengue virus capsid protein inhibitor peptide pep14-23: towards a novel drug target, 30th Anniversary Symposium of the Boehringer Ingelheim Fonds, Mainz, Germany, March 16, 2013. (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, F Almeida, AT Da Poian, NC Santos, IC Martins, Dengue virus capsid protein inhibitor peptide, pep14-23, becomes alpha-helical upon binding to negatively-charged lipids, Biophysical Society Meeting Membrane Protein Folding, Seoul, South Korea, May 19-22, 2013. (Poster presentation)

PM Matos, M Marin, B Ahn, W Lam, NC Santos, GB Melikyan, Imaging fusion of single vesicular stomatitis virus with supported lipid bilayers reveals dependence on anionic lipids, FEBS (Federation of European Biochemical Societies) – EMBO (European Molecular Biology Organization) Advanced Lecture Course Biomembranes: Molecular Architecture, Dynamics and Function, Cargèse (Corsica), France, June 10-20, 2013. (Poster presentation)

A Hollmann, PM Matos, MT Augusto, MARB Castanho, NC Santos, Conjugation of cholesterol to HIV-1 fusion inhibitor C34 increases peptide-membrane interactions potentiating its action, 23rd American Peptide Symposium, Waikoloa (Hawaii), USA. June 22-27, 2013. Abstract published on (2013) Biopolymers (Pept. Sci.), 100, 299 (Poster presentation)

JM Freire, AS Veiga, NC Santos, D Andreu, AT Da Poian, MARB Castanho, Nucleic acid delivery vectors derived from viral proteins: Cell Penetrating Peptides vs. Supercharged Proteins, 23rd American Peptide Symposium, Waikoloa (Hawaii), USA. June 22-27, 2013. Abstract published on (2013) Biopolymers (Pept. Sci.), 100, 249-250 (Poster presentation)

A Hollmann, F Vigant, MARB Castanho, B Lee, NC Santos, Singlet oxygen effects on lipid membranes: implication on viral fusion inhibitors mechanism of action, 38th FEBS (Federation of European Biochemical Societies) Congress – Mechanisms in Biology, San Petersburg, Russia, July 6-11, 2013. Abstract published on (2013) FEBS J., 280, 358 (Poster presentation)

AF Faustino, FA Carvalho, IC Martins, MARB Castanho, R Mohana-Borges, FCL Almeida, AT Da Poian, NC Santos, Dengue virus capsid protein interacts specifically with very low density lipoproteins, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S196 (Poster presentation)

A Hollmann, F Vigant, MARB Castanho, B Lee, NC Santos, New HIV fusion inhibitors LJ001 and JL103 act by modifying viral lipid membrane properties, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S123 (Poster presentation)

AF Guedes, FA Carvalho, C Duval, RAS Ariëns, NC Santos, AFM evaluation of the influence of different fibrinogen mutations on its binding to erythrocytes, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S111 (Poster presentation)

FA Carvalho, A Tavares, MTeodoro, G Miltenberger-Miltenyi, NC Santos, AFM based-force spectroscopy as a functional diagnostic nanotool for hematological diseases, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal. July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S110 (Poster presentation)

GM Guerra, S Abreu, NC Santos, IC Martins, Amyloid fibers formation using different peptides: A comparative approach.” EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S141 (Poster presentation)

M Rodrigues, BG de la Torre, D Andreu, NC Santos, Kinetic uptake profiles of cell penetrating peptides in lymphocytes and monocytes, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) Eur. Biophys. J., 42, S168 (Poster presentation)

presentation)

SM Vieira, IF Malho, FA Carvalho, NC Santos, Divalent cations dependence of the fibrinogen binding to its receptor on human erythrocytes, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S198 (Poster presentation)

AF Faustino, GM Guerra, A Hollmann, MARB Castanho, FCL Almeida, AT Da Poian, NC Santos, IC Martins, pep14-23, a peptide drug lead against dengue virus, binds anionic lipids becoming alpha-helical, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S64 (Poster presentation)

JM Freire, AS Veiga, IR de Figueiredo, BG de la Torre, NC Santos, D Andreu, AT Da Poian, MARB Castanho, Design and mechanism of dengue virus capsid-cell penetrating peptides for nucleic acid delivery, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S166 (Poster presentation)

MT Augusto, A Hollmann, MARB Castanho, A Pessi, NC Santos, Improvement of the HIV fusion inhibitor C34 activity by membrane anchoring and enhanced exposure, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S165 (Poster presentation)

PM Silva, S Gonçalves, LN de Medeiros, E Kurtenbach, NC Santos, Antifungal defensin Psd1 increases membrane roughness and promotes apoptosis in *Candida albicans*, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S106 (Poster presentation)

PM Matos, M Marin, B Ahn, W Lam, NC Santos, GB Melikyan, Imaging fusion of single vesicular stomatitis virus with supported lipid bilayers, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S102 (Poster presentation)

S Gonçalves, PM Silva, LN de Medeiros, E Kurtenbach, NC Santos, Biofilm formation by different *Candida albicans* variants and their antifungal agents' susceptibility, EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal, July 13-17, 2013. Abstract published on (2013) *Eur. Biophys. J.*, 42, S167 (Poster presentation)

AF Faustino, FA Carvalho, IC Martins, MARB Castanho, R Mohana-Borges, FCL Almeida, AT da Poian, NC Santos, Dengue virus capsid protein interacts specifically with very low-density lipoproteins, Modern Biophysical Methods for Protein Ligand Interactions – EMBO (European Molecular Biology Organization) Practical Course, Oulu, Finland, October 21-25, 2013 (Poster presentation)

V Artilheiro, AF Faustino, FCL Almeida, MARB Castanho, AT Da Poian, NC Santos, IC Martins, Understanding the mode of action of pep14-23, a novel Flavivirus drug candidate, 7th YES (Young European Scientist) Meeting, Porto, Portugal. November 14-16, 2013 (Poster presentation)

### Communications in National Conferences

MT Augusto, A Hollmann, MARB Castanho, M Porotto, A Pessi, NC Santos, Improvement of the HIV fusion inhibitor C34 efficacy by membrane anchoring and enhanced exposure, iMed Conference 5.0 – Innovating Medicine, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

IF Malho, L Sargento, AF Guedes, FA Carvalho, NC Santos, Molecular characterization of the fibrinogen-erythrocyte interaction and its influence on cardiovascular pathologies, iMed Conference 5.0 – Innovating Medicine, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

V Artilheiro, AF Faustino, GM Guerra, FCL Almeida, MARB Castanho, AT Da Poian, NC Santos, IC Martins, Structure-function study of the dengue virus capsid protein and its de novo designed inhibitor peptide, pep14-23, iMed Conference 5.0 – Innovating Medicine, Lisbon, Portugal, October 11-13, 2013 (Poster presentation)

GM Guerra, S Gonçalves, NC Santos, IC Martins, Development of amyloid-based biomaterials for nanotechnology, RECPAD 2013 – 2nd Portuguese Pattern Recognition Conference, Lisbon, Portugal, November 1, 2013 (Poster presentation)

P Silva, S Gonçalves, L Medeiros, E Kurntenbach, NC Santos, Antifungal defensin Psd1 increases membrane roughness and cell stiffness and promotes apoptosis in *Candida albicans*, RECPAD 2013 – 2nd Portuguese Pattern Recognition Conference, Lisbon, Portugal, November 1, 2013 (Poster presentation)

FA Carvalho, A Tavares, M Teodoro, G Miltenberger-Miltenyi, NC Santos, AFM based-force spectroscopy as a functional diagnostic nanotool for hematological diseases, RECPAD 2013 – 2nd Portuguese Pattern Recognition Conference, Lisbon, Portugal, November 1, 2013 (Poster presentation)

### Organisation of Conferences

Nuno C. Santos, Member of the scientific committee of the VIII Iberoamerican Congress of Biophysics, Valparaíso, Chile. October 1-4, 2013.

Nuno C. Santos and Sónia Gonçalves, Co-organization of Antimicrobial Peptides Course, Rio de Janeiro, Brazil. August 22-27, 2013.

Nuno C. Santos, Ivo C. Martins, Axel Hollman, Marcelo Augusto, André Faustino, Ana Filipa Guedes, Gabriela Guerra, Maria Inês Malho, Patrícia Silva and Margarida Rodrigues, Co-organization of EBSA 2013 – 9th European Biophysics Congress, Lisbon, Portugal. July 13-17, 2013.

### **Internationalisation**

Collaborative publications and/or funded projects with groups from the Federal University of Rio de Janeiro (Brazil), Pompeu Fabra University (Barcelona, Spain), Federal University of Ceará (Fortaleza, Brazil), University of Leeds (UK), University of Girona (Spain), 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), University of California at Los Angeles (USA), Mount Sinai Medical Center (New York, USA), University, Cornell University (New York, USA) 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 supervised two PhD students (Saulo Vieira and Virginia Amaral) from the Federal University of Rio de Janeiro (Brazil).

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

André Faustino won the Biophysical Society Best Poster Award at the 9th EBSA Conference, to support the participation at the 58th Biophysical Society Annual Meeting of 2014, Lisbon, Portugal, July 13-17, 2013.

Pedro Matos won a BIOVISION Next Fellowship to participate in the conference BIOVISION: The World Life Sciences Forum, Lyon, France, March 23-26, 2013.

Pedro Matos won the Runner-Up prize, Team Chemo and Bioengineering from Merck Serono Innovation Cup 2013, Seeheim-Jugenheim, Germany, August 25-30, 2013

André Faustino won the Biophysical Society International Travel Award to further support the participation at the 58th Biophysical Society Annual Meeting of 2014.

### **Advanced teaching**

Nuno C. Santos. Lecture on Nanotechnology and Nanomedicine, and on Atomic Force Microscopy based Force Spectroscopy, in the framework of the Lisbon Academic Medical Center (CAML) PhD Program nanocourse on “Nanomedicine”, Lisbon, Portugal, February 2013.

Nuno C. Santos. Lecture on Lipids and Biological Membranes classes in the framework of the doctoral program, Instituto de Tecnologia Química e Biológica (ITQB), Oeiras, Portugal, January 2013.

Nuno C. Santos, Ivo C. Martins. Organization of the Lisbon Academic Medical Center (CAML) PhD Program nanocourse on “Nanomedicine”, Lisbon, Portugal, February 18 - 20, 2013.

Nuno C. Santos. Lecture on Characterization of Colloidal Systems by Light Dispersion Techniques



and Force Spectroscopy in the Master of Biotechnology program, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa. Lisbon, Portugal, April 2013.

Nuno C. Santos. Lecture on AFM-based Force Spectroscopy: Biological and Biomedical Applications in the Master of Structural Biology program, Instituto Superior Técnico, Technical University of Lisbon. Lisbon, Portugal, April 2013.

Nuno C. Santos. Lecture on Antimicrobial Peptides in the post-graduation program of Biological Sciences (Biophysics, Biochemistry and Microbiology), Federal University of Rio de Janeiro. Rio de Janeiro, Brazil, August 2013.

Sónia Gonçalves. Lecture on Fluorescence Spectroscopy Methodologies in the post-graduation program of Biological Sciences (Biophysics, Biochemistry and Microbiology), Federal University of Rio de Janeiro. Rio de Janeiro, Brazil, August 2013.

Nuno C. Santos. Lecture on Light Dispersion Techniques and Atomic Force Microscopy in the Master of Biotechnology program, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa. Lisbon, Portugal, November 2013.

Nuno C. Santos. Lecture on Atomic Force Microscopy classes in the Master of Biochemistry for Health program, Instituto de Tecnologia Química e Biológica (ITQB) Oeiras, Portugal, November 2013.

### **Science and society**

The research work of Nuno Santos Lab was featured on mass media news on Expresso (May 4, 2013, pp.20-21), TSF (“Mundo Novo”, May 24, 2013), Público (May 26, 2013, p.2), RTP 2 (“Sociedade Civil”, June 11, 2013) and TSF (October 30, 2013).

With the aim of promoting the interest in science among young students, the Nuno Santos Lab organized visits for undergraduate students via presentations and “speed-dating” style contact with the different components the Unit’s Research work.

André Faustino participated in an outreach activity with children from Santa Casa da Misericórdia de Mafra (Portugal) to celebrate the “Dia Nacional da Cultura Científica”, on November 25, 2013.

Ivo C. Martins hosted at the Nuno Santos lab Lab high school students in the framework of the “Ciência Viva” program.

### **PhD theses completed**

Pedro Matos (2013) Shedding light on enveloped viruses entry and its inhibition using optical techniques. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Nuno C. Santos.

### **Msc theses completed**

Marcelo Augusto (2013) Interactions of HIV fusion inhibitors with biomembranes model systems and human blood cells. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Nuno C. Santos.

Maria Inês Malho (2013) Molecular characterization of the fibrinogen-erythrocyte interaction and its influence on cardiovascular pathologies by AFM-based force spectroscopy. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa. Supervisors: Nuno C. Santos, Filomena A. Carvalho.

Patrícia Oliveira e Silva (2013) Study of the effects of the antifungal defensin Psd1 in *Candida albicans* using atomic force microscopy and flow cytometry. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Nuno C. Santos, Sónia Gonçalves.

## LEONOR SAÚDE LAB

### Major Interests / Objectives

We would like to understand the cellular and molecular mechanisms that control the left-right asymmetric placement of internal organs and the bilateral symmetric formation of musculoskeletal elements in vertebrates. In addition we are interested in make 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 – Auxiliary professor, FMUL

### Research Team

Ana Catarina Esteves Ribeiro	PhD	Post-doctoral Investigator
Ana Margarida da Silva Figueira	Graduate	MSc Student
Ana Margarida Pereira Cristovão Pinto	Graduate	Technician
Benedict Paul Both	Graduate	MSc Student (started February)
João Duarte Tavares da Silva Pereira	Graduate	Post-doctoral Investigator
José Guilherme Pereira de Almeida Santos	Graduate	MSc Student
Raquel Valente Mendes	Graduate	PhD Student
Rita Alexandra Rodrigues Pinto	Master	PhD Student
Rita Joana Soares Serrano	Graduate	MSc Student
Rita Leonor Alvares Cabral de Figueiredo Fior Sousa Soares	PhD	Post-doctoral Investigator
Sara Maria Ferreira Fernandes	Master	PhD Student (started February)
Susana Alexandra Rodrigues Pascoal	PhD	Post-doctoral Investigator

### Keywords / Research Areas

Left-right asymmetry, Somite formation, Tissue/organ regeneration.

### Major scientific achievements

We published 1 paper:

Pascoal P., de Lima J.E, Leslie J.D., Hughes S.M. and Saúde L. Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. *PLoS ONE* **8**(6), e68021, 2013.

And managed to get 1 manuscript revised in *Developmental Cell*:

Mendes R.V., Martins G.G. and Saúde L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells.

Raquel V. Mendes, a PhD student in the unit was awarded The Best Poster Award at the 2nd Meeting of the Portuguese Society of Developmental Biology (SPBD) and Benedict Both, a medical student working in our unit was awarded The Best GAPIC project.

Leonor Saúde was the co-organizer of the the 2nd Meeting of the Portuguese Society of Developmental Biology (SPBD) jointly with the Spanish Society for Developmental Biology (SEBD) in association with the Portuguese Society for Stem Cells and Cell Therapies (SPCE-TC).

### Recent Most Relevant 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: 7.09, Citations: 2)

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: 2.79, Citations: 0)

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* **6**(7), e22820. (Journal IF: 4.092, Citations: 5)

Lopes S.S., Lourenço R., Pacheco L., Moreno N., Kreiling J. and Saúde L. (2012) Notch signalling regulates left-right asymmetry through ciliary length control. *Development* **137**(21), 3625-32. (Journal IF: 7.09, Citations: 26)

Saúde L., Lourenço R., Gonçalves A. and Palmeirim I. (2005) terra is a left-right asymmetry gene required for left-right synchronization of the segmentation clock. *Nature Cell Biology* **7**(9), 918-920. (Journal IF: 19.488, Citations: 32)

### Ongoing Research Projects

2010/2013 Uncover the importance of cilia as signaling structures during regeneration. Coordinator: Maria Leonor Tavares Saúde. Agency: FCT. Amount: €170.000,00

2010/2013 Searching for RNA regulators that control the segmentation clock. Coordinator: Maria Leonor Tavares Saúde. Agency: FCT. Amount: €188.743,00

2012/2015 Uncover the molecular mechanism downstream of Dmrt2a/Terra that coordinates symmetry versus asymmetry along the left-right axis. Coordinator: Maria Leonor Tavares Saúde. Agency: FCT. Amount: €109.755,00

2013/2014 Prémio L'Oreal Mulheres na Ciência - Ana Catarina Ribeiro. Coordinator: Maria Leonor Tavares Saúde. Agency: L'Oreal Portugal Lda. Amount: €20,000

2013/2015 Uncovering cellular mechanisms of spinal cord regeneration in zebrafish and their modulation with aging. Coordinator: Maria Leonor Tavares Saúde. Agency: FCT. Amount: €181.199,00

### Publications in peer review Journals

Pascoal P., de Lima J.E, Leslie J.D., Hughes S.M. and Saúde L. (2013) Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. *PLoS ONE* **8**(6), e68021.

### Invited lectures and seminars

N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. Centro Andaluz de Biología del Desarrollo, Seville, Spain, 2013.

N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. Making and breaking the left-right axis: laterality in development and disease. Satellite Symposium of The International Society of Developmental Biologists Congress, Cancun, Mexico, 2013.

An amputation resets positional information to a proximal identity in the regenerating zebrafish caudal fin. Interdisciplinary Approaches in Fish Skeletal Biology, Tavira, Portugal, 2013.

Cell movement choreographies that shape the vertebrate body plan. 3º Encontro de Biologia Molecular. Escola Superior de Saúde Egas Moniz, Monte da Caparica, Portugal, 2013.

### Communications in International Conferences

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Figueira, A.M. and Saúde, L. The role of Mesogenin1 in the dynamics of movement and differentiation of mesoderm progenitor cells. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. Molecular Biology in Portugal and EMBL, Lisbon, Portugal, July 18, 2013. (Poster presentation)

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. 8º Encontro da Sociedade Portuguesa de Células Estaminais e Terapia Celular, Universidade do Algarve, Faro, Portugal, May 9-10, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. Making and breaking the left-right axis: laterality in development and disease. International Society of Developmental Biologists Congress, Cancun, Mexico, June 16-20, 2013. (Poster presentation)

Azevedo A.S., Sousa S., Jacinto A. and Saúde L. An amputation resets positional information to a proximal identity in the regenerating zebrafish caudal fin. 5th Strategic Conference of Zebrafish Investigators, Pacific Grove, USA, January 19-23, 2013. (Poster presentation)

### **Communications in National Conferences**

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Pascoal, S., Esteves de Lima, J., Serrano R. and Saúde L. Hh signaling and cilia are getting divorced during regeneration: gossip or fact. 1st Postdoctoral Symposium, 10th anniversary of IMM, Lisbon, Portugal, October 17, 2013. (Oral communication)

Pascoal, S., Esteves de Lima, J., Leslie, J.D., Hughes, S.M., Saúde, L. Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. “Development in Action” – DIA Meeting, Oeiras, Portugal, June 2013. (Oral communication)

### **Organisation of Conferences**

Saúde, L., The 2nd Meeting of the Portuguese Society of Developmental Biology (SPBD) jointly with the Spanish Society for Developmental Biology (SEBD) in association with the Portuguese Society for Stem Cells and Cell Therapies (SPCE-TC), Lisbon, Portugal, October 24-26, 2013.

### **Internationalisation**

Collaborative publication with Simon M. Hughes, King's College London, UK.

Pascoal P., de Lima J.E., Leslie J.D., Hughes S.M. and Saúde L. Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. *PLoS ONE* (2013) **8**(6), e68021.

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

Benedict Both was awarded The Best GAPIC Project

Raquel Mendes was awarded The Best Poster Award at The 2nd Meeting of the Portuguese Society of Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013

### **Advanced teaching**

Rior, R. organized and lectured “Animal Developmental Biology”, The Molecular Genetics and Biomedicine Master Course. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Lisbon, Portugal, September 26 - November 15, 2013.

Saúde, L. lectured “Left-right asymmetry”, GAABA PhD Program. IMM, Lisbon, Portugal, March 26, 2013.

Saúde, L. lectured “Somitogenesis”, IGC PhD Program. IGC, Oeiras, Portugal, February 19, 2013.

Saúde, L. lectured “Left-right asymmetry”, FCUL Masters on Development and Evolution Programme. Faculdade de Ciências da Universidade de Lisboa, February 12, 2013.

Rior, R. lectured “Wnt signalling and cancer”, Oncobiology Master Course. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 16-17, 2013.

Pereira, J. lectured “Células estaminais e iPS-aplicações e trapeutica”, Master Course of Instituto Politécnico de Setúbal, Setúbal, Portugal, January 8, 2013.

### **Msc theses completed**

José Almeida Santos (2013) Molecular tools to dissect the role of Dmrt2a and Dmrt2b in left-right axis formation in zebrafish. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Lisbon, Portugal. Supervisor: Leonor Saúde.

Margarida Figueira (2013) The role of Mesogenin1 in the dynamics of movement and differentiation of mesoderm progenitor cells. Faculdade de Ciências da Universidade de Lisboa. Lisbon, Portugal. Supervisor: Leonor Saúde.

Lara Carvalho (2013) Control of somite number and size in zebrafish upon reduction of progenitors. Faculdade de Ciências e Tecnologia da Universidade do Algarve, Faro, Portugal. Supervisors: Rita Fior, Leonor Saúde.



## ANA SEBASTIÃO LAB

### Major Interests / Objectives

A challenge in Neurosciences is to correct abnormal synaptic function, a commonality of most brain diseases. Interfering with endogenous processes that adjust synaptic function to the circuit needs has been proposed as a promising strategy to correct synaptic dysfunction. We aim to elucidate how the neuronal and glial components of the tripartite synapse are fine-tuned under normal and dysfunctional situations, and how it affects neuronal excitability. Tuning of neurogenesis, neuronal maturation and degeneration is also under Unit interests. We focus on endogenous modulators, namely on adenosine, endocannabinoids, neurotrophins and glycine. As disease models we have been focusing on Alzheimer's and Parkinson's disease, developmental epilepsy and amyotrophic lateral sclerosis.

### Head of Unit

Ana M Sebastião, PhD, Full Professor, Faculdade de Medicina da Universidade de Lisboa,

### Research Team

Ana Filipa Ferreira da Cunha Ribeiro	Master	PhD Student
Ana Sofia Cristovão Ferreira	PhD	Post-doctoral Investigator
Ana Sofia Temudo Duarte António	Master	PhD Student
André Jerónimo Santos	Master	PhD Student
António Artur da Paz Ferreira Pinto Duarte	Master	PhD Student
Armando Dulcídio da Silva Cruz	Master	PhD Student (started April)
Bruno Miguel Ferreira Teixeira da Silva	PhD	Post-doctoral Investigator (started May)
Catarina Reis Orcinha	Master	Technician
Cátia Alexandra Pêgas Palminha	Graduate	MSc Student (started September)
Clara Cunha Matos Patrício	Graduate	MSc Student (left August)
Cláudia Alexandra dos Santos Valente de Castro	PhD	Investigator

Daniela Cristina Melo Magalhães	Graduate	MSc Student (started September)
Diana Gabriela Ribeiro Ferreira	Master	PhD Student (left May)
Diogo Miguel Rombo	Master	PhD Student
Fabio Marques Simoes de Souza	PhD	Principal Investigator
Filipa Fiel do Carmo Glórias Ferreira	Master	Investigator
Filipe Jorge Nascimento Xavier Fernandes	Graduate	MSc Student
Francisco Melo Albuquerque Saraiva Mouro	Master	PhD Student
Gabriela Antunes	MD/PhD	Post-doctoral Investigator (started August)
Gonçalo Luis Monteiro Ramos	Graduate	MSc Student (left September)
Haíssa de Castro Abrantes	Graduate	MSc Student (started September)
Joana Fernandes Esteves Soares Coelho	PhD	Post-doctoral Investigator (left May)
João Miguel Guerreiro Covita	Graduate	MSc Student
Joaquim Alexandre Ribeiro	MD/PhD	Principal Investigator
Luísa Maria Vaqueiro Lopes	PhD	Principal Investigator (left May)
Maria Alexandra Pereira Botelho	Undergraduate	Administrative
Maria José Diógenes	PhD	Principal Investigator
Mariana Colino Oliveira	Master	PhD Student
Noémia Marisa Félix Pereira	Graduate	MSc Student
Paula Alexandra Costa Marçal Correia	PhD	Investigator
Pedro Dinis Avelar Agostinho	Graduate	MSc Student (started September)
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 Artur Paiva Loureiro Gomes	PhD	Investigator, Assistant Professor (left

		June)
Sandra Cristina Henriques Vaz	PhD	Post-doctoral Investigator
Sara Alexandra Fernandes Carvalho	Graduate	MSc Student (left May)
Sara Alves Xapelli	PhD	Post-doctoral Investigator
Vânia Luisa Neves Batalha	Master	PhD Student (left May)

### Keywords / Research Areas

Tripartite synapse mechanisms, Neuronal excitation/inhibition balance, glia-to-neuron communication, Ageing, Neurodegenerative Mechanisms, Brain dysfunctions.

### Major scientific achievements

#### 1. Neuronal plasticity:

- a) Adenosine affords endogenous regulation of ischemia-induced plasticity (Dias *et al* Neuropharmac) and may contribute to adjust the threshold for plasticity according to prior experience (Dias *et al* TINS)
- b) A2ARs control the influence of BDNF TrkB receptors upon LTD (Rodrigues *et al*). A2A/TrkB interactions require lipid rafts (Assaife-Lopes *et al* 2013), which are perturbed in ageing (Sebastião *et al* 2013).

#### 2. Astrocytes:

- a) GlyT2 are expressed in astrocytes (Aroeira *et al* 2013).
- b) Adenosine acts via a heterocomplex of adenosine receptors in astrocytes to control GABA transport (Cristóvão-Ferreira *et al* 2013)

#### 3. Neurodegenerative diseases:

- a) In ALS there are subtle dysfunctions on neuromuscular transmission that start well before appearance of overt motor symptoms (Rocha *et al* 2013).

