

INSTITUTO DE MEDICINA MOLECULAR



2011 Activity Report



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Structure and Organization

Research and development in the Biomedical Sciences plays a central role in generating knowledge and in the application of this knowledge to improving the quality of life. ***The mission of the 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 Faculty of Medicine of the University of Lisbon, 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 2001, IMM results from the association of 5 former research units from the Faculty of Medicine of the University of Lisbon: 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
Fundação da Universidade de Lisboa
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.

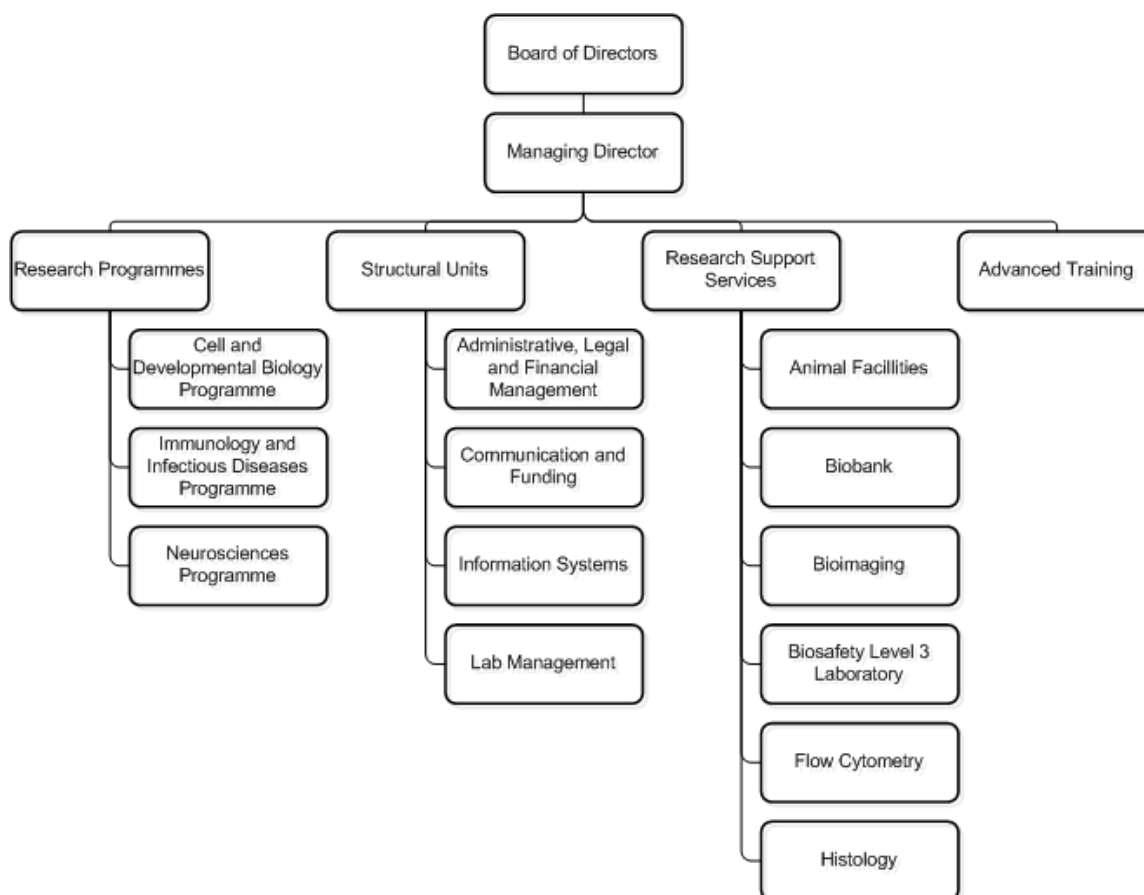
João Lobo Antunes, MD, PhD (President)
Maria Carmo-Fonseca, MD, PhD (Executive Director)
Joaquim Alexandre Ribeiro, MD, PhD (Vice-President)

Administration Board

The Administration Board is composed by the Directors, the Research Programme Coordinators, and the Directors of the *Faculdade de Medicina* and *Hospital de Santa Maria*. 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.

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

Cell and Developmental Biology Programme – 2006

Philip Ingham, University of Sheffield/Institute of Molecular and Cell Biology, Singapore

Frank Grosveld, Erasmus University, Rotterdam, the Netherlands

Outi Hovatta, Karolinska Institut, Stockholm, Sweden

Iain Mattaj, European Molecular Biology Laboratory, Heidelberg, Germany

Axel Pries, Department of Physiology, Charité-Berlin, Germany

Evaluation reports 2011

Summary of Review Report of the Scientific Advisory Board for the Neurosciences Program

Period of evaluation: 2006-2010

Scientific Advisory Board members:

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

Summary of the panel's overview:

The Neuroscience programme has some significant strengths with high impact outputs but also some PIs who are performing sub-optimally. The Neurological Clinical Research Unit demonstrated high quality output in stroke and neurodegenerative disease research although its use of the core facilities of the IMM was barely evident. Similarly the Neuromuscular Unit had some significant outputs but was only now beginning to be housed in IMM. For the future, the Programme would benefit by greater focus on these three high performing areas of clinical research and exploration of ways of integrating some of their research activity with complementary studies and the expertise of members of Units within Basic Medical Science (BMS). One resultant recommendation is that the Neuromuscular Unit be combined with the Autonomic Nervous System Unit to form a new Clinical Physiology Unit housed in the IMM (Dept. Physiol.).

This arrangement would facilitate these interdisciplinary interactions, and provide an opportunity for the development of the further use of animal models of disease. It would also provide an opportunity to provide bio-engineering support and more efficient use of space, facilities and resources. At present clinical research is largely, if not exclusively, conducted in the hospital and changes of the type proposed may lead to a cultural change that could heighten exchange. Other clinical research could also benefit from space in the IMM which would also facilitate exchange.

There was little evidence of IMM investment in appointments within the Programme. A single PI recruit and group Leader (Cell and Molecular Neuroscience) is the most closely integrated into the IMM. This unit also has collaborations within BMS and Clinical Units (CU). Unfortunately the Group Leader is leaving to take up a full Professor position in Gottingen. There are also some more junior appointments at staff scientist level (for example in the Neuroscience Unit) but far greater investment in such positions is essential. We were made aware of the difficulties encountered by clinical scientists in having protected research time. Accordingly we recommend that in addition to appointments at the PI level, consideration should be given to funding 50% of the time of a limited number of clinician scientists in training, for limited time periods, so that they can fully engage in research within the IMM helping to bring contemporary molecular and cellular approaches to the clinical problems being investigated in CU as an example. Also clinicians in IMM would help the basic scientists by identifying the potential clinical relevance of research. At present we do not believe that the wealth of clinical material available to the IMM through the clinical faculty is being utilised to its full potential. We also believe that a PI position should be targeted at a systems neuroscientist to further this objective and to assemble and support the groups with research interests in cognitive and behavioural disturbances.

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The BMS Units displayed a range of performance that varied from the well developed and respected (Neuroscience Unit) to the evolving and highly promising (Cell and Molecular Neuroscience Unit) to one that is in re-development (Autonomic Nervous System Unit) for which we have provided a suggested restructuring. Outputs were uneven across the BMS with high impact outputs in some areas but weaker output in others. A strategy of building collaboration between BMS and CU that can be facilitated by IMM offers an attractive model for future development.

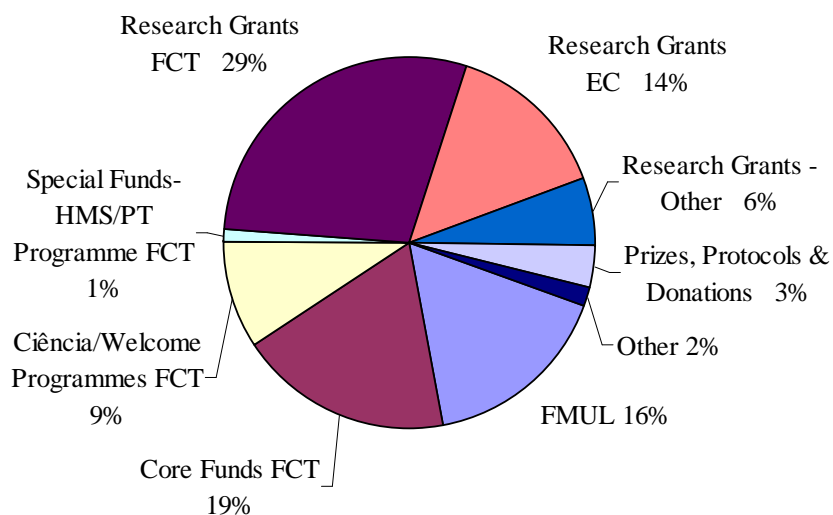
We noted across the Programme that many of the most successful PIs had developed, or participated, in established national and international research and clinical networks. This is a major benefit for the IMM, enhancing its recognition and reputation nationally and internationally, and is evidence of the vibrancy of the programme.

There was widespread recognition that the IMM provides excellent administrative support for PIs in obtaining FCT grants and in some cases European funding. Membership of the IMM was seen to enhance the likely success of applications and certainly assisted in attracting and funding good research students. We consider that the IMM should build on this by providing other services that could enhance a third stream funding, for example clinical trials and translational funding opportunities that could accommodate a Clinical Trials Unit.

Research Funding

Expenditure in 2011 by Funding Source

Total expenditure: 10.237.384,32 €

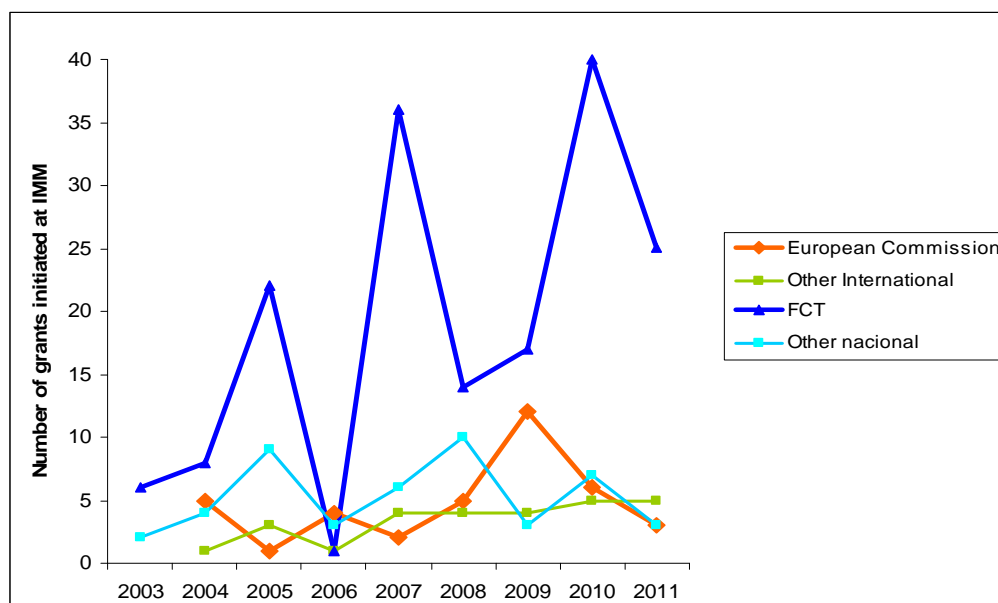


Number of Ongoing Research Grants in 2011

269 Research Grants

- 105 Public National FCT
- 15 Public Other National
- 29 Public European Commission
- 10 Public Other International
- 95 Private National
- 15 Private International

Number of Research Grants Initiated at IMM from 2003 to 2011



Research Funding Initiated in 2011

Research Grants (36)

- 3 European Commission; 5 Other International
- 25 FCT; 3 Other National

Funding Agency	reference	Title	PI at IMM	Duration	IMM Budget
EC	Sense Park	<i>Supporting and Empowering Parkinsons patients in their home environment using a Novel SEnsory information system</i>	J. Ferreira	24	277.440,00
EC	PIOF-2010-274037	<i>Evoaltsplice: Survey of tissue-specific alternative splicing in vertebrates by highthroughput sequencing</i>	M. Carmo Fonseca	36	210.446,00
EC	ITN-2011-289007	<i>RNPnet: RNP structure, function and mechanism of action</i>	M. Carmo Fonseca	48	187.017,00
EMBO	EMBO Young Investigator 2010	<i>Young Investigator Grant</i>	B. Silva Santos L.	36	45.000,00
EMBO	EMBO Instalation Grant	<i>Instalation Grant</i>	Figueiredo	36	150.000,00
Agência de Inovação, SA	EUROSTARS_E5553_PARK	<i>Identification of molecules to treat Parkinson's disease (PD) using a novel zebrafish model</i>	A. D. Correia	36	150.395,72
Bayer HealthCare	Bayer	<i>Boosting dendritic cell function to facilitate tolerance induction to recombinant clotting factors</i>	V. Oliveira Martins	24	119.299,22

Merck Sharp & Dohme	MISP Study Agreement	<i>Modulation of HIV replication and latency in human CD4 T cells by regulatory small RNAs</i>	A. Espada Sousa	24	92.000,00
Merck, S.A.	Merck	<i>Cancro Rectal-Efeitos Quimioterapia e Radioterapia</i>	L. Costa	8	20.000,00
Abbott Laboratorios, Lda	GWAS Abbott	<i>A national genome wide association study to predict the response to Anti-TNF treatment in rheumatoid arthritis</i>	H. Canhão	24	103.000,00
FCT	HMSP-ICJ/0003/2010	<i>N- Terminal of the brain natriuretic peptide as a biomarker of cardioembolic stroke</i>	C. Fonseca	24	126.540,00
FCT	HMSP-ICS/0004/2011	<i>Mechanisms of Invasion and Progression in Metastatic Bone Disease and Outcomes in HER2 Positive Metastatic Breast Cancer</i>	I. Luis	24	400.000,00
FCT	HMSP-ICT/0021/2010	<i>Pathogenesis of Kaposi's sarcoma herpesvirus LANA"</i>	J. P. Simas	36	294.892,00
FCT	PTDC/BIA-BCM/111451/2009	<i>Splicing-coupled mechanisms of chromatin remodeling and their global role in transcription.</i>	S. Almeida	36	141.967,00
FCT	PTDC/BIA-BCM/111617/2009	<i>Polyphenols as protective agents in cellular models of alpha-synucleinopathies, in particular Parkinson's disease.</i>	S. Tenreiro	36	58.089,00
FCT	PTDC/BIA-BCM/115864/2009	<i>The role of histone H1 in antigenic variation of African trypanosomes</i>	L. Figueiredo	36	189.828,00
FCT	PTDC/EIA-EIA/111239/2009	<i>NEUROCLINOMICS - Understanding NEUROdegenerative diseases through CLINical and OMICS data integration.</i>	A. de Mendonça	36	39.067,00
FCT	PTDC/EIA-EIA/113660/2009	<i>RAPS - Reading Analysis with neuroPhysiological Signals</i>	I. Pavão Martins	24	33.178,00
FCT	PTDC/QUI-BIQ/112929/2009	<i>LIPIDENGUE: The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies</i>	M. Castanho	36	130.000,00
FCT	PTDC/QUI-BIQ/114774/2009	<i>Membrane fusion mechanism of Influenza Hemagglutinin: a simulation and biophysical approach</i>	M. Castanho	36	44.186,00
FCT	PTDC/QUI-QUI/115712/2009	<i>Synthesis, Characterization and Biological Assessment of Multi-Functional Bone-Seeking Agents</i>	L. Costa	36	50.064,00
FCT	PTDC/SAU-BID/115264/2009	<i>Notch signalling in the specification and differentiation of thymic epithelial cells during embryogenesis</i>	H. Neves	36	140.000,00
FCT	PTDC/SAU-GMG/113440/2009	<i>The role of RNA polymerase II in splicing regulation</i>	M. Carmo Fonseca	36	170.000,00
FCT	PTDC/SAU-GMG/115652/2009	<i>Super-resolution Imaging of Gene Expression & Nuclear Architecture.</i>	M. Mhlanga	36	185.980,00

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FCT	PTDC/SAU-IMU/110303/2009	<i>Role of newly identified genes in in vivo antigen cross-presentation-dependent generation of CTL responses against tumors</i>	Â. Chora	36	136.840,00
FCT	PTDC/SAU-IMU/113541/2009	<i>Cellular and molecular requirements in human Regulatory T cell development</i>	I. Caramalho	36	158.360,00
FCT	PTDC/SAU-MIC/109786/2009	<i>HIV/AIDS: contribute of naïve CD4 T cell homeostasis</i>	A. Espada Sousa	36	159.694,00
FCT	PTDC/SAU-MIC/110887/2009	<i>Modulation of the cellular transcription factors NF-κB and MYC</i>	J. P. Simas	36	153.315,00
FCT	PTDC/SAU-MIC/113225/2009	<i>Screening of chromatin factors involved in antigenic variation in Trypanosoma brucei.</i>	L. Figueiredo	36	113.407,00
FCT	PTDC/SAU-MIC/113697/2009	<i>Mechanisms of Plasmodium liver infection: Subverting the host ubiquitin-proteasome pathway towards an immune evasion strategy</i>	V. Luis	36	157.162,00
FCT	PTDC/SAU-NMC/110838/2009	<i>Modulation of GABAergic transmission in the hippocampus by adenosine</i>	A. Sebastião	36	159.760,00
FCT	PTDC/SAU-ONC/113202/2009	<i>Identification of novel regulators of CK2 with impact on PTEN function in leukemia</i>	J. Barata	36	186.127,00
FCT	PTDC/SAU-ORG/113329/2009	<i>Autoregulation in acute stroke</i>	I. Rocha	24	54.982,00
FCT	PTDC/SAU-ORG/114083/2009	<i>Molecular determinants of microglial activation and neuronal dysfunction in in vivo models of Parkinson's disease</i>	T. Pais	36	115.664,00
FCT	PTDC/SAU-TOX/114424/2009	<i>Cellular therapy for liver-specific immune suppression</i>	L. Graça	36	173.000,00
Fund. Calouste Gulbenkian	ReNerve	<i>The Contribution of Innervation to Tissue Repair</i>	A. Jacinto	36	25.000,00

Protocols, Donations & Awards (25)

Funding Agency	Reference	PI at IMM	IMM Budget
Active Motif,S.A.	Support to seminars on Cromatin	L. Figueiredo	600,00
Boehringer Ingelheim, LDA	Support to research on Anticoagulation after dural sinus thrombosis	J. Ferro	5.000,00
Celgene Sociedade Unip., Lda.		J. Lacerda	2.500,00
Ciência Viva-Agência Nacional	Ciência Viva 2011	N. Santos	1.180,00
Delta Cafés	Support to PhD Programm	I. Crisóstomo	500,00
EMBO	Support to seminars	L. Figueiredo	5.000,00
Fund. Calouste Gulbenkian	Donation for aquisition of Microscope	M. Carmo Fonseca	60.000,00
FCT	Support to research on Adenosine A2A receptors and glucocorticoids in age-related hippocampal dysfunctions	L. V. Lopes	6.400,00
GHOP - Grupo Hemato-Oncológico	Support to research on oncology	L. Costa	5.000,00
GlaxoSmithKline	Sponsor - course of movement disorders	J. Ferreira	15.000,00
Grunenthal S.A.	Support to course on botulinic toxin	J. Ferreira	15.000,00
Grupo Taper	Support to seminars	D. Henrique	1.000,00
Laboratórios Pfizer,Lda	Support to PhD thesis	J. E. Fonseca	2.500,00
Linde Sogás, Lda	Support to research	M. de Carvalho	3.000,00
Merck Sharp & Dohme	Donation for aquisition of Microscope	M. Carmo Fonseca	100.000,00
Novartis Farma		L. Costa	4.040,00
Novartis Farma	support to meeting on Neuromuscular	M. de Carvalho	2.000,00
Novartis Farma	Support to research	S. Constantino	7.000,00
Roche Farmaceutica Quimica	support to meeting on Rheumatology	J. E. Fonseca	2.700,00
Roche Farmaceutica Quimica	Support to seminars on Rheumatology	J. E. Fonseca	12.000,00
Roche Farmaceutica Quimica		J. Lacerda	5.000,00
Soc. Portuguesa Neurociências	Organization of the XII SPN Meeting 2011	L. V. Lopes	10.300,00
Sojornal, S.A.	Prémio Pessoa 2010	M. Carmo Fonseca	60.000,00
Stab vida	Support to PhD Programm	I. Crisóstomo	500,00
University of Glasgow	Fellowship Award	L. Mancio	70.000,00

Number of Applications and Funding Secured from 2008 to 2011

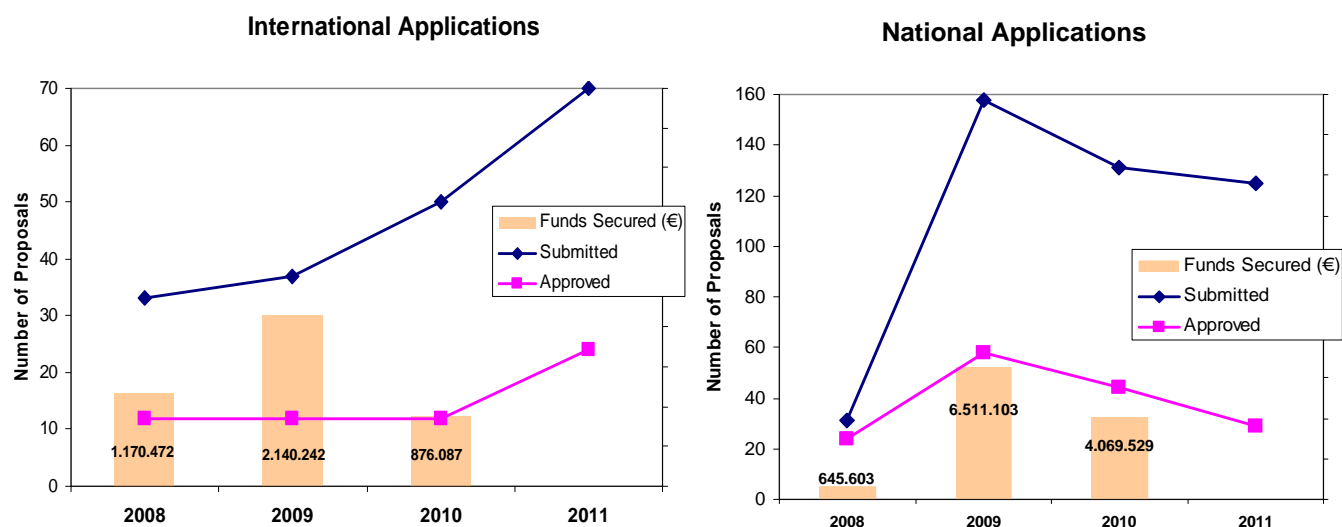


Figure.1 Number of total proposals submitted, number of approved applications, and amount of competitive funding secured by IMM researchers since 2008, for international and national funding. The data relies on the registration of the funding applications received by the Communication and Training Unit (researchers are not obliged to inform the Ucom when they submit a grant, thus this data may under represent the real number of IMM submissions). Proposals are displayed according to date of submission; funds secured correspond to the sum of the approved budgets for the IMM. 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 (international and national) by the IMM was €1,815,000 in 2008, €8,651,000 in 2009 and €4,945,000 in 2010.

Diversity of Funding Sources of IMM applications from 2008 to 2011

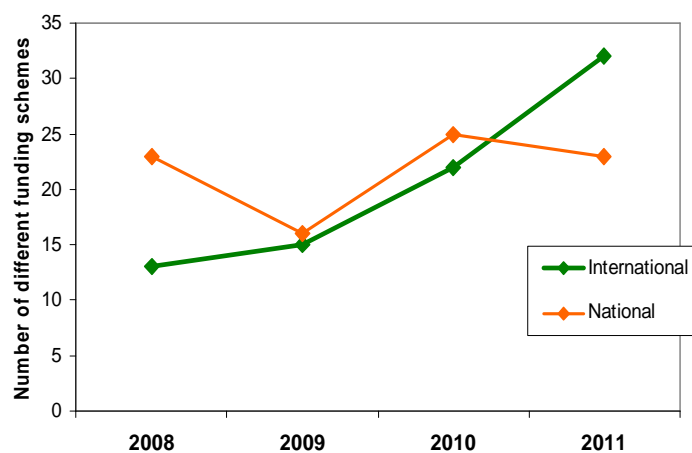


Figure 2. Diversity of funding sources since 2008 of IMM applications to international and national funding. Proposals were registered according to date of submission.

In 2011, IMM researchers have submitted grants to the following funding schemes:

<i>International</i>	<i>National</i>
Public FP7 Marie Curie Actions FP7 Cooperation Programme - Health FP7 Cooperation Programme - ICT FP7 IMI FP7 European Research Council FP7 Other European Science Foundation European Molecular Biology Organization Federation of European Biochemical Societies Human Frontier Science Program L'Agence Nationale de la Recherche, France National Institutes of Health, USA FEBS/EMBO Women in Science Award Nakasone/HFSP Award Private Axa Research Fund Alzheimer Association Baxter Foundation Boehringer Ingelheim Fonds European Calcified Tissue Society Ernst Schering Foundation Howard Hughes Medical Institute National Blood Foundation, US Parkinson Disease Canada Servier/International Osteoporosis Foundation Bayer Hemophilia EFSD/Novo Nordisk Exicon Merck Sharp & Dohme Pfizer The Company of Biologists Tahio Pharma Tcl Expression	Public FCT Projects in All Scientific Domains FCT Harvard Medical School-Portugal Programme FCT Coordenação Nacional para a Infecção VIH/Sida FCT Fundo de Apoio à Comunidade Científica Ciência Viva Private Fundação C. Gulbenkian - Programa de Estímulo à Investigação Liga Port. Contra o Cancro / Terry Fox Abbot Boehringer Ecbio GlaxoSmithKline Hematocológica Linde Merck Novartis Pfizer Sociedade Portuguesa Neurociências Prémio B. Manuel Mello Prémio Gulbenkian Prémio Jansen Neurociências Prémio Pfizer Prémio Nedai Prémio Medalhas de Honra L'Oréal

2011 IMM Activities Highlights

People in 2011

PhD Holders: 210

Total: 534

Productivity at a glance

Publications International Journals	287
...in journals with an impact factor higher than 10	23
...in journals with an impact factor between 5 – 10	58
Book/Book Chapters International	51
Communications in International Conferences	316
Communications in National Conferences	267
Seminars and Invited Lectures	316
Organization of Conferences	92
Prizes	42
PhD Thesis	22
Master Thesis	68

Selection of Prizes and Awards

Pfizer Award on Clinical Research 2011

Daniel Ribeiro, Nádia Correia, Bruno Cardoso, Leonor Sarmento and João Barata

Pfizer Award on Basic Research 2011

Sérgio de Almeida

Grand Challenges Bill & Melinda Gates Foundation

João Gonçalves

Discovery Early Career Research Award (Australian Research Council)

Sónia Henriques

NEDAI Prize in Autoimmunity Research 2011

Joana Duarte, Ana Água-Doce, João Eurico Fonseca e Luís Graça

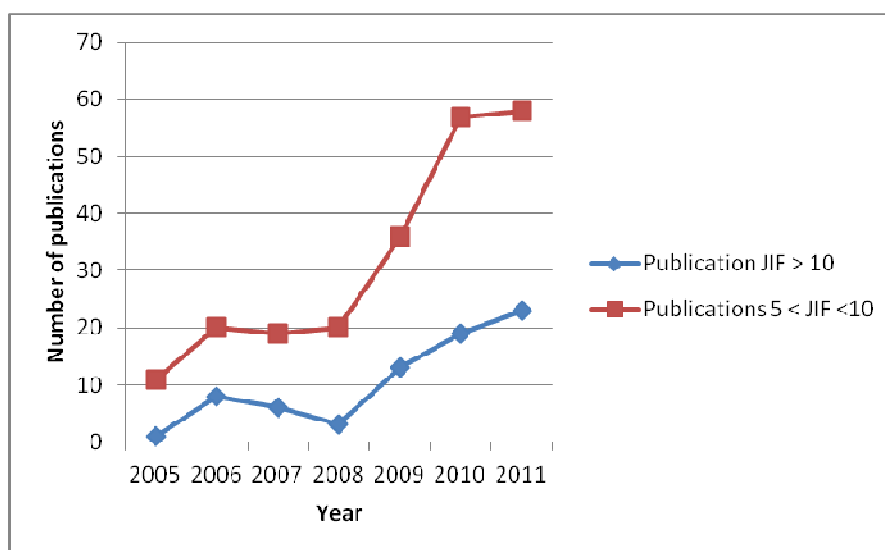
Basic Research Prize 2011 (Portuguese Society of Human Genetics)

Martins M, Rosa A, Guedes LC, Fonseca BV, Gotovac K, Violante S, Mestre T, Coelho M, Rosa MM, Martin ER, Vance JM, Outeiro TF, Wang L, Borovecki F, Ferreira JJ, Oliveira SA.

1st Prize from Liga Portuguesa Contra a Epilepsia 2011

Costa J, Fareleira F, Ascensão R, Borges M, Sampaio C, Vaz Carneiro A

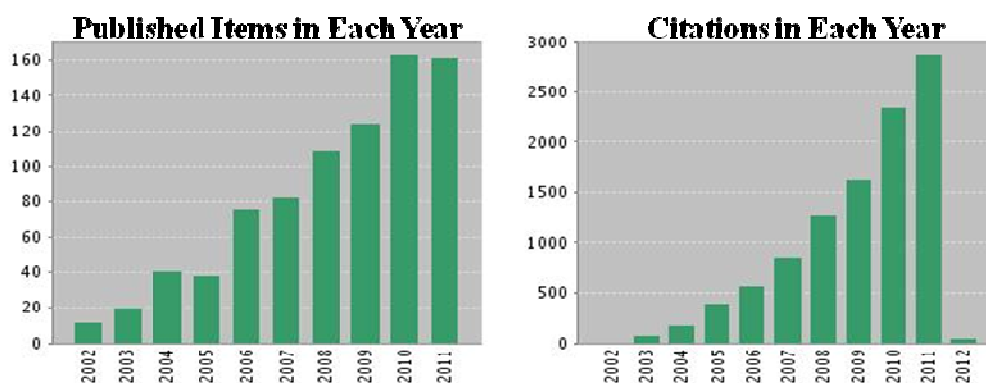
IMM Publications in International Journals



JIF = Journal Impact Factor

Citation Report

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



162 papers in 2011

829 since 2002

Sum of the Times Cited: **10292**

Average Citations per Item: **12.41**

h-index : **48**

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

Refined by: [excluding] Document Type=(EDITORIAL MATERIAL OR PROCEEDINGS PAPER OR CORRECTION OR MEETING ABSTRACT OR BOOK CHAPTER OR NEWS ITEM)

Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, CCR-EXPANDED, IC.

Note: This data is based on the information available on The Web of Science, hence it is not an exhaustive analysis of IMM publications

10 Most Cited Articles 2002-2011

Emre M; Aarsland D; Brown R; et al. (Sampaio C) (2007) Clinical diagnostic criteria for dementia associated with Parkinson's disease. *Movement Disorders*. **22** (12), 1689-1707 (Times cited: 245) (Journal IF: 4.48)

Di Fonzo A; Rohe CF; Ferreira RJ; et al. (Sampaio C) Italian Parkinson Genetics Network (2005) A frequent LRRK2 gene mutation associated with autosomal dominant Parkinson's disease. *Lancet*. **365** (9457), 412-415 (Times cited: 227) (Journal IF: 33.6)

Sousa AE; Carneiro J; Meier-Schellersheim M; et al.(2002) CD4 T cell depletion is linked directly to immune activation in the pathogenesis of HIV-1 and HIV-2 but only indirectly to the viral load. *Journal of Immunology*. **169** (6), 3400-3406 (Times cited: 219) (Journal IF: 5.74)

Ribeiro JA; Sebastiao AM; de Mendonca A (2002) Adenosine receptors in the nervous system: pathophysiological implications. *Progress in Neurobiology*. **68** (6), 377-392 (Times cited: 199) (Journal IF: 9.97)

Duarte A; Hirashima M; Benedito R; et al. (Henrique D) (2004) Dosage-sensitive requirement for mouse D114 in artery development. *Genes & Development*. **18** (20), 2474-2478 (Times cited: 181) (Journal IF: 13.89)

Healy G.; Falchi M; O'Sullivan S.; et al. (Ferreira J) (Int LRRK2 Consortium) (2008) Phenotype, genotype, and worldwide genetic penetrance of LRRK2-associated Parkinson's disease: a case-control study. *Lancet Neurology*. **7** (7), 583-590 (Times cited: 162) (Journal IF: 21.66)

Santos NC; Figueira-Coelho J; Martins-Silva J; et al.(2003) Multidisciplinary utilization of dimethyl sulfoxide: pharmacological, cellular, and molecular aspects. *Biochemical Pharmacology*. **65** (7), 1035-1041 (Times cited: 129) (Journal IF: 4.89)

Carmo-Fonseca M (2002) The contribution of nuclear compartmentalization to gene regulation. *Cell*. **108** (4), 513-521 (Times cited: 125) (Journal IF: 32.4)

Stamm S; Riethoven J; Le Texier V; et al. (Barbosa-Morais N) (2006) ASD: a bioinformatics resource on alternative splicing. *Nucleic Acid Research*. **34**, SI, D46-D55 (Times cited: 125) (Journal IF: 7.84)

Bonifati V; Rohe CF; Breedveld GJ; et al. (Sampaio C) Italian Parkinson Networks (2005) Early-onset parkinsonism associated with PINK1 mutations - Frequency, genotypes, and phenotypes. *Neurology*. **65** (1), 87-95 (Times cited: 109) (Journal IF: 8.17)

List of Publications in International Journals

Afonso P, Figueira L, Paiva T (2011) Schizophrenia patients with predominant positive symptoms have more disturbed sleep-wake cycles measured by actigraphy. *Psychiatry Res* **189**;62-66 (Journal IF: 2.344)

Afonso P, Figueira ML, Paiva T. (2011) Sleep-promoting action of the endogenous melatonin in schizophrenia compared to healthy controls. *Int J Psychiatry Clin Pract.* Nov;15(4):311-5. Epub. (Journal IF: 0.5)

Agua-Doce A, Graca L. (2011) Prevention of house dust mite-induced allergic airways disease in mice through immune tolerance. *PLoS ONE* 6(7):e22320. (Citations: 0) (Journal IF: 4.411)

Aguiar de Sousa D, Mestre T and Ferro JM (2011) Cerebral venous thrombosis in Behçet's disease: a systematic review. *J Neurol* 258, 719-27 (Journal IF: 3.853)

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(Total: 287)

Seminars and Workshops

IMM Seminars

17-01-2011

Jorge H. Leitão, Instituto Superior Técnico

Burkholderia cepacia complex: a group of pathogens endowed with a wide range of virulence determinants

(PFMA)

31-01-2011

Roland Liblau, Directeur du Centre de Physiopathologie de Toulouse Purpan INSERM UMR1043 - CNRS UMR5282 - Université Toulouse III

CNS inflammation: learning from animal models

07-02-2011

Eleonora Kurtenbach, Universidade Federal do Rio de Janeiro

Looking for functional domains involved in the Psd1 defensin antifungal activity

14-02-2011

Bruno Silva-Santos, IMM

From thymic differentiation to killing tumors: how gamma-delta T lymphocytes do it

28-02-2011

Robert A. S. Ariëns, University of Leeds, UK

Ultrastructure of the Fibrin Clot and its Physiological Regulation

07-03-2011

Maria Mota, IMM

Is Plasmodium detected by the host during the silent liver stage?

14-03-2011

Kent Golic, University of Utah, U.S.A.

New beginnings at chromosome ends

21-03-2011

Henrique Veiga-Fernandes, IMM

Regulation of haematopoietic cell functions by neurotrophic factors

28-03-2011

Joao Barata, IMM

A foe for a friend: IL-7-mediated signaling in T-cell leukemia

04-04-2011

Luis Graça, IMM

Reprogramming the immune system towards tolerance

03-05-2011

Hans Peter Peters

Societal contextualization of neuroscience by public communication: a research agenda and first results

09-05-2011

Vineet Gupta, University of Miami

Modulation of Inflammatory Injury with novel integrin Mac-1 agonists

16-05-2011

Helena Soares, Institute Pasteur

HIV-1 disrupts TCR signal amplification at immunological synapse

23-05-2011

Matthias Marti, Harvard School of Public Health

The biology of malaria transmission as a basis for intervention strategies

30-05-2011

David Lominadze, Health Sciences Center, University of Louisville, USA

Fibrinogen and remodeling of vascular wall

06-06-2011

Domingos Henrique, IMM

What's all this noise?

20-06-2011

Carmo-Fonseca, IMM

Imaging splicing in living cells with single-molecule precision

27-06-2011

Ana Espada de Sousa, IMM

Reversible and irreversible damage in HIV/AIDS: lessons from HIV-2

04-07-2011

Miguel Prudencio, IMM

Plasmodium infection: host factors, parasite molecules, and anti-malarial interventions

11-07-2011

Miguel Soares, IGC

Tissue damage control is a central component in the establishment of host tolerance to infection

18-07-2011

Stefan Kaufmann, MPI, Berlin

Vaccine and Biomarker Design for Tuberculosis

IMM Monday Lectures

12-09-2011

João Lobo Antunes, IMM

Egas Moniz - an unlikely scientist

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26-09-2011

Jacques van Dongen, Erasmus University Rotterdam

Normal, malignant and deficient lymphoid differentiation: From research to diagnostic patient care

10-10-2011

Piet Borst, NKI, Amsterdam, NL

Essential role for an unusual DNA modification in transcription in Leishmania

17-10-2011

Jannie Borst, NKI Amsterdam, NL

Shaping effector and memory CD8 T cell responses by TNF (receptor) family members

24-10-2011

Cláudio Sunkel, IBMC, Porto

Maintaining genomic stability through cell division

07-11-2011

David Andreu, Univ. Pompeu Fabra, Barcelona, Spain

From antimicrobial proteins to peptides; small is beautiful

14-11-2011

Jorge Pacheco, ATP-Group (U. Lisboa) & Dep. Matemática e Aplicações (U.Minho)

If cells play dice, can we gamble our way out of cancer?

21-11-2011

Detlev Boison, Portland, Oregon, USA

Homeostatic bioenergetic network regulation: towards a new philosophy to understand and to treat neurological disorders

28-11-2011

Alexandre Carmo, IBMC, Porto

Receptor-mediated signaling inhibition at the onset of T cell activation

12-12-2011

Jon Clardy, Harvard Medical School

Bacterial symbiosis and the discovery of new drugs

Oncology Series

24-01-2011

Michael Rogers, Bone & Musculoskeletal Research Programme Institute of Medical Sciences University of Aberdeen

Bisphosphonate drugs: mechanisms of action in bone diseases and potential anti-tumour properties

05-05-2011

Robert J. Motzer, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center, USA

Targeted Therapy for Advanced Renal Cell Carcinoma

27-10-2011

Chair: **Luis Costa** | Co-chair: **José Passos Coelho**

Triple Negative Breast Cancer

IMM Rheumatology Series

18-11-2011

Geraldine Cambridge, University College London

Rheumatoid Arthritis: Even more BAFF-ling than we thought

13-12-2011

Yrjö Kontinen, Helsinki University

The Macrophage

Hans Carlsten, Goteborg University

Estrogen and Arthritis

e-PI Seminar

05-01-2011

Élio Sucena, IGC

An evo-devo look into arthropod immunity

19-01-2011

João Relvas, IBMC

Myelin: ROCK and Rho in the nervous system

02-02-2011

Ana Ferreira, IGC

Sickle Hemoglobin Confers Tolerance to Plasmodium Infection

16-02-2011

Isabel Gordo, IGC

Rapid microbial adaptation to escape the sentinels of innate immunity

02-03-2011

Júlia Costa, ITQB

Protein glycosylation: implications in neuroscience and cancer

30-03-2011

Hélder Maiato, IBMC

How to make a precise chromosome segregation machine

13-04-2011

Henrique Teotónio, IGC

The genetic basis of adaptation in experimental C. elegans populations

27-04-2011

João Rodrigues, ITQB

Trypanosome Functional Glycomics: targeting the cell surface molecules responsible for the African sleeping sickness parasite survival and infectivity

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11-05-2011

Margardia Amaral, FCUL

From siRNA Screens to Drugs: Illuminating the Cell to Understand Cystic Fibrosis

08-06-2011

Rodrigo Cunha, CNC

Caffeine: a normalyser of brain function? - Behavior, circuits and receptors

22-06-2011

Carlos Ribeiro, CNP

Molecular and neuronal control of food choice in Drosophila

06-07-2011

José Belo, UAlg

Control of Nodal signaling in development and disease

20-07-2011

Fátima Martel, FMUP

Intestinal transport of some bioactive compounds: pathophysiological relevance

IMM Wednesday Lecture

19-10-2011

João Barata, IMM

Dr Jekyll and Mr Hyde Or Mistaking a foe for a friend: IL-7-mediated signaling in T-cell leukemia (take 2)

02-11-2011

Sérgio Almeida, IMM

Chromatin regulation during RNA Pol II transcription

16-11-2011

António Jacinto, IMM

How epithelia respond to a crisis

30-11-2011

Luis Moita, IMM

Sepsis: new uses for old drugs

14-12-2011

Alexandre Mendonça, IMM

Prodromal Alzheimer's Disease

Pizza Seminars

18-01-2011

Carolina Moreira, IMM

Drosophila haemocyte migration

Marta Ribeiro, IMM

Pin-pointing Pain: Biophysics and Kyotorphin peptides in Analgesia

01-02-2011

Alice Melão, IMM

Exploring the role of IL-7 and CK2 in T-cell acute lymphoblastic leukemia

Daniel Silva, IMM

Computer Modeling to predict and optimize E.Coli Growth

15-02-2011

Elsa Abranches, IMM

Into the heart of stemness

Catarina Ramos, IMM

Notch ligands and the regulation of spinal cord neurogenesis- Two is company, three is a crowd

01-03-2011

Marco Antunes, IMM

Drosophila wound healing

Joana Tato, IMM

Effects of chemotherapy and radiotherapy in rectal cancer: significance of different cellular outcomes in tumour behaviour

15-03-2011

Joana Xavier, IMM

Association of mitochondrial polymorphism m.709G>A with Behçet's disease

Rita Mateus, IMM

Size-control regulation during zebrafish caudal fin regeneration: a chemical screen approach

29-03-2011

Pedro Pereira, IMM

EZH2: a regulator of chromatin structure in the response to topoisomerase-mediated DNA lesions

Elisabete Martins, IMM

Molecular characterization of Streptococcus agalactiae isolates responsible for neonatal invasive infections in the Barcelona area

12-04-2011

Telma Lança, IMM

Understanding the dual role of murine gammadelta T-cells in tumour immune surveillance

Maurice Itoe, IMM

The role of host cell lipids during Plasmodium liver stage infection

26-04-2011

Miguel Prudêncio, IMM

The malaria parasite: getting in and out of the system

10-05-2011

Cristina Silva, IMM

Impact of different peptide-MHC/TCR affinities in CD8 T cell control of gammaherpesvirus latency

Vera Geraldes, IMM

Genetic modification of neural sympathetic regions to control hypertension chronically

24-05-2011

Diogo Rombo, IMM

Synapse-specific modulation of inhibitory signaling in the hippocampus

Nádia Correia, IMM

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

07-06-2011

Rita Cascão, IMM

The role of inflammasome in the initiation and perpetuation of Rheumatoid arthritis

Elisa Basso, IMM

Insight into the role of alpha-synuclein phosphorylation

21-06-2011

Sofia Ferreira, IMM

Adenosine A1R-A2AR heteromers modulate GAT-1- and GAT-3-mediated GABA uptake by astrocytes

Elisa Basso, IMM

Insight into the role of alpha-synuclein phosphorylation in Parkinson's disease

20-09-2011

Ana Água-Doce, IMM

Adjuvant can facilitate induction of therapeutic tolerance to recombinant factor VIII in a mouse model of hemophilia

Patricia Inácio, IMM

Not yet supplied

04-10-2011

Federico Herrera, IMM

Genetic and pharmacological modifiers of huntingtin oligomerization and toxicity

25-10-2011

Joana Monteiro, IMM

Dynamic extracellular proton fluxes during fin regeneration in Zebrafish

Susana Gonçalves, IMM

Modifying alpha-synuclein dimerization in living cells

08-11-2011

João Freire, IMM

Challenging the Viral Fusion "Dogma". Insights From Dengue Virus Capsid Protein Studies

Inês Perpétuo, IMM

Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis - a project overview

22-11-2011

Sandra Jacinto, IMM

The role of nuclear-encoded gene MPV17 in mtDNA maintenance

Ricardo Fernandes, IMM

About bronchiolitis, clinical trials and meta-analysis

06-12-2011

Ghislain Cabal, IMM

Plasmodium parasite scavenges host cell lipid droplets to complete malaria liver stage development

20-12-2011

Sofia de Oliveira, IMM

Role of CXCL8 chemokines in zebrafish neutrophil recruitment upon wounding

Frederico Couto, Instituto de Medicina Molecular

Is depression a risk factor for dementia?

Immunology Clubs

13-01-2011

Manuela Ferreira, IMM

Retinoic Acid in Enteric Lymphoid Organogenesis

20-01-2011

Carmen Penido, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

Gamma delta T lymphocyte migration during inflammation: involvement of CCL2/CCR2 and leukotriene B4/BLT1

03-02-2011

Catarina Almeida, IMM

The plasticity of NKT cells

10-02-2011

Rita Moura, IMM

B cell gene expression analysis in untreated very early Rheumatoid Arthritis patients

17-02-2011

Ana Gírio, IMM

Intracellular Reactive Oxygen Species are essential for PI3K/Akt/mTOR-dependent IL-7-mediated viability of T-cell Acute Lymphoblastic Leukemia Cells

24-02-2011

Ana Neves Costa, IMM

A role for the epigenetic regulator TET1 in innate immune responses

03-03-2011

Íris Caramalho, IMM

Investigating tools to increase the human regulatory T cell compartment

10-03-2011

Diogo Pereira, IMM

Role of RET tyrosine kinase in haematopoiesis

24-03-2011

Rita Azevedo, IMM e Division of Infection & Immunity, UCL

The role of IL-7 in the homeostasis of human naive and memory CD4 T cell subsets

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07-04-2011

Bruno Silva-Santos, IMM

Conference Report: World Immune regulation Meeting V

14-04-2011

Marta Caridade, IMM

What mathematics teaches about CD4 T cells

05-05-2011

Rita Cascão, IMM

Gambogic acid and celastrol are two powerful anti-inflammatory drugs in arthritis

12-05-2011

Gleb Turchinovich, IMM

Transcriptional control of $\gamma\delta$ T cell selection

19-05-2011

Magdalena Niedzielska, Friedrich-Alexander University of Erlangen-Nuremberg, Germany

DUSPs – from MAPK regulation to influence on the immune response

02-06-2011

Ana Água-Doce and Vanessa Oliveira, IMM

Enhancing tolerogenic antibodies to prevent Factor VIII inhibitors

16-06-2011

Alice Melão, IMM

Exploring the role of IL-7 and CK2 in T-cell acute lymphoblastic leukemia

30-06-2011

Jérémie Decalf, IMM

Gammaherpesviruses and their influence on B cells

07-07-2011

Andreia J. Amaral, IMM

Small Non-Coding RNAs in CD4 T cell activation and in HIV defence

14-07-2011

Ângela Afonso, IMM

Biobank-IMM - An Overview

06-10-2011

Manuela Ferreira, IMM

LTi differentiation depends on retinoic acid for the formation of Peyer's patches

13-10-2011

Rita Cascão, IMM

Celastrol: a potential new drug for RA

20-10-2011

Margarida Gomes, IMM

Activation of PI3K/Akt pathway in Acute Lymphoblastic Leukemia

27-10-2011

Rita Moura, IMM

The role of B cells in the early phase of Rheumatoid Arthritis

24-11-2011

Ana Neves-Costa, IMM

Regulation of Inflammatory Responses by TET1

Neuroscience Seminars

03-01-2011

Rita Almeida, Institut D'Investigacions Biomèdiques August Pi i Sunyer, Barcelona

Capacity and precision limitations of visual-spatial working memory

10-01-2011

Luís Pereira de Almeida, Faculdade Farmácia da Universidade de Coimbra

Modifying neurodegeneration in Machado-Joseph disease

17-01-2011

Joaquim Jacob, IMM

GABA Uptake and Calcium Signaling in Primary Cultures of Astrocytes: The Role of P2Y Receptors

24-01-2011

Rita Aroeira, IMM

Age-related changes of glycine receptor at the rat hippocampus: from the embryo to the adult

31-01-2011

André Santos, IMM

Chronic blockade of adenosine A2A receptor impairs the facilitatory effect of Brain-derived neurotrophic factor upon hippocampal LTP

07-02-2011

Ruben Gonçalves, IMM

The Neuroprotective Effect of BDNF in DNA Oxidative Damage in Cultured Rat Cortical Neurons by Comet Assay

14-02-2011

Diogo Rombo, IMM

Synapse-specific purinergic signalling in the hippocampus

21-02-2011

Christine Gall, Gillespie Neurosci. Res. Facility, University of California Irvine

Synaptic modulators, actin remodeling, and memory consolidation

28-02-2011 11:00 - 12:00

Júlia Pinho, IMM

Effect of memantine in aging: impact on hippocampus-dependent memory

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14-03-2011

Susana Ramos, Faculdade de Ciências e Tecnologia, Universidade Nova

Vanadium-actin interactions: effects on protein physiological function and structure

21-03-2011

Judith Pratt, Strathclyde Institute of Pharmacy and Biomedical Sci, University Strathclyde

Glutamate dysfunction in schizophrenia: from prefrontal cortex to disrupted networks

28-03-2011

Elisa Basso, IMM

Insight into the role of alpha-synuclein phosphorylation

04-04-2011

Raquel Dias, IMM

Journal Club: Erythropoietin enhances hippocampal long-term potentiation and memory

11-04-2011

Carlos Neves, Instituto de Fisiologia, Clinica Universitária de Oftalmologia

The role of autonomic nervous system in ocular hemodynamics and pupillar function

18-04-2011

Susana Gonçalves, IMM

Genetic modifiers of alpha-synuclein oligomerization

02-05-2011

Sandra H Vaz, IMM

Modulation of cholinergic neurotransmission by dopamine-galanin receptors in the rat ventral hippocampus

09-05-2011

Teresa Pais, IMM

Sirtuins: a novel link between neuroinflammation and neurodegeneration

16-05-2011

Mariana Oliveira, IMM

Molecular mechanisms underlying TrkB/A2A crosstalk

23-05-2011

Ana Correia, IMM

Zebrafish: a model system to study pain and Parkinson's disease

30-05-2011

Adelaide Fernandes, Faculdade de Farmácia da Universidade de Lisboa

Alterations in neuritic circuitry and myelinogenesis in a common neonatal pathological condition

06-06-2011

Paula Pousinha, IMM

Brain awareness week 2011: report

20-06-2011

Patrícia Guerreiro, IMM

LRRK2 and alpha-synuclein: intersecting pathways in the pathogenesis of Parkinson's disease

27-06-2011

Oldriska Marques, IMM

The role of alpha-synuclein in microglia activation

04-07-2011

Mariana Pereira, Universidade Federal Fluminense, Brasil

Expression and localization of adenosine receptors in avian retinal cells

11-07-2011

Hugo Miranda, IMM

Methylglyoxal glycation effects on alpha-synuclein aggregation

18-07-2011

Zrinka Marijanovic-Vultos, IMM

Autophagy in neurodegeneration

25-07-2011 11:00 - 12:00

Cláudia Valente, IMM

Mapping glycine receptor and glycine transporters in cultured cortical Astrocytes

12-09-2011

Luísa Lopes, IMM

Journal Club

26-09-2011 11:00 - 12:00

Tiago Maia, Instituto de Fisiologia

The catecholamines in cognition and in psychiatric disorders

03-10-2011

Rita Oliveira, IMM

Sirt2: Crossing the bridge between ageing and neurodegeneration

10-10-2011

Mariana Rocha, IMM

Is the neuromuscular transmission in the SOD1G93A mice, a model of Amyotrophic Lateral Sclerosis, compromised? What is the role of adenosine in those mice?

17-10-2011

Andreia Silva, IMM

Calcium signalling modulation in astrocytes by adenosine receptors

24-10-2011

Sandra Jacinto, IMM

The role of nuclear-encoded gene MPV17 in mtDNA maintenance

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31-10-2011

Rosa Chitolina Schetinger, Universidade Federal de Santa Maria, Brasil

Diabetes and ectonucleotidases in humans and experimental models

07-11-2011

Ângela Wyse, Universidade Federal do Rio Grande do Sul, Brasil

Toxicidade da homocisteína e possíveis estratégias de proteção

14-11-2011

Ana Filipa Ribeiro, IMM

The role of adenosine A2A receptor on neuronal outgrowth

21-11-2011

Federico Herrera, IMM

Protein quality control systems in health and disease

28-11-2011

Jana Sarkander, IMM

SIRT2 in neuronal differentiation

05-12-2011

Jorge Valadas, IMM

Adenosine A2A receptors overexpression in rats: effects on memory

12-12-2011

Sueli Marques, IMM

Chromatin remodeling in Alzheimer's disease

19-12-2011

Cecilia Gotti, Institute of Neuroscience, National Research Council of Italy

New tools to study the role of native brain $\alpha 6$ -containing nicotinic receptor subtypes

Bone Club

03-05-2011

Joana Lopes, IMM

Osteoblasts: to build or not to build

14-06-2011

Sandra Casimiro, Clinical and Translational Oncology Research Unit, IMM RANK-RANKL

Signaling Pathway Plays a Direct Role in the Tumor Compartment of Bone Metastases. A new window for anti-tumor therapeutics?

05-07-2011

Gabriel Miltényi, Genomed

FGFR gene related bone dysplasias from the perspective of human genetics

Lisbon Area Neuroscience Meetings

19-01-2011

Márcia M. Aranha, Research Institute for Medicines and Pharmaceutical Sciences, University of Lisbon

MiR-34a as a new player of neuronal differentiation

Hugo M. Botelho, ITQB, Universidade Nova de Lisboa

A β fibrils and metal ions modulate S100 amyloidogenesis: novel players in neurodegeneration?

16-02-2011

Alexandre de Mendonça, IMM

The beginning of Alzheimer's disease

Joaquim Ferreira, IMM

Disability milestones in Parkinson's disease: what really matters to the patients?

23-03-2011

Diogo S. Castro, Molecular Neurobiology, IGC

Transcriptional Control of Vertebrate Neurogenesis

Megan Carey, Champalimaud Neuroscience Programme, Champalimaud Centre for the Unknown

Endocannabinoid regulation of synaptic plasticity in the cerebellum

20-04-2011

Rita Aroeira, IMM

Temporal characterization of glycine receptor in rat hippocampus

Zrinka Marijanovic-Vultos, IMM

The role of autophagy in prion diseases

18-05-2011

Maria Luisa Vasconcelos, Champalimaud Neuroscience Programme, IGC

In search of the circuits of female fly courtship behavior

Sandra Tenreiro, IMM

Simple is good: Yeast as a model to study Parkinson's disease

22-06-2011

Sandra Morais Cardoso, Faculdade de Medicina e Centro de Neurociências e Biologia Celular, Universidade de Coimbra

Mitochondria breathe for autophagy

Michael Orger, Champalimaud Neuroscience Programme, Champalimaud Centre for the Unknown

Revealing neural circuits underlying visually guided behaviour in zebrafish

19-10-2011

João TS Fernandes, IST, INESC-Microsistemas e Nanotecnologias

Microfluidics in cell culture for neurosciences

Joana Coelho, Neuropharmacology laboratory, Boston University Medical School, Boston, Massachusetts, USA

The role of cellular localization of A2A adenosine receptors in psychostimulation

16-11-2011

Fábio Marques Simões de Souza, IMM

Electrophysiological recording and computational modeling of the olfactory system

Sara Xapelli, CNBC and IMM

Type 1 cannabinoid receptor (CB1R) activation promotes neurogenesis in murine subventricular zone cell cultures

14-12-2011

Diogo Rombo, IMM

Tuning inhibition with adenosine: synaptic vs extrasynaptic responses

Ricardo M. Santos., Redox Biology in Health and Disease Group, Center for Neuroscience and Cell Biology, University of Coimbra

Nitric oxide production, diffusion and inactivation in the rat brain: in vivo studies using microelectrodes

Other

05-01-2011

José Santos Victor, Instituto Superior Técnico

Reciprocal inputs between Neuroscience and Robotics

05-01-2011

Helder Coelho, Faculdade de Ciências, Universidade de Lisboa

Inteligência Artificial

13-01-2011

Michael Swash, The Royal London Hospital

How should we approach ALS?

01-02-2011

Alain Le Moine, Brussels

Transplantation: Relationships between Tregs, IL-17 and Th17 alloreactivity

04-02-2011

Sara Xapelli, Center for Neuroscience and Cell Biology, University of Coimbra

Type 1 cannabinoid receptor (CB1R) activation promotes neuronal differentiation in murine subventricular zone cell cultures

08-02-2011

Helene Dujardin, Application Scientist, Celeza GmbH

Flow cytometry analysis with FlowJo

15-03-2011

Cees Kallenberg, University Medical Center, Groningen, Holand

Vasculitis: turning complexity into simplicity

15-03-2011

Michèle Crozatier, Centre de Biologie du Développement, Université de Toulouse, France

Control of the size of the Drosophila hematopoietic niche by Dpp/BMP signaling reveals new parallels with mammals

16-03-2011

Steve Russell, University of Cambridge, UK

Transcription and Chromatin Architecture: a View from the Fly Genome

18-03-2011

Nobert Perrimon, Harvard Medical School, USA

Physiological and Regenerative Homeostasis in Drosophila

23-03-2011

Jonathon Blake, Gene Core Facility, EMBL, HD

Next Generation Sequencing, from Sequence Production towards Human Genetics

24-03-2011

Rob Pinnock, Merck Sharp & Dohme, UK

What is big pharma looking for?

25-03-2011

Patrício Soares da Silva, Bial, Portugal

Development of anti-epileptic eslicarbazepine acetate

29-03-2011

Ajay Chitnis, NIH, Bethesda, USA

Why does loss of Notch signaling affect lateral line morphogenesis?