#### 4. Cannabinoids:

- a) CB1Rs induce neuronal differentiation (Xapelli *et al* 2013) and interact with caffeine to control neuronal signaling and behavior (Sousa *et al* 2013)

### Recent Most Relevant 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: 66)

Diógenes MJ, Assaife-Lopes N, Pinto-Duarte A, Ribeiro JA, Sebastião AM (2007) Influence of age on BDNF modulation of hippocampal synaptic transmission: interplay with adenosine A2A receptors. *Hippocampus* **17**, 577-585. (Journal IF: 5.592, Citations: 40)

Diógenes, M.J., Fernandes, C.C., Sebastião, A.M., Ribeiro, J.A (2004) Activation of adenosine A2A receptor facilitates BDNF modulation of synaptic transmission in hippocampal slices. *Journal of Neuroscience* **24**, 2905-2913. (Journal IF: 6.908, Citations: 77)

Dias RB, Rombo DM, Ribeiro JA, Henley JM, Sebastião AM (2013) Adenosine: setting the stage for plasticity. *Trends in Neuroscience* **257**, 248. (Journal IF: 13.582, Citations: 0)

Sebastião AM, Ribeiro JA (2000) Fine tuning neuromodulation by adenosine. *Trends in Pharmacological Sciences (TIPS)* **21**, 341-346. (Journal IF: 9.250, Citations: 164)

### Ongoing Research Projects

2012/2015 Are Microglia a New Potential Pharmacological Target in Amyotrophic Lateral Sclerosis (ALS). Coordinator: Paula Alexandra Marçal Correia. Agency: FCT. Amount: €22000.00. €146273.000.

2011/2014 Modulação da transmissão GABAérgica no hipocampo pela adenosina. Coordinator: Ana Sebastião. Agency: FCT. Amount: €159760.00.

2010/2013 Interação entre receptores dos factores neurotróficos (TrkB) e receptores A2A da adenosina: implicações para a Esclerose Lateral Amiotrófica. Coordinator: Joaquim Alexandre Ribeiro. Agency: FCT. Amount: €111000.00.

2008/2013 Nestec - Research Agreement. Coordinator: Luísa Maria Vaqueiro Lopes. Agency: Nestec S.A.. Amount: €159.091,00

2013/2014 Modulação da toxicidade neuronal induzida pelo beta amiloide via JNK: um novo papel do ácido tauro-ursodesoxicólico. Coordinator: Rita Cruz Coelho Ramalho. Agency: FCT. Amount: €26.095,14

2013/2014 PhD in Biomedical Sciences, Specialty in Neuroscience. Coordinator: Ana M Sebastião. Agency: Cardlane Ltd. Amount: €33.044,00

### Publications in peer review Journals

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 (accepted and ePub in 2013). (Journal IF: 4.114)

Sousa VC, Ribeiro JA, Sebastião AM (2013) Caffeine and adenosine receptor modulation of cannabinoid influence upon cognitive function. *J Caffeine Research* **3**, 85-95. (Journal IF: ND)

Assaife-Lopes N, Sousa VC, Pereira DB, Ribeiro JA, Sebastião AM (2013) 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* (ePub ahead of print).

(Journal IF: 2.635)

Rocha, MC, Pousinha PA, Correia AM, Sebastião AM, Ribeiro JA (2013) Early changes of neuromuscular transmission in the SOD1(G93A) mice model of ALS start long before motor symptoms onset. *PLoS ONE*, **8**, e73846. (Journal IF: 3.730)

Cristóvão-Ferreira S, Navarro G, Brugarolas M, Pérez-Capote K, Vaz SH, Fattorini G, Conti F, Lluís C, Ribeiro JA, McCormick PJ, Casadó V, Franco R, Sebastião AM (2013) A1R-A2AR heteromers coupled to Gs and Gi/o proteins modulate GABA transport into astrocytes. *Purinergic Signalling*, **9**, 433-449. (Journal IF: 2.635)

Xapelli S, Agasse F, Sardà-Arroyo L, Bernardino L, Santos T, Ribeiro TF, Valero J, Bragança J, Schitine C, de Melo Reis RA, Sebastião AM, Malva JO (2013) Activation of Type 1 cannabinoid receptor (CB1R) promotes neurogenesis in murine subventricular zone cell cultures. *PLoS ONE*, **8**, e63529. (Journal IF: 3.730, Citations: 1)

Aroeira RI, Sebastião AM, Valente CA (2013) GlyT1 and GlyT2 in brain astrocytes: expression, distribution and function. *Brain Struct Funct* (ePub Mar 2013). (Journal IF 7.837)

Pimentel VC, Zanini D, Cardoso AM, Schmatz R, Bagatini MD, Gutierrez JM, Carvalho F, Gomes JL, Rubin M, Morsch VM, Moretto MB, Colino-Oliveira M, Sebastião AM, Schetinger MR. (2013) Hypoxia-Ischemia Alters Nucleotide and Nucleoside Catabolism and Na(+),K (+)-ATPase Activity in the Cerebral Cortex of Newborn Rats. *Neurochemical Research*, **38**, 886-894. (Journal IF 2.125)

Sebastião AM, Colino-Oliveira M, Assaife-Lopes N, Dias RB, Ribeiro JA (2013) Lipid rafts, synaptic transmission and plasticity: impact in age-related neurodegenerative diseases. *Neuropharmacology* **64**, 97-107. Journal IF : 4.114, Citations: 1)

Dias RB, Rombo DM, Ribeiro JA, Sebastião AM (2013) Ischemia-induced synaptic plasticity drives sustained expression of calcium-permeable AMPA receptors in the hippocampus. *Neuropharmacology*, **65**, 114-122. (Journal IF: 4.114, Citations: 1)

Ramalho RM, Nunes AF, Dias RB, Amaral JD, Lo AC, D'Hooge R, Sebastião AM, Rodrigues CM (2013). Tauroursodeoxycholic acid suppresses amyloid  $\beta$ -induced synaptic toxicity in vitro and in APP/PS1 mice. *Neurobiol Aging* **34**, 551-61. (Journal IF: 6.166, Citations: 1)

Batalha VL, Pego JM, Fontinha B, Costenla AR, Valadas J, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV (2013). Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *Molecular Psychiatry* **18**, 320-331. (Journal IF: 14.897, Citations: 2)

Hamilton TJ, Xapelli S, Larkum ME, Colmers WF (2013) Modulation of distal calcium electrogenesis by neuropeptide Y1 receptors inhibits neocortical long-term depression. *J Neurosci* **33**, 11184–11193. (Journal IF: 6.908)

Agasse F, Xapelli S, Coronas V, Christiansen SH, Rosa AI, Sardà-Arroyo L, Santos T, Ferreira R, Schitine C, Harnois T, Bourmeyster N, Bragança J, Bernardino L, Malva JO, Woldbye DP (2013) Galanin promotes neuronal differentiation in murine subventricular zone cell cultures. *Stem*

*Cells Dev* **22**, 1693-708. (Journal IF: 4.670)

Duarte ST, Armstrong J, Roche A, Ortez C, Pérez A, O'Callaghan Mdel M, Pereira A, Sanmartí F, Ormazábal A, Artuch R, Pineda M, García-Cazorla A (2013) Abnormal expression of cerebrospinal fluid cation chloride cotransporters in patients with Rett syndrome. *PLoS One* **8**, (7):e68851. doi: 10.1371/journal.pone.0068851 (Journal IF: 3.730)

Olafsdottir OB, Vandewalle E, Abegão Pinto L, Geirsdottir A, De Clerck E, Stalmans P, Gottfredsdottir MF, Kristjansdottir JV, Van Calster J, Zeyen T, Stefánsson E, Stalmans I (2013). Retinal oxygen metabolism in healthy subjects and glaucoma patients. *Br J Ophthalmol* doi:10.1136/bjophthalmol-2013-303162 (Journal IF: 2.725)

Ji B, Wang X, Pinto-Duarte A, Kim M, Caldwell S, Young JW, Behrens MM, Sejnowski TJ, Geyer MA, Zhou X (2013) Prolonged Ketamine Effects in Sp4 Hypomorphic Mice: Mimicking Phenotypes of Schizophrenia. *PLoS One* **8**, (6):e66327. (Journal IF: 3.730)

Wang X, Pinto-Duarte A, Sejnowski TJ, Behrens MM (2013) How Nox2-containing NADPH oxidase affects cortical circuits in the NMDA receptor antagonist model of schizophrenia. *Antioxid Redox Signal* **18**, 1444-62. doi: 10.1089/ars.2012.4907. (Journal IF: 7.189, Citations: 1)

#### Other publications International

Xapelli S, Agasse F, Ribeiro FF, Bernardino L, Schitine CS, Heimann A, Ferro ES, De Melo Reis RA, Sebastião AM, Malva JO. Hemopressin promotes oligodendrogenesis in murine subventricular zone cell cultures. *J Neurochem* **125**, (Supplement s1).

Colino-Oliveira, M.; Dias, R. B., Ribeiro, J. A and Sebastião AM (2013). Dual effects of BDNF on spontaneous GABAergic transmission in adult rat hippocampus. *J Neurochem* **125**, (Supplement s1):154.

Ribeiro, F. F., Silva, R., Fernandes, A, Brites, D, Ribeiro JA, Sebastião AM (2013). Adenosine A2A receptor: the mechanism behind axonal elongation in primary cortical cultures. *J Neurochem* **125**, (Supplement s1): 172

Sebastião AM, Cristóvão-Ferreira S, Ribeiro JA (2013). Downstream Pathways of Adenosine A key, link between Metabolism and Brain Activity, D Masino and D Boison (eds) , DOI 10.1007/978-1-4614-3903-5\_7\_1, Springer Science+Business Media New York. Adenosine.

#### Invited lectures and seminars

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, 2013.

Claudia Valente – Imaging molecules by immunofluorescence (Claudia Valente), Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2013.

Diogo Rombo - Evaluation of synaptic activity through electrophysiological recording Techniques, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2013.

Diogo Rombo - Synapse-specific modulation at the hippocampus, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2013.

Fábio Sousa - Modulation of olfactory sensory cells adaptation, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November, 2013.

Maria José Diógenes - Neurotrophic factors: key molecules for neuronal survival and plasticity, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, November, 2013.

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.

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

Sandra Vaz - Calcium signalling in astrocytes: relevance for excitability control, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2013.

Sofia Cristovão-Ferreira – GABA transport modulation: implications for excitability control, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October, 2013.

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 2013.

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

Diogenes MJ - Master in Computer Engineering, Master in Biological Engineering, Master in Electrical Engineering, Master in Biomedical Engineering” , Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Portugal, 2013.

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, 2013.

Sebastião AM. - Master in Physics, Instituto Superior Técnico, Lisbon, Portugal, 2013.

Sebastião AM – Master in Neuropsychology, Universidade Católica Portuguesa Lisboa, Lisbon, Portugal, 2013.

Dias RB - Curso Livre de Ciência, Tecnologia e Cidadania da Universidade Técnica de Lisboa, Lisbon, Portugal, 2013.

Lab members presented the following 'Neuroscience Seminars' at IMM:

Sofia Cristóvão-Ferreira "Role of GABA transporters on absence epilepsy seizures - project planning".

Tiago Rodrigues, "Adenosine A2A Receptors (A2ARs): novel upstream regulators of brain-derived neurotrophic factor (BDNF)-mediated attenuation of hippocampal long-term depression (LTD)", IMM, Lisbon, Portugal, 2013.

Diogo Rombo, "Hippocampal neuronal inhibition under control: a role for adenosine receptors", IMM, Lisbon, Portugal, 2013.

João Covita, "The effect of BDNF on synaptic and extrasynaptic NMDA currents upon aging", (project planning) IMM, Lisbon, Portugal, 2013.

Noémia Pereira, "Glycinergic transmission as a potential therapeutic target for epilepsy" (project planning) IMM, Lisbon, Portugal, 2013.

Sofia Duarte, Synaptic dysfunction in early epileptic encephalopathies, IMM, Lisbon, Portugal, 2013.

Sara Xapelli, "Hemopressin as a regulator of oligodendrogenesis in subventricular zone stem/progenitor cell cultures", IMM, Lisbon, Portugal, 2013.

Raquel Dias, "Erythropoietin: setting the tone for homeostatic plasticity?", IMM, Lisbon, Portugal, 2013.

Rita Aroeira, "Glycine transporters, GlyT1 and GlyT2, in brain astrocytes – recent insights" IMM, Lisbon, Portugal, 2013.

Sandra Vaz, BDNF-mediated enhanced LTP is modulated by astrocytes" IMM, Lisbon, Portugal, 2013.

Fábio Simões, "Mechanisms of regulation of olfactory adaptation by intracellular signaling cascades" IMM, Lisbon, Portugal, 2013.

Filipe Nascimento, "Neuromuscular transmission modulation by A1 and A2A adenosine receptors in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis" IMM, Lisbon, Portugal, 2013.

André Santos, "Amyloid- $\beta$  peptide dysregulates TrkB receptors and BDNF function by a calpain-dependent mechanism" IMM, Lisbon, Portugal, 2013.

Mariana Oliveira, "Synaptic modulation by adenosine in an aged-dependent epilepsy model" IMM, Lisbon, Portugal, 2013.



João Covita, “BDNF signaling upon aging: effect on NMDA receptor and glutamate transporter function” IMM, Lisbon, Portugal, 2013.

Rita Ramalho, “Deciphering the mechanisms underlying the lost of BDNF neuroprotection in Alzheimer’s disease”, IMM, Lisbon, Portugal, 2013.

Ana Filipa Ribeiro, “Deciphering the role of adenosine A2A receptor during neuronal development” IMM, Lisbon, Portugal, 2013.

Filipa Ferreira “Unravelling the role of BDNF on endocannabinoids-modulation of neurogenesis” IMM, Lisbon, Portugal, 2013.

Armado Cruz, "The cross-talk mechanism between adenosine A1 and cannabinoid CB1 receptors in the hippocampal synaptic plasticity", IMM, Lisbon, Portugal, 2013 (project planning)

Daniela Magalhães, “Glycinergic transmission molecular markers in vitro epilepsy model“,IMM, Lisbon, Portugal, 2013 (project planning)

### **Communications in International Conferences**

Aroeira RI, Sebastião AM and Valente CA (2013) “BDNF modulation of GlyT2-mediated glycine uptake in brain nerve terminals”, EMBO Young Scientists’ Forum, Lisbon, Portugal, July 15-16, 2013 (Poster presentation)

Aroeira RI, Sebastião AM and Valente CA (2013) “Glycine uptake in brain nerve terminals is decreased by BDNF through a reduction in GlyT2 membrane insertion”, Molecular Biology in Portugal and EMBL (and EMBL Alumni), Lisbon, Portugal, July 18, 2013 (Poster presentation)

Colino-Oliveira, M., Dias, R.B., Ribeiro, A.J., Sebastião, A.M., Dual effects of BDNF on spontaneous GABAergic transmission in the adult rat hippocampus, ISN-ASN meeting, Cancun, México, April 20-24, 2013 (Poster presentation)

Cortes-Saladelafont E, S Duarte, M Molero, M Casado, C Sierra, MO Callaghan-Gordo, X Sanmarti-Vilaplana, C Fons, V Gonzalez-Alvarez, B Perez-Duenas, P Poo, F Ramos, R Artuch, A Garcia-Cazorla. CSF vitamin B6 levels and response to pyridoxal 5-phosphate in diverse epileptic encephalopathies, 12th International Congress of Inborn Errors of Metabolism, Barcelona, Spain, September 3rd-6th, 2013 (Poster presentation)

Ferreira F, Ribeiro FF, Sebastião AM, Xapelli S. BDNF modulates type 1 cannabinoid receptor (CB1R)-stimulation of neurogenesis in murine dentate gyrus stem/progenitor cell cultures - 5th Conference on Advances in molecular mechanisms underlying neurological disorders, Bath, UK, June 23-26, 2013 (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 Amyloid- $\beta$  peptide dysregulates TrkB receptors

and BDNF function by a calpain-dependent mechanism, Molecular Biology in Portugal and EMBL (and EMBL Alumni), Lisbon, Portugal, 2013 (Poster presentation)

Ribeiro FF, Rui Silva, Adelaide Fernandes, Dora Brites, Joaquim A. Ribeiro, Ana M. Sebastião, Adenosine A2A receptor: the mechanism behind axonal elongation in primary cortical cultures, 24th Biennial ISN Meeting, Cancun, Mexico, April 20th – 24<sup>th</sup>, 2013. (Poster presentation)

Ribeiro FF, Telma Santos, Mónica Sousa, Ana M. Sebastião, Adenosine A2A receptor activation promotes microtubule dynamics, EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16th, 2013. (Poster presentation)

Vaz SH, Joaquim P. Jacob, Joaquim A. Ribeiro, and Ana M. Sebastião, P2Y1 receptor inhibits GABA transport through a calcium signalling-dependent mechanism in rat cortical astrocytes, 5th Conference on Advances in Molecular Mechanisms Underlying Neurological Disorders, Bath, UK, June 23-26, 2013 (Poster presentation)

Xapelli S, Agasse F, Ribeiro FF, Bernardino L, Schitine CS, Heimann A, Ferro ES, De Melo Reis RA, Sebastião AM, Malva JO. Induction of oligodendrogenesis by hemopressin in subventricular zone neural stem cell cultures - ISN/ FENS School 2013, Kolymbari, Crete (Greece), September 24-28, 2013. (Poster presentation)

Xapelli S, Agasse F, Ribeiro FF, Bernardino L, Schitine CS, Heimann A, Ferro ES, De Melo Reis RA, Sebastião AM, Malva JO. Hemopressin as a regulator of oligodendrogenesis in neural stem cell cultures from the subventricular zone – EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

### **Communications in National Conferences**

Aroeira RI, Ribeiro JA, Sebastião AM and Valente CA, (2013) “BDNF decreases glycine uptake in brain synaptosomes by reducing GlyT2 membrane insertion”. XIII Meeting of the Portuguese Society for Neurosciences, Luso, Portugal, May 30-June 1, 2013 (Oral presentation)

Colino-Oliveira, M., Dias, R.B., Ribeiro, A.J., Sebastião, A.M., Differential BDNF-mediated modulation of GABAergic spontaneous activity in the adult hippocampus. XLIII Reunião Anual da Sociedade Portuguesa de Farmacologia, Porto, Portugal, February 7, 2013 ( Oral Presentation)

Colino-Oliveira, M., Diogenes, M.J., Detlev, B., Sebastião, A.M., Synaptic modulation by adenosine on an age-dependent epilepsy model. VII IMM/CAML PhD Meeting, Lisbon, Portugal, December 6, 2013 (Oral Presentation)

Duarte ST, Cláudia Gaspar, Angels Garcia-Cazorla Estudo Molecular das alterações sinápticas na Síndrome de Ohtahara. 25º Encontro Nacional de Epileptologia, Porto, Portugal, March 8-9, 2013 (Oral presentation)

Duarte ST. Update on ataxias and SPG. Reunião da Sociedade Portuguesa de Doenças do Movimento Vimeiro, Portugal March 22-24, 2013 (Oral presentation – invited)

Fernandes I, Fernandes D, Pereira N, Sebastião AM and Valente CA (2013). Expression changes in GABAAR receptor subunits in a model of epileptiform activity in organotypic hippocampal slice cultures. 8th YES Meeting, Porto, Portugal, September 19-22, 2013 (Oral presentation)

Nascimento F., Correia A., Gomes R., Pousinha P.A., Sebastião A.M., Ribeiro J.A. Neuromuscular transmission modulation by adenosine A2A receptors in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis. XLIII Anual Reunion from the Portuguese Pharmacology Society, Porto, Portugal, February 6-8, 2013 (Oral presentation)

Ribeiro FF, Filipa Ferreira, Ana M. Sebastião, Sara Xapelli, Exploring the modulatory role of adenosine A2A receptor upon brain-derived neurotrophic factor (BDNF)-induced neurogenesis. 43rd Annual Meeting of the Portuguese Pharmacological Society, Porto, Portugal, February 6-8, 2013. (Oral presentation)

Ribeiro FF, Rui Silva, Dora Brites, Joaquim A. Ribeiro, Ana M. Sebastião, Are axonal elongation and dendritic branching induced by adenosine A2A receptor activation dependent on the endogenous BDNF?. 43rd Annual Meeting of the Portuguese Pharmacological Society, Porto, Portugal, February 6-8, 2013 (Oral presentation)

Rombo DM, Kathryn Newton, Karri Lamsa, Ana M. Sebastião, Adenosine A2A receptors mediate hippocampal network disinhibition specifically through parvalbumin expressing interneurons. XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal, May 30-31 and June 1, 2013 (Oral Presentation)

Rombo DM, Kathryn Newton, Karri Lamsa, Ana M. Sebastião, Disinhibitory action of A2A receptors through parvalbumin inhibitory synapses. XLIII Reunião Anual da Sociedade Portuguesa de Farmacologia, XXXI Reunião de Farmacologia Clínica e XII Reunião de Toxicologia, Instituto de Ciência Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal, February 6-8, 2013 (Oral Presentation)

Vaz SH BDNF-mediated enhancement of LTP is modulated by astrocytes. Pizza Seminars, Instituto de Medicina Molecular, Lisbon, Portugal, April 2, 2013 (Oral presentation)

Xapelli S, Agasse F, Ribeiro FF, Bernardino L, Schitine CS, Heimann A., Ferro ES, De Melo Reis RA, Sebastião AM, Malva JO Hemopressin stimulates oligodendrogenesis in neural stem cell cultures from the subventricular zone. XIII Annual meeting of The Portuguese Society for Neuroscience, Luso, Portugal, May 30, 31 and June 1, 2013 (Oral presentation)

Dias RB, Rombo DM, McGarvey J, Henley JM, Sebastião AM (2013) Erythropoietin modulates activity deprivation-induced regulation of synaptic transmission: a role for a hormone in homeostatic plasticity?. XIII Reunião da Sociedade Portuguesa de Neurociências, Luso, Portugal, May 30 and June 1, 2013 (Poster Presentation)

Mendes-Pedro D, Duarte-Samartinho M, Mendes-Pedro D, Ribeiro FF, Ferreira FF, Sebastião AM, Xapelli S. Modulatory role of Adenosine A2A receptors on brain-derived neurotrophic factor (BDNF)-induced neurogenesis in murine dentate gyrus stem/progenitor cell cultures. XIII Annual meeting of The Portuguese Society for Neuroscience, Luso, Portugal, May 30-31 and June 1, 2013 (Poster presentation)

Mouro F, Raquel Baptista Dias, Diogo Miguel Rombo, Ana Maria Sebastião. Modulation of NMDA receptor activity through A2A receptors in the hippocampus. Sociedade Portuguesa das Neurociências, Luso, Coimbra, Portugal, May 2013 (Poster presentation)

Ribeiro FF, Telma Santos, Mónica Sousa, Ana M. Sebastião, Adenosine A2A receptor activation promotes microtubule dynamics. XIII Meeting of the Portuguese Neuroscience Society, Lisbon, Portugal, May 30, 31 and June 1, 2013 (Poster presentation)

#### Other communications

Ribeiro FF, Mónica Sousa, Ana M. Sebastião, Adenosine A2A receptors and the elongation of the axon, Nerve Regeneration Group Lab Meeting, IBMC, Porto, Portugal, April 30, 31, 2013 (Oral presentation)

Aroeira RI, Ribeiro JA, Sebastião AM and Valente CA, (2013) “Glycine-mediated neurotransmission in rat brain – recent insights”. VII IMM PhD Students Meeting, Lisbon, Portugal, December 5-6, 2013 (Oral presentation)

Ribeiro FF, Ana M. Sebastião, The adenosine A2A receptor and microtubule dynamics during axon elongation. VII IMM PhD Students Meeting, Lisbon, Portugal, December 6, 2013 (Oral presentation)

Rombo DM, Kathryn Newton, Karri Lamsa, Ana M. Sebastião, Hippocampal network disinhibition of parvalbumin expressing interneurons by adenosine A2A receptors. VII IMM PhD Students Meeting, Lisbon, Portugal, December 5-6, 2013 (Oral presentation)

Duarte ST, Angels Garcia-Cazorla, Domingos Henrique, Ana Sebastião. Neuronal changes in neurodevelopmental disorders with epilepsy and autism. VII IMM PhD Students Meeting, Lisbon, Portugal, December 5-6, 2013 (Oral presentation)

Mouro F, Raquel Baptista Dias, Diogo Miguel Rombo, Ana Maria Sebastião. Adenosine A2A receptor activation facilitates synaptic NMDA receptor activity in the hippocampus. VII IMM PhD Students Meeting, Lisbon, Portugal, December 5-6, 2013 (Oral presentation)

Duarte ST, Angels Garcia-Cazorla, Joaquim Sampaio Cabral, Domingos Henrique, Ana Sebastião. From clinical to synaptic phenotype in neurodevelopmental disorders with epilepsy and autism. Champalimaud Neuroscience Program Retreat, Beja, Portugal, June 18-20, 2013 (Poster presentation)

### **Organisation of Conferences**

Sebastião AM – Neuroscience Symposium at the European Biophysical Congress, Lisbon, Portugal, 2013.

Sandra H. Vaz, Sara Xapelli, Inês Sousa and Cláudia Gaspar. The 1st IMM Post-doc day – Postdoctoral Association, IMM, Lisbon, Portugal, October 17th, 2013.

### Internationalisation

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.

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).

Eero Castren (Helsinki) and David Blum (Lille), 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).

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

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 under preparation).

Rafael Franco, (Pamplona) Carmen Lluís (Barcelona) and Francisco Conti (Ancona, Italy) on A1/A2A receptor heterodimers in astrocytes to control GABA transport (one paper was 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).

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

### Prizes, honours and awards

I Fernandes, D Fernandes, N Pereira, AM Sebastião and CA Valente (2013). Expression changes in GABAAR receptor subunits in a model of epileptiform activity in organotypic hippocampal slice cultures. 8th YES Meeting, September 19-22, Porto, Portugal. Best presentation in Neurosciences. Prize: €250

Jerónimo Santos A – Best oral presentation, VII PhD Students Meeting CAML, Lisbon, Portugal, December 5-6, 2013.

Duarte ST - Best Poster presentation. VII PhD Students Meeting CAML, Lisbon, Portugal,

December 5-6, 2013.

### **Advanced teaching**

Ribeiro FF, Mónica Sousa, Ana M. Sebastião, Adenosine A2A receptors and the elongation of the axon, Nerve Regeneration Group Lab Meeting, IBMC, Porto, Portugal, April 30, 31, 2013 (Oral presentation).

AM Sebastião – Member of the Scientific Board of the Ms/PhD in Neurosciences, Faculdade de Medicina da Universidade de Lisboa and of the Ms/PhD Programme in Cognitive Sciences, Universidade de Lisboa, Lisbon, Portugal, 2013.

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, Lisbon, Portugal, 2013.

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, Lisbon, Portugal, 2013.

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 Module on Neuroethics, Ms/PhD in Neurosciences.

### Advanced training and Post-graduate Supervision of non-Lab members

Dias RB - Supervision of Maria do Carmo Pinto Basto in her final thesis entitled “O cérebro e a reabilitação neuropsicológica” developed as part of Curso Livre de Ciência, Tecnologia e Cidadania, Universidade Técnica de Lisboa, Lisbon, Portugal, 2013.

Dias RB - Advanced training of the GAPIC student Afonso José Félix de Oliveira, as co-supervisor with Professor Ana Maria Sebastião, Lisbon, Portugal, 2013.

Ana M Sebastião, Maria José Diógenes, Claudia Valente, Sara Xapelli, Sandra Vaz and Sofia Cristóvão Ferreira: Advanced training of the following GAPIC students:

Carla Filipa Guerreiro, Carla Nunes Ferreira, Denise Fernandes, Diogo Filipe Andrade Guimarães, Diogo Mendes Pedro, Gabriel da Fonseca Matos, Inês Cristina Fernandes, Marta Samartinho, Raquel Lopes Brás, Sara Parreira, Sofia Lérias, Tiago Rodrigues.

Lab Members invited the following speakers to give lectures at IMM, attended by Master and PhD Students:

Asla Pitkänen (Kuopio Finland) – Onset of epilepsy after a traumatic brain injury: molecular and cellular mechanisms, IMM, Lisbon, Portugal, 2013.

Jeremy Henley (Bristol) - 'Plasticity, death and SUMOylation, IMM, Lisbon, Portugal, 2013.

Karri Lamsa, (Oxford) Cell type specific plasticity rules in hippocampal interneurons”, IMM, Lisbon, Portugal, 2013.

Paula Pousinha (Valbonne France) Role of APP C-terminal fragment, AICD, in hippocampal function”, IMM, Lisbon, Portugal, 2013.

Mariana Rocha (Newcastle) Mitochondrial dysfunction in ageing skeletal muscle, IMM, Lisbon, Portugal, 2013.

Patrícia Coelho de Velasco (Rio de Janeiro) Impact of omega-3 fatty acids nutritional restriction on the development of the rodent visual system, IMM, Lisbon, Portugal, 2013.

### Science and society

Members of the Lab were involved in the activities regarding the Brain Awareness Week (BAW) - 2013, which included lectures and hands-on activities with the goal of increasing public awareness of the progress and benefits of brain research. These activities were a collaboration between IMM and “Ciência Viva - Pavilhão do Conhecimento” included in “Clube C60+”, “O Cérebro e a Memória” and “Deste-me um nome de rua – O Cérebro”.

Mouro F - Iniciativa Braço Direito – Semana Global do Empreendedorismo 2013, Novembro. Iniciativa suportada pela empresa Junior Achievement Portugal

Aroeira R was invited to participate in the television program “Sociedade Civil”, under the topic “Segredos do Cérebro”.

Colino-Oliveira M - session about the brain at Colégio Pedro Arrupe to students from the 10th grade.

Diogenes MJ - Session at Escola Casa Santa Ana, primary school (7 years old students) under the topic “Vamos olhar para o cérebro”.

Sandra H Vaz talk at St. Julian Secondary School on the brain, as part of the brain awareness week.

Sebastião AM – talk on Drugs and the Brain to students at the Secondary School ‘Escola Secundária Sebastião e Silva.

Simoes de Souza, FM and Mouro F gave a speech about the brain in the highschool Dom Manuel Martins, Setubal, Portugal, as part of the brain awareness week organized by the Portuguese Society for Neurosciences.

Valente C- two sessions untitled “Nós e o cérebro” to children of the 4th year of Colégio Manuel Bernardes.

Xapelli S. Talk during the Brain Awareness Week to students of “Colégio Laranja e Meia” (Lisboa).

Xapelli S. Talk during the Brain Awareness Week to students of “Escola Secundária de Carcavelos”, Cascais.

#### **Msc theses completed**

Filipe Jorge do Nascimento Xavier Fernandes (2013) Neuromuscular transmission modulation by A2A adenosine receptors in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis. Universidade de Lisboa. Supervisor: Joaquim Alexandre Ribeiro.

João Covita (2013) Effect of BDNF on Synaptic and extrasynaptic NMDA currents. Universidade de Lisboa. Supervisors: Maria José Diógenes, Ana M Sebastião.

António Caetano (2013) Unraveling the effect of different Abeta species upon hippocampal synaptic plasticity and the neuroprotective role of BDNF. Universidade de Lisboa. Supervisor: 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, Faculdade de Medicina da Universidade de Lisboa.

**Research Team**

Ana de Oliveira Rodrigues Amorim	Graduate	MSc Student (started August)
Ana Maria de Amarante Pamplona Dias dos Santos	PhD	Principal Investigator
Anita Raquel Quintal Gomes	PhD	Investigator
Artur Manuel Rodrigues Nixon Martins	Graduate	MSc Student
Daniel Vargas Correia	PhD	Post-doctoral Investigator
Eva Sofia Alves Rolo	Master	Investigator (left May)
Francisco Landeck Moreira Franco Caiado	PhD	Post-doctoral Investigator
Haakan Rolf Norell	PhD	Principal Investigator
Ingrid Cecilia Brok	Graduate	MSc Student (left February)
Joana Luísa de Barros Martins	Graduate	MSc Student (started August)
Julie Cecile Caroline Ribot	PhD	Principal Investigator
Karine Serre	PhD	Post-doctoral Investigator

Maria Margarida Sousa Gonçalves Rei	Graduate	PhD Student
Michael Hamm	Graduate	MSc Student (started April) (left July)
Miguel Muñoz Ruiz	Master	PhD Student (started September)
Natacha Maria Gonçalves Silva Sousa	Master	Lab manager
Nina Alexandra Schmolka	Master	PhD Student
Rita Maria de Almeida Neres	PhD	Post-doctoral Investigator
Sérgio Tiago de Freitas Ribeiro	Master	PhD Student
Sofia Mensurado Santos	Graduate	Investigator (started July)
Telma Sofia Martins Lança	Graduate	PhD Student (left February)
Tomás Laia McGuire	Graduate	MSc Student

#### Keywords / Research Areas

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

#### Major scientific achievements

Published 10 papers in peer-reviewed international journals, including in Nature Immunology (IF 26.2) and Journal of Experimental Medicine (IF 13.2).

Were awarded 2 Exploratory Project Grants from Fundação para a Ciência e Tecnologia (PIs: Haakan Norell e Julie C. Ribot).

Had a total of 21 communications in international conferences, of which four as invited speaker, including in the most prestigious International Congress of Immunology (B. Silva-Santos).  
Telma Lança successfully defended her PhD thesis with distinction and honours.

#### Recent Most Relevant Publications

Correia DV, Fogli M, Hudspeth K, da Silva MG, Mavilio D and Silva-Santos B. (2011) Differentiation of human peripheral blood Vdelta1+ T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells. *Blood* . **118**, 992-1001. (Journal IF: 10.555, 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 (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**, 715. (Journal IF: 13.216, Citations: 4)

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 gd T-cell cytotoxicity. *Blood*. **115**, 2407-11. (Journal IF: 10.555, Citations: 24)

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-g- and IL-17-producing gd T cell subsets. *Nature Immunology*. **10**, 427-36. (Journal IF: 26.218, Citations: 124)

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 gd T cell subsets. *Nature Immunology*. **14**, 1093. (Journal IF: 26.199, Citations: 0)

### Ongoing Research Projects

2010/2013 Relevance of Cholesterol - rich diet on protection from experimental cerebral malaria. Coordinator: Ana Maria de Amarante Pamplona Dias dos Santos. Agency: FCT. Amount: €148.246,00

2010/2015 Differentiation of pro-inflammatory T cell subsets in vivo. Coordinator: Bruno Silva Santos. Agency: FP7. Amount: €1.500.000,00.

2011/2013 Epigenetic regulation of T lymphocyte differentiation in vivo. Coordinator: Bruno Silva Santos. Agency: PRIV-UE. Amount: €45.000,00

2013/2014 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: FCT. Amount: €50.000,00

### Publications in peer review Journals

Serre K, Silva-Santos B. 2013. Molecular Mechanisms of Differentiation of Murine Pro-Inflammatory gd T Cell Subsets. *Front Immunol*. **4**, 431. (Journal IF: na, Citations: 0)

Norell H, Moretta A, Silva-Santos B, Moretta L. 2013. At the Bench: Preclinical rationale for exploiting NK cells and gd T lymphocytes for the treatment of high-risk leukemias. *J Leukoc Biol*. **94**(6):1123-39. (Journal IF: 4.568, Citations: 1)

Prinz I, Silva-Santos B, Pennington DJ. 2013. Functional development of gd T cells. *Eur J Immunol*. **43**, (8):1988-94. Review. (Journal IF: 4.970, Citations: 0)

Lança T, Silva-Santos B. 2013. Recruitment of gd T lymphocytes to tumors: A new role for the pleiotropic chemokine CCL2. *Oncoimmunology*. **2**, (8):e25461. (Journal IF: na, Citations: 0)

Lança T, Costa MF, Gonçalves-Sousa N, Rei M, Grosso AR, Penido C, Silva-Santos B. 2013. Protective role of the inflammatory CCR2/CCL2 chemokine pathway through recruitment of type 1 cytotoxic gd T lymphocytes to tumor beds. *J Immunol*. **190**, (12):6673-80. (Journal IF: 5.520, Citations: 1)

Ribot JC, Silva-Santos B. 2013. Differentiation and activation of gd T Lymphocytes: Focus on CD27 and CD28 costimulatory receptors. *Adv Exp Med Biol*. **785**, 95-105. Review. (Journal IF: 1.825, Citations: 0)

Hudspeth K, Silva-Santos B, Mavilio D. 2013. Natural cytotoxicity receptors: broader expression patterns and functions in innate and adaptive immune cells. *Front Immunol*. **4**, 69. (Journal IF: na, Citations: 6)

Correia DV, Lopes A, Silva-Santos B. 2013. Tumor cell recognition by gd T lymphocytes: T-cell receptor vs. NK-cell receptors. *Oncoimmunology*. **2**, (1):e22892. (Journal IF: na, Citations: 1)

#### Invited lectures and seminars

Serre K., Schmolka N., Ribot J., Gomes A. and Silva-Santos B. Regulation of IL-17 and IFN- $\gamma$  expression in gd T cells. "16e Colloque Cytokines et Chimioquines du Croisic (CCCC16), Croisic, France, May 27-29, 2013 (Invited Oral Presentation)

Caiado F. Quantitative analysis of clonal evolution in relapsing Acute Myeloid Leukemia. Clinical research seminar at IPO-Lisboa. Lisbon, Portugal, June 26, 2013 (Oral Presentation)

Caiado F. Driving relapse of Acute Myeloid Leukemia: preprogrammed populations versus stochastic events. Lecture in the research seminar series at IPO-Lisboa. Lisbon, Portugal, December 18 2013 (Oral Presentation)

B. Silva-Santos. Molecular determinants of tumor cell recognition by gd T lymphocytes. Instituto de Tecnologia Química e Biológica, Oeiras, Portugal, January 17, 2013.

B. Silva-Santos. Molecular mechanisms of differentiation of effector and regulatory T cells. Department of Immunology, University of Toronto, Canada, January 24, 2013.

B. Silva-Santos. T cells in cancer and autoimmunity. Harvard Medical School-Portugal Symposium on Immunomedicine. University of Coimbra, Coimbra, Portugal, April 13, 2013.

B. Silva-Santos. Differentiation and activation of anti-tumor human gd T cells. University of Bilbao, Bilbao, Spain, June 18, 2013.

B. Silva-Santos. Imunoterapia do Melanoma. 1º Congresso Nacional de Melanoma, Lisbon, Portugal, June 29, 2013.

B. Silva-Santos. Molecular mechanisms of differentiation of gd T lymphocytes. 15th International Congress of Immunology, Milan, Italy, August 22-27, 2013.

B. Silva-Santos. Stress-inducible proteins in cancer immune surveillance. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal, September 20, 2013.

B. Silva-Santos. Activation of gd T cells for targeting of human tumours. Symposium of the Tumour Infiltrating Myeloid Cells Consortium, London, UK, October 7, 2013.

B. Silva-Santos. Molecular mechanisms of differentiation of immunoregulatory T cell subsets. Annual Meeting of the French Society of Immunology, Paris, France, November 4-7, 2013.

B. Silva-Santos. Oncoimunologia e imunoterapia do cancro. II Forum de Oncologia José de Mello Saúde, Fundação Doutor António Cupertino de Miranda, Porto, Portugal, November 15, 2013.

### Communications in International Conferences

Ribot J.C., Coquet J.M., Middendorp S., van der Horst G., Xiao Y., Neves J.F., Pennington D.J., Jacobs H.B., Borst J. and Silva-Santos B. Epithelial and dendritic cells in the thymic medulla promote CD4+Foxp3+ regulatory T cell development via the CD27/CD70 pathway. 2nd World Immunology Online Conference (Target Meeting). March 27-29, 2013 (Oral Presentation)

Ribot J.C., Ribeiro T.R, Correia D.V, Sousa A.E, and Silva-Santos B. Human gd thymocytes are functionally immature and differentiate into cytotoxic type 1 effector T cells upon IL-2/ IL-15 signaling. EMBO Young Scientists's Forum. Lisbon, Portugal, July 27-29, 2013 (Poster Presentation)

Ribot J.C. Molecular determinants of thymocytes differentiation. SPI Workshop Thymus @ Porto II. Porto, Portugal, December 19, 2013 (Oral Presentation)

Serre K., Schmolka N., Grosso A., Rei M., Pennington D., Gomes A. and Silva-Santos B. In vivo molecular signatures of stable versus plastic gamma delta T cell subsets." Congrès Annuel de la Société Française d'Immunologie (SFI), France, Paris, November 27-29, 2013 (Oral presentation)

Schmolka N., Gomes A.Q., and Silva-Santos B. MicroRNA-146a controls proliferation and differentiation of pro-inflammatory gd T lymphocytes. 8th Microsymposium on Small RNAs, Vienna, Austria, May 27-29 2013 (Poster presentation)

Schmolka N., Gomes A.Q., and Silva-Santos B. MicroRNA-146a controls proliferation and differentiation of pro-inflammatory gd T lymphocytes. EMBO young scientists' forum, Lisbon, Portugal, July 15-16, 2013 (Poster presentation)

Rei M., Lança T., Thompson R., Balkwill F., Kulbe H., Silva-Santos B. and Pennington D.J. Major contribution of gd T cells to IL-17A production and ovarian cancer cell growth in vivo. EMBO Young Investigator's Forum. Lisbon, Portugal, July 15-16 2013 (Poster presentation)

Rei M., Lança T., Thompson R., Balkwill F., Kulbe H., Silva-Santos B. and Pennington D.J. Major contribution of gd T cells to IL-17A production and ovarian cancer cell growth in vivo. 15th International Congress of Immunology. Milan, Italy, August 22-27, 2013 (Oral presentation)

Rei M., Lança T., Thompson R., Balkwill F., Kulbe H., Silva-Santos B. and Pennington D.J. Major contribution of ?? T cells to IL-17A production and ovarian cancer cell growth in vivo. British Society for Immunology Congress 2013. Liverpool, UK, December 2-5, 2013 (Poster presentation)

Caiado F., Carvalho T., Gomes da Silva M., Schumacher T., Silva-Santos B., Norell H. Quantitative analysis of clonal evolution and characterization of escape variants in relapsing acute myeloid leukemia. 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, 18-20 September 2013 (Poster & Oral Communication - Best Poster Award)

Schmolka N, Gomes A.Q., and Silva-Santos B. MicroRNA-146a controls proliferation and differentiation of pro-inflammatory gamma-delta T lymphocytes. EMBO/EMBL Symposium: The Non-Coding Genome. Heidelberg, Germany, October 9-13, 2013 (Poster presentation)

Lança T., Costa M.F., Gonçalves-Sousa N., Penido C., and Silva-Santos B. An unanticipated protective role for the CCR2/CCL2 pathway through recruitment of gd tumor-infiltrating lymphocytes. Keystone Symposium on Cancer Immunology and Immunotherapy, Vancouver, Canada, January 28-31, 2013 (Poster presentation)

Schmolka N., Serre K., Grosso A.R., Rei M., Pennington D.J., Gomes A.Q., and Silva-Santos B. Thymic differentiation and peripheral plasticity of IL-17-producing gd T-cells. VII World Immune Regulation Meeting, Davos, Switzerland, March 13-16, 2013 (Poster presentation)

### **Communications in National Conferences**

Schmolka N, Gomes A.Q., and Silva-Santos B. MicroRNAs regulate interleukin-17 and interferon- $\gamma$  expression during T cell development and differentiation. XXXIX Annual Meeting of the Portuguese Society of Immunology (SPI), Coimbra, Portugal, November 13-15, 2013. (Oral Presentation)

Neres R.\*, Ribot J.C.\*, Rolo E., Zuzarte-Luis V., Mota M.M., Silva-Santos B. and Pamplona A. Hepatic gd T cells producing IL-17A and IFN- $\gamma$  are critical for the development of experimental cerebral malaria upon Plasmodium sporozoite infection. XXXIX Annual Meeting of the Portuguese Society of Immunology (SPI), Coimbra, Portugal, November 25-27, 2013. (\*equal contribution) (Oral presentation)

Serre K., Schmolka N., Grosso A., Rei M., Pennington D., Gomes A. and Silva-Santos B. In vivo molecular signatures of stable versus plastic gamma delta T cell subsets. XXXIX Annual Meeting of the Portuguese Society of Immunology (SPI), Coimbra, Portugal, November 13-15, 2013. (Oral presentation)

### **Organisation of Conferences**

B. Silva-Santos co-organized the Cancer immunotherapy workshop, Encontros de Primavera em Oncologia, Hotel Évora, Évora, Portugal, April 18, 2013.

B. Silva-Santos co-organized the Young Investigator Forum of the European Molecular Biology Organization (EMBO) Young Investigator Programme, Instituto de Medicina Molecular, Lisbon, Portugal, July 15-17, 2013.

### **Internationalisation**

Collaborative work with Drs. Daniel J. Pennington (Blizard Institute, Queen Mary College, London, UK), Adrian Hayday (Cancer Research UK, London, UK), Ton Schumacher and Jannie Borst (The Netherlands Cancer Institute, Amsterdam, The Netherlands), Domenico Mavilio (Istituto Clinico Humanitas, Milan, Italy) and Carmen Penido, Instituto Oswaldo Cruz, Rio de Janeiro, Brazil.

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

Best Poster Award - Caiado F., Carvalho T., Gomes da Silva M., Schumacher T., Silva-Santos B., Norell H. Quantitative analysis of clonal evolution and characterization of escape variants in relapsing acute myeloid leukemia. 3rd Global Cancer Genomics Consortium Symposium. Lisbon, Portugal, September 18-20, 2013.

SPI travel Award to Karine Serre and Margarida Rei.

### **Advanced teaching**

Serre, K. Challenges in T cell differentiation. Nanocourse “Challenges in Immunology” within the PhD Programme of Centro Académico de Medicina de Lisboa, IMM, Lisbon, Portugal, June 3, 2013.

B. Silva-Santos. Differentiation and function of gd T cells. GABBA PhD Program course, Instituto de Biologia Molecular e Celular, Universidade do Porto, Porto, Portugal, February 8, 2013.

B. Silva-Santos. Diferenciação de linfócitos T e sua aplicação em imunoterapia do cancro. Jornadas de Tecnologia: Bio&Chemistry Today! Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Monte de Caparica, Portugal, February 22, 2013.

B. Silva-Santos. Diferenciação e respostas anti-tumorais de linfócitos T. Biochemistry Sessions. Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, March 6, 2013.

B. Silva-Santos. T lymphocytes for cancer immunotherapy. 1st Research Meeting, Universidade de Coimbra, Coimbra, Portugal, April 21, 2013.

B. Silva-Santos. T cells in inflammation and autoimmunity. PhD Program course, Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisbon, Portugal, May 9, 2013.

B. Silva-Santos co-organized and lectured in the course “Oncoimmunology”, MSc Program of Centro Académico de Medicina de Lisboa, Lisbon, Portugal, May 21-24, 2013.

B. Silva-Santos organized and lectured in the course “Challenges in Immunology”, PhD Program of Centro Académico de Medicina de Lisboa, Lisbon, Portugal, June 3-5, 2013.

B. Silva-Santos. How to start your own group. Post-doctoral training course of the European Calcified Tissue Society, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, May 17, 2013.

### **Science and society**

B. Silva-Santos participated in a documentary for “Maratona da Saúde”, Rádio e Televisão de Portugal, November 11, 2013.

### **PhD theses completed**

Telma Lança (2013) gd T cell responses to tumours: recruitment, recognition and functions. Faculdade de Medicina da Universidade de Lisboa Supervisor: B. Silva-Santos



**PEDRO SIMAS LAB****Major Interests / Objectives**

We utilize murine herpesvirus 4, which causes persistent infection in laboratory mice. We have identified two viral proteins critical for the virus life cycle. M2 that functions as an adaptor protein that assembles a signalosome with cellular proteins involved in the activation and differentiation of B-cells. The other, mLANA, secures viral episome persistence by tethering the viral genomes to mitotic chromosomes to segregate viral DNA to daughter nuclei. mLANA also regulates transcription and cell growth through E3 ubiquitin-ligase activity. The objective is that our work will enable future strategies to disrupt LANA function and control disease associated with persistent infection by herpes viruses.

**Head of Unit**

João Pedro Monteiro e Louro Machado de Simas, PhD.

**Research Team**

Cristina Sofia Godinho da Silva	No degree	Investigator
Diana Marisa Pinto Freire Fontinha	Master	PhD Student
Inês Marques Basto	Graduate	MSc Student (started July)
Lénia Marisa Pereira Rodrigues	PhD	Post-doctoral Investigator (left June)
Marta Bebiano Alenquer	Graduate	PhD Student (left March)
Marta Pires de Miranda	PhD	Post-doctoral Investigator
Sofia Isabel Arriaga Mimoso Cerqueira	Master	PhD Student
Sofia Pinto Guia Marques	PhD	Post-doctoral Investigator (left February)

**Keywords / Research Areas**

herpes virus, B lymphocytes, E3 ubiquitin ligase, SH2 and SH3, B cell signalosome, MuHV-4.

### Major scientific achievements

During 2013 with our collaborators Maria Arménia Carrondo and Colin McVey at ITQB and Ken Kaye at Harvard Medical School, we have resolved 3D structure of the DNA binding domain of LANA, which includes the SOCS box E3 ligase motif. In addition we have defined that in addition to NF- $\kappa$ B, LANA also targets the cellular oncogene MYC for polyubiquitination. In contrast to NF- $\kappa$ B, where polyubiquitination mediated by LANA is degradative, MYC polyubiquitination is heterotypic and increases the stability of MYC. It turns out that MYC is essential for virus induced lymphoproliferation, offering a new target for blocking LANA, hence virus-induced lymphoproliferative disease.

### Recent Most Relevant Publications

Rodrigues L, Filipe J, Seldon MP, Anrather J, Soares MP and Simas JP (2009). Termination of NF- $\kappa$ B activity via a  $\gamma$ herpesvirus protein that assembles an EC5S ubiquitin-ligase. *The EMBO Journal* 6;**28**(9):1283-95. Epub 2009 Mar 26 (Citations: 23)

Marques S, Efstathiou S, Smith KGC, Haury M, Simas JP (2003) Selective Gene Expression of Latent Murine Gammaherpesvirus 68 in B Lymphocytes. *Journal of Virology* 77:7308-7318 (Citations: 71)

Stevenson PG, May JS, Smith XG, Marques S, Adler H, Koszinowski HU, Simas JP, Efstathiou S (2002) CD8+ T cell evasion by K3 plays a critical role in the amplification of a latent  $\gamma$ -herpesvirus. *Nature Immunology* 3:733-40. (Citations: 110)

Bridgeman A, Stevenson PG, Simas JP, Efstathiou S (2001). A secreted chemokine binding protein encoded by murine gammaherpesvirus 68 is necessary for the establishment of a normal latent load. *Journal of Experimental Medicine* 194: 1-13. (Citations: 78)

Parry CN, Simas JP, Smith VP, Stewart CA, Minson AC, Efstathiou S, Alcami A (2000). A broad spectrum secreted chemokine binding protein encoded by a herpesvirus. *Journal of Experimental Medicine* 191: 573-578. (Citations: 147)

### Ongoing Research Projects

2011/2013 Pathogenesis of gamma-herpesvirus: modulation of the cellular transcription factors NF- $\kappa$ B and MYC. Coordinator: João Pedro Monteiro e Louro Machado de Simas. Agency: FCT. Amount: €153.315,00

2011/2014 Pathogenesis of Kaposi's sarcoma herpesvirus LANA. Coordinator: João Pedro Monteiro e Louro Machado de Simas. Agency: FCT. Amount: €294.892,00

**Publications in peer review Journals**

Correia, B., Cerqueira, S.A., Beauchemin, C., Pires de Miranda, M., Li S., and 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: 8.136, Citations: 1)

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: 8.136, Citations: 0)

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**(6), 3858. (Journal IF: 4.651, Citations: 0)

Nuno Figueiredo, Angelo Chora, Helena Raquel, Nadja Pejanovic, Pedro Pereira, Björn Hartleben, Ana Neves-Costa, Catarina Moita, Dora Pedroso, Andreia Pinto, Sofia Marques, Hafeez Faridi, Paulo Costa, Raffaella Gozzelino, Jimmy L. Zhao, Miguel P. Soares, Margarida Gama-Carvalho, Jennifer Martinez, Qingshuo Zhang, Gerd Döring, Markus Grompe, J. Pedro Simas, Tobias B. Huber, David Baltimore, Vineet Gupta, Douglas R. Green, João A. Ferreira, and Luis F. Moita. (2013) Anthracyclines Induce DNA Damage Response-Mediated Protection against Severe Sepsis. *Immunity*. Oct 30, 2013. doi:pil: S1074-7613(13)00465-2. 10.1016/j.immuni.2013.08.039. [Epub ahead of print]

**ANA E. SOUSA LAB****Major Interests / Objectives**

Our work is focused 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 our research effort is centered on HIV/AIDS immunopathogenesis, mainly through the study of HIV-2 infection, a naturally attenuated form of HIV disease.

We prioritize the “bedside to the bench” approach and, given the transversal nature of Clinical Immunology, bring together physician/clinical researchers, from different medical areas, and basic researchers.

**Head of Unit**

Ana Espada de Sousa, Md, PhD Agregação, Associate Professor, Faculdade de Medicina da Universidade de Lisboa.