31-03-2011

Tristan Rodriguez, MRC CSC, UK

Dissecting the pathways underlying neuronal specification in mammals

01-04-2011

Ana Pombo, MRC Clinical Sciences Centre, London, UK

Gene regulation by Polycomb repressor complexes in ES cells

05-04-2011

Arne Akbar, Division of Infection and Immunity, University College London

Decreased immunosurveillance in the skin during ageing

07-04-2011

Irina Budunova, Associate Professor, Departments of Dermatology and Urology, Northwestern University, Chicago, IL, USA

Novel approach to prostate cancer treatment via differential regulation of steroid receptors

20-05-2011

Dave Barry, Wellcome Trust Centre for Molecular Parasitology, Glasgow, Scotland

Systems biology of trypanosome antigenic variation

31-05-2011

Miguel Maroto, Dundee University

Mechanisms controlling segmentation during embryonic development

08-06-2011

Li Tang, BGI-Europe

Next Generation Sequencing on Human Disease Research

30-06-2011

Brian G. Spratt, Imperial College London

Web applications for MLST, population genomics and field epidemiology

07-09-2011

Pedro Beltrão, University of California San Francisco

Evolution of cellular networks: from interactions to phenotypes

06-10-2011

Paolo Ghia, Università Vita-Salute San Raffaele, Milano

When a lot becomes too much: the tale of Chronic Lymphocytic Leukemia

14-10-2011

Javier Martínez, Institute of Molecular Biotechnology, Vienna, Austria

The RNAi revolution

14-10-2011

Marcos Malumbres, Grupo de division celular y cancer, Centro Nacional de Investigaciones Oncológicas, Madrid, Spain

Control of cell proliferation and tumor growth by microRNAs

21-10-2011

Clare M. Waterman, Director, Cell Biology and Physiology Center, National Heart, Lung and Blood Institute, National Institutes of Health, USA

Integrating Actin dynamics with Adhesion in Cell Migration

08-11-2011

Steve Renshaw, MRC Centre for Developmental and Biomedical Genetics and Department of Infection and Immunity, University of Sheffield, UK

Understanding neutrophilic inflammation: what we can learn from zebrafish models

15-11-2011

Claudia G. Almeida, Laboratory of Morphogenesis and Intracellular Signaling, CNRS UMR144, Institute Curie, Paris

How does intracellular trafficking contribute to neuronal (dys)function?

23-11-2011

Klaus Ley, Division of Inflammation Biology of La Jolla Institute Allergy Immunology

New mechanisms of neutrophil adhesion under shear

07-12-2011

Edward Feil, University of Bath, UK

The micro-evolution and transmission of bacterial pathogens as revealed by next-generation sequencing

29-12-2011

Pedro Moreira, EMBL-Monterotondo

Implementation of Transgenic Technology at EMBL-Monterotondo

Courses

02-02-2011

Miguel Prudêncio, IMM

Training Course: IMM BSL3 Facility

28- 03-2011 - 01- 04-2011

Joana Almeida, IMM

Course on Animal Experimentation

24- 25-02-2011

Margarida Trindade, IMM and **Sheila Vidal**, IGC

CAML Advanced Course: Preparing for research: the grant environment

28-02-2011

Nuno C. Santos, IMM

CAML Advanced Course: Nanomedicine

09-10-03-2011

Francisco Enguita, IMM

CAML Advanced Course: Get the best from your sequences

17-02-2011

João Lobo Antunes, IMM

CAML Advanced Course: Scientific integrity

23-03-2011 - 13-04-2011

António Gouveia de Oliveira

CAML Advanced Course: Biostatistics

24-25-03-2011

Miguel Castanho, IMM

CAML Advanced Course: Improving technology transfer from academia in translational medicine

21-05-2011

Joaquim Ferreira, IMM

*III Teaching Course in Movement Disorders of the Neurological Clinical Research Unit
Instituto de Medicina Molecular*

30-05-2011 - 01-06-2011

Inês Crisóstomo, **Margarida Trindade** and **Marta Agostinho**, IMM

CAML Advanced Course: Launching your research career

13-14-10-2011

Francisco Enguita, IMM

CAML Advanced Course / Small RNAs in cell biology and human disease

17-11-2011

Communication and Training Unit, IMM

Training course on communicating science in the media - for post docs and PIs

05-06-12-2011

José Rino, IMM

CAML Advanced Course: BioImaging Nano Course on Microscopy

Workshops

16-05-2011

Workshop: Applying for funding from the Health FP7 Programme

04-09-2011

Workshop Emerging Tools in Quantitative Fluorescence Microscopy for Systems Biology

14-10-2011

Workshop em Estimulação Magnética Transcraniana (EMT)

11-11-2011

Primeiro Seminário Luso-Afro-Brasileiro sobre Poliomielite e Síndrome Pós-Poliomielite

IMM Advanced Training

The Advanced Training Programme has the support of Bayer

The IMM is strongly committed to Advanced Training in Biomedicine, in particular through the Lisbon Academic Medical Centre Doctoral Programme.

Team

Director: Miguel Carneiro de Moura, MD, PhD

Executive Coordinator: Inês Crisóstomo, PhD

*Scientific Consultants: António Jacinto, PhD
Ana Espada de Sousa, MD, PhD
Isabel Pavão Martins, MD, PhD*

IMM recruits every year highly motivated students to join one of the three IMM research programmes: Cell & Developmental Biology, Immunology & Infectious Diseases and Neurosciences. IMM's mission is to enable these students to be able to carry out independent, original and scientifically significant research, and become critical thinkers.

IMM co-organizes the **Lisbon Academic Medical Centre Doctoral Programme**, a joint PhD Programme between IMM, Faculdade de Medicina da Universidade de Lisboa (FMUL) and the Santa Maria University Hospital (HSM-CHLN). This programme focus on the excellence of the research proposals, and features a flexible and modular training component. The CAML PhD Programme, seeks to promote new questions at the bedside and take them to the lab. And reciprocally bridge questions from the lab to the clinic. By bringing together clinical and non-clinical researchers the program fosters new collaborative approaches and a more effective communication among fundamental and clinical investigators.

Advanced Training in numbers

111 PhD Students (70 Students registered in the CAML Doctoral Programme)

83 out of the 111 PhD students have individual fellowships

- 71** *Fundação para a Ciência e Tecnologia*
- 1** *Axa Research Fund*
- 2** *Marie Curie Initial Training Network*
- 2** *MD-PhD / Fundação para a Ciência e Tecnologia (Resident-PhD)*
- 4** *Programa de Formação Médica Avançada (FCG;FC;FCT;Min-Saúde)*
- 1** *Harvard Medical School-Portugal Program – Junior Award*
- 2** *IMM*

21 out of the 111 PhD students are MDs

- 15** MDs doing their PhD training in part-time

New PhD Students

Ana Filipa Ribeiro, Ana Londral, Ana Pena, Ana Rodrigues, Augusto Ministro, Bruno Gil Rosa, Carla Bentes, Catarina Mota, Daniel Ribeiro, Diana Ferreira, Fernando Domingos, Francisca Monjardino, Inês Perpétuo, João Freire, José Fonseca, Margarida Rei, Mariana Verdelho Machado, Maurício Martins, Patrícia Meireles, Paula Oliveira, Sandra Jacinto, Sérgio Laranjo, Telmo Pereira, Teresa Moreno, Tomás Fonseca. (Total: 25)

Advanced Courses

A total of 11 Advanced Courses were organized

Courses organized under the CAML PhD Programme

Get the best from your sequences

Organizer: Francisco Enguita, IMM/FMUL

Date: Feb 11-12 (1 ECTS)

Nº of Participants: 15

The students were trained to use online tools on the analysis of sequence properties of the more relevant biological molecules, DNA, RNA and proteins, and also how to present their data.

Scientific Integrity

in partnership with “Programa de Formação Médica Avançada”

Organizer: João Lobo Antunes, IMM/FMUL/CHLN

Date: Feb 17 –Apr 18 (1 ECTS)

Nº of Participants: 14

Principles of scientific integrity and ethics in experimentation.

Biostatistics

Organizer: António Gouveia de Oliveira, FCM/UNL

Date: Feb 23 –Apr 13 (2 ECTS)

Nº of Participants: 20 (37 Applications)

Basic principles and methods of biostatistics and data analysis, which are essential to design a study, select the appropriate statistical methods and interpret results.

Preparing for research: the grant environment

in partnership with “Programa de Formação Médica Avançada”

Organizer: Margarida Trindade, IMM & Sheila Vidal, IGC

Date: Feb 24 – 25 (1 ECTS)

Nº of Participants: 4

Practical tools to help search and apply for funding, write grants and get a better understanding of the present national and international research funding environments.

Nanomedicine

Organizer: Nuno Santos, IMM/FMUL

Date: Feb 28 - Mar 2

Nº of Participants: 15 (1.5 ECTS)

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”.

Improving technology transfer from basic research in translational medicine

Organizer: Miguel Castanho, IMM/FMUL

Date: Mar 24-25

Nº of Participants: 14 (1 ECTS)

Letting the researchers in academia know the potentialities of tech transfer, what industry expects from them, and the means by which basic research is suitable to carry on and be developed as industrial research.

Methodologies in clinical research

in partnership with “FMUL MSc/PhD in Neurosciences Programme”

Organizer: José Ferro, Patrícia Canhão, Cristina Sampaio & Joaquim Ferreira HSM-IMM/FMUL/CHLN

Date: May 3 – Jun 16 (2 ECTS)

Nº of Participants: 2

The course introduces the methodologies used in clinical research and describes the different types of studies. The second part of the course focus on therapeutic research.

Launching your research career

Organizer: Inês Crisóstomo, Margarida Trindade & Marta Agostinho, IMM

Date: May 30 – Jun 1 (1.5 ECTS)

Nº of Participants: 15 (19 applications)

This course aimed to help plan a research career and develop complementary skills, such as: manage time and data; present your work in posters, presentations, papers and grants; communicating with peers, funding agencies, media and other publics.

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

Organizer: Francisco Enguita, IMM/FMUL

Date: Oct 13-14 (1 ECTS)

Nº of Participants: 20 (35 applications)

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.

BioImaging Nano Course on Microscopy

Organizer: José Rino, IMM

Date: Dec 5 – 6 (0.5 ECTS)

Nº of Participants: 70

Targeted for beginner or intermediate microscope users, this course taught participants the theoretical background in fluorescence widefield and confocal microscopy as well as practical information on how to efficiently prepare samples, acquire data and obtain publication quality images.

Other Advanced Courses

Training course on communicating science in the media - for postdocs and PIs

Organizer: Marta Agostinho, IMM

Date: Nov 17 – 18

Nº of Participants: 5

This course aims at helping participants explore the opportunities of contacting with the media, define communication goals, manage expectations and take the most of media contacts.

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”.

2011 PhD Students commission

Alice Melão, Carolina Moreira, Diogo Pereira, Diogo Rombo, Irina Alho, Joana Xavier, João Freire, Jorge Santos, Rita Mateus, Rosangela Frita and Telma Lança.

2011 PhD Students representatives

Margarida Rodrigues and Henri Franquelim

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, every four sessions there is an “invited speaker” (Full list at Seminars Section)

IMM Changer

Date: June 14

Place: Instituto Superior de Agronomia

Late afternoon gather of IMMers for a traditional game circuit followed by dinner and an after-hour party.

IV IMM PhD Students Retreat

Date: September 25-27

Place: Pousada da Juventude de Alvados, Porto de Mós

Participants: 30: PhD students (21), post-docs (2), master students (1), technicians (5) and staff scientists (1).

Programme:

- 1) “Breaking the ice”, introduction of all participants.
- 2) Scientific discussion - Round table.
- 3) Hiking to Fórnea - Cova da velha.
- 4) IMM Quiz and Traditional games.

V PhD Students Meeting IMM/CAML

Date: October 17-18

Place: IMM/FMUL

Participants: 62 PhD students, 1 Guest, 7 Moderators, 1 Members of Jury, 2 PhD Team (Total: 73), plus audience

October 17

Opening Session

Rui Victorino (FMUL), João Correia da Cunha (CHLN) and Carmo Fonseca (IMM) and Miguel Carneiro de Moura (IMM).

Oral Presentation Session I

Moderators: Filomena Carvalho and Susana Pascoal

Speakers: Aida Costa, Joana Monteiro, Cristina Silva, Henri Franquelim, Sofia Cristóvão-Ferreira and Joana Xavier.

Poster Presentation Session

Nina Schmolka, Rita Mateus, Rita Aroeira, Patrícia Meireles, Tomás Fonseca, Inês Perpétuo, João Freire, Elisa Basso, Mariana Oliveira, Sofia Oliveira, Alice Melão and Sandra Jacinto.

October 18

Oral Presentation Session II

Moderators: Patrícia Silva and Rita Moura

Speakers: Marta Caridade, Maurice Itoe, Marco Antunes and Rita Cascão.

Oral Presentation Session III

Moderators: Daniel Carapau and Filipe Vilas-Boas

Speakers: Telma Lança, Leonor Fleming, Margarida Rodrigues and Joana Tato Costa.

Keynote Lecture

Introduction by Prof. Lobo Antunes (CAML)

Keynote speaker: Prof. Martin Raff (MRC Lab. for Molecular Cell Biology, UCL, London, UK)

Poster Presentation Session II

Jorge Santos, Carolina Moreira, André Santos, Rosangela Frita, Vânia Batalha, Diogo Rombo, Ana Pena, Inês Cristo, Filipa Ribeiro, Daniel Ribeiro, Telmo Pereira, and Susana Fernandes.

Oral Presentation Session IV

Moderators: Madalena Martins and Sandra Aguiar

Speakers: Ana Água-Doce, Marco Domingues, Angélica Vittori, Marta Ribeiro, Diogo Pereira and Daniel Silva

Oral Presentation Session V

Moderators: Manuela Ferreira and Sandra Tenreiro

Speakers: Rita Barbosa, Raquel Mendes, Susana Gonçalves and Pedro Pereira.

Awards Ceremony and Closing Remarks

Inês Crisóstomo; Henri Franquelim; Margarida Rodrigues

Meeting Dinner

PhD thesis

Filipe Vilas Boas (January 14, 2011) Functional analysis of the Notch signalling cascade in neural progenitors. Faculdade de Medicina da Universidade de Lisboa. Supervisor: D. Henrique

Joana Duarte (February 16, 2011) Reprogramming the immune system with anti-CD4 monoclonal antibodies. Faculdade de Medicina da Universidade de Lisboa. Supervisor: L. Graça

Raquel Lourenço (March 4, 2011) Symmetry-OUT, Asymmetry-IN, The role of DMRT2. Instituto de Tecnologia Química e Biológica da Universidade Nova de Lisboa. Supervisor: L. Saúde

Vasco C. Sousa (March 21, 2011) Cross-talk mechanisms between adenosine and cannabinoid implications for the effects of Δ^9 -tetrahydrocannabinol on spatial memory. Faculdade Medicina da Universidade de Lisboa. Supervisors: A.M. Sebastião; Co-supervisor: R. Brett

Rita Azevedo (April 5, 2011) The role of IL-7 in the Homeostasis of Human Naive and Memory CD4⁺ T cell subsets. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Soares

Tiago Krug Coelho (April 13, 2011) Stroke Genetics and Genomics. Faculdade de Medicina da Universidade de Lisboa. Supervisors: S.A. Oliveira; Co-supervisor: J.M. Ferro

Catarina Guerreiro (April 14, 2011) Nutrição e Genes em Doenças Intestinais. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M.E. Camilo

Rui Manuel da Silva Soares (May 23, 2011) Papel da Carga Viral Celular na Imunodeficiência HIV/SIDA: Contributo do Estudo da Infecção pelo HIV-2. Faculdade de Medicina da Universidade de Lisboa. Supervisor: A.E. Sousa

Sandra Aguiar (July 1, 2011) Molecular epidemiology of *Streptococcus pneumoniae*: impact of PCV7 in the pneumococcal population responsible for invasive pediatric infections. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Ramirez

Raquel Dias (July 8, 2011) Modulation of glutamate AMPA receptors by adenosine, in physiology and hypoxic/ischemic conditions. Faculdade Medicina da Universidade de Lisboa. Supervisor: A.M. Sebastião

Ana Inês Domingues (September 20, 2011) Molecular mechanisms and relevance of the nuclear internalization of VEGF and VEGFR2 (KDR) on endothelial cells. Faculdade de Ciências da Universidade de Lisboa. Supervisors: S. Constantino; Co-supervisor: P. de Lanerolle

Ricardo Henriques PhD (October 17, 2011) Beyond Rayleigh's limit: Achieving real-time super-resolution fluorescence microscopy. Faculdade de Medicina da Universidade de Lisboa. Supervisors: M. Mhlanga; Co-supervisor: A. Jacinto

Ivonne Wollenberg (October 17, 2011) The role of regulatory T cells in the control of B cell mediated immune responses. Faculdade de Medicina da Universidade de Lisboa. Supervisor: L. Graça; Co-supervisor: J. Faro

Rita Moura (November 18, 2011) The role of B cells in the early phase of rheumatoid arthritis. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.E. Fonseca; Co-supervisor: L. Graça

Inês Sofia Vala (November 24, 2011) Vascular activation and tumor regrowth after radiotherapy. Faculdade de Ciências da Universidade de Lisboa. Supervisor: S. Constantino

Maria João Frias (November 25, 2011) Lysis strategy of *Streptococcus pneumoniae* bacteriophages: Mechanisms and host implications. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Ramirez

Elisabete Martins (November 28, 2011) *Streptococcus agalactiae* causing human infections. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Ramirez

Sandra Vaz (December 7, 2011) Regulation of GABA transporter in neuronal cells: role of Brain-Derived Neurotrophic Factor. Faculdade Medicina da Universidade de Lisboa. Supervisor: A.M. Sebastião

Margarida Carrolo (December 9, 2011) New insights into the sociomicrobiology of *Streptococcus pneumoniae*: exploring biofilm formation. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Ramirez

Joana Caetano Lopes (December 13, 2011) Effect of inflammation on bone biological, structural and mechanical behavior. Faculdade de Medicina de Lisboa. Supervisors: J.E. Fonseca; Co-supervisor: Y. Konttinen

Catarina Fernandes (December 19, 2011) Dynamics and function of nicotinic acetylcholine receptors in the nervous system. Faculdade Medicina da Universidade de Lisboa. Supervisors: A.M. Sebastião; Co-supervisor: D.K. Berg

Bruno Cardoso (December 20, 2011). IL-4 and TAL1 in T-cell acute lymphoblastic leukemia: studies on the participation of microenvironmental cues and cell-autonomous alterations in leukemogenesis. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata; Co-supervisor: L. Parreira

(Total: 22)

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.

IMM and Inserm, aware of the need to develop international co-operation in the fields of life sciences and health research and of health, have decided, through a **agreement** signed in 2010 to collaborate in order to promote the exchange of scientific, medical, and technical knowledge, and to support actions conducive to high-quality scientific exchanges. The partnership builds on sound research expertise of both institutions to deliver scientific international workshops, short-term staff exchanges and research mentoring for MD students.

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** and **Thelial** (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 2011, IMM hosted 29 research units.

Of these:

- 26 are located at Edifício Egas Moniz (IMM)
- 1 at Hospital Santa Maria (Neurological Clinical Research Unit)
- 2 at the Faculdade de Farmácia da Universidade de Lisboa (Mycobacteria Host Interactions Unit and Retrovirus Research Unit)

Cell and Developmental Biology programme

Programme Coordinators: António Jacinto and Luís Moita

Heads of Unit:

Susana Constantino Santos, PhD

Nuno C. Santos, PhD

João Taborda Barata, PhD

M. Carmo Fonseca, MD, PhD

Luís Ferreira Moita, MD, PhD

Luís Costa, MD, PhD

Domingos Henrique, PhD

Leonor Saúde, PhD

Musa Mhlanga, PhD

Carlota Sadanha, PhD

Miguel Castanho, PhD

António Jacinto, PhD

Principal Investigators:

Susana Constantino Santos

Nuno C. Santos

João Taborda Barata

M. Carmo-Fonseca, Francisco Enguita,
Sérgio de Almeida

Luís Ferreira Moita, Ângelo Chora

Luís Costa

Domingos Henrique

Leonor Saúde

Musa Mhlanga

Carlota Sadanha, Ângelo Calado

Miguel Castanho

António Jacinto, Soren Prag, Nina
Matova

Angiogenesis Unit

Major interests / Objectives

The Angiogenesis Unit studies molecular and cellular mechanisms that regulate the angiogenic process in order to devise novel therapeutic approaches. Our specific aims are 1) to study the molecular mechanisms whereby low doses of ionizing radiation induce angiogenesis and consequently metastasis after radiotherapy; 2) To investigate the potential therapeutic effects of low doses of ionizing radiation through neovascularization promotion; 3) To investigate the effect of the wild-type or mutated Transthyretin (TTR) in the differential response of the hepatic vasculature.

Head of Unit

Susana Constantino Rosa Santos, PhD – Auxiliary Professor, FMUL

Research Team

Raquel Sampaio, PhD	Post Doc Fellowship, FCT
Augusto Ministro, MD	PhD Student
Ana Inês Domingues	PhD Fellowship, FCT (left September 2011)
Inês Sofia Vala	PhD Fellowship, FCT (left October 2011)
Rui Perdigoto	MD, Hospital Curry Cabral
Paula Oliveira	IEFP/IMM fellowship
André Rocha	Md Student, FMUL
Joana Simões	Msc Student
Teresa Freitas	Technician, FMUL

Keywords/Research Areas

Angiogenesis; Vasculogenesis; Metastasis ; Ischemia

Major scientific achievements

- 1) VEGFR-2 activates its own promoter and by this mechanism could be involved in amplifying the angiogenic response. Work published in PLoS ONE.
- 2) Low doses of ionizing radiation (IR) promote tumor growth and metastasis by enhancing angiogenesis. We identified several genes whose expression is significantly altered by low doses of IR and play a role in pro-angiogenic response. The results obtained will provide a new rationale basis to the improvement of current radiotherapy protocols. Moreover, we found that low doses of IR enhance vascularisation in ischemic tissues, having important implications in the use of low doses of IR in nonmalignant diseases.

3) V30M transthyretin induces endothelial cell apoptosis but not migration, as opposed to the WT. Molecularly, TTR WT increases the levels of mRNA for proteins that promote angiogenesis. These results are important to understand why FAP patients have more hepatic artery thrombosis incidence after transplantation.

Recent Most Relevant Publications

Domingues I, Rino J, Demmers JAA, de Lanerolle P, Santos SCR (2011) VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. *PLoS ONE* **6**, e25668 (Journal IF: 4.4, Citations: 0)

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 (Journal IF: 4.4, Citations: 0)

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. (Journal IF: 5.4, Citations: 17)

Constantino Rosa Santos S, Miguel C, Domingues I, Calado A, Zhu Z, Wu Y and Dias S (2007) VEGF and VEGFR-2 (KDR) internalization is required for endothelial recovery during wound healing. *Exp Cell Res* **313**, 1561-1574. (Journal IF: 3.7, Citations: 36)

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. (Journal IF: 10.6, Citations: 92)

Ongoing Research Projects

2009/2012 The biological effects of ionizing radiation in the vasculature, Roche Farmacêutica, Novartis Farma, Astellas Farma, Wyeth Lederle Portugal and Merck Sharp & Dohme. Coordinator: Susana Constantino. €50 000

2009/2012 The effect of the wild-type or mutated Transthyretin (TTR) in the differential response of the hepatic vasculature, Hospital Curry Cabral. Coordinator: Susana Constantino. €40 000

2009/2012 The differential effect of WT and V30M Transthyretin in the hepatic microenvironment and vasculature response, FCT. Coordinator: Susana Constantino and Rui Perdigoto. PIC/IC/83062/2007. €190 000

2011/2012 The biological effects of ionizing radiation in the vasculature, Novartis, Medtronic. Coordinator: Susana Constantino. €7 000

2011/2013 Molecular targets and cellular mechanisms whereby low doses of IR induce a pro-angiogenic response. Coordinator: Susana Constantino (no funding)

Publications in peer review Journals

Domingues I, Rino J, Demmers JAA, de Lanerolle P, Santos SCR (2011) VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. PLoS ONE 6, e25668 (Journal IF: 4.4, Citations: 0)

Mareel M. and Constantino S. (2011) Ecosystems of invasion and metastasis in mammary morphogenesis and cancer. Int. J. Dev. Biol. 55, 671 – 684 (Journal IF: 2.9, Citations: 0)

Communications in International Conferences

Rocha, A. Ionizing radiation: boosting angiogenesis in ischemic diseases, Leiden International Medical Student Conference, Leiden, Netherlands, March 16-20, 2011(Oral presentation).

Constantino Rosa Santos S. Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis, Champalimaud Cancer Center, Lisbon, Portugal, June 25-28, 2011 (Poster presentation)

Sousa J. Molecular mechanisms whereby low doses of ionizing radiation induce angiogenesis, Advances in the cellular and molecular biology of angiogenesis, Birmingham, UK, June 26-29, 2011 (Poster presentation)

de Oliveira, P. A new strategy for therapeutic angiogenesis: Low doses of Ionizing Radiation, Advances in the cellular and molecular biology of angiogenesis, Birmingham, UK, June 26-29, 2011 (Poster presentation)

Ministro A. A Novel Approach for Therapeutic Angiogenesis: Low Doses of Ionizing Radiation, 20th European Chapter Congress of the International Union of Angiology, Ljubljana, Slovenia, October 6-8, 2011 (Oral presentation)

Internationalization

Collaborative Publication:

Domingues I, Rino J, Demmers JAA, de Lanerolle P, Santos SCR (2011) VEGFR2 Translocates to the Nucleus to Regulate Its Own Transcription. PLoS ONE 6, e25668

Collaborative Research:

Primal de Lanerolle, University of Illinois, Chicago, USA. Research Project: The role of nuclear VEGFR-2.

Curzio Ruegg, Division of Experimental Oncology, Centre Pluridisciplinaire d'Oncologie, Faculty of Biology and Medicine, University of Lausanne, and NCCR Molecular Oncology ISREC-EPFL, Epalinges, Switzerland. Research Project: Molecular mechanisms and relevance of angiogenesis induced by low-dose ionizing radiation.

Marc Mareel, Ghent University Hospital, Ghent, Belgium. Research Project: Molecular mechanisms and relevance of angiogenesis induced by low-dose ionizing radiation.

Collaborative PhD Training:

Primal de Lanerolle, University of Illinois, Chicago, USA. Co-supervisor of PhD project of Ana Inês Domingues.

Advanced teaching

Constantino, S. Tumoral Angiogenesis lecture for the Master in Neurosciences - Pathology of the Nervous System, FMUL, Lisbon. February 15, 2011

Science and Society

Susana Constantino. Participation in the TV program “Com Ciência”, RTP2, 29 June, 2011

Master and PhD thesis completed (3000 ca.)

PhD thesis

Ana Inês Domingues (2011). Faculdade de Ciências da Universidade de Lisboa. Molecular mechanisms and relevance of the nuclear internalization of VEGF and VEGFR2 (KDR) on endothelial cells. Supervisors: Susana Constantino and Primal de Lanerolle

Inês Sofia Vala (2011). Vascular activation and tumor regrowth after radiotherapy. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Susana Constantino

Master thesis

Joana Simões (2011). Molecular mechanisms and relevance of angiogenesis induced by low-dose ionizing radiation. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Susana Constantino

Biomembranes Unit

Major interests / Objectives

Biochemical and biophysical processes occurring at the level of the membranes of human cells, as well as of their viral and bacterial pathogens. Study of the two steps of the life cycle of enveloped viruses (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 at the molecular level of antimicrobial peptides (AMP) and cell-penetrating peptides (CPP). On the Nanotechnology / Nanomedicine area, the structural characterization of metal nanoparticles conjugated with proteins or nucleic acids, for biomedical application.

Head of Unit

Nuno C. Santos, PhD – Assistant Professor with Habilitation, FMUL.

Research Team

Sónia Gonçalves, PhD	Researcher, FMUL
Ivo Martins, PhD	Post Doc Fellowship, FCT
Andrea Santos, PhD	Post Doc Fellowship, FCT
Axel Hollmann, PhD	Post Doc Fellowship, FCT (since April 2011)
Filomena Carvalho	Assistant, FMUL
Marco Domingues	PhD Fellowship, FCT
Pedro Matos	PhD Fellowship, FCT
Margarida Rodrigues	PhD Fellowship, FCT
André Faustino	PhD Fellowship, FCT
Rita Inácio	Master Student
Teresa Freitas	Technician, FMUL

Keywords/Research Areas

Membranes, HIV, Antimicrobial peptide, AFM, Fibrinogen, Nanomedicine.

Major scientific achievements

Dengue virus capsid protein binding to hepatic lipid droplets is K⁺-dependent and mediated by droplets surface proteins:

Dengue virus (DENV) affects millions of people, causing more than 20 thousand deaths annually. No effective treatment for the disease caused by DENV infection is currently available, partially due to the lack of knowledge on the basic aspects of the viral life cycle, including the molecular basis of the interaction between viral components and cellular compartments. Here, we

characterized the properties of the interaction between DENV capsid (C) protein and hepatic lipid droplets (LDs), which was recently shown to be essential for the virus replication cycle. Zeta-potential analysis revealed a negative surface charge of LDs, with an average of -19 mV. Titration of LDs with C protein led to an increase of the surface charge, which reaches a plateau at +13.7 mV, suggesting that the viral protein-LD interaction exposes the protein cationic surface to the aqueous environment. Atomic force microscopy (AFM)-based force spectroscopy measurements were performed using C protein-functionalized AFM tips. C protein-LDs interaction was found to be strong, with a single (un)binding force of 33.6 pN. This binding was dependent on high intracellular concentrations of potassium ion but not sodium. Inhibition of Na^+/K^+ -ATPase in DENV-infected cells resulted in C protein dissociation from LD and a 50-fold inhibition of infectious virus production but not in RNA replication, indicating a biological relevance for the potassium dependent-interaction. Limited proteolysis of LDs surface impaired C protein-LDs interaction and force measurements in the presence of specific antibodies indicate perilipin 3 (TIP47) as the major DENV C protein ligand on LDs surface.

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: 9.865, Citations: 6)

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: 4.411, Citations: 6)

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: 11.050, Citations: 4)

Matos PM, Franquelim HG, Castanho MARB, Santos NC (2010) Quantitative assessment of peptide-lipid interactions. Ubiquitous fluorescence methodologies. *Biochim. Biophys. Acta* **1798**, 1999-2012. (Journal IF: 4.647, Citations: 7)

Domingues MM, Castanho MARB, Santos NC (2009) rBPI₂₁ promotes lipopolysaccharide aggregation and exerts its antimicrobial effects by (hemi)fusion of PG-containing membranes. *PLoS ONE* **4**, e8385. (Journal IF: 4.411, Citations: 8)

Ongoing Research Projects

2007/2011 Fibrinogen-dependent signalling in microvascular blood cell function – implications of inflammation and cardiovascular disease. Participant PI: N.C. Santos. FCT - PTDC/SAU-OSM/73449/2006, €101 736.

2007/2011 The role of lipid membranes on cell infection by Dengue virus. Participant PI: N.C. Santos. FCT - PTDC/QUI/69937/2006, €120 000.

2009/2011 Interação da proteína capsídica do vírus da dengue com membranas e corpúsculos lipídicos – Relevância para a patogénese viral. Coordinator: N.C. Santos. FCT-CAPES Project, €20 000.

2010/2013 Cell membrane features in HIV entry and its inhibition. Coordinator: N.C. Santos. FCT - PTDC/QUI-BIQ/104787/2008, €174 130.

2010/2013 Inherent antibacterial activity in peptide-based hydrogels for tissue regeneration. Participant PI: N.C. Santos. FCT - PTDC/SAU-BEB/099142/2008, €199 350.

2010/2013 MEMPEPACROSS: Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration. Coordinator: N.C. Santos. Programme “People” – Marie Curie International Research Staff Exchange Scheme – Call identifier: FP7-PEOPLE-2009-IRSES. Coordinator: N.C. Santos, €200 000.

2010/2013 Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease. Coordinator: N.C. Santos. Calouste Gulbenkian Foundation, €12 500.

2010/2013 The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation. Coordinator: I.C. Martins. Calouste Gulbenkian Foundation, €50 000.

2011/2014 LIPIDENGUE: The role of hepatic lipid membranes and lipid droplets in Dengue virus encapsidation. A gateway to new therapies. Coordinator: M. Castanho. FCT - PTDC/QUI-BIQ/112929/2009, €130 000.

Publications in peer review Journals

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 (2011) Dengue virus capsid protein binding to hepatic lipid droplets (LD) is potassium ion dependent and is mediated by LD surface proteins. *J. Virol.*, Epub 2011 Nov 30. (Journal IF: 5.189, Citations: 0)

Eaton P, Zuzarte-Luis V, Mota MM, Santos NC, Prudêncio M (2011) Infection by Plasmodium changes shape and stiffness of hepatic cells, *Nanomedicine (NBM)*, Epub 2011 Oct 25. (Journal IF: 4.882, Citations: 0)

dos Santos AM (2011) Thermal effect on aequorea green fluorescent protein anionic and neutral chromophore forms fluorescence. *J. Fluoresc.*, Epub 2011 Aug 10. (Journal IF: 1.966, Citations: 0)

Franquelim HG, De-Sousa FF, Veiga AS, Santos NC, Castanho MARB (2011) Cationic liposomes are possible drug-delivery systems for HIV fusion inhibitor Sifuvirtide. *Soft Matter* **7**, 11089-11092. (Journal IF: 4.457, Citations: 0)

Rodrigues M, de la Torre BG, Rádis-Baptista G, Santos NC, Andreu D (2011) Efficient cellular delivery of β -galactosidase mediated by NrTPs, a new family of cell-penetrating peptides. *Bioconjugate Chem.* **22**, 2339-2344. (Journal IF: 5.002, Citations: 0)

Ribeiro MM, Pinto AR, Domingues MM, Serrano I, Heras M, Bardaji ER, Tavares I, Castanho MARB (2011) Chemical conjugation of the neuropeptide kyotorphin and ibuprofen enhances brain targeting and analgesia. *Mol. Pharm.* **8**, 1929-1940. (Journal IF: 5.400, Citations: 0)

Henriques ST, Huang YH, Rosengren KJ, Franquelim HG, Carvalho FA, Johnson A, Sonza S, Tachedjian G, Castanho MARB, Daly NL, Craik DJ (2011) Decoding the membrane activity of the cyclotide kalata B1: the importance of phosphatidylethanolamine phospholipids and lipid organization on hemolytic and anti-HIV activities. *J. Biol. Chem.* **286**, 24231-24241. (Journal IF: 5.328, Citations: 2)

Vitorino C, Carvalho FA, Almeida AJ, Sousa JJ, Pais AA (2011) The size of solid lipid nanoparticles: an interpretation from experimental design. *Colloids Surf. B Biointerfaces.* **84**, 117-30. (Journal IF: 2.780, Citations: 2)

Ascenso A, Guedes R, Bernardino R, Diogo H, Carvalho FA, Santos NC, Silva AM, Marques HC (2011) Complexation and full characterization of the tretinoin and dimethyl- β -cyclodextrin complex. *AAPS PharmSciTech* **12**, 553-563. (Journal IF: 1.211, Citations: 1)

Martins AP, Lopes PA, Costa ASH, Martins SV, Santos NC, Prates JAM, Moura TF, Soveral G (2011) Differential mesenteric fat deposition in bovines fed on silage or concentrate is independent of membrane permeability to glycerol. *Animal* **5**, 1949-1956. (Journal IF: 1.458, Citations: 0)

Carvalho FA, de Oliveira S, Freitas T, Gonçalves S, Santos NC (2011) Variations on fibrinogen-erythrocyte interactions during cell aging. *PLoS ONE* **6**, e18167. (Journal IF: 4.411, Citations: 2)

Freire JM, Domingues MM, Matos J, Melo MN, Veiga AS, Santos NC, Castanho MARB (2011) Using zeta-potential measurements to quantify peptide partition to lipid membranes. *Eur. Biophys. J.* **40**, 481-487. (Journal IF: 2.387, 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* **25**, 419-428. (Journal IF: 6.348, Citations: 3)

Other publications International

Castanho M, Santos NC (2011) Peptide drug discovery and development: Translational research in academia and industry. Wiley-VCH, Weinheim.

Castanho M, Santos NC (2011) The timeliness of peptide drugs. *In*: Castanho M, Santos NC (eds.), Peptide drug discovery and development: Translational research in academia and industry. Wiley-VCH, Weinheim, pp. xiii-xiv.

Franquelim HG, Matos PM, Veiga AS (2011) HIV vs. HIV: turning HIV-derived peptides into drugs. *In*: Castanho M, Santos NC (eds.), Peptide drug discovery and development: Translational research in academia and industry. Wiley-VCH, Weinheim, pp. 209-229.

Other publications National

Santos NC (2011) Nanomedicina – Ciência, Tecnologia e Educação. *In: Nanotecnologias e O.G.M. – Ciência, Ética, Sociedade. Coleção Bioética*, vol. 12, Conselho Nacional de Ética para as Ciências da Vida, Lisbon, pp. 27-34.

Domingues MM, Matos PM, Carvalho FA, Santos NC (2011) Protein-Biomembrane interactions as therapeutic targets. *Canal BQ*, **8**, 4-11.

Invited Lectures and Seminars

Santos, N.C. Atomic Force Microscopy and Force Spectroscopy. Biological and Biomedical Applications. Workshop MIT Portugal, Lisbon, Portugal, January 14, 2011.

Santos, N.C. Protein-Biomembrane interactions as therapeutic targets. Faculdade de Farmácia da Universidade de Lisboa, Lisbon, Portugal, February 18, 2011.

Carvalho, F.A., Santos, N.C. Identification and single-molecule recognition of the fibrinogen receptor on human erythrocytes. Exploring Beyond the Shore: A Trans-Atlantic Meeting on Biochemistry and Molecular Biology, Seville, Spain, May 24-26, 2011.

Castanho, M.A.R.B., Freire, J.M., Santos, N.C., Veiga, A.S., Da Poian, A.T. Dengue: viral cellular infection reappraised. 22nd American Peptide Symposium, San Diego, USA, June 25-30, 2011.

Castanho, M.A.R.B., Freire, J.M., Santos, N.C., Veiga, A.S., Da Poian, A.T. Dengue: viral cellular infection reappraised. XXXIV Congreso de la Sociedad Española de Bioquímica y Biología Molecular (SEBBM), Barcelona, Spain, September 5-8, 2011.

Carvalho, F.A. Microscopia de Força Atómica – Reconhecimento molecular do receptor do fibrinogénio nos eritrócitos. Encontro dos técnicos de diagnóstico e terapêutica, Lisbon, Portugal, November 12, 2011.

Santos, N.C. AFM-based Force Spectroscopy. 10th Short Course of the Portuguese Biophysical Society – Nanosciences for Life, Santarém, Portugal, November 17-19, 2011.

Communications in International Conferences

Carvalho, F.A., Connell, S., Miltenberger-Miltenyi, G., Pereira, S.V., Tavares, A., Ariëns, R.A.S., Santos, N.C. Identification of the fibrinogen receptor on human erythrocyte by AFM-based force spectroscopy. Biophysical Society's 55th Annual Meeting, Baltimore, USA, March 5-9, 2011 (Poster presentation).

Martins, I.C., Carneiro, F.A., Mohana-Borges, R., Faustino, A., Pereira, R.M., Carvalho, F.A., Castanho, M., Almeida, F., Santos, N.C., Da Poian, A.T. Characterization of the interaction of the dengue virus capsid protein with lipid droplets. Biophysical Society's 55th Annual Meeting, Baltimore, USA, March 5-9, 2011 (Poster presentation).

Domingues, M.M., Castanho, M., Santos, N.C. rBPI₂₁ causes (hemi)fusion and leakage of membranes and promotes massive lipopolysaccharide aggregation. Biophysical Society's 55th Annual Meeting, Baltimore, USA, March 5-9, 2011 (Poster presentation).

Faustino, A., Martins, I.C., Carneiro, F.A., Carvalho, F.A., Pereira, R.M., Castanho, M.A.R.B., Mohana-Borges, R., Almeida, F.C.L., Da Poian, A.T., Santos, N.C. Molecular insights into the interaction between dengue virus capsid protein and lipid droplets. 40th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, April 30 - May 3, 2011 (Poster presentation).

Carvalho, F.A., de Oliveira, S., Freitas, T., Gonçalves, S., Santos, N.C. AFM-based force spectroscopy evaluation of the variations on fibrinogen-erythrocyte interactions during cell aging. 40th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, April 30 - May 3, 2011 (Poster presentation).

Gonçalves, S., Teixeira, A., Abade, J., de Medeiros, L., Kurtenbach, E., Santos, N.C. Antimicrobial peptides Psd1 and HNP-1: comparison of lipid selectivities. 40th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, April 30 - May 3, 2011 (Poster presentation).

Carvalho, F.A., Carneiro, F.A., Martins, I.C., Faustino, A., Pereira, R., Castanho, M., Mohana-Borges, R., Da Poian, A.T., Santos, N.C. Characterization of the interaction of the dengue virus capsid protein with lipid droplets. Keystone Symposium Lipid Biology and Lipotoxicity, Killarney, Ireland, May 15-20, 2011 (Poster presentation).

Freire, J.M., Veiga, A.S., Santos, N.C., Kowalczyk, W., Andreu, D., Da Poian, A.T., Castanho, M. Assigning a role to the Dengue Virus Capsid Protein during cellular infection. 11th FEBS (Federation of European Biochemical Societies) Young Scientist Forum, Torino, Italy, June 23-25, 2011 (Poster presentation).

Rodrigues, M., Santos, A., de la Torre, B.G., Rádis-Baptista, G., Castanho, M., Andreu, D., Santos, N.C. A new family of CPPs – Membrane interactions and translocation assays for nucleolar-targeting peptides (NrTP) in cells and biomembrane model systems. 36th FEBS (Federation of European Biochemical Societies) Congress – Biochemistry for Tomorrows Medicine, Torino, Italy, June 25-30, 2011 (Poster presentation).

Santos, A., Rodrigues, M., de la Torre, B.G., Rádis-Baptista, G., Castanho, M., Andreu, D., Santos, N.C. Screening and characterization of membrane-peptide interactions in new crotamine-derived CPPs. 36th FEBS (Federation of European Biochemical Societies) Congress – Biochemistry for Tomorrows Medicine, Torino, Italy, June 25-30, 2011 (Poster presentation).

Freire, J.M., Veiga, A.S., Santos, N.C., Kowalczyk, W., Andreu, D., Da Poian, A.T., Castanho, M. Assigning a role to the Dengue Virus Capsid Protein during cellular infection. 36th FEBS (Federation of European Biochemical Societies) Congress – Biochemistry for Tomorrows Medicine, Torino, Italy, June 25-30, 2011 (Oral presentation).

Franquelim, H.G., Veiga, A.S., Santos, N.C., Castanho, M. Membrane mode of action of HIV inhibitor peptides enfuvirtide and T-1249 unraveled by atomic force microscopy and dipole potential fluorescence spectroscopy. 22nd American Peptide Symposium, San Diego, USA, June 25-30, 2011 (Poster presentation).

Ribeiro, M.M.B., Pinto, A., Domingues, M., Heras, M., Bardaji, E., Tavares, I., Castanho, M. Development of novel analgesic Kyotorphin-derived peptides: linking peptide-membrane interaction, Blood-Brain barrier crossing and in vivo efficacy. 22nd American Peptide Symposium, San Diego, USA, June 25-30, 2011 (Poster presentation).

Freire, J.M., Veiga, A.S., Santos, N.C., Kowalczyk, W., Andreu, D., Da Poian, A.T., Castanho, M. Quantifying Molecular Partition of Supramolecular Complexes in Lipid Model Systems – Studies on Dengue Virus Supramolecular Components. EBSA 2011 – 8th European Biophysics Congress, Budapest, Hungary, August 23-27, 2011 (Poster presentation).

Rodrigues, M., Santos, A., de la Torre, B.G., Rádis-Baptista, G., Castanho, M., Andreu, D., Santos, N.C. Membrane interactions and translocation assays for nucleolar-targeting peptides. EBSA 2011 – 8th European Biophysics Congress, Budapest, Hungary, August 23-27, 2011 (Poster presentation).

Santos, A., Rodrigues, M., de la Torre, B.G., Rádis-Baptista, G., Castanho, M., Andreu, D., Santos, N.C. Screening and characterization of membrane-peptide interactions in new crotamine-derived CPPs. EBSA 2011 – 8th European Biophysics Congress, Budapest, Hungary, August 23-27, 2011 (Poster presentation).

Gonçalves, S., Teixeira, A., Abade, J., Santos, N.C. Lipid selectivity as a determinant factor for HNP1 biological activity. EBSA 2011 – 8th European Biophysics Congress, Budapest, Hungary, August 23-27, 2011 (Poster presentation).

Carvalho, F.A., de Oliveira, S., Freitas, T., Gonçalves, S., Santos, N.C. Force spectroscopy characterization of fibrinogen-erythrocyte binding and its conditioning by aging. EBSA 2011 – 8th European Biophysics Congress, Budapest, Hungary, August 23-27, 2011 (Poster presentation).

Torcatto, I.M., Huang, Y.H., Franquelim, H.G., Gaspar, D., Santos, N.C., Craik, D.J., Castanho, M.A.R.B., Henriques, S.T. Novel antimicrobial peptides with activity against Gram-negative and Gram-positive bacteria. 14th European Conference on the Spectroscopy of Biological Molecules, Coimbra, Portugal, August 29 - September 3, 2011 (Oral presentation).

Communications in National Conferences

Santos, A., Rodrigues, M., de la Torre, B.G., Rádis-Baptista, G., Castanho, M., Andreu, D., Santos, N.C. Novel crotamine-derived CPPs: how they interact with model membranes? XXII Encontro Nacional da Sociedade Portuguesa de Química, Braga, Portugal, July 3-6, 2011 (Poster presentation).

Internationalization

Collaborative publications and 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), University of Queensland (Brisbane, Australia), Technical University of Dresden (Germany), Oswaldo Cruz Foundation (Rio de Janeiro, Brazil) and Agency for Science, Technology and Research (Singapore), as well as with Biotech companies from the United States and China.

Nuno C. Santos coordinates a Marie Curie International Research Staff Exchange Scheme (IRSES) Project, funded by the European Commission through the 7th Framework Program.

Sónia Gonçalves and Ivo C. Martins received and oriented research students from University of Birmingham (UK) and Pontifical Catholic University (Campinas, Brazil), respectively.

Patents/prototypes

Martins IC, Almeida FC, Santos NC, Da Poian AT (2011) Means and methods for the inhibition of Flavivirus replication. Portuguese Intellectual Property Protection Institute, provisional patent application Nr. 20111000041319.

Advanced teaching

Santos, N.C. “Atomic Force Microscopy and Force spectroscopy”, MIT-Portugal PhD Program (NanoBio modulus), Lisbon. January 14, 2011.

Santos, N.C. “Atomic Force Microscopy and Force spectroscopy”, PhD Program, Instituto de Tecnologia Química e Biológica (ITQB), Oeiras. January 31, 2011.

Santos, N.C. organized and lectured on the Lisbon Academic Medical Center (CAML) PhD Program nanocourse on “Nanomedicine”, Lisbon. February 28 - March 2, 2011.

Carvalho, F.A. lectured the practical teaching for Lisbon Academic Medical Center (CAML) PhD Program nanocourse on “Nanomedicine”, Lisbon. February 28 - March 2, 2011.

Santos, N.C. “Force spectroscopy”, Master in Structural Biology and PhD Program, Instituto Superior Técnico, Universidade Técnica de Lisboa, Lisbon. March 23, 2011.

Carvalho, F.A. lectured the academic teaching for REQUIMTE Hands-on Workshop “AFM-based Force Spectroscopy. Biological and Biomedical Applications.” Faculdade Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica. September 14-16, 2011.

Santos, N.C. lectured on the Experimental Biochemistry Course of Federal University of Rio de Janeiro (UFRJ) / Federal University of Pará (UFPA) / Federal University of Western Pará (UFOPA). September 19-23, 2011.

Santos, N.C. “Light scattering techniques and their Biochemical applications”, Master in Structural and Functional Biochemistry, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Lisbon. December 16, 2011.

Domingues, M.M. co-organized and lectured the practical teaching of Light Scattering Spectroscopy in the Master of Structural and Functional Biochemistry, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Lisbon. December 16, 2011.

Science and Society

During 2011, the Research work of the Biomembranes Unit of IMM was addressed at several mass media news and interviews; namely, on ScienceDaily (March 8, 2011), Jornal de Leiria (March 24, 2011, pp. 14-15), CienciaPT (March 31, 2011), Diário de Notícias on-line (April 1, 2011), CiênciaHoje (April 1, 2011), Diário de Notícias (April 2, 2011, pp. 40-41), Público on-line (April 3, 2011), Biomedicina Brasil (April 4, 2011), IP Jornal (April 4, 2011), Destak (April 4, 2011, p. 4), Drugs News (April 4, 2011) and TVNET (May 17, 2011).

Carvalho FA, Domingues MM, Faustino A, Freitas T, Gonçalves S, Martins IC, Matos PM, Rodrigues M, Santos A, Santos NC. Visit of Escola Secundária José Belchior Viegas (São Brás de Alportel) to the Biomembranes Unit, including presentation and “speed-dating” style contact with the different components the Unit’s Research work, Lisbon, February 25, 2011.

Martins IC, Rodrigues M. Hosting at the Biomembranes Unit of “Ciência Viva” students, Lisbon, July, 2011.

Santos, N.C. Seminar “Membranas biológicas como alvos terapêuticos”. Semana da Ciência e Tecnologia 2011, Escola Secundária Ferreira Dias, Agualva-Cacém, November 22, 2011.

Master thesis completed

André Faustino (2011) Molecular level evaluation of the dengue virus capsid protein role(s) on the virus life cycle. Mestrado em Bioquímica, Faculdade de Ciências da Universidade de Lisboa. Supervisors: N.C Santos and I.C. Martins.

Cancer Biology Unit

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 Taborda Barata, PhD

Research Team

Ana Gírio, PhD	Post-Doc Fellowship, FCT
Leonor Sarmento, PhD	Post-Doc Fellowship, FCT; Assistant Professor, FMUL
Inês Antunes	Post-Doc Fellowship, FCT
Leila Martins	PhD Fellowship, FCT
Nádia Correia	PhD Fellowship, FCT
Alice Melão	PhD Fellowship, FCT
Daniel Ribeiro	PhD Fellowship, FCT
Vanda Póvoa	BI Fellowship, FCT (since September)
Michael Svaton	Short-term SCORE internship (July)

Keywords/Research Areas

Oncobiology; Leukemia; Signal transduction; Cellular and molecular biology

Major scientific achievements

In 2011, we have made significant advances in one of our research lines: to characterize the molecular and functional impact of IL-7/IL-7R-mediated signaling in T-cell acute lymphoblastic leukemia (T-ALL). We have shown that IL-7 accelerates human T-cell leukemia development in vivo (Cancer Research 71: 4780) and that reactive oxygen species crosstalk with PI3K/Akt pathway and are essential for IL-7-mediated survival of T-ALL cells (Leukemia 25: 960).

Remarkably, we found that around 9% of T-ALL patients harbor gain-of-function oncogenic mutations in IL7R. These mutations are tumorigenic in vivo and targetable by using JAK/STAT

pathway inhibitors (Nature Genetics 43: 932). This study was awarded the 2011 Pfizer Award in Clinical Research from Sociedade das Ciências Médicas de Lisboa and led to a Vote of Congratulations in the Portuguese Parliament for the excellence of the scientific research in Portugal.

We are also interested in identifying the mechanisms by which TAL1/SCL (a major T-cell oncogene) is regulated in T-ALL. We recently we showed for the first time that TAL1 protein expression is strikingly downregulated by treatment with histone deacetylase inhibitors (HDACi) in T-ALL cells. This is due to decreased TAL1 gene transcription in cells with native TAL1 promoter, and due to impaired TAL1 mRNA translation in cells that harbor the TAL1d microdeletion and consequently express TAL1 under the control of the SCL/TAL1 interrupting locus (SIL) promoter. Notably, HDACi-triggered apoptosis of T-ALL cells is significantly reversed by TAL1 forced overexpression. Our results indicate that the HDACi-mediated apoptotic program in T-ALL cells is partially dependent on their capacity to downregulate TAL1 and provide support for the therapeutic use of HDACi in T-ALL (Leukemia 25: 1578).

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. Sarmento, N. Correia, M.L. Toribio, J. Kobarg, M. Horstmann, R. Pieters, S.R. Brandalise, A.A. Ferrando, J.P. Meijerink, S.K. Durum, J.A. Yunes, J.T. Barata (2011). Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia. Nature Genetics 43 (10): 932-939. (Journal IF: 36.377)

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: 3762-3774. (Times cited: 61) (Journal IF: 14.152)

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. J. Exp. Med. 200: 659-669. (Times cited: 78) (Journal IF: 14.776)

J.T. Barata, A.A. Cardoso, L.M. Nadler, V.A. Boussiotis (2001). Interleukin-7 promotes survival and cell cycle progression of T-cell acute lymphoblastic leukemia cells by down-regulating the cyclin-dependent kinase inhibitor p27kip1. Blood 98 (5): 1524-1531. (Times cited: 78) (Journal IF: 10.558)

Ongoing Research Projects

2011/2013 Identification of novel regulators of CK2 with impact on PTEN function in leukemia. FCT. Coordinator: J.T. Barata. PTDC/SAU-ONC/113202/2009, € 186 000

2010/2012 Cell-intrinsic and microenvironmental signals intertwined: novel targets for therapeutic intervention in acute lymphoblastic leukemia? FCT. Coordinator: J.T. Barata. PTDC/SAU-ONC/104816/2008, € 190 000

2010/2011 Reciprocal regulation between TAL1 and miRNA expression in T-cell leukemia. Liga Portuguesa Contra o Cancro – “TERRY FOX”. Coordinator: J.T. Barata, € 15 000

2009/2011 Regulation of ZAP-70 and PTEN activity and stability in chronic lymphocytic leukemia: prognostic and therapeutic implications. FCT. Coordinator: J.T. Barata, € 134 000

2009/2011 Clinical implications of activation of PI3K/Akt signaling pathway in primary adult acute lymphoblastic leukemia. FCT. Coordinator: J. Lacerda (UIC), € 134 000

Publications in Peer Reviewed International Journals

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 (10): 932-939. (Journal IF: 36.377)

A. Silva, A.B.A. Laranjeira, L.R. Martins, B.A. Cardoso, J. Demengeot, J.A. Yunes, B. Seddon, J.T. Barata (2011). IL-7 contributes to the progression of human T-cell acute lymphoblastic leukemias. *Cancer Research* 71 (14): 4780-4789. (Journal IF: 8.234)

L.R. Martins, P. Lúcio, M.C. Silva, P. Gameiro, M.G. Silva, J.T. Barata (2011). On CK2 regulation of chronic lymphocytic leukemia cell viability. *Molecular and Cellular Biochemistry* 356 (1-2): 51-55. (Journal IF: 2.168)

L.M. Sarmiento, J.T. Barata (2011). The therapeutic potential of Notch inhibition in T-cell acute lymphoblastic leukemia: rationale, caveats and promises. *Expert Review of Anticancer Therapy* 11 (9): 1403-1415. (commissioned review) (Journal IF: 2.976)

B.A. Cardoso, S.F. de Almeida, A.B.A. Laranjeira, M. Carmo-Fonseca, J.A. Yunes, P.J. Coffey, J.T. Barata (2011). TAL1/SCL is down-regulated upon histone deacetylase inhibition in T-cell acute lymphoblastic leukemia cells. *Leukemia* 25 (10): 1578-1586. (Journal IF: 8.966)

A. Silva, A. Gírio, I. Cebola, C.I. Santos, F. Antunes, J.T. Barata (2011). Intracellular Reactive Oxygen Species are Essential for PI3K/Akt/mTOR-dependent IL-7-mediated Viability of T-cell Acute Lymphoblastic Leukemia Cells. *Leukemia* 25 (6): 960-967. (Journal IF: 8.966)

A. Batista, J.T. Barata, E. Raderschall, S.E. Sallan, L.M. Nadler, N. Carlesso, A.A. Cardoso (2011). Targeting of active mtor inhibits primary leukemia T-cells and synergizes with cytotoxic drugs and signaling inhibitors. *Experimental Hematology* 39 (4): 457-472. (Journal IF: 3.198)

Invited Lectures and Seminars

J.T. Barata. Mr Hyde revealed: IL-7/IL-7R signaling in acute T-cell leukemia. Department of Cell Signalling and Immunology, College of Life Sciences, University of Dundee, Dundee, UK, 20 September 2011.

J.T. Barata. Transdução de sinal em leucemia: novos alvos moleculares – futuras terapias? Ciência e Ensino – 100 anos da FMUL (Celebrations of the 100th Anniversary of the Faculty of Medicine of Lisbon University), Faculdade de Medicina da Universidade de Lisboa, 6-7 May 2011.

J.T. Barata. Leucemia e transdução de sinal: as células tumorais também ouvem. 1o Encontro de Biologia Molecular em Saúde, Escola Superior de Saúde Egas Moniz, Caparica, Portugal, 18-19 March 2011.

J.T. Barata. Lectures Signal Transduction Aberrations in Cancer and 'Novel' Concepts in Cancer Signal Transduction. Advanced Course on Oncobiology, BEB PhD Program of the Center for Neuroscience and Cell Biology (CNC), University of Coimbra, 21 February 2011.

Communications in International Conferences

J.T. Barata. Signals from the outside, signals from within: finding new molecular therapeutic targets in T-cell leukemia. International-attended, Istanbul Technical University 5th National Molecular Biology and Genetics Student Congress, Istanbul, Turkey, 19-22 August 2011. (Invited speaker)

A.B. Silveira, P. Leal, B.A. Cardoso, B. Nogueira, R.A. Yunes, S.R. Brandalise, N.I.T. Zanchin, J.T. Barata, J.A. Yunes. Inhibition of PI3K sensitizes T-ALL cells to chemotherapy. Targeting PI3K/mTOR Signaling in Cancer AACR Special Conference, San Francisco, CA, USA, 24-27 February 2011. (Poster presentation).

Communications in National Conferences

D. Ribeiro, C.I. Santos, M.C. Silva, A. Silva, L. Vinagre, B.A. Cardoso, L.F. Moita, J.T. Barata. STAT5 Activation is Required for IL-7-mediated Viability and Growth of Human Leukemia T-cells. SINAL 2011 – 5th Annual Meeting on Cell Signalling, University of Coimbra, Portugal, 28-30 April 2011. (Poster presentation).

Organisation of Conferences

J.T. Barata was a Member of the Scientific Committee and Chair of Session 7, SINAL 2011 – 5th Annual Meeting on Cell Signalling, University of Coimbra, Portugal, 28-30 April 2011.

J.T. Barata was a Member of Jury for the selection of the best poster of the XXXVII Annual Meeting of the Portuguese Society of Immunology, Instituto Gulbenkian de Ciência, Oeiras, Portugal, 29-30 November 2011.

Internationalization

All the projects at the Cancer Biology Unit involve some degree of collaborative work with international research groups in Europe, United States and Brazil. Our publication track record illustrates this extensively (for example, see our 2011 list of publications). Our FCT funded projects systematically include foreign researchers as consultants or participants.

Current collaborators include: Dr. J. Andres Yunes (Centro Infantil Boldrini, Campinas, SP, Brazil), Prof. Paul Coffey (Utrecht University Medical Center, The Netherlands), Prof. Jules Meijerink (Erasmus MC Rotterdam - Sophia Children's Hospital, The Netherlands), Dr. Ben Seddon (National Institute for Medical Research, London, UK), Prof. Adolfo Ferrando (Columbia University, New York, NY, USA), Dr. Scott Durum (National Cancer Institute, Frederick, MD, USA), and Dr. Nick Leslie (Dundee University, UK).