**Research Team**

Adriana Silva de Albuquerque	PhD	Post-doctoral Investigator
Alcinda Melo	Graduate	Technician
Ana Berta da Fonseca Vieira Álvares e Sousa Ferrand de Almeida	MD/PhD	Investigator, Clinical Specialist, Assistant Professor
Ana Isabel Gouveia Costa da Fonseca Lopes	MD/PhD	Investigator, Clinical Specialist, Assistant Professor
Ana Luisa Caetano	Graduate	Technician
Ana Margarida Fernandes Pereira de Matos	Graduate	Lab Manager
Ana Rita Correia Pires	Graduate	Lab Manager, Investigator
Andreia de Jesus Amaral Gomes Barbosa Fonseca	PhD	Post-doctoral Investigator
Daniela Filipa Alves Ferreira	Graduate	Investigator(left June)
Helena Nunes Cabaço	PhD	Post-doctoral Investigator

Inês Filipa dos Santos Martins	Master	Consultant
Íris Maria Ferreira Caramalho	PhD	Principal Investigator
Isabel Cristina e Castro de Menezes Esteves	Graduate	Investigator, MD, Clinical Specialist, Teaching Assistant
Jorge Andrade	PhD	Post-doctoral Investigator (started February)
José Gonçalo Duque Pereira Monteiro Marques	Graduate	Investigator, MD, Clinical Specialist, Teaching Assistant
Maria Catarina Mota da Silva	Graduate	PhD Student, MD
Maria da Conceição Galvão Barata Pinto Pereira dos Santos	PhD	Investigator
Paula Cristina Frade dos Santos Matoso	Master	Lab Manager, Investigator
Rita Maria Vitorino Tendeiro Pereira Rêgo	PhD	Post-doctoral Investigator (left September)
Rui Manuel Martins Victorino	MD, PhD Agregação	Principal Investigator, Full Professor, Clinical Service Director
Russell Bourne Foxall	PhD	Post-doctoral Investigator
Sara Branco Pereira da Silva	Graduate	Investigator, MD, Clinical Specialist
Susana Clara Barão Lopes da Silva dos Anjos	Master	PhD Student, MD, Clinical Specialist, Teaching Assistant
Susana Mendes Fernandes	Graduate	PhD Student, MD, Teaching Assistant

### Keywords / Research Areas

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

### Major scientific achievements

Our investigation of HIV/AIDS immunopathogenesis is focused on HIV-2 infection, which features a much slower course than HIV-1, often being asymptomatic for over 20 years without therapy. We showed preserved telomere length within naive and memory CD4 subsets, despite

increased CD4 T-cell turnover. We also found a heightened state of monocyte and dendritic cell activation throughout HIV-2 infection with overexpression of the inhibitory molecule PD-L1, which may act by limiting inflammation, given the role of these cells as main orchestrators of immune responses. These data challenge current paradigms in HIV/AIDS and open new perspectives regarding potential strategies to modulate inflammatory states.

Our research related to the Primary Immunodeficiency Centre (a partnership with University Hospital de Santa Maria), was strengthened by the organization of 1st International Primary Immunodeficiency Congress/International Patient Organization for Primary Immunodeficiencies.

### Recent Most Relevant Publications

Markert ML, Marques JG, Neven B, Devlin BH, McCarthy EA, Chinn IK, Albuquerque AS, Silva SL, Pignata C, de Saint Basile G, Victorino RM, Picard C, Debre M, Mahlaoui N, Fischer A, Sousa AE. (2011) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of 2 cases. *Blood* **117**, 688. (Journal IF: 9.060, Citations: 10)

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: 9.060, Citations: 27)

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: 8,136, Citations: 14)

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: 5.520, Citations: 265)

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: 24.302, Citations: 296)

### Ongoing Research Projects

2013/2015 Bee Venom as a tool to expand the human regulatory T-cell compartment. Coordinator: Rui Manuel Martins Victorino. Agency: FCT. Amount: €145.000,00

2011/2013 Factores celulares e moleculares no desenvolvimento de Células T Reguladoras humanas. Coordinator: Íris Maria Ferreira Caramalho. Agency: FCT. Amount: €158.360,00

2011/2014 Infecção HIV/SIDA: contributo da homeostasia dos linfócitos T CD4+ naïves. Coordinator: Ana Espada de Sousa. Agency: FCT. Amount: €159.694,00

2013/2015 Plataforma para o Desenvolvimento de Médicos-Cientistas. Coordinator: Ana Espada de Sousa. Agency: Fundação Calouste Gulbenkian. Amount: €100.000,00

2013/2015 Reservatórios e replicação viral nas células T CD4 de memória-central e foliculares na infecção HIV-2. Coordinator: Ana Espada de Sousa. Agency: Gilead Sciences, Lda. Amount: €14.500,00

2011/2013 Modulation of HIV replication and latency in human CD4 T cells by regulatory small RNAs. Coordinator: Ana Espada de Sousa. Agency: Merck Sharp & Dohme. Amount: €142.000,00

### Publications in peer review Journals

Tendeiro R, Albuquerque AS, Foxall RB, Cavaleiro R, Soares RS, Baptista AP, Soares MV, Gomes P, Sousa AE (2013) Preserved CD4 T-cell telomere length during long-lasting HIV-2 infection. *AIDS*, Jan 14, **27**(2):289-92. (Journal IF: 6.348, Citations: 0)

Cavaleiro R, Tendeiro R, Foxall RB, Soares RS, Baptista AP, Gomes P, Valadas E, Victorino RM, Sousa AE (2013) Monocyte and myeloid dendritic cell activation occurs throughout HIV type 2 infection, an attenuated form of HIV disease. *J Infect Dis.*, Jun 1, **207**(11):1730-42. (Journal IF: 5.848, Citations: 1)

Nunes-Cabaço H, Sousa AE (2013) Repairing Thymic Function. *Current Opinion in Organ Transplantation*, **18**(3), 363-8. URL: <http://journals.lww.com/co-transplantation/pages/articleviewer.aspx?year=2013&issue=06000&article=00019&type=abstract> (Journal IF: 3.272, Citations: 0)

Paiva RS, Lino AC, Caramalho I, Sousa AE, Zelenay S, Demengeot J (2013) Recent thymic emigrants are the preferential precursors of regulatory T cells differentiated in the periphery. *Proc Natl Acad Sci USA* **110**(16),6494-9. (Journal IF: 9.737, Citations: 1)

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**, 703-12. (Journal IF: 3.94, Citations: 0)

Miskinyte M, Sousa A, Ramiro RS, de Sousa JA, Kotlinowski J, Caramalho I, Magalhães S, Soares MP, Gordo I. (2013). The Genetic Basis of Escherichia coli Pathoadaptation to Macrophages. *PLoS Pathog* **9** (12): e1003802. (Journal IF: 8.136, Citations: 0)

Brás-Rosário Luis, Matsuda Alex, Pinheiro Ana Isabel, Gardner Rui, Lopes Telma, Amaral Andreia, Gama-Carvalho, Margarida (2013) Expression Profile of microRNAs Regulating Proliferation and Differentiation in Mouse Adult Cardiac Stem Cells. *PLoS one* **8**(5),e63041. (Journal IF: 3.730, Citations: 0)

Michael V Dodson, Sihem Boudina, Elke Albrecht, Luke Bucci, Melinda Fernyhough Culver, Shengjuan Wei, Werner G Bergen, Andreia J Amaral, Naima Moustaid-Moussa, Sylvia Poulos, Gary J Hausman (2013) A long journey to effective obesity treatments: is there light at the end

of the tunnel? *Experimental biology and medicine* **238**(5), 491-501. (Journal IF: 2.803, Citations: 0)

Manco L, Pires S, Lopes AI, Figueiredo I, Albuquerque D, Alvarez M, Rocha J, Abade A. (2013) Distribution of the -13910C>T polymorphism in the general population of Portugal and in subjects with gastrointestinal complaints associated with milk consumption. *Ann Hum Biol* **40**, (2):205-8. doi:10.3109/03014460.2012.754943. Epub Jan 18, 2013. PubMed PMID: 23327608. (Journal IF: 1.484 Citations: 0)

Esposito G., de Falco F., Neri I., Graziano C., Toschi B., Auricchio L., Gouveia C., Sousa A.B., Salvatore F. (2013) “Different TGM1 mutation spectra in Italian and Portuguese patients with autosomal recessive congenital ichthyosis: evidence of founder effects in Portugal”. *Brit J Dermatol* **168**, (6):1364-7. (Journal IF: 3.759, Citations: 0)

#### Other publications International

Pinto MV, Palha AM, Marques JG, da Silva SL, Lopes AI. (2013) Chronic Granulomatous Disease and Crohn's Disease Histopathological Distinctive Features: A Pediatric Study. *Journal of Gastroenterology and Hepatology Research* **2**, (11):863-867. URL: <http://www.ghrnet.org/index.php/joghr/article/view/529>

J.Caiado, L. Venemalm, M. C Pereira Santos, L. Costa, M. Pereira Barbosa, M. Castells. (2013) Carboplatin, Oxaliplatin and Cisplatin specific IgE: Cross reactivity and value in the diagnosis of Carboplatin and Oxaliplatin allergy. *J. Allergy Clinical Immunology: In Practice* **1**, 494-500

Pinto MV, Esteves I, Bryceson Y, Ferrão A. (2013) Hemophagocytic syndrome with atypical presentation in an adolescent. *BMJ Case Rep*. pii: bcr2013200929. doi: 10.1136/bcr-2013-200929.

#### Other publications National

Dias JG; Silva SL; Luz S; Silva SP; Santos AS; Pedro E; Pereira Santos MC; Barbosa MP. (2013). Estudo comparativo de métodos de rastreio de atopia em doentes com rinite (ImmunoCAP® Rapid versus Phadiatop® e testes cutâneos em picada). *Rev Port Imunoalergol* **21**, (1): 41– 47.

Rocha G, Marques JG, Marques L, Cavaco A, Rodrigues F. (2013) Vacinação em circunstâncias especiais. Comissão de Vacinas da Sociedade Portuguesa de Pediatria. *Sociedade de Infeciologia Pediátrica*, ed. Coimbra 2013.

Gonçalves C, Lobo L, Anjos R, Salgueiro C, Lopes AI. (2013) Giant infantile hepatic hemangioma: which therapeutic options? *Acta Med Port* **26**, (6):750-4.

#### Invited lectures and seminars

I. Caramalho. “Development of FOXP3+ cells in the human thymus”. Thymus@Porto II, Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Porto, Portugal, December 19, 2013.



R.B. Foxall. “The elite controllers follow-up programme”. Partnering for Cure Portugal, Bristol-Myers Squibb, Lisbon, Portugal, November 30, 2013.

S.L. Silva. “Immunoglobulin replacement therapy: the journey so far”. International Primary Immunodeficiency Congress 2013, Estoril, Portugal, November 7-8, 2013.

A.E. Sousa. Reconstituição imunológica. Reunião do Grupo Português de Trabalho sobre Infecção VIH na Criança, Lisbon, Portugal, September 20, 2013.

A.E. Sousa. “Infecção latente: o que nos separa da cura?”. Jornadas do Núcleo de Estudos de Infecção VIH da Sociedade Portuguesa de Medicina Interna, Tomar, Portugal, June, 2013.

R.B. Foxall. “AIDS Immunopathogenesis: what we can learn from HIV-2?”. XXXVII Congresso Nacional de Inmunología, Sociedade Española de Inmunología, Salamanca, Spain, May 29-June 1, 2013.

A.B. Sousa. “Genodermatosis: from etiopathogenesis to prenatal diagnosis”. 2º Simpósio de Genodermatoses, Lisbon, Portugal, May 31- June 1, 2013.

A.E. Sousa. “HIV Immunopathogenesis in 2013: what are we missing”. XIII Congresso Sociedade Ibérica de Citometria, Aveiro, Portugal, May, 2013.

A.B. Sousa “Aconselhamento genético em obstetrícia”. Simpósio de Obstetrícia do Hospital da Luz, Lisbon, Portugal, May 17, 2013.

S. L. Silva, S.P. Silva. “Imunodeficiência primária: abordagem diagnóstica”. 4ª Reunião do Núcleo de Estudos de Bronquiectasias da Sociedade Portuguesa de Pneumologia, Coimbra, Portugal, May 4, 2013.

### **Communications in International Conferences**

Ana Célia Costa, Fátima Duarte, Elisa Pedro, Alcinda Melo, Manuel Pereira-Barbosa, Conceição Pereira Santos. Efficacy and safety of Sublingual Specific Immunotherapy with Pru p 3 in a Portuguese population - Clinical and Immunological evaluation during 12 months, WAO Symposium of Immunotherapy and Biologics, Chicago, USA. December 2013 (Poster presentation)

Pereira Santos MC, Silva P, Costa C, Pestana L, Pereira Barbosa M. Frequency of LTP (Pru p 3) and Profilin (Pru p 4) sensitisation in 1052 patients referenced to an immunoallergy department in Lisbon, International Symposium on Molecular Allergology, Viena, Austria. December 2013. (Poster presentation)

S. Silva, A. Albuquerque, A. Melo, M. Lucas, R. Cheynier, R.M.M. Victorino, A.E. Sousa. Chronic granulomatous disease in adulthood: indication for hematopoietic stem cell transplantation. Chronic granulomatous disease – a Portuguese survey, International Primary Immunodeficiencies Congress 2013, Estoril, Portugal, November 2013. (Poster presentation)

A. Serra-Caetano, A. Albuquerque, A. Ferrão, S. Lopes da Silva, A.B. Sousa, I. Esteves, A. Campos Melo, J.G. Marques, A. Figueiredo, E. Faria, J. Fabela Neves, S. Melo, M.C. Pereira Santos, R.M. Victorino, A.E. Sousa. Towards the definition of a local algorithm for the diagnosis of autoimmune lymphoproliferative syndrome, International Primary Immunodeficiencies Congress 2013, Estoril, Portugal, November 2013. (Poster presentation)

SP Silva, SL. Silva, M. Laiges, E. Pedro, M. Barbosa. Adult primary immunodeficiencies clinic – 8 years experience, International Primary Immunodeficiencies Congress 2013, Estoril, Portugal, November 2013. (Poster presentation)

M. Guedes, A. Cordeiro, E. Faria, L. Marques, B. Vitor, J.G. Marques, S.L. Silva, S. Lemos, C. Neves, I. Soares, J.F. Neves, A.E. Sousa, E. Neves. Chronic granulomatous disease – a Portuguese survey, International Primary Immunodeficiencies Congress 2013, Estoril, Portugal, November 2013. (Poster presentation)

Catarina Ferreira, Ana Russo, Paula Ravasco, Sara Azevedo, Maria Camilo, Ana Isabel Lopes. Inflammatory bowel disease in Pediatrics: The impact on nutritional status and intake, 35th European Society for Clinical Nutrition (ESPEN) Congress, Leipzig, Germany, September 2013. (J Clin Nutr suppl.) (Poster presentation)

M Almeida, T Rodrigues, A Palha, M Oleastro, AI Lopes Helicobacter infection in pediatric digestive endoscopy: prevalence trend and clinical profile, XXVth International Workshop of the European Helicobacter Study Group, Madrid, Spain, September 2013 (Helicobacter suppl.). (Poster presentation)

Ana Margarida Matos, Jorge Andrade, Andreia Fonseca, Mariana Santa-Marta, Ana Serra-Caetano, Russell B Foxall, Paula Matoso, Rui Soares, João Gonçalves, Ana E Sousa, Margarida Gama-Carvalho (2013). A role for miR-34c-5p in T-cell activation and response to HIV infection, Molecular Biology in Portugal and EMBL (and EMBL Alumni) Meeting, Lisbon, Portugal, July 2013. (Poster presentation)

Andreia J Amaral, Jorge Andrade, Ana Margarida Matos, Paula Matoso, Rui Soares, Russel Foxall, Rita Tendeiro, Margarida Gama-Carvalho, João Gonçalves, Ana Espada Sousa (2013). Deep-sequencing profile of small ncRNAs in human CD4+ T cells upon TCR-mediated activation and its modulation by HIV infection, Molecular Biology in Portugal and EMBL (and EMBL Alumni), Lisbon, Portugal, July 2013. (Poster presentation)

Batalha S, Oom P, Torres J, Cravo M, Oliveira H, Lopes AI. Diagnosis of inflammatory bowel disease: not always an easy task, ESPGHAN Summer School on Nutrition, Prague, Czech Republic, July 2013. (JPGN suppl.) (Oral communication)

Silveira-Santos R., Serafim S., Custódio S., Ávila M., Sousa A., Sousa A.B., Cordeiro I. “Early array-CGH diagnosis of Mowat-Wilson syndrome in two children”, 9th European Cytogenetics Conference, Dublin, Ireland, June 29– July 2 2013. (Poster presentation)

Andreia J Amaral, Jorge Andrade, Ana Margarida Matos, Russell B Foxall, Paula Matoso, Mariana Santa-Marta, Rita Tendeiro, Ana Serra-Caetano, Rui S Soares, João Gonçalves, Ana E Sousa,

Margarida Gama-Carvalho. miR-34c-5p is a novel regulator of naive T-cell activation that impacts HIV replication. RNA 2013 - The 18th Annual Meeting of the RNA Society, Davos, Switzerland, June 2013. (Oral communication)

Sousa A.B., Dupont J., Kalscheuer V.M., Medeira A., de Brouwer A.P.M., Cordeiro I. “Non-syndromic X-linked intellectual disability caused by a missense mutation in RPS6KA3, the gene responsible for Coffin-Lowry syndrome”, European Human Genetics Conference 2013, Paris, France, June 2013. (Poster presentation)

Justino A., Dias P., Pina M.J., Ribeiro C., Sousa S., Cirnes L., Sousa A.B., Costa J.L., Machado J.C. “Comprehensive massive parallel DNA sequencing strategy for the genetic diagnosis of the RAS/MAPK related syndromes”, European Human Genetics Conference 2013, Paris, France, June 2013. (Poster presentation)

Sousa A.B., Serafim S., Santo S., Barreta A., Custódio S., Silveira-Santos R., Ávila M., Melo A., Pinto L., Sousa A., Cordeiro I. “Beyond the karyotype: aCGH uncovers pathogenic 4p16.1 submicroscopic deletion in apparently balanced reciprocal translocation”, 17th International Conference on Prenatal Diagnosis and Therapy, Lisboa, Portugal, June 2013. (Poster presentation)

L. Barbosa L, Martins R, Jacinto T, Sousa R, Esteves I, Prata F, Mouzinho A, Borges A, Marques JG. Kawasaki disease: when the lab doesn't fit, 31th Annual Meeting of the ESPID, Milan, Italy, May 28 – June 1, 2013. (Poster presentation)

Sousa R, Almeida S, Esteves I, Prata F, Mouzinho A, Marques JG. Co-infection with hepatitis B and hepatitis C viruses among HIV-infected children, 31th Annual Meeting of the ESPID, Milan, Italy, May 28 – June 1, 2013. (Poster presentation)

Almeida S, Sousa R, Esteves I, Prata F, Mouzinho A, Marques JG. HIV diagnosis in children: two different populations, 31th Annual Meeting of the ESPID, Milan, Italy, May 28 – June 1, 2013. (Poster presentation)

Fernandes, S.M., Pires, R.A. C., Foxall, R.B. Veiga-Fernandes, H., Sousa A. Major IL-22 depletion in the gut of long term treated HIV-1 infected individuals. "Immune Activation in HIV Infection: Basic Mechanisms and Clinical Implications" Keystone Symposia conference, Breckenridge, USA, April, 2013. (Poster presentation)

Esteves I, Quintas S, Bustamante J, Casanova JL, Marques JG. Partial IFN- $\gamma$  R1 deficiency: beyond mycobacterial susceptibility, 2nd São Paulo Advanced School on Primary Immunodeficiencies: the interface of autoimmunity and immunodeficiency, São Paulo, Brasil, March, 2013. (Poster presentation)

A. Serra-Caetano, S.P. Silva, S.L. Silva, R.R. Barbosa, A. Melo, L.V. Paulos, M. Costa, J.E. Fonseca, M.P. Barbosa, A.E. Sousa. Infliximab treatment in a CVID patient with severe non-infectious manifestations, II São Paulo Advanced School on Primary Immunodeficiencies: The interface of autoimmunity and immunodeficiency, São Paulo, Brasil, March 2013. (Oral communication and poster presentation)

M. Valente Pinto\*, S. Azevedo, H. Loreto, P. Mourato, C. Maltez, A.I. Lopes . Iron deficiency anemia in Pediatric Crohn's Disease: preliminary evaluation of parenteral iron therapy, 8th Congress of European Crohn's and Colitis Organization (ECCO) - Inflammatory Bowel Diseases, Vienna, Austria, February, 2013 (Journal of Crohn's and Colitis suppl.) (Poster presentation)

### Communications in National Conferences

Helena Nunes-Cabaço, Paula Matoso, Russell B. Foxall, Rita Tendeiro, Ana R. Pires, Rui S. Soares, Ana I. Pinheiro, Ana E. Sousa; Infection of the human thymus by HIV-2, Thymus@Porto II, Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Porto, 19th December 2013. (Poster presentation)

Caramalho, I., V. Nunes-Silva, A.R. Pires, A.I. Pinto, C. Mota and A. E. Sousa, IL-2 and IL-15 impact on Regulatory T cell commitment and are expressed within discrete non-overlapping niches in the human thymus, XXXIX Meeting of the Portuguese Society of Immunology, Coimbra, November 13-15, 2013. (Oral presentation)

A S. Albuquerque, SL Silva, A Serra-Caetano, AI Pinheiro, SM Fernandes, RB. Foxall, J Ferreira, R. M. M. Victorino, AE. Sousa. A role for IL-7 in the homeostasis of human naive regulatory T-cells XXXIX Meeting of the Portuguese Society of Immunology, Coimbra, November 13-15, 2013. (Oral Presentation)

Mota, C., V. Nunes-Silva, A. E. Sousa, R. M. M. Victorino and I. Caramalho. Delta like-1 enhances the in vitro conversion of human memory CD4 cells into FOXP3-expressing Regulatory T Cells, XXXIX Meeting of the Portuguese Society of Immunology, Coimbra, November 13-15, 2013. (Poster presentation)

A. Serra-Caetano, A. Albuquerque, A. Ferrão, S. Lopes da Silva, A.B. Sousa, I. Esteves, A. Campos Melo. J.G. Marques, A. Figueiredo, E. Faria, J. Fabela Neves, S. Melo, M.C. Pereira Santos, R.M. Victorino, A.E. Sousa. Towards the definition of a local algorithm for the diagnosis of autoimmune lymphoproliferative syndrome, XXXIX Meeting of the Portuguese Society of Immunology, Coimbra, November 13-15, 2013. (Poster presentation)

Sousa A.B., Medeira A., Peixoto M., Singh S., Matyas G., Cordeiro I. "TGFB2 mutation causing a phenotype in the Marfan spectrum in a large Portuguese family", XVII Reunião da Sociedade Portuguesa de Genética Humana, Coimbra, November 21-23, 2013. (Poster presentation)

Peixoto M., Durães A., Serafim S., Sousa A.B. "Duplication of 11p13 involving the PAX6 gene". XVII Reunião da Sociedade Portuguesa de Genética Humana, Coimbra, November 21-23, 2013. (Poster presentation)

Machado C., Dupont J., Medeira A., Pereira C., Custódio S., Sousa A., Sousa A.B. "Tetraploid/diploid mosaicism: clinical characterization of a further case of a rare mixoploidy syndrome", XVII Reunião da Sociedade Portuguesa de Genética Humana, Coimbra, November 21-23, 2013. (Poster presentation)

Ana Célia Costa, Fátima Duarte, Elisa Pedro, Alcinda Melo, Manuel Pereira Barbosa, M. Conceição Pereira Santos. Eficácia e tolerância de imunoterapia específica sublingual com Pru p 3 em doentes com alergia grave ao pêsego-evolução clínica e imunológica ao longo de 12 meses, XXXIV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Vale de Lobo, October 11-13, 2013. (Poster presentation)

Pedro Silva, Leticia Pestana, Ana Célia Costa, M. Conceição Pereira Santos, Manuel Pereira Barbosa. Sensibilização A LTP (Pru p 3) e profilina(Pru p 4) em 1052 doentes referenciados a um Serviço de Imunoalergologia em Lisboa, XXXIV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Vale de Lobo, October 11-13, 2013. (Poster presentation)

M. Isabel Mascarenhas, I. Costa Silva, A. Campos Melo, MC Pereira Santos, J. Rosado Pinto. Anafilaxia com hidrocortisona- raro mas existe, XXXIV Reunião Anual da Sociedade Portuguesa de Alergologia e Imunologia Clínica, Vale de Lobo, October 11-13, 2013. (Poster presentation)

Joana Extreia, Andreia Abrantes, Sara Azevedo, Ana Isabel Lopes. Casuística de Doença de Crohn numa Unidade de Gastreenterologia Pediátrica dum Hospital Terciário, Congresso Nacional de Pediatria, Porto, October 2013. (Oral communication)

Morais A, Costa NF, Silva S, Silva LO, Seves G, Marques JG. Neutropenia grave em duas gémeas, XIII Jornadas Nacionais de Infecçiology Pediátrica, Coimbra, July 4-5, 2013. (Best Oral communication)

Lígia Paulos, Sara Azevedo, Paula Mourato, Helena Loreto, Ana Isabel Lopes. Doença inflamatória em idade pediátrica: série retrospectiva de um centro terciário, Reunião Anual da Sociedade de Gastreenterologia e Nutrição Pediátrica, Semana Digestiva, Vilamoura, June 2013. (Oral communication)

### **Organisation of Conferences**

Adriana Albuquerque, Ana Luísa Caetano and Isabel Esteves. Co-organisation of V Reunião de Imunodeficiências Primárias, Estoril, November 9, 2013.

Susana Lopes da Silva. Co-organisation of the 1st International Primary Immunodeficiency Congress (IPIC) from the IPOPI (International Patient Organization for Primary Immunodeficiencies), Estoril, November 6-8, 2013.

### **Internationalisation**

Established international collaborations in the area of HIV/AIDS and/or Primary Immunodeficiency with:

- Alain Fischer, Hôpital Necker-Enfants malades, Paris, France
- Claudio Pignata, “Federico II” University, Naples, Italy
- Jeffrey Platt, University of Michigan, Ann Arbor, USA
- Lennart Hammarstrom, Karolinska Institute, Stockholm, Sweden

- Louise Markert, Duke University Medical Center, Durham, USA
- Marilia Cascalho, University of Michigan, Ann Arbor, USA
- Nicolas Manel, Institut Curie, Paris, France
- Rémi Cheynier, Institut Cochin, Paris, France
- Zvi Grossman, NIH, Bethesda, USA

#### Prizes, honours and awards

Prize for the best Abstract - WAO Symposium of Immunotherapy and Biologics. Chicago, USA, 13-14 December 2013 - Ana Célia Costa, Fátima Duarte, Elisa Pedro, Alcinda Melo, Manuel Pereira-Barbosa, Conceição Pereira Santos. Efficacy and safety of Sublingual Specific Immunotherapy with Pru p 3 in a Portuguese population - Clinical and Immunological evaluation during 12 months.

Poster award - 2nd prize - Molecular Biology in Portugal and EMBL (and EMBL Alumni) Meeting, Lisbon, Portugal, 18th July 2013 - Andreia Fonseca, Jorge Andrade, Ana Margarida Matos, Paula Matoso, Rui Soares, Russel Foxall, Rita Tendeiro, Margarida Gama-Carvalho, João Gonçalves, Ana Espada Sousa (2013). Deep-sequencing profile of small ncRNAs in human CD4+ T cells upon TCR-mediated activation and its modulation by HIV infection.

2º Prémio Comunicação Oral, SPAIC– Merck Sharp Dome 2013 - Ana Célia Costa, Fátima Duarte, Elisa Pedro, Alcinda Melo, Manuel Pereira Barbosa, M. Conceição Pereira Santos. Eficácia e tolerância de imunoterapia específica sublingual com Pru p 3 em doentes com alergia grave ao pêsegue-evolução clínica e imunológica ao longo de 12 meses. *Rev. Portuguesa Imunoalergologia* 2013; **21**(1):16.

#### Industry contract research

Ana E. Sousa, Principal Investigator/Coordinator of the Project entitled: Modulation of HIV replication and latency in human CD4 T cells by regulatory small RNAs. Merck Investigators Study Program, funded by the Merck Sharp & Dome Corporation, 2011-2013, 142,000€. Merck & Co., Inc.

Ana E. Sousa, Principal Investigator/Coordinator of the 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.

Susana Lopes da Silva; Principal Investigator/Coordinator of the 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.

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

José G. Marques and Susana Lopes da Silva, Members of “Comissão Técnica de Vacinação da Direcção-Geral de Saúde” (Portaria nº 243/2013, de 22 de Abril)

Members of the Directive Board of the Sociedade de Ciências Médicas de Lisboa. Ana E. Sousa (left in May 2013) and Rui MM Victorino (since May 2013).

Rui MM Victorino, Member of the Scientific Council for Health and Life Science from FCT (Portuguese Foundation for Science and Technology) (left in 2013).

Rui MM Victorino, Chairman, and Ana E Sousa, Member, of the Scientific Council of the PhD Program from the Lisbon Academic Medical Center.

Maria Conceição Pereira-Santos, José G. Marques: Members of the Coordinator Board of the Portuguese Group for Primary Immunodeficiencies (GPIP).

Rui MM Victorino, Member of the Scientific Council of the Fundação Pulido Valente.

Rui MM Victorino, Member of the Jury for the Annual Prizes in clinical research from the University of Hospital Santa Maria.

Rui MM Victorino, Member of the Clinical Research Committee from University Hospital Santa Maria.

Rui MM Victorino, Chairman, and Ana E Sousa, Member, of the Scientific Council of the Faculdade de Medicina da Universidade de Lisboa.

### **Advanced teaching**

Ana E Sousa, Maria Conceição Pereira-Santos, Rui MM Victorino, Susana L. Silva, Susana M Fernandes, and Ana Serra-Caetano: Clinical Immunology teaching in the core curriculum for Medical Students, Area: Medicine 2, 5th year, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Ana E Sousa, Rui MM Victorino: full-responsibility in the organization of the Clinical Immunology optional courses for Medical Students, 4th and 5th year, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Adriana Albuquerque, Susana Lopes Silva. 2013. Contribution in the teaching of the Discipline of Clinical Immunology of the 4th and 5th year of the Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal.

Isabel Esteves. Advanced Formation Institute of Lisbon Medical Faculty and Pediatrics Department of Santa Maria Hospital. “Specialization in Pediatrics: innovation and technology” - Postgraduate course. Santa Maria Hospital, 10 sections, one weekend/month, Lisbon, Portugal. January-June and September-December, 2013.

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

Ana Berta Sousa. Coordenação e ensino no Módulo de Risco Oncológico Familiar do Mestrado de Oncobiologia da Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal. May, 2013.

Isabel Esteves. Infectious Diseases in Childhood: new epidemics. XI Meeting of Pediatrics Department of Algarve Hospital Center, Faro, Portugal, December 5, 2013.

Isabel Esteves. Meningococcal disease: past and future of prevention. XI Meeting of Pediatrics Department of Algarve Hospital Center, Faro, Portugal, December 5, 2013.

Marques JG. Classificação das IDPs e sinais de alerta. Curso satélite das XI Jornadas do Serviço de Pediatria do C.H. do Algarve, Faro, Portugal, December 4, 2013.

Marques JG. Terapêutica com Imunoglobulinas, Curso satélite das XI Jornadas do Serviço de Pediatria do C.H. do Algarve, Faro, Portugal, December 4, 2013.

Isabel Esteves. Pediatrics Department of Algarve Hospital Center and PID Centre of the Lisbon Medical Academic Centre. “Primary Immunodeficiencies” – satellite course of XI Meeting of Pediatrics Department of Algarve Hospital Center, Faro, Portugal, December 4, 2013.

Isabel Esteves. How to manage the child with probable primary immunodeficiency, “Primary Immunodeficiencies” – satellite course of XI Meeting of Pediatrics Department of Algarve Hospital Center, Faro, Portugal, December 4, 2013.

Marques JG. Imunodeficiências Primárias, Curso satélite das XI Jornadas do Serviço de Pediatria do C.H. do Algarve, Faro, Portugal, December 4, 2013.

Isabel Esteves. Invasive Fungal Infections in Pediatrics, 34<sup>o</sup> Edition of Infectious Diseases Conferences, Hospital Santa Maria, Lisbon, Portugal, November 22, 2013.

Isabel Esteves. BCGitis 15<sup>o</sup> Meeting of the Pediatrics Department of Cascais Hospital, Cascais Cultural Centre, Cascais, Portugal, November 8, 2013.

Ana Isabel Lopes. Doença Celíaca. I Curso Pós-Graduado de Actualização -Diferenciação em Pediatria Formação Avançada em Gastrenterologia Pediátrica, Departamento de Pediatria do HSM-CHLN/ Clínica Universitária de Pediatria, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 2013.

Ana Isabel Lopes. Esofagite Eosinofílica, I Curso Pós-Graduado de Actualização -Diferenciação em Pediatria, Formação Avançada em Gastrenterologia Pediátrica, Departamento de Pediatria do HSM-CHLN/ Clínica Universitária de Pediatria, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 2013.

Ana Isabel Lopes. Doença Hepática Auto-Imune, I Curso Pós-Graduado de Actualização -Diferenciação em Pediatria, Formação Avançada em Gastrenterologia Pediátrica, Departamento



de Pediatria do HSM-CHLN/ Clínica Universitária de Pediatria, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, October 2013.

Ana Isabel Lopes. A Criança com Hepatite Vírica, IV Curso Avançado de Hepatites Viricas, Serviço de Gastrenterologia do HSM-CHLN (Presidentes: Prof. J Velosa, Prof. Rui Marinho), Lisbon, Portugal, October 2013.

Ana E Sousa. Challenges in HIV research, Course “Challenges in Immunology”, PhD Program of the Lisbon Academic Medical Centre, Lisbon, Portugal, June 5, 2013.

Ana Isabel Lopes. Doença Inflamatória em Idade Pediátrica, ABBVIE Medical Department, Lisbon, Portugal, June 2013.

Ana E Sousa. Imunodeficiência associada à infecção VIH, Instituto de Ciências Biomédicas Abel Salazar, Porto, Portugal, May 30, 2013.

Ana Isabel Lopes. Doença Hepática Autoimune em Idade Pediátrica, 2º Curso ABC de Hepatologia, Unidade de Hepatologia, Hospital Pediátrico de Coimbra, Nazaré, Portugal, May 2013.

Paula Matoso. A user’s perspective - Biosafety training for use of the IMM BSL3 Facility, IMM, Lisbon, Portugal, March 2013.

Susana Lopes da Silva. Curso de Diferenciação em Pediatria, Módulo de Infecologia - Imunodeficiências primárias e doenças auto-inflamatórias: O laboratório de imunologia na perspectiva do clínico, Lisbon, Portugal, March 22, 2013.

Marques JG. Curso de diferenciação em pediatria, módulo de Infecologia, Departamento de Pediatria do HSM/CHLN, Lisbon, Portugal, March 1, 8, 15, 22, 2013.

Isabel Esteves. Severe Combined Immunodeficiencies. Pediatric Infectious Diseases Section of the postgraduate course “Specialization in Pediatrics: innovation and technology”, Hospital de Santa Maria, Lisbon, Portugal, March 22, 2013.

Isabel Esteves. New Primary Immunodeficiencies. Pediatric Infectious Diseases Section of the postgraduate course “Specialization in Pediatrics: innovation and technology”, Hospital de Santa Maria, Lisbon, Portugal, March 22, 2013.

Isabel Esteves. Neutropenia: diagnosis, complications and treatment, Pediatric Infectious Diseases Section of the postgraduate course “Specialization in Pediatrics: innovation and technology”, Hospital de Santa Maria, Lisbon, Portugal, March 22, 2013.

Isabel Esteves. Adjuvant Therapies of viral infections, Pediatric Infectious Diseases Section of the postgraduate course “Specialization in Pediatrics: innovation and technology”, Hospital de Santa Maria, Lisbon, Portugal, March 15, 2013.

Iris Caramalho. Lectured at the Oncobiology Module of the Doctoral Programme in Experimental Biology and Biomedicine, Coimbra, Portugal, February 2013.

Ana E. Sousa. HIV pathogenesis, GABBA PhD Program, Porto, Portugal, February 8, 2013.

Ana Isabel Lopes. Esofagite e Gastroenteropatia Eosinofílica, Curso Avançado de Imunoalergologia Pediátrica (2ª Edição), Universidade Católica de Lisboa, Lisbon, Portugal, January 2013.

#### **Science and society**

Susana Lopes da Silva, Medical Advisor for Associação Portuguesa de Doentes com Imunodeficiências Primárias

Ana E Sousa, Participation in the TSF radio program “Alerta SIDA” to increase HIV/AIDS awareness.

#### **Msc theses completed**

Ana Margarida Fernandes Pereira de Matos (2013) Characterization of differentially expressed microRNAs in HIV-1 and HIV-2 infection in Human CD4-T cells: A role for miR-34c-5p in T-cell activation and response to HIV infection MSc thesis in Emerging Infectious Diseases. Faculdade de Medicina da Universidade de Lisboa. Supervisors: Margarida Gama Carvalho (BioFig/FCUL) and Ana Espada de Sousa, (IMM/FMUL).

**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, DVM, PhD

**Research Team**

Afonso Rocha Martins de Almeida	PhD	Post-doctoral Investigator
Ana Teresa Veríssimo Alves Bento	Graduate	MSc Student (started February)
Bethania García Cassani	Master	PhD Student
Carlos Diogo Labão Alpiarça Sousa de Almeida	Graduate	MSc Student
Diogo da Fonseca Pereira	PhD	PhD Student
Fátima Sofia dos Santos Cardoso	Graduate	Investigator (started November)
Hélder Manuel Piedade Ribeiro	Graduate	Technician
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

#### Publications:

Klein Wolterink, R.G. *et al.* "Essential, dose-dependent role for the transcription factor Gata3 in the development of IL-5+ and IL-13+ type 2 innate lymphoid cells", *Proceeding of National Academy of Science* 110, 2013.

Baptista AP *et al.* Colonic patch and colonic SILT development are independent and differentially regulated events, *Mucosal Immunol*, 2013 May, **6** (3), 511-21.

#### Prize:

Innovator Award of the Kenneth Rainin Foundation (KRF) from Kenneth Rainin Foundation, USA, Aug 2013.

#### Patents:

The use of ret agonist molecules are critical to haematopoietic stem cell expansion protocols and transplantation therapy and a ret agonist. Submitted to WIPO as nr. 47679-13 (not published). Inventors: Henrique Veiga-Fernandes, Diogo Fonseca-Pereira, Silvia Madeira

#### Organisation of international conference:

Young Scientist Forum EMBO. Lisbon, Portugal, 15-16 July 2013

### Recent Most Relevant Publications

Patel, A, Harker, N, Moreira-Santos, L, Ferreira, M, Alden, K, Timmis, J, Foster, K, Garefalaki, A, Pachnis, P, Andrews, P, Enomoto, H, Milbrandt, J, Pachnis, V, Coles, M, Kioussis, D, Veiga-Fernandes, H. (2012) Differential RET Signaling Pathways Drive Development of the Enteric Lymphoid and Nervous Systems. *Science signaling* ra55. (Journal IF: 7.6, Citations: 2)

Veiga-Fernandes H, Kioussis D, Coles M. Natural killer receptors: the burden of a name (2010). Natural killer receptors: the burden of a name. *J Exp Med* **207**, 269-72. (Journal IF: 13.2, Citations: 9)

Veiga-Fernandes, H., Coles, M.C., Foster, K.E., Patel, A., Williams, A., Natarajan, D., Barlow, A., Pachnis, V. and Kioussis, D. (2007). Tyrosine kinase receptor Ret is a key regulator in Peyer's Patch organogenesis. *Nature* **446**, 547-51. (Journal IF: 38.6, Citations: 69)

Peixoto, A., Evaristo, C., Munitic, I., Monteiro, M., Charbit, A., Rocha, B. and Veiga-Fernandes, H. (2007). CD8 single-cell co-expression reveals three different effector types present at distinct phases of the immune response. *J. Exp. Med.* **204**, 1193-205. (Journal IF: 13.2, Citations: 43)

Veiga-Fernandes, H. and Rocha, B. (2004). High expression of active CDK6 in the cytoplasm of

CD8 memory cells favors rapid division. *Nature Immunol*, **5**, 31-37. (Journal IF: 26, Citations: 63)

### Ongoing Research Projects

2008/2013 “Role of the proto-oncogene Ret in lymphocyte function” Coordinator: José Henrique Veiga Fernandes, Agency: FP7. Amount: €1.901.400,00

2010/2013 “Role of the Tyrosine kinase RET in foetal and adult haematopoiesis” Coordinator: José Henrique Veiga Fernandes, Agency: FCT. Amount: €182.000,00

2010/2013 “Role of haematopoietic cell subsets during lymphoid organogenesis” Coordinator: José Henrique Veiga Fernandes, Agency: FCT. Amount: €197.802,00

2012/2013 “Enteric Microbiota and Innate Lymphoid Cells” Coordinator: José Henrique Veiga Fernandes, Agency: PRIV-UE. Amount: €10.000,00

2012/2015 “Stromal Cell – Immune cell interactions in health and disease” Coordinator: José Henrique Veiga Fernandes, Agency: FP7. Amount: €220.204,56

2012/2014 “Modulation of RET signaling in hematopoietic stem cell transplantation” Coordinator: José Henrique Veiga Fernandes, Agency: National Blood Foundation. Amount: €59.027,23

2008/2013 “Role of neurotrophic factors in the immune system” Coordinator: José Henrique Veiga Fernandes. Agency: EMBO. Amount: €250.000,00

2013/2016 “Controlo da função das células inatas linfóides e da homeostasia intestinal por fatores neurotróficos”. Coordinator: José Henrique Veiga Fernandes, Agency: FCT. Amount: €250.000,00

2013/2014 “Control of innate lymphoid cells and intestinal homeostasis by neurotrophic factors” Coordinator: José Henrique Veiga Fernandes. Agency: Kenneth Rainin Foundation. Amount: €72.632,19

### Publications in peer review Journals

Coles M, Veiga-Fernandes H. (2013). Insight into lymphoid tissue morphogenesis. *Immunol Lett*. 2013 Aug 14. doi:pii: S0165-2478(13)00103-X.

Klein Wolterink RG, Serafini N, van Nimwegen M, Vosshenrich CA, de Bruijn MJ, Fonseca Pereira D, Veiga Fernandes H, Hendriks RW, Di Santo JP (2013). Essential, dose-dependent role for the transcription factor Gata3 in the development of IL-5+ and IL-13+ type 2 innate lymphoid cells. *Proc Natl Acad Sci USA*. **110**, (25):10240-5. (Journal IF: 9.74)

Alden K, Read M, Timmis J, Andrews PS, Veiga-Fernandes H, et al. (2013) **Spartan**: A Comprehensive Tool for Understanding Uncertainty in Simulations of Biological Systems. *PLoS*

Comput Biol 9(2): e1002916. doi:10.1371/journal.pcbi.1002916 (Journal IF: Citations: 2)

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

Veiga-Fernandes, H. Lymphoid organogenesis in brief. IBMC / Gabba programme, Porto, Portugal February 7, 2013.

Veiga-Fernandes, H. Beyond neuroregulatory functions of neurotrophic factors. Gaslini Institute, Genova, Italy, May 9-10, 2013.

Veiga-Fernandes, H. Lymphoid organogenesis in brief, Porto Conte, Italy, May 27-31, 2013.

Veiga-Fernandes, H. Prebirth world and the regulation of immune fitness. Young Scientist Forum EMBO, Lisbon, Portugal, July 15-16, 2013.

Veiga-Fernandes, H. Prebirth world and the regulation of immune fitness. 3rd international lymphoid tissue meeting, Rotterdam, Netherlands, September 15-17, 2013.

Veiga-Fernandes, H. Prebirth world and the regulation of immune fitness. VUMC, Netherlands, Amsterdam, September 19, 2013.

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

Fonseca-Pereira, D., Madeira, S. et al., "The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function", Hematopoiesis, Keystone Symposia, 55, Steamboat Springs. Colorado, USA, January 14-19, 2013.

Fonseca-Pereira, D., Arroz-Madeira, S. et al. "The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function", The Hemato-vascular System: Development and Disease, Baeza, Spain, October 21-23, 2013.

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

M.Ferreira, R. G. Domingues, H.Ribeiro, H. Veiga-Fernandes, "Maternal retinoic acid controls lymphoid tissue inducer cell differentiation and lymphoid organ size", EMBO Young Scientists' Forum – Instituto de Medicina Molecular, Lisbon, Portugal, July 2013.

Fonseca-Pereira, D., Arroz-Madeira, S. et al. "The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function", VII PHD STUDENTS MEETING, Lisbon Academic Medical Centre, Lisbon, Portugal, December 5-6, 2013.

R.G. Domingues, M. Ferreira, D. Fonseca-Pereira, L. Moreira-Santos, H.Ribeiro, H. Veiga-Fernandes, "The transcription factor NFIL3 regulates foetal innate lymphoid cell development", VII PhD Students Meetin, Lisbon Academic Medical Centre, Lisbon, Portugal, December 5-6, 2013.

B.Garcia-Cassani, S.Ibiza, H.Ribeiro, H. Veiga- Fernandes, "Stroma-innate lymphoid cell interaction in enteric lymphoid tissue formation", VII PhD Students Meeting, Lisbon Academic Medical Centre, Lisbon, Portugal, December 5-6, 2013.

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

Innovator Award of the Kenneth Rainin Foundation (KRF) from Kenneth Rainin Foundation, USA, August 2013.

### **Patents/prototypes**

The use of RET agonist molecules are critical do haematopoetic stemm cell expansion protocols and transplantations therapy and a RET agonist kit. Submitted to WIPO as nr. 47679-13 (not published). Inventors: Henrique Veiga-Fernandes, Diogo Fonseca-Pereira, Silvia Madeira

### **Advanced teaching**

Diogo Pereira: Participation in Hematopoiesis, Keystone Symposia, 55, Steamboat Springs, Colorado, USA.

Bethania Cassani, Rita Domingues and Silvia Madeira: Participation in VII PhD Students Meeting 5-6 December 2013 Lisbon Academic Medical Centre, Lisbon, Portugal.

Henrique Veiga-Fernandes: Invited Speaker in 3rd international Lymphoid Tissue Meeting, 15-17 September 2013, Congress Centre Engels, Rotterdam, The Netherlands.

Henrique Veiga-Fernandes: Invited Speaker in Gabba programme. 7 February 2013. Porto, Portugal.

Bethania Cassani: Participation in Stromal Immunology Group/ British Society for Immunology meeting 6-7 November 2013, Moller Centre, Cambridge, UK.

Bethania Cassani: Participation in Stroma ITN Mid-Term Review Meeting 6 November 2013, Moller Centre, Cambridge, UK.

Bethania Cassani: Participation in 2nd Stroma ITN Meeting 5 November 2013, Moller Centre, Cambridge, UK

### **Science and society**

Veiga-fernandes, H. Lymphoid organogenesis in brief. IBMC / Gabba programme. Porto, Portugal. 7 February 2013.

3rd Stroma Training Course, Bethania Cassani, Kantosspital St Gallen, Switzerland. 25 February-1 March 2013.

2nd Stroma Training Course, Bethania Cassani, University of York, UK. 4-8 February 2013.

Organisation of international conference: Young Scientist Forum EMBO. Lisbon. 15-16 July 2013

Science to the lay public: "the conversation that never took place", Pavilhão do Conhecimento, Lisbon, Portugal. November 24<sup>th</sup> 2013.

#### **PhD theses completed**

Diogo da Fonseca Pereira (2013) "Role of the neurotrophic factor receptor RET in haematopoiesis". Faculdade de Medicina da Universidade de Lisboa. Supervisor: José Henrique Veiga - Fernandes

#### **Msc theses completed**

Ana Teresa Bento (2013) "Role of RET signals in human hematopoietic stem cell transplantation. Instituto Técnico de Lisboa. Supervisor: José Henrique Veiga - Fernandes



## ELSA ANES LAB

### Major interests / Objectives

The ability of Koch's bacilli (Mtb) to create tuberculosis or a latent infection relay, in part, on the powerful mechanisms it has evolved to parasitize host macrophages and dendritic cells. Our major aim for the current period was to better understand the molecular mechanisms by which 1) Mtb controls the acquisition of cathepsins and their inhibitors cystatins within phagosomes, an important phenomenon for antigen presentation or bacteria intracellular killing; 2) trafficking host factors are involved in Mtb internalization by macrophages, phagosome maturation and exosome secretion; 3) micro RNAs controls actin dynamics during early steps of Mtb phagocytosis and finally 4) micro RNAs controls distinct phases of Mtb infection within macrophages.

### Head of Unit

Elsa Anes, (PharmD. PhD), Associate Professor with Habilitation, FFUL.

### Research Team

David Pires	PhD Student
Joana Bugalhão	MsC student
Joana Marques	MsC student
João Pombo	MsC student
Nuno Baltazar Carmo	PhD Student
Paulo Bettencourt	Post-Doc Investigator
Pedro Timóteo	MsC student
Vera Fernandes	MsC student

### Keywords/Research Areas

Innate immunity, Intracellular trafficking, Host-pathogen interactions, Tuberculosis.

### Major scientific achievements

- 1) We found that Mtb activates the over-expression of miRNA 142-3p during macrophage phagocytosis. We showed that miR142-3p is involved in controlling actin dynamics during infection (Bettencourt et al., Front Cell Infect Microbiol, 2013, PhD thesis). Indeed the group found a microRNA over-expressed early during Mtb infection involved on the control of cathepsin S (Pires et al., in prep) while others are controlling pro-inflammatory events.
- 2) By using RNA silencing we deciphered the role of cathepsins S, B and L during *M. tuberculosis* infection of macrophages and dendritic cells (DCs) (Pires et al., in prep) relatively to pathogen intracellular survival or antigen presentation. Indeed an overall map of the gene expression of all cathepsins and their natural inhibitors cystatins during Mtb infection was clarified during the year in resting vs activated macrophages or in immature vs mature DCs .
- 3) In collaboration with Maria José Umbelino (iMed.Ulisboa), we evaluated the antimycobacterial effect of extracts from medicinal plants from Mozambique and their effect *in vitro* and *ex vivo* (Luo, Pires et al., J Ethnopharmacol, 2013).
- 4) Indeed chemical compounds prodrugs derived with activity against PZA resistance mycobacteria strains and species were characterized (World patent 2013/WO2013084214; Pires et al., in prep).
- 5) We assessed the role of efflux pumps inhibitors and in combination with nanoparticles delivery systems containing antibiotics on the killing of intracellular Mtb (Machado, Pires et al., Microbiotec2013, manuscript in prep).
- 6) The group organized the “VI-Science-shop: TUBERCULOSE: development of new strategies to treat TB” FFUL, May, 21; Elsa Anes was part of the Scientific Committee of Microbiotec2013; David Pires was awarded with the prize Immunotools 2013; We organized the Course Cellular Microbiology as part of the Master/PhD program at FFUL.

### Recent Most Relevant Publications

Mishra BB, Moura- Alves P, Sonawane A, Hacohe N, Griffiths G, Moita LF and Anes E. (2010). *Mycobacterium tuberculosis* protein ESAT-6 is a potent activator of the NLRP3/ASC inflammasome. *Cell Microbiol.* **12**(8), 1046-63 (Journal IF: 5.8; Citations: 65)

Kuehnel M, Rybin V, Anand P, Anes E and Gareth Griffiths. 2009. Lipids regulate P2X7 receptor-dependent actin assembly by phagosomes via ADP translocation and ATP synthesis in the phagosome lumen. *J Cell Science* **122**(Pt 4), 499-504. (Journal IF: 6.4; Citations: 20)

Gutierrez, MG\*, Mishra, BB\*, Jordao, ML, Elliot, E, Anes, E and Griffiths, G. 2008. NF-kappa B activation controls phago-lysosome fusion-mediated killing of mycobacteria by macrophages. *J. Immunology* **18**(4), 2651-63 \*joined first authors (Journal IF: 6.1; Citations: 28)

Jordao, L., Bleck, CKE., Mayorga, L., Griffiths, G, and Anes, E. 2008. On the killing of mycobacteria by macrophages. *Cell Microbiol* **10**(2), 529-48. (Journal IF: 5.6; Citations: 39)

Anes, E., Kuhnel, M.P., Bos, E., Moniz-Pereira, J., Habermann, A. & Griffiths, G. 2003. Selected lipids activate phagosome actin assembly and maturation resulting in killing of pathogenic mycobacteria. *Nat Cell Biol*; **5**(9), 793-802. (Journal IF: 20.8; Citations: 126)

### Ongoing Research Projects

2010/2013. Role of *M. tuberculosis* in microRNA controlling of actin assembly and other pro-inflammatory signals in infected macrophages. Agency: FCT. Coordinator: Elsa Anes. Amount: €198.830,00.

2010/2013. Dissecting the intracellular trafficking factors involved in *M. tuberculosis* killing/survival within human macrophages using RNA interference. Agency: FCT. Coordinator: Elsa Anes. Amount: €149.652,00

2010/2013. Enhancing the killing of intracellular multi-drug resistant tuberculosis (MDRTB) by human macrophages: a new chemotherapeutic strategy to fight MDRTB. Agency: FCT. Coordinator: Miguel Viveiros. Amount: €25 000 Total amount: €191.134,00

2010/2013. A new life for old antimycobacterial drugs: development of prodrugs of pyrazinoic acid activated by mycobacterial esterases as a way to circumvent resistance to pyrazinamide. Agency: FCT. Coordinator: Luis Constantino. Amount: €25 000. Total amount: €192.882,00

### Publications in peer review Journals

Bettencourt P, Marion S, Pires D, Santos L, Lastrucci C, Carmo N, Blake J, Benes V, Griffiths G, Neyrolles O, Lugo-Villarino G and Anes E 2013. Actin-binding protein regulation by microRNAs as a novel microbial strategy to modulate phagocytosis by host cells: the case of N-Wasp and miR-142-3p. *Front. Cell. Infect. Microbiol.* **3**, 19. doi: 10.3389/fcimb.2013.00019 (Journal IF: ND; Citations: 1)

Luo X., David P., Ainsa J.A., Gracia B., Duarte N, Mulhovo S., Anes E.\*, Ferreira M.J.U.\* 2013 Zanthoxylum capense constituents with antimycobacterial activity against Mycobacterium tuberculosis in vitro, and ex vivo within human macrophages. accepted in *Journal of Ethnopharmacology*, **146**(1), 417-22, doi: 10.1016/j.jep.2013.01.013\*Joined corresponding authors. (Journal IF: 3.728; Citations: 1)

### Other publications International

#### Patents

Constantino L, Anes E, Valente E, Almeida T, Carmo N. Pyrazinoic Acid Prodrugs activated by Esterases of Mycobacteria. World patent 2013/ WO2013084214. Universidade de Lisboa, Lisbon, Portugal.