The lab head, Dr. J.T. Barata, is regularly invited to give talks at research institutes abroad and at international meetings (e.g. see meeting in Istanbul in 2011). Furthermore, Dr. Barata was asked to act as referee for prestigious international journals (including The Journal of Clinical Investigation, Blood, Leukemia, etc). He is an Associate Editor of the American Journal of Cancer Research since October 2011 and ad hoc Section Editor for Leukemia.

In addition, the Cancer Biology Unit welcomes regularly foreign students (e.g. in 2011 - undergrad SCORE internship).

Prizes, honours and awards

2011 Pfizer Award on Clinical Research. Sociedade das Ciências Médicas de Lisboa to D. Ribeiro, N. Correia, B.A. Cardoso, L.M. Sarmiento and J.T. Barata.

Advanced teaching

J.T. Barata lectured the topics Signal Transduction Aberrations in Cancer and 'Novel' Concepts in Cancer Signal Transduction. Advanced Course on Oncobiology, BEB PhD Program of the Center for Neuroscience and Cell Biology (CNC), University of Coimbra, 21 February 2011.

MD students from FMUL and Universidade do Algarve were hosted in the lab during 2011.

Science and Society

Members of the Cancer Biology Unit hosted a school visit from high school students to the Unit in order to explain the aims and strategies of the research performed in the lab and to demonstrate some of the technical approaches used. The Unit also hosted a high school student from Egypt for a three-week internship. Likewise, an MD student from Universidade do Algarve.

Master and Ph.D. thesis completed

PhD Thesis

Bruno Cardoso (2011). PhD Thesis "IL-4 and TAL1 in T-cell acute lymphoblastic leukemia: studies on the participation of microenvironmental cues and cell-autonomous alterations in leukemogenesis". Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata. Co-supervisor: L. Parreira.

Cell Biology Unit

Description and Objectives

Understanding the genomic programme of the human organism requires knowledge of how the information encoded in DNA is processed to generate messenger RNAs that can be translated into proteins, the building blocks of the different tissues in the body. In the cell, extensive modification and alternative processing of the initial products of gene transcription can profoundly affect the diversity and function of the proteins that are generated from a single gene. Our lab is interested in identifying mechanisms of mRNA biogenesis to better understand diseases caused by errors that affect these processes. Making use of a multidisciplinary approach that combines live-cell microscopy, computational modeling, molecular biology, biochemistry and bioinformatics, our group developed expertise to study how the dynamic properties of RNA-protein complexes contribute to post-transcriptional gene regulation.

Head of Unit

Maria Carmo-Fonseca, MD, PhD – Full Professor, FMUL

Principal Investigators

Francisco Enguita, PhD - Auxiliary Professor, FMUL

Sérgio de Almeida, PhD – Post-Doc Fellow, FCT

Research Team

Teresa Carvalho, MD, PhD	Auxiliary Professor, FMUL
Joana Desterro, PhD	Auxiliary Professor, FMUL
Célia Carvalho, PhD	Auxiliary Professor, FMUL
Noélia Custódio, PhD	Auxiliary Professor, FMUL
Sandra Martins, PhD	Auxiliary Professor, FMUL
José Rino, PhD	Investigator, IMM
Rute Marcelino, M.Sc	Invited Investigator, IMM
Robert Manfred Martin, PhD	Post-Doc Fellowship, FCT
Ana Rita Grosso, PhD	Post-Doc Fellowship, FCT
Marina Costa, PhD	Post-Doc Fellowship, FCT
Jorge Andrade	PhD Fellowship, FCT (left in 2011)
Rita Mendes de Almeida	PhD Fellowship, FCT
Filipa Martins	Masters Student, FCUL
Ana Cláudia Raposo, MSc	Research trainee, IEFP
Marco Pinheiro	ERASMUS, University of Manchester, UK
Marisa Cabrita	Technician, FMUL
Sérgio Marinho	Technician, FMUL
Sílvia Carvalho	Technician, IMM

Research Areas

Cell and Molecular Biology; Biogenesis of messenger RNA; RNA splicing; Diseases of RNA metabolism

Major scientific achievements

It has long been realized that introns stimulate mRNA production, but precisely how splicing may influence transcription remains unclear. Early studies proposed that components of the splicing apparatus stimulate transcription elongation through direct interaction with elongation factors. A more recent study suggests that splicing factors may facilitate transcriptional elongation even before participating in spliceosome assembly. We set out to determine how inhibition of splicing affects transcription dynamics using a combination of live-cell imaging, chromatin immunoprecipitation and quantitative real-time PCR approaches. Our data reveal that correct spliceosome assembly is linked to RNAPII pausing for transcriptional termination, and that uncoupling these processes results in leakage of unspliced transcripts to the nucleoplasm.

We have used the well characterized human β -globin (HBB) gene as a model system to study in real-time the dynamics of transcription by RNAPII. We engineered human osteosarcoma-derived cells (U2OS Tet-On) to stably express tetracycline-inducible β -globin transgenes integrated in tandem in the genome. Six MS2 coat protein binding sequences were inserted in frame in exon3 of the HBB gene. We analyzed the dynamics of RNAPII at the site of transcription using fluorescence recovery after photobleaching (FRAP). Contrasting to the full recovery of mCherry-MS2 fluorescence intensity, which implies that all bleached RNAs have been released from the DNA template and replaced by new MS2-containing transcripts, the RNAPII-GFP signal failed to recover to pre-bleach values. We consider it most likely that the immobile fraction corresponds to RNAPII molecules paused downstream of the poly(A) site for termination. To determine whether RNAPII molecules are paused downstream of the poly(A) site in our system, chromatin immunoprecipitation (ChIP) was carried out to compare RNAPII density throughout the β -globin gene.

To investigate the effect of splicing inhibition on RNAPII dynamics, we used a mutant variant of β -globin that lacks completely the second intron. In these experiments splicing was inhibited due to deletion of an intron that prevents recruitment of the spliceosome. We next examined another scenario of splicing inhibition in which spliceosomal components are partially recruited. For this we used spliceostatin A (SSA), a potent antitumor compound that targets SF3b, a multimeric protein component of the U2 snRNP. Surprisingly, FRAP experiments performed in SSA-treated cells reveal distinct results compared to those obtained with the splicing mutant. Taken together, our results indicate that SSA abolishes pausing of RNAPII downstream the poly(A) site of the β -globin gene. Absence of RNAPII pausing at the 3'-end of the gene is consistent with faster dissociation from the template thereby explaining the lack of immobile fraction detected by FRAP. Next, we were interested in determining whether the effect of SSA on 3'-end pausing of RNAPII happens particularly in the β -globin gene or rather represents a more general characteristic of human genes. The results suggest that coupling between spliceosome assembly for splicing and RNAPII pausing for transcriptional termination is a novel general feature of human genes. (Martins, Rino, et al. *Nature Struct. Mol. Biol.* 18: 1115, 2011)

Several lines of recent evidence support a role for chromatin in splicing regulation. We have explored the possibility that splicing may influence histone modification, namely H3K36 trimethylation. If so, then the chromatin of exons that are constitutively spliced should have higher H3K36me3 enrichment than exons excluded by alternative splicing. This had been

observed in *C. elegans* and mouse cells, but not in human cells. If splicing influences H3K36 trimethylation, another prediction is that intron-containing and intronless genes should differ in the marking.

We used chromatin immunoprecipitation coupled to high throughput sequencing (ChIP-seq) to compare the distribution of histone H3 methylation in intron-containing and intronless genes across the mouse and human genomes. Our results show that irrespective of gene size and expression level, H3K36me3 marking is significantly higher on intron-containing genes than in intronless genes. This difference had not been observed before and suggests that the chromatin landscape can be influenced not only by transcription but also by splicing. To further investigate a potential relation between H3K36me3, H3K4me3 and H3K4me1 modifications and splicing, we used poly(A) RNA-seq data from mouse CD4⁺ CD8⁺ T cells to identify genes with similar expression levels that contain a second exon that is either constitutively included in the mature transcript or is excluded by alternative splicing. Plotting H3K36me3 signals across aligned first, second and third exons revealed that the levels of H3K36me3 remain relatively low from the TSS to the first intron-exon boundary, raise sharply over the second exon when this is included, persist constant over the second intron, and raise sharply again over the third exon. In contrast, genes that contain an excluded second exon have much weaker enrichment of H3K36me3 levels at the first intron-exon boundary. No significant differences are detected in levels of H3K4me1 and H3K4me3 associated with included or excluded second exons. These observations suggest that splicing preferentially affects specific chromatin modifications, namely H3K36me3.

Because H3K36 trimethylation in mammalian cells is catalyzed by the Huntingtin-interacting protein HYPB/Setd2 histone methyltransferase, we wondered whether inhibition of splicing affects recruitment of this enzyme to the chromatin. ChIP experiments using anti-HYPB/Setd2 antibodies revealed a distribution pattern very similar to that of H3K36me3, suggesting that recruitment of the histone methyltransferase and subsequent H3K36me3 modification are splicing-dependent. According to this view, the levels of HYPB/Setd2 and H3K36me3 associated with alternatively spliced exons should increase when the splicing pattern is induced to shift from exon exclusion to exon inclusion. To address this possibility, we took advantage of the CD44 gene that contains multiple clustered variant exons, the splicing of which can be induced in response to activation of signalling pathways. ChIP experiments revealed that PMA treatment significantly increased the levels of Pol II, H3K36me3 and HYPB/Setd2 in exons v5 and v10 but not in the constitutive exons located upstream and downstream the alternative exons. In summary, we observe that splicing inhibition in human cells impairs recruitment of H3K36 methyltransferase HYPB/Setd2 and reduces H3K36me3, whereas inclusion of alternative exons has the opposite effect, increasing HYPB/Setd2 recruitment and H3K36me3. We therefore demonstrate that H3K36me3 marking is directly influenced by splicing and we propose a model in which co-transcriptional pre-mRNA splicing enhances H3K36 trimethylation by promoting the recruitment of HYPB/Setd2 to elongating Pol II. (de Almeida et al. *Nature Struct. Mol. Biol.* 18: 977, 2011).

Recent Most Relevant Publications

Grosso, A.R., Gomes, A.Q., Barbosa-Morais, N.L., Caldeira, S., Thorne, N.P., Grech, G., von Lindern, M., and Carmo-Fonseca, M (2008) Tissue-specific splicing factor gene expression signatures. *Nucleic Acids Research* 36: 4823-32. (Times cited: 35)*

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. (Times cited: 113)*

Desterro, J., Keegan, L., Lafarga, M., Berciano, M.T., O'Connell, M., and Carmo-Fonseca, M. (2003) Dynamic association of RNA editing enzymes with the nucleolus. *J. Cell Sci.* 116: 1805-1818. (Times cited: 87)*

Calapez, A., Pereira, H.M., Calado, A., Braga, J., Rino, J., Carvalho, C., Tavanez, J.P., Wahle, E., Rosa, A.C., and Carmo-Fonseca, M. (2002) The intranuclear mobility of messenger RNA binding proteins is ATP-dependent and temperature-sensitive. *J. Cell Biol.* 159:795-805 (Times cited: 91)*

Calado, A., Tomé, F.M.S., Brais, B., Rouleau, G.A., Kühn, U., Wahle, E., and Carmo-Fonseca, M. (2000) Nuclear inclusions in oculopharyngeal muscular dystrophy consist of poly(A) binding protein 2 aggregates which sequester poly(A) RNA. *Human Molecular Genetics* 9:2321-2328. (Times cited: 142)*

(*Google Scholar citations)

Ongoing Research Projects

2009/2012 Transcription-coupled mechanisms of gene regulation (FCT- PTDC/BIA-BCM/101575/2008)

PI: M. Carmo-Fonseca; total funding € 199.350,00.

2010/2013 The role of RNA polymerase II in splicing regulation (FCT-PTDC/SAU-GMG/113440/2009)

PI: M. Carmo-Fonseca; total funding € 170.000,00.

2011/2014 Splicing-coupled mechanisms of chromatin modification and their global role in transcription (PTDC/BIA-BCM/111451/2009)

PI: Sérgio de Almeida; total funding € 146.000,00

2010/2013 Circulating miRNAs as a prognosis factor for acute cardiac infarction (CHLN-2010)

PI: F.J. Enguita; total funding € 25.000,00.

Publications in peer review Journals

Carmo-Fonseca, M., Rino J. (2011) RNA seeds nuclear bodies. *Nature Cell Biol.* 13 (2): 110-112. (JIF: 19.527)

de Almeida, SF, Grosso, AR, Koch, F, Fenouil, R, Carvalho, S, Andrade, J, Levezinho, H, Gut, M, Eick, D, Gut, I, Andrau, JC, Ferrier P, Carmo-Fonseca, M (2011) Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36. *Nature Struct. Mol. Biol.* 18 (9): 977-983. (JIF: 13.69)

Martins, SB, Rino, J., Carvalho, T., Carvalho, C., Yoshida, M., Klose JM, de Almeida, SF, Carmo-Fonseca, M. (2011) Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. *Nature Struct. Mol. Biol.* 18 (10): 1115-1123. (JIF: 13.69)

Cardoso BA, de Almeida SF, Laranjeira A, Carmo-Fonseca M, Yunes JA, Coffey PJ and Barata JT. "TAL1/SCL is down-regulated upon histone deacetylase inhibition in T-cell acute lymphoblastic leukemia cells" *Leukemia*, 2011 Oct;25(10):1578-86 (JIF: 9,0)

de Oliveira RM, Marijanovic Z, Carvalho F, Miltényi GM, Matos JE, Tenreiro S, Oliveira S, Enguita FJ, Stone R, Outeiro TF. (2011) Impaired proteostasis contributes to renal tubular dysgenesis. *PLoS One*. 2011;6(6):e20854. (JIF: 4.41)

Invited Seminars

Carmo-Fonseca, M. The exosome and its role in RNA surveillance. Stockholm University, 11 February 2011.

Carmo-Fonseca, M. Why is pre-mRNA processing coupled to transcription? The Wellcome Trust Centre for Cell Biology, The University of Edinburgh, 14 February 2011.

Carmo-Fonseca, M. Genes e genomas – na fronteira entre a Medicina e a Biologia Molecular Universidade Estadual Paulista, Campus de Botucatu, Brazil, 21 September 2011.

de Almeida SF. "Global regulation of transcription by local histone modifications" CBAA Seminars, Centro de Botânica Aplicada à Agricultura, Instituto Superior de Agronomia, December 20, 2011. Invited speaker

de Almeida SF. "Uso de drogas e engenharia genética como armas terapêuticas no combate à Atrofia Muscular Espinhal" VI Mini Congresso de Ciência, Rio Maior, April 8, 2011 - Invited speaker.

Communications in International Conferences

the EMBO Workshop on Chromatin structure, organization and dynamics. Prague, Czech Republic, April 9-13, 2011.

Carmo-Fonseca, M. Co-transcriptional RNA checkpoints. Invited lecture presented at the 36th FEBS Congress. Torino, Italy, June 25-30, 2011.

Carmo-Fonseca, M. et al. The communication between splicing and chromatin is bi-directional. Invited lecture presented at the 19th Annual International Conference on Intelligent Systems for Molecular Biology & 10th European Conference on Computational Biology. Vienna, Austria, July 15-16, 2011.

Carmo-Fonseca et al. Transcription and splicing imaged alive in mammalian cells. Invited lecture presented at the INSERM Workshop on Emerging tools in quantitative fluorescence microscopy for systems biology. Lisboa, September 4-6, 2011.

de Almeida SF et al. "Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36" Workshop "Frontiers in Epigenomics" Baeza, Spain, October 17-19, 2011. Oral communication

de Almeida SF et al. "Dynamic methylation of histone H3K36 is splicing-dependent" Eurasnet Meeting on Alternative Splicing Granada, Spain. February 28-March3, 2011. Oral communication

de Almeida SF et al. "Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36" Workshop "Frontiers in Epigenomics" Baeza, Spain, October 17-19, 2011. Poster presentation

Organisation of National and International Conferences

Carmo-Fonseca, M. co-organized the INSERM Atelier de Formation #210 on Emerging tools in quantitative fluorescence microscopy for systems biology. Lisboa, September 4-6, 2011.

M. Carmo-Fonseca co-organized the EMBO Conference Series on Nuclear structure and dynamics. L'isle sur la sorgue, France, September 28- October 2, 2011.

Internationalization

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".

Host lab for the following ERASMUS students:

- 1) Jasmin Klose, MSc student from the University of Duisburg-Essen, Germany
- 2) Marco Pinheiro, Bs student from the University of Manchester, UK

Prizes, honours and awards

Prémio Pfizer 2011 awarded to Sérgio de Almeida

Maria Carmo-Fonseca was awarded a visiting professorship at Harvard Medical School.

The 2011 João Porto Grant for research in Cardiology (Portuguese Society for Cardiology) was awarded to N. Cortez-Dias, F. J. Enguita, M. Costa, P. Carrilho-Ferreira, C. Calisto, J. Carvalho de Sousa, J. Cravino, R. Ferreira, M. Mendes, F. J. Pinto, M. Fiúza, J. de Sousa, A. Nunes Diogo. "miRNAs na fibrilhação auricular".

Francisco J. Enguita was awarded a COST fellowship for visiting the National Center for Cardiovascular Research, Madrid, Spain. July 2011 (ECOST-STSM-BM0804-170711-010478).

Advanced teaching

Carmo-Fonseca, M. Biologia molecular e genoma humano. Mestrado em Genética Forense, Instituto de Medicina Legal, Lisboa, 7 Janeiro 2011.

Enguita, F.J. lectured "miRNAs: master regulators of cell biology". Gulbenkian Program for Advanced Medical Education, Instituto Gulbenkian de Ciência, October 4, 2011.

Enguita, F.J. lectured "miRNAs and aging". Master in Molecular and Cell Biology, University of Coimbra, April 11, 2011.

Enguita, F.J. lectured and organized "Get the best from your sequences". CAML PhD. Programme advanced courses, Instituto de Medicina Molecular, March 9-10, 2011.

Enguita, F.J. organized "miRNAs and non-coding RNAs in cell biology and human disease". CAML PhD. Programme advanced courses, Instituto de Medicina Molecular, October 13-14, 2011.

Science and Society

Carmo-Fonseca, M. Biologia Sintética: uma versão bacterial de Frankenstein. VII Conferência Indústria Farmacêutica “Os Desafios da Inovação nos Sistemas de Saúde”, Lisboa, 20 Janeiro 2011.

Carmo-Fonseca, M. Da Biologia Molecular ao Feto. II Simpósio Gravidez depois dos 40 anos, Hospital da Luz, Lisboa, 25 Fevereiro 2011.

Carmo-Fonseca, M. Uma Medicina, Vários caminhos. 10º Seminário de Saídas Profissionais, Associação dos Estudantes da Faculdade de Medicina da Universidade de Lisboa, Lisboa, 27 Fevereiro 2011.

Carmo-Fonseca, M. Investigação com células estaminais. Conferência Conselho Nacional de Ética para as Ciências da Vida, Porto, 17 Maio 2011.

Carmo-Fonseca, M. O potencial das sinergias Universidade-Indústria. Seminário “Inovação Biofarmacêutica: por uma Europa mais competitiva, Lisboa, 24 Maio 2011.

Carmo-Fonseca, M. Escutar a Sociedade - Investigação. VII Encontro Luso-Espanhol de Fundações, Évora, 20 Outubro 2011.

Carmo-Fonseca, M. Inovação e Desenvolvimento. Conferência Anual do INFARMED, Lisboa, 10 Outubro 2011.

Francisco J. Enguita. Science road-show. Instituto Español de Lisboa Giner de los Ríos, 15 Fevereiro 2011.

Master thesis completed

Master thesis

Ana Cláudia Raposo, MSc in Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa. September 2011. (Final Grade 19/20) Supervisor: Sérgio F. de Almeida.

Fernando Magalhães Martins. (2011). *In silico* analysis of miRNA promoters. Master in Bioinformatics and Computational Biology, Faculty of Sciences, University of Lisbon. Supervisor: Francisco J. Enguita.

Cell Biology of the Immune System Unit

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 signaling pathways that regulate central processes of an immune response, their targets and role in an *in vivo* immune response.

Head of Unit

Luís Ferreira Moita, M.D., Ph.D. Assistant Professor at FMUL

Principal Investigators

Ângelo Chora, Ph.D. Post-Doc Fellowship, FCT

Research Team

Maria Helena Raquel, PhD	Post Doc Fellowship, FCT
Raquel Rodrigues, PhD	Post Doc Fellowship, FCT
Ana Neves-Costa, PhD	Post Doc Fellowship, FCT
Catarina Moita, PhD	Post Doc Fellowship, FCT
Iris Cadima- Couto, PhD	Post Doc Fellowship, FCT
Dora Pedroso, PhD	Technician Fellowship, FCT
Nuno Figueiredo, MD	MD, PGFMA
Richard Staats, MD	MD, Lung Specialist at HSM
Susana Moreira, MD	MD, Lung Specialist at HSM

Keywords/Research Areas

Innate Immunity; Antigen Cross-Presentation; Sepsis; Cancer; Multiple Sclerosis; Sleep

Major scientific achievements

The anthracycline epirubicin triggers an ATM-dependent protective response against sepsis

Sepsis remains a poorly understood systemic inflammatory condition with high mortality rates and limited therapeutic options in addition to organ support measures. Most often, sepsis is triggered by a bacterial infection that causes excessive production of pro-inflammatory mediators, including the initial critical tumor necrosis factor (TNF) and interleukin 1 β (IL-1 β), leading to the activation of spiraling signaling cascades ultimately causing multi-organ failure and death. We have used a drug screen to identify the clinically approved group of anthracyclines as potent *in vitro* inhibitors of two key initiators of sepsis, TNF and IL-1 β . *In vivo*, anthracyclines confer strong protection against severe sepsis induced by cecal ligation and puncture (CLP) in mice. This protective effect relies on the induction of autophagy and on an anti-inflammatory program

that increase the tolerance to infection without reducing bacterial burden. Using an shRNA-based screen we identified the Ataxia Telangiectasia Mutated (ATM) as a mediator of the protective effect of anthracyclines. ATM deficient (*Atm*^{-/-}) mice are refractory to this protective effect succumbing to severe sepsis with similar kinetics to the non-treated wild-type mice. Our results have identified the group of anthracyclines as effective therapeutic options in sepsis, and ATM as a potential molecular target in inflammation-driven conditions.

The anthracycline epirubicin triggers an ATM-dependent protective response against severe sepsis. Nuno Figueiredo, Angelo Chora, Helena Raquel, Ana Neves-Costa, Catarina Moita, Hafeez Faridi, João A. Ferreira, Paulo Costa, Raffaella Gozzelino, Jimmy L. Zhao, Vineet Gupta, Miguel P. Soares, Margarida Gama-Carvalho, David Baltimore and Luis F. Moita, ***Submitted for publication***.

The anthracycline epirubicin triggers an ATM-dependent protective response against severe sepsis - ***Patent application filed*** (September 8th, 2011)

Recent Most Relevant Publications

Cebrian I, Visentin G, Blanchard N, Jouve M, Bobard A, Moita C, Enninga J, Moita LF, Amigorena S, Savina A. Sec22b regulates phagosomal maturation and antigen crosspresentation by dendritic cells.

Cell. 2011 Dec 9;147(6):1355-68. (Journal IF: 32.406, Citations: 0)

Richard A. Colvin, Terry K. Means, Thomas J. Diefenbach, **Luis F. Moita**, Robert P. Friday, Sanja Sever, Gabriele S.V. Campanella, Tabitha Abrazinski, Lindsay A. Manice, **Catarina Moita**, Norma W. Andrews, Dianqing Wu, Nir Hacohen, and Andrew D. Luster. Synaptotagmin mediated vesicle fusion regulates cell migration.

Nature Immunology, 2010, Jun;11(6):495-502. (Journal IF: 25.934, Citations: 8)

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.*. Rab27 controls constitutive exosome secretion.

Nat Cell Biol. 2010 Jan;12(1):19-30. *Corresponding authors. (Journal IF: 19.407, Citations: 44)

Savina, A., Peres, A., Cebrian, I., Carmo, N., Moita, C., Hacohen, N., **Moita, L.F.**, and Amigorena, S. Rac2 controls phagosomal alkalization and crosspresentation selectively in CD8⁺ dendritic cells.

Immunity, 2009 Apr;30(4):544-55. (Journal IF: 24.221, Citations: 33)

Oberdoerffer, S., **Moita, L.F.**, Neems, D., Freitas, R.P., Hacohen, N., Rao, A. Regulation of CD45 alternative splicing by heterogeneous ribonucleoprotein, hnRNPLL.

Science. 2008 Aug 1;321(5889):686-91. (Journal IF: 31.377, Citations: 41)

Ongoing Research Projects

2009 – 2011 Immunological basis for the association of hypersomnic sleep disorders and cardiovascular disease, FCT. Coordinator: Luís Ferreira Moita (PIC/IC/82991/2007) - 170.795 Euros

2010 – 2013 Role of ASF/SF2 and SRp20 in IL-1 β secretion, FCT Coordinator: Luís Ferreira Moita (PTDC/SAU-MII/100780/2008) - 198.591 Euros

2011 – 2014 - Role of newly identified genes in in vivo antigen cross-presentation-dependent generation of CTL responses against tumors. FCT. Coordinator: Ângelo Chora / Luís Ferreira Moita (PTDC/SAU-IMU/110303/2009) – 136.840 Euros

Publications in peer review Journals

Cebrian I, Visentin G, Blanchard N, Jouve M, Bobard A, Moita C, Enninga J, **Moita LF**, Amigorena S, Savina A. Sec22b regulates phagosomal maturation and antigen crosspresentation by dendritic cells. *Cell*. 2011 Dec 9;147(6):1355-68. (Journal IF: 32.406, Citations: 0)

Dony Manguel, Mohd Hafeez Faridi, Changli Wei, Yoshihiro Kuwano, Keir Balla, Dayami Hernandez, Constantinos J. Barth, Geanncarlo Lugo, Mary Donnelly, Ali Nayer, **Luis F. Moita**, Stephan Schürer, David Traver, Phillip Ruiz, Roberto I. Vazquez-Padron, Klaus Ley, Jochen Reiser and Vineet Gupta. Small molecule mediated activation of integrin CD11b/CD18 reduces inflammatory disease. *Science Signaling*. 2011 Sep 6;4(189):ra57. (Journal IF: 6.354, Citations: 3)

Pedro Moura-Alves, Ana Neves-Costa, Helena Raquel, Teresa Raquel Pacheco, Bruno D'Almeida, Raquel Rodrigues, Iris Cadima-Couto, Ângelo Chora, Mariana Oliveira, Margarida Gama-Carvalho, Nir Hacohen and **Luis F. Moita**. An shRNA-Based Screen of Splicing Regulators Identifies SFRS3 as a Negative Regulator of IL-1 β Secretion. *PLoS One*, 2011;6(5):e19829. Epub 2011 May 17. (Journal IF: 4.411, Citations: 0)

Communications in International Conferences

Luís Ferreira Moita. Cold Spring Harbor Asia. Infection and Immunity. Suzhou, China. September 8 – 12, 2011. *The anthracycline epirubicin triggers an ATM-dependent protective response against severe sepsis*. Best Poster Award.

Organisation of Conferences

Lus Ferreira Moita

January 2009 – July 2011

Coordinator of IMM external seminars.

Internationalization

Cebrian I, Visentin G, Blanchard N, Jouve M, Bobard A, Moita C, Enninga J, Moita LF, Amigorena S, Savina A. Sec22b regulates phagosomal maturation and antigen crosspresentation by dendritic cells.

Cell. 2011 Dec 9;147(6):1355-68. (Journal IF: 32.406, Citations: 0)

Dony Manguel, Mohd Hafeez Faridi, Changli Wei, Yoshihiro Kuwano, Keir Balla, Dayami Hernandez, Constantinos J. Barth, Geanncarlo Lugo, Mary Donnelly, Ali Nayer, Luis F. Moita, Stephan Schürer, David Traver, Phillip Ruiz, Roberto I. Vazquez-Padron, Klaus Ley, Jochen Reiser and Vineet Gupta. Small molecule mediated activation of integrin CD11b/CD18 reduces inflammatory disease.

Science Signaling. 2011 Sep 6;4(189):ra57. (Journal IF: 6.354, Citations: 3)

Patents/prototypes

The anthracycline epirubicin triggers an ATM-dependent protective response against severe sepsis - Patent application filed (September 8th, 2011)

Clinical and Translational Oncology Research Unit

Major interests / Objectives

Our Unit major interests are to study the mechanisms of invasion and progression of solid tumors in bone; determining the existence of a molecular signature of bone metastazition; unravel new “partners” and mechanisms of the “vicious cycle” of bone metastases, to identify prognostic and/or predictive markers, and therapeutic targets.

We are also interested in the mechanisms of invasion and progression of colorectal cancer in liver, and identifying a molecular signature of colorectal cancer metastazition. Also to determine if chemotherapy-induced cell senescence may be related with rectal tumors relapse.

Another objective of our Unit is to understand how tumors modulate the sensitivity to antineoplastic agents such as topoisomerase inhibitors, somatostatin analogues and aromatase inhibitors.

Head of Unit

Luís Costa, MD, PhD – Director of the Oncology Division, HSM; Auxiliary Professor, FMUL

Research Team

Teresa Raquel Pacheco, PhD	Auxiliary Professor, FMUL
Ana Cristina Santos, PhD	Auxiliary Investigator, FMUL
Sandra Casimiro, PhD	Post Doc Fellowship, FCT
Joana Tato-Costa	PhD Fellowship, FCT
Irina Alho	PhD Fellowship, FCT
Isabel Fernandes, MD	Medical Oncologist, HSM
Inês Luis, MD	Oncology Fellow, HSM
Joana Ribeiro, MD	Oncology Fellow, HSM
Margarida Matias, MD	Oncology Fellow, HSM
Mafalda Peres, MD	Oncology Fellow, HSM
Ricardo Pires	Technician, FCT

Keywords/Research Areas

Bone metastases; bone “vicious cycle”; colorectal cancer metastases; chemotherapy-induced cell senescence.

Major scientific achievements

In 2011 we could demonstrate for the first time the presence in human bone metastases of a bone metastasis gene expression signature previously identified using human breast cancer cells in a mouse model. Importantly, our data supports the cooperative function of these proteins in the bone microenvironment, and the potential functional role of these genes in the establishment of bone metastases in vivo.

In the context of our projects we successfully increased our repository of human tumor samples. Clinicians (Oncologists, Pathologists, Surgeons) and life sciences researchers are committed in this task, creating a network, starting at the Surgery/Oncology Departments and ending in our Lab. We are also strongly dedicated to provide support to research projects assigned to Oncology fellows from HSM. During 2011, two new projects were implemented. The diffusion of hot topics in translation oncobiology is also one of our priorities. The Oncology Series organized in 2011 was a success, as in previous years, gathering together basic researchers and clinicians in a same audience.

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, 155-164, published online in 2 December 2011. (Journal IF: 4.113, Citations: N.A.)

Ha N et al. (2011) Lactoferrin- Endothelin-1 Axis Contributes to the Development and Invasiveness of Triple Negative Breast Cancer Phenotypes. *Cancer Res* 71(23), 7259-7269 (Journal IF: 8.234, citations: 0)

Luis I, Casimiro S, Ribeiro J and Costa L (2010) Zoledronic Acid: Its Use in the Treatment of Breast Cancer. *Clinical Medicine Insights: Therapeutics* 2, 903-926. (Journal IF: N.A., Citations: 0)

Casimiro S, Guise TA, Chirgwin J (2009) The critical role of the bone microenvironment in cancer metastases. *Mol. Cel. Endoc.*, 310, 71-81. (Journal IF: 4.119, citations: 21)

Costa L, Major PP (2009) Effect of bisphosphonates on pain and quality of life in patients with bone metastases. *Nat. Clin. Prac. Oncol.*, 6(3), 163-174. (Journal IF: 8.08, citations: 31)

Ongoing Research Projects

2011/2014 Multi-Functional Bone Seeking Agents for the Treatment of Skeletal Metastatic Disease, FCT. Coordinator: Luis Costa. PTDC/QUI-QUI/115712/2009, €36 300

2011/2014 Molecular markers in multiple myeloma, Novartis. Coordinator: Inês Luis, €5 000

2011/2014 Mechanisms of invasion and progression in metastatic bone disease and outcomes in HER2 positive metastatic breast cancer. FCT and Harvard Medical School. Coordinator: Inês Luis. HMSP-ICS/0004/2011, €400 000

2011/2012 Senescence in rectal cancer. Coordinator: Luis Costa. Merck, €20 000

2011/2012 D-dimmers in gastric cancer. CHLN-Sanofi Aventis. Coordinator: Inês Luis, € 5 000

2009/2012 Prognostic Signatures in Colorectal Cancer, FCT. Coordinator: Luis Costa. PIC/IC/82821/2007, €183 600

Publications in peer review Journals

Coleman R, Costa L, et al. (2011) Consensus on the Utility of Bone Markers in the Malignant Bone Disease Setting. *Critical Reviews in Oncology/Hematology* 80(3), 411-32 (Journal IF: 4.689, citations: 0)

Ha N et al. (2011) Lactoferrin- Endothelin-1 Axis Contributes to the Development and Invasiveness of Triple Negative Breast Cancer Phenotypes. *Cancer Res* 71(23), 7259-7269 (Journal IF: 8.234, citations: 0)

Costa L, Harper P, Coleman R, Lipton A (2011) Anticancer evidence for zoledronic acid across the cancer continuum. *Critical Reviews in Oncology/Hematology* 77(1), S31-7 (Journal IF: 4.689, citations: 3)

Lipton A, Costa L, Coleman RE (2011) Bone Turnover markers: Tools for prognosis and monitoring response to bisphosphonates. *Breast Dis.* 2011 Dec. 5 [Epub ahead of print] (Journal IF: N.A., citations: N.A.)

Invited Lectures and Seminars

Costa L. Clinical Impact of Bone-Targeted Therapies in Cancer. Gregorio Marañón Hospital, Madrid. January 17, 2011

Costa L. Established Benefits of Bisphosphonates in Early Breast Cancer. Special lecture at the 8th Kyushu Regional Meeting of the Japanese Breast Cancer Society, Japan February 19- 2011

Costa L. Metastases Prevention in Breast Cancer. Skeletal Care Academy; Madrid; February 25, 2011.

Costa L. Molecular Therapy in Breast Cancer with Bone Metastases. The 1st Global Cancer Genomics Consortium. TMC Symposium: the interface between genomics and cancer medicine. Mumbai, India (2011)

Casimiro, S. Pathophysiology of bone metastases. XXXI Congresso Nacional de Ortopedia e Traumatologia, 19th October 2011, Lisbon, Portugal.

Communications in International Conferences

Ribeiro J, Luis I Correia L, Casimiro S, Fernandes A, Quintela A, Mestan J, Ramos M and Costa L. Correlation between aromatase expression in metastatic and primary breast cancer. Santo Antonio Breast Cancer Symposium. San Antonio, Texas, USA, December 6-10, 2011.

Communications in National Conferences

Tato-Costa J, Casimiro S, Fernandes A, Costa L. The impact of therapy-induced cellular senescence in rectal cancer: a retrospective study. V PhD Students Meeting IMM/CAML, Lisbon October 17-18, 2011.

Organisation of Conferences

Costa, L. organized the Oncology Series 2011, Instituto de Medicina Molecular, Lisbon, Portugal. Invited speakers and title of Conferences:

- Michael Rogers, “Biophosphonate drugs: mechanisms of action in bone diseases and potential anti-tumour properties”. January 24, 2011.
- Robert J. Motzer, “Targeted Therapy for Advanced renal Cell carcinoma”. May 5, 2011.
- Fernando Schmit, Miguel Martin and Rakesh Kumar, “Triple Negative Breast Cancer”. October 27, 2011.

Internationalization

During 2011 we integrated the Global Cancer Genomics Consortium that 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.

Advanced teaching

In 2011, L. Costa (Chairman) and S. Casimiro, I. Luis, J. Ribeiro, I. Fernandes, A. C. Santos (Invited Professors), participated in the organization and lecturing of Oncobiology, a mandatory course for the 3rd year Medical students from FMUL. 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.

Master thesis completed

Sofia de Figueiredo Ribeiro, 2010/2011, FMUL, Master Thesis: “Development of anti-RANKL targeted therapies for bone metastatic disease”. Supervisor: Sandra Casimiro

Rui Pedro Lourenço Teixeira, 2010/2011, FMUL, Master Thesis: “The role of metalloproteinase-1 in cancer metastasis”. Supervisor: Sandra Casimiro

Developmental Biology Unit

Major interests / Objectives

The research work being developed at the DBU aims to elucidate the molecular mechanisms that regulate the genesis of neurons in vertebrate embryos. Our goal is to understand how the establishment of neural precursors is regulated in vertebrate embryos, how these cells are maintained throughout development, and how they give rise to the multitude of neurons that compose the adult CNS. A better knowledge about these fundamental mechanisms is a prerequisite for the future development of cellular therapies to treat neurodegenerative diseases.

An additional area of research at the Developmental Biology Unit is aimed at investigating the molecular mechanisms underlying the establishment of pluripotency in embryonic stem cells, focusing on the central role of Nanog in these molecular networks.

Head of Unit

Domingos Henrique, PhD – Investigator, FMUL

Research Team

Elsa Abranches, PhD	Post Doc Fellowship, FCT
Catarina Ramos, PhD	Post Doc Fellowship, FCT
Cláudia Gaspar, PhD	Post Doc Fellowship, FCT
Alexandra Rosa, PhD	Post Doc Fellowship, FCT
Filipe Vilas-Boas, PhD	Post Doc Fellowship, FCT
Aida Costa	PhD Fellowship, FCT
Sara Ferreira	Technician, Fellowship IGC
Ana Guedes	MSc Student, FCUL (left in September 2011)
Inês Honório	MSc Student, FCUL (left in September 2011)
Joana Neves	MSc Student, FCUL (left in September 2011)
Ricardo Miragaia	MSc Student, FCUL (left in September 2011)

Keywords/Research Areas

Spinal Cord and Retina Neurogenesis
 Cell and Molecular Biology of Notch signalling
 Stem cell biology
 Pluripotency

Major scientific achievements

- Establishment of a novel reporter to monitor Notch signalling in neural progenitors, with single-cell resolution, reported in a paper published in BMC Biology
- Characterization of the neural phenotype due to Dll4 deletion in the developing neural retina and spinal cord of mouse embryos. Manuscript in preparation.

- Establishment of ES cell lines with a Nanog fluorescent reporter and characterization of the dynamic behavior of the pluripotent network in ES cells. Manuscript submitted.
- Organization of the major national meeting on Neurosciences, with ca. 300 participants.
- Training of 4 master's students, and organization of two advanced courses for PhD students, with participation of 8 international speakers.
- Organization of the EpiSeminar series at IMM (bi-weekly), with participation of ca. 15 national speakers.
- Organization of the Chalk Talk series at IMM (bi-weekly), with participation of ca. 20 PIs from IMM as speakers.

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. (Journal IF 2010: 5.20)
www.biomedcentral.com/1741-7007/9/58 (on 1/2/12, 3.646 accesses since 31/8/11)

Ramos C, Rocha S, Gaspar C, Henrique, D. (2010): "Two Notch ligands, *Dll1* and *Jag1*, are differently restricted in their range of action to control neurogenesis in the mammalian spinal cord"; *PLoS One* 24;5(11):e15515. (Journal IF 2010: 4,411)
www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0015515
(4 Citations and 1.014 accesses on 1/2/12)

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 (Journal IF 2010: 4,411)
www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0006286
(32 Citations and 10.771 accesses on 1/2/12)

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"; *Dev. Biology* 328:54-65 (Journal IF: 4,42)
www.sciencedirect.com/science/article/pii/S0012160609000293
(11 Citations)

Henrique, D. Bally-Cuif, L. (2010) "A cross-disciplinary approach to understanding neural stem cell in development and disease", *Development* 137(12): 1933-8 (Journal IF 2008: 9,162)
<http://dev.biologists.org/content/137/12/1933.short>

Ongoing Research Projects

2010-2012 - "The dialectics of "Stemness": from biology to mathematics", Coordinator: Domingos Henrique. PTDC/SAUOBD/100664/2008, €140.000.

Publications in International Journals

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. (Journal IF 2010: 5.20)
www.biomedcentral.com/1741-7007/9/58 (on 1/2/12, 3.646 accesses since 31/8/11)

Invited Lectures and Seminars

Henrique, D., Abranches, E., “Nanog and the pluripotent state in ES cells”, STEMBRYO 2011 Meeting- From Oocyte to Embryo: Workshop on Early Mammalian Embryogenesis, Madrid, October 26-28.

Organisation of Conferences

Henrique, D. co-organized the SPN Meeting 2011 (Sociedade Portuguesa Neurociências), May 26-28, Lisbon, Portugal.

Advanced teaching

Henrique, D. - organized the “Advanced Course on Regenerative Medicine”, as part of the Programa Gulbenkian de Formação Médica Avançada (PFMA), IMM, Portugal, February 24th to 28th.

Henrique, D. - organized the “Advanced Course on Developmental Biology”, as part of the GABBA PhD program, Oporto University, IMM, Portugal, March 28th to April 1st.

Henrique, D. – Lectures on “Development of the nervous system” – Masters Program on Neuroscience, Faculdade Medicina Lisboa

Abranches, E. – Course on Stem Cell Biology, Mestrado em Ciência Biológicas, Univ. Algarve, Faro, October 20th.

Abranches, E., Lectures on "Neural differentiation in vitro and in vivo" , FCUL Mestrado Biologia e Tecn. das Células Estaminais , October 2011.

Science and Society

Domingos Henrique is a member of the Conselho Nacional para a Procriação Medicamente Assistida (CNPMA), the regulatory authority for medically-assisted reproduction (www.cnpma.org.pt).

Master and PhD thesis completed

Filipe Vilas Boas (2011): “Functional analysis of the Notch signalling cascade in neural progenitors”, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Domingos Henrique.

Ricardo Miragaia (2011): “Proneural bHLH and cell population dynamics in mouse retina”, Mestrado em Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Cláudia Gaspar

Joana Neves (2011): “Regulation of Dll4 expression in cells committing to differentiation in the V2 domain of the developing spinal cord”, Mestrado em Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Catarina Ramos

Inês Honório (2011): “A novel reporter of *Fgf5* expression to monitor the "stemness" ground state in mouse Embryonic Stem cells”, Mestrado em Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Abranches.

Ana Guedes (2011): “Monitoring the activity of the Notch pathway in neural progenitor cells”, Mestrado em Biologia Molecular e Genética, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Domingos Henrique

Embryonic Development of Vertebrates Unit

Major interests / Objectives

The design of the vertebrate body plan involves the creation of asymmetries between the left and the right side of the lateral plate mesoderm, in order to correctly position the internal organs. In addition, it also comprises the control of symmetry between the left and the right side of the presomitic mesoderm to ensure the symmetric formation of the somites and therefore the correct allocation of symmetric body structures such as the axial skeleton and skeletal muscles. We would like to understand the cellular and molecular mechanisms that control the left-right (LR) 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

Leonor Saúde, PhD – Invited Auxiliary Professor, FMUL

Research Team

Susana Pascoal, PhD	Post Doc Fellowship, FCT
Rita Fior, PhD	Post Doc Fellowship, FCT
Ana Ribeiro, PhD	Post Doc Fellowship, FCT
Raquel Mendes	PhD Fellowship, FCT
Sofia Azevedo	PhD Fellowship, FCT
Margarida Cristovão	BTI, FCT
Joana Lima	BTI, FCT
Sara Fernandes	Master student, FCUL
Lúcia Barriga Negra	Master student, ICBAS (left in December 2011)
Pedro Henriques	Visitor (left in September 2011)

Keywords/Research Areas

Left-right asymmetry
Somite formation
Tissue/organ regeneration
Cilia formation and function

Major scientific achievements

1. The regenerative capacity of zebrafish caudal fin is not affected by repeated amputations or ageing

We demonstrated that the zebrafish caudal fin has an almost unlimited capacity to regenerate. Even after inhibition of regeneration caused by the loss of Wnt/ β catenin signalling, a new

amputation resets the regeneration capacity within the caudal fin, suggesting that blastema formation does not depend on a pool of stem/progenitor cells that require Wnt/ β -catenin signalling for their survival.

This work was published in PlosOne.

2. Identification and expression analysis of two novel members of the Mesp family in zebrafish

We have completed the description of the Mesp family in zebrafish, which will enable correct genome annotation and facilitate further functional studies on the role of these proteins in zebrafish. The newly identified *mesp-ab* and *mesp-bb* are expressed in early mesoderm with *mesp-ab* expression starting during late blastula stages and *mesp-bb* expression initiating later, at the end of gastrulation. During somitogenesis, both *mesp* genes are expressed dynamically in the anterior presomitic mesoderm. We showed that the segmentation clock program regulates expression of these newly identified zebrafish *mesp* genes in a similar manner to their ohnologs, *mesp-aa* and *mesp-ba*. We also presented evidence that zebrafish, minnow and salmon retained these additional *mesps* after the teleost whole genome duplication, while medaka, stickleback, fugu and tetraodon did not. We also showed that although expression and regulation of zebrafish *mesps* appears highly comparable there is no conservation in non-coding regions to other teleosts.

This work is in press in The International Journal of Developmental Biology.

3. Differentiation and movement of presomitic mesoderm progenitor cells are coupled by Mesogenin1

We showed in zebrafish, using loss- and gain-of-function experiments and heat-shock transgenics, that *Msgn1* acts with *Spt* to initiate and drive the program of PSM differentiation. *Msgn1* allows progression of the PSM differentiation program by negatively regulating the progenitor maintenance genes *wnt* and *ntl*. *msgn1* is itself positively regulated by Wnt/*Ntl*, creating a negative feedback loop that may be critical for maintaining the progenitor population until somitogenesis ends. We show, through live imaging, that *Msgn1* also regulates the ventral diving of progenitors as they move from the tailbud into the PSM. Thus, in the conversion of progenitors into PSM, differentiation is coupled with cell movement through *Msgn1*.

This work is being reviewed in Development.

4. Notch signalling controls pectoral fin development in zebrafish.

A functional pectoral fin is composed of an endochondral disk associated with skeletal muscle fibres. We showed that in the absence of Notch signalling, the endochondral disk is not a cohesive mass of cells and the skeletal muscle fibres become wavy and loose. Our findings highlight the role that developing muscles have on the development of bone structures.

This work is being prepared for publication.

5. The cell adhesion molecule N-cadherin controls cell movement in the Hensen's node after the establishment of left-right asymmetry.

We show that N-cadherin asymmetric expression in the chicken's node becomes asymmetric downstream of the leftward movements that occur in the node at stage 4. The asymmetric N-cadherin expression seems to be required to stop cell movement once the asymmetry is established and in this was helps to maintain the asymmetric information.

This work is being prepared for publication.

Recent Most Relevant Publications

Cutty S.J., Fior F., Henriques P.M., Saúde L. and Wardle F.C. Identification and expression analysis of two novel members of the Mesp family in zebrafish. The International Journal of Developmental Biology in press.

Azevedo A.S., Grotek B., Jacinto A., Weidinger G. and Saúde L. (2011) The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. PloS ONE Vol. 6(7); e22820. (Journal IF: 4.351, Citations: 0)

Lourenço R, Lopes S S and Saúde L (2010) Left-right function of *dmrt2* genes is not conserved between zebrafish and mouse. PlosONE 5(12); e14438. (Journal IF: 4.351, Citations: 0)

Lopes S S, Lourenço R, Pacheco L, Moreno N, Kreiling J and Saúde L (2110) Notch signalling regulates left-right asymmetry through ciliary length control. Development 137(21); 3625-32. (Journal IF: 8.064, Citations: 5)

Ongoing Research Projects

2009/2011 Searching for RNA regulators that control the segmentation clock, FCT. Coordinator: Leonor Saúde. PTDC/BIA-BCM/101282/2008, €188.743,00

2009/2011 Uncover the importance of cilia as signaling structures during regeneration, FCT. Coordinator: Leonor Saúde. PTDC/SAU-OB/100202/2008, €170.000,00

2007/2010 Functional study of the molecular clock during vertebrate limb development, FCT. Coordinator: Leonor Saúde. PTDC/SAU-OB/64628/2006, €129.700,00 (ended 12-02-2011)

Publications in peer review Journals

Cutty S.J., Fior F., Henriques P.M., Saúde L. and Wardle F.C. Identification and expression analysis of two novel members of the Mesp family in zebrafish. The International Journal of Developmental Biology in press.

Azevedo A.S., Grotek B., Jacinto A., Weidinger G. and Saúde L. The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. PloS ONE (2011), Vol. 6(7); e22820. (Journal IF: 4.351, Citations: 0)

Communications in International Conferences

Fior, R., Lewis, J. and Saúde, L. The role of mesogenin in mesoderm formation. 9th International Zebrafish European Conference, Edinburgh, UK, July 5-9, 2011 (Oral presentation).

Mendes, R. and Saúde, L. N-cadherin is asymmetrically expressed in the Hensen's node. What for? Gordon Research Conference on Regeneration and Tissue Repair, Andover, NH, USA, June 19-24, 2011 (Poster presentation).

Pascoal, S., Lima, J. and Saúde, L. The role of Shh signaling during larvae caudal fin regeneration. Gordon Research Conference on Regeneration and Tissue Repair, New London, NH, USA, June 5-10, 2011 (Poster presentation).

Mendes, R. and Saúde, L. N-cadherin is asymmetrically expressed in the Hensen's node. What for? EMBO Workshop Biophysical Mechanisms of Development, Oeiras, Portugal, May 24-27, 2011 (Poster presentation).

Pascoal, S., Lima, J. and Saúde, L. Mind bomb is a ubiquitin ligase required for proper formation of cartilage and muscle fibers in zebrafish pectoral fins. EMBO Workshop Biophysical Mechanisms of Development, Oeiras, Portugal, May 24-27, 2011 (Poster presentation).

Henriques, P., Fior, R. and Saúde, L. Mesp2 defines a segmental prepatter in the presomitic mesoderm of zebrafish. EMBO Workshop Biophysical Mechanisms of Development, Oeiras, Portugal, May 24-27, 2011 (Poster presentation).

Barriga-Negra, L., Gonçalves, J., Soares, H. and Saúde, L. Study of centrosomal TBCCD1 protein function during the Danio rerio development. EMBO Workshop Biophysical Mechanisms of Development, Oeiras, Portugal, May 24-27, 2011 (Poster presentation).

Fior, R., Lewis, J. and Saúde, L. The role of mesogenin in mesoderm formation. EMBO Workshop Biophysical Mechanisms of Development, Oeiras, Portugal, May 24-27, 2011 (Poster presentation).

Pascoal, S., Lima, J. and Saúde, L. Mind bomb is a ubiquitin ligase required for proper formation of cartilage and muscle fibers in zebrafish pectoral fins. Interdisciplinary Approaches in Fish Skeletal Biology, Tavira, Portugal, April 26-28, 2011 (Poster presentation).

Pascoal, S., Lima, J. and Saúde, L. The role of Shh signaling during larvae caudal fin regeneration. Gordon Research Conference on Cilia, Mucus & Mucociliary Interactions, Ventura, CA, USA, February 13-18, 2011 (Poster presentation).

Fior, R., Lewis, J. and Saúde, L. Mesogenin throws the switch that converts mesodermal progenitors into paraxial mesoderm. 4th Strategic Conference of Zebrafish Investigators, Asilomar, USA, January 29-February 2, 2011 (Oral presentation).

Communications in National Conferences

Saúde, L. Patterning the vertebrate embryo along the left-right axis. 5th National Meeting on Signal Transduction, Coimbra, Portugal, April 28-30 (Oral presentation).

Internationalization

-Collaborative publication with Gilbert Weidinger from Center for Regenerative Therapies University of Technology Dresden, Germany and António Jacinto from IMM, Portugal.
Azevedo A.S., Grotek B., Jacinto A., Weidinger G. and Saúde L. The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. PloS ONE (2011), Vol. 6(7); e22820.

-Collaborative publication with Fiona Wardle, King's College London, UK.
Cutty S.J., Fior F., Henriques P.M., Saúde L. and Wardle F.C. Identification and expression analysis of two novel members of the Mesp family in zebrafish. The International Journal of Developmental Biology in press.

-Collaborative project (manuscript in revision in Development) with Julian Lewis from CRUK, UK, Sharon Amacher from University of California at Berkeley, USA and Cecilia Moens from Fred Hutchinson Cancer Research Center Seattle, USA.

Fior R., Maxwell, A.A., Ma, T.P., Vezzaro, A., Moens, C.B., Amacher, S.L., Lewis, J. and Saúde, L. Differentiation and movement of presomitic mesoderm progenitor cells are coupled by Mesogenin1.

-Collaborative project with Margarida Gama-Carvalho from BioFIG-FCUL on “Identification of the RNA regulators of the segmentation clock”. Co-supervision of a Masters student: Sara Fernandes.

-Collaborative project with Helena Soares from FCUL on the “Role of TBCCD1 on ciliogenesis and development”. Co-supervision of a Masters student: Lúcia Barriga Negra

Prizes, honours and awards

Honorable Mention, Olympus BioScapes Competition 2011 to Rita Fior.

Advanced teaching

Fior, R. organized and lectured “Animal Developmental Biology” in The Molecular Genetics and Biomedicine Master course. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, September 15 - December 15, 2011.

Pascoal, S. lectured The Molecular Genetics and Biomedicine Master course. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, November 10, 2011.

Mendes, R. lectured The Molecular Genetics and Biomedicine Master course. Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, September 29 and October 6, 2011.

Saúde, L. lectured the FMUC PhD programme. Faculdade de Medicina da Universidade de Coimbra. November 3, 2011.

Saúde, L. Round table “Scientific reasoning” Programa Gulbenkian de Formação Médica Avançada. IMM, Lisbon, September 29, 2011.

Saúde, L. lectured the PhD programme “Molecular and Cellular Biology of the Epithelium in Health and Disease”. Faculdade de Ciências da Universidade de Lisboa. September 23, 2011.

Science and Society

Rita Fior (2011) selected movies to the “corpoIMAGEM” exhibition promoted by Ciência Viva, Pavilhão do Conhecimento, Lisboa, Portugal

Rita Fior (2011) selected pictures to The Physics of Life exhibition promoted by EMBO. Instituto Gulbenkian de Ciência, Oeiras, Portugal

Raquel Mendes (2011) selected pictures to The Physics of Life exhibition promoted by EMBO. Instituto Gulbenkian de Ciência, Oeiras, Portugal

Susana Pascoal (2011) selected pictures to The Physics of Life exhibition promoted by EMBO. Instituto Gulbenkian de Ciência, Oeiras, Portugal

Leonor Saúde (2011) APIFARMA visit to the IMM. A guided-visit to the Fish Facility to members of different Portuguese Patients Associations.

Leonor Saúde (2011) L'Oréal visit to the IMM. A guided-visit to the Fish Facility to L'Oréal collaborators.

Leonor Saúde (2011) Conversas com Cientistas, Galerias Mês da Ciência, Oeiras Parque, Oeiras, Portugal

Master and PhD thesis completed

Lúcia Barriga-Negra (December 28, 2011). Caracterização da proteína centrossomal TBCCD1 durante o desenvolvimento embrionário do peixe zebra. Instituto de Ciências Biomédicas Abel Salazar. Masters Co-Supervisor: Leonor Saúde

Sara Fernandes (December 2, 2011). Identification of the RNA regulators operating in the segmentation clock. Faculdade de Ciências da Universidade de Lisboa. Masters Co-Supervisor: Leonor Saúde

Raquel Lourenço (March 4, 2011). Symmetry-OUT, Asymmetry-IN, The role of DMRT2. Instituto de Tecnologia Química e Biológica da Universidade Nova de Lisboa. PhD Supervisor: Leonor Saúde

Gene Expression & Biophysics Unit

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 M. Mhlanga PhD – Research Group Leader (IMM Associate Investigator)

Research Team

Luis Pedro Coelho PhD	Post Doc Fellowship, FCT
Ricardo Henriques	PhD Fellowship, FCT (left in Dec 2011)

Research Areas

RNA biology
Super-resolution
Nuclear Architecture
Gene Expression
Host-Pathogen Interactions

Major scientific achievements

The laboratory published two publications this year and also developed new releases of its QuickPALM software for super resolution microscopy. In addition a European patent was awarded to the PI of the laboratory in late 2011. The lab also was actively involved in organizing an EMBO workshop in South Africa in November 2011.

Henriques R., Lelek M., Fornasiero E. F., Valtorta F., Zimmer C., Mhlanga M. M. (2010) QuickPALM: 3D real-time photoactivation nanoscopy image processing in ImageJ. Nature Methods 7,5 339

Henriques, R., Griffiths, C., Rego, E. H. and Mhlanga, M.M. (2011) PALM and STORM: unlocking live-cell super-resolution. Biopolymers, n/a. doi: 10.1002/bip.21586

QuickPALM Super-resolution algorithm & microscopy hardware control. Language: Java & Python. Mhlanga M. & Henriques R (2010)

Single cell based reporter assay to monitor gene expression patterns with high spatio-temporal resolution

M Mhlanga, J Enninga, P Sansonetti, U Nehrbass

EP Patent 2,195,457

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 (5), 339-340 (Journal IF: 20.717, Citations: 21)

R Henriques, MM Mhlanga (2009) PALM and STORM: What hides beyond the Rayleigh limit? *Biotechnology journal* 4 (6), 846-857 (Journal IF: ND Citations: 17)

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 (6), 1902-1912 (Journal IF: 7.836 Citations: 81)

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 of the United States of ...* (Journal IF: 9.771 Citations: 214)

LG Kostrikis, S Tyagi, MM Mhlanga, DD Ho, FR Kramer (1998) Spectral genotyping of human alleles *Science* 279 (5354), 1228 (Journal IF: 31.36 Citations: 288)

Ongoing Research Projects

2010/2013: Super-resolution Imaging of Gene Expression & Nuclear Architecture, FCT. Coordinator: M Mhlanga. PTDC/SAU-GMG/115652/2009, €185.000

Publications in Peer Review International Journals

Henriques, R., Griffiths, C., Rego, E. H. and Mhlanga, M.M. (2011) PALM and STORM: unlocking live-cell super-resolution. *Biopolymers*, n/a. doi: 10.1002/bip.21586 (Journal IF: 2.572 Citations: 7)

Invited Lectures and Seminars

Musa Mhlanga: Imaging from systems biology to single molecules, Janelia Farm, USA April 2011

Musa Mhlanga: Imaging from systems biology to single molecules, Johns Hopkins Univ. School of Medicine, USA April 2011

Musa Mhlanga: Imaging from systems biology to single molecules, Cold Spring Harbor Laboratory Suzhou, China, USA April 2011

Musa Mhlanga: Super-resolution microscopy PALM/STORM for biology, Beijing Nanocenter China August 2011

Musa Mhlanga: Imaging from systems biology to single molecules, Janelia Farm, USA
September 2011

Musa Mhlanga: Imaging from systems biology to single molecules, RIKEN, Yokohama, Japan
Oct 2011

Musa Mhlanga: Super-resolution microscopy PALM/STORM for biology, A-STAR, Singapore,
Nov 2011

Organisation of Conferences

Musa Mhlanga. co-organized the EMBO Practical Course – Imaging Infection. November 2-13, 2011, Pretoria, South Africa.