([http://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013084214&recNum=48&docAn=IB2012057149&queryString=\(FP/enzyme\)%20&maxRec=13106](http://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013084214&recNum=48&docAn=IB2012057149&queryString=(FP/enzyme)%20&maxRec=13106))

### Proceedings

Luo X., Pires D., Ainsa J.A., Mulhovo S., Duarte A, Anes E., Ferreira M.J.U (2012) Searching for natural antituberculars from Mozambican medicinal plants. Congresso Internacional Saber Tropical em Moçambique: História, Memória e Ciência IICT-JBT, Palácio Condes da Calheta, Lisbon, Portugal. October 24-26. ISBN 978-989-742-006-1

### Conferences and seminars

Anes E. For host factors weddings and a Koch's bacillus funeral: actin, lipids, phagosome maturation and inflammasome activation. "VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB". Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

Paulo Bettencourt, Anes E. "Role of pro and anti-inflammatory lipids in intracellular survival and killing of mycobacteria". "VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB". Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

David Pires, Anes E. To control or to be controlled during M. tuberculosis infection? Cathepsins and their inhibitors in TB immune response. "VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB". Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

João Pombo, Anes E. Cathepsin regulation via MicroRNA's during mycobacteria infection. "VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB". Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

Pedro Timoteo, Anes E. Deciphering host factors for mycobacteria internalization during phagocytosis "VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB". Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

### Invited Lectures and Seminars

Elsa Anes. Innate immunity mechanisms for bacterial infections. Módulo Microbiologia e Saúde do mestrado de Microbiologia Aplicada UL. 2013

Elsa Anes. Cellular assays for Phagolysosome maturation. Mestrado/doutoramento em Ciências Biofarmacêuticas. 2013

Elsa Anes. Cellular assays for Phagolysosome maturation. Mestrado Biologia Molecular em Saúde ICSS. 2013

Elsa Anes. Innate Immunity in tuberculosis. Mestrado Biologia Molecular em Saúde ICSS. 2013

Elsa Anes. Immunity to tuberculosis. Imunologia, Integrated master in Pharmaceutical Sciences FFUL. 2013

### Communications in National Conferences

Carmo, N., Pires D., Bugalhão J., Marques J., Bettencourt P., Timóteo P and Anes E. Host Factors Affecting Mycobacterium tuberculosis Macrophage Infection. pg112 5th iMed.UL Postgraduate Students Meeting, Lisbon, Portugal. July 18th, 2013. (poster presentation)

Pires D., Carmo, N., Marques J., Pombo J., Timóteo P, Bettencourt P., and Anes E. Cut or be Cut: Cathepsins and their Inhibitors During Mycobacterial Infection of Macrophages and Dendritic Cells. pg103 5th iMed.UL Postgraduate Students Meeting, Lisbon, Portugal. July 18th 2013. (poster presentation)

Machado D, Pires D, Perdigão J, Ramos J, Couto I, Portugal I, Anes E, and Viveiros M. EFFLUX INHIBITORS AGAINST DRUG RESISTANT ANTIMICROBIAL AGENTS AND ENHANCERS OF MACROPHAGE KILLING ACTIVITY. P233/F12 Microbiotec, Aveiro, Portugal. December 6-8, 2013 (poster presentation)

### Organisation of Conferences

Elsa Anes, Associação de Estudantes da FFUL .“VI-Scienceshop: TUBERCULOSE: development of new strategies to treat TB”. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, May 21, 2013.

### Internationalization

Collaborative Research:

- Gareth Griffiths (Oslo University, Norway);
- Olivier Neyrolles (CNRS, Toulouse , Fr);
- Maximiliano Gutierrez (Helmholtz Centre for Infection Research, Braunschweig, Ger);
- Michael Niederweis (Univ. Alabama at Birmingham, USA).

### Prizes, honours and awards

**ImmunoTools** IT-Box-139 Award 2013  
(<http://www.immunotools.de/html/award/DavidPires.pdf>)

### Patents/prototypes

Constantino L, Anes E, Valente E, Almeida T, Carmo N. Pyrazinoic Acid Prodrugs activated by Esterases of Mycobacteria. World patent 2013/ WO2013084214. Universidade de Lisboa, Lisbon, Portugal. Pt patent 106051 W  
([http://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013084214&recNum=48&docAn=IB2012057149&queryString=\(FP/enzyme\)%20&maxRec=13106](http://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013084214&recNum=48&docAn=IB2012057149&queryString=(FP/enzyme)%20&maxRec=13106))

### Advanced teaching

Elsa Anes organized the Course Cellular Microbiology as part of the Master/PhD program on Biopharmaceutical Sciences at Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal.

Elsa Anes. Innate immunity mechanisms for bacterial infections. Módulo Microbiologia e Saúde do Mestrado de Microbiologia Aplicada UL. 2013

Elsa Anes. Cellular assays for Phagolysosome maturation. Mestrado/Doutoramento em Ciências Biofarmacêuticas Mach 21, 2013.

Elsa Anes. Cellular assays for Phagolysosome maturation. Mestrado Biologia Molecular em Saúde ICSS. April 29, 2013.

Elsa Anes. Innate Immunity in tuberculosis. Mestrado Biologia Molecular em Saúde ICSS. April 30, 2013.

Elsa Anes. Biologia Celular. Coordinator. Integrated Master in Pharmaceutical Sciences. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal. 2013.

Elsa Anes. Immunity to tuberculosis. Imunologia, Integrated Master in Pharmaceutical Sciences, Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal. 2013.

### Msc theses completed

Vera Alexandra Canária Fernandes (2013) O papel de porinas e de bombas de efluxo de micobactérias na imunidade inata e resistência aos antibióticos. Tese de Mestrado Integrado em Ciências Farmacêuticas, Faculdade de Farmácia da UL. Supervisor: Elsa Anes

Joana Margarida Nunes Bugalhão (2013) Mycobacterium tuberculosis subversion of host vesicular traffic pathways Mestrado em Microbiologia Aplicada. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes

Pedro Manuel Dias Timóteo (2013) Deciphering host factors for mycobacteria internalization during phagocytosis. Mestrado em Microbiologia Aplicada. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes

Joana Pereira Marques (2013) Mycobacteria manipulation of host proteases and inflammatory pathways during infection within human macrophages and dendritic cells. Mestrado em Microbiologia Aplicada. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes

João Palma Neves Pombo (2013) Manipulation of cystein cathepsins during Mycobacterium tuberculosis infection of human macrophages. Mestrado em Microbiologia Aplicada. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes

## JOÃO GONÇALVES LAB

### Major interests / Objectives

Molecular virology has contributed greatly to the understanding of cellular responses to infection. Lentiviruses are valuable tools in applied biotechnology and gene therapy. We previously identified cellular proteins involved in the multistep processes of HIV-1 replication. We manipulated the transcription of genes that control HIV-1 to answer questions related to viral latency and antiviral restriction. We also developed small antibody scaffolds that inhibit HIV-1 infection and helped the specific targeting of lentiviral vectors. We now aim to explore reactivation of HIV-1 latency and expression of restriction cellular factors to control and eradicate the virus. The use of validated pharmaceutical compound libraries will help us in this endeavour of modulating viral expression and cellular antiviral defences. Alternative strategies that combine antibody engineering, genetic delivery systems and synthetic biology are being developed to eliminate cells containing viral genomes. Given the uniqueness and innovative strategies to approach these problems of HIV we believe to be well positioned at the international scientific level to contribute with original and groundbreaking research.

### Head of Unit

João Gonçalves, PhD – Associate Professor, FFUL.

### Research Team

Mariana Santa-Marta, PhD	Principal Investigator
Paula Brito, PhD	Principal Investigator
Cátia Cantante	PhD Student
Ana Catarina Cunha Santos	PhD Student
Ana Catarina G. Santos	PhD Student (left June 2013)
Luis Ferreira	PhD Student
Pedro Perdigão	PhD Student

### Keywords/Research Areas

Antibody, HIV, drug screening, therapy.

### Major scientific achievements

The Lab has a consolidated track record in several aspects of molecular microbiology and pathogenesis with strong emphasis in biotechnology. We foster the molecular understanding of microbial pathogenesis and the identification of essential steps in the infectious process that can constitute novel targets for therapeutic intervention. We aimed to manipulate the transcription of genes that control HIV-1 to answer questions related to viral latency and antiviral restriction. We also developed small antibody scaffolds that inhibit HIV-1 infection and helped the specific targeting of lentiviral vectors. The use of validated pharmaceutical compound libraries will help us in this endeavor of modulating viral expression and cellular antiviral defenses. Alternative strategies that combine antibody engineering, genetic delivery systems and synthetic biology are being developed to eliminate cells containing viral genomes.

### Recent Most Relevant Publications

Santa-Marta M, de Brito PM, Godinho-Santos A, Goncalves J. Host Factors and HIV-1 Replication: Clinical Evidence and Potential Therapeutic Approaches. *Front Immunol.* 2013 Oct **24**(4), 343. eCollection 2013. Review. (Journal IF: na, Citations: 2)

da Silva, F. A., Li, M., Rato, S., Maia, S., Malhó, R., Warren, K., Harrich, D., Craigie, R., Barbas, C. and Goncalves, J. (2012), Recombinant rabbit single-chain antibodies bind to the catalytic and C-terminal domains of HIV-1 integrase protein and strongly inhibit HIV-1 replication. *Biotechnology and Applied Biochemistry*, **59**: 353–366. doi: 10.1002/bab.1034. (Journal IF: 3,03, Citations: 4)

Cadima-Couto I, Saraiva N, Santos AC, Goncalves J. HIV-1 Vif Interaction with APOBEC3 Deaminases and its Characterization by a New Sensitive Assay. *J Neuroimmune Pharmacol.* 2011 Jan 29. (Journal IF: 4.5, Citations: 15)

Rato S, Maia S, Brito PM, Resende L, Pereira CF, et al. 2010. Novel HIV-1 Knockdown Targets Identified by an Enriched Kinases/Phosphatases shRNA Library Using a Long-Term Iterative Screen in Jurkat T-Cells. *PLoS ONE* 5(2): e9276. doi:10.1371/journal.pone.0009276. (Journal IF: 5,3, Citations: 24)

### Ongoing Research Projects

2013/2015 ArmAb: Antibody strategy of ADC to cancer therapy. Coordinator: João Gonçalves. Amount: €99.000,00



2012/2014 Albumin-binding peptides to increase pharmacokinetics of therapeutic proteins.  
Coordinator: João Gonçalves. Amount: €125.000,00

### **Communications in International Conferences**

Albumin-binding domains Zag and ProTH improve pharmacokinetics and affect biodistribution of an anti-TNF VHH. Cátia Cantante, Sara Lourenço, João Leandro, Maurício Morais, Soraia Oliveira, Lurdes Gano, Carlos Fontes, Paula Leandro, João Correia, Frederico Silva, João Gonçalves. PEGS 2013 (Poster presentation)

João D. G. Correia, Maurício Morais, Lurdes Gano, Isabel Santos, Cátia Cantante, Sara Lourenço, Catarina Santos, Carlos Fontes, Frederico Silva, João Gonçalves. Pharmacokinetic properties of a <sup>67</sup>Ga-labeled anti-TNF VHH single domain antibody containing a bacterial albumin-binding domain (Zag). WIPR 2013: Workshop on Innovative Personalized Radioimmunotherapy (Poster presentation)

### **Patents/prototypes**

U.S. Provisional Patent Application No. 61/771,562; Filed: March 1, 2013. Inventors: João Manuel Braz Gonçalves et al. Titled: "Cell-Based Methods for Coupling Protein Interactions and Binding Molecule Selection and Diversification".

## 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
Education & Advanced Training	Alexandra Manaia
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	Maria Soares
Histology Service	Sandra Casimiro
IMM Biobank	João Eurico Fonseca
Zebrafish Facility	Leonor Saúde

## COMMUNICATION UNIT

### Major 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.

### Team

Ana Cristina Borges Marques do Carmo	Master	Director (left July)
Andreia Sofia Moita Machado	Graduate	Administrative
Maria Margarida Ferreira Trindade	PhD	Manager (left January)
Silvana Daniela Fonseca Paules	Graduate	Administrative (started August)

### Keywords

Corporate and Institutional Communication, Science Communication, Public Affairs.

### Major achievements

Produced materials to promote the corporate image of IMM (report, folders videos) and reinforced IMM presence in the social networks and national and international press. A new website is being developed and should be online in 2014.

By the celebration of IMM's 10th anniversary it organized two major events (one that aimed to foster the collaboration with decision makers and scientific partners and another that was

focused on the IMM community) and produced merchandising materials to celebrate and disseminate the information.

It communicated several national and international events (e.g.: PEPBRAIN, 3rd GCGC, EMBO Young Scientists Forum 2013, Health Cluster Portugal conference, 1st Post Doc Day etc.) and was responsible for a wide range of media relations to communicate several awards, grants and the publication of relevant papers of the IMM researchers. It also organized official meetings with foreign delegations and national and international students.

### **Communications in International Conferences**

de Almeida, L. "Citizenship and the Portuguese NHS", Association for Contemporary Iberian Studies 35th Annual Conference, Lisbon, September 19th-11th 2013. (Oral presentation)

### **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 (e.g.: Brazil, Libya).

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.

School visits to IMM from all levels of schooling, most particularly secondary school, engaged in school visits to IMM, co-organized by the communication unit with the presence of international students (Semester at Sea program) that also visited IMM.

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.

In 2013 we've increased IMM image in the Social Media, namely on Facebook a social media that grew about 45% (+1069 fans) and reached a total of 8903 people in the end of December.

## EDUCATION & ADVANCED TRAINING UNIT

### Major 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.
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### Head of Unit

Maria Alexandra Gama Mendonça Simões Manaia, PhD.

### Team

Sónia Silva Arroz	Graduate	Administrative (started June)
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### Keywords

Education, Advanced-Training, PhD-Program, Postdoctoral-Program, Career Development, Advanced Courses.

### Major achievements

#### Transversal Managerial Achievements

- Help desk: Standardized email messages and info packages for regular requests: FCT grant applications, renewals, spontaneous applications, general queries etc
- 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.

**Ongoing Research Projects**

2012/2013 Programa Mobilidade Académica PhD. Coordinator: Maria Alexandra Gama Mendonça Simões Manaia. Agency: Fundação Calouste Gulbenkian. Amount: €20.000,00

2013/2014 Cursos (Formação avançada. Coordinator: Maria Alexandra Gama Mendonça Simões Manaia. Agency: Financiadores vários (inscrições). Amount: 1.000,00

## FUNDING PROGRAMS OFFICE

### Major 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 research organizations for the development of scientific collaborations. Our specific goals include: i) promote a service of funding opportunities tailor-made for IMM researchers; ii) promote academic/entrepreneurial scientific collaborations underpinning the establishment of national/international applications; iii) promote partnerships with companies and explore relevant financial opportunities; iv) assist obtaining funding for entrepreneurial projects.

### Head of Unit

Ana Filipa Duarte Nunes Almeida, PhD.

### Team

Joana Costa	PhD	Manager
Rudolfo Pais Mendes Ferreira Francisco	Graduate	Administrative (started May)

### Keywords

Research funding, Funding opportunities dissemination, Scientific and entrepreneurial collaborations, Networking, Funding agencies.

### Major achievements

- We tested and implemented an online platform for matching funding opportunities to individual profiles of IMM researchers (ProQuest Pivot). Using this tool, we managed to bi-weekly disseminate a newsletter - Funding Opportunities Announcement - and to increase the time-to-deadline to 5 months for the funding opportunities disseminated via Pivot;
- An important step to improve the quality of the services our Office provides and the success of IMM researchers' grant applications was the establishment of rules for requests to grant application support;
- We established contacts to build a specialized network of consultants/grant-writers;

- We established partnerships with companies (Wise Consulting, Roche) to explore financial opportunities to IMM research projects;
- We managed to establish a better communication/articulation with the Management Unit;
- We organized an “Entrepreneurial Workshop” and several institutional visits, including Pfizer Internacional and Peter Andersen (EFPIA).

### **Ongoing Research Projects**

2012/2014 SIAC - Dinamização da Participação Portuguesa no 7PQ: Saúde - Lisboa Ana Filipa Duarte Nunes Almeida. Amount: €305.007.13

### **Organisation of Conferences**

Filipa Nunes, Entrepreneurial Workshop: Making Private Investment Work for Health Sciences, Lisbon, June 25, 2013.

Filipa Nunes, Seminar by Peter Andersen (European Federation of Pharmaceutical Industries and Associations): "IMI2 – a new ecosystem for European health care?" followed by Round Table discussion: "Main challenges to successful participation in IMI2", Lisbon, December 19, 2013.

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

Filipa Nunes, selected to attend the Course: Entrepreneurs in Clinical Academia, INSEAD, Fontainebleau, France, September 23–27, 2013 (one of only 21 candidates accepted, all expenses covered).



## INFORMATION SYSTEMS UNIT

### Major Objectives

The primary goal of the Information Systems Unit (USI) is to help researchers reach their maximum productivity by using adequate Information Technology resources and following best practices. By accompanying the latest technological trends we also aim at providing researchers and managers at IMM with tools for enhancing data analysis and processing, communication and decision taking. To achieve this USI operates in several areas:

1. Planning, implementation and maintenance of the IT infrastructure to protect and secure research data. This involves constant monitoring of backups, storage and connectivity;
2. Designing and integrating Information Systems;
3. Maintenance of IMM website (with the Communication and Training Unit);
4. Documentation and Information Workflow;
5. IT Support.

### Head of Unit

José Joaquim Carvalho da Costa Braga, PhD

### Team

Daniel Alexandre Felício da Silva	Graduate	PhD Student (left April)
Daniel José Vilhena Guerreiro	Graduate	Technician
Emanuela Simões	Master	Technician
Nuno Andrade da Cruz Henriques	Master	Technician (started September)
Pedro Miguel Bernardino Eleuterio	Graduate	Technician
Tito Lívio Santos Silva	PhD	Consultant (left April)

### Keywords

Data protection, Information integration, Web Services, IT support.

### **Major achievements**

In 2013, due to the ever increasing reliance upon Information technologies, support tickets averaged 250 per month. During this year USI deployed several new services. An FTP server was configured to facilitate dissemination and sharing of large amounts of data between IMM and other research institutions.

Significant savings were achieved by configuring a cost-effective storage that will increase the space available for data. To increase efficiency in lab processes of all units, USI also developed web applications for online purchases, for requisitions of the Histology Unit and for generating the annual IMM activity reports.

USI also planned and designed the hardware and software infrastructure that is necessary to reach a fully integrated Information System, offering better tools for IMM researchers and managers in the near future during 2014.

## MANAGEMENT UNIT

### Major Objectives

The Management Unit is responsible for the overall IMM legal, human resources, administrative and financial issues. The main areas are:

- Accounts – general accounting and preparation of IMM statutory accounts and tax returns; cost accounting per project/activity; submission of statistical information to Bank of Portugal, Intrastat and Tax Office- SAFT;
- Budget management - overall budget control, for Institutional Funding and Research Projects, including Facilities, Support Units and Management;
- Projects management - contractual, administrative and financial issues, from start to termination; contacts with donors and funding institutions; all administrative support to researchers (projects adjustments, transfer of funds, fellowships and HR contracts, preparation of scientific reports, etc);
- Human resources - new appointments/contracts, registrations, organization of individual files, salary preparation and other procedures, including statistical information;
- Legal – support to researchers, namely on intellectual property and consortium agreements; all types of contracts (funding, HR, suppliers, scientific collaborations, MTA, etc); support to staff and fiscal matters;
- Scientific protocols management – current support and updating;
- Quality Management System;
- General Administrative support – to all units and researchers.

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

Margarida Pinto Gago, Degree in Management, ISEG-UTL.

### Team

#### Legal

Ana Isabel Fernandes Braz Panão	No degree	Lawyer started June)
André Rebelo da Silva Fialho	Graduate	Lawyer

**Human Resources**

Cláudia Aurora Mira Soeiro	Graduate	Administrative
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**Accounts**

Annie Cibele Guerreiro Semião	Graduate	Accountant (started September)
Diogo Miguel de Sousa Henriques	Graduate	Accountant, (left June)
Eduarda Maria Seabra Rosmaninho	Master	Accountant (started July)
Joana Filipe Reis	Graduate	Accountant (left October)
Nuno Manuel Barradas da Fonseca	Graduate	Accountant (started November)
Sandra Paula da Silva Duarte	Graduate	Accountants manager
Tânia Cristina Torres Pereira Ascensão	Graduate	Administrative
Vera Cristina Felício Conceição Rego	Undergraduate	Administrative

**Project Management**

Andreia Sofia Gonçalves Almeida Vaz Veiga	Graduate	Project manager
Daniela Filipa Ferreira Madeira	Graduate	Administrative
Isabel Pequenino Roque	Graduate	Administrative
Kendrik Graça do Sacramento	Graduate	Project officer (started March) (left July)
Maria José Flores Marques Antunes	Graduate	Administrative
Mónica Aurora Malheiro Vieira	Graduate	Administrative
Mónica Raquel Carvalho Paquete	Graduate	Administrative (started September)

**Support**

Patricia McCarthy da Cunha		Board Secretary
Susana Isabel dos Santos Pedroso	Undergraduate	Front office (started July)

**Quality Management System**

Alexandre Manuel Raposo de Jesus	Master	Quality Manager
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**Keywords**

Continuous improvement and challenges; Human Resources; Accounts and budget control; Project Management; Funding strategy; Legal and Tax; Quality Management System.

**Major achievements**

Effective response to a continually increasing number of scientific collaboration protocols and HR contracts, namely, related to Research Projects. This work is performed both, by Dr. André Fialho, as legal support for IMM and HR - Cláudia Soeiro; Accounts Manager - Sandra Duarte - and Project Manager, Andreia Vaz. The team work is one of keys to improve and achieve the highest level of performance.

Quality Management System – the first internal audit was carried out in 2011 but due to major changes in the management system, the process was re-launched in 2013 and is now in the final stage – with the second certification audit scheduled for next April. This process would not have been possible without the collaboration and hard work of the Lab Management Team. Alexandre, as Quality Manager, has been doing an excellent job.

Organization and participation in periodic meetings with IMM Board and the other support units, mostly to find the best ways to cope with the current government funding restrictions and to continue with the high level of support to science.

## QUALITY AND SAFETY IN LABORATORY

### Major Objectives

The Quality and Safety in laboratory (QSL) is divided in three main areas, each one dedicated to improve the quality of research of IMM and comply with National and International guidelines and best practices. The Lab Management works as an advisor and authority regarding safety with products and equipments. Training and development of standard operating procedures is the key to achieve high standards of safety and effectiveness in the use of equipment and infrastructures. It is also responsible for the design of (re) new laboratory infrastructures. The Purchasing Office is responsible for the Internal Storehouse and External Orders, centralizing all acquisitions. It also provides updated information on prices, ongoing promotions and new products. The Washing Room provides researchers cleaned and sterilized material, according to each specific requirement.

### Head of Unit

Alexandra Maralhas, Graduate

### Team

#### Lab Management

Alexandre Manuel Raposo de Jesus	Master	Technician
André Paiva Antunes	Graduate	Technician
Cátia Vanessa Sanches Mesquita	Graduate	Technician
Rita Isabel Ganchas Soares Alves	Master	Technician (left April)

#### Washing Room

Ana Cristina dos Santos Anunciação Silva	Undergraduate	Technician
Carlos Filipe Ferreira Curado	Undergraduate	Technician (left January)
Edna Neias F. Gomes	Graduate	Technician
Susana Maria Andrade	Undergraduate	Technician

**Purchasing Office**

Ana Patrícia de Freitas Roque	Graduate	Technician (left January)
Ana Rita Fonseca Vicente	Graduate	Administrative
Sandra Isabel Francisco Lopes	Graduate	Administrative
Vânia Isabel Estevens Polido Marques Paula	Graduate	Administrative

**Keywords**

Infrastructure and equipments maintenance, Health and Safety in Work, Laboratory Design, Purchasing Management, Laboratory Management, budgeting; cost controlling, technical consultant; integrated management systems.

**Major achievements**

In 2013 we have changed to Quality and Safety in Laboratory. The online Purchase System implemented last year, was in 2013 expanded to all IMM acquisitions, streamlining the work required to purchase and also allowing a better control by Structural Units concerning purchases of general and IT equipment's.

The Unit was actively involved in several re-modelings of laboratory spaces and research support structures, such as histology room, tritium room, a new -80°C common room, new laboratory spaces for existing research units - Sérgio Almeida; Luís Costa; Miguel Prudêncio and Maria Mota Labs and the reorganization of the IMM Biobank lab and for new research units – Gonçalo Bernardes; Edgar Gomes and Nuno Morais Labs.

The equipments management was improved with the ongoing inventory of all IMM equipments, essential for an excellent level of support to over 300 equipments with maintenance contracts.

**Advanced Teaching**

Maralhas, A. lectured a theoretical session for the BLS3 course “Biosafety training for use of the IMM BSL3 Facility”, Instituto de Medicina Molecular, Lisboa, 28February - 01 March, 2013; and 15 April 2013.

## ANIMAL FACILITY

### Major Objectives

The IMM's Rodent Facility aims to maintain the highest standards of animal welfare and to promote a responsible use of laboratory animals, hence providing the conditions for state-of-the-art animal-based research. The facility has capacity to host 15000 rodents and comprises one conventional unit and one SPF unit. The SPF unit includes one Production which hosts 70 genetically altered strains and one Experimental area, with four housing rooms and three rooms for experimental work with animals. All husbandry and manipulations are performed according to high standards of biocontainment and bioexclusion, in order to ensure the best possible conditions in terms of health and safety. This unit is highly committed to follow the 3Rs – Replacement, Reduction, Refinement - and provides education and guidance for researchers, according to the Portuguese and international laws/recommendations for good practices and animal welfare.

### Head of Unit

Joana Margarida da Silva Marques, PhD.

### Team

Ana Catarina Jorge Mendes	Undergraduate	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
Janaina Gonçalves dos Santos de Barcelos	Graduate	Technician
Maria Dolores Paulos Bonaparte Figueira	Graduate	Veterinarian
Nuno Manuel Ribeiro Inácio	No degree	Technician
Olena Pavlovska Borges de Pinho	Undergraduate	Technician
Pedro Manuel Nogueira dos Santos	Undergraduate	Technician
Wilma Eliandra de Lemos Zovo	Undergraduate	Lab Technician



### **Keywords**

Rodents, Welfare, Husbandry.

### **Major scientific achievements**

During 2013, the major achievements of the facility were mainly related to the human resources, namely their reorganization hence increasing the efficiency of the services provided as well as in their education, increasing the quality of the services provided. During 2013 we considerably increased the housing capacity of the facility by acquiring new housing equipments. We also added two animal caretakers to the team - Catarina Mendes and Pedro Santos - which allowed us to accommodate new researchers and projects without compromising the quality standard of the services we provide.