Industry contract research

Development of Super-resolution microscopy hardware and software tools for use in
PALM/STORM

Advanced teaching

EMBO Practical Course – Imaging Infection. November 2-13, 2011, Pretoria, South Africa.

Science and Society

Lecturer on Synthetic Biology . Synthetic Biology Forum: August 24, 2011

PhD thesis completed

Ricardo Henriques PhD (2011) Beyond Rayleigh's limit: Achieving real-time super-resolution
fluorescence microscopy. Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor:
Musa Mhlanga & Antonio Jacinto.

Microvascular Biology and Inflammation Unit

Major interests / Objectives

Inflammation aims to eliminate noxious agents to regain body homeostasis. At the microcirculation level, it involves the action of inflammatory mediators and vascular and blood cells that conduct the process either onto resolution or to a chronic stage. In this respect, we aim to dissect the cellular and molecular mechanisms that control leukocyte recruitment and erythrocyte function by studying: (1) the CD47/fibrinogen binding mechanisms and its repercussions on NO metabolism in blood and microvascular cells in acute and chronic inflammation; (2) the role of systemic hemorheological and inflammatory biomarkers in disease progress and as prognostic markers and (3) how distinct inflammatory cues, as chemokines and hydrogen peroxide, concert their action in driving leukocyte migration.

Head of Unit

Carlota Saldanha, PhD – Associated Professor with Habilitation, FMUL.

Principal Investigators

Ângelo Calado, PhD – Auxiliary Professor, FMUL (Proposed for PI in 2011)

Research Team

Henrique Sobral do Rosário, MD, PhD	Auxiliary Professor, FMUL
Ana S. Silva-Herdade, Master Degree	Assistant, FMUL
Patrícia Napoleão	Post Doc Fellowship, FCT
Vanda Vitorino de Almeida	PhD Fellowship, FCT
Sofia de Oliveira	PhD Fellowship, FCT
Cláudia Ferreira, PhD	Auxiliary Professor, Lusófona University
Daniel Guerreiro	Master student
Nuno Duro	Master student
Teresa Freitas	Lab Technician, FMUL

Keywords/Research Areas

Inflammation; Leukocyte-endothelium interaction; Microcirculation; Hemorheology ; Non-Neuronal Cholinergic System

Major scientific achievements

Fibrinogen interacts with RBC membrane in a discrete punctuated pattern and in an age-dependent way. A higher interaction is established with younger RBCs that decrease in the

presence of anti-CD47 antibodies arguing erythrocyte membrane CD47 is a molecular target for plasma fibrinogen.

High concentrations of fibrinogen and acetylcholine increase the levels of nitrites, nitrates, GSNO and erythrocyte deformability without significant changes in RBCs NO. The efflux is reinforced when band 3 is phosphorylated in presence of high fibrinogen level. Erythrocyte NO efflux is negatively associated with carotid intima-media thickness and independently associated with early stages of atherosclerosis.

Zebrafish encodes two distinct CXCL8 chemokines. Both genes, *cxcl8-11* and *cxcl8-12*, are up-regulated on tail transected larvae. Importantly, ablation of their expression by specific morpholinos has shown that both chemokines are important for normal neutrophil response in inflammation.

Recent Most Relevant Publications

de Oliveira, S, de Almeida, VV, Calado, A, Rosario, HS, Saldanha, C. (2011) Integrin-associated protein (CD47) is a putative mediator for soluble fibrinogen interaction with human red blood cells membrane. *Biochim Biophys Acta* 1818 (3), 481-490 (Journal IF: 4.647, Citations: 0)

Artoli, AM, Sequeira, A, Silva-Herdade, AS, Saldanha, C. (2007) Leukocytes rolling and recruitment by endothelial cells: hemorheological experiments and numerical simulations. *J Biomech* 40 (15), 3493-502. (Journal IF: 2.463, Citations: 5)

Santos, NC, Martins-Silva, J, Saldanha, C. (2005) PTEN "meets" DMSO. *Leuk Res* 29 (4), 361-362 (Journal IF: 4.626, Citations: 3).

Lund, E., Guttinger, S., Calado, A., Dahlberg, J.E., Kutay, U. (2004) Nuclear export of microRNA precursors. *Science* 303, 95-98. (Journal IF: 31.377, Citations: 827).

Rosário HS, Waldo SW, Becker SA, Schmid-Schönbein GW. (2004) Pancreatic trypsin increases matrix metalloproteinase-9 accumulation and activation during acute intestinal ischemia-reperfusion in the rat. *Am J Pathol.* 164, 1707-16. (Journal IF: 5.244, Citations: 32)

Ongoing Research Projects

2007/2011 Fibrinogen-dependent signalling in microvascular blood cell function – implications of inflammation and cardiovascular disease, FCT. Coordinator: Carlota Saldanha. PTDC/SAU-OSM/73449/2006, €101736 (total).

2009/2011 Cardiovascular risk and inflammation- contribution to the etiopathogenesis of atherosclerosis and cardiovascular disease, FCT. Coordinator: João Eurico, IMM, FMUL, UL. PIC/IC/82920/2007. € 23307,98 (UBIMI), € 150000 (total).

2009/2011 Development and validation of vaso-occlusion early predictors in a mendelian model of vascular disease, FCT. Coordinator: João Lavinha, INSA. PIC/IC/83084/2007, € 65010 (IMM), € 185000 (total).

2007/ 2012 The relationship of circulating biomarkers of apoptosis and endothelial function with the plaque composition using VH IVUS, FCT. Coordinator: Teresa Pinheiro, Grupo de Estudos Biomédicos, Instituto Tecnológico e Nuclear (ITN). FCT project PIC/IC/82734/2007, €155000 (total).

2009/2013 Interrelationship of circulating haemostatic, hemorheologic and inflammatory markers in acute myocardial infarction – a longitudinal approach. Coordinator: Carlota Saldanha. Patrícia Napoleão Post-Doc Fellowship SFRM/BPD/63908/2009, FCT. (No funding)

2009/2013 Regulatory interactions between the metabolic sensors SIRT1 and AMPK in modulating PPARalpha-linked functions in liver in health and disease, Co-Coordinator: Carlota Saldanha. Marta Silvestre PhD Fellowship SFRH /BD/62927/2009, FCT. (No funding)

2009/2013 In vivo imaging of inflammation in zebrafish: the role of chemokine system in the neutrophil and macrophage migration, Coordinator: Ângelo Calado. Sofia de Oliveira, PhD Fellowship SFRH/BD/62674/2009, FCT. (No funding)

Publications in peer review Journals

Lopes de Almeida, JP, Freitas-Santos, T, Saldanha, C. (2011) Evidence that the degree of band 3 phosphorylation modulates human erythrocytes nitric oxide efflux - in vitro model of hyperfibrinogenemia. *Clinical Hemorheology and Microcirculation* 49 (1), 407-16. (Journal IF: 2.838)

Saldanha, C, Lopes de Almeida, JP. (2011) Erythrocyte as a link between basic and clinical research. *Clinical Hemorheology and Microcirculation* 49 (1), 463-72. (Journal IF: 2.838)

Moura, RA, Cascao, R, Perpetuo, I, Canhao, H, Vieira-Sousa, E, Mourao, AF, Rodrigues, AM, Polido-Pereira, J, Queiroz, MV, Rosario, HS, Souto-Carneiro, MM, Graca, L, Fonseca, JE. (2011) Cytokine pattern in very early rheumatoid arthritis favours B-cell activation and survival. *Rheumatology* 50 (2), 278-282 (Journal IF: 4.171)

de Oliveira, S, de Almeida, VV, Calado, A, Rosário, HS, Saldanha, C. (2011) Integrin-associated protein (CD47) is a putative mediator for soluble fibrinogen interaction with human red blood cells membrane. *Biochim Biophys Acta* 1818 (3), 481-490 (Journal IF: 4.647)

Santos, MJ, Pedro, LM, Canhão, H, Fernandes e Fernandes, J, Canas da Silva, J, Fonseca, JE, Saldanha C. (2011) Hemorheological parameters are related to subclinical atherosclerosis in systemic lupus erythematosus and rheumatoid arthritis patients. *Atherosclerosis* 219(2), 821-6. (Journal IF: 4.086)

Silva-Herdade, AS, Saldanha, C. (2011) Hemorheological effects of valsartan in L-NAME induced hypertension in rats. *The Open Circ Vasc J* 4, 1-5. (Journal IF: not available)

Lopes de Almeida JP, Freitas-Santos, T, Saldanha C. (2011) Erythrocyte deformability dependence on Band 3 protein in an in vitro model of hyperfibrinogenemia. *Clin Hemorh Microc* 44, 1-6. (Journal IF: 2.838)

Lopes de Almeida, JP, de Oliveira, S, Saldanha, C. (2011) Erythrocyte as a Biological Sensor. *Clin Hemorh Microc* 48, 1-20. (Journal IF: 2.838)

Invited Lectures and Seminars

Carlota Saldanha, Red Blood Cell as a Link between Basic and Clinic Research, Symposium Rheology and Hemostasis, European Society of Hemorheology and Microcirculation, Munich, Germany, 18-21 June 2011.

Communications in International Conferences

Moura, RA, Cascão, R, Perpetuo, I, Canhão, H, Vieira-Sousa, E, Mourao, AF, Rodrigues, AM, Polido-Pereira, J, da Silva, JAP, Rosario, HS, Souto-Carneiro, MM, Graca, L, Fonseca, JE. Spondyloarthritis and Rheumatoid arthritis: different clinical manifestations, similar cytokine network, 31st European Workshop for Rheumatology Research, Amsterdam, Netherlands, 3-6 March 2011. (Poster Presentation)

Saldanha, C, de Oliveira, S, de Almeida, VV, Calado, A, Rosário, HS. Imaging of Fibrinogen Binding to Erythrocytes, Nano Meets Spectroscopy, NPL, Tedington, UK, 14-15 September 2011. (Oral Presentation)

Saldanha, C, de Oliveira S, Almeida, J. Modulation of erythrocyte ATP level by PKC activity and Band3 phosphorylation degree, Joint Meeting of the European Society for Microcirculation (ESM)/Society of Microcirculation and Vascular Biology (GfMVB), Munich, Germany, 13-16 October 2011 (Oral Presentation)

de Oliveira, S, Mulero, V, Calado, A. CXCL8 is involved in zebrafish neutrophil recruitment, 10th World Congress on Inflammation, Paris, France, 25-29 June 2011 (Oral Presentation)

Saldanha, C, Lopes de Almeida, JP. Influence of fibrinogen on erythrocyte nitric oxide efflux induced by acetylcholine, Third International Symposium on Non-neuronal Acetylcholine, Groningen, The Netherlands, 24-26 August 2011. (Poster Presentation)

Lopes de Almeida, JP, Saldanha, C. Evidence that the degree of band3 Phosphorylation modulates human erythrocytes Nitric Oxide Efflux – In vitro model for Hyperfibrinogenemia, European Society of Hemorheology and Microcirculation, Munich, Germany, 18-21 June 2011. (Poster Presentation)

Communications in National Conferences

Napoleão, P. Biomarkers of inflammation and endothelial dysfunction in coronary syndromes, Santa Marta – Lisbon Summer Meeting on Interventional Cardiology, Lisbon, Portugal, 2 July 2011. (Oral presentation)

Calado, A. Animal and cell models to study mechanisms of inflammation and cell-cell interaction, Santa Marta – Lisbon Summer Meeting on Interventional Cardiology, Lisbon, Portugal, 2 July 2011. (Oral Presentation).

de Oliveira, S., Mulero, V. and Calado, A. CXCL8 is involved in zebrafish neutrophil recruitment, 2011 PhD Student Meeting IMM/CAML, Lisbon, October 17-18, 2011. (Poster Presentation).

Organisation of Conferences

Saldanha, C. Organizer of Microcirculation and Microrheology of Blood Cells in Health and Diseases Symposium, Joint Meeting of the European Society for Microcirculation (ESM)/Society of Microcirculation and Vascular Biology (GfMVB), Munich, Germany, 13-16 October 2011.

Internationalization

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” and performed under the co-supervision of Dr. Ângelo Calado and Dr. Victor Mulero (Univ. Murcia, Spain) in the two laboratories.

Rosario, HS. Post Doc fellowship FMUL. The hypercholesterolemic *Drosophila*: a novel high throughput animal model to study macrophage biology in atherosclerosis. At: Monocyte Lab – Centre for Molecular Biology of Inflammation Guy’s Campus, King’s College, London.

Saldanha, C. Member of the “European Clinical Hemorheology Coordinating Committee” since 1991

Saldanha, C. Member of the “Strategic Group of the European Society of Microcirculation” since 2000

Saldanha, C. Member of the Editorial Board of the Clinical Hemorheology between 1994-1997

Saldanha, C. Member of the Editorial Board of the Clinical Hemorheology and Microcirculation since 1997

Saldanha, C. Member of the Editorial Board of the Open Circulation and Vascular Journal since 2009

Industry contract research

Since 2010: contract research with Biosurfit (Portugal).

Science and Society

Saldanha, C. “President of Portuguese Society of Hemorheology and Microcirculation, www.hemorreologia.com

Saldanha, C. “Editor-in-Chief of the Bulletin of the Portuguese Society of Hemorheology and Microcirculation.

Saldanha, C. “Editor-in-Chief of the Bulletin of the Portuguese Society of Hemorheology and Microcirculation.

Saldanha, C. “Blood Cell Components” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2011: 26 (1) :3-4

Saldanha, C. “Hemorheology Renewal” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2011: 26 (2) :3-4

Saldanha, C. “Intravital Microscopy and Hemorheology” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2011: 26 (3) :3-4

Saldanha, C. “Is Nitric Oxide an Hemorheological Parameter? ” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2011: 26 (4) :3-4

Physical Biochemistry Unit

Major interests / Objectives

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, antimicrobials and transfection agents. Peptide-lipid biomembranes interactions are ubiquitous in the living world and a fertile ground for drug discovery and development. At the UBqF 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. More recently, we are focused on the central nervous system and translocation of the blood-brain barrier.

Head of Unit

Miguel ARB Castanho, PhD – Full Professor, FMUL

Research Team

Ana Salomé Veiga, PhD	Post Doc Fellowship Marie Curie (FP7)
Diana Gaspar, PhD	Post Doc Fellowship, FCT
Isa Domingues Serrano, PhD	Post Doc Fellowship, FCT
Katia da Conceição	Post Doc Fellowship, Marie Curie (FP7)
Sónia Sá Santos, PhD	Post Doc Fellowship (FCT support to IAPP, Marie Curie Actions in FP7)
Sónia Troeira Henriques, PhD	Post Doc Fellowship, Marie Curie (FP7)
Henri Girão Franquelim	PhD Fellowship, FCT
João M. Freire	PhD Fellowship, FCT
Marta Maria B. Ribeiro	PhD Fellowship, FCT
Inês Torcato	Master Research Student
Ahmet Asci	Undergraduate Research Student from the program SCORE, project IFMSA
Amr Shaarawi	Undergraduate Research Student from the program SCORE, project IFMSA
Francisco Cunha	Undergraduate Research Student (FMUL)
Georgia Protonotariou	Undergraduate Research Student from the program SCORE, project IFMSA
Guilherme Trigo Romana	Undergraduate Research Student (FMUL)
Inês Isabel Lopes Leão	Undergraduate Research Student (FMUL)
Inês Figueiredo	Undergraduate Research Student (FMUL)
Joana Estrela	Undergraduate Research Student (FMUL)
Raquel Brás	Undergraduate Research Student (FMUL)

Keywords/Research Areas

Analgesic peptides; Antimicrobial peptides; Blood-brain barrier; Cell-penetrating peptides; Viral fusion inhibitors

Major scientific achievements

We have:

- Proved that a covalent conjugation of an anti-inflammatory hydrophobic molecule (ibuprophen) with a previously designed kyotorphin derivative (analgesic dipeptide) has improved, synergistic, efficacy. This new drug resulted from an innovative drug design strategy (Ribeiro M.M., et al., 2011, Molecular Pharmaceutics, Oct 3;8);
- Demonstrated a correlation between the efficacy of both HIV fusion inhibitors and anti-HIV antibodies with their membrane-interaction properties (Franquelim H.G., et al., 2011, AIDS, Feb 20;25; Franquelim H.G., et al., 2011, Soft Matter, Oct; 7);
- Optimized the imaging of bacteria with lesions resulting from the local action of antimicrobial peptides (AMP's) using Atomic Force Microscopy, which brought significant advancements both to imaging of bacteria itself and the mechanism of action of AMP's.

Recent Most Relevant Publications

Franquelim H.G., Chiantia S., Veiga A.S., Santos N.C., Schwille P., Castanho M.A.R.B. (2011) Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes. AIDS Feb 20;25(4):419-28. (Journal IF = 6.348, Citations: 0).

Henriques S.T., Huang Y.-H., Rosengren K. J., Franquelim H.G., Carvalho F.A., Johnson A., Sonza, S., Tachedjian G., Castanho M.A.R.B, Daly N.L., Craik D.J. (2011) Decoding membrane activity of the cyclotide kalata B1: the importance of phosphatidylethanolamine phospholipids and lipid organization on hemolytic and anti-HIV activities, J Biol Chem, Jul 8;286(27):24231-41. (Journal IF= 5.32, Citations: 2).

Ribeiro M.M., Pinto A.R., Domingues M.M., Serrano I., Heras M., Bardaji E.R., Tavares I., Castanho M.A. (2011) Chemical conjugation of the neuropeptide kyotorphin and ibuprofen enhances brain targeting and analgesia, Molecular Pharmaceutics, Oct 3;8(5):1929-40. (Journal IF 5.400, Citations: 0).

Ribeiro M.M., Pinto A., Pinto M., Heras M., Martins I., Correia A., Bardaji E., Tavares I., Castanho M. (2011) Inhibition of nociceptive responses after systemic administration of amidated kyotorphin, British Journal of Pharmacology, Jul;163(5):964-73. 964-973. (Journal IF: 4.925, Citations: 0).

Franquelim H.G., De-Sousa F.F., Veiga A.S., Santos N.C., Castanho M.A.R.B. (2011) Cationic liposomes are possible drug-delivery systems for HIV fusion inhibitor sifuvirtide, Soft Matter, Oct; 7: 11089-11092. (Journal IF = 4.457, Citations: 0).

Ongoing Research Projects

2007/2011 Targeting kyotorphin derivatives to the brain, FCT. Coordinator: Miguel Castanho. PTDC/SAU-FCF/69493/2006, €80 000 (Total: €100 000).

2007/2011 The role of lipid membranes on cell infection by Dengue virus, FCT. Coordinator: Miguel Castanho. PTDC/QUI/69937/2006, €120 000 (Total: €120 000).

2011/2014 LIPIDENGUE , FCT. Coordinator: Miguel Castanho. PTDC/QUI-BIQ/112929/2009, €130 000 (Total: €130 000).

2009/2012 Selected peptides as drug candidates directed to pain and neurodegeneration (PEP2BRAIN), EC-FP7. Coordinator: Miguel Castanho. Marie Curie Industry-Academia Partnerships and Pathways (IAPP) Call: FP7-PEOPLE-2007-3-1-IAPP (Grant no. 230654), €300 000 (Total: €660 000).

2009/2012 Elucidating the mechanism of action of cyclotides ultra-stable proteins from plants, European Commission. Coordinator: Miguel Castanho. PIOF-GA-2008-220318 (joint project with the Institute for Molecular Biosciences, The University of Queensland, Australia), €55 647,53 (Total: €222 590,10).

2009/2012 Toward the development of peptide-based hydrogels for tissue regeneration applications with inherent antibacterial activity, European Commission. Coordinator: Miguel Castanho. PIOF-GA-2008-235154, (joint project with National Institute of Health, USA), €58 775,50 (Total: €235 102).

2010/2012 Inherent antibacterial activity in peptide-based hydrogels for tissue regeneration, FCT. Coordinator: Ana Salomé Veiga. PTDC/SAU-BEB/099142/2008, €199 350 (Total: €199 350).

2010/2012 Cell membrane features in HIV entry and its inhibition, FCT. Participant: Miguel Castanho. PTDC/QUI-BIQ/104787/2008, (Coordinator: Nuno Santos, IMM), €174 130 (Total: €174 130).

2010/2013 Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration (MEMPEPACROSS). Participant PI: Miguel Castanho. Marie Curie International Research Staff Exchange Scheme (IRSES) Call: FP7-PEOPLE-2009-IRSES, (Coordinator: Nuno Santos, IMM), €200 000 (Total: €200 000).

2005 - Joint agreement with biotech companies Xoma (USA), Fusogen (China), and Roche (USA), with published work. Non-funding.

Publications in peer review Journals

Melo M.N., Ferre R., Feliu L., Bardaji E., Planas M., Castanho M.A.R.B. (2011) Prediction of antibacterial activity from physicochemical properties of antimicrobial peptides, PLoS One, Dec 14;6(12):e28549. (Journal IF=4.411)

Chan L.Y., Gunasekera S., Henriques S.T., Worth N.F., Le S.J., Clark R.J., Campbell J.H., Craik D.J., Daly N.L. (2011) Engineering pro-angiogenic peptides using stable disulfide-rich cyclic scaffolds, *Blood*, Dec 15;**118**(25):6709-17. (Journal IF=10.56)

Sando L.,* Henriques S.T.,* Foley F., Simonsen S.M., Rosengren K. J., Daly N.L., Kristopher N.H., Aguilar M-I, Craik D.J. (2011) A synthetic mirror image of kalata B1 reveals that cyclotide activity is independent of a protein receptor, *ChemBioChem*, Nov 4;**12**(16):2456-62 (*Co-first authors). (Journal IF=3.94)

Cascales L., Henriques S.T., Kerr M.C., Huang Y.-H., Sweet M.J., Daly N.L., Craik D.J. (2011) Identification and characterization of a new family of cell penetrating peptides: cyclic cell penetrating peptides, *J Biol Chem*, Oct 21;**286**(42): 36932-43. (Journal IF= 5.32)

Franquelim H.G., De-Sousa F.F., Veiga A.S., Santos N.C., Castanho M.A.R.B. (2011) Cationic liposomes are possible drug-delivery systems for HIV fusion inhibitor sifuvirtide, *Soft Matter*, Oct; **7**: 11089-11092. (Journal IF = 4.457)

Ribeiro M.M., Pinto A.R., Domingues M.M., Serrano I., Heras M., Bardaji E.R., Tavares I., Castanho M.A. (2011) Chemical conjugation of the neuropeptide kyotorphin and ibuprofen enhances brain targeting and analgesia, *Molecular Pharmaceutics*, Oct 3;**8**(5):1929-40. (Journal IF 5.400).

Saraiva T.C., Grund L.Z., Komegae E.N., Ramos A.D., Conceição K., Orie N.M., Lopes-Ferreira M., Lima C. (2011) Nattectin a fish C-type lectin drives Th1 responses in vivo: Licenses macrophages to differentiate into cells exhibiting typical DC function, *Int Immunopharmacol*, Oct;**11**(10):1546-56. (Journal IF: 2.325).

Carvalho A.V., Sá Santos S., Carrondo M.J.T. (2011). Extracellular purine and pyrimidine catabolism in cell culture, *Biotechnology Progress*, Sep-Oct;**27**(5):1373-82. (Journal IF: 2.398).

Monteiro-Dos-Santos J., Conceição K., Seibert C.S., Marques E.E., Ismael Silva P. Jr, Soares A.B., Lima C., Lopes-Ferreira M. (2011) Studies on pharmacological properties of mucus and sting venom of *Potamotrygon* cf. *Henlei*, *Int Immunopharmacol*, Sep;**11**(9):1368-1377. (Journal IF: 2.325).

Henriques S.T., Huang Y.-H., Rosengren K. J., Franquelim H.G., Carvalho F.A., Johnson A., Souza, S., Tachedjian G., Castanho M.A.R.B, Daly N.L., Craik D.J. (2011) Decoding membrane activity of the cyclotide kalata B1: the importance of phosphatidylethanolamine phospholipids and lipid organization on hemolytic and anti-HIV activities, *J Biol Chem*, Jul 8;**286**(27):24231-41. (Journal IF= 5.32)

Ribeiro M.M., Pinto A., Pinto M., Heras M., Martins I., Correia A., Bardaji E., Tavares I., Castanho M. (2011) Inhibition of nociceptive responses after systemic administration of amidated kyotorphin, *British Journal of Pharmacology*, Jul;**163**(5):964-73. 964-973. (Journal IF: 4.925).

Sá Santos S., Sonnewald U., Carrondo M.J.T. and Alves P.M. (2011). The role of glia in neuronal recovery following anoxia: in vitro evidence of neuronal adaptation, *Neurochemistry International*, May;**58**(6):665-75. (Journal IF: 3.601).

Daly N.L., Rosengren, K. J., Henriques S.T., Craik D.J. (2011) NMR and Protein Structure in Drug Design: application to cyclotides and conotoxins, *Eur Biophys J*, Apr;**40**(4):359-70. (Journal IF=2.39)

Freire J.M., Domingues M.M., Matos J., Melo M.N., Veiga A.S., Santos N.C., Castanho M.A. (2011). Using zeta-potential measurements to quantify peptide partition to lipid membranes. *Eur Biophys J*. Apr;**40**(4):481-7. (Journal IF: 2.387)

Conceição K., Bruni F.M., Santos J.M., Lopes R.M., Marques E.E., Fernandez J.H., Lopes-Ferreira M. (2011) The action of fish peptide Orpotrin analogs on microcirculation, *J Pept Sci*, Mar;**17**(3):192-199. (Journal IF: 1.954).

Franquelim H.G., Chiantia S., Veiga A.S., Santos N.C., Schwille P., Castanho M.A.R.B. (2011) Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes, *AIDS*, Feb 20;**25**(4):419-28. (Journal IF = 6.348)

Other publications International

Books

Peptide Drug Discovery and Development: Translational Research in Academia and Industry. Castanho M. and Santos N. (Eds) WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany ISBN: 978-3-527-32891-8.

The Researching, Teaching, and Learning Triangle. Castanho M. and Güner-Akdogan G. (Eds) Springer, USA. ISBN: 978-1-4614-0567-2.

Book Chapters

Franquelim H.G., Matos P.M., Veiga A.S. (2011) HIV vs. HIV: turning HIV-derived peptides into drugs, In: Castanho M. and Santos N. (Eds), *Peptide Drug Discovery and Development: Translational Research in Academia and Industry*, first ed. WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany pp. 209-229. ISBN: 978-3-527-32891-8.

Ribeiro M.M.B., Serrano I.D. and Sá Santos S. (2011) Turning endogenous peptides into New Analgesics: the example of Kyotorphin derivatives, In: Castanho M. and Santos N. (Eds), *Peptide Drug Discovery and Development: Translational Research in Academia and Industry*, first ed. WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany pp 171-188. ISBN: 978-3-527-32891-8.

Abstract

Franquelim H.G., Veiga A.S., Santos N.C., Castanho M.A.R.B. (2011) Membrane mode of action of HIV inhibitor peptides enfuvirtide and T-1249 unraveled by atomic force microscopy and dipole potential fluorescence spectroscopy. *Biopolymers*. 96, P504

Invited Lectures and Seminars

Castanho M.A.R.B. “Dengue: viral cellular infection reappraised” 22nd American Peptide Symposium, San Diego, USA, 25-30 June, 2011.

Castanho M.A.R.B. “Dengue vírus capsid protein translocates nucleic acids” XXXIV Congreso de la Sociedad Española de Bioquímica y Biología Molecular, Barcelona, Spain, 5-8 September, 2011.

Castanho M.A.R.B. “Inhibition of nociceptive responses after systemic administration of amidated kyotorphinBarrier Systems in Health and Disease Symposium, Lisbon, Portugal, May 30, 2011.

Ribeiro M.M. “Distinguished characteristics of BBB endothelial cells membrane and functionality – membrane charge by zeta potential”. Barrier Systems in Health and Disease Symposium, Lisbon, Portugal, May 30, 2011.

Ribeiro M.M. “Kyotorphin, from a peptide to a pharmaceutical drug lead”. Improving technology transfer from academia in translational medicine, Lisbon, Portugal, 24-25 March, 2011.

Communications in International Conferences

Castanho M.A.R.B., Melo M.N., Ferre R. and Ribeiro M.M. MICs go Molecular with AMP - linking partition, activity and high membrane concentrations. Gordon Research Conference Antimicrobial Peptides in Innate Immunity - New Insights on an Ancient System, Lucca, Italy, 25-20 May, 2011. Poster presentation.

Franquelim H.G., Veiga A.S., Santos N.C., Castanho M.A.R.B. Membrane mode of action of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 determined by atomic force microscopy and dipole potential fluorescence spectroscopy. 22nd American Peptide Symposium, San Diego, USA, 25-30 June, 2011. Oral Communication.

Franquelim H.G., Veiga A.S., Santos N.C., Castanho M.A.R.B. Membrane mode of action of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 determined by atomic force microscopy and dipole potential fluorescence spectroscopy. 22nd American Peptide Symposium, San Diego, USA, 25-30 June, 2011. Poster Presentation.

Freire J.M., Veiga A.S., Conceição T.M., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Dengue virus life cycle reappraised: Putative role of the capsid protein. 2nd Institute for Research in Biomedicine (IRB) Barcelona PhD Student Symposium, Barcelona, Spain, 17-18 November, 2011. Oral Communication.

Freire J.M., Castanho M.A.R.B. A Drug Delivery System Derived From Dengue Virus Structural Proteins. A focus on siRNA Therapy. VI YES Meeting, Oporto, Portugal, 16-18 September, 2011. Oral Communication.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Quantifying Molecular Partition of Supramolecular Complexes in Lipid Model

Systems – Studies on Dengue Virus Supramolecular Components. 8th European Biophysics Congress (EBSA), Budapest, Hungary, 23-27 August, 2011. Poster Presentation.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Assigning a role to the Dengue Virus Capsid Protein During Cellular Infection. 8th EBSA congress Satellite Meeting on FCS in Cell Biology, Debrecen, Hungary, August 22, 2011. Poster Presentation.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Assigning a role to the Dengue Virus Capsid Protein During Cellular Infection. 36th FEBS Congress: Biochemistry for Tomorrow's Medicine, Torino, Italy, 25-30 June, 2011. Oral Communication.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Assigning a role to the Dengue Virus Capsid Protein During Cellular Infection. 36th FEBS Congress: Biochemistry for Tomorrow's Medicine, Torino, Italy, 25-30 June, 2011. Poster Presentation.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Andrea T. Da Poian, Castanho M.A.R.B. Assigning a role to the Dengue Virus Capsid Protein During Cellular Infection. 11th FEBS-Young Scientist Forum: Biochemistry for Tomorrow's Medicine, Torino, Italy, 23-25 June, 2011. Poster Presentation.

Henriques S.T., Huang Y.-H., Rosengren K. J., Franquelim H.G., Carvalho F.A., Johnson A., Sonza, S., Tachedjian G., Castanho M.A.R.B, Daly N.L., Craik D.J., "The anti-HIV activity of the cyclotide kalata B1 is explained by peptide-membrane interactions", Natural Peptides to Drugs, 5th International Congress, Zermatt, Switzerland, December 2011. Oral presentation.

Henriques S.T., Huang Y.-H., Rosengren K. J., Franquelim H.G., Carvalho F.A., Johnson A., Sonza, S., Tachedjian G., Castanho M.A.R.B, Daly N.L., Craik D.J., "Differences in bactericidal, hemolytic and anti-HIV efficiencies of the cyclotides kalata B1 are explained by distinct cell membrane compositions", 22nd American Peptide Symposium, San Diego, California, USA, 25-30 June 2011. Oral presentation.

Henriques S.T., Huang Y.-H., Rosengren K. J., Franquelim H.G., Carvalho F.A., Johnson A., Sonza, S., Tachedjian G., Castanho M.A.R.B, Daly N.L., Craik D.J. (2011) "Differences in bactericidal, hemolytic and anti-HIV efficiencies of the cyclotide kalata B1 are explained by distinct cell membrane compositions". 22nd American Peptide Symposium", San Diego, California, USA, 25-30 June 2011. Poster presentation.

Ribeiro M.M.B., Pinto A., Domingues M., Heras M., Bardaji E., Tavares I. and Castanho M. Development of novel analgesic Kyotorphin-derived peptides: linking peptide-membrane interaction, Blood-Brain barrier crossing and in vivo efficacy. 22nd American Peptide Symposium, San Diego, USA, 25-30 June, 2011. Poster presentation.

Torcato I.M., Huang Y.H., Franquelim H.G., Gaspar D., Santos N.C., Craik D.J., Castanho M.A.R.B., Henriques S.T. Novel antimicrobial peptides with activity against Gram-negative and Gram-positive bacteria. 14th European Conference on the Spectroscopy of Biological Molecules, Coimbra – Portugal, 29 August to 03 September, 2011. Oral presentation.

Veiga A.S., Schneider J.P. Design of arginine containing peptide-based hydrogels with improved material properties and inherent antibacterial activity. “22nd American Peptide Symposium”, San Diego, California, USA, 25-30 June, 2011. Poster presentation.

Communications in National Conferences

Castanho M.A.R.B. “Em busca de um novo fármaco: derivados do péptido quiotrofina desde a molécula ao efeito analgésico”. Congresso iMed3.0-Inovar a Medicina, Lisbon, Portugal, October 29, 2011. Invited speaker.

Castanho M.A.R.B. “Bio-química de fio a pavio: derivados da quiotrofina desde a molécula até ao efeito analgésico.” Ciência QB. Encontros de alunos de DQB-FCUL, Lisbon, Portugal, June 7, 2011. Invited speaker.

Conceição K., Monteiro-dos-Santos J., Seibert C.S., Marques E, E., Ismael Silva Jr. P; Soares A.B., Lima C., Lopes-Ferreira M. *Potamotrygon cf. henlei* Stingray Mucus: Biochemical Properties of a Novel Antimicrobial Protein. 2011. XL Annual Meeting of SBBq. Foz do Iguaçu, Brasil. May, 2011. Poster presentation.

Franquelim H.G., Veiga A.S., Santos N.C., Castanho M.A.R.B. Decoding distinct membrane interactions of HIV-1 inhibitors T-20 and T-1249 using atomic force microscopy combined with fluorescence methodologies. 5th IMM/CAML PhD Students Meeting, Lisbon, Portugal, 17-18 October, 2011. Oral Communication.

Freire J.M., Veiga A.S., Santos N.C., Kowalczyk W., Andreu D., Castanho M.A.R.B. Assigning a role to Dengue virus Casid Protein during cellular infection. 5th IMM/CAML PhD Students Meeting, Lisbon, Portugal, 17-18 October, 2011. Poster presentation.

Nimo L.G., Martínez T.B., Ribeiro M.M., Castanho M.M., Rocha H., Cocho de Juan J.A. Desarrollo de un método para la determinación de quiotorfina endógena por espectrometría de masas en tándem acoplada a cromatografía líquida. V Congreso Nacional del Laboratorio Clínico, Malaga, Spain. 9-11 November, 2011. Poster presentation.

Organisation of Conferences

Castanho M.A.R.B “Improving Technology: transfer from academia in translational medicine”, Lisbon, Portugal, 24-25 March, 2011. Funded by FP7-Marie Curie Actions (IAPP)

Freire J.M. co-organized the 5th IMM/CAML PhD Students Meeting

Internationalization

UBqF is engaged in collaborative projects with several international research teams, such work being supported by international grants:

1) “Selected peptides as drug candidates directed to pain and neurodegeneration”, FP7-PEOPLE-2007-3-1-IAPP, Grant no. 230654. Coordinator: M Castanho. This project involves intersectorial

(industry-academia) training of young researchers, international technology transfer and drug R&D. Consortia: U Girona (Spain), U Tuebingen (Germany), Synovo GmbH (Germany) and Bioalvo (Portugal). M Ribeiro spent 6 months in Synovo, a Pharma Company, acquired skills in Pharmacokinetic and Pharmacodynamic methodologies, cell culture and in vivo tests.

2) “Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration. FP7-PEOPLE-2009-IRSES. Coordinator: N Santos, IMM. This is specially devoted to research staff exchange, involving teams of U Pompeu Fabra (Spain), Federal U Rio de Janeiro and U Fortaleza (Brazil) that work jointly in training, research and outreaching activities.

3) “The role of lipid membranes on cell infection by Dengue virus”, FCT, PTDC/QUI/69937/2006. Coordinator: M Castanho. This collaboration between UBqF and Dr Andrea da Poian’s group at Federal U. Rio Janeiro, involves exchange of PhD students and young post-docs.

4) Sónia T. Henriques is a Marie Curie fellow who collaborates with Prof David Craik at IMB, U Queensland, Australia (transfer of knowledge and training).

S.T. Henriques is also chief investigator of the Australian Research Council project “Elucidating the chemical and the biophysical basis for the bioactivity of cyclotides: ultra-stable proteins from plants”. The researcher has spent a short-term in Prof. Patrick Daugherty laboratory at the University of California, Santa Barbara, USA. A collaboration was established to develop the project: “Preparation of a knotted library on bacterial surface display to identify peptide leads”.

5) Ana Salomé Veiga was awarded with a Marie Curie International Outgoing Fellowships for Career Development (IOF) under the framework of the collaboration between UBqF and the Dr Joel Schneider’s group at the National Cancer Institute, NIH, USA.

Prizes, honours and awards

Franquelim H. and Ribeiro M.M. APS travel grant, awarded by the 22nd American Peptide Symposium, San Diego, USA, 25-30 June, 2011

Franquelim H. and Ribeiro M.M. Finalists of COHiTEC Entrepreneurship Program (member of team) – COTEC & ISCTE, Lisbon, Portugal, February-July, 2011.

Freire J.M. Best lecture, awarded by the VI YES Meeting, Oporto, Portugal, September 16-18 (Supervisor of the work presented by Inês Rego de Figueiredo).

Henriques S.T. UQ Postdoctoral Research fellowship, awarded by the University of Queensland, Australia.

Henriques S.T. Discovery Early Career Research Award, awarded by the Australian Research Council, Australia.

Advanced teaching

Thesis Supervision/ Examination

Miguel Castanho and Sónia T. Henriques supervised the Master Thesis of Inês Mota Torcato: “Aumento do espectro de acção de péptidos antimicrobianos – Actividade sobre bactérias Gram-negativas e Gram-positivas”, Faculdade de Ciências da Universidade de Lisboa, October 19, 2011.

Miguel Castanho co-supervised the PhD Thesis of Carla S.B.A.S. Alves: “Computational and experimental strategies for assessing the conformational and dynamic properties of proteins and peptides”, Universidade da Madeira, Portugal, November 30, 2011.

Isa Serrano examined the Master Thesis of Inês Sá Pereira: “Basement membrane alterations in kernicteric brain microvasculature and pericyte response to bilirubin”, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, November 25, 2011.

Miguel Castanho, Henri Franquelim, João Freire, Diana Gaspar, Sónia T. Henriques, Sónia S. Santos, Isa Serrano, Marta M. Ribeiro, and Inês Torcato, were engaged in the supervision and tutoring of undergraduate research students from the Faculdade de Medicina da Universidade de Lisboa.

João Freire supervised and tutored an undergraduate M.D. student from the Faculdade de Medicina da Universidade de Lisboa. The project were funded by GAPIC.

João Freire, Diana Gaspar, Sónia S. Santos, and Marta M. Ribeiro supervised International M.D. Students under the International Federation of Medical Students’ Association (IFMSA) Research Exchange Program.

Workshops/Courses Attended

Franquelim H., Freire J.M., Gaspar D., Henriques S.T., Santos S.S., Ribeiro M.M., and Torcato I. participated in the IMM Nanocourse: “Improving technology transfer from academia in translational medicine”, IMM-FMUL, Lisboa, Portugal, 24-25 March, 2011.

Freire J.M. also participated in:

- “Theoretical part of the 210# course Emerging Tools in Quantitative Fluorescence Microscopy for systems Biology”, INSERM Workshop, Lisbon, Portugal, 4-6 September.
- “Studying Protein-Protein Interactions by Advanced Light Microscopy and Spectroscopy”, EMBO Practical Course, Debrecen, Hungary, 16-22 August.
- IMM Nanocourses, IMM-FMUL, Lisboa, Portugal: “miRNAs and non-coding RNAs in cell biology and human disease” 13-14 October, 2011; “Biostatistics” February 23 to April 13, 2011; “Nanomedicine Course” February 28 to March 2, 2011; “Scientific Integrity” 17-18 February, 2011.

Gaspar D. and Serrano I. attended the workshop: Cell/Tissue Culture Biocant, Cantanhede – Portugal, November 15, 2011.

Ribeiro M.M., Sa Santos S., and Serrano I. participated in the Symposium “Barrier Systems in Health and Disease” organized by Neuron Glia Biology in Health and Disease Unit - iMed.UL, CPM-FFUL, Lisboa, Portugal, May 30, 2011.

Sá Santos S. also participated in:

- “Nanosciences for Life” 10th Short Course of the Portuguese Biophysical Society, Santarém, Portugal. 17-19 November, 2011.
- “Laboratory Animal Science 2011 – Theoretical course (according to FELASA cat. B)”, IMM-FMUL, Lisboa, Portugal. March 28 to April 1, 2011.
- IMM Nanocourses, IMM-FMUL, Lisboa, Portugal: “BioImaging Nanocourse on Microscopy”, 5-6 December, 2011; “Nanomedicine Course”, Feb 28 to March 2, 2011.

Science and Society

Castanho M.A.R.B. “Café da Ciência: Química para um futuro sustentável”, Comissão Parlamentar da Educação, Ciência e Cultura, September 7.

Castanho M.A.R.B. Scientific consultant for Biochemistry, Harvard Medical School - Portugal Programme, on-line repository for students.

Franquelim H.G. Represented the IMM PhD Students

Freire J.M. “A day watching Life in Motion”, Organizing and tutoring an elementary school visit to IMM and to UBqF Lab facilities. (5th and 6th grades – Nature Sciences class), Colégio Planalto (Telheiras), Lisbon, Portugal, December 13, 2011.

Freire J.M. “The Colourful Life”, Theoretical and Practical Workshop about the origin of light and the colour of things. (5th and 6th grades), Colégio Planalto (Telheiras), Lisbon, Portugal, June 15-16, 2011.

Ribeiro M.M. Represented IMM at the “Health Innovation & Technology Transfer Showcase – Health Cluster Portugal” 27 September, 2011, ICVS, Universidade do Minho, Braga, Portugal.

Master and Ph.D. thesis completed

PhD Thesis

Carla S.B.A.S. Alves (2011). “Computational and experimental strategies for assessing the conformational and dynamic properties of proteins and peptides”. PhD Thesis, Universidade da Madeira, Portugal, November 30, 2011. Co-supervisor: Miguel A.R.B. Castanho.

Master Thesis

Inês Mota Torcato (2011). “Aumento do espectro de acção de péptidos antimicrobianos – Actividade sobre bactérias Gram-negativas e Gram-positivas”. Master degree in Biochemistry,

Specialization in Medical Biochemistry, Faculdade de Ciências da Universidade de Lisboa, Portugal, October 19, 2011. Co-Supervisor: Miguel A.R.B. Castanho.

Tissue Morphogenesis and Repair Unit

Major interests / Objectives

Our group is interested in understanding molecular and cellular processes that regulate tissue repair and regeneration. We use model organisms such as *Drosophila* and zebrafish due to their amenability to genetic manipulation and live imaging analysis. Currently we are studying wound healing in epithelial tissues, regeneration of complex organs and the recruitment of immune system cells to clear damaged cells in wounds.

Head of Unit

António Jacinto, PhD – Assistant Professor, FMUL

Principal Investigators

Soren Prag, PhD Staff scientist
Nina Matova, PhD Staff scientist

Research Team

Marta Carapuço, PhD	Post Doc Fellowship, IMM (left in December 2011)
Dulce Azevedo, PhD	Post-Doc Fellowship, FCT (left in August 2011)
Patricia Abrantes, PhD	Post-Doc Fellowship, FCT
Anna Zaidman, PhD	Post-Doc Fellowship, IMM (Jan-June 2011) Post-Doc Fellowship, FCT (from July 2011)
Ana Cristina Silva, PhD	Post-Doc Fellowship, FCT
Duarte Mesquita	Post-Doc Fellowship, EMBO
Jennifer Regan, PhD	Post-Doc Fellowship, EMBO until June 2011 Post-Doc Fellowship, IMM (from July to December; left in December 2011)
Lara Jesus Carvalho, PhD	Post-Doc Fellowship, Marie Curie
João Cordeiro, PhD	Post-Doc Fellowship, FCT
Ana Cristina Borges	Post-Doc Fellowship, FCT
Teresa Cabral Braga	PhD Fellowship, FCG
Neuza Teixeira	PhD Fellowship, FCT
Sara Maurício de Sousa	PhD Fellowship, IMM (left in July 2011)
Mariana Simões	PhD Fellowship, IMM
Marco Antunes	PhD Fellowship, FCT
Rita Mateus	PhD Fellowship, FCT
Carolina Moreira	PhD Fellowship, FCT
Telmo Pereira	PhD Fellowship, FCT
Inês Cristo	PhD Fellowship, FCT
Susana Ponte	Technician, IMM
Ana Sofia Azevedo	Technician, IMM
Vânia Francisco	Technician, IMM
Fábio Valério	Technician, IMM

Ângela Dias	Technician, IMM
Tiago Krug Coelho	Technician, IMM (left in March 2011)
Ana Sofia Brandão	Masters Student (left in December 2011)
Cátia Crespo	Masters Student
Gonçalo Miguel Brito	Masters Student Technician, IMM (left in December 2011)

Keywords/Research Areas

Cell and Developmental Biology, *Drosophila* Genetics , Cell Migration, Wound Healing, Regeneration, Inflammation

Major scientific achievements

We have started the detailed characterization of *Drosophila* wound healing mutants that we have identified in a genetic screen (Campos et al., 2010). The publication Geiger et al. (2011) describes a novel mutant, *Hole-in-one*, that is required for efficient epithelial repair and seems to be involved in EGFR/ERK signalling.

We have established *Drosophila* larva as a tool to study immune cell migrations and homing. We have shown that PI3K regulates a discrete population of hemocytes (macrophage-like cells) at the gut proventriculus (Zaidman-Rémy et al., 2011).

We have characterized molecularly the process of bone regeneration during caudal fin regeneration demonstrating that the cells that contribute to formation of new bone originate from dedifferentiation of pre-existing bone tissue (Sousa et al., 2011), and we have demonstrated that, similarly to amphibians, re-innervation is essential for fin regeneration in zebrafish.

Recent Most Relevant Publications

Zaidman-Rémy A, Regan JC, Brandão AS, Jacinto A (2011) The *Drosophila* larva as a tool to study gut-associated macrophages: PI3K regulates a discrete hemocyte population at the proventriculus. *Dev Comp Immunol* [Epub ahead of print] (Journal IF: 3.293, Citations: -)

Sousa S, Afonso N, Bensimon-Brito A, Fonseca M, Simões M, Leon J, Roehl H, Cancela ML, Jacinto A (2011) Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. *Development* **138**(18),3897-905. (Journal IF: 6.898, Citations: 1)

Geiger JA, Carvalho L, Campos I, Santos AC, Jacinto A (2011) Hole-in-one mutant phenotypes link EGFR/ERK signaling to epithelial tissue repair in *Drosophila*. *PLoS One* **6**(11), e28349. (Journal IF: 4.411, Citations: 0)

Brodland GW, Conte V, Cranston PG, Veldhuis J, Narasimhan S, Hutson MS, Jacinto A, Ulrich F, Baum B, Miodownik M (2010) Video force microscopy reveals the mechanics of ventral furrow invagination in *Drosophila*. *Proc Natl Acad Sci U S A* **107**(51), 22111-6. (Journal IF: 9.771, Citations: 7)

Campos I, Geiger JA, Santos AC, Carlos V, Jacinto A (2010) Genetic screen in *Drosophila melanogaster* uncovers a novel set of genes required for embryonic epithelial repair. *Genetics* **184**(1), 129-40. (Journal IF: 4.087, Citations: 7)

Ongoing Research Projects

2007/2010 Integrating the genetics, mechanics, phenomenology of embryonic wound healing, Human Frontier Science Program. Coordinator: António Jacinto. HFSP-RGP21-07, €244 976

2009/2010 The role of re-innervation in zebrafish fin regeneration. Coordinator: António Jacinto. GAPIC – 2009041, €1 180

2008/2011 Embryonic wound healing: a genetic approach, FCT. Coordinator: António Jacinto. PTDC/BIA-BCM/65872/2006, €150 000

2008/2014 ERC-Epithelial Resealing, Comissão Europeia. Coordinator: António Jacinto. ERC - 208631 Epithelial Resealing, €1 150 000

2011 FCT Base. Coordinator: António Jacinto.

2010/2013 The role of reinervation in tissue regeneration, FCT. Coordinator: António Jacinto. PTDC/SAU-OB/100200/2008, €126 000

2010/2013 Genetics of Nonsyndromic Cleft Lip and Palate (NSCLP), FCT. Coordinator: António Jacinto. PTDC/SAU-GMG/101537/2008, €196 176

2010/2012 Development and characterization of zebrafish stem cells: implications for the development of transgenics – Fishcell, FCT. Participant: António Jacinto; Coordinator: Leonor Cancela, €18 739

2010/2012 The role of EGF/ERK signaling pathway during the wound healing response in *Drosophila* and zebrafish epithelia, Marie Curie, Comissão Europeia. Fellowship: Lara Carvalho, €146 783

2011/2012 Microarray analysis of transcription during nerve-dependent fin regeneration in zebrafish, GAPIC. GAPIC-2011013, €2 160

2010/2012 Function of Integrins in *Drosophila* Haemocyte Migration, FCT. Coordinator: Soren Prag. PTDC/SAU-OB/101259/2008, €120 000

Publications in peer review Journals

Zaidman-Rémy A, Regan JC, Brandão AS, Jacinto A (2011) The *Drosophila* larva as a tool to study gut-associated macrophages: PI3K regulates a discrete hemocyte population at the proventriculus. *Dev Comp Immunol*. [Epub ahead of print] (Journal IF: 3.293, Citations: -)

Sousa S, Afonso N, Bensimon-Brito A, Fonseca M, Simões M, Leon J, Roehl H, Cancela ML, Jacinto A (2011) Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. *Development* **138**(18), 3897-905. (Journal IF: 6.898, Citations: 1)

Geiger JA, Carvalho L, Campos I, Santos AC, Jacinto A (2011) Hole-in-one mutant phenotypes link EGFR/ERK signaling to epithelial tissue repair in *Drosophila*. *PLoS One* **6**(11), e28349. (Journal IF: 4.411, Citations: 0)

Azevedo D, Antunes M, Prag S, Ma X, Hacker U, Brodland GW, Hutson MS, Solon J, Jacinto A (2011) DRhoGEF2 regulates cellular tension and cell pulsations in the Amnioserosa during *Drosophila* dorsal closure. *PLoS One* **6**(9), e23964. (Journal IF: 4.411, Citations: 0)

Azevedo AS, Grotek B, Jacinto A, Weidinger G, Saúde L (2011) The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. *PLoS One* **6**(7), e22820. (Journal IF: 4.411, Citations: 0)

Madsen, L, Kriegenburg F, Vala, A, Best, D, Prag S, Hofmann K, Seeger M, Adams, IR, Hartmannm-Petersen R: The tissue-specific Rep8/UBXD6 recruits p97 to the endoplasmic reticulum membrane for degradation of misfolded proteins (2011) PLoS ONE. **6**(9):e25061 (Journal IF: 4.411, Citations: 0)

Other publications International

Moreira CG, Regan JC, Zaidman-Rémy A, Jacinto A, Prag S (2011) *Drosophila* hemocyte migration: an in vivo assay for directional cell migration. *Methods Mol Biol* **769**, 249-60. Book chapter.

Invited Lectures and Seminars

Jacinto A. Epithelial Repair in *Drosophila*, Department of Zoology, University of Cambridge, UK, February 24, 2011.

Jacinto A. Wound Repair in *Drosophila*. Seminar in the Centre for Regenerative Medicine, University of Bath, UK, June 20, 2011.

Communications in International Conferences

Jacinto A. Regulation of Tissue Repair in *Drosophila*. The 26th European Cytoskeletal Forum (ECF) Meeting, Actin-Based Motility: From Molecules to Model Organisms, Stresa, Italy, 29 October - 2 November, 2011. (Oral Presentation)

Antunes M., Cordeiro J., Pereira T., Jacinto A. Regulation of Tissue Repair in *Drosophila*. The 26th European Cytoskeletal Forum (ECF) Meeting, Actin-Based Motility: From Molecules to Model Organisms, Stresa, Italy, 29 October - 2 November, 2011. (Poster Presentation)

Carvalho L., Azevedo D., Campos I., and Jacinto A. The role of Septate Junctions during epithelial wound healing. 22nd European *Drosophila* Research Conference, Lisbon, Portugal, September 21-24, 2011. (Poster presentation)

Antunes M., Cordeiro J., Pereira T., Jacinto A. Regulation of tissue repair in *Drosophila*. 22nd European *Drosophila* Research Conference, Lisbon, Portugal, September 21-24, 2011. (Poster presentation)

Prag, S. Increased Oscillations of Actomyosin in Tail Retraction During Hemocyte Directed Migration, 22nd European *Drosophila* Research Conference, Lisboa, Portugal, September, 2011. (Oral presentation)

Zaidman-Rémy A., Regan J. (co-first author), Brandão A., Jacinto A. The *Drosophila* larva as a tool to study gut-associated macrophages: PI3K regulates a discrete hemocyte population at the proventriculus. 22nd European *Drosophila* Research Conference, Lisbon, Portugal, September 21-24, 2011. (Oral presentation)

Moreira, C., Jacinto, A., Prag, S. The Role of Adhesion in Hemocyte Migration, 22nd European *Drosophila* Research Conference, Lisbon, Portugal, September 21-24, 2011. (Poster Presentation)

Teixeira N., Remy-Zaidman A., Jacinto A., Lopes M. F. 22nd European *Drosophila* Research conference. Lisboa, Portugal, September 21-24, 2011. (Poster Presentation)

Prag, S. Increased Oscillations of Actomyosin in Tail Retraction During Hemocyte Directed Migration, Gordon Research Conference on Gradient Sensing and Directed Cell Migration, Les Diablerets, Switzerland, June 2011. (Oral and poster presentation)

Carvalho L. *, Geiger J. *, Campos I., Azevedo D., Jacinto A. *These authors contributed equally to this work. Hole-in-one and ERK signaling are required for epithelial tissue repair in *Drosophila*, EMBO Workshop on Biophysical Mechanisms of Development, Lisbon, Portugal, May 2011. (Poster presentation)

Antunes M., Cordeiro J., Pereira T., Jacinto A., Integrating the genetics, mechanics and phenomenology of wound healing. EMBO Workshop on Biophysical Mechanisms of Development, May 24–27, 2011. (Poster presentation)

Prag, S. “Increased Oscillations of Actomyosin in Tail Retraction During Hemocyte Directed Migration”, EMBO Workshop on Biophysical Mechanisms Of Development, Oeiras, Portugal, May 2011. (Oral presentation)

Mateus, R., Pereira, T., Jacinto, A. In vivo tissue dynamics underlying zebrafish fin fold regeneration. Conference: 7th European Zebrafish Meeting. Edinburgh, UK, 5-9 July, 2011. (Poster presentation)

Antunes, M., Cordeiro, J., Pereira, T., Jacinto, A. Regulation of tissue repair in *Drosophila* The 26th European Cytoskeletal Forum (ECF) Meeting, Actin-Based Motility: From Molecules to Model Organisms, Stresa, Italy, October 29 - November 2, 2011. (Poster presentation)

Moreira, C., Regan, J., Zaidman-Rémy, A., Jacinto, A., Prag, S. *Drosophila* Hemocyte Migration - an in vivo assay for Directional Cell Migration in Fibronectin, Integrins & Related Molecules, a Gordon-Kenan Research Seminar, Lucca (Barga), Italy, April 30 - May 1, 2011. (Poster presentation)

Communications in National Conferences

Antunes M., Cordeiro J., Pereira T., Jacinto A. V PhD Student Meeting IMM/CAML, IMM, Lisbon, Portugal, October 17-18, 2011 (Oral presentation)

Rita Mateus, António Jacinto. Size-control Regulation During Regeneration: How to stop growth. Pizza Seminar, IMM Lisbon. 15th March, 2011 (Oral presentation)

Mateus R., Pereira T., Jacinto A. In vivo tissue dynamics underlying zebrafish fin fold regeneration. V PhD Student Meeting IMM/CAML. IMM, Lisbon, Portugal, October 17-18, 2011. (Poster presentation)

Cristo I., Silva A. C., Borges A. C., Jacinto A. What a healing! The role of tight junctions in embryonic wound repair, V PhD Student Meeting IMM/CAML. IMM, Lisbon, Portugal, October 17-18, 2011. (Poster presentation)

Moreira C., Jacinto A., Prag S. The Role of Adhesion in Hemocyte Migration, V PhD Student Meeting IMM/CAML, IMM, Lisbon, Portugal, October 17-18, 2011. (Poster presentation)

Moreira C., Drosophila haemocyte migration, Pizza Seminar talk, Student's Seminar Series, IMM, Lisbon, January 18, 2011. (Oral presentation)

Teixeira N., Palmer K., Zaidman-Rémy A., Hancock L., Jacinto A., Gilmore M., Lopes M. F. PhD meeting ITQB. Oeiras, Portugal. October 2011. (Oral presentation)

Organisation of Conferences

Jacinto A. co-organized 22nd European Drosophila Research Conference, Lisbon, Portugal, September 21-24, 2011.

Prag S. organized and lectured the EMBO Practical Course on Drosophila Techniques, Lisbon, Portugal, March 2011.

Prag S. and Jacinto A. co-organized and lectured the Faculty on Inserm/IMM Workshop on “Emerging Tools in Quantitative Fluorescence Microscopy for Systems Biology”, Lisbon, Portugal, September 2011.

Soren Prag organized and lectured the Faculty on BioImaging Nano Course on Microscopy, Lisbon, Portugal, December 2011.

Moreira C. co-organized the V PhD Student Meeting IMM/CAML (in the context of the IMM PhD Student Committee 2010-2011), IMM, Lisbon, October 17-18, 2011.

Moreira C. co-organized the IV PhD Student Retreat (in the context of the IMM PhD Student Committee 2010-2011), September 25-27, 2011.

Internationalization

Jacinto A. is a member of the steering committee of QuanTissue, a Research Network Programme of the European Science Foundation.

Prizes, honours and awards

1st prize for Poster Presentation at V PhD Student Meeting IMM/CAML, IMM, Lisbon, Portugal, October 17-18, 2011, Carolina Moreira.

1st Prize for Oral presentation at V PhD Student Meeting IMM/CAML, IMM, Lisbon, Portugal, October 17-18, 2011, Marco Antunes.

Advanced teaching

Jacinto A. lectured in the GABBA PhD programme, “Regeneration in Zebrafish: the contribution of the nerves” in the module Nerve Regeneration, IBMC, Porto, June 13, 2011.

Prag S. organized and lectured the EMBO Practical Course on Drosophila Techniques, Lisbon, Portugal, March 2011.

Prag S. and Jacinto A. co-organized and lectured the Faculty on Inserm/IMM Workshop on “Emerging Tools in Quantitative Fluorescence Microscopy for Systems Biology”, Lisbon, Portugal, September 2011.

Moreira C. lectured the Live Imaging classes at the EMBO Practical course: Drosophila techniques, IMM, Lisbon, March 3-8, 2011.

Antunes A. lectured the Live Imaging classes at the EMBO Practical course: Drosophila techniques, IMM, Lisbon, March 3-8, 2011.

Mateus R. lectured the teaching class "Regeneração" as a part of the subject "Biologia do Desenvolvimento" for the Masters "Genética Molecular e Biomedicina", Universidade Nova - Faculdade de Ciências e Tecnologia, 15th December, 2011

Science and Society

Mateus R. and Jacinto A. Participation in movie "Documentário 100 anos UL - O Desejo do Saber", Universidade de Lisboa, 2nd June, 2011.

Master thesis completed

Gonçalo Miguel Brito (2011), “The role of Hippo pathway in zebrafish fin regeneration”, Mestrado em Biologia do Desenvolvimento, Faculdade de Ciências da Universidade de Lisboa. Supervisors: António Jacinto.

Ana Sofia da Silva Pereira Brandão (2011), “Analysis of GPCR functions in hemocyte navigation in *Drosophila melanogaster*”, Mestrado em Biologia do Desenvolvimento, Faculdade de Ciências da Universidade de Lisboa. Supervisors: António Jacinto, Jennifer Claire Regan, Anna Zaidman-Remy.

Immunology & Infectious Diseases Programme

Programme Coordinators: Mário Ramirez, José Moniz Pereira, Rui Victorino

Heads of Unit:

Luis Graça, MD, PhD

Ana Espada de Sousa, MD, PhD

Henrique Veiga-Fernandes, PhD

Maria Mota, PhD

Bruno Silva-Santos, PhD

Mário Ramirez, PhD

Gunnar Rudolf Mair, PhD

Maria Ermelinda Camilo, MD, PhD

Luísa Figueiredo, PhD

João Eurico da Fonseca, MD, PhD

João Pedro Simas, DVM, PhD

Elsa Anes, PhD, FFUL

João Gonçalves, PhD, FFUL

Principal Investigators:

Luis Graça

Ana Espada de Sousa, Rui Victorino, M^a.
Conceição Santos, João Lacerda, Iris
Caramalho

Henrique Veiga-Fernandes

Maria Mota, Miguel Prudêncio

Bruno Silva-Santos, Ana Pamplona

Mário Ramirez, José Melo Cristino, Thomas
Hänscheid, João Carriço

Gunnar Rudolf Mair

Maria Ermelinda Camilo, Helena Cortez
Pinto, Isabel Monteiro-Grillo, Paula Ravasco

Luísa Figueiredo, PhD

João Eurico da Fonseca, Helena Canhão

João Pedro Simas

Elsa Anes

João Gonçalves, Mariana Santa Marta, Paula
Brito

Cellular Immunology Unit

Major interests / Objectives

The Cellular Immunology Unit studies the mechanisms underlying the 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 like as it happens in 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 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 diseases such as allergy, autoimmunity and transplant rejection.

Head of Unit

Luis Graça, MD, DPhil – Assistant Professor, FMUL

Research Team

Ana Água-Doce	PhD Fellowship, FCT
Catarina Almeida	MSc Student, IEFEP (left in June 2011)
Alexandre Varela	Research Assistant, IMM
Ivonne Wollenberg	PhD Fellowship, FCT (left in October 2011)
Joana Duarte	PhD Fellowship, FCT (left in March 2011)
Marta Caridade, MSc	PhD Fellowship, FCT
Marta Monteiro, PhD	Post-doctoral Fellowship, FCT
Patricia Santos, PhD	Post-doctoral Fellowship, FCT (left in November 2011)
Vanessa Oliveira, DPhil	Post-doctoral Fellowship, FCT
Silvia Almeida, PhD	Post-Doctoral Fellowship, FCT

Research Areas

Immune tolerance; Regulatory T cells; Natural Killer T cells (NKT); Allergy, Transplantation; Autoimmunity

Major scientific achievements

1. CD4-blockade can induce long-term tolerance in a mouse model of multiple sclerosis. Tolerance is associated with alteration of Th17/Treg ratio in the synovial, as well as elimination of pre-committed effector cells.

We found treatment with non-depleting anti-CD4 monoclonal antibody (MAb) could prevent the development of EAE in mice, as well as prevent the progression of the disease when mice were treated after the onset of EAE. Using TCR-transgenic cells we were able to follow the fate of T cells as tolerance is established, thus unveiling the underlying regulatory mechanisms.

2. Long-term tolerance to allergens can be induced with anti-CD4 antibodies, including in an animal model of peanut-induced anaphylaxis.

CD4 blockade at the time of allergen exposure induces antigen-specific tolerance in mice, sparing immune competence to unrelated antigens.

3. A subset of Follicular helper T cells (Tfh) express Foxp3 and regulate the germinal centre reaction.

We found that Foxp3⁺ cells, with phenotypic characteristics of Tfh, can be identified in the GC – we named these cells Tfr. Tfr cells accumulate in the GC during the course of GC reaction, and control the overall magnitude of the response and the amount of antibodies produced.

Recent Most Relevant Publications

Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira V, Faro J, Graça L. (2011) Regulation of germinal centre reaction by Foxp3⁺ follicular regulatory T cells. *J Immunol.* 187(9):4553-60. (Journal IF 2009: 5.646; Citations: 1)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Agua-Doce A, Wollenberg I, Silva-Santos B, Graça L. (2010) Identification of Regulatory Foxp3⁺ Invariant NKT Cells Induced by TGF- β . *J Immunol.* 185: 2157-2163. (Journal IF 2009: 5.646; Citations: 11)

Graça L, Le Moine A, Lin C-Y, Fairchild PJ, Cobbold SP, Waldmann H. (2004) Donor-specific transplantation tolerance: the paradoxical behavior of CD4⁺CD25⁺ T cells. *Proceedings of the National Academy of Sciences USA.* 101: 10122-10126. (Journal IF 2004: 10.452, Citations: 59)

Graça L, Cobbold SP, Waldmann H. (2002) Identification of regulatory T cells in tolerated allografts. *Journal of Experimental Medicine.* 195: 1641-1646. (Journal IF 2003: 15.302, Citations: 300)

Graça L*, Lin C-Y*, Cobbold SP, Waldmann H. (2002) Dominant transplantation tolerance impairs CD8⁺ T cell function but not expansion". *Nature Immunology.* 3: 1208-1213. [* Joint first authors]. (Journal IF 2003: 28.180, Citations: 99)

Ongoing Research Projects

2009/2011 Invariant Natural Killer T Cells in Allergic Asthma and Tolerogenic Therapy, FCT. Coordinator: L. Graça. PIC/IC/82895/2007, €155 000

2010/2012 Tolerance induction to recombinant clotting factors in a murine model of hemophilia, FCT. Coordinator: Vanessa G. Oliveira. PTDC/SAU-OSM/108267/2008, €200 000

2011/2013 Cellular therapy for liver-specific immune suppression, FCT. Coordinator: L. Graça. PTDC/SAU-TOX/114424/2009, €198 000

2009/2012 Improving Immunotherapy. European Commission. Participant: L. Graça. FP7/SUDOE/Immunonet, €117 000 (total).

2011/2013 Boosting dendritic cell function to facilitate tolerance induction to recombinant clotting factors, Bayer Global Hemophilia Awards. Coordinator: Vanessa G Oliveira, US\$170,000.

2012/2013 Cellular therapy to induce local immune suppression in islet transplantation, Novo Nordisk/European Foundation for the Study of Diabetes. Coordinator: L. Graça. €100,000.

2012/2014 Regulation of germinal centre reaction by Foxp3+ follicular T cells, FCT. Coordinator: L. Graça. PTDC/SAU-IMU/120225/2010, €49,755.

2011/2012 Contract research, ECBio. Approximately €30,000.

Publications in Peer Review International Journals

Moura RA, Cascao R, Perpetuo I, Canhao H, Vieira-Sousa E, Mourao AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosario HS, Souto-Carneiro MM, Graça L*, Fonseca JE*. (2011) Cytokine pattern in very early rheumatoid arthritis favours B-cell activation and survival. *Rheumatology*. 50: 278-282. (Citations: 4; IF 2009: 4.236) *JOINT SENIOR AUTHOR

Oliveira VG, Caridade M, Paiva RS, Demengeot J, Graça L. (2011) Sub-optimal CD4 T cell activation triggers autonomous TGF- β -dependent conversion to Foxp3+ regulatory T cells. *Eur J Immunol*. 41: 1249-1255. (Citations: 5; IF 2009: 5.179)

Agua-Doce A, Graça L. (2011) Prevention of house dust mite-induced allergic airways disease in mice through immune tolerance. *PLoS ONE* 6(7):e22320. (Citations: 0; IF 2010: 4.411)

Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira V, Faro J, Graça L. (2011) Regulation of germinal centre reaction by Foxp3+ follicular regulatory T cells. *J Immunol*. 187: . doi: 10.4049/jimmunol.1101328 (Citations: 1; IF 2010: 5.745)

Duarte J, Caridade M, Graça L. (2011) CD4-blockade can induce protection from peanut-induced anaphylaxis. *Front Immunol*. 2: 56. Doi: 10.3389/fimmu.2011.00056 (Citations: 0; IF 2010: ND).

Invited Lectures and Seminars

Graça L. Tolerance induction in allergy. At “New perspectives in immunotherapy” workshop, Fundacion Dr. Antonio Esteve, Barcelona, Spain, April 29, 2011.

Graca L. Induction of immune tolerance with monoclonal antibodies. International workshop: New trends of immunotherapy, Hospital Universitario Puerta de Hierro, Madrid, Spain, May 20, 2011.

Graca L. Immune tolerance and cancer immunotherapy. 4th Biomedical Research Workshop of Vigo. Vigo, Spain, May 24, 2011.

Graca L. Regulation of germinal centre reaction and antibody production. New trends of immunotherapy symposium. Montpellier, France, November 7, 2011.

Graca L. Immunogenicity in cellular therapies. Advanced Therapeutics Workshop. Faculdade de Farmácia da Universidade de Lisboa, Portugal, November 24 – 25, 2011

Communications in International Conferences

Oliveira VG, Caridade M, Paiva RS, Demengeot J and Luis Graca, Sub-optimal CD4 T cell activation triggers TGF- β -dependent conversion of Foxp3⁺ regulatory T cells, The Keystone Symposia ‘TGF-beta in Immune Responses: From Bench to Bedside’, held in Snowbird, Utah, USA, January 7-12, 2011. (Poster presentation)

Monteiro M, Almeida CF, Caridade M, Duarte J, Agua-Doce A, Graca L. Peripheral induction of invariant NKT cells producing Foxp3, IL-9 and IL-17. The Keystone Symposia “NK and NKT cell biology”. Breckenridge, Colorado, USA, January 9-14, 2011. (Poster presentation)

Monteiro M, Almeida CF, Caridade M, Duarte J, Graca L. Upregulation of Foxp3 by invariant NKT cells in the cervical lymph nodes correlates with protection from EAE. The Keystone Symposia “NK and NKT cell biology”. Breckenridge, Colorado, USA, January 9-14, 2011. (Poster presentation)

Monteiro M, Almeida CF, Agua-Doce A and Graca L. Reprogramming the fate of iNKT cells towards IL-9 production. 6th International Symposium on CD1 and NKT Cells. Chicago, Illinois, USA, September 23 - 27, 2011. (Poster presentation)

Wollenberg I, Agua-Doce A, Hernandez A, Almeida CF, Oliveira VG, Faro J, Graca L. iRegulation of the germinal centre reaction by Foxp3⁺ follicular T cells. 16th Germinal Centre Conference, Birmingham, UK, September 4 – 8, 2011. (Oral presentation)

Água-Doce A, Oliveira V, Graca L, Enhancing tolerogenic antibodies to prevent Factor VIII inhibitors. World Immune Regulation Meeting V, Davos, Switzerland, March 24-27, 2011 (Poster presentation)

Caridade M., Agua-Doce A., Oliveira V., Ribeiro R.M., Graca L. The Role of microenvironment in Tolerance Induction to Foreign Antigens. Keystone Symposia – Immunoregulatory Networks, Breckenridge, CO, USA, April 01-05, 2011 (Poster presentation)

Communications in National Conferences

Caridade M., Oliveira V., Agua-Doce A., Ribeiro R.M., Graca L. The fate of CD4+ T cells under tolerogenic stimulation: a modeling perspective. XXXVII SPI Annual Meeting –“Portrait of the immune system: history and perspective” Instituto Gulbenkian de Ciência, Oeiras, Portugal, November 29-30, 2011 (Poster presentation)

Organisation of National and International Conferences

Graca L. Organizer and lecturer of International workshop: New trends of immunotherapy, Hospital Puerta de Hierro, Madrid, Spain, May 20, 2011.

Graca L. Organizer and lecturer of New trends of immunotherapy symposium. Montpellier, France, November 7, 2011.

Graca L. Organizer of New Frontiers in biological therapy Symposium, under the auspices of Sociedade Portuguesa de Imunologia, Instituto de Medicina Molecular, Lisbon, Portugal, November 26, 2011.

Internationalization

Collaborative research with Dr. José Faro (University of Vigo, Spain) – co-supervision of PhD student. Led to common publication and co-supervision of PhD student.

Collaborative research with Dr. Ruy M. Ribeiro (Los Alamos National Laboratory, NM, USA) – co-supervision of PhD student. Support from Collaboratorium Programme Fundação Calouste Gulbenkian.

Collaborative research with Dr. Lennart Mars (University of Toulouse, France). Exchange of materials and joint experiments involving one PhD student. Supported under a FP7 network SUDOE/Immunonet.

Collaborative research with Dr. Florain Kreppel (University of Ulm, Germany). Exchange of reagents and training. Supported by a FCT grant.

Participation in a European Network involving several laboratories interested in immunotherapy: FP7/ SUDOE/Immunonet.

Prizes, honours and awards

NEDAI Prize in Autoimmunity Research 2011 to Joana Duarte, Ana Agua-Doce, João Eurico Fonseca e Luís Graça for the publication of the paper “Modulation of synovial IL-17 and Foxp3 expression in the prevention of autoimmune arthritis” in 2010.

Travel Award from the Portuguese Society of Immunology to Vanessa Oliveira to attend The Keystone Symposia ‘TGF-beta in Immune Responses: From Bench to Bedside’, held in Snowbird, Utah, January 7-12, 2011.

Industry contract research

Contract research with ECBio, Lisbon

Advanced teaching

Graca L. Coordinator of the Immunology module for the Programa Gulbenkian de Formação Médica Avançada – Programa Doutoral para Médicos. Held at IMM in January 2011.

Graca L, Monteiro M. Participation in of the Immunology module for the GABBA PhD Programme. Held at Instituto de Biologia Molecular e Celular, Porto, March 2011.

Science and Society

Graca L, Scientific advisor for the development of art and science project by artist Maria Manuela Lopes, 2011.

Graca L, Scientific advisor for the development of art and science project by artist Marta de Menezes, 2011.

PhD Thesis completed

Ivonne Wollenberg (2011) The role of regulatory T cells in the control of B cell mediated immune responses. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luis Graca; Co-supervisor: José Faro (University of Vigo).

Joana Duarte (2011) Reprogramming the immune system with anti-CD4 monoclonal antibodies. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luis Graca.

Rita Moura (2011) The role of B cells in the early phase of rheumatoid arthritis. Faculdade de Medicina da Universidade de Lisboa. Supervisor: João Eurico Fonseca; Co-supervisor: Luís Graça.

Clinical Immunology Unit

Major interests / Objectives

UIC's research focuses on human T cell homeostasis and immune regulation with the ultimate goal of identifying new strategies for immunological reconstitution and targets for immune-based therapies.

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

UIC prioritizes the "bedside to the bench" approach and, given the transversal nature of Clinical Immunology, brings together physician/clinical researchers, from different medical areas, and basic researchers.

Head of Unit

Ana E. Sousa, MD, PhD – Investigator and Auxiliary Professor, FMUL

Principal Investigators

Rui MM Victorino, MD, PhD – Full Professor, FMUL

Maria Conceição Pereira-Santos, PharmD, PhD – Investigator, FMUL

Iris Caramalho, PhD – Investigator, IMM

João Lacerda, MD, PhD – Associate Professor, FMUL

Maria Soares, PhD - Investigator, IMM (Left in November; Head of Flow Cytometry Unit. IMM)

Research Team

Russell B Foxall, PhD	Post Doc Fellowship, FCT
Andreia Fonseca, PhD	Post Doc Fellowship, EMBO
Adriana S. Albuquerque, PhD	Post Doc Fellowship, FCT
Helena Nunes Cabaço, PhD	Post Doc Fellowship, FCT
Rui Soares, MSc	PhD Fellowship, FCT (left in August)
Rita Tendeiro, BSc	PhD Fellowship, FCT
Ana Rita Barbosa, BSc	PhD Fellowship, FCT
Rita Azevedo, BSc	PhD Fellowship, FCT (left in April)
Susana Mendes Fernandes, MD	PhD Fellowship, FCT
Catarina Mota, MD	PhD Fellowship, FCT
Paula Matoso, MSc	Research Fellowship, FCT
Ana Rita Pires, BSc	Research Fellowship, FCT (since January)
Ana Isabel Pinheiro, MSc	Research Fellowship, FCT (since February)
Vânia Nunes Silva, MSc	Research Fellowship, FCT (since June)
Ana Luisa Caetano, BSc	Technician, FMUL (since October)
Inês Filipa dos Santos Martins, MSc	Information Technician, IEPF (since April)

Susana Lopes da Silva, MD, MSc	Immunoallergologist, HSM, Lecturer, FMUL
José Gonalo Marques, MD	Consultant Pediatrician, HSM, Lecturer, FMUL
Ana Isabel Lopes, MD, PhD	Paediatric Gastroenterology Unit Coordinator (Chief of Service), Auxiliary Professor, FMUL
Francisca Fontes, MD, PhD	Auxiliary Professor, FMUL, Consultant Internist, HSM (left in April)
Carlos Ferreira, MD, PhD	Auxiliary Professor, FMUL, Consultant Internist, HSM
Ana Margarida Amaral Gomes, BSc	Research Fellowship, FCT
Teresa Moscoso MD	Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Pulido Valente (left in February)
José Geraldo Dias MD	Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Santa Maria (left in April)
Joana Bruno Soares MD	Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Santa Maria (March to July)
Pedro Tiago Silva, MD	Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Santa Maria (since October)

Keywords/Research Areas

Human T cell homeostasis ; Immune regulation; HIV/AIDS immunopathogenesis; HIV-2 infection.; Primary immunodeficiencies; Immunological reconstitution.

Major scientific achievements

- Human T cell homeostasis / Immune regulation

Our studies of human thymic tissue, removed under current standard protocols of reconstructive cardiac surgery in children, provided new insights into the steps involved in human regulatory T cell development.

- Primary immunodeficiencies (Primary Immunodeficiency Centre HSM/FMUL/IMM)

We published in Blood the first case of thymic transplantation in the context of human FOXP1 deficiency. Moreover, through the study of B-cell deficiencies, we revealed a link between B-cell differentiation and homeostasis of Th17 cells, a CD4 T-cell subset critical in inflammation and response to microbes.

- HIV/AIDS immunopathogenesis / HIV-2 infection

We developed assays to quantify HIV-2 spliced and unspliced RNA transcripts that revealed significant amounts of ongoing viral replication, despite low to undetectable levels of circulating virus in HIV-2 infection. Additionally we pursued the investigation of factors underlying immune activation and its regulation during HIV/AIDS by publishing the first data on regulatory T cells in HIV-2 infected patients.

Recent Most Relevant Publications

Cavaleiro R, Baptista AP, Soares RS, Tendeiro R, Foxall RB, Gomes P, Victorino M, and Sousa AE. (2009) Major Depletion of Plasmacytoid Dendritic Cells in HIV-2 Infection, an Attenuated

Form of HIV Disease. *PLoS Pathog* **5(11)**: e1000667. doi:10.1371/journal.ppat.1000667 (Journal IF: 9.079, Citations: 10).

Azevedo RI, Soares MV, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE. (2009) IL-7 sustains CD31 expression in human naïve CD4⁺ T cells and preferentially expands the CD31⁺ subset in a PI3K-dependent manner. *Blood* **113**:2999-3007 (Jornal IF: 10.558, Citations: 14).

Pereira-Santos MC, Baptista AP, Melo A, Alves RR, Soares RS, Pedro E, Pereira-Barbosa M, Victorino RMM, Sousa AE. (2008) Expansion of circulating Foxp3(+) CD25(bright) CD4(+) T cells during specific venom immunotherapy. *Clin Exp Allergy*, **38**:291-297. (Journal IF: 4.195, Citations: 27)

Sousa AE, Carneiro J, Meier-Schellersheim M, Grossman Z, and Victorino RM. (2002) CD4 T cell depletion is linked directly to immune activation in the pathogenesis of HIV-1 and HIV-2 but only indirectly to the viral load. *J Immunol* **169**:3400-3406. (Journal IF: 5.745, Citations: 221)

Grossman Z, Meier-Schellersheim M, Sousa AE, Victorino RM, and Paul WE. (2002) CD4⁺ T-cell depletion in HIV infection: are we closer to understanding the cause? *Nature Medicine* **8**:319-321. (Journal IF: 25.430, Citations: 266)

Ongoing Research Projects

2007/2011 HIV-2 infection and the thymus, FCT, Coordinator: Ana E Sousa, FCT/PTDC/SAU-MII/66248/2006, €136.621

2007/2011 HIV/AIDS Program IMM-FCG, Fundação Calouste Gulbenkian, Coordinator: Ana E Sousa, €150.000

2008/2011 Immune Reconstitution after Unrelated and Haplotype-Mismatched Stem Cell Transplantation, FCT, Coordinator: Maria Soares, PTDC/SAU-MII/67662/2006, €122.986

2009/2012 Long-term impact of thymectomy performed in early infancy, FCT, Coordinator: Rui MM Victorino, PIC/IC/83068/2007, €75.000

2009/2012 Clinical implications of activation of PI3K/Akt signaling pathway in primary adult acute lymphoblastic leukemia, FCT, Coordinator: João F. Lacerda, PIC/IC/83023/2007, €134.000

2009/2012 Lymphoid Tissues in HIV-2 Infected patients, FCT, Coordinator: Ana E Sousa, PIC/IC/82712/2007, €195.000

2011/2013 Modulation of HIV replication and latency in human CD4 T cells by regulatory small RNAs, Merck Investigator Studies Program. Merck & Co., Inc. Coordinator: Ana E. Sousa, IISP ID#: 39114, €142,000

2011/2014 HIV/AIDS: contribute of naïve CD4 T cell homeostasis, FCT. Coordinator: Ana E. Sousa. PTDC/SAU-IMU/109786/2009, €159.694

2011/2014 Cellular and molecular requirements in human regulatory T cell development, FCT. Coordinator: Iris Caramalho. PTDC/SAU-IMU/113541/2009, €158.360

Publications in peer review Journals

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, and Sousa AE (2011) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of two cases. *Blood* **117**, 688-96. (Journal IF: 10.558)

Soares RS, Tendeiro R, Foxall RB, Baptista AP, Cavaleiro R, Gomes P, Camacho R, Valadas E, Doroana M, Lucas M, Antunes F, Victorino RM, and Sousa AE (2011) Cell-associated viral burden provides evidence of ongoing viral replication in aviremic HIV-2 infected patients. *J Virol* **85**, 2429-38. (Journal IF: 5.189)

Soares RS, Matoso P, Calado M, and Sousa AE (2011) Strategies to quantify unspliced and multiply spliced mRNA expression in HIV-2 infection. *J Virol Methods* **175**, 38-45. (Journal IF: 2.139)

Fabre-Mersseman V, Dutrieux J, Louise A, Rozlan S, Lamine A, Parker R, Rancez M, Nunes-Cabaço H, Sousa AE, Lambotte O, and Cheynier R (2011) CD4⁺ Recent Thymic Emigrants Contribute to Human Immunodeficiency Virus (HIV) Reservoir In Vivo, Implication for HIV Pathogenesis. *AIDS* **25**, 1153-62. (Journal IF: 6.348)

Barbosa RR, Silva SP, Silva SL, Melo AC, Pedro E, Barbosa MP, Pereira-Santos MC, Victorino RM, and Sousa AE (2011) Primary B-Cell Deficiencies Reveal a Link between Human IL-17-Producing CD4 T-Cell Homeostasis and B-Cell Differentiation. *PLoS ONE* **6**, e22848. (Journal IF: 4.411)

Foxall RB, Albuquerque AS, Soares RS, Baptista AP, Cavaleiro R, Tendeiro R, Gomes P, Victorino RM, and Sousa AE (2011) Memory and naïve-like regulatory CD4⁺ T cells expand during HIV-2 infection in direct association with CD4⁺ T-cell depletion irrespectively of viremia. *AIDS* **25**, 1961-70. (Journal IF: 6.348)

Nunes-Cabaço H, Caramalho I, Sepúlveda N and Sousa AE (2011) Differentiation of human thymic regulatory T cells at the double positive stage. *Eur J Immunol* **41**, 3604-3614. (Journal IF: 4.942)

Caramalho I, Rodrigues-Duarte L, Perez A, Zelenay S, Peha-Gonçalves C and Demengeot J (2011) Regulatory T cells contribute to diabetes protection in lipopolysaccharide-treated non-obese diabetic mice. *Scand J Immunol* **74**, 585-595. (Journal IF: 1.935)

Di Mitri D, Azevedo RI, Henson SM, Libri V, Riddell NE, Macaulay R, Kipling D, Soares MV, Battistini L, Akbar AN (2011) Reversible senescence in human CD4⁺CD45RA⁺CD27⁻ memory T cells. *J Immunol* **187**, 2093-100. (Journal IF: 5.745)

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 (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* **132**, 326-39. (Journal IF: 3.302)

Amaral AJ, Ferretti L, Megens H-J, Crooijmans RPMA, Nie H, Ramos-Onsins SE, Perez-Enciso M, Schook LB, Groenen MA. (2011) Genome-Wide Footprints of Pig Domestication and Selection Revealed through Massive Parallel Sequencing of Pooled DNA. *PLoS ONE* **6**, e14782. (Journal IF: 4.411)

Monteiro PH, Pinheiro LS, Alvoeiro L, Lucas M, Victorino RMM (2011) Clopidogrel-induced liver failure. *J Roy Soc Med* **2**, 40. (Journal IF: 1.366)

Carvalho A, Cunha C, Almeida AJ, Osório NS, Saraiva M, Teixeira-Coelho M, Pedreiro S, Torrado E, Domingues N, Gomes-Alves AG, Marques A, Lacerda JF, da Silva MG, Gomes M, Pinto AC, Torres F, Rendeiro P, Tavares P, Di Ianni M, Medeiros R, Heutink P, Bracci PM, Conde L, Ludovico P, Pedrosa J, Maciel P, Pitzurra L, Aversa F, Marques H, Paiva A, Skibola CF, Romani L, Castro AG, Rodrigues F. (2011) The rs5743836 polymorphism in TLR9 confers a population-based increased risk of non-Hodgkin lymphoma. *Genes Immun* Aug 25. doi: 10.1038/gene.2011.59. [Epub ahead of print] (Journal IF: 4.367)

Oleastro M, Pelerito A, Nogueira P, Benoliel J, Santos A, Cabral J, Lopes AI, Ramalho PM, Monteiro L. (2011) Prevalence and incidence of *Helicobacter pylori* Infection in a healthy pediatric population in the Lisbon area. *Helicobacter* **16**, 363-72. (Journal IF: 3.109)

Vitoriano I, Saraiva-Pava KD, Rocha-Gonçalves A, Santos A, Lopes AI, Oleastro M, Roxo-Rosa M. (2011) Ulcerogenic *Helicobacter pylori* strains isolated from children: a contribution to get insight into the virulence of the bacteria. *PLoS ONE* **6**, e26265. (Journal IF: 4.411)

Sologuren I, Boisson-Dupuis S, Pestano J, Vincent QB, Fernández-Pérez L, Chappier A, Cárdenes M, Feinberg J, García-Laorden MI, Picard C, Santiago E, Kong X, Janniére L, Colino E, Herrera-Ramos E, Francés A, Navarrete C, Blanche S, Faria E, Remiszewski P, Cordeiro A, Freeman A, Holland S, Abarca K, Valerón-Lemaur M, Gonçalo-Marques J, Silveira L, García-Castellano JM, Caminero J, Pérez-Arellano JL, Bustamante J, Abel L, Casanova JL, Rodríguez-Gallego C (2011). Partial recessive IFN- γ R1 deficiency: genetic, immunological and clinical features of 14 patients from 11 kindreds. *Hum Mol Genet* **20**, 1509-23. (Journal IF: 8.085)

Other publications National

Ana E Sousa, Rui MM Victorino (2011) Imunopatogénese e resposta imunológica. In: *Manual sobre SIDA* - Ed. F. Antunes - Permanyer Portugal, 4ª Edição.

Emília Faria, Susana Lopes da Silva (2011) Imunodeficiências primárias. In: *Fundamentos de Imunoalergologia. Da Epidemiologia ao Tratamento*. Taborda Barata L, eds: Lisboa; Lidel.

Marques JG (2011) Chapters In: *Protocolos de Urgência em Pediatria*. Correia M, Levy Gomes AL, Camilo C, Abecasis F, Vieira M, Quintas F, eds. 3ª edição. ACSM Editora, Lisboa.

Esteves I, Silva S, Marques JG (2011) Infecção e Imunodeficiências Primárias. *Infecção e Sépsis* **10**, 5-13.

Reis Boto ML, Sandes AR, Brites A, Silva S, Stone R, Almeida M (2011) Severe immune haemolytic anaemia due to ceftriaxone in a patient with congenital nephrotic syndrome. *Acta Paediatr* **100**, e191-3.

Mascarenhas MI, Silva SL, Mendes A, Santos AS, Pedro E, Barbosa MP (2011) Alergia aos anestésicos locais. *Acta Med Port* **24**, 293-298.

Invited Lectures and Seminars

Pereira Santos MC, New in vitro testing methods in drug allergy, 2nd International Congress Southern European Allergy Societies, Estoril, Portugal, 29-31 March, 2011

Lopes da Silva S. News on curative therapeutic of PIDs. 2nd International Congress of SEAS (Southern European Allergy Societies). Estoril, March 31- April 2, 2011.

Caramalho, I. Regulatory T cells as a therapeutic target in autoimmunity. II National Congress on Autoimmunity, Almancil, Portugal, April 29, 2011.

Sousa AE. Do desenvolvimento das células T ao transplante tímico. Ciência e Ensino - 100 anos da FMUL. Faculdade de Medicina da Universidade de Lisboa, May 6, 2011

Lopes da Silva S. Imunoglobulinas. 1ª Reunião sobre derivados do sangue. Porto. July 1-2, 2011.

Caramalho I. Immunology of Regulatory T cells. I International Summer Course ASIA, Troia, Portugal, September 17, 2011.

Lacerda JF. Cellular Immunotherapy post-stem cell transplantation. IX encontro de Engenharia Biomédica. FMUL, November 11, 2011

Ana E. Sousa. Discordância Imuno-Viológica na infecção HIV. 1º Reunião Infecção e Imunologia, Vila do Conde, Portugal, November 12, 2011.

Susana M. Fernandes. GALT (Gut associated lymphoid tissue). 1º Reunião Infecção e Imunologia, Vila do Conde, Portugal, November 12, 2011.

Pereira Santos MC, Imunoterapia específica- Novos conceitos, 50 anos Imunoalergologia Hospitalar em Portugal, Lisboa, Portugal, November 25, 2011

Pereira Santos MC, Para lá do paradigma Th1 Th2, 1ª Reunião Associação dos Serviços de Imunoalergologia-ASIA, Lisboa, Portugal, December 9-10, 2011

Communications in International Conferences

Tendeiro R, Soares M, Baptista AP, Cavaleiro R, Foxall R, Soares RS, Gomes P, Victorino RMM, Sousa AE. Naïve CD4+ T-Cell Disturbances and HIV/AIDS, HIV Evolution, Genomics and Pathogenesis, Keystone Symposia, Whistler, Canada, March 20-25, 2011. (Poster presentation)

Barbosa RR, Silva SL, Silva SP, Melo A, Pedro E, Barbosa MP, Santos MCG, Victorino RMM, Sousa AE. BAFF-R and TACI expression in Common Variable Immunodeficiency B Cells: New Insights into Normal versus Dysregulated Function, Keystone Symposia, Whistler, Canada, April 12-17, 2011. (Poster presentation)

Caramalho I, Nunes-Cabaço H and Sousa AE. Role of common-gamma chain cytokines in human Treg development, EUThyme-Rolduc Meeting, Leeuwenhorst, Netherlands, May 21-24, 2011 (Poster presentation)

Gomes CL, Pinto MV, Ferreira C, Pereira J, Prata F, Marques JG Intravenous immunoglobulin as a treatment option in severe Kikuchi-Fujimoto disease. ESPID Meeting, The Hague, June 7-11, 2011. (Poster presentation)

Pereira Santos MC, Batista A, Campos Melo A, Pedro E, pereira Barbosa M, Victorino RMM, Sousa AE. Foxp3+CD25brightCD4+Tcells expand in correlation with specific IgE/IgG4 changes during long term specific venom immunotherapy. XXX Congress of the European Academy of Allergy and Clinical Immunology, Istambul, 11-15 June, 2011. (Poster presentation)

Caiado J, Pereira Santos MC, Venenalm L, Costa L, Pedro E, Barbosa M, Castells M *In vitro* diagnosis in hypersensitivity to platins. XXX Congress of the European Academy of Allergy and Clinical Immunology, Istambul, 11-15 June, 2011. (Oral presentation)

Pinto MV, Palha AM, Marques JG, Silva S, Lopes AI. Gastrointestinal involvement in Chronic Granulomatous disease and Crohn's Disease: a distinctive histopathological pattern? 5th Europediatrics. Wien, Austria, June, 2011. (Poster presentation)

Foxall R, Tendeiro R, Baptista AP, Soares RS, Cavaleiro R, Gomes P, Victorino RMM, Sousa AE. PD-1/PD-L1 over-expression in HIV-2 infection: a naturally occurring attenuated form of HIV/AIDS, 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention. Rome, Italy, July 17-20, 2011. (Poster presentation)

Fernandes SM, Tendeiro R, Pires AR, Paulo SE, Ferreira C, Foxall RB, Victorino RMM, Sousa AE. HIV 2 impact on mucosa associated lymphoid tissue, 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention. Rome, Italy, July 17-20, 2011. (Poster presentation)

Pinto M, Luis P, Alves A, Palha AM, Marques JG, Silva S, Rute A, Lopes AI. Gastrointestinal involvement in chronic granulomatous disease and crohn's disease: a distinctive histopathological pattern. 23rd European Congress of Pathology, Helsinki, August 27- September 1, 2011 (Oral presentation)

Alves A, Palha AM, Matos M, Lopes AI. Morphological and immunophenotypic esophageal mucosa characterization in children with Eosinophilic Esophagitis: which contribution to the differential diagnosis with Gastroesophageal reflux disease? 23rd European Congress of Pathology, Helsinki, August 27- September 1, 2011 (Oral presentation)

Santos-Sanches I, Pires R, Lino L, Semedo-Lemsaddek T, Tenreiro R, Rolo D, Brito-Avô A, Morais A, Marques JG. Non-random distribution of virulence genes in Group A Streptococcus (GAS) from colonization and infection. XVIII Lancefield International Symposium on Streptococci and Streptococcal Diseases. Palermo, Italy, September 4 - 8, 2011. (Poster presentation)

Vitoriano I, Saraiva-Pava KD, Rocha -Gonçalves A, Santos A, Lopes AI, Oleastro M, Roxo-Rosa M. Ulcerogenic profile of *Helicobacter pylori* pediatric strains: a contribution to get insight into the virulence of the bacteria. The XXIVth International Workshop of the European Helicobacter Study Group, Dublin, September 11-13, 2011 (Oral presentation)

Prata F, Oliveira L, Pestana L, Esteves I, Mouzinho A, Viegas MP, Guerreiro C, Marques JG, Valente P. Mother-to-child transmission of HIV1 from mothers with negative serology on the third trimester of pregnancy – report of three cases. 7th World Congress of the WSPID. Melbourne, Australia, November, 16-19, 2011. (Poster presentation)

Communications in National Conferences

Tendeiro R, Soares M, Baptista AP, Cavaleiro R, Foxall R, Soares RS, Gomes P, Victorino RMM, Sousa AE. Naïve CD4+ T-cell disturbances and HIV/AIDS. SPI International School of Immunology 2011, Portuguese Society for Immunology, Tavira, March 28 – April 1, 2011. (Oral presentation)

Silva SL, Albuquerque AS, Marques JG, Ligeiro D, Devlin BH, Dutrieux J, Cheynier R, Pignata C, Victorino RM, Markert ML, Sousa AE. Long-term impact of thymectomy performed in early infancy. SPI International School of Immunology 2011, Portuguese Society for Immunology, Tavira, March 28 – April 1, 2011. (Oral presentation)

Fernandes SM, Tendeiro R, Foxall R, Victorino RMM, Sousa AE. HIV 2 impact on lymphoid tissues. SPI International School of Immunology 2011, Portuguese Society for Immunology, Tavira, March 28 – April 1, 2011. (Oral presentation)

Pinto MV, Palha AM, Marques JG, Silva SL, Lopes AI. Envolvimento gastrointestinal na doença granulomatosa crónica e na doença de Crohn: um padrão histopatológico distintivo? XXIV Reunião da Sociedade de Gastrenterologia Pediátrica, Ofir, March 17-18, 2011(Oral presentation)

Durão F, Esteves I, da Silva SL, Morais A, Marques JG. Infecção por BCG em doentes com SCID. XII Jornadas Nacionais de Infecçologia Pediátrica. Braga, 19-21 May, 2011. (Poster presentation)

Moutinho A, Esteves I, Janeiro P, Palaré MJ, Gaspar A, Marques JG, Sousa AB. Síndrome de Barth: uma forma rara de neutropenia cíclica. XII Jornadas Nacionais de Infecçologia Pediátrica. Braga, 19-21 May, 2011. (Poster presentation)

Susana M. Fernandes^{1,2}, Rita Tendeiro¹, Sérgio E. Paulo³, Cristina Ferreira⁴, Luís Correia⁵, Ana Rita Pires¹, Rui M.M. Victorino^{1,2}, Ana E Sousa. HIV-2 infection acquired early in life. Conference on HIV/AIDS. A Collaborative Solution for Tropical Diseases: the Luso-American Response. Luso-American Development Foundation (FLAD). Lisbon. September 7-9, 2011. (Poster presentation).

Soares RS, Tendeiro T, Foxall RB, Baptista AP, Cavaleiro R, Gomes P, Camacho R, Valadas E, Doroana M, Lucas M, Antunes F, Victorino RMM, Sousa AE. Cell-associated viral burden provides evidence of ongoing viral replication in aviremic HIV-2 infected patients. Conference on HIV/AIDS. A Collaborative Solution for Tropical Diseases: the Luso-American Response. Luso-American Development Foundation (FLAD). Lisbon. September 7-9, 2011. (Oral presentation).

Tendeiro R, Fernandes S, Foxall RB, Soares RS, Baptista AP, Cavaleiro R, Gomes P, Victorino RMM, Sousa AE. B-cell compartment in HIV-2 infection. Conference on HIV/AIDS. A

Collaborative Solution for Tropical Diseases: the Luso-American Response. Luso-American Development Foundation (FLAD). Lisbon. September 7-9, 2011. (Poster presentation).

Foxall RB, Albuquerque AS, Soares RS, Baptista AP, Cavaleiro R, Tendeiro R, Cortesão CS, Gomes P, Victorino RMM, Sousa AE. Memory and naïve-like regulatory CD4⁺ T cells expand during HIV-2 and HIV-1 infections in direct association with CD4⁺ T-cell depletion but only indirectly with viral load. Conference on HIV/AIDS. A Collaborative Solution for Tropical Diseases: the Luso-American Response. Luso-American Development Foundation (FLAD). Lisbon. September 7-9, 2011. (Poster presentation).

Soares JB, Melo AC, Caiado J, Mendes A, Lopes A, Ferreira MB, Barbosa MP, Pereira Santos MC Contributo do Teste de Activação de Basófilos para o diagnóstico de hipersensibilidade aos anti-inflamatórios não-esteróides. Portuguese Society for Immunoallergology and Clinical Immunology XXXII Annual Meeting, Porto, 1-3 October, 2011. (Oral presentation)

Sousa F, Melo A, Caiado J, Barbosa MP, Sousa AE, Pereira Santos MC. Estudo longitudinal da expressão de FcεRI e da IgE em basófilos e células dendríticas em associação com a função dos basófilos numa doente com asma alérgicagrade tratada com Omalizumab. Portuguese Society for Immunoallergology and Clinical Immunology XXXII Annual Meeting, Porto, 1-3 October, 2011. (Poster presentation)

Costa AC, Duarte FC, Silva P, Caiado J, Pedro E, Bento ML, Pereira Santos MC, Barbosa MP. Indução de tolerância oral específica em jovens/adultos com alergia persistente grave ao leite de vaca. Portuguese Society for Immunoallergology and Clinical Immunology XXXII Annual Meeting, Porto, 1-3 October, 2011. (Poster presentation)

Albuquerque AS, Marques JG, Silva SL, Ligeiro D, Devlin BH, Dutrieux J, Cheynier R, Pignata C, Victorino RM, Markert ML, Sousa AE. Deciphering the human FOXP1-null phenotype through thymic transplantation, Thymus@Porto, Porto, October 14, 2011 (Poster presentation).

Nunes-Cabaço H, Caramalho I, Sepúlveda N, Sousa AE. Differentiation of human thymic regulatory T cells at the double positive stage. Thymus@Porto, Porto, October 14, 2011 (Poster presentation).

Caramalho I, Nunes-Silva V, Pires AR, Pinto AI, Mota C, Nunes-Cabaço H and Sousa AE. Impact of common-gamma chain cytokines on human thymic regulatory T cell development, XXXVII Annual Meeting of the Portuguese Society for Immunology, Oeiras, November 29-30, 2011 (Poster presentation).

Mota C, Nunes-Silva V, Victorino RMM, Sousa AE and Caramalho I. Notch signaling enhances the *in vitro* differentiation of human Regulatory T cells, XXXVII Annual Meeting of the Portuguese Society for Immunology, Oeiras, November 29-30, 2011 (Poster presentation).

Barbosa RR, Silva SL, Silva SP, Barata JT, Sousa AE. BAFF-R and TACI expression in Common Variable Immunodeficiency – insights into receptor dynamics. XXXVII Annual Meeting of the Portuguese Society for Immunology, Oeiras, November 29-30, 2011 (Poster presentation).

Fernandes SM, Pires AR, Foxall RB, Ferreira C, Veiga-Fernandes H, Sousa AE. Lymphoid tissue inducer (LTi)-like cells in human tonsils and colon mucosa. XXXVII Annual Meeting of the Portuguese Society for Immunology, Oeiras, November 29-30, 2011. (Poster presentation).

Nunes-Cabaço H, Tendeiro R, Foxall RB, Soares RS, Pinheiro AI, Matoso P, Sousa AE. HIV-2 has a reduced ability to infect the human thymus, XXXVII Annual Meeting of the Portuguese Society for Immunology, Oeiras, November 29-30, 2011 (Oral presentation).

Organisation of Conferences

Lopes da Silva S. Organizer and Lecturer of the Workshop "Imunodeficiências Primárias" at the XXXII Reunião Anual SPAIC. Porto, October 1-3, 2011.

Sousa AE. Co-organizer of the SPI International School of Immunology 2011, Portuguese Society for Immunology, Tavira, March 28 – April 1, 2011.

Internationalization

List of publications revealing international network collaborations:

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, and Sousa AE (2011) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of two cases. *Blood* **117**, 688-96.

Fabre-Mersseman V, Dutrieux J, Louise A, Rozlan S, Lamine A, Parker R, Rancez M, Nunes-Cabaço H, Sousa AE, Lambotte O, and Cheynier R (2011) CD4⁺ Recent Thymic Emigrants Contribute to Human Immunodeficiency Virus (HIV) Reservoir In Vivo, Implication for HIV Pathogenesis. *AIDS* **25**, 1153-62.

Di Mitri D, Azevedo RI, Henson SM, Libri V, Riddell NE, Macaulay R, Kipling D, Soares MV, Battistini L, Akbar AN (2011) Reversible senescence in human CD4⁺CD45RA⁺CD27⁻ memory T cells. *J Immunol* **187**, 2093-100.

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 (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* **132**, 326-39.

Amaral AJ, Ferretti L, Megens H-J, Crooijmans RPMA, Nie H, Ramos-Onsins SE, Perez-Enciso M, Schook LB, Groenen MA. (2011) Genome-Wide Footprints of Pig Domestication and Selection Revealed through Massive Parallel Sequencing of Pooled DNA. *PLoS ONE* **6**, e14782.

Sologuren I, Boisson-Dupuis S, Pestano J, Vincent QB, Fernández-Pérez L, Chappier A, Cárdenes M, Feinberg J, García-Laorden MI, Picard C, Santiago E, Kong X, Jannièrè L, Colino E, Herrera-Ramos E, Francés A, Navarrete C, Blanche S, Faria E, Remiszewski P, Cordeiro A, Freeman A, Holland S, Abarca K, Valerón-Lemaur M, Gonçalo-Marques J, Silveira L, García-Castellano JM, Caminero J, Pérez-Arellano JL, Bustamante J, Abel L, Casanova JL, Rodríguez-Gallego C (2011). *Partial recessive IFN- γ R1 deficiency: genetic, immunological and clinical features of 14 patients from 11 kindreds*. *Hum Mol Genet*;20 (8):1509-23.

Government/Organization contract research

Rui MM Victorino. Member of the Advising Committee for the National Board for HIV/AIDS (Ministry of Health)

Rui MM Victorino. Member of the National Scientific Council for Health and Life Sciences, FCT

Rui MM Victorino. Collaborator in the National Health Plan 2011-2016 (Ministry of Health)

Maria Conceição Pereira Santos, Member of the Coordinator Board of the Portuguese Group for Primary Immunodeficiencies (GPIP)

José G Gonçalves, Member of the Coordinator Board of the Portuguese Group for Primary Immunodeficiencies (GPIP)

Ana I Lopes, President of the Portuguese Society of Pediatric Gastroenterology

Ana E Sousa. Member of the Assessment Board for PhD and Post-Doc Fellowships, FCT

Ana E Sousa. Treasurer of the Sociedade de Ciências Médicas de Lisboa (SCML)

Ana E Sousa. President of the Portuguese Society for Immunology (SPI)

Advanced teaching

Sousa AE. Organized the course of “Immunology” and gave lectures. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 3-17, 2011.

Soares MV. Imaturidade e senescência no sistema imunitário. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 3, 2011.

Lopes da Silva S. Imunodeficiências Primárias. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 10, 2011.

Albuquerque AS and Foxall RB. Laboratory demonstrations in practical immunology. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 10 and 17, 2011.

Foxall RB. Evaluation of specific immune responses. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 17, 2011.

Tendeiro R. Vacinas. VIII Mestrado de Infecções Emergentes. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 17, 2011.

Sousa AE. Imunopatogénese da infecção VIH/SIDA. III Curso Pós-Graduado de Farmacoterapia na Infecção por VIH/SIDA. Faculdade de Medicina da Universidade de Lisboa. Lisboa, January 17, 2011.

Lacerda JF, Transplantation of hematopoietic progenitors and adoptive cell therapy. Programa de Doutoramento em Ciências da Saúde. Faculdade de Medicina da Universidade de Coimbra. Coimbra, March 2011

Lopes AI, Hepatite autoimune. Curso de Hepatologia Pediátrica, Hospital Pediatrico de Coimbra, Coimbra, April, 2011

Sousa AE. Imunodeficiência associada à infecção VIH. Instituto de Ciências Biomédicas Abel Salazar. Porto, June 9, 2011.

Sousa AE. Immunopatologia da infecção VIH/SIDA. VII Curso Pós-Graduado de Actualização em Tuberculose e infecção por VIH. FMUL, Lisboa, July 6, 2011.

Pereira Santos MC, Inflamação virus e sensibilização alérgica, Formação Avançada em Alergologia Pediátrica -Instituto de Ciências da saúde - Universidade Católica Portuguesa, Lisboa, Portugal, October, 2011

Marques JG. Organizer and lecturer of the course “Vacinas”. XII Congresso Nacional de Pediatria. Albufeira, October, 2011

Lopes da Silva S. Gave a lecture in: Curso 1 - Satélite ao Congresso Nacional de Pediatria 2011 - "Vacinas" Temas: "Bases Imunológicas da Vacinação" e "Reacções de hipersensibilidade - como Lidar? Albufeira, October 8, 2011

Lopes AI, Esofagite eosinofílica – Up to date Session, Jornadas Anuais do Departamento de Pediatria do HSM- CHLN, Lisboa, November 25, 2011

Amaral AJ, gave lecture in the “Workshop on Bioinformatics and Systems Modeling”, Faculdade de Ciências, Universidade de Lisboa, November 21-25, 2011.

Science and Society

Lopes da Silva S. Manifestações de Imunodeficiências Primárias. Assembleia Geral da APDIP (Associação Portuguesa de Doentes com Imunodeficiências Primárias). Odivelas, November 19, 2011.

Lopes da Silva S. Bases Imunológicas da Vacinação. PNV (Plano Nacional de Vacinação) - Divulgação de Boas Práticas. INFARMED. Lisboa, December 13-14, 2011

Master and PhD thesis completed

PhD thesis completed

Rita Isabel Silva de Azevedo (2011) “The role of IL-7 in the Homeostasis of Human Naive and Memory CD4+ T cell subsets”. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria Soares.

Rui Manuel da Silva Soares (2011) “Papel da Carga Viral Celular na Imunodeficiência HIV/SIDA: Contributo do Estudo da Infecção pelo HIV-2”. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana E Sousa.

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

Teresa Moscoso, M.D. Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Pulido Valente (2011) Supervisor: Maria Conceição Pereira Santos.

José Geraldo Dias, M.D. Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Santa Maria (2011) Supervisor: Maria Conceição Pereira Santos

Joana Bruno Soares, M.D. Resident in Immunoallergology, Centro Hospitalar Lisboa Norte, Hospital Pulido Valente (2011) Supervisor: Maria Conceição Pereira Santos

Master thesis completed

Orlando Galego (2011) “Severe prolonged CD4 T-cell lymphopenia in a patient with a phagocytic disorder, X-linked chronic granulomatous disease.” Mestrado Integrado em Medicina, da Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana E Sousa.

Immunobiology Unit

Major interests / Objectives

Immunological studies are crucial for public health providing knowledge for vaccine development and for the treatment of immune disorders, transplantation, infectious diseases and cancer. Understanding the mechanisms underlying differentiation of immune cells and the control of immune responses involves analyses ranging from lymphoid organogenesis to lymphocyte differentiation and function.

Our research projects are centred on the cellular and molecular mechanisms governing lymphoid organogenesis and lymphocyte development and function.

Head of Unit

Henrique Veiga-Fernandes, DVM, PhD

Research Team

Afonso Almeida, PhD	Post-Doc Fellowship, FCT
Manuela Ferreira, PhD	Post-Doc Fellowship, FCT
Sales Ibiza, PhD	Post-Doc Fellowship, Spanish MCE
Diogo Pereira	PhD Fellowship, FCT
Lara dos Santos	Technician
Silvia Madeira	Technician
Rita Domingues	Technician
Helder Ribeiro	Technician
Inês Barbosa	Technician (Left May 2011)

Keywords/Research Areas

Lymphoid organogenesis; Haematopoiesis; Innate Lymphocyte function; Lymphocyte development

Major scientific achievements

Differential mechanisms for enteric organogenesis: We have found that LT α cells are critical players in the earliest phases of enteric lymphoid organ development. Thus, adhesion mediated motility arrest of Lymphoid Tissue initiator (LT α) cells determine early maturation of enteric mesenchymal cells in a RET dependent, chemokine independent manner. This work has been recently submitted for publication

Role of neurotrophic factors during haematopoiesis: Neurotrophic factors of the GDNF family ligands (GFLs) signal through the RET tyrosine kinase receptor and are critical molecules for nervous system function. Our work showed that RET is a novel and critical molecule for HSCs

survival, opening new horizons for the usage of RET/GFL signalling axes as therapeutic targets in HSC transplantation protocols. This work is currently being prepared for submission. Moreover, despite previous studies indicating a role of RET in thymic differentiation, we found that this kinase is not required for normal thymopoiesis. A manuscript describing this work is also currently being prepared.

Role of RET in enteric homeostasis: Using a RET reporter mouse line we found that this kinase is highly expressed in mucosal lymphocytes. Using loss and gain of RET function models we have found a critical role of RET in mucosal homeostasis. This work will require one additional semester to be submitted for publication.

Generation of transgenic models for de-regulated Ret expression in lymphocytes: In the laboratory we have generated different genetically modified mouse models: Ret conditional KO mice; Ret KI in the Rosa26 locus; *hCD2-Ret*; *hCD2-Ret^{MEN2A}* and *hCD2-Ret^{MEN2B}* transgenic mice. We have obtained several founders and part of them had germ-line transmission. These transgenic lines are currently being characterised.

Role of Retinoic Acid (RA) in enteric lymphoid organogenesis: Genetic analysis revealed that RA signalling is critically involved in haematopoietic cell differentiation. A manuscript describing this work is also currently being prepared.

Recent Most Relevant Publications

Veiga-Fernandes H, Kioussis D, Coles M (2010). Natural killer receptors: the burden of a name. *J Exp Med.* 207(2):269-72. (Journal IF: 14.77; Citations: 7).

Gascoyne DM, Long E, Veiga-Fernandes H, de Boer J, Williams O, Seddon B, Coles M, Kioussis D, Brady HJ. (2009) The basic leucine zipper transcription factor E4BP4 is essential for natural killer cell development. *Nat Immunol.* 10:1118-24. (Journal IF: 25.60; Citations: 54).

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: 36.1; Citations: 51).

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: 14.77; Citations: 35).

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: 25.6; Citations: 54).

Ongoing Research Projects

2008/2013 Role of neurotrophic factors in the immune system. Coordinator: H. Veiga-Fernandes. EMBO installation grant, 1648. €250 000.

2008/2013 Role of the proto-oncogene Ret in lymphocyte function. Coordinator: H. Veiga-Fernandes. ERC starting grant, 207057. €1 901 400.

2010/2012 Role of haematopoietic cell subsets during lymphoid organogenesis. Coordinator: H. Veiga-Fernandes. PTDC/SAU-MII/100016/2008. €197 802

2010/2012 Role of the tyrosine kinase RET in foetal and adult haematopoiesis. Coordinator: H. Veiga-Fernandes. PTDC/SAU-MII/104931/2008. €182 600

Publications in peer review Journals

Zaragoza B, Evaristo C, Kissenpfennig A, Libri V, Malissen B, Rocha B, Freitas AA, Almeida AR (2011). Cell-to-cell interactions and signals involved in the reconstitution of peripheral CD8 T(CM) and T(EM) cell pools. *PLoS One*. 14;6(3):e17423. (Journal IF: ND; Citations: 0)

Narita M, Young ARJ, Arakawa S, Samarajiwa SA, Nakashima T, Yoshida S, Hong S, Berry LS, Reichelt S, Ferreira M, Tavaré S, Inoki K, Shimizu S, Narita M. (2011) Spatial Coupling of mTOR and Autophagy Augments Secretory Phenotypes. *Science*. May 20;332(6032):966-70. (Journal IF: 31,3; Citations: 6)

Fujiwara H, Ferreira M, Donati G, Marciano DK, Linton JM, Sato Y, Hartner A, Sekiguchi K, Reichardt LF, Watt FM. (2011). The basement membrane of hair follicle stem cells is a muscle cell niche. *Cell*, Feb 18;144(4):577-89. (Journal IF: 32,4; Citations: 8)

Other publications International

Cupedo T, Coles M, Veiga-Fernandes H. (2011). Development and structure of lymph nodes in humans and mice. In: *Developmental Biology of Peripheral Lymphoid Organs*. Springer (Heidelberg). P. 59-74.

Cupedo T, Coles M, Veiga-Fernandes H. (2011). Structure and development of Peyer's patches in humans and mice. In: *Developmental Biology of Peripheral Lymphoid Organs*. Springer (Heidelberg). P. 97-106.

Ferreira M, Santos L, Ferreira-Almeida F, Domingues R, Barbosa I, Veiga-Fernandes H. (2011). "Retinoic Acid in the development of Peyer's patches" International School of Immunology. Tavira, Algarve, Portugal.

Fonseca-Pereira, D., Madeira, S. et al. (2011). "Role of RET tyrosine kinase in haematopoiesis", EMBO/ENII conference "Homeostasis and perturbations of immunity", 97, Capo Caccia, Sardinia, Italy

Other publications National

Ferreira M, Santos L, Ferreira-Almeida F, Domingues R, Barbosa I, Veiga-Fernandes H. (2011). "Retinoic Acid in the development of Peyer's patches" XXXVII SPI Annual Meeting. Instituto Gulbenkian de Ciência, Oeiras, Portugal.

Fonseca-Pereira, D., Madeira, S. et al. (2011). "Role of neurotrophic factors in haematopoiesis", V IMM/CAML PhD Student Meeting, 26, Lisboa, Portugal.

Fonseca-Pereira, D., Madeira, S. et al. (2011). "Role of neurotrophic factors in haematopoiesis", "XXXVII Annual Meeting of the Portuguese Society of Immunology", Oeiras, Portugal.

Afonso R. M. Almeida, Diogo Pereira, Silvia Madeira and Henrique Veiga-Fernandes (2011) Role of the tyrosine kinase receptor RET in T cell function. XXXVII SPI Annual Meeting, November 29-30. Oeiras, Portugal.

Invited Lectures and Seminars

Veiga-Fernandes H. Lymphoid organogenesis. ENII Summer School. Cappel Caccia. May 2011

Veiga-Fernandes, H. Neurotrophic factors and Immune cell functions. SFB854 International Symposium. Magdeburg, Germany. September 2011.

Veiga-Fernandes, H. Neurotrophic factors and Immune cell functions. EMBL, Monterotondo, Italy, November 2011.

Communications in International Conferences

Ferreira M, Santos L, Ferreira-Almeida F, Domingues R, Barbosa I, Veiga-Fernandes H. (2011). "Retinoic Acid in the development of Peyer's patches" International School of Immunology. Tavira, Algarve, Portugal.

Fonseca-Pereira, D., Madeira, S. et al. (2011). "Role of RET tyrosine kinase in haematopoiesis", EMBO/ENII conference "Homeostasis and perturbations of immunity", 97, Capo Caccia, Sardinia, Italy.