The team had the chance to participate in a national congress about alternatives to animal experimentation. Furthermore, the two technicians (Carlos and Iolanda) and one caretaker (Cecília) accompanied the facility director to the FELASA congress. Participation in these events is extremely important as it allows the members of the team to learn about the scientific and technical advances in the field of Laboratory Animal Science. Besides, it allows the team to take part and understand the context of animal experimentation and to establish contacts with people who work in the same field around the world. Later in 2013, one of our animal caretakers – Ana Rafaela Coelho was promoted to animal technician, with the role to manage the transgenic colonies of Henrique Veiga Fernandes Lab.

From 2014 Ana will also play a crucial role on the development and implementation of the cryopreservation services. Another important achievement was the reorganization of process of ethical evaluation of projects. This allowed to greatly improve the efficiency of the process.

## BIOIMAGING UNIT

### Major 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. We research novel microscopy techniques and develop image processing software tools for quantitative microscopy applications.

### 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.

### Major scientific achievements

Scientific collaboration with 2 IMM research units resulted in 3 publications in which José Rino is co-author:

- Carvalho S et al, Nucleic Acids Res (PMID: 23325844; IF: 8.278)
- Rino J et al, Methods (PMID: 23969316; IF:3.641)
- Martin R et al, Cell Reports (PMID: 24035393)

In 2013 the BioImaging Unit services were used by 197 users from 39 different research units, 5 of them from outside the IMM. We trained 103 new users in different microscopy systems during the year. We implemented monthly quality control checks of objective performance and

illumination stability on all fluorescence microscopes.

### Recent Most Relevant Publications

Martins SB\*, Rino J\*, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M. \* These authors contributed equally to this work (2011) Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. *Nat Struct Mol Biol* **18**, 1115. <http://www.nature.com/nsmb/journal/v18/n10/full/nsmb.2124.html>. (Journal IF: 12.712, Citations: 24)

Martin RM\*, Rino J\*, Carvalho C\*, Kirchhausen T, Carmo-Fonseca M \* These authors contributed equally to this work (2013) Live-cell visualization of pre-mRNA splicing with single molecule sensitivity. *Cell Reports* **4**(6), 1144-1155. <http://www.sciencedirect.com/science/article/pii/S2211124713004373>. (Journal IF: N/A, Citations: 0)

Henriques CM, Rino J, Nibbs RJ, Graham GJ, Barata JT (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7Ralpha in T cells. *Blood* **115**, 3269-77. <http://bloodjournal.hematologylibrary.org/content/115/16/3269.long>. (Journal IF: 10.558, Citations: 26)

Domingues I, Rino J, Demmers JA, de Lanerolle P, Santos SC (2011) VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. *PLoS One* **6**, e25668. <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0025668>. (Journal IF: 4.092, Citations: 11)

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: 7)

### Publications in peer review Journals

Rino J, Martin RM, Carvalho T, Carmo-Fonseca M (2013) "Imaging dynamic interactions between spliceosomal proteins and pre-mRNA in living cells". *Methods*, Aug 19, S1046-2023(13), URL: <http://www.sciencedirect.com/science/article/pii/S1046202313003150> (Journal IF: 3.641, Citations: 0)

### Invited lectures and seminars

Rino J, "Imaging Gene Expression Inside Living Cells", invited seminar for the XI Encontro de Engenharia Biomédica, Lisbon, Portugal, November 2013.

### **Internationalisation**

Apr 2013: José Rino participated in the Course “Quantitative Imaging: from cells to molecules” organized by Torsten Wittmann and Jennifer Waters at Cold Spring Harbor Lab, NY

### **Advanced teaching**

José Rino lectured (both theoretical lectures and hands-on practicals) at the "1st Advanced Course on Fluorescence Microscopy and Image Analysis" held on 22-24 November 2013 at the Faculty of Health Sciences at the University of Beira Interior, Covilhã, Portugal. The course was attended by students of master's, doctoral and post-doctoral researchers, health professionals and teachers.

José Rino lectured at the course "Innovation in Microscopy", organized by the Sociedade Portuguesa de Microscopia; lecture entitled "Introduction to confocal microscopy", Cooperativa de Ensino Superior CRL, Monte da Caparica, Portugal. December 11, 2013.

## BIO SAFETY LEVEL 3 LABORATORY

### Major 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.

### Head of Unit

Miguel Prudêncio, PhD.

### Research Team

Inês Antunes Cabral Queiroz de Matos	Graduate	Technician
Maria Dolores Paulos Bonaparte Figueira	Graduate	Veterinarian

### Keywords / Research Areas

Biosafety level 3, HIV, Mycobacterium tuberculosis, ABSL3.

### Major scientific achievements

During 2013, the IMM BSL3 facility was used in research projects involving both Mycobacterium tuberculosis and HIV, carried out by IMM as well as external units. Besides, the facility organized and delivered 2 theoretical and practical courses on biosafety intended for future users of the facility. During this year, the IMM BSL3 facility established itself as a key partner of LabPTBioNet, a network of National BSL3 facilities whose main aim is to establish common procedures and foster cooperation between high containment facilities in Portugal. Also in the context of this network, the facility participated in a consortium that applied for European funding within the "Roteiro de Infraestruturas" program of FCT. The facility also participated in one course and one workshop organized by Instituto Nacional de Saúde Dr. Ricardo Jorge, where Dr. Miguel Prudêncio served as a lecturer and a chairman, respectively.

### **Invited lectures and seminars**

Miguel Prudêncio: “Biossegurança em Laboratórios de Nível 2 e 3”, "Management of a Biosafety Program Applied to Research - The IMM experience", INSARJ, Lisbon, Portugal. December 11-13, 2013.

### **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**

Course “IMM BSL3 Facility”, IMM, Lisbon, Portugal. February 28 - March 1, 2013.

Course “IMM BSL3 Facility”, IMM, Lisbon, Portugal. April 15, 2013.

### **Science and society**

3rd Workshop “Biosafety: design, construction and decontamination of biocontainment laboratories”, INSARJ, Lisbon, Portugal. November 8, 2013.

## FLOW CYTOMETRY UNIT

### Major Objectives

The Flow Cytometry Unit (UCF) provides training and support to researchers performing flow cytometry studies. UCF users comprise a very diverse and challenging set of researchers, creating a very stimulating working environment that demands from our staff a constant knowledge of new developments in the field.

Training in flow cytometry concepts, experimental controls and instrument operation is achieved through workshops and one-to-one tuition. UCF staff also provides support in experiment planning and data analysis. In addition, our trained staff operates the High Speed Cell Sorters providing a cell purification service.

UCF staff further ensures quality control and maintenance procedures on all instruments and the implementation the Quality Management System, according to ISO 900.

### Head of Unit

Maria Godinho A.V. Duarte Soares, PhD.

### Research Team

Ana Isabel da Silva Vieira	Graduate	Technician
Sofia Pinto Guia Marques	PhD	Lab manager (started February) (left August)

### Keywords / Research Areas

Flow Cytometry, High Speed Cell Sorting, Phenotyping, Training in Flow Cytometry.

### Major scientific achievements

In 2013 the Flow Cytometry unit provided direct support to approximately 140 users from 32 research labs of which 6 were external to the IMM and one company. We trained 65 new users and organized a Flow Cytometry Course under the Lisbon AMC Doctoral Program. This course included theoretical and practical modules on the basic concepts of flow cytometry, instrument setup, experimental controls, as well as high speed cell sorting and data analysis using Flowjo.

We experienced a 29% increase in analyser usage as compared to 2012. This was partly due to the installation of a High Throughput Sampler (HTS) in one of the analysers in February 2013. This device allows the automated acquisition of samples from 96 and 384 well plates which greatly facilitates the work of researchers.

### Recent Most Relevant 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.” *Biol Blood Marrow Transplant* Azevedo and Soares joint first authors, Maria Soares corresponding author, **19**, 703. <http://www.sciencedirect.com/science/article/pii/S1083879113000530#>. (Journal IF: 3.04, Citations: 0)

Libri V, Azevedo RI, Jackson SE, Di Mitri D, Lachmann R, Fuhrmann S, Vukmanovic-Stejic M, Yong K, Battistini L, Kern F, Soares MV, Akbar AN. . Mar;132(3):-339. Journal Impact Factor; Times Cited 17 (2011) “Cytomegalovirus infection induces the accumulation of short-lived, multifunctional CD4+ CD45RA+CD27- T cells: the potential involvement of interleukin-7 in this process.” *Immunology* **123**, 326. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3044899/>. (Journal IF: 3.705, Citations: 24)

Henson SM, Franzese O, Macaulay R, Libri V, Azevedo RI, Kiani-Alikhan S, Plunkett FJ, Masters JE, Jackson S, Griffiths SJ, Pircher HP, Soares MV, Akbar AN . (2009) “KLRG1 signaling induces defective Akt (ser473) phosphorylation and proliferative dysfunction of highly differentiated CD8+ T cells.” *Blood* **113**, 6619. <http://bloodjournal.hematologylibrary.org/content/113/26/6619.long>. (Journal IF: 9.898, Citations: 53)

Azevedo RI\*, Soares MV\*, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE. (2009) *Blood* \*Azevedo and Soares joint first authors, Maria Soares corresponding author. **13**, 2999. <http://bloodjournal.hematologylibrary.org/content/113/13/2999.long>. (Journal IF: 9.898, Citations: 28).

### Ongoing Research Projects

2011/2014 Infecção HIV/SIDA: contributo da homeostasia dos linfócitos T CD4+ naïves.  
Coordinator: Ana Espada de Sousa. Agency: FCT. Amount: €159.694,00

### Publications in peer review Journals

Tendeiro R, Albuquerque AS, Foxall RB, Cavaleiro R, Soares RS, Baptista AP, Soares MV, Gomes P, Sousa AE; (2013); “Preserved CD4 T-cell telomere length during long-lasting HIV-2 infection”. *AIDS* **27**(2), 289-92. (Journal IF: 6.407, Citations: 0)

### Invited lectures and seminars

Maria Soares was a moderator on the session on Cell Sorting Applications at the 13th Congress of the Flow Cytometry Iberian Society; Aveiro, Portugal, May 9-11, 2013.



### **Organisation of Conferences**

Maria Soares was a member of the Scientific Committee at the 13th Congress of the Flow Cytometry Iberian Society, Aveiro, Portugal, May 9-11, 2013.

### **Advanced teaching**

Maria Soares organized the Flow Cytometry Nanocourse for the IMM PhD program (June 17-21, 2013). Lecturers: Prof. Artur Paiva from Centro de Histocompatibilidade do Centro, Maria Soares (UCF), Ana Isabel Vieira (UCF IMM), Rui Gardner (UIC, IGC) and Andreia Mendonça (Enzifarma). This course focused on the Basic concepts of flow cytometry, instrument calibration/compensation and controls as well as flow cytometry potential applications and High Speed Cell Sorting. The course included theoretical and practical modules for “hands-on” instrument operation as well as data analysis using FlowJo.

Maria Soares lectured at the Oncobiology MSc Course from Faculdade de Medicina da Universidade de Lisboa. This included a theoretical lecture on Flow Cytometry and practical lab rotations at the Flow Cytometry Unit (July 2-4, 2013)

## HISTOLOGY SERVICE

### Major Objectives

Implemented in IMM on September 09, the Histology Service is devoted to provide technical and scientific support to all researchers from IMM, or other academical, medical or industry-related research teams, in the areas of histology and histopathology. We aim to continuously enlarge and optimize the services available at our Laboratory. We also provide tutorship in the design and implementation of any procedures not performed in the Service. Currently, the techniques available in the Histology Service include: processing of tissue samples and routine histochemical procedures; processing and visualization of samples for Transmission Electron Microscopy; processing of samples for Laser Capture Microdissection; automated immunohistochemistry.

### Head of Unit

Sandra Cristina Cana de Anjo Casimiro, PhD.

### Research Team

Ana Margarida Biscaia Fernandes dos Santos	Graduate	Technician
Andreia Lúcia do Nascimento Pinto	Master	Technician (started March)

### Keywords / Research Areas

Histology, Histopathology, Tissue processing.

### Major scientific achievements

From an average of 24 requisitions per month in 2009, the service received in average 76.7 requisitions/month in 2013, representing an increase of 219.4%. The users (Units) of the Histology Service were 13 in 2009 (all IMMers), and were 40 in 2013 (32 IMM Units/Pis and 8 external users). External users represented 13.8% in terms of total billing in the first semester of 2013.

The Histology Service tried from the beginning to fulfil the needs of the researchers in terms of available services. From beginning we offered the basic histopathology techniques, like tissue processing, embedding (OCT, paraffin), decalcification, sectioning (microtome and cryostat), and staining (H&E and special stains). In 2010 we implemented the protocols for TEM, with visualization at IGC; in 2012 we established a protocol with HPP for the use of a new electron

microscope, and implemented LCM processing, and automated immunohistochemistry; since 2013 we offer veterinary pathology services.

#### **Recent Most Relevant Publications**

Casimiro S, Luis I, Fernandes A, Pires R, Pinto A, Gouveia AG, Francisco AF, Portela J, Correia L, and Costa L (2012) Analysis of a bone metastasis gene expression signature in patients with bone metastasis from solid tumors. *Clin Exp Metastasis* **29**, 155. (Journal IF: 3.524, Citations: 2)

## IMM BIOBANK

### Major Objectives

The vision of the Biobanco-IMM, Lisbon Academic Medical Centre, is to position itself as a major member of the European Network of Biobanks within the next 5 years, offering excellent opportunities for translational and clinical research. Our mission is to promote and facilitate biomedical research that will lead to the identification of new diagnostic and prognostic tests, as well as to new therapeutic targets. We have set as our goals to collect a wide variety of high quality human biological samples associated with detailed relevant clinical information and to promote its use for research purposes based on scientific and ethical criteria.

### Head of Unit

João Eurico Fonseca, MD/PhD - Professor, FMUL

### Research Team

Ana Filipa Rodrigues Lopes	Master	Lab manager
Ana Filipa Soares Garcia	Graduate	Technician (started October)
Ana Rita Cascão Rodrigues	PhD	Technician
Ana Sofia Zhao	Master	Technician
Ângela Maria Cerqueira Coelho Afonso	Graduate	Technician
Joana Ribeiro Caetano Lopes	PhD	Post-doctoral Investigator
Joaquim Miguel Polido Pereira	No degree	Investigator
Vanessa Gonçalves Silva	Graduate	MSc Student

### Keywords / Research Areas

Biobanks, samples and clinical information.

### Major scientific achievements

- Collected 7 thousand donors and 60 thousand samples across 20 collections;
- More than 1500 Samples from the Biobanco-IMM CAML have been requested for research projects and contributed to 8 scientific papers;

- Organization of meetings in all medical departments of the Lisbon Academic Medical Centre, 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 infrastructures (cell culture facilities);
- Launch of the national biobank concept (Biobanco.pt), based on a network of biobanks with a common information system.

### Recent Most Relevant Publications

Fonseca JE. (2013) Biobanco-IMM CAML: a case study. . *Acta Med Port* **26**:312-314. (Journal IF: 0.679, Citations: 0)

### Other Projects

2012/2013 Collection of samples from patients with early arthritis. Coordinator: Rita Cascão. (No Funding)

2013/2014 Collection of samples from young patients with auto-inflammatory diseases. Coordinator: Filipa Ramos. (No Funding)

2013/2014 Collection of samples from patients with Bipolar Disorders. Coordinator: Maria Luisa Figueira. (No Funding)

2013/2014 Collection of samples from transplanted patients.. Coordinator: João Lacerda. (No Funding)

2012/2013 Collection of samples from rheumatic diseases patients.. Coordinator: Jaime Branco. (No Funding)

2012/2014 Collection of femoral epiphysis, including bone and cartilage, from hip replacement surgery patients.. Coordinator: Helena Canhão. (No Funding)

2012/2014 Collection of samples from controls, based on a questionnaire and interviewed by a physician.. Coordinator: Biobanco-IMM CAML. (No Funding)

2012/2013 Collection of samples from patients with endocrinology disorders.. Coordinator: Sónia do Vale. (No Funding)

2012/2013 Collection of samples from a national epidemiological study on rheumatic diseases. A prospective follow-up is ongoing.. Coordinator: Jaime Branco. (No Funding)

2012/2013 Collection of samples from patients with heart failure.. Coordinator: Dulce Brito.(No Funding)

2012/2013 Collection of samples from patients with brain metastasis.. Coordinator: Cláudia Faria. (No Funding)

2012/2013 Collection of samples from patients with neurological movement disorders, including Parkinson's disease.. Coordinator: Joaquim Ferreira.(No Funding)

2012/2013 Collection of samples from patients with rheumatoid arthritis. Link with detailed clinical data on Reuma.pt.. Coordinator: Helena Canhão.(No Funding)

2012/2013 Collection of samples from patients with brain tumors. Coordinator: Claudia Faria.(No Funding)

2012/2013 Collection of samples from patients with Spondyloarthritis. Link with detailed clinical data on Reuma.pt.. Coordinator: Elsa Sousa.(No Funding)

2012/2013 Collection of samples from patients with stroke, and controls.. Coordinator: Ruth Geraldes, Sofia Oliveira.(No Funding)

2012/2013 Collection of samples from patients with rheumatic diseases. Coordinator: Helena Canhão.  
(No Funding)

2012/2013 Collection of samples from patients with rheumatic diseases.. Coordinator: Elsa Sousa.  
(No Funding)

2012/2013 Collection of samples from gastrointestinal tract cancer and breast cancers.. Coordinator: Luis Costa. (No Funding)

### **Invited lectures and seminars**

Outreach sessions across all Hospital de Santa Maria departments, University of Lisbon Medical School, institutes and IMM Units.

Caetano-Lopes J. “Biobanco-IMM CAML: the first steps”. 3º Encontro de Biologia Molecular em Saúde, Escola Superior de Saúde Egas Moniz, Caparica, Portugal. March 16, 2013

Seminar “The experience of the National DNA Bank Carlos III” by Dr. F Javier Garcia, hosted by Biobanco-IMM CAML. April 16, 2013

Afonso A. “Biobanco-IMM CAML, os primeiros passos”. Associação Portuguesa de Doentes com Immunodeficiências Primárias meeting, Belém, Portugal. May 18, 2013

Fonseca JE. “O Biobanco-IMM CAML como fulcro do desenvolvimento da investigação médica na pediatria”. Congresso Nacional de Pediatria. October 4, 2013

Fonseca JE. “Biobanco-IMM CAML: uma oportunidade para todos?”. XIII Congresso Nacional da Sociedade Portuguesa de Menopausa. October 17, 2013.

### **Communications in International Conferences**

Visiongain’s 4th Biobanking UK conference, Biobanco-IMM: An overview. London, England. June 20-21, 2013.

Biobanco-IMM: An overview. 3rd Global Cancer Genome Consortium symposium, Lisbon, Portugal. September 18-20, 2013.

Biobanco-IMM: An overview. ESBB congress, Verona, Italy. October 9-11, 2013 (No Funding)

### **Communications in National Conferences**

Biobanco-IMM os primeiros passos. 3º Encontro de Biologia Molecular em Saúde, Escola Superior de Saúde Egas Moniz, Caparica, Portugal. March 15-16, 2013.

### **Internationalisation**

We are now participating in several international networks and samples from the Biobanco-IMM CAML have started to be requested for research projects. Up until now, 1520 samples have left the Biobanco-IMM CAML mostly through collaboration with research institutions:

- Institute of Clinical Medicine, Department of Medicine, Biomedicum Helsinki, Helsinki, Finland;
- Neurology Department, Hospital de Santa Maria, Lisbon, Portugal;
- Genomic Oncology department, Parque Tecnológico de Ciencias de la Salud and Unit of Clinical and Laboratory of Hematology and Transfusion, Unidad de Gestión Clínica de Hematología y Hemoterapia, Granada, Spain;
- Laboratório de Biologia Molecular do Hemocentro de Botucatu, Faculdade de Medicina, UNESP, São Paulo, Brazil;
- Labatt Brain Tumour Research Centre, The Hospital for Sick Children, Toronto and RS McLaughlin Professor and Chair of the Department of Surgery, University of Toronto, Canada.

### **Advanced teaching**

Biobanco-IMM CAML has collaborated in a master course on oncobiology (June-July 2013) by contributing with technical skills on molecular biology.

For the period of 2013/2014 Biobanco-IMM CAML has two masters students that will contribute to the development of improved methods for sample quality control.

## ZEBRAFISH FACILITY

### Major 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.

### Research Team

Aida Gonçalves Lino Barros	No degree	Technician
Lara Carvalho	Master	Lab manager
Sara Mulenas Sá de Matos	Master	Technician (started May) (left November)

### Keywords / Research Areas

Embryonic development, Regeneration, Angiogenesis, Neuropathology, Drug screening.

### Major scientific achievements

- A major upgrade in our facility was the acquisition of a new room specific for the production of live food for the zebrafish;
- We generated a Casper-Fli-GFP line for the use of the users;
- We set up a cell transplantation technique in embryos;
- We optimised an angiography technique in adults;
- The facility staff followed and gave support to the generation of the first zebrafish mutants using the TALEN technology.

### Recent Most Relevant 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), 4656-4665. (Journal IF: 7.09, Citations: 2)



Sousa S., Afonso N., Bensimon-Brito A., Fonseca M., Simões M., Leon J., Roehl H., Cancela M.L., Jacinto A. (2011) Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. *Development* **138**(18), 3897-905. (Journal IF: 7.09, Citations: 16)

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* **6**(7), e22820. (Journal IF: 4.092, Citations: 5)

Vala, I., Martins, L., Imaizumi, N., Nunes, R., Rino, J., Kuonen, F., Carvalho, L., Rüegg, C., Grillo, I., Barata, J., Mareel, M. and Santos S.C.R. (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *PLoS ONE* **5**(6), e11222. (Journal IF: 4.092, Citations: 16)

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* **137**(21), 3625-32. (Journal IF: 7.09, Citations: 26)

#### Publications in peer review Journals

Pascoal P., de Lima J.E, Leslie J.D., Hughes S.M. and Saúde L. (2013) Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. *PLoS ONE* (2013) **8**(6):e68021. (Journal IF: Citations: 0)

de Oliveira S., Reyes-Aldasoro C.C., Candel S., Renshaw S.A., Mulero V., and Calado A. (2013) Cxcl8 (IL-8) mediates neutrophil recruitment and behavior in the zebrafish inflammatory response. *J. Immunol.* **190**(8):4349-59. (Journal IF: 5.520, Citations: 2)

#### Communications in International Conferences

Sofia de Oliveira, Azucena López-Muñoz, Sergio Candel, Pablo Pelegrín, Ângelo Calado and Victoriano Mulero, ATP and Calcium modulate the inflammatory response via Duox 1 activation and hydrogen peroxide release, Zebrafish Disease Models 6, Murcia, Spain 2013. (oral communication)

Sergio Candel, Sofia de Oliveira, Diana Garcia-Moreno, Raquel Espin, Maria L Cayuela, Sylwia D Tyrkalska, Stephen A Renshaw, José Meseguer, Maria P Sepulcre and Victoriano Mulero, TNFR2 deficiency triggers skin inflammation in the zebrafish via the production of H<sub>2</sub>O<sub>2</sub> and the Activation of the NF- $\kappa$ B signaling pathway, Zebrafish Disease Models 6, Murcia, Spain 2013. (Oral communication)

ATP and Calcium modulate the inflammatory response via Duox 1 activation and hydrogen peroxide release, Sofia de Oliveira, Azucena López-Muñoz, Sergio Candel, Pablo Pelegrín, Ângelo Calado and Victoriano Mulero, Semmelweis Symposium 2013, Budapest, Hungary 2013. (Oral communication)

Identification of new therapeutic targets for the treatment of skin inflammatory diseases using the zebrafish, Sergio Candel, Sofia de Oliveira, Diana Garcia-Moreno, Azucena López-Muñoz,

Raquel Espin, Maria L Cayuela, Sylwia D Tyrkalska, Stephen A Renshaw, José Meseguer, Maria P Sepulcre and Victoriano Mulero, Semmelweis Symposium 2013, Budapest, Hungary 2013 (Poster Presentation)

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Figueira, A.M. and Saúde, L. The role of Mesogenin1 in the dynamics of movement and differentiation of mesoderm progenitor cells. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. 2nd Meeting of the Portuguese Society for Developmental Biology (SPBD), Lisbon, Portugal, October 24-26, 2013. (Poster presentation)

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. Molecular Biology in Portugal and EMBL, Lisbon, Portugal, July 18, 2013. (Poster presentation)

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. EMBO Young Scientists' Forum, Lisbon, Portugal, July 15-16, 2013. (Poster presentation)

Ribeiro, A. and Saúde, L. Uncovering cellular mechanisms of spinal cord regeneration in zebrafish. 8º Encontro da Sociedade Portuguesa de Células Estaminais e Terapia Celular.

Universidade do Algarve, Faro, May 9-10, 2013. (Poster presentation)

Mendes, R.V., Martins, G.G. and Saúde, L. N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. Making and breaking the left-right axis: laterality in development and disease. International Society of Developmental Biologists Congress, Cancun, Mexico, June 16-20, 2013. (Poster presentation)

Azevedo A.S., Sousa S., Jacinto A. and Saúde L. An amputation resets positional information to a proximal identity in the regenerating zebrafish caudal fin. 5th Strategic Conference of Zebrafish Investigators, Pacific Grove, USA, January 19-23, 2013. (Poster presentation)

### **Communications in National Conferences**

Fernandes S.F., Fior R., Gama-Carvalho M. and Saúde L. Quaking A - a post-transcriptional regulator of early patterning in zebrafish. VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Pinto R.A., Almeida-Santos J. and Saúde L. Uncover the molecular mechanism downstream of Dmrt2a/Terra, a transcription factor that coordinates symmetry versus asymmetry along the left-right axis. VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Vaz R, Chapela D, Afonso N, Outeiro TF, Sousa S. Zebrafish as an in vivo model system for the identification of novel therapeutic approaches for Parkinson's disease. VII IMM/CAML PhD Students meeting, Lisbon, Portugal, December 5-6, 2013. (Poster presentation)

Pascoal, S., Esteves de Lima, J., Serrano R. and Saúde L. Hh signaling and cilia are getting divorced during regeneration: gossip or fact? 1st Postdoctoral Symposium, 10th anniversary of IMM, Lisboa, Portugal, October 17, 2013. (Oral presentation)

Pascoal, S., Esteves de Lima, J., Leslie, J.D., Hughes, S.M., Saúde, L. Notch signalling is required for the formation of structurally stable muscle fibres in zebrafish. "Development in Action" – DIA Meeting, Oeiras, Portugal, June 2013. (Oral presentation)

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

Benedict Both was awarded The Best GAPIC Project. December 11, 2013.

### **Advanced teaching**

Carvalho L., Lectured the course on Laboratory Animal Science at IMM, Lisbon, 2013

### **Science and society**

Carvalho L, Barros A, Experimental Biochemistry free Course - A guided visit to the fish facility, February 2013.

Carvalho L, Barros A, Candidates`day - A guided visit to the fish facility, April 2013.

Afonso N, Japanese pharmaceutical - A guided visit to the fish facility, June 2013.

Saude L, Visit from the president of FAPESP, October, 2013

### **Msc theses completed**

José Almeida Santos (2013) Molecular tools to dissect the role of Dmrt2a and Dmrt2b in left-right axis formation in zebrafish. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa. Supervisor: Leonor Saúde.

Margarida Figueira (2013) The role of Mesogenin1 in the dynamics of movement and differentiation of mesoderm progenitor cells. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Leonor Saúde.

Lara Carvalho (2013) Control of somite number and size in zebrafish upon reduction of progenitors. Faculdade de Ciências e Tecnologia da Universidade do Algarve. Supervisors: Rita Fior, Leonor Saúde.

## COMPANIES

### GENOMED

#### Major Interests / Objectives

GenoMed is a spin-off company of IMM created in 2004. The mission of GenoMed is to provide cutting-edge technology transfer services relevant for medical applications. Currently, GenoMed offers over 350 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, Oftalmology, Otorhinolaryngology, Pediatrics, Urology and Pharmacogenetics. Additionally, GenoMed provides parental and ancestry DNA testing.

#### Head of Unit

Teresa Cristina de Almeida Porta Nova, Master.

#### Research Team

Alexandra Manuela Lemos Oliveira	Graduate	MSc Student (started October)
Ana Aidé Martins Marques Flores	Undergraduate	Administrative
Ana Carla Almeida da Silva e Sousa	Graduate	Technician
Ana Margarida Trindade dos Santos Coutinho	PhD	Technician
André Madeira Janeiro	Graduate	Technician
Catarina Sofia Urbano Silveira	Master	Technician
Fabíola Carina Costa Paulo Faria da Rosa	Undergraduate	Administrative
Gabriel Miltenberger Miltényi	MD/PhD	Principal Investigator
Hélia Filipa Lourenço Guerreiro	Graduate	Technician
Inês Filipa Rodrigues da Silva	Master	Technician
Paula Costa	Graduate	Technician
Paula Cristina Maximino Mimoso	Graduate	Technician

Sara Sofia Santos Malveiro Gongó Carvalhêda	Graduate	Technician
Sónia de Jesus Ramalho Proença dos Santos	PhD	Technician
Sónia Maria Lopes de Matos	Master	Technician
Viviana Alexandra Sequeira Martins	Graduate	Investigator (started November)

### Major scientific achievements

Currently, GenoMed offers over 350 different tests that are used in diagnosis, prognosis and therapeutic follow up.

### Recent Most Relevant Publications

Pires C, Coelho M, Valadas A, Barroso C, Pimentel J, Duyckaerts C, de Mendonça A, Verdelho A, Miltenberger-Miltenyi G (2013) Phenotypic Variability of Familial and Sporadic Progranulin p.Gln257ProfsX27 Mutation. *Journal of Alzheimer's Disease* **37**(2), 335-42. (Journal IF: 4.170, Citations: 0) doi: 10.3233/JAD-130146.

Madruza Dias J, Rosa R, Perpétuo I, Rodrigues A, Janeiro A, Costa MM, Gaião L, Pereira da Silva J, Fonseca JE, Miltenberger-Miltenyi G (2013) Pachydermoperiostosis in an African patient caused by a Chinese/Japanese SLCO2A1 mutation – case report and review of literature. *Seminars in Arthritis and Rheumatism* Sep 5, (Journal IF: 3.806, Citations: 0) pii: S0049-0172(13)00163-7. doi: 10.1016/j.semarthrit.2013.07.015.

Dijkstr J.R., Boers J.E., Diebold J., Hirschmann A, Heideman D.A.M., Hoefler G., Miltenberger-Miltenyi G., Richman S.D., Rouleau E., Tejpar S., van Krieken J.H.J.M (2013) KRAS mutation analysis on low percentage of colon cancer cells: the importance of quality assurance. *Virchows Archiv* **462**(1), 39-46. (Journal IF: 2.676, Citations: 1)

### Other Projects

2008/present: Study of Ras mutations in tumorous tissue of colorectal cancer. Merck Funding. Coordinators: Gabriel Miltenberger-Miltenyi

2010/---- 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. Ammount: € 18.000,00

2011/---- 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. Ammount: € 16.000,00

2012/---- 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. Coordinator: Gabriel Miltenberger-Miltenyi. Amount: € 18.000,00

2010/---- Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease. Calouste Gulbenkian Foundation. Participant::Gabriel Miltenberger-Miltenyi. Coordinator PI: N.C. Santos.

2011/---- Investigação translacional em Alzheimer. Quadro de Referência Estratégico Nacional. Participant: Gabriel Miltenberger-Miltenyi. Coordinator PI: S. Corte-Real.

2012/---- Biomarkers for Alzheimer's disease and Parkinson's disease (BIOMARKADO). European research projects for the optimisation of biomarkers and harmonisation of their use between clinical centers. Joint Programming in Neurodegenerative Disease. Participant: Gabriel Miltenberger-Miltenyi. Coordinator PI: A. de Mendonça.

2013/---- Randomized, Double-blind, Placebo-controlled Phase 3 Study of Ibrutinib, a Bruxton'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: Sónia Santos. Coordinator PI: João Raposo.

2013/---- Analysis of CD34+ peripheral blood cells by FISH as cytogenetic monitoring of MDS. Celgene. Coordinator: Sónia Santos. Coordinator PI: Maria João Costa. Amount: € 14.460,00

2012/2014 Diagnosis and monitoring of Chronic Myeloid Leukemia (CML) patients: Molecular and Cytogenetic analysis. Bristol-Myers Squibb.. Coordinator: Sónia Santos, Sónia Matos. Coordinator PI: José Alves do Carmo.

### Publications in peer review Journals

van der Zee J, Gijssels I, Dillen L, Van Langenhove T, Theuns J, Engelborghs S, Philtjens S, Vandenbulcke M, Slegers K, Sieben A, Bäumer V, Maes G, Corsmit E, Borroni B, Padovani A, Archetti S, Pernecky R, Diehl-Schmid J, de Mendonça A, Miltenberger-Miltenyi G, Pereira S, Pimentel J, Nacmias B, Bagnoli S, Sorbi S, Graff C, Chiang HH, Westerlund M, Sanchez-Valle R, Llado A, Gelpi E, Santana I, Almeida MR, Santiago B, Frisoni G, Zanetti O, Bonvicini C, Synofzik M, Maetzler W, Vom Hagen JM, Schöls L, Heneka MT, Jessen F, Matej R, Parobkova E, Kovacs GG, Ströbel T, Sarafov S, Tournev I, Jordanova A, Danek A, Arzberger T, Fabrizi GM, Testi S, Salmon E, Santens P, Martin JJ, Cras P, Vandenbergh R, De Deyn PP, Cruts M, Van Broeckhoven C, van der Zee J, Gijssels I, Dillen L, Van Langenhove T, Theuns J, Philtjens S, Slegers K, Bäumer V, Maes G, Corsmit E, Cruts M, Van Broeckhoven C, van der Zee J, Gijssels I, Dillen L, Van Langenhove T, Philtjens S, Theuns J, Slegers K, Bäumer V, Maes G, Cruts M, Van Broeckhoven C, Engelborghs S, De Deyn PP, Cras P, Engelborghs S, De Deyn PP, Vandenbulcke M, Vandenbulcke M, Borroni B, Padovani A, Archetti S, Pernecky R, Diehl-Schmid J, Synofzik M, Maetzler W, Müller Vom Hagen J, Schöls L, Synofzik M, Maetzler W, Müller Vom Hagen J, Schöls L, Heneka MT, Jessen F, Ramirez A, Kurzwelly D, Sachtleben C, Mairer W, de Mendonça A, Miltenberger-Miltenyi G, Pereira S, Firmo C, Pimentel J, Sanchez-Valle R, Llado A, Antonell A, Molinuevo J, Gelpi E, Graff C, Chiang

HH, Westerlund M, Graff C, Kinhult Ståhlbom A, Thonberg H, Nennesmo I, Börjesson-Hanson A, Nacmias B, Bagnoli S, Sorbi S, Bessi V, Piaceri I, Santana I, Santiago B, Santana I, Helena Ribeiro M, Rosário Almeida M, Oliveira C, Massano J, Garret C, Pires P, Frisoni G, Zanetti O, Bonvicini C, Sarafov S, Tournev I, Jordanova A, Tournev I, Kovacs GG, Ströbel T, Heneka MT, Jessen F, Ramirez A, Kurzweily D, Sachtleben C, Mairer W, Jessen F, Matej R, Parobkova E, Danel A, Arzberger T, Maria Fabrizi G, Testi S, Ferrari S, Cavallaro T, Salmon E, Santens P, Cras P; European Early-Onset Dementia Consortium. A pan-European study of the C9orf72 repeat associated with FTL: geographic prevalence, genomic instability and intermediate repeats. *Human Mutat* 2013 Feb;**34**(2):363-73. (Journal IF: 5.213, Citations: 14)

### **Invited lectures and seminars**

Miltenberger-Miltenyi, G. A Genética da Doença de Gaucher. At Simpósio doença de Gaucher em foco. Quinta das Lágrimas, Coimbra, Portugal. September 28, 2013.

Miltenberger-Miltenyi, G. Aspectos moleculares das demências. XXV Congresso Brasileiro De Genética Médica. Florianópolis – SC, Brazil. June 11-15, 2013.

Miltenberger-Miltenyi, G. Desafios das novas regras europeias referentes aos ensaios clínicos e farmacovigilância. II Reunião anual da Revista Portuguesa de Farmacoterapia. Oeiras, Portugal. June 4, 2013.

Miltenberger-Miltenyi, G. Os avanços da Genética no diagnóstico, tratamento e prevenção de Doenças Genéticas e Hereditárias. Palestra internacional sobre avanços genéticos no diagnóstico, tratamento e prevenção de doenças. 1º Encontro Médico RDOVIVER. Hospital RDOVIVER, Ribeirão Preto, Brazil. October 9, 2013.

Miltenberger-Miltenyi, G. “O efeito Angelina” – Os avanços da Genética no diagnóstico e tratamento do câncer – medicina personalizada. Palestra internacional sobre avanços genéticos no diagnóstico, tratamento e prevenção de doenças. 1º Encontro Médico RDOVIVER, Hospital RDOVIVER, Ribeirão Preto, Brazil. October 9 2013.

### **Communications in International Conferences**

G. Miltenberger-Miltenyi. Casa dos Marcos – From bed to bench in rare diseases. 7th Cornelia de Lange World Conference. Buenos Aires, Argentina. November 14-16, 2013. (Oral presentation)

### **Communications in National Conferences**

Pricila Bernardi, Ines Silva, Francisco J.Enguita, Adrian Danek, Benedikt Bader, Katia Lin, Gabriel Miltenberger-Miltenyi. Novel heterozygous mutation in a Brazilian chorea- acanthocytosis case – pitfalls of diagnostics. 4th Congress of the SPDMov - Sociedade Portuguesa das Doenças do Movimento. Vimeiro, Portugal. March 22-24, 2013. (Oral presentation)



Gabriel Miltenberger-Miltenyi, Leonor Correia Guedes, Tiago Mendes, Raquel Pinho, Miguel Coelho, Tiago Mestre, Anabela Valadas, Patrícia Lobo, Dulce Neutel, Mário Miguel Rosa, Joaquim J. Ferreira, Tiago Outeiro. Slow versus Rapid Progression Parkinson's Disease: Molecular Determinants and Biomarkers. 4th Congress of the SPDMov - Sociedade Portuguesa das Doenças do Movimento. Vimeiro, Portugal. March 22-24, 2013. (Oral presentation)

Gabriel Miltenberger-Miltenyi, Ana Rita Sandes, Leonor Real Mendes, Catarina Silveira, Margarida Almeida, F. Coelho Rosa. Caracterização genética da síndrome nefrótica corticorresistente em doentes portugueses. Encontro Renal (Congress of the Portuguese Society of Nephrology), Vilamoura, Portugal. April 11-13, 2013. (Poster presentation)

Gabriel Miltenberger-Miltenyi, Fernanda Carvalho, Helena Viana, Ana Rita Santos, Carina Ferreira, Laia Ejarque, Elisabet Ars, Edgar Almeida, Joaquim Calado. Lessons in medullary cystic kidney disease – pitfalls in diagnostics. Encontro Renal (Congress of the Portuguese Society of Nephrology), Vilamoura, Portugal. April 11-13, 2013. (Poster presentation)

Brito, D, Moldovan, O, Miltenberger-Miltenyi, G, Silva, D, Almeida, A, Nunes-Diogo, A, Madeira, H. Phenotypic and prognostic diversity of cardiac troponin T gene mutations in hypertrophic cardiomyopathy patients. XXXIV Congresso Português de Cardiologia, Vilamoura, Portugal. April 28-30, 2013. (Poster presentation)

Brito, D, Moldovan, O, Miltenberger-Miltenyi, G, Silva, D, Almeida, A, Nunes-Diogo, A, Madeira, H. Cardiac troponin T gene mutations: genotype-phenotype correlations in a Portuguese population with hypertrophic cardiomyopathy. XXXIV Congresso Português de Cardiologia, Vilamoura, Portugal. April 28-30, 2013. (Poster presentation)

Sousa AC, Janeiro A, Miltenberger-Miltenyi, G. Five year experience on diagnostic K-ras testing at GenoMed - Instituto de Medicina Molecular. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal. September 18-20, 2013. (Poster presentation)

Coutinho AM, Silva I, Miltenberger-Miltenyi, G. Molecular genetic diagnostics of BRCA1 and BRCA2 mutations in breast cancer - five year experience of GenoMed - Instituto de Medicina Molecular. 3rd Global Cancer Genomics Consortium Symposium, Lisbon, Portugal. September 18-20, 2013 (Poster presentation)

Factores citogenéticos e moleculares preditivos de resposta em doentes com LMC tratados com Imatinib em primeira linha. A. Ferreira; M. Neves; S. Matos; S. Santos; S. Malveiro; P. Costa; C. Lopes; S. Valle; G. Esteves; B. Polo; J. Raposo; M. Costa; L. Guerra; J. Alves do Carmo. Reunião Anual da Sociedade Portuguesa de Hematologia 2013, Porto, November 14-16, 2013 (Oral Communication)

Monitorização citogenética de Síndrome Mielodisplásico em células CD34+ de sangue periférico – resultados preliminares. A. Ferreira, M. Costa, S. Santos, E. Espada, J. Alves do Carmo. Reunião Anual da Sociedade Portuguesa de Hematologia 2013, Porto, November 14-16, 2013 (Poster presentation)

Impact of additional cytogenetic aberrations and variant Philadelphia translocations at diagnosis in CML patients treated with imatinib as first-line therapy: a Portuguese center series. A. Ferreira; M. Neves; S. Santos; S. Matos; C. Lopes; S. Valle; L. Guerra; J.A. Carmo ESH-iCMLf International Conference on CML – Biology and Therapy, Estoril, Portugal. September 26-29. (Poster presentation)

BCR-ABL mutation analysis in an Portuguese series of chronic myeloid leukemia patients A. Ferreira; S. Santos; S. Matos; C. Lopes; L. Guerra; J.A. Carmo ESH-iCMLf International Conference on CML – Biology and Therapy, Estoril, Portugal. September 26-29, 2013. (Poster presentation)

BCR-ABL(p210) fusion transcript type: is it a prognostic factor? A. Ferreira; S. Matos; S. Santos; S. Malveiro; P. Costa; M. Neves; L. Guerra; J. Alves do Carmo. ESH-iCMLf International Conference on CML – Biology and Therapy, Estoril, Portugal, September 26-29, 2013. (Poster presentation)

### Internationalisation

The BIOMARKAPD project is an international multicenter project of the Joint Programme in Neurodegenerative Disease Research initiative (JPND) and including various Working packages (WPs) on the research of Alzheimer's disease (AD) and Parkinson's Disease (PD).

Genomed is participating in the BIOMARKAPD project in collaboration with the Neuroscience group of IMM (coordinator: Alexandre Mendonça).

The aim of BIOMARKAPD is to standardise the assessment of established and new fluid biomarkers for AD and PD. To this end we will:

- Create and validate detailed standardised operating procedures for sample collection, storage, analytical procedures and clinical use of biomarkers for AD and PD.
- Create an assay qualification algorithm specifying technical characteristics that must be fulfilled to employ the assay in AD and PD biomarker studies and in clinical routine and trials.
- Create a network of harmonised laboratories around Europe and also implement a certification system for laboratories and technicians with yearly hands-on training events and external quality control surveys four times per year.
- Define a workflow for how new biomarkers can be developed from proof-of concept studies to established biomarkers with reference limits, cut-offs and controlled confounders.
- Build a biobank for validating new biomarker candidates.
- Establish certified reference materials for biomarker measurements.

This is by far the most ambitious AD and PD biomarker standardisation programme to date, covering whole Europe, as well as one Canadian site. The harmonisation of biomarker-related procedures across Europe will facilitate clinical trials and allow for general implementation of the newly proposed diagnostic guidelines for AD and new diagnostic approaches for PD in clinical routine.

### Prizes, honours and awards

Miltenberger-Miltenyi, G. Annual Scientific Award of the Portuguese Society of Nephrology, “Estudo de associações genótipo-fenótipo na síndrome nefrótica corticorresistente – descrição de seis novas mutações.” Encontro Renal, Congress of the Portuguese Society of Nephrology, Vilamoura, Portugal. April 11-13, 2013.

### Advanced teaching

Miltenberger-Miltenyi, G. O Diagnóstico Genético rotina das Doenças Hereditárias. Seminar for students of Ciências Biomédicas as part of the discipline Genética Humana at Universidade de Algarve, Faro, Portugal. December 4, 2013.

Miltenberger-Miltenyi, G. What is new in cerebrospinal fluid biomarkers? New Perspectives in the Study of Age-related Cognitive Decline (Symposium). Master/PhD in Neurosciences - Cognitive Deterioration in Ageing and Dementia (Module 10), Faculdade de Medicina da Universidade de Lisboa, Portugal. April 3, 2013.

Miltenberger-Miltenyi, G. Doenças metabólicas ligadas ao cromossoma X. Mestrado em doenças metabólicas e do comportamento alimentar. Programa do Módulo Genética Faculdade de Medicina da Universidade de Lisboa, Portugal. 2013

### Science and society

Participant: Gabriel Miltenberger-Miltenyi

- EURORDIS Membership Meeting; May 30 – June 1, 2013, Dubrovnik, Croatia.
- Fabry Masterclass V. Madrid, Spain. May 17-18, 2013.
- European Symposium on Lysosomal Storage Disorders – ESLSD, Brussels, Belgium. June 5-6, 2013
- International Summer School "Rare Disease and orphan drug registries", Rome, Italy. September 16-20, 2013.
- 2nd International Workshop on Rare Disease and orphan drug registries, Italian National Institute of Health – Rome, Italy. October 21-22, 2013.

### Msc theses completed

Catarina Sofia Urbano Silveira (2013) Nephrotic syndrome in childhood: genotype - phenotype association studies and screening for novel mutations. Faculdade de Ciências da Universidade de Lisboa Supervisor: G. Miltenberger-Miltenyi.



## **LYMPHACT S.A.**

### **Major interests / Objectives**

Lymphact is a biopharmaceutical start-up focused on developing innovative personalized 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.

### **Keywords/Research Areas**

Cellular Therapies, Immunology, Oncology, Immunotherapies, Start-up, Business Development.

### **Major achievements**

- Initiated Regional Phase of our patent;
- Initiated partnership with Instituto Português de Oncologia;
- Initiated partnership with Instituto Superior Técnico;
- Initiated partnership with Universidade de Évora.

### **Patents/prototypes**

Licensee Patent- PCT IB2012/052545



## 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	Technician
Laura Felício, MSc	Technician
Alexandra Maralhas, BSc	Consultant Lab Manager

### Keywords/Research Areas

Human induced pluripotent stem cells; disease modelling; primary cultures of human fibroblasts

### Major achievements

Consolidation of the QREN project initiated in 2012: development of an optimized protocol for the establishment of fibroblast culture from human skin biopsy and subsequent reprogramming into hiPSCs.

Initiation of a second project funded by QREN dedicated to the exploration of potential markets, and internationalization of the company and its products/services.

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.

It is ongoing the implementation of the Integrated Management Systems (IMS) that comprises the certification in Quality (ISO 9001:2008), Environment (ISO 14001:2004), Health and Safety (ISO 18001:2007).

### **Ongoing Research Projects**

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

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**

Nunes, F. Regenerative Medicine Curricular Unit of the Master Degree in Biomedical Technologies, FMUL, Lisbon, Portugal, May 27, 2013.

### **Advanced teaching**

Nunes, F. lectured a seminar integrated in the Regenerative Medicine Curricular Unit of the Master Degree in Biomedical Technologies, FMUL, Lisbon, Portugal, May 27, 2013.



**TECHNOPHAGE, SA****Major Interests / Objectives**

TechnoPhage S.A. is a biopharmaceutical company engaged in the R&D of therapeutics and diagnostics in three main programs, managed by different Business Units:

1) TechnoPhage: R&D of novel bacteriophage-based products, for the treatment, diagnosis and prevention of bacterial infections.

2) TechnoAntibodies: R&D of recombinant single domain antibody fragments (sdAbs), for therapeutic and diagnostic of human diseases.

3) TechnoZeb: Innovative approaches to drug discovery by using the zebrafish as an in vivo model system.

The strategy of the company is to use these platforms to identify new therapeutic molecules in various areas. Molecules are taken into in vivo studies to provide data on efficacy and safety. Partnering deals are sought for preclinical or clinical development or both.

**Head of Unit**

Miguel Ângelo da Costa Garcia, PhD, MBA, TechnoPhage, SA.

**Research Team**

Ana Raquel Martins Barbosa	Master	Investigator
Bruno Miguel Parreiras Gimbra	Graduate	Accountant
Cátia Sofia Simões Família	Graduate	MSc Student (left in December)
Clara Isabel Rodrigues Leandro	Master	Investigator
Daniela Sofia Moreira Proença	Master	PhD Student
Diana Sofia Chapela Duarte Pires	Master	Technician
Frederico Nuno C. Aires da Silva	PhD	Principal Investigator
Joana Henriques Ministro	Master	Investigator
João João Duarte Alves Mendes	Graduate	PhD Student
João Miguel Sotinho Oliveira	Master	Administrative (started in October)
Mariana Lima de Faria Trigo Pereira	Master	Project manager (started in October)
Nuno Miguel Duarte Afonso	PhD, MBA	Manager
Patricia Alexandra Norte Ferreira Pinto	No degree	Technician

Patrícia Cavaco Silva Montez	PhD	Director
Pedro Manuel Correia Canhão	Graduate	MSc Student
Rita Leitão Landeiro Vaz	Master	PhD Student
Sara Cristina Mauricio de Sousa	Graduate	Investigator
Sara Ferreira Llorente Grancho Lourenço	Master	Investigator
Sofia Volker Corte-Real	PhD	Project manager
Soraia Rafaela Santiago de Oliveira	PhD	Investigator (started February)

### Keywords / Research Areas

R&D of therapeutics for human disease, Bacteriophage Therapeutics, Small domain Antibodies, Zebrafish models for in vivo screening.

### Major scientific achievements

Mar 2013- Manuscript on animal efficacy for bacteriophage cocktail for the treatment diabetic cutaneous wounds accept

May 2013- TechnoPhage selected by UK Trade and Investment for entry as a National Champion in the European Business Awards 2013-14.

Jun 2013 - TechnoPhage invited to present at APIFARMA.

Oct 2013 - Benefits for the SME - TA101 GOCLIN European funded project for the development of an innovative product for the treatment of rheumatoid arthritis – 1,7M€ total budget

Oct 2013 - Patent Granted to TechnoPhage partner company Lusomedicamenta Antibacterial Phage Peptides and Methods of Use Thereof (USPTO); 22 October 2013; Patent No: US 8,563,504 B2 .

Oct 2013 -Patent Granted to TechnoPhage; Engineered Rabbit Antibody Variable Domains and Uses Thereof (Singapore); 11 October 2013; Patent No: 156768 [WO 2008/136694]

Oct 2013 - TechnoPhage invited to present Rheumatoid Arthritis therapeutics development programme at ANDAR symposium at Gulbenkian Foundation, Lisbon, Portugal.

### Recent Most Relevant Publications

João J. Mendes, MD<sup>1,2</sup>; Clara Leandro, MSc<sup>1</sup>; Sofia Corte-Real, PhD<sup>1</sup>; Raquel Barbosa, MSc<sup>1</sup>; Patrícia Cavaco-Silva, PharmD, PhD<sup>1,4</sup>; José Melo-Cristino, MD, PhD<sup>3</sup>; Andrzej Górski, MD,

PhD5; and Miguel Garcia, PharmD, PhD1 (2013) Wound healing potential of topical bacteriophage therapy on diabetic cutaneous wounds. *Wound Repair and Regeneration*, 21, Issue 4, pages 595–603, July-August 2013 (Journal IF: 2.757, Citations: NA)

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

TechnoPhage invited to present Rheumatoid Arthritis therapeutics development programme at National Association of Rheumatoid Arthritis Patients (ANDAR) symposium “Disclosing the future in RA: the Portuguese contribution” at Gulbenkian Foundation, Lisbon, Portugal, October 2013.

TechnoPhage invited to present at National Symposium of Portuguese Association of the Pharmaceutical Industry - APIFARMA: “O Valor da Inovacao: Da Investigacao ao Doente” , Seminar title: “Desafios da Terapêutica Inovadora no séc. XXI” at Centro Cultural de Belém, Lisbon, Portugal, June 2013.

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

TechnoPhage selected by UK Trade and Investment for entry as a National Champion in the European Business Awards 2013-14 for Commercial success, Innovation, and Business Ethics. (<http://www.businessawardseurope.com/national-champion/2013>)

#### **Patents/prototypes**

OCT 2013 Patent Granted to TechnoPhage partner company Lusomedicamenta Title: Antibacterial Phage Peptides and Methods of Use Thereof Office: United States Patent and Trademark Office Date: 22 October 2013 Patent No: US 8,563,504 B2 .

OCT 2013 Patent Granted to TechnoPhage Title: Engineered Rabbit Antibody Variable Domains and Uses Thereof Office: The Registry of Patents Singapore Date: 11 October 2013 Patent No: 156768 [WO 2008/136694]

#### **Msc theses completed**

Pedro Canhão 04/12/2013 Selection of small domain antibodies against b-amyloid peptides University of Lisbon Frederico Aires da Silva João Gonçalves.

Cátia Família 22/11/2013 Avaliação de bacteriófagos com actividade antibacteriana em isolados provenientes de doentes com pneumonia associada ao ventilador Universidade Nova de Lisboa Patrícia Cavaco Silva Montez.