Communications in National Conferences

Ferreira M, Santos L, Ferreira-Almeida F, Domingues R, Barbosa I, Veiga-Fernandes H. (2011). "Retinoic Acid in the development of Peyer's patches" XXXVII SPI Annual Meeting. Instituto Gulbenkian de Ciéncia, Oeiras, Portugal.

Fonseca-Pereira, D., Madeira, S. et al. (2011). "Role of neurotrophic factors in haematopoiesis", "XXXVII Annual Meeting of the Portuguese Society of Immunology", Oeiras, Portugal.

Afonso R. M. Almeida, Diogo Pereira, Silvia Madeira and Henrique Veiga-Fernandes (2011) Role of the tyrosine kinase receptor RET in T cell function. XXXVII SPI Annual Meeting, November 29-30. Oeiras, Portugal.

Internationalization

Cupedo T, Coles M, Veiga-Fernandes H. (2011). Development and structure of lymph nodes in humans and mice. In: Developmental Biology of Peripheral Lymphoid Organs. Springer (Heidelberg). P. 59-74.

Cupedo T, Coles M, Veiga-Fernandes H. (2011). Structure and development of Peyer's patches in humans and mice. In: Developmental Biology of Peripheral Lymphoid Organs. Springer (Heidelberg). P. 97-106.

Zaragoza B, Evaristo C, Kissenpfennig A, Libri V, Malissen B, Rocha B, Freitas AA, Almeida AR (2011). Cell-to-cell interactions and signals involved in the reconstitution of peripheral CD8 T(CM) and T(EM) cell pools. *PLoS One*. 14;6(3):e17423. (Journal IF: ND; Citations: 0)

Narita M, Young ARJ, Arakawa S, Samarajiwa SA, Nakashima T, Yoshida S, Hong S, Berry LS, Reichelt S, Ferreira M, Tavaré S, Inoki K, Shimizu S, Narita M. (2011) Spatial Coupling of mTOR and Autophagy Augments Secretory Phenotypes. *Science*. May 20;332(6032):966-70. (Journal IF: 31,3; Citations: 6)

Fujiwara H, Ferreira M, Donati G, Marciano DK, Linton JM, Sato Y, Hartner A, Sekiguchi K, Reichardt LF, Watt FM. (2011). The basement membrane of hair follicle stem cells is a muscle cell niche. *Cell*, Feb 18;144(4):577-89. (Journal IF: 32,4; Citations: 8)

Advanced teaching

Veiga-Fernandes H. Lymphoid organogenesis. GABBA PhD programme. Universidade do Porto, Portugal. May 2010.

Malaria Unit

Major interests / Objectives

Malaria is still estimated to be responsible for 1 million deaths in vast parts of our planet. Within the human host, *Plasmodium*, malaria's causative agent, infects very distinct cells types: liver hepatocytes and red blood cells. While in hepatocytes *Plasmodium* replicates in a single cycle of infection into thousands of new parasites, later in the blood *Plasmodium* replicates only in 10-20 parasites but in consecutive cycles of infection that are the cause of disease and death. We aim not only to uncover *Plasmodium* requirements to establish in its host but also to elucidate the major virulence mechanisms used by this parasite to obtain its key needs and how these processes impact human health.

Head of Unit

Maria M. Mota, MSc, PhD - Principal Investigator, Laboratório Associado, IMM

Principal Investigators

Miguel Prudêncio, PhD – Principal Investigator, Staff Scientist, IMM-FCT

Research Team

Ana Margarida Vigário	PhD – Post-doc	Invited researcher, University of Madeira
Ana Filipa Cruz	PhD – Post-doc	FCT Fellowship until 31 st July
António Mendes	PhD – Post-doc	Fellowship (from Melinda & Bill Gates Foundation grant) between 1 st January to 31 st December
Claúdia Cunha	PhD – Post-doc	FCT Fellowship
Daniel Carapau	PhD – Post-doc	FCT Fellowship
Eliana Real	PhD – Post-doc	FCT Fellowship
Ghislain Cabal	PhD – Post-doc	Marie Curie Fellowship until 21 st April FCT Fellowship since 1 st May
Inês Gomes	PhD – Post-doc	FCT Fellowship
Iset Vera	PhD – Post-doc	Fellowship (from FCT grant) since 16 th July
Kirsten Hanson	PhD – Post-doc	FCT Fellowship
Liliana Mancio	PhD – Post-doc	EMBO Fellowship until 10 th January Fellowship (from EVIMALAR grant) since 1 st October
Peter Liehl	PhD – Post-doc	FCT Fellowship
Vanessa Luís	PhD – Post-doc	EMBO Fellowship until 31 st August Fellowship (from FCT grant) between 1 st September to 31 st October Scientific career development Fellowship (from FCT grant) since 1 st November
Patricia Inácio	PhD Student	FCT Fellowship until 30 th September
Maurice Itoe	PhD student	Marie Curie ITN Fellowship
Patrícia Meireles	PhD student	Fellowship (from FCT grant) since 1 st April
Fernanda Baptista	Laboratory and Project manager	Fellowship (from EVIMALAR grant)
Ana Parreira	Laboratory and Insectary technician	Fellowship (from EVIMALAR grant)
Maria Rebelo	Researcher	Fellowship (from FCT grant)

Inês Albuquerque	Msc student	Until 26 th October
	Researcher	Fellowship (from FCT grant) since 1 st August
Audrey Lopes	Msc student	Since 1 st February
Francisco Vidal	Msc student	Since 27 th September
Joana Carrelha	Msc student	Until 30 th October
Joana Sales	Msc student	Until 5 th December

Keywords/Research Areas

Host-*Plasmodium* Cellular and Molecular Interactions; *Plasmodium* biology ; Superinfection and co-infections; Innate immunity sensors; *Plasmodium* sensors; *Plasmodium* and host metabolism
Malaria Pathogenesis; Anti-malarial intervention

Major scientific achievements

Aiming to uncover *Plasmodium* requirements to establish in its host, we have performed the first large-scale studies that identified key host factors involved in hepatocyte infection by *Plasmodium* (Rodrigues *et al.*, 2008. *Cell Host & Microbe*; Prudêncio *et al.*, 2008. *PLoS Pathogens*). Additionally, we have revealed that during the liver stage of infection *Plasmodium* co-opts a host enzyme, HO-1, to be protected from the host inflammatory response (Epiphany *et al.*, 2008. *Cell Host & Microbe*). Interestingly, we also show that this same host enzyme and its end-product carbon monoxide promote host survival during blood stage of infection (Pamplona *et al.*, 2007. *Nature Medicine*; Epiphany *et al.*, 2010. *PLoS Pathogens*). As such, we then became extremely interested on how liver and the blood stages of infection influence each other. We showed that blood-stage parasitaemia impairs the establishment of a subsequent liver infection, explaining why *Plasmodium* superinfection is rarely found in young non-immune children (Portugal *et al.* 2011. *Nature Medicine*).

Recent Most Relevant Publications

1. Gomes-Santos CS, Braks J, Prudêncio M, Carret C, Gomes AR, Pain A, Feltwell T, Khan S, Waters A, Janse C, Mair GR, Mota MM. 2011. Transition of *Plasmodium* sporozoites into liver stage-like forms is regulated by the RNA binding protein pumilio. *PLoS Pathog.* 7(5):e1002046. (IF: 9.079; Citations: 2)
2. Portugal S, Carret C, Recker M, Armitage A, Sullivan D, Roy Cindy, Newbold CJ, Drakesmith H, Mota MM. 2011. Host-mediated control of Malaria Superinfection. *Nature Medicine.* 17(6):732. (Highlighted in *Nature Reviews Microbiology*; evaluated in *F1000 Biology*; Commented in *EMBO Mol.Med.*) (IF: 25.430; Citations: 8)
3. Epiphany 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 Pathog.* 6(5):e1000916. (IF: 9.079; Citations: 8)
4. Prudêncio M, Rodrigues CD, Hannus M, Martin C, Real E, Gonçalves LA, Carret C, Dorkin R, Röhl I, Jahn-Hoffmann K, Luty AJ, Sauerwein R, Echeverri CJ, Mota MM. 2008. Kinome-wide RNAi screen implicates at least 5 host hepatocyte kinases in *Plasmodium* sporozoite infection. *PLoS Pathog.* 4(11):e1000201. (IF: 9.079; Citations: 20)

5. Rodrigues CD, Hannus M, Prudêncio M, Martin C, Gonçalves LA, Portugal S, Epiphanyo S, Akinc A, Hadwiger P, Jahn-Hofmann K, Röhl I, van Gemert GJ, Franetich JF, Luty AJF, Sauerwein R, Mazier D, Koteliansky V, Vornlocher HP,⁵ Echeverri CJ and Mota MM. 2008. Host scavenger receptor SR-BI plays a dual role in the establishment of malaria parasite liver infection. *Cell Host & Microbe*. 4(3):271-82. (*comment in Cell Host & Microbe*) (IF: 13.728; Citations: 26)
6. Epiphanyo S, Mikolajczak SA, Gonçalves LA, Pamplona A, Portugal S, Albuquerque S, Goldberg M, Rebelo S, Anderson DG, Akinc A, Vornlocher HP, Kappe SH, Soares MP, Mota MM. 2008. Heme oxygenase-1 is an anti-inflammatory host factor that promotes murine plasmodium liver infection. *Cell Host & Microbe*. 3(5):331-8. (*comment in Nature Reviews Microbiology*) (IF: 13.728; Citations: 22)
7. Pamplona A, Ferreira A, Balla J, Jeney V, Balla G, Epiphanyo S, Chora A, Rodrigues CD, Gregoire IP, Cunha-Rodrigues M, Portugal S, Soares MP, Mota MM. 2007. Heme oxygenase-1 and carbon monoxide suppress the pathogenesis of experimental cerebral malaria. *Nature Medicine*. 13:703. (*comment in Nature Medicine; evaluated in F1000 Biology and F1000 Medicine*) (IF 25.430, Citations: 108)
8. Prudêncio M, Rodriguez A, Mota MM. (2006). The silent path to thousands of merozoites: the *Plasmodium* liver stage. *Nat Rev Microbiol*. Nov;4(11):849-56. (IF: 20.686; Citations: 79)

Ongoing Research Projects

- 2010/2015 Towards the establishment of a permanent European Virtual Institute dedicated to Malaria Research (EViMalaR) – EU FP7 European Network of Excellence. IMM coordinator: Maria M. Mota, 12.000.000,00 € (for the entire consortium).
- 2011/2014 Subverting the host ubiquitin-proteasome pathway towards an immune evasion strategy. FCT. Coordinator: Vanessa Luis. PTDC/SAU-MIC/113697/2009, 148.385,00 €
- 2010/2013 The influence of bile acids on malaria liver infection. FCT. Coordinator: Miguel Prudêncio. PTDC/SAU-MII/099118/2008, 171.482,00 €
- 2010/2013 New drugs for treating and eradicating malaria. FCT. Coordinator: Maria M. Mota. HMSP-CT/SAU-ICT/0068/2009, 300.000,00 €
- 2010/2013 Respiratory tract & malaria co-infections. FCT. Coordinator: Maria M. Mota, MM. PTDC/SAU-MII/108578/2008, 190.850,00 €
- 2010/2013 Unravelling the secrets of *Plasmodium* liver stage. FCT. Coordinator: Maria M. Mota. PTDC/SAU-GMG/100313, 199.943,00 €
- 2010/2012 A new whole-organism vaccine against Malaria. Grand Challenges Explorations, Bill & Melinda Gates Foundation. Coordinator: Miguel Prudêncio, 100.000,00 USD
- 2008/2011 The role of SR-BI in malaria infection. FCT. Coordinator: Miguel Prudêncio. PTDC/BIA-BCM/71920/2006, 118.000,00 €

Publications in peer review Journals

1. Douradinha B, van Dijk M, van Gemert GJ, Khan SM, Janse CJ, Waters AP, Sauerwein RW, Luty AJ, Silva-Santos B, Mota MM, Epiphany S. 2011. Immunization with genetically attenuated P52-deficient *Plasmodium berghei* sporozoites induces a long-lasting effector memory CD8⁺ T cell response in the liver. *J Immune Based Ther Vaccines* 17;9(1):6.
2. Capela R, Cabal GG, Rosenthal PJ, Gut J, Mota MM, Moreira R, Lopes F, Prudêncio M. 2011. Design and Evaluation of Primaquine-Artemisinin Hybrids as a Multistage Anti-Malarial Strategy. *Antimicrob Agents Chemother.* 55(10):4698.
3. Liesenfeld O, Parvanova I, Zerrahn J, Han SJ, Heinrich F, Muñoz M, Kaiser F, Aebischer T, Buch T, Waisman A, Reichmann G, Utermöhlen O, von Stebut E, von Loewenich FD, Bogdan C, Specht S, Saeftel M, Hoerauf A, Mota MM, Könen-Waisman S, Kaufmann SH, Howard JC. 2011. The IFN- γ -Inducible GTPase, Irga6, Protects Mice against *Toxoplasma gondii* but Not against *Plasmodium berghei* and Some Other Intracellular Pathogens. *PLoS One* 6(6):e20568.
4. Gomes-Santos CS, Braks J, Prudêncio M, Carret C, Gomes AR, Pain A, Feltwell T, Khan S, Waters A, Janse C, Mair GR, Mota MM. 2011. Transition of *Plasmodium* sporozoites into liver stage-like forms is regulated by the RNA binding protein pumilio. *PLoS Pathog.* 7(5):e1002046.
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6. Frita R, Rebelo M, Pamplona A, Vigarito AM, Mota MM, Grobusch MP, Hänscheid T. Simple flow cytometric detection of haemozoin containing leukocytes and erythrocytes for research on diagnosis, immunology and drug sensitivity testing. 2011. Frita R, Rebelo M, Pamplona A, Vigarito AM, Mota MM, Grobusch MP, Hänscheid T. *Malar J.* 10:74. (*highly accessed article*)
7. Douradinha B, Augustijn KD, Moore SG, Ramesar J, Mota MM, Waters AP, Janse CJ, Thompson J. 2011. *Plasmodium* Cysteine Repeat Modular Proteins 3 and 4 are essential for malaria parasite transmission from the mosquito to the host. *Malar J.* 10(1):71. (*highly accessed article*)
8. Slavic K, Delves MJ, Prudêncio M, Talman AM, Straschil U, Derbyshire ET, Xu Z, Sinden RE, Mota MM, Morin C, Tewari R, Krishna S, Staines HM. 2011. Use of a selective inhibitor to define the chemotherapeutic potential of the plasmodial hexose transporter in different stages of the parasite's life cycle. *Antimicrob Agents Chemother.* 55(6):2824-30.
9. Lavrado J, Cabal GG, Prudêncio M, Mota MM, Gut J, Rosenthal PJ, Díaz C, Guedes RC, Dos Santos DJ, Bichenkova E, Douglas KT, Moreira R, Paulo A. 2011. Incorporation of Basic Side Chains into Cryptolepine Scaffold: Structure-Antimalarial Activity Relationships and Mechanistic Studies. *J Med Chem.* 54(3):734.
10. Prudêncio M, Mota MM, Mendes AM. 2011. A toolbox to study liver stage malaria. *Trends Parasitol.* 27(12):565.
11. Portugal S, Drakesmith H and Mota MM. 2011. Superinfection in malaria: *Plasmodium* shows its iron will. *EMBO Rep.* 12(12):1233.
12. Derbyshire ER, Mota MM, Clardy J. 2011. The next opportunity in anti-malaria drug discovery: the liver stage. *PLoS Pathog.* 7(9):e1002178.

13. malERA Consultative Group on Basic Science and Enabling Technologies, Baum J, Billker O, Bousema T, Dinglasan R, McGovern V, Mota MM, Mueller I, Sinden R. 2011. A research agenda for malaria eradication: basic science and enabling technologies. PLoS Med. 8(1):e1000399.
14. Langhorne J, Buffet P, Galinski M, Good M, Harty J, Leroy D, Mota MM, Pasini E, Renia L, Riley E, Stins M, Duffy P. 2011. The relevance of non-human primate and rodent malaria models for humans. *Malar J.* 10(1):23. (*highly accessed article*)

Invited Lectures and Seminars

- Mota, M.M. American Society of Tropical Medicine and Hygiene 60th Annual Meeting. December 4-8, 2011. Philadelphia, USA.
- Zuzarte-Luis V. "Innate Immunity and the Malaria liver infection". Immunology Meeting. Nov 11, 2011. Instituto Gulbenkian de Ciência, Oeiras.
- Mota, M.M. "Infection, superinfection and co-infections: from simple models to complex interactions". August 10, 2011. National Institutes of Health, Bethesda, USA.
- Prudêncio, M. "*Plasmodium* infection: host factors, parasite molecules and anti-malarial interventions". Institutional Seminar. July 15, 2011. Instituto Gulbenkian de Ciência, Oeiras.
- Mota, M.M. Workshop on Innate Immunity and Malaria. Belo Horizonte (Brazil). June 8-9, 2011.
- Mota, M.M. "Searching for new drugs against *Plasmodium* liver stage". Jun 2-3, 2011. Johns Hopkins Malaria Research Institute Research Advances in Malaria Conference - Resistance to Existing Drugs and New Drug Development. GSK Medicines Development Campus. Tres Cantos (Spain).
- Zuzarte-Luis, V. "Host response mechanisms to malaria liver infection". May 18, 2011. University of Massachusetts. Boston, USA.
- Mota, M.M. "*Plasmodium*-Host-*Plasmodium* interactions". April 12, 2011. Strasbourg University, France.

Communications in International Conferences

- Liehl, P. Toll 2011 Meeting - Decoding Innate Immunity, Riva del Garda, Italy, May 4-7 2011 (Poster presentation: "*Type I interferons induced by Plasmodium control malaria liver stage infection*").
- Carrelha, J. Young Researchers in Life Sciences Congress, Paris, France, May 9-11, 2011 (Poster presentation: "*Role of host peroxisomal proteins in malaria liver stage*").
- Itoe, M. 7th Annual BioMalPar Conference - Biology and Pathology of the Malaria Parasite, Heidelberg, Germany, May 15-22, 2011 (Poster presentation: "*Altered lipid composition in Plasmodium-infected hepatocytes*").
- Itoe, M. 22nd Annual Molecular Parasitology Meeting. Woods Hole, USA, September 11-15, 2011 (Poster presentation: "*Altered lipid composition in Plasmodium-infected hepatocytes*").
- Hanson, K. 22nd Annual Molecular Parasitology Meeting. Woods Hole, USA, September 11-15, 2011 (Poster presentation: "*Plasmodium liver stage growth modulates host hepatocyte size in a cell-cycle independent manner*")

Cabal, G. EMBO Conference - Nuclear receptors: from molecular mechanism to health and disease, Barcelona, Espanha, September 16-20, 2011 (Poster presentation: *"Hepatocyte nuclear receptors and Plasmodium liver infection: from biology to anti-malarial prophylactic intervention"*).

Prudêncio, M. BIT's 9th Annual Congress of International Drug Discovery Science and Technology, Shenzhen, China, November 3-6, 2011 (Oral Presentation: *"Novel Multistage Strategies Against Malaria"*).

Mota, M.M. American Society of Tropical Medicine and Hygiene 60th Annual Meeting, Philadelphia, USA, December 4-8, 2011 (Oral presentation: *"How is Plasmodium recognized by the host during the liver phase of infection"*).

Communications in National Conferences

Carrelha, J. 1.º Encontro de Biologia Molecular em Saúde, Lisboa, Portugal, March 18-19, 2011 (Poster presentation: *"Role of host peroxisomal proteins in malaria liver stage"*)

Organisation of Conferences

Mota M and Del Portillo HA. Organizers of 3rd meeting of Plataforma Ibérica de Malária. June 23 - 24, 2011. Instituto de Medicina Molecular, Lisbon, Portugal

Prizes, honours and awards

Carrelha, J. 1.º Encontro de Biologia Molecular em Saúde, Lisboa, Portugal, March 18-19 2011 (Poster presentation: poster price winner)

Patents/prototypes

1. Method for the prevention of malaria infection of humans by hepatocyte growth factor antagonists, South Africa: Issued Patent No.: 2005/08178. Based on International PCT Publication No. WO2004/080420, African Reg. Ind. Prop. Org. – Application No. AP/P/2005/003411, Brazil – Application No. PI0408268-0, China – Publication No. CN1809382A, Europe – Publication No. 1601378, Hong Kong – Publication No. 1093903A, Japan – Application No. 2006-507105, United States - Publication No.: US 2004-0185050 A1.
2. Use of inhibitors of scavenger receptor class proteins for the treatment of infectious diseases (WO/2007/101710), International Application No. PCT/EP2007/002110, National phases initialized in EU, US, CA and China in Oct. 2008.
3. Use of inhibitors of host kinases for the treatment of infectious diseases, US provisional application NO. 61/110,217, filed 31.10.2008.
4. Ruthenium carbon monoxide releasing molecules and uses thereof. US provisional application NO. 61/510,136, filed 7.21.2011.

Advanced teaching

Mota, M.M. MalVecBlok FP7 PhD Program. April 10-12, 2011. Strasbourg University, France.

Prudêncio, M and Mota, M.M. GABBA PhD Program. January 25, 2011, IBMC, Porto, Portugal.

Master and PhD thesis completed

Joana Carrelha (2011) "Uncovering the role of host peroxisomal functions in *Plasmodium* liver stage infection". Faculdade de Ciências da Universidade de Lisboa. Supervisors: Ghislan Cabal (IMM) e Margarida Ramos (FCUL). Msc degree.

Joana Dias (2011) "The role of glucose in *Plasmodium* liver infection". Faculdade de Ciências da Universidade de Lisboa. Supervisors: Miguel Prudêncio (IMM) e Margarida Telhada (FCUL). Msc degree.

Maria Inês Albuquerque (2011) "Cytoadherence capabilities of *Plasmodium berghei* ANKA and NK65 infected red-blood cells in different malaria models". Faculdade de Ciências da Universidade de Lisboa. Supervisors: Ana Margarida Vigário (IMM) e Ana Rita Zilhão (FCUL). Msc degree.

Molecular Immunology Unit

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 – Auxiliary Professor, Faculdade de Medicina, Universidade de Lisboa

Principal Investigators

Ana Pamplona, PhD – Principal Investigator (Staff Scientist), IMM

Research Team

Anita Q. Gomes, PhD	Auxiliary Professor, ESTSL
Julie Ribot, PhD	Post Doc Fellowship, FCT
Rita Neres, PhD	Post Doc Fellowship, FCT
Karine Serre, PhD	Post Doc Fellowship, FCT
Daniel V. Correia	PhD Fellowship, FCT
Telma Lança	PhD Fellowship, FCT
Ana deBarros	PhD Fellowship, FCT
Nina Schmolka	PhD Fellowship, ERC/ IMM
Natacha Gonçalves Sousa	Research grant, FCT

Keywords/Research Areas

T cell development/ differentiation; T cell activation; Tumour immunology; Immunopathogenesis of Severe Malaria

Major scientific achievements in 2010

- Our Unit published 7 papers in peer-reviewed international journals, 5 of which with an impact factor >5.

- Submitted two PhD thesis and one Master thesis.
- Submitted one provisional patent.
- Successfully recruited a senior post-doctoral fellow through the Wellcome II program.
- Bruno Silva-Santos was selected for the editorial board of *Oncoimmunology*.

Recent Most Relevant Publications

Lança T., Correia D. V., Moita C. F., Raquel H., Ferreira C., Ramalho J. S., Barata J. T., Moita L. F., Gomes A. Q. and Silva-Santos B. (2010). The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. *Blood*: 115(12):2407-11. (Journal IF: 10.555) (Citations: 16)

Ribot J. C., Chaves-Ferreira M., d'Orey F., Wencker M., Gonçalves-Sousa N., Decalf J., Simas J. P., Hayday A. C. and Silva-Santos B. (2010). Cutting Edge: Adaptive *versus* innate signals selectively control the pool sizes of IFN- γ - or IL-17-producing $\gamma\delta$ T cells upon infection. *J Immunol*: 185(11):6421-5. (Journal IF: 5.646) (Citations: 10)

Gomes A. Q., Correia D. V., Grosso A. R., Lança T., Ferreira C., Lacerda J. F., Barata J. T., Gomes da Silva M. and Silva-Santos B. (2010). Identification of a panel of ten cell surface protein antigens associated with immunotargeting of leukemias and lymphomas by peripheral blood $\gamma\delta$ T cells. *Haematologica*: 95(8):1397-404. (Journal IF: 6.416) (Citations: 7)

Ribot J. C., deBarros A., Pang D. J., Neves J. F., Peperzak V., Girardi M., Borst J., Hayday A. C., Pennington D. J. and Silva-Santos B. (2009). CD27 is a thymic determinant of the balance between IFN- γ - and IL-17-producing $\gamma\delta$ T cell subsets. *Nature Immunology* 10: 427-436. (Journal IF: 26.218) (Citations: 66)

Pennington, D. J., Silva-Santos, B., Silberzahn, T., Escorcio-Correia, M., Dyson P. J., and Hayday, A. C. (2006). Early events in the thymus affect the balance of effector and regulatory T cells. *Nature* 444, 7122: 1073-7. (Journal IF: 32.182) (Citations: 62)

Ongoing Research Projects

2007/2011	Innate Mechanisms of Tumor Immunosurveillance. European Molecular Biology Organization, Installation Grant, €250 000. PI: B.Silva-Santos.
2008/2011	Mechanisms of tumor resistance to $\gamma\delta$ T cell-based cancer immunotherapy. Fundação Calouste Gulbenkian, SDH Oncologia 2008 - Projecto 99293, €50 000. PI: B. Silva-Santos.
2010/2011	Regulation of T cell differentiation and activation by CD27-CD70 receptor-ligand interactions in the thymus and in the periphery. Fundação para a Ciência e Tecnologia, PTDC/SAU-MII/104158/2008, €194 000. PI: B. Silva-Santos.
2010/2015	Differentiation of pro-inflammatory T cell subsets in vivo. European Research Council, StG 260352, €1 500 000 PI: B. Silva-Santos

2011/2013 (Epi)genetic regulation of T lymphocyte differentiation in vivo. European Molecular Biology Organization, Young Investigator Programme, €45 000. PI: B. Silva-Santos.

Publications in peer reviewed Journals

Mahtani-Patching J., Neves J. F., Pang D. J., Stoenchev K. V., Aguirre-Blanco A. M., **Silva-Santos B.** and Pennington D. J. (2011), “PreTCR and TCR $\gamma\delta$ signal initiation in thymocyte progenitors does not require domains implicated in receptor oligomerization. *Science Signal* 4, ra47. (Journal IF: 6.12)

- Pena A. C., Penacho N., Mancio-Silva L., Neres R., Seixas J. D., Fernandes A. C., Romão C. C., Mota M. M., Bernardes G. J., Pamplona A. (2011), “A novel Carbon Monoxide-Releasing Molecule (CO-RM) fully protects mice from Severe Malaria”, *Antimicrob Agents Chemother*: Epub 12 Dec 2011. (Journal IF: 4.672)

- Correia D. V., Fogli M., Hudspeth K., da Silva M. G., Mavilio D. and **Silva-Santos B.** (2011), “Differentiation of human peripheral blood V δ 1⁺ T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells”, *Blood*: Epub 1 Jun 2011. (Journal IF: 10.555)

- Douradinha B, van Dijk M, van Gemert GJ, Khan SM, Janse CJ, Waters AP, Sauerwein RW, Luty AJ, **Silva-Santos B.**, Mota MM and Epiphany S (2011), “Immunization with genetically attenuated P52-deficient Plasmodium berghei sporozoites induces a long-lasting effector memory CD8⁺ T cell response in the liver”. *J Immune Based Ther Vaccines* 9(1):6.

- **Silva-Santos B.** (2011), “ $\gamma\delta$ cells making IL-17”, *Blood* 118 (1): 3-5. Review. (Journal IF: 10.555)

- Ribot J. C., deBarros A., and **Silva-Santos B.** (2011), “Searching for “signal 2”: costimulation requirements of $\gamma\delta$ T cells”, *Cell Mol Life Sci*: Epub 4 May 2011. Review. (Journal IF: 7.047)

- deBarros A., Chaves-Ferreira M., d'Orey F., Ribot J. C. and **Silva-Santos B.** (2011), “CD70-CD27 interactions provide survival and proliferative signals that regulate T cell receptor-driven activation of human $\gamma\delta$ peripheral blood lymphocytes”, *Eur J Immunol* 41(1):195-201. (Journal IF: 5.179)

Invited Lectures and Seminars

B. Silva-Santos. Caring for a minority: differentiation and activation of $\gamma\delta$ T lymphocytes. Instituto Gulbenkian de Ciência, Oeiras (Portugal). 18 February 2011.

B. Silva-Santos. Differentiation and activation of $\gamma\delta$ T lymphocytes. Universidade Federal do Rio de Janeiro (Brasil). 28 February 2011.

B. Silva-Santos. Molecular mechanisms of tumor cell recognition by human $\gamma\delta$ T lymphocytes. Institut Necker, Faculté de Médecine, Université Paris Descartes, Paris (France). 16 May 2011.

B. Silva-Santos. Activation and expansion of Th17- or Th1-like $\gamma\delta$ cell subsets are controlled by distinct receptors associated with innate or adaptive immunity. 4th Angean Conference on Crossroads in Innate and Adaptive Immunity. Mykonos (Greece), 11-16 September 2011.

B. Silva-Santos. Education at birth: the development of $\gamma\delta$ T cells. European Research Council, Brussels (Belgium). 9 December 2011.

Communications in International Conferences

Lança T.^{*}, Correia D.V.^{*}, Gomes A.Q., Mavilio D., and Silva-Santos B. NKG2D and Natural Cytotoxicity Receptors play critical roles in leukemia cell recognition by human $\gamma\delta$ peripheral blood lymphocytes. Keystone Symposium on Tumor Immunology. Santa Fe (USA), 12-17 February 2011 (Poster presentation)

Ribot J., Coquet J., Neves J. F., deBarros A., Ferreira A., Wencker M., Hayday A. C., Pennington D. J., Borst J., and Silva-Santos B. Thymic CD70-CD27 interactions control the development of agonist-selected effector and regulatory T cells. 5th World Immune Regulation Meeting. Davos (Switzerland), 24-27 March 2011 (Oral Presentation).

Schmolka N., Gomes A.Q. and Silva-Santos B. Pre- and post-transcriptional mechanisms of $\gamma\delta$ T cell differentiation in vivo. SPI International School of Immunology 2011, Tavira (Portugal), 28 March – 1 April 2011 (Oral presentation)

Gomes A.Q., Schmolka N. and Silva-Santos B. Epigenetic regulation of Ifng and Il17 gene expression in $\gamma\delta$ T lymphocytes. Epigenetics and RNAi World Congress”, Boston (USA), 26-28 April 2011 (Poster presentation).

Lança T.^{*}, Rei M.^{*}, Pennington D.J. and Silva-Santos B. Understanding the dual role of murine $\gamma\delta$ T cells in tumour immunosurveillance. European Network of immunology Institutes Summer School. Capo Caccia (Italy), 15-22 May 2011 (Poster presentation)

Schmolka N., Gomes A.Q. and Silva-Santos B. Molecular mechanisms of $\gamma\delta$ T cell differentiation in vivo, EMBO Young Investigator PhD course 2011, Heidelberg (Germany), 26 September-1 October 2011 (Oral presentation)

Communications in National Conferences

Ribot J.C., Coquet J.M., Middendorp S., van der Horst G., Xiao Y., Babala N., Neves J.F., Pennington D.J., Jacobs H.B., Borst J. and Silva-Santos B. CD70 on dendritic and epithelial cells in the thymic medulla promotes CD4⁺ regulatory T cell development via CD27. Thymus Workshop of the Portuguese Society for Immunology (Porto), 14 October 2011 (Poster Presentation).

Lança T, Correia DV, Mavilio D, Gomes A.Q.^{*} and Silva-Santos B^{*}. The NKG2D and NCR receptors are critical for tumour recognition by human $\gamma\delta$ T cells, 6th National Meeting of the Health Sciences and Technologies, Lisbon (Portugal), 20-22 October 2011 (Poster presentation).

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. CD70 on dendritic and epithelial cells in the thymic medulla promotes CD4⁺ regulatory T cell development via CD27. XXXVII Annual Meeting of the Portuguese Society for Immunology (Oeiras), 29-30 November 2011 (Oral Presentation).

Lança T.*, Rei M.* , Pennington D.J. and Silva-Santos B. Understanding the dual role of murine $\gamma\delta$ T cells in tumour immunesurveillance. XXXVII Annual Meeting of the Portuguese Society of Immunology, Oeiras, Portugal, 29-30 November 2011 (Poster presentation)

Schmolka N., Gomes A.Q. and Silva-Santos B. Molecular mechanisms of differentiation of pro-inflammatory $\gamma\delta$ T-cell subsets. XXXVII Annual Meeting of the Portuguese Society of Immunology, Oeiras (Portugal), 29-30 November 2011 (Poster presentation).

Correia D.V., Fogli M., Hudspeth K., Gomes da Silva M., Mavilio D., Silva-Santos B. Differentiation of human peripheral blood $V\delta 1^+$ T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells. XXXVII Annual Meeting of the Portuguese Society of Immunology, Oeiras (Portugal), 29-30 November 2011 (Poster presentation).

Internationalization

Collaborative work with Drs. Daniel J. Pennington (Blizard Institute, Queen Mary College, London, UK), Adrian Hayday (Cancer Research UK, London, UK), Jannie Borst (The Netherlands Cancer Institute, Amsterdam, The Netherlands), Domenico Mavilio (Istituto Clinico Humanitas, Milan, Italy), Benedita Rocha (Institut Necker, Faculté de Médecine, Université Paris Descartes, France), António Freitas (Institut Pasteur, Paris, France), Carmen Penido (Instituto Oswaldo Cruz, Rio de Janeiro, Brasil).

Advanced teaching

Silva-Santos B. lectured at the GABBA PhD course, Instituto de Biologia Molecular e Celular, Universidade do Porto, Portugal, 22 February 2011.

Silva-Santos B. lectured on “Tumor immunology” at Faculdade de Ciências e Tecnologias, Universidade do Algarve, Faro (Portugal), 29 March 2011.

Silva-Santos B. co-organized the SPI International School of Immunology 2011, Tavira (Portugal), 28 March – 1 April 2011.

Silva-Santos B. co-organized and lectured in the EMBO YIP PhD course “Spotlights on current biology”, EMBL, Heidelberg, Germany, 26-30 September 2011.

Silva-Santos B. and Schmolka N. supervised the student Waleed Al Humaid during a one-month student’s laboratory training under the SCORE programme of the *International Federation of Medical Students’ Association*.

Science and Society

Silva-Santos B. (<http://www.cienciahoje.pt/index.php?oid=50454&op=all>) and his group (<http://www.cienciahoje.pt/index.php?oid=50918&op=all>) featured in two articles in *Ciência Hoje*.

Lança T. lectured in EB23 High School for the Celebration of the International Day of Immunology (29 April 2011).

Master and PhD theses completed

Duarte Saraiva Martins (2011). Targeting $\gamma\delta$ T-lymphocytes for cancer immunotherapy: from novel mechanistic insight to clinical application. MSc Thesis. Faculdade de Medicina, Universidade de Lisboa. Supervisor: B. Silva-Santos.

Molecular Microbiology And Infection Unit

Major interests / Objectives

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. Current work focuses on characterizing the effect of antimicrobial use and human vaccination on the bacterial population. 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 Ramirez, PhD – Associate professor, FMUL

Principal Investigators

José Melo Cristino, MD, PhD – Full Professor, FMUL

Thomas Hänseid, MD, PhD - Assistant Professor, FMUL

João Carriço, PhD - Assistant Investigator, FMUL

Research Team

Sandra Aguiar	Postdoc Fellowship, FCT
Maria João Frias	Postdoc Fellow, FCT
Elisabete Martins	PhD Fellowship, FCT
Margarida Carrolo	PhD Fellowship, FCT
Rosangela Frita	PhD Fellowship, FCT
Patricia Batista	Research Fellowship
Ana Severiano	Research Fellowship
Andreia Horácio	Research Fellowship
Catarina Pato	Research Fellowship
Jorge Miranda	Research Fellowship
Sandra Matos	Research Fellowship
Joana Lopes	Research Fellowship

Keywords/Research Areas

Population biology and epidemiology; Interactions of malaria and other infectious diseases
Diagnostic tools; Bioinformatics

Major scientific achievements

Identification of lineages of *S. pneumoniae* with different invasive disease potential within groups sharing the same serotype.

Description of a stable population of *S. agalactiae* causing invasive neonatal disease in a period of 10 years.

Evaluation of different sampling methodologies to determine confidence intervals of congruence agreement measures and identification of the best approach. Proposal of a new directional agreement metric.

Development of a novel and rapid flow cytometry based assay for antimalarial drug sensitivity testing, using detection of haemozoin without any further reagents.

Synthesis and purification of synthetic haemozoin and from *P. falciparum* culture, and evaluation of its immunomodulatory properties in human and mouse leukocytes. In-vivo effect of haemozoin in a mouse model on re-infection with *Plasmodium* spp. Interactions of haemozoin with M. tuberculosis in an in-vitro model using mouse monocytes. Effect of haemozoin on phagocytosis using a *Salmonella* model.

Recent Most Relevant Publications

Ramirez M., and J. Melo-Cristino. 2010. Expanding the diagnosis of pediatric bacteremic pneumococcal pneumonia from blood cultures to molecular methods: advantages and caveats. Clin. Infect. Dis 51:1050-1052. [IF= 8.186, Times cited 1]

Aguar S. I., F. R. Pinto, S. Nunes, I. Serrano, J. Melo-Cristino, R. Sá-Leão, M. Ramirez, and H. de Lencastre. 2010. Increase of Denmark¹⁴-230 clone as a cause of pneumococcal infection in Portugal within a background of diverse serotype 19A lineages. J. Clin. Microbiol. 48:101–108. [IF= 4.220, Times cited 10]

Francisco, A. P., M. Bugalho, M. Ramirez, and J. A. Carriço. 2009. Global optimal eBURST analysis of multilocus typing data using a graphic matroid approach. BMC Bioinformatics 10:152. [IF= 3.029, Times cited 19]

Silva-Costa, C., F. R. Pinto, M. Ramirez, J. Melo-Cristino, and the Portuguese Surveillance Group for the Study of Respiratory Pathogens. 2008. Decrease in macrolide resistance and clonal instability among *Streptococcus pyogenes* in Portugal. Clin. Microbiol. Infect. 14:1152-1159. [IF= 4.784, Times cited 4]

Hänscheid, T., Egan, T.J., Grobusch, M.P. 2007. Haemozoin: from melatonin pigment to drug target, diagnostic tool, and immune modulator. Lancet Infect. Dis. 7:675-685. [IF= 15.583, Times cited 23]

Ongoing Research Projects

2009/2012 Implications for therapy and disease presentation of the changes triggered by the use of the pneumococcal 7-valent conjugate vaccine, FCT. Coordinator M. Ramirez. PIC/IC/83065/2007, €180 000.

2009/2012 CAREPNEUMO - Combating antibiotic resistance pneumococci by novel strategies based on in vivo and in vitro host-pathogen interactions, European Commission. Participant: M. Ramirez. FP7-HEALTH-2007-223111, €155 100 (total €2 999 999)

2009/2012 Does malaria increase susceptibility to tuberculosis? The role of malaria-pigment induced immune-suppression, FCT Coordinator T. Hänscheid. PIC/IC/83214/2007. €150 000

2008/2012 Population and genomic consequences of vaccination against *Streptococcus pneumoniae*, FCT. Coordinator M. Ramirez. PTDC/SAU-ESA/64888/2006, €150 778.

2008/2011 A computational biology approach using *Streptococcus pneumoniae* as a model towards an integrative view of bacteria/host interactions and evolution, FCT. Coordinator M. Ramirez. PTDC/SAU-ESA/71499/2006, €94 984.

2008/2011 *Streptococcus pyogenes* invasive disease and antimicrobial resistance – two faces of a changing pathogen, FCT. Coordinator J. Melo Cristino. PTDC/SAU-ESA/72321/2006, €156 195

2010/2012 Malaria drug-resistance: development of a novel, clinically useful drug-sensitivity assay for *Plasmodium* species. Fundação Luso-Americana (LACR awards). Coordinator Thomas Hänscheid. B-A.V-109-09/07 €17 000

Publications in peer review Journals

Costa, S. S., C. Falcão, M. Viveiros, D. Machado, M. Martins, J. Melo-Cristino, L. Amaral, and I. Couto. 2011. Exploring the contribution of efflux on the resistance to fluoroquinolones in clinical isolates of *Staphylococcus aureus*. BMC Microbiol 11:241. (Journal IF: 2.960, Citations: 0)

Narciso, A., F. Nunes, T. Amores, L. Lito, J. Melo-Cristino, and A. Duarte. 2011. Persistence of uropathogenic *Escherichia coli* strains in the host for long periods of time: relationship between phylogenetic groups and virulence factors. Eur J Clin Microbiol Infect Dis (Journal IF: 2.631, Citations: 0)

Carreiro, A. V., O. Anunciação, J. A. Carriço, and S. C. Madeira. 2011. Prognostic prediction through biclustering-based classification of clinical gene expression time series. J Integr Bioinform 8:175 (Journal IF: NA, Citations: 0)

Severiano A., F. R. Pinto, M. Ramirez, and J. A. Carriço. 2011. Adjusted Wallace as a measure of congruence between typing methods. J Clin Microbiol 49:3997-4000 (Journal IF: 4.220, 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 (Journal IF: 4.220, Citations: 0)

Severiano A., J. A. Carriço, D. A. Robinson, M. Ramirez, and F. R. Pinto. 2011. Evaluation of jackknife and bootstrap for defining confidence intervals for pairwise agreement measures. PLoS ONE 6:e19539. (Journal IF: 4.411, Citations: 2)

Hänscheid T., R. Romão, M. P. Grobusch, T. Amaral, and J. Melo-Cristino. 2011. Limitation of malaria diagnosis with the Cell-Dyn® analyser: not all haemozoin-containing monocytes are detected or shown. Int J Lab Hematol 33:e14-16. (Journal IF: 1.368, Citations: 0)

Frita R., M. Rebelo, A. Pamplona, A. M. Vigarrio, M. M. Mota, M. P. Grobusch, and T. Hänscheid. 2011. Simple flow cytometric detection of haemozoin containing leukocytes and erythrocytes for research on diagnosis, immunology and drug sensitivity testing. Malar. J 10:74. (Journal IF: 3.49, Citations: 0)

Nordmann P, Picazo JJ, Mutters R, Korten V, Quintana A, Laeuffer JM, Seak JC, Flamm RK, Morrissey I; on behalf of the COMPACT study group. 2011. Comparative activity of carbapenem testing: the COMPACT study. J Antimicrob Chemother. 66:1070-1078 (Journal IF: 4.659, Citations: 4)

Hänscheid T., R. Badura, M. L. Fernandes, F. Antunes, and J. Melo-Cristino. 2011. The case of the disappearing mycobacteria in Ziehl-Neelsen-stained smears. Int. J. Infect. Dis 15:e291. (Journal IF: 2.529, Citations: 0)

Sá-Leão R., F. Pinto, S. I. Aguiar, S. Nunes, J. A. Carriço, N. Frazão, N. Gonçalves-Sousa, J. Melo-Cristino, H. de Lencastre, and M. Ramirez. 2011. Analysis of invasiveness of pneumococcal serotypes and clones circulating in Portugal before widespread use of conjugate vaccines reveals heterogeneous behavior of clones expressing the same serotype. J. Clin. Microbiol 49:1369-1375. (Journal IF: 4.220, Citations: 1)

T. Hänscheid, M. Boura, A. Góis, R. Frita. The issue if the phagocytosis of digestive vacuoles or hemozoin causes immune suppression may be more complex than presented. Blood (e-letter). http://bloodjournal.hematologylibrary.org/content/118/18/4946.abstract/reply#bloodjournal_el_3294. December 23rd, 2011. Accessed 23 January 2012.

Other publications National

C Candeias, C Marcos, T Ferreira, T Hänscheid, J Melo Cristino, A Duarte. Bombas de efluxo em *Pseudomonas aeruginosa*. Importância clínica na terapêutica. Revista Portuguesa de Doenças Infecciosas 6: 66-71, 2011.

Invited Lectures and Seminars

Ramirez, M.. More than meets the eye in the relationship between pneumococci and its bacteriophages. Microbiotec'11. Braga, Portugal, 1-3 December, 2011

Ramirez, M.. Resistencias en *Streptococcus pneumoniae*. XI Congreso nacional Sociedad Española Quimioterapia. Hospital Clínico San Carlos, Madrid, Spain, 5-8 October, 2011.

J.A Carriço. Linked Data for Microbial Typing: are we there yet? Applied Bioinformatics & Public Health Microbiology Conference, Wellcome Trust Genome Campus , Hinxton, Cambridge, UK, 1-3 June, 2011.

J. Melo Cristino. Impacto e panorama actual da resistência aos antimicrobianos nas infecções respiratórias em Portugal. Reunião da Sociedade Portuguesa de Pneumologia. Reunião da Comissão de Infecçologia Respiratória da Sociedade Portuguesa de Pneumologia. Óbidos, Janeiro de 2011.

J. Melo Cristino. Pneumonia adquirida na comunidade: o que mudou desde 2003. Reunião da Sociedade Portuguesa de Pneumologia. Reunião da Comissão de Infecçologia Respiratória da Sociedade Portuguesa de Pneumologia. Óbidos, Janeiro de 2011.

J. Melo Cristino. Pneumococos: a última década. Curso de Infecçologia Pediátrica. Coimbra, Janeiro de 2011.

J. Melo Cristino. O Microbiologista e o Pediatra. Curso de Infecçologia Pediátrica. Hospital Pediátrico de Coimbra. Fevereiro de 2011.

J. Melo Cristino. As Infecções Respiratórias – Um desafio multifactorial. Resistência aos antimicrobianos, situação em Portugal. II Congresso da Fundação Portuguesa do Pulmão. Outubro de 2011.

J. Melo Cristino. Resistência bacteriana aos antibióticos em Portugal. Encontro dos Técnicos de diagnóstico e Terapêutica. Faculdade de Medicina da Universidade de Lisboa, Novembro de 2011.

J. Melo Cristino. A microbiologia das infecções respiratórias: o que mudou nos últimos 10 anos. XXVII Congresso de Pneumologia. Porto, Outubro de 2011

Communications in International Conferences

E.R. Martins, J. Melo-Cristino and M. Ramirez. 2011. Clonal analysis of the invasive group B streptococcal population in non-pregnant adults in Portugal. XVIII Lancefield International Symposium, Palermo, Italy, 4-8 September.

E.R. Martins, A. Andreu, T. Juncosa, J. Bosch, J. Melo-Cristino and M. Ramirez 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 streptococcal neonatal infection in Barcelona area: 18-year surveillance. XVIII Lancefield International Symposium, Palermo, Italy, 4-8 September.

S. S. Costa, C. Mourato, M. Viveiros, J. Melo-Cristino, L. Amaral, I. Couto 2011. Description of a novel pC194-family plasmid carrying the smr efflux pump gene (C1-617). 51st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, IL, 17-20 September.

A. Horacio , J. Miranda, S. Aguiar, M. Ramirez, J. Melo-Cristino, the Microbiology and Pediatric pneumococcal working group. 2011. After 7 years of PCV7 (7-valent pneumococcal conjugate vaccine) PCV13 still covers the majority of invasive pneumococcal disease (IPD) in Portugal

(G3-778). 51st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, IL, 17-20 September, 2011.

C. Pato, A. Friães, M. Ramirez, J. Melo-Cristino. 2011. Molecular characterization and antimicrobial resistance of *Streptococcus pyogenes* causing skin and soft tissue infections in Portugal. XVIII Lancefield International Symposium, Palermo, Italy, 4-8 September.

A. Friães, J. Lopes, M. Ramirez, J. Melo-Cristino. 2011. Molecular changes in *Streptococcus pyogenes* invasive isolates recovered during ten years in Portugal. XVIII Lancefield International Symposium, Palermo, Italy, 4-8 September.

A. Friães, C. Silva-Costa, F. Pinto, M. Ramirez, J. Melo-Cristino. 2011. Identification of clones with enhanced invasive capacity among Group A Streptococci isolated in Portugal. XVIII Lancefield International Symposium, Palermo, Italy, 4-8 September.

F.R. Pinto, P.A. Batista, M. Ramirez. 2011. Asymmetry of age group sizes contributes to high child carriage and leads to the underestimation of pneumococcal transmission dynamics in adults (H08). 10th European Meeting on the Molecular Biology of the Pneumococcus (Europneumo), Amsterdam, Netherlands, 23-26 June.

M.S.M. Carrolo, F.R. Pinto, J. Melo-Cristino, M. Ramirez. 2011. Pherotype influences biofilm growth and recombination in *Streptococcus pneumoniae* (P11). 10th European Meeting on the Molecular Biology of the Pneumococcus (Europneumo), Amsterdam, Netherlands, 23-26 June.

M.J.R. Frias, J. Melo-Cristino, M. Ramirez. 2011. Pneumococcal phage lysins are targeted to the cell wall independently of holin activity but activated by holin induced membrane depolarization. 10th European Meeting on the Molecular Biology of the Pneumococcus (Europneumo), Amsterdam, Netherlands, 23-26 June.

M. Carrolo, M.J. Frias, F.R. Pinto, J. Melo-Cristino, M. Ramirez. 2011. Lysogenic phages promote pneumococcal biofilm development (O189). 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milan, Italy, 7-10 May.

S. Preziuso, M. Pinho, A.R. Attili, J. Melo-Cristino, M. Ramirez, V. Cuteri. 2011. The streptokinase gene as a candidate target for differentiation between *Streptococcus dysgalactiae* subsp. *equisimilis* causing infections in humans and horses (P980). 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milan, Italy, 7-10 May.

A. Tavares, M. Miragaia, R. Mato, J. Rolo, J. Melo-Cristino, L.M. Lito, F. Martins, E. Gonçalves, G. Ribeiro, L. Boaventura, J. Amorim, R. Campinha, A. Fonseca, M. Guimarães, M. Gonçalves, A.M. Costa, J. Mairos, S. Francisco, M.A. Guimarães, C. Lameiras, M. Ribeiro, L. Branco, D. Tuna, A. Faustino, M.T. Vaz, M. Gião, P. Paixão, C. Febra, M.A. Read, M.J. Soares, M.J. Nunes, A. Coutinho, M. Carvalho, T. Sardinha, L. Sancho, G. Sousa, P. Correia, R.M. Barros, C. Gouveia, M. Pinto, M.J. Brito, I. Daniel, G.C. Ferreira, A. Morais, I. Valadares, H. de Lencastre. 2011. High prevalence of hospital-associated *Staphylococcus aureus* epidemic clones in the community in Portugal: evidence for blurring of community/hospital boundaries (O350). 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milan, Italy, 7-10 May.

E. Martins, M. Gimenez, M. Sierra, M. Lite, J. Melo-Cristino, M. Ramirez 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 streptococcal neonatal infection in the Barcelona area: 18-year surveillance (O357). 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milan, Italy, 7-10 May.

M. Pinho, M. Ramirez, J. Melo-Cristino on behalf of the Portuguese group for the study of streptococcal infections. 2011. Multilocus sequence typing characterisation of *Streptococcus dysgalactiae* subsp. *equisimilis* isolates from Portugal (P1715). 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milan, Italy, 7-10 May.

T. Hänscheid. 2011. Novel methods to diagnose malaria by detecting hemozoin in intra-erythrocytic parasites -possible limitation. Oral presentation MO22. Sixth EDCTP Forum, Addis Abba, Ethiopia, 9-12 October 2011

J.J. Mendes, L. Prata, C. Vilela, J. Neves, N. Candeias, P. Cavaco Silva, J. Melo Cristino. Epidemiological survey of diabetic foot infections in Lisbon. (P 1082). European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milão, Itália, 7 a 10 de Maio de 2011.

C. Caneiras, F. Calisto, A. Narciso, S. Arriaga, J. Melo Cristino, A. Duarte. Resistance and virulence characterisation of CTX-M15 and KPC-3 *Klebsiella pneumoniae* clinical isolates. (P 1043). European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milão, Itália, 7 a 10 de Maio de 2011.

C. Caneiras, F. Calisto, R. Moura, M. Augusto, G. Da Silva, J. Melo Cristino, A. Duarte. Multicentre evaluation of in vitro activity of tigecycline against extended-spectrum beta-lactamases and multidrug-resistant *Enterobacteriaceae* clinical isolates. (R 2314). European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) and 27th International Congress of Chemotherapy (ICC), Milão, Itália, 7 a 10 de Maio de 2011.

Communications in National Conferences

R. Frita, D. Carapau, P. Liehl, A. Góis, M.M. Mota, T. Hänscheid. 2011. Pigmento Malarico como possível adjuvante numa vacina de malária com esporozoítos irradiados (P51). IV Congresso Pandemias na Era da Globalização. Coimbra, Portugal, 16-18 June.

M Rebelo, Sousa C, Machado M, Lopes D, Lopes, T, Gardner R, Hanscheid T. 2011. Pigmento malarico: um outro olhar sobre Plasmodium spp., Poster number 50, 4º Congresso Pandemias na Era da Globalização, Coimbra, Portugal, 16-18 June

Márcia Boura, Ana Góis, Thomas Hänscheid. 2011. A imunomodulação do pigmento malárico (hemozoína) aumenta a susceptibilidade para infeções bacterianas disseminadas? 12º Encontro de Atualização em Infeciologia. Porto, Portugal . 25-28 October.

A. Francisco, C. Vaz, P. Monteiro, M. Ramirez, J. Carriço. 2011. Fooled by trees: when simple can be misleading (PS4:1). Microbiotec'11. Braga, Portugal, 1-3 December.

AS Moreira, C Coutinho, P Azevedo, L Lito, J Melo Cristino, I Sá-Correia. Pulmonary co-infection by *Burkholderia dolosa* and *Burkholderia cenocepacia* and clonal variation during long-term colonization of a cystic fibrosis patient. (274). Microbiotec 11. Braga, 1 a 3 de Dezembro de 2011.

S Francisco, D Machado, M Viveiros, J Ramos, T Pacheco, J Melo Cristino, LM Lito, I Portugal, L Amaral, I Couto. Application of molecular methods for the direct detection of MDR-TB. (372). Microbiotec 11. Braga, 1 a 3 de Dezembro de 2011.

32nd Annual Congresso f the European Society of Mycobacteriology. P127. Lübeck, Alemanha, Junho de 2011.

D Espadinha, NA Faria, M Miragaia, L Lito, L Monteiro, J Melo Cristino, H de Lencastre. Massive clonal replacement and increase in MRSA prevalence in a major portuguese central hospital. (384). Microbiotec 11. Braga, 1 a 3 de Dezembro de 2011.

C Mourato, SS Costa, M Viveiros, C Falcão, J Melo Cristino, L Amaral, I Couto. Multidrug resistance in methicillin-resistant *Staphylococcus aureus* (MRSA) clinical isolate mediated by efflux pump QacA. (391). Microbiotec 11. Braga, 1 a 3 de Dezembro de 2011.

SS Costa, C Mourato, M Viveiros, J Melo Cristino, L Amaral, I Couto. Description of a novel staphylococcal pC194-Family plasmid carrying the *smr* efflux pump gene. (404). Microbiotec 11. Braga, 1 a 3 de Dezembro de 2011.

Internationalization

- We have started a collaboration with Italian and German colleagues on animal streptococci.
- We are continuing work with other European, South American and Indian colleagues within the context of CAREPNEUMO.
- Laboratory capacity building in Africa, within the CANTAM (Central African Network for Tuberculosis, AIDS and Malaria) network, involving Cameroon, Gabon and Congo. With special emphasis on low cost solutions for laboratories to conduct routine and research work with *Mycobacterium tuberculosis*.
- 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
- Sensitivity testing using flow cytometric principles to detect hemozoin – set-up of a 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

Advanced teaching

J. Melo Cristino, T. Hänscheid and M. Ramirez. Master Course in Emerging Infectious Diseases 2009-2010, Faculty of Medicine of Lisbon. Responsible for the organization of a module in Microbiology and teaching of multiple courses.

Master and PhD thesis completed

Sandra Aguiar (2011) “Molecular epidemiology of *Streptococcus pneumoniae*: impacto f PCV7 in the pneumococcal population responsible for invasive pediatric infections” Doutoramento em Ciências e Tecnologias da Saúde, Especialidade de Microbiologia, Faculdade de Medicina, Universidade de Lisboa, Supervisor: Mario Ramirez

Maria João Frias (2011) “Lysis strategy of *Streptococcus pneumoniae* bacteriophages: Mechanisms and host implications” Doutoramento em Ciências e Tecnologias da Saúde, Especialidade de Microbiologia, Faculdade de Medicina, Universidade de Lisboa, Supervisor: Mario Ramirez

Elisabete Martins (2011) “*Streptococcus agalactiae* causing human infections” Doutoramento em Ciências e Tecnologias da Saúde, Especialidade de Microbiologia, Faculdade de Medicina, Universidade de Lisboa, Supervisor: Mario Ramirez

Margarida Carrolo (2011) “New insights into the sociomicrobiology of *Streptococcus pneumoniae*: exploring biofilm formation”, Doutoramento em Ciências e Tecnologias da Saúde, Especialidade de Microbiologia, Faculdade de Medicina, Universidade de Lisboa, Supervisor: Mario Ramirez

Catarina Pato (2011) “*Streptococcus pyogenes* como agente de infecção da pele e tecidos moles”, Mestrado em Microbiologia Aplicada, Faculdade de Ciências, Universidade de Lisboa. Supervisor: Mario Ramirez

Andreia Horácio (2011) “Infecção pneumocócica invasiva no adulto em Portugal em 2008 e 2009”, Mestrado em Microbiologia Aplicada, Faculdade de Ciências, Universidade de Lisboa. Supervisor: José Melo Cristino

Jorge Diamantino Miranda (2011) “Infecção pneumocócica invasiva no idoso em Portugal em 2008 e 2009”, Mestrado em Microbiologia Aplicada, Faculdade de Ciências, Universidade de Lisboa. Supervisor: José Melo Cristino

Molecular Parasitology Unit

Major interests / Objectives

The *Plasmodium* parasite alternates between mosquito vector and vertebrate host. Transmission relies on highly specialized parasite stages that once inside the new host, quickly give rise to fundamentally different parasite forms adapted to their new environments. This sudden transition between hosts requires a rapid molecular and cellular re-programming, which may only be realized by parasites that are in a state of molecular preparedness, while maintaining a quiescent state until transmission occurs. Our unit explores the transcriptional and post-transcriptional gene expression control mechanisms during the transmission of the rodent malaria parasite from and to the mammalian host.

Head of Unit

Gunnar Mair, PhD - Assistant Professor

Principal Investigators

Celine Carret, PhD (left in March 2011)

Research Team

Ana Guerreiro, MSc	Research Fellow, FCT
Natalia Kozlova, PhD	Post Doctoral Fellowship, FCT
Marcelo Perreira	Master's Student (left October 2011)
Jorge Santos, MSc	PhD Fellowship, FCT
Patricia Silva, PhD	Post Doctoral Fellowship, FCT

Keywords/Research Areas

Malaria; Transmission; Gene expression control; RNA binding protein

Major scientific achievements

A universal feature of sexual development is the storage of mRNA to provide coding potential for proteins during early post-fertilisation development. Stabilisation of quiescent mRNA pools in *Plasmodium* gametocytes depends on an evolutionarily conserved protein core. Gene deletion mutants of key components of the mRNP (DOZI, CITH) are fertilization-competent, but zygotes fail to develop further. Through RNA pull down and immunoprecipitation, and global expression profiling of mutants we highlighted crucial repressors of maternally supplied mRNAs. Our data define P bodies as critical components for development in the initial stages of *Plasmodium*

mosquito infection. During transmission from mosquito vector to mammalian host we have identified the RNA binding protein Pumilio as a regulator of development; in its absence sporozoites develop prematurely into liver stage forms with accompanying changes in gene expression profiles that are typical of liver stage development.

Recent Most Relevant Publications

Laurentino EC, Taylor S, Mair GR, Lasonder E, Bartfai R, Stunnenberg HG, Kroeze H, Ramesar J, Franke-Fayard B, Khan SM, Janse CJ, Waters AP. Experimentally controlled down regulation of the histone chaperone FACT in *Plasmodium berghei* reveals that it is critical to male gamete fertility. *Cell Microbiol.* 2011 Dec;13(12):1956-74. (Journal IF: 5.625, Citations: 0)

Gomes-Santos CSS, Braks JAM, Prudêncio M, Carret CK, Gomes ARB, Pain A, Feltwell T, Khan SM, Waters AP, Janse CJ, Mair GR, Mota MM. Transition of *Plasmodium* Sporozoites into Liver-Stage Forms is Regulated by the RNA Binding Protein Pumilio. *PLoS Pathogens* 2011, 7(5):e1002046. (Journal IF: 9.079, Citations: 1)

Mair GR, Lasonder E, Garver LS, Franke-Fayard B, Carret CK, Wiegant J, Dirks R, Dimopoulos G, Janse CJ, Waters AP. An evolutionarily ancient P body controls sexual development in the protozoan *Plasmodium*. *PLoS Pathog.* 2010 Feb 12;6(2):e1000767. (Journal IF: 9.079, Citations: 15)

Tonkin CJ, Carret CK, Duraisingh MT, Voss TS, Ralph SA, Hommel M, Duffy MF, Silva LM, Scherf A, Ivens A, Speed TP, Beeson JG, Cowman AF (2009) Sir2 paralogs cooperate to regulate virulence genes and antigenic variation in *Plasmodium falciparum*. *PLoS Biology* Apr 14;7(4):e84. (Journal IF: 12.916, Citations: 19)

Baum J, Papenfuss AT, Mair GR, Janse CJ, Waters AP, Cowman AF, Crabb BS, de Konig-Ward T. Molecular genetics and comparative genomics suggests RNAi is not functional in malaria parasites. *Nucleic Acid Research* 2009 Jun;37(11):3788-3798 (Journal IF: 7.836, Citations: 24)

Ongoing Research Projects

2012/2014 Pumilio-regulated gene expression of malaria during mosquito vector to mammalian host transmission, FCT. Coordinator: GR Mair PTDC/SAU-MIC/122082/2010; €114000

2010/2012 Transcriptional regulation of *Plasmodium* during host-vector transmission, FCT. Coordinator: GR Mair PTDC/BIA-BCM/105610/2008; €19710

2010/2012 Non coding RNA in malaria parasites, FCT. Coordinator: CK Carret PTDC/SAU-GMG/104392/2008; €103581

2010/2012 Unravelling the secrets of *Plasmodium* liver stage: a multi-directional approach. FCT. Coordinator MM Mota PTDC/SAU-GMG/100313/2008; €199943; CK Carret Bolseiro 10% (until March 2011)

Publications in peer reviewed Journals

Leah Mwai, Abdi Diriye, Victor Masseno, Steven Muriithi, Theresa Feltwell, Jennifer Musyoki, Jacob Lemieux, Avi Feller, Gunnar R. Mair, Kevin Marsh, Chris Newbold, Alexis Nzila, Céline K. Carret. Genome wide adaptations of *Plasmodium falciparum* in response to Lumefantrine selective drug pressure, PLoS ONE accepted for publication. (Journal IF: 4.411, Citations: 0)

Gajjar DU, Pal AK, Santos JM, Ghodadra BK, Vasavada AR. Severe pigmented keratitis caused by *Cladorrhinum bulbiliosum*. Indian Journal of Medical Microbiology 2011, 29:434-437. (Journal IF: 1.006, Citations: 0).

Laurentino EC, Taylor S, Mair GR, Lasonder E, Bartfai R, Stunnenberg HG, Kroeze H, Ramesar J, Franke-Fayard B, Khan SM, Janse CJ, Waters AP. Experimentally controlled down regulation of the histone chaperone FACT in *Plasmodium berghei* reveals that it is critical to male gamete fertility. Cell Microbiol. 2011 Dec;13(12):1956-74. (Journal IF: 5.625, Citations: 0)

Gomes-Santos CSS, Braks JAM, Prudêncio M, Carret CK, Gomes ARB, Pain A, Feltwell T, Khan SM, Waters AP*, Janse CJ, Mair GR, Mota MM. Transition of *Plasmodium* Sporozoites into Liver-Stage Forms is Regulated by the RNA Binding Protein Pumilio. PLoS Pathogens 2011, 7(5):e1002046

McVeigh P, Mair GR, Novozhilova E, Day A, Zamanian M, Marks NJ, Kimber MJ, Day TA, Maule AG. Schistosoma I/Lamides – A new family of bioactive helminth neuropeptides. Int J Parasitol. 2011 Jul;41(8):905-13. Epub 2011 Apr 21.

Invited Lectures and Seminars

Santos, J. M. Invited lecture under the subject of Regulation and Differentiation class, Molecular Biology and Genetics MSc Course, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal, May 26, 2011

Mair, G.R. Seminar at Department für Infektionsbiologie, Heidelberg University, Heidelberg, Germany, May 23, 2011

Communications in International Conferences

Kozlova, N.V., Lasonder E., Mair G.R. Mechanisms of translational repression in *Plasmodium berghei*, Plataforma Ibérica da Malária, 3rd meeting, Lisbon, Portugal, June 23-24, 2011 (Oral presentation)

Santos, J. M., Rao, P. N., Guerreiro, A., Carret, C. K., Templeton, T. J., Mair, G. R. Molecular characterisation of *Plasmodium* translationally repressed gene products during sexual development, 7th BioMalPar Conference, Heidelberg, Germany, May 16-18, 2011 (Poster presentation)

Rao, P., Santos, J. M., Mair, G., Templeton, T. Translational repression of the CPW-WPC family of genes in the malarial parasite *Plasmodium*, XXII MPM, Woods Hole, USA, September 11-15, 2011 (Poster presentation)

Prizes, honours and awards

Wellcome Trust Bursary to Jorge M. Santos for the attendance of the workshop “Working with Parasite Database Resources”, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK. October 3-7, 2011.

Fundação para a Ciência e a Tecnologia subsidies to Jorge M. Santos for a collaborative short stay at the Leiden Malaria Research Group, Leiden University Medical Center, Leiden, The Netherlands, November 1-December 18, 2011.

Advanced teaching

Santos, J. M. lectured under the subject of Regulation and Differentiation class, Molecular Biology and Genetics MSc Course, Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal. May 26, 2011.

Master thesis completed

Marcelo Luís Monteiro Pereira (October 17, 2011) Localization of mRNA storage complexes in *Plasmodium berghei* throughout the life cycle. Mestrado em Microbiologia Aplicada, Faculdade de Ciências da Universidade de Lisboa. Supervisor: Gunnar Mair

Nutrition And Metabolism Unit

Major interests / Objectives

The Unit focus is: clinical and translational biomedical/nutritional research in nutrition/metabolism. Topics are in tune with investigators' backgrounds/interests. Disease management, nutrition/life-style related risk factors always prevail, e.g. nutrition and cancer, nutrition and Quality of Life, metabolic dysfunction, body composition and genetic predisposition for cachexia, nutrients and disease modulation/therapy/prognosis, obesity, fatty liver and insulin resistance. We also 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 cancer and alcoholic/non-alcoholic liver disease.

Head of Unit

Maria Ermelinda Camilo, MD, PhD – retired since June 2008 from Auxiliary Professor FMUL and Consultant of Gastroenterology HSM, remains voluntarily as Head of Unit.

Principal Investigators

Helena Cortez-Pinto, MD, PhD - Consultant of Gastroenterology HSM, Associate Professor with “Agregação” FMUL.

Isabel Monteiro-Grillo, MD, PhD - Director of the Oncology Department and of the Radiotherapy Service HSM.

Paula Ravasco, PhD - Auxiliary Professor FMUL.

Research Team

Catarina Sousa Guerreiro	MsC and PhD in Nutrition, Assistant FMUL
Mariana Verdelho Machado	MD, Specialist in Gastroenterology HSM; PhD student in the PhD Doctoral Programme for Advanced Medical Education (Doctoral Programme for Physicians-FCT, Champalimaud Foundation, Gulbenkian)
Carolina Boléo-Tomé	Research dietician
Ana Isabel Almeida	Research dietician
Catarina Ferreira	Research dietician

Keywords/Research Areas

- Hepatology: steatohepatitis, insulin resistance, alcoholic liver disease;
- Cancer: nutrition, outcomes, cachexia, radiotherapy.

Major scientific achievements

The only Research Nutrition and Metabolism Unit 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, e.g. *Hepatology/Journal of Hepatology/The Oncologist/Journal of Clinical Oncology/The Lancet Oncologist*, and in the internationalization with major roles in international bodies, lectures in major national and 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 Unit is increasingly involved in advanced teaching: chosen for the integrated Master Degree in Medicine, Nutrition Master and PhD Programs.

Recent Most Relevant Publications

Ratzliff 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: 9.334, Citations: 31)

Guerreiro CS, Cravo ML, Brito M, Vidal PM, Fidalgo PO, Leitão CN. (2007). The D1822V APC polymorphism interacts with fat, calcium, and fiber intakes in modulating the risk of colorectal cancer in Portuguese persons. *American Journal of Clinical Nutrition* **85**: 1592-1597 (Journal IF: 6.606, Citations: 11)

Marques-Vidal P, Ravasco P, Camilo ME. (2006). Foodstuffs and colorectal cancer risk: A review. *Clinical Nutrition* **25**: 14-36 (Journal IF: 3.410, Citations: 24)

Machado M, Cortez-Pinto H. (2006). Non-alcoholic steatohepatitis and metabolic syndrome. *Current Opinion in Clinical Nutrition and Metabolic Care* **9**: 637-642 (Journal IF: 4.333, Citations: 40)

Plauth M, Cabré E, Riggio O, Assis-Camilo M, Pirlich M, Kondrup J, Ferenci P, Holm E, von Dahl S, Müller MJ, Nolte W (2006). ESPEN Guidelines on Enteral Nutrition: Liver disease. *Clinical Nutrition* **25**: 285-294 (Journal IF: 3.410, citations: 94)

Ongoing Research Projects

HEPATOLOGY

PI: Helena Cortez-Pinto

2008/2011 Nutraceuticals: a shield against chronic disease? Contribution for the rationale of a new therapeutic option. Coordinator: A. Sousa-Guerreiro. PTDC/SAU-OSM/66323/2006, total € 170.000.

2009/2012 Prevalence and severity of fatty liver in morbid obesity: correlation and mechanisms related with the role of ectopic fat in insulin resistance. Coordinator: H.Cortez-Pinto. PTDC/SAU-OSM/100878/2008, total €139.010.

2010/2013 Targeting microRNA-34, a Potential Link between Apoptosis and Nonalcoholic Fatty Liver Disease Pathogenesis. Coordinator: C.M. Rodrigues. PTDC/SAU-ORG/111930/2009, total € 120.000.

2009/2011 Efficacy, Safety and Tolerability of Levodopa-Carbidopa Intestinal Gel in Levodopa-Responsive Parkinson's Subjects. Our participation pertains to the placement of the PEG/PEJ device. Coordinator: Joaquim Ferreira. Industry sponsored.

CANCER/ RADIOTHERAPY

PI: Isabel Monteiro Grillo

Collaborations in Research Projects with the Faculty of Sciences. Coordinator: Ducla Soares

Salvage External Beam Radiotherapy after Biochemical Recurrence or following prostatectomy (differs) in prostatectomized patients. Coordinator: I. Monteiro Grillo. (No funding)

Combined HDR BT and 3D-CRT in intermediate and high risk prostate cancer patients: a dose escalation method. Coordinator: I. Monteiro Grillo. (No funding)

NUTRITION AND CANCER

PI: Paula Ravasco

2009/2012 Nutrition in Cancer: relevance and guidelines for clinical practice. Coordinator: Paula Ravasco. (No funding)

2008/2012 Body composition, metabolic pattern and cancer histological aggressiveness,. Coordinator: Paula Ravasco. (No funding)

2003/2012 Cancer: metabolic dysfunction, nutrition intervention, Quality of Life and prognosis. Coordinator: Paula Ravasco. (No funding)

2011/2014 How to evaluate body composition in cancer: validation of 3 methods for clinical use. Coordinator: Paula Ravasco. (No funding)

Publications in peer review Journals

Machado MV, Cortez-Pinto H (2011) Osteopontin: A Missing Link between Hedgehog Signaling and Fibrosis in Nonalcoholic Steatohepatitis. Editorial. *Hepatology* 53: 382-384. (Journal IF: 10.885)

Machado MV, Cortez-Pinto H (2011) The dark side of sports: using steroids may harm your liver. *Liver International* 31: 280-281 (Journal IF: 3.840)

Machado MV, Cortez-Pinto H (2011). No need for a large belly to have NASH. *J Hepatol* 54:1090-1093 (Journal IF: 9.334)

Ferreira, DM, Castro R, Machado MV, Evangelista T, Silvestre AR, Costa A, Coutinho J, Carepa F, Cortez-Pinto H, Rodrigues CM (2011). Apoptosis and insulin resistance in liver and peripheral tissues of morbidly obese patients is associated with different stages of non-alcoholic fatty liver disease. *Diabetologia* 54:1788-1798 (Journal IF: 6.973)

Machado MV, Cortez-Pinto H (2011). Cell death and nonalcoholic steatohepatitis: where is ballooning relevant? *Expert Rev Gastroenterol Hepatol* 5:213-222 (new journal, no IF yet)

Machado MV, Oliveira AG, Cortez-Pinto H (2011). Hepatic steatosis in hepatitis B virus infected patients: Meta-analysis of risk factors and comparison with hepatitis C infected patients. *Journal of Gastroenterology and Hepatology* 26:1361-1367 (Journal IF: 2.410)

Machado MV, Gonçalves G, Carepa F, Coutinho J, Costa A, Cortez-Pinto H (2011). Impaired renal function in morbid obese patients with nonalcoholic fatty liver disease. *Liver International* Aug 31. doi: 10.1111/j.1478-3231.2011.02623.x. [Epub ahead of print] (Journal IF: 3.840)

Antunes MI, Bujor L, Monteiro Grillo I (2011) Anal canal plasmacytoma – an uncommon presentation site. *Reports of Pratical Oncology and Radiotherapy* 16, 36-39 (new Journal, no IF)

Ferreira M, Amado A, Jorge M, Monteiro Grillo I (2011) Stevens Johnson Syndrome in a patient undergoing gynaecological brachytherapy: An association or an incident?. *Reports of Pratical Oncology and Radiotherapy* 16, 115-117 (new Journal, no IF)

Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G, Mellar D, Muscaritoli M, Ottery F, Radbruch L, Ravasco P, Walsh D, Wilcock A, Kaasa S, Baracos V (2011). Definition and classification of cancer cachexia: an international consensus statement. *The Lancet Oncology* 12: 489-495 (Journal IF: 17.764)

Ravasco P (2011). Nutrition support in head and neck cancer: how and why? Invited Special Review *AntiCancer Drugs* 22: 639-646 (Journal IF: 2.376)

Marques-Vidal P, Marcelino G, Ravasco P, Oliveira JM, Paccaud F (2011). Increased body fat is independently and negatively related with cardiorespiratory fitness levels in normal weight children and adolescents. *European Journal of Cardiovascular Prevention and Rehabilitation* 17: 649-654 (Journal IF: 2.638)

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: 5.826)

Marques-Vidal P, Paccaud F, Ravasco P (2011). Obesity is underdiagnosed and undertreated in the Portuguese population. *Archives of Internal Medicine* 171:1511-1512 (Journal IF: 10.639)

Marques-Vidal P, Paccaud F, Ravasco P (2011). Ten year trend in overweight and obesity in the adult Portuguese population, 1995 to 2005". *BMC Public Health* 11: 772-779 (Journal IF: 2.364)

Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo ME, Ravasco P (2011). Validation of the Malnutrition Universal Screening Tool (MUST) in cancer. *British Journal of Nutrition* Epub ahead of print Dec 6:1-6 (Journal IF: 3.072)

Almeida AI, Correia M, Camilo M, Ravasco P (2011). Nutritional risk screening in surgery: valid, feasible, easy! *Clinical Nutrition* Epub ahead of print Nov 1:1-6, <http://dx.doi.org/10.1016/j.clnu.2011.10.003> (Journal IF: 3.410)

Other publications International

Jonkers – Schuitema CF, Camilo M E: Nutrition therapy for neurological disorders and Sobotka L, Camilo M E: Metabolic complications of parenteral nutrition. In: Luboš Sobotka (Eds). *ESPEN Book - Basics in Clinical Nutrition*, 4th Edition, Prague, Czech Republic. Galen press (ISBN 978-80-7262-821-6 September 2011)

Machado M, Cortez-Pinto H. Genética e Fígado gordo não alcoólico. In: Viana DL (Ed). *Doença Hepática Gordurosa não alcoólica. Esteato-hepatite e suas correlações*. São Caetano do Sul, Brasil, 2011 (ISBN 978-85-7728-277-2).

Ravasco P. Counselling and Intervention (2011). In: Halteren HV, Jatoi A (Eds). *ESMO Handbook of nutrition and cancer*. Switzerland: ESMO Press: 57-63 (ISBN: 978-88-906359-0-8).

Planas M, Alvarez J, Ravasco P. “Ética en nutrición especializada (2011). In: Prado RA, Márquez HA, Moya DA (Eds.). *Nutrición Enteral y Parenteral*, 2a edición. McGraw-Hill InterAmericana Editores, S.A. de C.V.: 49-63.

Ravasco P. Nutrition in Cancer (2011). In: Ayhan A, Gultekin M and Dursun P, (Eds). *Textbook of Gynaecological Oncology (Official ESGO Reference Book)*. Ankara: Gunes Publishing: 102-108.

Other publications National

Duarte MJ, Guerreiro CS, Bernardo B, Caldas de Almeida M, Mendes L (2011). Avaliação do estado nutricional de indivíduos com demência. *APNEP V*: 80-87.

Invited Lectures and Seminars

Cortez-Pinto H. NAFLD. Evaluating of disease severity and prognosis in chronic liver diseases. Monothematic Conference of the European Association for the Study of the Liver (EASL), Nice, France, 28-29 January 2011.

Cortez-Pinto H. Increased burden of alcoholic liver disease in 2011. 13th ESBRA (European Society for Biochemical Research on Alcoholism), Vienna, Austria, 4-7 September 2011.

Cortez-Pinto H. NAFLD: Long-term prognosis in liver diseases and impact of treatment. 19th United European Gastroenterology Unit (UEGW), Stockholm, Sweden, 22-26 October, 2011.

Cortez-Pinto H. Lunch Session: Update on NAFLD. 19th United European Gastroenterology Unit (UEGW), Stockholm, Sweden, 22-26 October, 2011.

Cortez-Pinto H. Lunch Session: Update on nonalcoholic fatty liver disease. 19th United European Gastroenterology Unit (UEGW), Stockholm, Sweden, 22-26 October, 2011.

Cortez-Pinto H. Lunch Session: How to manage NAFLD/NASH. 19th United European Gastroenterology Unit (UEGW), Stockolm, Sweden, 22-26 October, 2011.

Cortez-Pinto H. Estudo epidemiológico do fígado gordo em Portugal. Reunião dos Clínicos Gerais. Gaia, Portugal, 19 February 2011.

Cortez-Pinto H. Uso de Albumina no contexto de Urgência. Reuniões da Urgência do Hospital de Santa Maria, Lisboa, Portugal, 24 February 2011.

Cortez-Pinto H. Esteatohepatite não alcoólica. O que há de novo. 4º Congresso Português de Hepatologia, Aveiro, Portugal, 10-12 March 2011

Cortez-Pinto H. Muito peso, pouca saúde: benefícios de exercício para a saúde do fígado. Desporto e Saúde do Fígado, Porto, Portugal, 18 March 2011

Cortez-Pinto H. Cirrose biliar primária: O que há de novo? II Congresso de Auto-imunidade, Almancil, Portugal, 29 April 2011.

Cortez-Pinto H. Doença hepática na obesidade. A Medicina Familiar e a Endocrinologia, V Jornadas "A Endocrinologia e a Medicina Geral e Familiar" Lisboa, Portugal, 30 April 2011

Cortez-Pinto H. NASH e Ácidos Biliares – Conversa binária. Workshop Fígado e intestino. Semana Digestiva, Estoril, Portugal, June 2011.

Monteiro Grillo I. Moderator at: "Cancro da Mama" and "Módulo IV". Jornadas internacionais de Cirurgia, Faculdade de Ciências Médicas, Lisboa, Portugal, 21 January 2011.

Monteiro Grillo I. "Técnicas de tratamento avançadas" and "Innovation in Adjuvant Radiotherapy for Breast Cancer". 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011

Monteiro Grillo I. Follow-up for Prostate cancer Patients Modern Brachytherapy. Nucletron Prostate Meeting, Sintra, Portugal, 17-19 March 2011

Monteiro Grillo I. Seguimiento del paciente con cancer de próstata, III Congreso de Asociación Latinoamericana de Terapia Radiante Oncológica (ALATRO), Panamá 20-24 June 2011

Monteiro Grillo I. Prostate Cancer Clinical Case Battles, EMUC, Barcelona, Spain 3-6 November 2011.

Ravasco P. Envelhecimento saudável: nutrição e estilos de vida. Academia das Ciências de Lisboa, Lisboa, Portugal, January 4th, 2011.

Ravasco P. The impact of nutritional intervention in cancer patients. Annual Congress of NSKE (Norwegian Society of Clinical Nutrition), Oslo, Norway, January 20th, 2011

Ravasco P. Soja: um real contributo para a saúde? Associação Portuguesa de Dietistas em parceria com a DANONE®, Lisboa, Portugal. January 24th, 2011.

Ravasco P. Nutrição no doente cardíaco e respiratório: problemática da obesidade e subnutrição". Reunião Conjunta de Reabilitação Cardíaca e Respiratória, Tróia, Portugal, March 26th, 2011.

Ravasco P. The impact of nutritional status on Quality of Life: the value of nutritional intervention in cancer patients. 2nd International Conference on Cancer Therapy, Edimburgh, Scotland, March 29th, 2011.

Ravasco P. A patofisiologia do Síndrome Anorexia-Caquexia: uma actualização. Sessão comemorativa dos 55 anos da Unidade Assistência Domiciliária do IPOFG-EPE, Lisboa, Portugal, April 15th, 2011.

Ravasco P. Caquexia Oncológica. X Congresso de Nutrição e Alimentação e II Congresso Ibero-Americano de Nutrição, Lisboa, Portugal, May 13th, 2011.

Ravasco P. Mechanisms of wasting in cancer cachexia. XXIX Congreso Nacional de Oncología promovido pela SMEO (Sociedad Mexicana de Oncología), Ixtapa, Zihuatanejo, México. October 26-29th 2011.

Ravasco P. Impact of nutritional status on Quality of Life: the value of intervention. XXIX Congreso Nacional de Oncología promovido pela SMEO (Sociedad Mexicana de Oncología), Ixtapa, Zihuatanejo, México, October 26-29th, 2011

Ravasco P. Medicina Geral e Familiar: primeira escolha de Especialidade em alunos de Medicina? Encontro Nacional da Associação dos Docentes e Orientadores de Medicina Geral e Familiar (ADSO). Faro, Portugal, November 11-12th, 2011

Ravasco P. Alimentação e Cancro. 4^a Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal, November 25-26th, 2011

Ravasco P. Caquexia oncológica: presente e futuro. 4^a Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 25-26th, 2011

Guerreiro CS. Avaliação de Risco e Estado Nutricional. VI Encontro Nacional das Ciências e Tecnologias da Saúde, Lisbon, Portugal, 20 October 2011

Guerreiro CS. Nutrição e genes em doenças intestinais: Ciclo de Conferências – Encontros com a Ciência na ESTeSL, Lisbon, Portugal, 27 October 2011

Guerreiro CS. A saúde nas nossas mãos – ambiente vs genes – *1^a Aula*. Comemorações oficiais da abertura do ano lectivo 2011-2012 da ESTeSL. Lisbon, Portugal, Setembro 2011

Guerreiro CS. Plano nutricional adaptado ao idoso. Ciclo de Conferências em Cuidados Continuados da Universidade Lusófona. Lisbon, Portugal, 20 September 2011

Guerreiro CS. Nutrição em pacientes disfágicos. Seminário “Criando Iniciativas - Comemorações Dia Europeu da Terapia da Fala. Entroncamento, Portugal, 19 March 2011

Communications in International Conferences

Vale do Gato I, Machado J, Chaves P, Cortez-Pinto H, Guerreiro AS. Comparison of gut microbiota composition between two animal models of non alcoholic steatohepatitis. EASL International Conference 2011, *J Hepatology*, 2011, 54, S363–S534 (Poster presentation)

Ferreira D, Borralho P, Machado MV, Cortez-Pinto H; Rodrigues C, Castro R. Increased expression of microrna-34 in nafld patients and targeting by ursodeoxycholic acid in rat liver. 19th United European Gastroenterology Week - UEGW, Estocolmo, Sweden, 22-26 de Outubro 2011. *Gut*, Supl 2011(Oral presentation).

Vieira C, Machado M, Correia L, Cortez-Pinto H, Velosa J. Ascites: one piece in a diagnostic jigsaw – selected clinical case presentation. 19th United European Gastroenterology Week - UEGW, Estocolmo, Sweden, 22-26 de Outubro 2011. *Gut*, Supl 2011 (Oral presentation).

Machado MV, Ferreira D; Castro D; Silvestre; Evangelista T; Coutinho J; Carepa F; Costa F; Rodrigues C; Cortez-Pinto H. Fatty muscle associates with severity of nonalcoholic fatty liver and insulin resistance: how liver and muscle interplay when facing energy surplus. 19th United European Gastroenterology Week - UEGW, Estocolmo, Sweden, 22-26 de Outubro 2011. *Gut*, Supl 2011 (Poster presentation).

Vieira C, Machado M; Carvalho R, Nobre E, Cortez-Pinto H; Velosa J. Medium to long term results of 100 intragastric balloons placed in 94 patients with morbid obesity. 19th United European Gastroenterology Week - UEGW, Estocolmo, Sweden, 22-26 Outubro 2011 (poster presentation). *Gut*, Supl 2011 (Poster presentation)

Ferreira D, Borralho P, Machado MV, Cortez-Pinto H, Rodrigues C, Castro R. MIR-34/SIRT1 in NALFD patients and targeting by ursodeoxycholic acid in rat liver. AASLD, November 2011, San Francisco USA.. *Hepatology* Supl 2011 (Poster presentation)

Ferreira CN, Rodrigues T, Cortez-Pinto T, Serejo F, Ramalho F, Alexandrino, Velosa F. Acute renal dysfunction at hospital admission in cirrhotics: the new workingparty definition of acute renal injury may not be better in predicting hospital mortality than the conventional value of serum creatinine $\geq 1.5\text{mg/dl}$. AASLD, November 2011, San Francisco USA. *Hepatology* Supl 2011 (Poster presentation)

Ferreira CN, Rodrigues T, Cortez-Pinto T, Serejo F, Ramalho F, Alexandrino, Velosa F. The MIC score improves the ability of meld score in predicting in-hospital mortality risk in decompensated liver cirrhosis. AASLD, November 2011, San Francisco USA. *Hepatology* Supl 2011 (Poster presentation)

Mareco V, Bujor L, Monteiro Grillo I. Reirradiation of brain tumors in the University Hospital of Santa Maria of Lisbon. EORTC-EANO Conference 2011 Trends in Central Nervous System Malignancies, Bucharest, Romania, 25-26 March 2011. *Proceedings Book*. 2011: 46. (Poster presentation)

Carreira P., Ribeiro T.N, Madureira L., Prudêncio L., Mota M., Pontes M., Monteiro Grillo I. Monitor Unit Comparison Between a Treatment Planning System and an Independent Monitor Unit Calculation Software. ESTRO Anniversary Congress, London, UK, 8-12 May 2011, *Proceedings Book* 2011:276(Poster presentation)

Mareco V, Bujor L, Pimentel Serra N, Monteiro Grillo I. Utility of the tractography in radiotherapy planning of brain primary tumors. 8th Annual World Congress of IBNISPS on Brain, Spinal Cord Mapping and Image Guided Therapy. San Francisco, USA. 2011. <http://www.worldbrainmapping.org/posters/> (Poster presentation)

Mareco V, Bujor L, Monteiro Grillo I. Human Immunodeficiency Virus- Associated Plasmablastic Lymphoma. 2011 European Multidisciplinary Cancer Congress. Stockholm, Sweden. 16-20 October 2011. <http://www.poster-submission.com/board/> (Poster presentation)

Amado A, Vasconcelos AL, Jorge M, Monteiro Grillo I. Carcinosarcomas Uterinos – La Experiencia de una institución. XVI Congreso Nacional SEOR, Madrid, Spain, 14-17 June 2011. *Resúmenes de comunicaciones* (Poster presentation)

Vasconcelos AL, Santa Cruz O, Amado A, Pina F, Monteiro Grillo I. Clinica y Terapéutica del Carcinoma Celulas Anillo de Sello Próstata. XVI Congreso Nacional SEOR, Madrid, Spain, 14-17 June 2011 *Resúmenes de comunicaciones*. (Poster presentation)

Mareco V, Amado A, Jorge Lemos M, Monteiro Grillo I. Irradiación del cáncer de mama después de radioterapia al tórax. La actualidad en medicina y cirugía y 16 Congreso de la Sociedad Española de Oncología Radioterápica, Madrid, Spain, 14-17 June 2011 *Resúmenes de comunicaciones* 2011: 129-130 (Poster presentation)

Mareco V, Bujor L, Pimentel Serra N, Monteiro Grillo I. Fractionated External Radiotherapy for Choroidal Hemangioma. PROS Congress, Venice, Italy, 21-24 June 2011. *Abstract Scientific Programme* 2011: 33 (Poster presentation)

Mareco V, Pimentel Serra N, Bujor L, Monteiro Grillo I. Localized Radiotherapy of Pineal Pure Germinoma. PROS Congress, Venice – Italy, 21-24 June 2011. *Abstract Scientific Programme* 2011: 33. (Poster presentation)

Reis Ferreira M, Bujor L, Jesus C, Monteiro Grillo M, Monteiro Grillo I. Interstitial high-dose rate brachytherapy for inferior eye-lid basal and squamous cell carcinoma: a feasibility study. 53rd ASTRO Annual Meeting. Miami Beach, FLA, USA. October 2-6 2011. <http://www.abstractsonline.com/Plan/ViewSession.aspx?sKey=b8eeab7e-5771-43f2-9aff-4b40e8fb32ff&mKey=%7bCCCE7E125-D766-49E6-91B0BC792B0063A%7d+> (Poster presentation)

Ferreira C, Camilo M, Pena R, Ravasco P. Undernutrition and nutritional supplements in Oncology: what do family and caretakers know?" 33rd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Gothenburg, Sweden, September 2011. *Clinical Nutrition* 2011; 6 (suppl 1): 45 (Poster presentation)

Ferreira C, Camilo M, Pena R, Ravasco P. Health professionals, undernutrition and nutritional supplements in Oncology: a pilot survey. 33rd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Gothenburg, Sweden, September 2011. *Clinical Nutrition* 2011; 6 (suppl 1): 45 (Poster presentation)

Almeida AI, Ornelas M, Neto E, Monteiro-Grillo M, Camilo M, Ravasco P. Are nutrition and cataract linked?. 33rd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Gothenburg, Sweden, September 2011. *Clinical Nutrition* 2011; 6 (suppl 1): 61-62 (Poster presentation)

Almeida AI, Correia M, Camilo M, Ravasco P. Nutritional risk in surgical patients: how to screen? 33rd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Gothenburg, Sweden, September 2011. *Clinical Nutrition* 2011; 6 (suppl 1): 71. Travel Award for the 20 best research works of the congress (Poster presentation)

Ferreira C, Camilo M, Pena R, Ravasco P. Undernutrition and nutritional supplements in Oncology: what do family and caretakers know? 11th European Nutrition Conference FENS 2011: "Diversity vs Globalization – a nutritional challenge for a changing Europe, Madrid, Spain, October 2011. *Annals of Nutrition and Metabolism* 2011; 58 (suppl 3): 40 (Oral communication)

Ferreira C, Camilo M, Pena R, Ravasco P. Health professionals, undernutrition and nutritional supplements in Oncology: a pilot survey. 11th European Nutrition Conference FENS 2011: "Diversity vs Globalization – a nutritional challenge for a changing Europe, Madrid, Spain, October 2011. *Annals of Nutrition and Metabolism* 2011; 58 (suppl 3): 39 (Oral communication)

Almeida AI, Ornelas M, Neto E, Monteiro-Grillo M, Camilo M, Ravasco P. Are nutrition and cataract linked?. 11th European Nutrition Conference FENS 2011: "Diversity vs Globalization – a nutritional challenge for a changing Europe, Madrid, Spain, October 2011. *Annals of Nutrition and Metabolism* 2011; 58 (suppl 3): 63 (Oral communication)

Almeida AI, Correia M, Camilo M, Ravasco P. Nutritional risk in surgical patients: how to screen? 11th European Nutrition Conference FENS 2011: "Diversity vs Globalization – a nutritional challenge for a changing Europe, Madrid, Spain, October 2011. *Annals of Nutrition and Metabolism* 2011; 58 (suppl 3): 412 (Poster presentation)

Communications in National Conferences

Ferreira CF, Rodrigues T, Cortez-Pinto H, Serejo F, Ramalho F, Velosa J. Melhoria significativa na predição de mortalidade hospitalar em cirróticos pelo escore meld tomando em conta infecções e colesterol total. XXXI Congresso Nacional de Gastroenterologia, Endoscopia Digestiva e Hepatologia, June 2011, Estoril, Portugal. *Semana Digestiva 2011 GE-Jornal Português de Gastroenterologia*, 2011; 18 (Oral presentation)

Ferreira D.M.S, Machado M.V., Cortez-Pinto H., Rodrigues C.M.P., Castro R.E. Expressão do mirna-34 no fígado de doentes com fígado gordo não alcoólico e sua potencial modulação. XXXI Congresso Nacional de Gastroenterologia, Endoscopia Digestiva e Hepatologia, June 2011, Estoril, Portugal. *Semana Digestiva 2011. GE-Jornal Português de Gastroenterologia*, 2011; 18 (Oral presentation)

Vale do Gato I, Cortez-Pinto H, Machado J, Chaves P, Santos A. M., Pereira T., Lopes T., Guerreiro A.S. Comparação da composição da microbiota entre dois modelos de dieta de esteatohepatite não alcoólica no ratinho. XXXI Congresso Nacional de Gastroenterologia, Endoscopia Digestiva e Hepatologia, June 2011, Estoril, Portugal. *Semana Digestiva 2011. GE-Jornal Português de Gastroenterologia*, 2011; 18 (Oral presentation)

Machado M.V., Gonçalves S., Costa A., Carepa F., Coutinho J., Cortez-Pinto H. A esteatohepatite não alcoólica associa-se a alterações precoces na taxa de filtração glomerular, na obesidade mórbida. *GE-Jornal Português de Gastroenterologia*, XXXI Congresso Nacional de

Gastroenterologia, Endoscopia Digestiva e Hepatologia, June 2011, Estoril, Portugal. Semana Digestiva 2011. *GE-Jornal Português de Gastroenterologia*, 2011; 18 (Oral presentation)

Machado M.V., Oliveira A.G., Cortez-Pinto H. Prevalência de esteatose hepática em doentes infectados pelo VHB: meta-análise de factores de risco e comparação com infectados pelo VHC. XXXI Congresso Nacional de Gastroenterologia, Endoscopia Digestiva e Hepatologia, June 2011, Estoril, Portugal. Semana Digestiva 2011. *GE-Jornal Português de Gastroenterologia*, 2011; 18 (Oral presentation)

Jesus C, Batista V, Monteiro Grillo I. Desenvolvimento de um Software de verificação independente do cálculo de dose em Braquiterapia HDR”. 4º Congresso Sociedade Portuguesa de Radioterapia Oncologia (SPRO), Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Ferreira M R, Jorge M, Amado A, Monteiro Grillo I. Radioquimioterapia no carcinoma do colo do útero: um tratamento potencialmente agressivo. 4º Congresso SPRO, Porto, Portugal 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Amado A, Ferreira M, Vasconcelos A, Mendonça V, Jorge M, Monteiro Grillo I. Carcinoma Mínimo da Mama (T1a,b N0 M0): sinónimo de bom prognóstico? 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Amado A, Vasconcelos A, Ferreira M, Bujor L, Pimentel N, Monteiro Grillo I. Tumor Mucoepidermoide da Parótica - a propósito de um caso clínico. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Vasconcelos A L, Monteiro Grillo I. Tumores microinvasivos da mama. 4º Congresso SPRO, Porto Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Mareco V, Bujor L, Pimentel Serra N, Monteiro Grillo I. Neoplasia secundária à distância após radioterapia com fotões de alta energia e produção de neutrões secundários. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011 <http://abstracts2011.spro.pt/> (Poster presentation)

Vasconcelos AL, Mendonça V, Amado A, Antunes I, Jorge M, Monteiro Grillo I. Tumor Desmóide - A propósito de um caso clínico”. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Vasconcelos A L, Monteiro Grillo I. O Papel da radioterapia nos sarcomas retroperitoneais. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Carreira P., Ribeiro T.N, Madureira L., Prudêncio L., Mota M., Pontes M., Monteiro Grillo I. Comparação do cálculo de Unidades Monitor entre um sistema de planeamento e um sistema dedicado independente. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Marques de Jesus C, Malveiro R, Ribeiro T, Monteiro Grillo I. Controlo de qualidade geométrico de um sistema de aquisição de imagens de Raios-X para utilização em Braquiterapia (IBU). 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Pontes M., Madureira L., Rato A., Mota M., Jacob K., Fernandes P., Carreira P., Clemente A., Mateus D., Carvoeiras P., Dias C., Malveiro R., Batista V., Prudêncio L., Galhardas J., Ribeiro T., Duarte A., Ferreira A., Teixeira N., Monteiro Grillo I. Aquisição e validação de dados de dois Aceleradores Lineares para quatro Sistemas de Planeamento. 4º Congresso SPRO, Porto, Portugal, 27-29 January 2011. <http://abstracts2011.spro.pt/> (Poster presentation)

Amado A., Vasconcelos A., Pina F., Jorge M., Monteiro Grillo I. Sarcoma de Ewing Extra-Ósseo – uma Entidade Rara. Encontros da Primavera-Oncologia, Hospital do Espírito Santo, Évora, Portugal, 31 March- 3 April 2011 (Poster presentation)

Amado A., Mareco V., Vasconcelos A., Pina F., Jorge M., Monteiro Grillo I. Carcinoma Ductal Invasivo em Tecido Mamário Ectópico na Vulva – Caso Clínico e Breve Revisão da Literatura. Encontros da Primavera-Oncologia, Hospital do Espírito Santo, E.P.E., Évora, Portugal, 31 March- 3 April 2011 (Poster presentation)

Ferreira C., Pena R., Camilo M., Ravasco P. Profissionais de saúde, desnutrição e suplementos nutricionais em oncologia: inquérito nacional. XIII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Porto, Portugal. April 2011. *Revista da APNEP* 2011; vol. V, Nº1: 59 (Poster presentation)

Ferreira C., Pena R., Camilo M., Ravasco P. Desnutrição e suplementos nutricionais em oncologia – o que sabem familiares e cuidadores? XIII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Porto, Portugal. April 2011. *Revista da APNEP* 2011; vol. V, Nº1: 57 (Poster presentation)

Almeida AI, Camilo M., Ravasco P. Nutrição e catarata: que relação? XIII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Porto, Portugal. April 2011. *Revista da APNEP* 2011; vol. V, Nº1: 58 (Poster presentation)

Almeida AI, Camilo M., Ravasco P. Risco nutricional no doente cirúrgico: como avaliar? XIII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Porto, Portugal. April 2011. *Revista da APNEP* 2011; vol. V, Nº1: 56 (Poster presentation)

Ferreira C., Pena R., Camilo M., Ravasco P. Profissionais de saúde, desnutrição e suplementos nutricionais em oncologia: Inquérito nacional. X Congresso de Nutrição e Alimentação e II Congresso Ibero-Americano de Nutrição. Lisboa, Portugal. May 2011. *Livro de Resumos do Congresso* 2011; 38 (Poster presentation)

Ferreira C., Pena R., Camilo M., Ravasco P. Desnutrição e suplementos nutricionais em oncologia – o que sabem familiares e cuidadores? X Congresso de Nutrição e Alimentação e II Congresso Ibero-Americano de Nutrição. Lisboa, Portugal. May 2011. *Livro de Resumos do Congresso* 2011; 39-40 (Poster presentation)

Almeida AI, Camilo M., Ravasco P. Nutrição e catarata: que relação? X Congresso de Nutrição e Alimentação e II Congresso Ibero-Americano de Nutrição. Lisboa, Portugal. May 2011. *Livro de Resumos do Congresso* 2011; 39 (Poster presentation)

Almeida AI, Camilo M., Ravasco P. Da Teoria à Prática: Avaliação de Risco Nutricional no Doente Cirúrgico”. X Congresso de Nutrição e Alimentação e II Congresso Ibero-Americano de Nutrição. Lisboa, Portugal. May 2011. *Livro de Resumos do Congresso* 2011; 27-28. (Oral communication).

Almeida AI, Ferreira C, Marques Vidal P, Ravasco P. Ten-year trends in overweight and obesity in the adult Portuguese population, 1995 to 2005. 15º Congresso Português de Obesidade promovido pela SPEO: Combater a Obesidade: uma missão possível. Coimbra, Portugal. November 2011. *Revista Portuguesa de Cirurgia* (Supl Novembro 2011); 36 (Oral communication)

Almeida AI, Ferreira C, Marques Vidal P, Ravasco P. Obesity is underdiagnosed and undertreated in the Portuguese population. 15º Congresso Português de Obesidade promovido pela SPEO: Combater a Obesidade: uma missão possível. Coimbra, Portugal. November 2011. *Revista Portuguesa de Cirurgia* (Supl Novembro 2011); 36 (Oral communication)

Almeida AI, Ferreira C, Monteiro Grillo I, Camilo ME, Ravasco P. Composição corporal do doente oncológico: uma nova realidade? 4ª Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 2011 (Poster presentation)

Almeida AI, Boléo-Tomé C, Ferreira C, Monteiro Grillo I, Camilo ME, Ravasco P. Cancro, excesso de peso e obesidade: prioridade para intervenção nutricional? 4ª Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 2011. Prémio de 3º melhor trabalho de investigação apresentado no congresso (Poster presentation)

Almeida AI, Boléo-Tomé C, Ferreira C, Monteiro Grillo I, Camilo ME, Ravasco P. Qual é actualmente a dieta do doente oncológico? 4ª Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 2011 (Poster presentation)

Ravasco P, Ferencova J, Krajnak S, Almeida AI, Boléo-Tomé C, Monteiro Grillo I, Camilo ME. Programa internacional de intercâmbio entre Faculdades de Medicina: A importância de um estágio de investigação clínica em nutrição. 4ª Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 2011 (Poster presentation)

Ravasco P, Stambolliu E, Bogataj J, Almeida AI, Boléo-Tomé C, Monteiro Grillo I, Camilo ME. O 2º intercâmbio sobre Nutrição entre Faculdades de Medicina. 4ª Jornada Luso-Brasileira de Nutrição Oncológica, Porto, Portugal. November 2011 (Poster presentation)

Almeida AI, Ornelas M, Neto E, Monteiro-Grillo M, Camilo M, Ravasco P. Nutrição e catarata: que relação? 54º Congresso Português de Oftalmologia, Vilamoura, Portugal. December 2011. *Livro de Resumos do Congresso 2011*; 39 (Poster presentation)

Duarte MJ, Guerreiro CS, Bernardo B, Caldas de Almeida M, Mendes L. Índice de Massa Corporal e perímetro geminal em indivíduos idosos com demência. II Congresso Anual de Cuidados Continuados, Lisbon, Portugal, November 2011 (Poster presentation)

Duarte MJ, Guerreiro CS, Bernardo B, Caldas de Almeida M, Mendes L. Aplicação do Mini Nutritional Assessment vs Mini Nutritional Assessment short form em indivíduos com demência. XIII Congresso da Associação Portuguesa de Nutrição Entérica e Parentérica, Porto, Portugal, April 2011. *Revista da APNEP 2011* (Poster presentation)

Garagarza C, Matias P, Guerreiro CS, Amaral T, Ferreira C, Jorge C, Gil C, Ferreira A. Massa celular corporal como indicador do estado nutricional e inflamatório dos doentes em hemodiálise. C. XIII Congresso da Associação Portuguesa de Nutrição Entérica e Parentérica. Porto, Portugal, April 2011. *Revista da APNEP 2011* (Poster presentation)

Duarte MJ, Guerreiro C, Bernardo A, Almeida M, Mendes L. Avaliação da ingestão alimentar de indivíduos idosos com demência. VI Encontro Nacional das Ciências e Tecnologias da Saúde, Lisbon, Portugal, 20 October 2011 (Poster presentation)

Marques S, Calha R, Guerreiro C, Mendes L. Percepção corporal pós-parto: influência do IMC pré-gestacional e ganho de peso gestacional. VI Encontro Nacional das Ciências e Tecnologias da Saúde, Lisbon, Portugal, 20 October 2011 (Poster presentation).

Carmona B, Guerreiro C, Cravo M, Brito M. Influência dos genes timidilato sintetase e metionina sintetase no desenvolvimento de cancro colo-rectal. VI Encontro Nacional das Ciências e Tecnologias da Saúde, Lisbon, Portugal, 20 October 2011 (Poster presentation)

Organisation of Conferences

Cortez-Pinto H. Member of the Organizing Committee of the XIXth United European Gastroenterological Week (UEGW) 2011, held in Stockholm. Presently preparing the XXth UEGW Meeting to be held in Amsterdam in 2012.

Monteiro Grillo I. Multidisciplinary Teaching Course on Prostate Cancer 2011, ESTRO, Lisbon, Portugal, 6-10 February 2011

Monteiro Grillo I. Clinical Workshop- Image Guided HDR Brachytherapy for Prostate cancer: Live Case in Radiotherapy Department. Nucletron Prostate Meeting – HSM, Lisbon, Portugal 15-16 March 2011

Monteiro Grillo I. Modern Brachytherapy. The future of prostate cancer treatment” Sintra, Portugal, 17-19 March 2011.

Monteiro Grillo I. IMRT- IGRT Workshop, Lisbon, Portugal, 25 May 2011.

Ravasco P. Member of the Organizing Committee of the 11th FENS European Nutrition Conference (Federation of European Nutrition Societies). October 26-29, 2011 Madrid, Spain.

Guerreiro CS. Scientific Committee of II Congresso Anual de Cuidados Continuados, November 25-26, 2011, Lisbon, Portugal.

Internationalization

Camilo ME. TOOLTIPS Partner = Erasmus EU financed Intensive Programme “Tools targeted on obesity intervention and prevention strategies for efficient and sustained implementation”.

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

Cortez-Pinto H. Collaborative multicenter study to assess non-invasive tests to detect liver disease in NAFLD. Coordinator: Musso G, University of Turin/Italy

Cortez-Pinto H. Collaborating on “EASL Clinical Practice Guidelines on Alcoholic Liver Disease” of the European Association for the Study of Liver Disease to be published in 2012

Monteiro Grillo I. Editorial board J of Contemporary Brachytherapy (Polish Brachytherapy Society)

Monteiro Grillo I. Editorial board Reports of Practical Oncology and Radiotherapy.

Monteiro Grillo I. Editorial board Current Nutrition and Food Science

Monteiro Grillo I. Regional Representative of ESTRO at ALATRO- Asociación Latinoamericana de Terapia Radiante Oncológica.

Ravasco P. Invited member of the *Nature reader panel*; panelists role: to shape NATURE Journal publication, value, sustain, develop the research community and others interested in science and its impacts. This role ensures the highest standards of professional research and privacy in using the information that the panelists provide.

Ravasco P. Member of the ESPEN Faculty (*European Society for Clinical Nutrition and Metabolic Care*), which serve as a Board of international expertise. Members may be asked to give expert opinions on clinical nutrition and metabolism, represent ESPEN in other Societies, as a source of knowledge for governments or other bodies related to health care.

Ravasco P. Scientific consult for the area of Nutrition in the Harvard Medical School-Portugal Program.

Ravasco P, Guerreiro CS. Erasmus EU network DIETS= Dieticians Improving Education Training Standards across Europe.

Guerreiro CS. *E-learning for Health Agents Program in Europe - Equity creating equality in health through capacity building in Europe between health care workers*; a Life Learning Programme financed by the European Commission

Guerreiro CS. *Key-Member* representing Portugal at ESPEN (European Society for Clinical Nutrition and Metabolism).

Prizes, honours and awards

Prize for the best Oral presentation of the session entitled: Increased expression of microrna-34 in NAFLD patients and targeting by ursodeoxycholic acid in rat liver; awarded to: Ferreira D, Borralho P, Machado MV, Cortez-Pinto H; Rodrigues C, Castro R. 19th United European Gastroenterology Week - UEGW, Stockholm, Sweden, 22-26 October 2011.

Prize for the best communication presented at the 4º Congresso da Sociedade Portuguesa de Radioterapia e Oncologia, Porto, Portugal 27-29 January 2011, entitled: “Implementação de dosimetria in vivo com MOSFET em braquiterapia de alta taxa de dose da próstata”. Authors: Ribeiro T.N., Jesus C.M., Peralta L., Monteiro-Grillo I.

Travel Award to young investigators (one per country) for their best first presented abstract at the ESPEN 33rd Congress of European Society for Clinical Nutrition and Metabolism (ESPEN) to

Ana Isabel Almeida, Gothenburg, Sweden, 2011. Almeida AI, Correia M, Camilo M, Ravasco P. "Nutritional risk in surgical patients: how to screen?" 33rd Congress of European Society for Clinical Nutrition and Metabolism (ESPEN), Gothenburg, Sweden, 3-6 of September 2011.

Prize for the 3rd best research work presented at the Congress 4^a Jornada Luso-Brasileira de Nutrição Oncológica, Porto Novembro de 2011, entitled: "*Cancro, excesso de peso e obesidade: prioridade para intervenção nutricional?*" Authors: Almeida AI, Boléo-Tomé C, Ferreira C, Monteiro Grillo I, Camilo ME, Ravasco P.

Ravasco P. Selected scientist by the Scientific Committee of Atomium Culture with the work: "Nutrition and food: real determinants in cancer", to represent Portugal in Brussels, Belgium at the Permanent Platform for European Excellence.

Guerreiro CS. Honorable Mention in Nutrition Awards at Communication in Nutrition category. "Alimentação & Doença Inflamatória do Intestino - A importância de uma alimentação adequada".

Guerreiro CS. Best poster at VI Encontro Nacional das Ciências e Tecnologias da Saúde, Lisbon, Portugal, 20 October 2011. entitled: "*Avaliação da ingestão alimentar de indivíduos idosos com demência*". Authors: Duarte MJ, Guerreiro C, Bernardo A, Almeida M, Mendes L.

Advanced teaching

Cortez-Pinto H. President of the Scientific board of the Post-Graduate Course in Clinical Nutrition (2011/2012), 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 Stockholm, Sweden, November 2011.

Cortez-Pinto H. Lecturer at the Master Degree on Metabolic Diseases and Behaviour, Faculdade de Medicina da Universidade de Lisboa. Lisbon, February 2011.

Monteiro Grillo I. Lecturer "Terapia Radiações I" at the Master Program Applied Technologies and Radiations to Health, II edition. Technical Institute of Lisbon, May to June 2011

Monteiro Grillo I. Lecturer "Palliative Radiotherapy " at the 9^{ed}. of Master Program in Palliative Care of the Faculty of Medicine of Lisboa, January 2011

Monteiro Grillo I. Moderator: "A Radioterapia no Controlo da Dor". 1^a Curso da Dor Crónica para médicos Internos, HFF, Lisboa 20-29 October 2011

Ana Oliveira (2011) Cuidados Paliativos: Dificuldades dos Enfermeiros do HSM. Master Program in Cuidados Paliativos, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Monteiro Grillo I.

Ana Rita Simões (2011) IGRT com CBCT: o impacto da precisão em Radioterapia, Master Program Applied Technologies and Radiations to Health, 1st ed. Technical Institute of Instituto Politécnico de Lisboa Supervisor: Monteiro Grillo I.

Alexandra Oliveira (2011) "Medida da Qualidade de Vida do doente oncológico na prática clínica diária. Master Program in Cuidados Paliativos, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Monteiro Grillo I.

Luísa Maria Leitão Moreira (2011): "Hipodermoclise uma Forma de Dignificar a Vida na Prestação de Cuidados de Saúde no Domicílio. Master Program in Cuidados Paliativos, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Monteiro Grillo I.

Ravasco P. Lecturer at the advanced teaching program Educational Long Life Learning (CME) on Mechanisms of wasting in cancer cachexia in the module "Nutritional support in cancer" of ESPEN (European Society for Clinical Nutrition and Metabolism), Gothenburg, Sweden, September 2011.

Ravasco P. Lecturer on The relevance of nutrition and body composition in cancer patients at the clinical session of the Radiotherapy Department of the University Hospital of Santa Maria, Lisboa, May 5th 2011.

Ravasco P. Carcinogénese alimentar e tubo digestivo. Curso de Nutrição em Cirurgia promovido e organizado pela Sociedade Portuguesa de Cirurgia, Lisboa, Portugal, March 5th, 2011.

Ravasco P: Teacher at the 20th Advanced Course in Clinical Nutrition (ACCN course) organized by ESPEN (European Society for Clinical Nutrition and Metabolism). Maastricht, Holland, May 12th 2011.

Ravasco, P. Various lectures addressing "Patologias e Terapêutica Nutricional", in the module "Nutrição" at the Master Program in Nutrition of the Faculty of Medicine of Lisboa, Lisboa, Portugal, from January to March 2011.

Ravasco P. Lecturer on "A escolha da especialidade de MGF nos alunos de Medicina" in the pre-graduate session of General and Family Medicine at the FMUL. Lisboa, Portugal, 21 July 2011.

Ravasco P. Lecturer on Integração do screening nutricional, impacto da nutrição e composicao corporal no prognóstico e marcadores geneticos de caquexia: o que ainda temos para saber? at the clinical session of the Radiotherapy Department of the University Hospital of Santa Maria, Lisboa, Portugal, 8 September 2011.

Ravasco P. Lecturer on Obesidade, alimentação e estilos de vida em pediatria: que implicações futuras? at the clinical session of the Research Center of the Pediatrics Department of the University Hospital of Santa Maria, Lisboa, Portugal, 20 October 2011.

Ravasco, P. President of the Master Program Board in Nutrition 2010-2012. Other board members: Camilo M E. and Cortez-Pinto H.

Ravasco, P. Scientific Coordinator of the Course of Specialization in Clinical Nutrition (2011-2013), and Coordinator of the Module "Nutrition and Cancer". Faculdade de Medicina da Universidade de Lisboa.

Pedro Fortes (2009-2012) Avaliação do Risco e do Estado Nutricionais em meio hospitalar. Master Program in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ravasco P.

Maria José Mirotres (2008-2012) Estudo da associação entre a estrutura familiar e o regime alimentar dos idosos no concelho de Serpa. Master Program in Dietetics and Nutrition, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ravasco P.

Maria José Pires Aurélio Duarte (2009-2012) Avaliação do estado nutricional e hábitos alimentares das crianças do pré-escolar em Santarém. Master Program in Dietetics and Nutrition. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ravasco P.

Maria José Casas Novas Patação (2010-2012) O risco nutricional e a desnutrição hospitalar: que influência na atitude dos profissionais de saúde face à Nutrição? Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ravasco P.

Carolina Maria Pinto Basto Coutinho (2010-2012) Impacto das dietas hiperproteicas na percepção e na composição corporal: intervenção num contexto clínico. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Inês Barbosa (2010-2012) Alimentação e cálculos urinários. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

João Carlos Vieira da Silva Sampaio (2010-2012) Dieta sem amido no tratamento da Espondilite Anquilosante: uma mais valia? Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Mariana Pavão Abecasis (2010-2012) A gravidez, o aumento de peso e suas consequências na mulher. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Vanda Filipa da Silva Gonçalves Paiva (2010-2012) Fibromialgia: qual a relevância da vitamina D na dor crónica? Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Vanessa Mealha (2010-2012) Qual o risco de distúrbios alimentares em estudantes de Dietética e Nutrição? Comportamento e hábitos alimentares, estado nutricional e composição corporal. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Verónica Machado Jorge Lopes (2010-2012) Escolhas alimentares em Instituição do Ensino Secundário. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Salomé Almeida (2010-2012) Caracterização e comparação do perfil nutricional e composição corporal em atletas de elite ao longo da época desportiva. Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Cláudia Marinho Alves Parreira (2010-2012) O que sabe a população sobre factores de risco para a Diabetes tipos 2? Master Program in Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Ravasco P.

Guerreiro CS. Lecturer at the Postgraduate course of the Escola Superior de Hotelaria e Turismo do Estoril. Estoril, June 2011.

Guerreiro CS. Lecturer “Malnutrição” module “Nutrição” at the Master Program in Nutrition of the Faculty of Medicine of Lisboa.

Guerreiro CS. Scientific Board of Clinical Nutrition Post Graduate Course. FMUL/ESTeSL

Science and Society

Ravasco P. Participation in a session for a structured group of 4 students of the 12th grade of the *Escola Secundária de Ferreira Dias - Lisboa*, in the context of the discipline “Project” under the theme: “What is the influence of food in cancer incidence?” at FMUL (*Public Perception of Science*).

Master and PhD thesis completed

Guerreiro CS. PhD thesis - Nutrição e Genes em Doenças Intestinais, defense “with honours” in 15th April 2011, Supervisor: Camilo M.

Rita Machado da Silva Barroso (2011) Condições para o desenvolvimento de acções paliativas em unidades de internamento de agudos, Faculdade de Medicina Universidade de Lisboa – President of the Examination Board: Monteiro Grillo I.

Amanda Fernandes (2011) Avaliação do Risco e do Estado Nutricionais em meio hospitalar.. Master Degree in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ravasco P; Members of the Examination Board: Ravasco P, Cortez-Pinto H.

Inês Chaparro Roque dos Santos (2011) Obesidade e ingestão nutricional em crianças Portuguesas dos 2 aos 5 anos de idade. Master Degree in Dietetics and Nutrition, Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor and Member of the Examination Board: Ravasco P.

Rita Margarida Ascenso Roldão (2011) Avaliação da composição corporal e ingestão nutricional em crianças com Perturbações de Hiperactividade e Défice de Atenção medicadas com Metilfenidato. Master Degree in Dietetics and Nutrition, Faculdade de Medicina da Universidade de Lisboa. Supervisor and Member of the Examination Board: Ravasco P.

Parasite Molecular Genetics Unit

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 M Figueiredo, PhD – Group Leader, IMM

Research Team

Ana Filipa Ferreira	PhD fellow (GABBA program)
Ana Martins Ribeiro	Masters student (left in September 2011)
Ana Pena	PhD fellow, FCT
Fabien Guegan	Post-Doc fellow
Francisco Aresta Branco	Training fellowship, FCT
Mafalda Pimentel	Masters student
Silvia Pimenta	Medical student (left in August 2011)

Keywords/Research Areas

antigenic variation; chromatin; gene expression; parasitology

Major scientific achievements

2011 was my second year as a Group Leader. It was a very important year for three main reasons.

First, I significantly increased the size of my group (which was possible due to the funding I obtained at the end of 2010). I hired two PhD students, from IMM and GABBA PhD programs. I also hired the first international member of my group, a post-doc from France. Hosting a medical student was a very rewarding experience that, I hope will bring my lab closer to FMUL and to translational medicine.

Second, I obtained an extremely prestigious, competitive and wealthy funding from Howard Hughes Medical Institute (HHMI). There were 760 candidates, from 18 different countries, to the

new International Early Career Scientist award. After two rounds of selection, I was one of the 28 awardees of a €560.000 award, for a period of 5 years.

Third, I began exploring a new area of interest in African trypanosomiasis, which includes a collaboration with an extremely successful scientist in the USA. This project will be at the crossroads of parasitology, neurobiology and ageing.

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 Cell*, **9**: 148-154 (Journal IF: 3,395, Citations: 10)

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: 23)

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: 59)

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: 26)

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: 36)

Ongoing Research Projects

2009/2012 Epigenetics of antigenic variation: defining new drug targets that make African trypanosomes more susceptible to the host immune response; Fundação Calouste de Gulbenkian. Coordinator: Luisa M Figueiredo. P-105333 (57 657 €)

2010/2013 Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes; Marie Curie International Reintegration Grant; Coordinator: Luisa M Figueiredo. FP7-PEOPLE-RG-2009 “HistoneH1Tryp” (100 000 €)

2011/2014 Screening of chromatin factors involved in antigenic variation in *Trypanosoma brucei*; Fundação para a Ciência e Tecnologia; Coordinator: Luisa M Figueiredo. PTDC/SAU-MIC/113225/2009 (113 407 €)

2011/2014 The role of histone H1 in antigenic variation of African trypanosomes; Fundação para a Ciência e Tecnologia; Coordinator: Luisa M Figueiredo. PTDC/BIA-BCM/115864/2009 (189 828 €)

2011/2013 The role of chromatin in antigenic variation of African Trypanosomes; EMBO Installation Grant; Coordinator: Luisa M Figueiredo. Project No. 2151 (150 000 €)

Other publications International

Luisa M Figueiredo and David Horn (book chapter currently in edition) *Trypanosoma brucei* subtelomeres: Monoallelic expression and antigenic variation. Ed: Subtelomeres.

Invited Lectures and Seminars

Figueiredo LM. Histone H1 modulates antigenic variation of African Trypanosomes. University of Regensburg. Regensburg, Germany. July 2011

Communications in International Conferences

Figueiredo LM. The role of chromatin in antigenic variation of African Trypanosomes. Royal Society Subtelomere meeting. Buckinghamshire, England. Jan 2011 (Oral presentation)

Figueiredo LM. Histone H1 modulates antigenic variation in African trypanosomes. EMBO Young Investigator meeting. EMBL, Heidelberg, Germany. April 2011 (Oral presentation)

Pena A, Ferreira AF, Figueiredo LM. Histone H1 controls variant surface glycoprotein silencing in African trypanosomes. The 3rd EMBO meeting, Vienna, Austria. September 2011 (Poster presentation)

Communications in National Conferences

Figueiredo LM. The role of chromatin in antigenic variation of African Trypanosomes. Microbiotec11 meeting, Braga. 1-3 December 2011. (oral presentation)

Organisation of Conferences

I am responsible for organizing the weekly institutional seminar series of IMM (Sept 2011 – July 2012).

Internationalization

International funding from EMBO and Marie Curie.

Collaborators: Christian Janzen (Germany), Nina Papavasiliou and George Cross (New York, USA), Joseph Takahashi (Dallas, USA), Vladimir Benes (EMBL).

Advanced teaching

Figueiredo LM. Control of antigenic variation in African trypanosomes. IGC PhD program, Oeiras, Portugal. October 2011

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Figueiredo LM. African trypanosomes and epigenetics. Masters in Medical Parasitology, IHMT, Lisboa, Portugal. May 2011

Figueiredo LM. African trypanosomes and epigenetics. Masters in Emerging Infectious Diseases, FMUL, Lisboa, Portugal. March 2011

Figueiredo LM. African trypanosomes and epigenetics. Masters in Evolution and Development Biology, FCUL, Lisboa, Portugal. March 2011

Figueiredo LM. The role of chromatin in antigenic variation of African Trypanosomes. GABBA PhD program. Porto, Portugal. January 2011

Science and Society

May 2011 Guest at “Prós e Contrás”, TV show of RTP1.

Master thesis completed

Ana Martins Ribeiro (2011) The role of chromatin remodelling enzymes in antigenic variation of *Trypanosoma brucei*. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Luisa Figueiredo.

Rheumatology Research Unit

Major interests / Objectives

The Rheumatology Research Unit (RRU) results from a partnership between the Instituto de Medicina Molecular/Faculdade de Medicina da Universidade de Lisboa and the Rheumatology Department of the Santa Maria Hospital. Basic scientists and clinicians closely work together to promote translational research and clinical excellence in the field of Rheumatology.

Our specific research objectives are the study of the pathogenesis of inflammatory joint diseases (Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis, Spondylarthritis (SpA) and Systemic Lupus Erythematosus (SLE)) and bone disorders (osteoporosis) in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies.

The long-term objective of the RRU is to achieve recognition as a European League Against Rheumatism Centre of Excellence in Rheumatology.

Head of Unit

João Eurico Fonseca, MD, PhD – Assistant Professor with Habilitation (“Agregação”), Faculdade de Medicina da Universidade de Lisboa (FMUL); Rheumatologist, Rheumatology Department, Santa Maria Hospital (HSM); Lisbon, Portugal

Principal Investigator

Helena Canhão, MD, PhD – Assistant Professor, Faculdade de Medicina da Universidade de Lisboa (FMUL); Rheumatologist, Rheumatology Department, Santa Maria Hospital (HSM); Lisbon, Portugal

Research Team

Joaquim Pereira, MD	Assistant, FMUL and Training Fellowship
Ana Rodrigues, MD	Assistant, FMUL and Training Fellowship
Susana Capela, MD	Assistant, FMUL, Rheumatologist
Filipa Ramos, MD	Assistant, FMUL, Rheumatologist
Elsa Sousa, MD	Assistant, FMUL, Rheumatologist
João Dias, MD	Training Fellowship
Cristina Ponte, MD	Training Fellowship
Raquel Marques, MD	Training Fellowship
Saba Abdulghani, PhD	Post Doc Fellowship, ECTS/Servier grant
Márcio Navalho, MD, PhD student	Radiologist in Hospital da Luz
Rita Moura, PhD	PhD Fellowship, FCT
Joana Caetano-Lopes, PhD	PhD Fellowship, FCT
Rita Cascão, PhD student	PhD Fellowship, FCT
Luís Santos, PhD student	PhD Fellowship, FCT
Ana Catarina Vale, PhD student	PhD Fellowship, FCT

Maria José Santos, MD, PhD student	Rheumatologist in Hospital Garcia de Orta
Ana Filipa Mourão, MD, PhD student	PhD Fellowship, FCT, assistant, FCML, Rheumatologist in Hospital Egas Moniz
Inês Perpétuo, PhD student	PhD Fellowship, FCT
Ana Lopes, MSc	Lab Manager, IMM
Bruno Vidal	Research grant, FCT
Diana Fernandes, MSc	Assistant Researcher, IMM

JE Fonseca, H Canhão, MJ Santos, Elsa Sousa, Ana Filipa Mourão, Joaquim Pereira, Ana Rodrigues, Susana Capela, João Dias, Filipa Ramos, Cristina Ponte e Raquel Marques are full time Rheumatologists (at least 35 hours of clinical activity per week).

JE Fonseca, H Canhão, Elsa Sousa, Ana Rodrigues, Susana Capela, Filipa Ramos are responsible for all Rheumatology teaching in the medical course (around 4 hours per week)

JE Fonseca, H Canhão are supervising 3 post docs, 9 PhD students and 2 rheumatology trainees.

Keywords/Research Areas

- Joint inflammatory diseases - pathogenesis, early diagnosis, prognosis and pharmacogenetics
- Inflammatory cells and Inflammation
- Bone biology, structure and biomechanics
- Epidemiology of Rheumatic Diseases, Cohorts, Registries and Databases. Recommendations and Guidelines

Major scientific achievements

The main achievements of the Rheumatology Research Unit in 2011 were:

- 1- Describing the degradation of bone biomechanical properties in patients with arthritis.
- 2- Describing the gene expression pattern of the early phase of fragility fractures and the contribution of inflammation related genes for this biologic process.
- 3- Describing the cytokine network in very early rheumatoid arthritis.
- 4- Describing the B cell behavior in very early rheumatoid arthritis.
- 5- Contribution of inflammasome activation for early rheumatoid arthritis.
- 6- Describing the differences in cardiovascular risk between RA and SLE patients.
- 8- Coordination of the Portuguese national databases and registries of the Portuguese Society of Rheumatology for rheumatic diseases treated with biotechnology drugs.
- 9- Coordination of the Portuguese Rheumatology Biobank, a part of the IMM biobank.
- 10- Participation in multinational clinical trials as national coordinators allowing refractory patients to have access to the state of art in biotechnological therapies.
- 11- Establishment of a research network with the Harvard Medical School based on the study of genetic and biochemical markers of RA in the context of a Senior Clinical Award (Helena Canhão) of the Harvard Portugal Program.
- 12- Creation of 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.
- 13- Creation of IMM Rheumatology Series.

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, Edwards CJ, Hamuryudan V, Kvien TK, Leeb BF, Martín-Mola EM, Mielants H, Müller-Ladner U, Murphy G, Østergaard M, Pereira IA, Ramos-Remus C, Valentini G, Zochling J, Dougados M. (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: 1086-93. (Journal IF: 9.082 Citations: 73)

Fonseca JE, Santos MJ, Canhão H, Choy E. (2009) Interleukin-6 as a key player in systemic inflammation and joint destruction. *Autoimmun Rev*; 8: 538-42. (Journal IF: 6.556, Citations: 60)

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: 793-4. (Journal IF: 9.082, Citations: 35)

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):185-92 (Journal IF: 2.358, Citations: 20)

Fonseca JE, Edwards JC, Blades S, Goulding NJ. (2002) Macrophage subpopulations in rheumatoid synovium: reduced CD163 expression in CD4+ T lymphocyte-rich microenvironments. *Arthritis Rheum*; 46: 1210-6. (Journal IF: 8.435, Citations: 25)

Ongoing Research Projects

2009/ 011. Cardiovascular risk and inflammation- contribution to the etiopathogenesis of atherosclerosis and cardiovascular disease, FCT: JE Fonseca (ref. PIC/IC/82920/2007), 150.000€

2009/2011. Evaluation of bone quality and its relation to osteoporotic fracture risk, Associação Portuguesa de Osteoporose, Merck Research Grant, Servier Research Grant. Coordinator: H Canhao, 40.000€

2009/2012. The role of B cells in early Rheumatoid Arthritis, Portuguese Society of Rheumatology. Coordinator: JE Fonseca, no funding

2010/2012. Development of carbon monoxide releasing molecules for the treatment of rheumatoid arthritis (COMRA), European Union FP7 call Program "Research for the benefit of SMEs". Local Coordinator: JE Fonseca Call identifier: FP7-SME-2008-1. General Coordinator: N Arantes-Oliveira. Proposal No: 230629, 400.000€

2010/2012. An assessment of bone mineral and organic phases in an osteoporosis mice model and their influence on the mechanical properties of bone. Coordinator: Saba Abdulghani. European Calcified Tissue Society /Servier Fellowship 2010, 40.000€

2010/2014. Response to anti-TNF treatment biomarkers in Rheumatoid Arthritis. Coordinator: Canhão H (ref. HMPS-ICS/SAU-ICT/002/2010), 398.000€

2009/2011. The role of inflammasome in the initiation and perpetuation of Rheumatoid Arthritis: Contribution for new targeted therapies. Coordinator: JE Fonseca. Pfizer Research Grant. 21.000€

2006/2012 Research Projects involving National and International Databases and Registries. Cooperation with Institutional Health Organizations. Coordinator: JE Fonseca, no funding

2006/2012. National and International Guidelines for the diagnosis and treatment of rheumatic diseases, Portuguese Society of Rheumatology. Coordinators: JE Fonseca, H Canhão, MJ Santos, no funding.

2011/2014 -Portuguese Epidemiologic Study of Rheumatic Diseases – EpiReumaPt. Coordinator: H Canhao, no funding

2012/2014 Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis. Coordinator: JE Fonseca. Pending funding from MSD, 30.000€

2011/2013 Clinical, serological and genetic predictors of evolution, outcome and response to treatment in Portuguese patients with Juvenile Idiopathic Arthritis. Coordinator: JE Fonseca. Pending funding from Abbott, 40.000€

2011/2012 Fabry disease investigation in Juvenile Idiopathic Arthritis patients Funding from Shire Pharmaceuticals Portugal. Coordinator: H Canhao 9.500€

2011/2012 Gaucher disease investigation in Juvenile Idiopathic Arthritis patients. Funding from Shire Pharmaceuticals Portugal. Coordinator: H Canhao Funding from Shire Pharmaceuticals Portugal. 9.500€

2011/2013- Collaboration in “A National Genome Wide Association Study to Predict the Response to Anti-TNF Treatment in Rheumatoid Arthritis”. Coordinator: H Canhao Funding from Abbott Laboratories, 100.000€

Publications in peer review Journals

Machado P, Castrejon I, Katchamart W, Koevoets R, Kuriya B, Schoels M, Silva-Fernández L, Thevissen K, Vercoetere W, Villeneuve E, Aletaha D, Carmona L, Landewé R, van der Heijde D, Bijlsma JW, Bykerk V, Canhão H, Catrina AI, Durez P, Edwards CJ, Mjaavatten MD, Leeb BF, Losada B, Martín-Mola EM, Martínez-Osuna P, Montecucco C, Müller-Ladner U, Østergaard M, Sheane B, Xavier RM, Zochling J, Bombardier C (2011) Multinational evidence-based recommendations on how to investigate and follow-up undifferentiated peripheral inflammatory arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. *Ann Rheum Dis*. **70**(1):15-24 (Journal IF: 9.082, Citations: 4)

Moura RA, Cascão R, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graca L, Fonseca JE (2011)

Cytokine pattern in very early rheumatoid arthritis favours B-cell activation and survival. *Rheumatology (Oxford)* **50**(2):278-82. (Journal IF: 4.171, Citations: 4)

Gossec L, Bijlsma JW, Bombardier C, Canhão H, Devlin J, Edwards CJ, Hamuryudan V, Kvien TK, Leeb BF, Martín-Mola EM, Mielants H, Müller-Ladner U, Ostergaard M, Pereira IA, Ramos-Remus C, Zochling J, Dougados M (2011) Dissemination and evaluation of the 3E initiative recommendations for use of methotrexate in rheumatic disorders: results of a study among 2233 rheumatologists. *Ann Rheum Dis* **70** (2): 388-9. (Journal IF: 9.082, Citations: 0)

Caetano-Lopes J, Lopes A, Rodrigues A, Fernandes D, Perpétuo I, Monjardino T, Lucas R, Monteiro J, Konttinen YT, Canhão H, Fonseca JE (2011) Upregulation of inflammatory genes and downregulation of sclerostin gene expression are key elements in the early phase of fragility fracture healing. *PLoS One*. **11**;6(2):e16947. (Journal IF: 4.411, Citations: 0)

Navalho M, Resende C, Rodrigues AM, Gaspar A, Fonseca JE, Canhão H, Campos J (2012) Dynamic contrast-enhanced 3-T magnetic resonance imaging: a method for quantifying disease activity in early polyarthritis. *Skeletal Radiol*. **41**(1):51-9. Epub 2011 Feb 12. (Journal IF: 1.387, Citations:0)

Pérez Alamino R, Maldonado Cocco JA, Citera G, Arturi P, Vazquez-Mellado J, Sampaio-Barros PD, Flores D, Burgos-Vargas R, Santos H, Chavez-Corrales JE, Palleiro D, Gutierrez MA, Vieira-Sousa E, Pimentel-Santos FM, Paira S, Berman A, Moreno-Alvarez M, Collantes-Estevez E; RESPONDIA Group (2011) Differential features between primary ankylosing spondylitis and spondylitis associated with psoriasis and inflammatory bowel disease. *J Rheumatol*. 2011 **38**(8):1656-60(Journal IF: 3.551, Citations: 0)

Pimentel-Santos FM, Ligeiro D, Matos M, Mourão AF, Costa J, Santos H, Barcelos A, Godinho F, Pinto P, Cruz M, Fonseca JE, Guedes-Pinto H, Branco JC, Brown MA, Thomas GP (2011) Whole blood transcriptional profiling in ankylosing spondylitis identifies novel candidate genes that might contribute to the inflammatory and tissue-destructive disease aspects. *Arthritis Res Ther*. **7**;13(2):R57. (Journal IF: 4.357, Citations: 0)

van de Sande MG, Gerlag DM, Lodde BM, van Baarsen LG, Alivernini S, Codullo V, Felea I, Vieira-Sousa E, Fearon U, Reece R, Montecucco C, Veale DJ, Pitzalis C, Emery P, Klareskog L, McInnes IB, Tak PP (2011) Evaluating antirheumatic treatments using synovial biopsy: a recommendation for standardisation to be used in clinical trials. *Ann Rheum Dis* **70** 423-427 (Journal IF: 9.082, Citations: 4)

Hasija R, Pistorio A, Ravelli A, Demirkaya E, Khubchandani R, Guseinova D, Malattia C, Canhao H, Harel L, Foell D, Wouters C, De Cunto C, Huemer C, Kimura Y, Mangge H, Minetti C, Nordal EB, Philippet P, Garozzo R, Martini A, Ruperto N; Pediatric Rheumatology International Trials Organization (PRINTO) (2011) Therapeutic approaches in the treatment of juvenile dermatomyositis in patients with recent-onset disease and in those experiencing disease flare: an international multicenter PRINTO Study. *Arthritis Rheum*. **63**(10):3142-52. (Journal IF: 9.082, Citations: 0)

Hazlewood G, Aletaha D, Carmona L, Landewé RB, van der Heijde DM, Bijlsma JW, Bykerk VP, Canhão H, Catrina AI, Durez P, Edwards CJ, Leeb BF, Mjaavatten MD, Martinez-Osuna P, Montecucco C, Ostergaard M, Serra-Bonett N, Xavier RM, Zochling J, Machado P, Thevissen K, Vercoutere W, Bombardier C (2011) Algorithm for identification of undifferentiated peripheral

inflammatory arthritis: a multinational collaboration through the 3e initiative. *J Rheumatol* **38** Suppl. 87:54-8. (Journal IF: 3.551, Citations: 1)

Santos MJ, Fernandes D, Capela S, Canas da Silva J, Fonseca JE (2011) Interleukin-6 promoter polymorphism -174 G>C is associated with nephritis in Portuguese Caucasian systemic lupus erythematosus patients. *Clin Rheumatol* **30**:409-13. (Journal IF: 1.687, Citations: 3)

Santos MJ, Fernandes D, Caetano-Lopes J, Perpetuo IP, Vidal B, Canhao H, Fonseca JE. (2011) Lymphotoxin- α 252 A>G polymorphism: a link between disease susceptibility and dyslipidemia in rheumatoid arthritis? *J Rheumatol.* **38**(7):1244-9. (Journal IF: 3.551, Citations: 0)

Santos MJ, Carmona-Fernandes D, Caetano-Lopes J, Perpetuo IP, Vidal B, Capela S, Canas da Silva J, Fonseca JE (2011) TNF promoter -308 G>A and LTA 252 A>G polymorphism in Portuguese patients with Systemic Lupus Erythematosus. *Rheumatol Int.* **5** [Epub ahead of print] (Journal IF: 1.431, Citations:0)

Santos MJ, Vinagre F, Canas da Silva J, Gil V, Fonseca JE (2011) Body composition phenotypes in systemic lupus erythematosus and rheumatoid arthritis: a comparative study of Caucasian female patients. *Clin Exp Rheumatol.* **29**(3):470-6. (Journal IF: 2.358, Citations: 0)

Polido-Pereira J, Vieira-Sousa E, Fonseca JE (2011) Rheumatoid arthritis: What is refractory disease and how to manage it? *Autoimmun Rev.* **10**(11):707-13. (Journal IF: 6.556, Citations: 1)

Haraoui B, Smolen JS, Aletaha D, Breedveld FC, Burmester G, Codreanu C, Da Silva JP, de Wit M, Dougados M, Durez P, Emery P, Fonseca JE, Gibofsky A, Gomez-Reino J, Graninger W, Hamuryudan V, Jannaut Peña MJ, Kalden J, Kvien TK, Laurindo I, Martin-Mola E, Montecucco C, Santos Moreno P, Pavelka K, Poor G, Cardiel MH, Stanislawski-Biernat E, Takeuchi T, van der Heijde D; Treat to Target Taskforce. (2011) Treating Rheumatoid Arthritis to Target: multinational recommendations assessment questionnaire. *Ann Rheum Dis.* **70** (11): 1999 -2002. (Journal IF: 9.082, Citations: 0)

Carmona-Fernandes D, Santos MJ, Perpétuo IP, Fonseca JE, Canhão H (2011) Soluble receptor activator of nuclear factor kappa B ligand/osteoprotegerin ratio is increased in systemic lupus erythematosus patients. *Arthritis Res Ther.* **25**; 13(5): R175. (Journal IF: 4.357, Citations:0)

Pimentel-Santos FM, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Pinto P, Godinho F, Cruz M, Vieira-Sousa E, Santos RA, Rabiais S, Félix J, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC; CORPOREA Study Group (2011) Spectrum of ankylosing spondylitis in Portugal. Development of BASDAI, BASFI, BASMI and mSASSS reference centile charts. *Clin Rheumatol* **19**. [Epub ahead of print] (Journal IF: 1.687, Citations:0)

Polido-Pereira J, Rodrigues AM, Canhão H, Saraiva F, da Silva JA, Fonseca JE (2011) Primary biliary cirrhosis in a rheumatoid arthritis patient treated with rituximab, a case-based review. *Clin Rheumatol.* **26**. [Epub ahead of print] (Journal IF: 1.687, Citations:0)

Cascão R, Polido-Pereira J, Canhão H, Rodrigues AM, Navalho M, Raquel H, Mourão AF, Resende C, Fonseca JE, Moita LF (2011) Caspase-1 is active since the early phase of Rheumatoid Arthritis. *Clin Exp Rheumatol.* **2012** **23**. [Epub ahead of print] (Journal IF: 2.358, Citations:0)

Pimentel-Santos FM, Ligeiro D, Matos M, Mourão AF, de Sousa EV, Pinto P, Ribeiro A, Santos H, Barcelos A, Godinho F, Cruz M, Fonseca JE, Guedes-Pinto H, Trindade H, Brown MA,

Branco JC (2011) ANKH and Susceptibility to and Severity of Ankylosing Spondylitis. *J Rheumatol*. **15**. [Epub ahead of print]. (Journal IF: 3.551, Citations: 0)

Pereira JP, Barroso C, Evangelista T, Fonseca JE, Pereira da Silva JA (2011) Macrophagic myofasciitis: a case report of autoimmune/inflammatory syndrome induced by adjuvants (ASIA). *Acta Reumatol Port*. **1**:75-76. (Journal IF: 0.451, Citations: 1)

Canhão H, Faustino A, Martins F, Fonseca JE; on behalf Comissão Coordenadora do Registo Nacional de Doentes Reumáticos da Sociedade Portuguesa de Reumatologia: Sousa E, Pereira da Silva JA, Santos MJ, Canas da Silva J, Melo Gomes JA, Duarte C, Silva JA, Cunha-Miranda L, Teixeira A, Castelão W, Branco JC, Costa JA, Araujo D, Nóvoa T, Figueiredo G, Jesus H, Quintal A, Cravo AR, Sequeira G, Pinto P, André R, Bernardes M, Ventura F, Cunha I, Barcelos A, Nero P, Cruz M (2011) Reuma.pt - the rheumatic diseases portuguese register. *Acta Reumatol Por* **1**:45-56. (Journal IF: 0.451, Citations: 0)

Carvalho JF, Barros SM, Branco JC, Fonseca JE (2011) Asia or Shoenfeld's syndrome: highlighting different perspectives for diffuse chronic pain. *Acta Reumatol Port*. **1**:10-12. (Journal IF: 0.451, Citations: 0)

Nunes J, Marinho RT, Fonseca JE, Pereira da Silva JA, Velosa J (2011) Prophylaxis of hepatitis B reactivation with immunosuppressive therapy in rheumatic diseases. Orientations for clinical practice. *Acta Reumatol Port*. **36** (2):110-118. (Journal IF: 0.451, Citations: 1)

Mourão AF, Canhão H, Moura RA, Cascão R, Weinmann P, Rodrigues A, Polido-Pereira J, Resende C, Capela S, Pereira da Silva JA, Fonseca JE (2011) Markers of progression to rheumatoid arthritis: discriminative value of the new ACR/EULAR rheumatoid arthritis criteria in a Portuguese population with early polyarthritis. *Acta Reumatol Port* **36**:370-376 (Journal IF: 0.451, Citations: 0)

Branco JC, Canhão H. (2011) Epidemiological study of rheumatic diseases in Portugal – EpiReumaPt. *Acta Reumatol Port*. **36**(3):203-4, (Journal IF: 0.451, Citations: 0)

Canhao H (2011) Practical guides and clinical recommendations – why are they important? *Acta Reumatol Port*. **36**(2):99-100. (Journal IF: 0.451, Citations: 0)

Fonseca JE; Bernardes M; Canhão H; Santos MJ; Quintal A; Malcata A; Neto A; Cordeiro A; Rodrigues A; Mourão AF; Ribeiro AS; Cravo AR; Barcelos A; Cardoso A; Vilar A; Braña A; Faustino A; Silva C; Duarte C; Araújo D; Nour D; Sousa E; Simões E; Godinho F; Brandão F; Ventura F; Sequeira G; Figueiredo G; Cunha I; Matos JA; Branco J; Ramos J; Costa JA; Gomes JA; Pinto J; Silva JC; Silva JA; Patto JV; Costa L; Miranda LC; Inês L; Santos LM; Cruz M; Salvador MJ; Ferreira MJ; Rial M; Queiroz MV; Bogas M; Araújo P; Reis P; Abreu P; Machado P; Pinto P; André R; Melo R; Garcês S; Cortes S; Alcino S; Ramiro S; Capela S (2011) Portuguese guidelines for the use of biological agents in rheumatoid arthritis – October 2011 update. *Acta Reumatol Port* **36**:385-388 (Journal IF: 0.451, Citations: 0)

Mourão AF; Fonseca JE; Canhão H; Santos MJ; Bernardo A; Cordeiro A; Cravo AR; Ribeiro A; Teixeira A; Barcelos A; Malcata A; Faustino A; Duarte C; Ribeiro C; Nour D; Araújo D; Sousa E; Mariz E; Ramos F; Vinagre F; Ventura FS; Sequeira G; Santos H; Branco JC; Gomes JA; Silva JA; Ramos J; Santo JE; Costa JA; Silva JA; Ribeiro JS; Inês L; Miranda L; Sampaio L; Costa ML; Rodrigues M; Afonso MC; Cunha MI; Saavedra MJ; Queiroz MV; Couto M; Bernardes M; Bogas M; Pinto P; Valente P; Coelho P; Abreu P; Cortes S; Pimenta S; Ramiro S;

Figueira R; Nóvoa T (2011) Guia prático de utilização de terapêuticas biotecnológicas na artrite reumatóide - actualização de Dezembro 2011. *Acta Reumatol Port* **36**:389-395 (Journal IF: 0.451, Citations: 0)

Other publications International

Sousa E, Fonseca JE, McInnes I, Treatment of Rheumatoid Arthritis in EULAR Compendium on Rheumatic Diseases 2011 (online course and book in press)

Carmona- Fernandes D and Fonseca JE. IL-6 y autoinmunidade (Chapter 3) and IL-6 y Artritis Reumatoide (Chapter 5) In: Interleucina 6 (IL-6) Factores inmunológicos en la artritis reumatoide y tocilizumab, anticuerpo monoclonal humanizado dirigido contra el receptor de IL-6. Published by ROCHE. México 2011.

Vaz MF, Canhão H and Fonseca JE. Advances in Composite Materials - Analysis of Natural and Man-Made Materials, ISBN 978-953-307-449-8. Bone: A Composite Natural Material. Published by InTech.

Other publications National

Canhão H (2011) Current treatment of post-menopausal osteoporosis, *Acta Obstet Ginecol Port* **5**(3):137-142

Invited Lectures and Seminars

Fonseca JE. Tuberculosis and Biologics. 31º Ciclo de conferências de Infecçiology do Hospital de Santa Maria, Lisbon, Portugal, January 7, 2011

Fonseca JE. Cytokines, bone and biomechanics. 9th Medinterna International Meeting “Pearls in connective tissue diseases”, Porto, Portugal, January 26-29, 2011

Mourão AF. Laboratório nas Artrites Juvenis. 1º Curso SPR de Reumatologia Pediátrica, Lisbon, Portugal, January 23, 2011

Canhão H. Clinical and genetic predictors of response to anti-tnf treatment in patients with rheumatoid arthritis. Longitudinal Clinical Research Seminar Serie, Tostesan Medical Education Center, Harvard Medical School, Boston, USA, February 15, 2011

Mourão AF. DAPSA na Artrite Psoriática. IV Forum das Espondilartrites. Viseu, Portugal, February 25-26, 2011

Sousa E. Doença Psoriática - Caso Clínico. IV Fórum das Espondilartrites, Viseu, Portugal, February 25-26, 2011

Santos MJ. O efeito do LES sobre o osso: como preveni-lo. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31 March-02 April 2011

Fonseca JE. Serão as terapêuticas utilizadas na fase crónica da AR as melhores opções para tratar

a fase muito inicial da doença? 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011

Canhão H. Terá o FRAX um significado biológico? 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011

Sousa E. Novas possibilidades terapêuticas para inibir a reabsorção óssea. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011

Fonseca JE. Diagnóstico de AR: a importância do anti-CCP. Reunião da Associação Nacional de Doentes com AR, Lisbon, Portugal, April 5, 2011

Santos MJ. Assessing atherosclerosis and risk of thrombosis in SLE: Adipokines and inflammation, Porto, Portugal, April 7-9, 2011

Canhão H. Defining disease activity and identifying response to therapy from EMRs narrative data. Autoimmune and Cardiovascular Disease Meeting New Research Building, Harvard Medical School, Boston, USA, April 8, 2011

Fonseca JE. Meet the professor: Rheumatoid arthritis and lupus: Similarities and differences in therapeutic management, 8th European Lupus Congress, Porto, Portugal, April 7-9, 2011

Fonseca JE. Serão as terapêuticas utilizadas na fase crónica das doenças autoimunes a melhor opção para a fase muito inicial da doença? 2º Congresso Nacional de Auto-imunidade | XVII Reunião Anual do NEDAI Almanil, Portugal, April 28-30, 2011

Mourão AF. Aspectos Imunológicos da Artrite Inicial. 2º Congresso Nacional de Auto-imunidade | XVII Reunião Anual do NEDAI Almanil, Portugal, April 28-30, 2011

Sousa E. Segurança dos tratamentos biológicos, III Jornadas dos Novos Centros de Reumatologia, Caldas da Rainha, Portugal, April 30, 2011

Caetano Lopes. Biobank , Rheumatology Department Session, Hospital de Santa Maria, Lisbon, Portugal, May 3, 2011

Canhão H. BioRePortAR. Rheumatoid Arthritis :Making and Meet, Lisbon, Portugal May 12, 2011

Mourão AF. Integração dos “Consensus Statement” do Rituximab e documento CRI sobre tocilizumab. Arthritis: Making and Meet, Lisbon, Portugal, May 12, 2011

Sousa E. New Concepts in the design of clinical trials. Rheumatoid Arthritis: Making and Meet, Lisbon, Portugal, May 12, 2011

Fonseca JE. Estratégia de indexação de uma Revista. Congresso Português de Gastroenterologia, Estoril, Portugal, June 4, 2011

Moura RA. The role of B cells in the early phase of Rheumatoid Arthritis. Institut Pasteur, Immunology Department, Molecular and Cellular Allergology Unit, Paris, France, June 7, 2011

Moura RA. The role of B cells in the early phase of Rheumatoid Arthritis. Rheumatology Department Session, Hospital de Santa Maria, Lisbon, Portugal, June 14, 2011

Canhão H. Disease Activity and Response to Anti-TNF Treatment in Patients with Rheumatoid Arthritis. Pharmacoepi/Quality. Harvard, USA, July 20, 2011

Mourão AF. Doenças Reumáticas Periarticulares: 4^{as} Jornadas de Reumatologia Prática do CHLO/FCML. Lisbon, Portugal, September 22, 2011

Fonseca JE. Actuar sobre todos los parámetros del hueso. IX Congreso SIBOMM (Sociedad Iberoamericana de Osteología y Metabolismo Mineral), Madrid, Spain Octubre 6-8, 2011

Fonseca JE. Fracture risk reduction in osteoporosis: a matter of bone quality and bone strength, Satellite Symposium-IOF Regionals 1st Middle-East & Africa Osteoporosis Meeting Dubai, UAE, October 19-22, 2011

Fonseca JE. Interecção das terapêuticas biológicas imunomodeladoras com o sistema imunológico. Seminário Terapêutica Biológica Imunomoduladora e Infecção. Porto, Portugal, Octubre 14, 2011

Canhão H. Compreender para agir: como funciona o osso? XXII Curso de Reumatologia Hospitais da Universidade de Coimbra. Coimbra, Portugal, October 13-14, 2011

Sabatina. Agora pergunto eu. Osteoporose. XXII Curso de Reumatologia Hospitais da Universidade de Coimbra. Coimbra, Portugal, October 13-14, 2011

Sousa E. Manifestações cutâneas das doenças reumáticas, XIII Fórum Liga Portuguesa Contra as Doenças Reumáticas, Lisbon, Portugal October 21, 2011

Mourão AF. Descontinuação de terapêutica anti-TNF em doentes com artrite reumatóide em remissão “Rheumatology in Practice”. Funchal, Madeira, Portugal Octubre 22, 2011

Carmona-Fernandes D. Anti-ribosomal P protein IgG autoantibodies in Portuguese SLE patients. Rheumatology Department Session, Hospital de Santa Maria, Lisbon, Portugal, Octubre 25, 2011

Fonseca JE. Terapêuticas actuais e perspectivas para o futuro. Jornadas do aparelho locomotor. Escola de Ciências da Saúde da Universidade do Minho. Braga, Portugal, Octubre 28-29, 2011

Communications in International Conferences

Moura RA, Canhão H, Polido-Pereira J, Rodrigues AM, Navalho M, Mourão AF, Resende C, Pereira da Silva JA, Graça L, Fonseca JE. BAFF and TACI mRNA expression are increased in very early Rheumatoid Arthritis patients. 31st European Workshop for Rheumatology Research (EWRR), Amsterdam, The Netherlands, March 3-6, 2011(Poster Presentation)

Fernandes D, MJ Santos, JE Fonseca. Antiribosomal P protein IgG autoantibodies are highly specific for SLE and might be associated with disease activity, 31st European Workshop for

Rheumatology Research (EWRR), Amsterdam, The Netherlands, March 3-6, 2011 (Poster Presentation).

Cascão R, Vidal B, Fonseca JE, Moita LF. Gambogic acid and Celastrol are two powerful anti-inflammatory drugs in arthritis 31st European Workshop for Rheumatology Research (EWRR), Amsterdam, The Netherlands, March 3-6, 2011 (Poster Presentation).

Moura RA*, Cascão R*, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Pereira da Silva JA, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Spondyloarthritis and rheumatoid arthritis: Two different diseases, a similar cytokine network. 31st European Workshop for Rheumatology Research (EWRR), Amsterdam, The Netherlands, March 3-6, 2011 *contributed equally. (Poster Presentation)

Fernandes D, Perpétuo IP, Vinagre F, Canhão H, Santos MJ, Fonseca JE. sRANKL/OPG ratio is increased in systemic lupus erythematosus patients. 8th European Lupus Congress, Porto, Portugal, April 7-9, 2011 Porto (Poster presentation)

Fernandes D, Santos MJ, Fonseca JE. Anti-ribosomal P protein IgG autoantibodies in Portuguese SLE patients. 8th European Lupus Congress, Porto, Portugal, April 7-9, 2011 Porto (Poster presentation)

Cordeiro I, Santos MJ, Canas da Silva J, Fonseca JE, Gil V. Endothelial dysfunction in systemic lupus erythematosus. 8th European Lupus Congress, Porto, Portugal, April 7-9, 2011 Porto (Poster presentation)

De La Torre I, Moura RA, Leandro MJ, Edwards JCW, Cambridge G. BAFF Binding Receptors (BBR) related to relapse after Rituximab in patients with Rheumatoid Arthritis (RA). Rheumatology 2011 (British Congress of Rheumatology), Brighton, United Kingdom, April 12-14, 2011 (Poster Presentation)

Caetano-Lopes J, A Lopes A, Rodrigues A, Fernandes D, Perpétuo I, Monteiro J, Canhão H, Fonseca J. Upregulation of Inflammatory genes and downregulation of sclerostin gene expression are key elements in the early phase of fragility fracture healing, 3rd Joint Meeting of ECTS & IBMS Athens, Greece, 7-11 May, 2011 (Poster Presentation).

Perpétuo I, Caetano-Lopes J, Polido-Pereira J, Pereira da Silva JA, Fonseca JE, Canhão H. Gene Expression on osteoclast precursors from Rheumatoid Arthritis patients. 3rd Joint Meeting of ECTS & IBMS Athens, Greece, 7-11 May, 2011 (Poster Presentation).

Cristino J, Canhão H, Perelman J, Santos C, Pereira JA. Cost-utility analysis of denosumab vs. standard care in the treatment of post-menopausal osteoporosis in Portugal. International Society for Pharmacoeconomics and Outcomes Research 16th Annual International Meeting, , Baltimore, MD, USA, May 21-25, 2011 (Poster Presentation)

Fernandes D, Perpétuo IP, Vinagre F, Canhão H, Santos MJ, Fonseca JE. sRANKL/OPG ratio is increased in systemic lupus erythematosus patients. European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, London, United Kingdom, May 25-28, 2011 (Poster Presentation)

Santos MJ, Cordeiro I, Canas da Silva J, Fonseca JE, Gil V. The influence of rheumatoid arthritis on endothelial function as assessed by peripheral artery tonometry. European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, London, United Kingdom, May 25-28, 2011 (Poster Presentation)

Santos MJ, Capela S, Vinagre F, Canhao H, Canas da Silva J, Fonseca JE, Saldanha C. Hemorheological disturbances and its clinical correlates among women with systemic lupus erythematosus. European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, London, United Kingdom, May 25-28, 2011 (Poster Presentation)

Cascão R, Polido-Pereira J, Canhão H, Rodrigues AM, Navalho M, Mourão AF, Resende C, Fonseca JE, Moita LF. Caspase-1 is active since the early phase of Rheumatoid Arthritis. European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, London, United Kingdom, May 25-28, 2011 (Poster Presentation)
31st European Workshop for Rheumatology Research (EWRR), Amsterdam, The Netherlands, March 3-6, 2011 (Poster presentation)

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.
European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, London, United Kingdom, May 25-28, 2011 (Poster Presentation)
ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation).

Dias JM, Costa MM, Saraiva F., da Silva JPJ Musculo-skeletal Ultrasound in paediatric rheumatology: experience of one University Hospital, 18th Pediatric Rheumatology European Society (PReS) Congress Bruges, Belgium, September 14-18, 2011(Poster Presentation)

Campanilho-Marques R, Mourão AF, Melo Gomes S, Fonseca JE, Canhão H, Macieira C, Ramos F, Pereira da Silva JA. Off-label use of biological agents in the management of uveitis: experience from a Pediatric Rheumatology centre, 18th Pediatric Rheumatology European Congress, Bruges, September 14-18, 2011 (Poster Presentation)

Dias JM, Costa MM, Romeu J, de Almeida LS, Filipe P, da Silva JP A case of pachydermodactyly in a 16 year-old male. 18th Pediatric Rheumatology European Society (PReS) Congress Bruges, Belgium, September 14-18, 2011(Poster Presentation)

Rodrigues A, Caetano-Lopes J, Lopes A Vale AC, Aleixo I, Perpétuo I, Pena AS, Faustino A,

Sepriano A, Polido-Pereira J, Vieira-Sousa E, Romeu JC, Amaral PM, Rosa LG, Pereira da Silva JA, Monteiro J, Vaz MF, Fonseca JE, Canhão H. Apolipoprotein E and undercarboxylated osteocalcin are associated with bone fragility but not with bone mineral density in osteoarthritis patients. 6th European Workshop on Immune-Mediated Inflammatory Diseases. Nice, France, November 23-25, 2011. (Poster Presentation).

ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation).

Caetano-Lopes J, Rodrigues A, Lopes A, Vale AC, Pitts-Kiefer MA, Vidal B, Perpétuo I, Monjardino T, Monteiro J, Konttinen YT, Vaz MF, Nazarian A, Canhão H, Fonseca JE. Rheumatoid Arthritis Bone Fragility Is Associated with Increased Dickkopf-1 Expression and Disturbances in the Bone Turnover Regulating genes.

6th European Workshop on Immune-Mediated Inflammatory Diseases. Nice, France, November 23-25, 2011. (Poster Presentation).

ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation).

Chatzidionysiou K, Lie E, Evgeny L, Nasonov E, Lukina G, Merete L, Hetland ML, Tarp U, Ancuta I, Pavelka K, Nordström DC, Gabay C, Canhao H, Tomsic M, van Riel PL, Gomez-Reino J, Kvien TK, van Vollenhoven RF. Seropositivity and Response to RTX: Data From the CERERRA Collaboration. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011 (Oral Presentation).

Chatzidionysiou K, Lie E, Evgeny L, Nasonov E, Lukina G, Merete L, Hetland ML, Tarp U, Ancuta I, Pavelka K, Nordström DC, Gabay C, Canhao H, Tomsic M, van Riel PL, Gomez-Reino J, Kvien TK, van Vollenhoven RF. Efficacy of Different Doses of Rituximab for the Treatment of RA: Data From the CERERRA Collaboration. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011 (Oral Presentation).

Ramiro S, Machado P, Roque R, Santos H, Pereira J, Peixoto D, Duarte C, Marques A, Pimentel-Santos F, Silva C, Teixeira F, Marques A, Araújo F, Branco JC, Pereira da Silva JA, Costa J, Pereira Silva JA, Miranda L, Canas da Silva J, Canhão H, Van Tubergen AM, Desire'e van der Heijde Landewe R, Santos MJ. Performance of the Ankylosing Spondylitis Disease Activity Score (ASDAS) in Patients Under Biological Therapies in Daily Practice—Results From the Portuguese Register Reuma.Pt ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011 (Poster Presentation)

Lie E, Chatzidionysiou K, Nasonov E, Lukina G, Pavelka K, Nordström DC, Tomsic M, Hetland ML, Gabay C, Ancuta I, van Riel PL, , Gomez-Reino J, Fonseca JE, Trap U, van Vollenhoven RF, Kvien TK. Early Versus Delayed Retreatment with Rituximab (RTX) in Relation to Long Term Clinical Response – Data From the CERERRA Collaboration ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation)

Lie E, Chatzidionysiou K, Nasonov E, Lukina G, Pavelka K, Nordström DC, Tomsic M, Gabay C, Ancuta I, Piet LC, van Riel, Juan J. Gomez-Reino JJ, Fonseca JE, Hetland ML, Tarp U, Kvien TK and Ronald F. van Vollenhoven. Characterization of Long-Term Responders to First

Treatment Course of Rituximab (RTX) – Results From the CERERRA Collaboration. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation)

Moura RA, De la Torre I, Leandro MJ, Edwards JCW, Cambridge G. 9G4 expression on antibodies to citrullinated residues in patients with early inflammatory arthritis and established rheumatoid arthritis. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation).

Pimentel-Santos FM, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Sousa E, Pinto P, Godinho F, Cruz M, Santos RA, Sequeria G, Rabiais S, Félix J, Fonseca JE, Guedes-Pinto H, Branco JC. Clinical and Radiological Manifestations of Ankylosing Spondylitis:Gender Differences. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011(Poster Presentation)

Canhão H. Predictors of response and anti-TNF drugs comparative efficacy, 6th European Workshop on Immune-Mediated Inflammatory Diseases. Nice, France, November 23-25, 2011. (Poster Presentation).

Cascão R, Vidal B, Raquel H, Gupta V, Fonseca JE, Moita LF. Drugs that simultaneously down-regulate IL-1 and TNF secretion significantly reduce inflammation in a rat model of antigen-induced arthritis. 6th European Workshop on Immune-Mediated Inflammatory Diseases. Nice, France, November 23-25, 2011. (Poster Presentation).

Dias JM, Costa MM, Pereira da Silva J, Viana de Queiroz M. Syndrome de Parry-Romberg chez un enfant de 11 ans avec manifestations neurologiques sans altérations cérébrales à l'imagerie, 24 Congrès Français de Rhumatologie, Paris, December 11-14, 2011 (Poster Presentation)

Dias JM, Miltenberger-Milteny G, Rodrigues A, Janeiro A, Costa M.M, Gaião L, Fonseca, JE, Pereira da Silva J. Pachydermopériostose avec arthrite exubérante, sans mutation du gène HPGD 24 Congrès Français de Rhumatologie, Paris, December 11-14, 2011 (Poster Presentation)

Communications in National Conferences

Cascão R, Vidal B, Fonseca JE, Moita LF. Gambogic acid and Celastrol are two powerful anti-inflammatory drugs in arthritis. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Oral Presentation)

Dias JM, Costa MM, Saraiva F, Pereira da Silva J.Ecografia musculo-esquelética em Reumatologia Pediátrica: experiência de um centro. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Oral Presentation)

Moura RA, Canhão H, Polido-Pereira J, Rodrigues AM, Navalho M, Mourão AF, Rosa CM, Resende C, Campanilho-Marques R, Dias JM, Ribeiro da Silva J, Bexiga M, Pereira da Silva JA, Fonseca JE. BAFF and TACI gene expression are increased in untreated very early rheumatoid

arthritis patients. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Moura RA*, Cascão R*, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Pereira da Silva JA, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Spondyloarthritis and rheumatoid arthritis: Two different diseases, a similar cytokine network. 2º Simpósio da Sociedade Portuguesa de Reumatologia: Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation) *contributed equally.

Cascão R, Polido-Pereira J, Canhão H, Rodrigues AM, Navalho M, Mourão AF, Resende C, Fonseca JE, Moita LF. Caspase-1 is active since the early phase of Rheumatoid Arthritis. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Mourão AF, Canhão H, Moura RA, , Weinmann P, Rodrigues AM, Resende C, Capela S, Pereira da Silva JA, Queiroz MV, Fonseca JE. Markers of progression to Rheumatoid Arthritis and the discriminative value of the new ACR/EULAR classification criteria for Rheumatoid Arthritis in an untreated polyarthritis cohort with less than 6 weeks of disease duration. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Ponte C, Marques R, Rodrigues AM, Romeu JC, Pereira da Silva JE. As principais causas da Osteoporose masculina nos doentes seguidos em consulta de Reumatologia no Hospital de Santa Maria, Lisboa. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Polido-Pereira J, Rodrigues AM, Geraldês R, Henriques V, Zagalho A, Canhão H, Rosa CM, Pereira da Silva JA, Fonseca JE. Neuro- Behçet mimicking acute meningitis: Differential Diagnosis. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Santos L, Fernandes PR, Fonseca JE, Rodrigues H. Modelação computacional do processo de mineralização óssea e da actividade de BMUS na avaliação da distribuição de Densidades de Mineralização Óssea (BMDD). 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Pimentel-Santos FM, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Sousa E, Pinto P, Godinho F, Cruz M, Santos RA, Sequeria G, Rabiais S, Félix J, Fonseca JE, Guedes-Pinto H, Branco JC. Manifestações clínicas e radiológicas na espondilite anquilosante numa população portuguesa: A influência do sexo. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Polido-Pereira J, Madruga JD, Costa M, Fonseca JE, Pereira da Silva JA. ANCA vasculitis induced by propylthiouracil, a disease with heterogeneous presentations: Report of 2 cases. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Perpétuo I, Caetano-Lopes J, Polido-Pereira J, Pereira da Silva JA, Fonseca JE, Canhão H. Gene Expression on osteoclast precursors from Rheumatoid Arthritis patients. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Fernandes D, Perpétuo IP, Vinagre F , Canhão H , Santos MJ , Fonseca JE. Serum evaluation of sRANKL/OPG ratio does not reflect increased bone loss in rheumatoid arthritis patients. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Dias JM, Costa MM, Pinto L, Marques A, Graça L, Pereira da Silva J. Fractura de stress do 3º metatarso durante a gravidez, 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Dias JM, Costa MM; Pereira da Silva J. Relembrar a fractura de insuficiência como causa importante de incapacidade na Artrite Reumatóide de longa duração, 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Dias JM, Costa MM, Marques A, Pinto L, Conceição I, Graça L, Pereira da Silva J. Miastenia Gravis Ocular em grávida com Lúpus Eritematoso Sistémico, 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Dias JM, Costa MM; Pereira da Silva J. Sinovite vilonodular pigmentada circunscrita do ombro, 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Dias JM, Miltenberger-Miltenyi G, Rodrigues A, Janeiro A, Costa M, Gaião L, Fonseca JE, Pereira da Silva J. Paquidermoperiostose com artrite exuberante, sem mutações no gene HPGD. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Polido-Pereira J, Rodrigues AM, Borges R, Saavedra MJ, Marques A, Catita C, Canhão H, Pereira da Silva JA, Fonseca JE. Aplicação da BioRePortEA na avaliação de eficácia dos agentes anti-TNF no Hospital de Santa Maria 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Polido-Pereira J, Pereira da Silva JA, Fonseca JE Macrophagic myofasciitis presenting as fibromyalgia. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Moura RA, Cascão R, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graca L, Fonseca JE. Spondyloarthritis and Rheumatoid Arthritis: Different clinical manifestations similar cytokine network. 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011 (Poster Presentation)

Organisation of Conferences

Fonseca JE. Organized and chaired the meeting 2º Simpósio SPR Artrite e Osso, Aveiro, Portugal, 31March-02April 2011

Santos MJ. Organized and chaired the meeting 8th European Lupus Congress, Porto, Portugal, 7-9 April, 2011

Fonseca JE and RRU Organized and chaired the meeting Rheumatoid Arthritis: Making and Meet, Lisbon, Portugal 12 May, 2011

Fonseca JE Chaired the session in New Frontiers in Biological Therapy. Instituto Medicina Molecular, Lisbon, Portugal November 26, 2011

Fonseca JE. Chairman in lecture Towards Prevention of Atherosclerosis Progression in Rheumatoid Arthritis: Insights into the Relationship between Inflammation and Cardiovascular Disease. ACR/ARHP Annual Scientific Meeting, Chicago, IL November 4 – 9, 2011

Fonseca JE. Co Chair in Lecture BioRePortAR and CERRERA Rheumatoid Arthritis: Making and Meet, Lisbon, Portugal, May 12 , 2011

Fonseca JE chairman in “Rheumatology in Practice”. Funchal, Madeira, Portugal Octobre 22, 2011

Fonseca JE and RRU. Created and organized “IMM Rheumatology Series”, every month in Instituto de Medicina Molecular, Lisbon, Portugal, 2011

Sousa E. Organized “ 1º Curso de Formação para Enfermeiros em Espondilartrites”, Fátima, Portugal, November 12, 2011

Fonseca JE created IMM Rheumatology Series. Monthly lectures on translational research in the field of rheumatology

Internationalization

Internationalization is considered by RRU one important strategic pathway. Over the last years, international collaborations have been set and strengthened, allowing the development of networking, collaborative projects and publications:

- Joint inflammatory diseases - pathogenesis, early diagnosis, prognosis and pharmacogenetics (in collaboration with Broad Institute and Brigham Women Hospital, Harvard Medical School (Robert Plenge); Laboratorio de Investigacion and Rheumatology Unit, Hospital Clinico Universitario de Santiago, Santiago de Compostela (Antonio Gonzalez);
- Inflammatory cells and Inflammation (in collaboration with University College of London (J Edwards, M Leandro, G Cambridge); Amsterdam Academic Medical Centre (PP Tak and Dominique Baeten); University of Helsinki (YT Konttinen Mari and Ainola))
- Bone biology, structure and biomechanics (in collaboration with University of Helsinki (YT Konttinen and Mari Ainola) and CAOS, BIMDC, Harvard Medical School (Ara Nazarian)).
- Epidemiology of Rheumatic Diseases, Cohorts, Registries and Databases. Recommendations and Guidelines (in collaboration with Brigham Women Hospital, Harvard Medical School (Daniel Solomon and Elizabeth Karlson)).

Prizes, honours and awards

Classification as one of the most interesting posters presented at EULAR 2011. EMEUNET Newsletter (EMEUNews, Issue 1, Year 2, May 2011) 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.

Best Presenting Poster Award in 2º Simpósio da Sociedade Portuguesa de Reumatologia: Artrite e Osso, Aveiro, Portugal, March 31-April2, 2011. 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 mRNA expression are increased in very early Rheumatoid Arthritis patients.

Best oral communication Award in 2º Simpósio da Sociedade Portuguesa de Reumatologia: Artrite e Osso, Aveiro, Portugal, March31 - April2, 2011. SPOCK2 E EP300: Dois novos genes envolvidos na neo-formação óssea da espondilite anquilosante? Pimenel-Santos FM, Matos M, Ligeiro D, Mourão AF, Ribeiro A, Santos H, Barcelos A, Vieira-Sousa E, Fonseca JE, Guedes-Pinto H, Brown MA, Thomas G, Branco JC

NEDAI/MSD Award on Autoimmunity Research was awarded in April 2011 to Duarte J, Aguiar-Doce A, Oliveira VG, Fonseca JE, Graca L for the project “Modulation of IL-17 and Foxp3 expression in the prevention of autoimmune arthritis in mice”.

Bolsa de Investigação Sociedade Portuguesa de Reumatologia/ MSD 2011 was awarded to Sousa E, Caetano Lopes J, Lopes A, Perpétuo I, Navalho M, Rodrigues AM, Capela S, Madruga Dias J, Ponte C, Antunes J, Filipe P, Pereira da Silva JA, Canhão H, McInnes I, Fonseca JE for the project- “Linking biomechanics and the immune system in early Psoriatic Arthritis - a translational approach”.

Industry contract research

2011-2012 - Collection of peripheral blood samples and associated biological & clinical data from RA patients, in order to develop a blood-based gene expression signature able to discriminate responders from non-responders to anti-TNF therapy. Pending funding from TcLand expression, 21600 euros

Rheumatoid arthritis causes considerable direct costs (treatment, hospitalization, surgery) and indirect costs (disruption of professional activity, sick leave). In 2006, in the classification of the 15 best selling bio drugs worldwide for all pathologies, 3 were for RA treatments occupying 1st, 4th and 12th place (etanercept, infliximab and adalimumab respectively) representing 4.5, 3.8 and 2 billion dollars' sales (10.5%, 9.1% and 4.8% of total sales, almost 25% for this pathology alone). Predicting non-response to a specific anti-TNF treatment such as etanercept might represent an advantage by reducing unnecessary costs relating to the prescription of “ineffective” treatment for patients or state or private health insurance.

This study aims at collecting whole blood and associated biological & clinical data on a large cohort of RA patients in order to develop a blood-based gene expression signature able to discriminate responders and non-responders to a given anti-TNF prior to initiation of therapy.

The collected samples associated with clinical and biological data will be stored at TcLand Expression to be used for future research programs. This research could involve discovery, development or pilot validation studies on gene expression biomarkers for rheumatoid arthritis.

Government/Organization contract research

Jaime Branco, Viviana Tavares, Eugénia Simões, Helena Canhão authored the “Norma da Direcção Geral da Saúde para Tratamento Farmacológico da Osteoporose Pós-menopáusia”

Jaime Branco, José António de Melo Gomes, Elisabete Melo Gomes, Helena Canhão, João Eurico da Fonseca, Maria José Santos e Marta Conde created the “Norma da Direcção Geral da Saúde para Prescrição de Agentes Biológicos nas Doenças Reumáticas”

João Eurico da Fonseca, Augusto Faustino, Jaime Branco have made a critical appraisal of the norma “Anti-inflamatórios não esteróides sistémicos em adultos: orientações para a utilização de inibidores da COX-2”

Advanced teaching

Fonseca JE. Imunologia Inata nas Doenças Reumaticas Juvenis.
Canhão H. Auto-imunidade nas Doenças Reumaticas Juvenis.
I Curso Reumatologia Pediatrica para Internos de Reumatologia. Organização SPR
Lisbon, Portugal, January 21-23, 2011

Fonseca JE, Canhão H, Ramos Filipa, Sousa E, Polido-Pereira J, Rodrigues A and Capela S are responsible for all the Rheumatology teaching in Faculdade de Medicina da Universidade de Lisboa

Mourão AF. Aula Teórica de Medicina I – Doenças reumáticas sistémicas. Disciplina do 4º ano do Curso de Medicina, Faculdade de Ciências Médicas da Universidade Nova de Lisboa. Lisbon, Portugal, April 6, 2011

Fonseca JE. Diagnóstico imagiológico das doenças inflamatórias das articulações periféricas. XVII Curso pós graduado de actualização da Escola Superior de Tecnologias da Saúde e Faculdade de Ciências Médicas, Lisboa, Portugal, April 6, 2011

Fonseca JE was a member of the faculty of XVI Curso de Reciclagem do Centro de Estudos de Reciclagem e de Investigação em Reumatologia do Estado de São Paulo, Brasil, April 14 -17, 2011

“O que há de novo na terapêutica da osteoartrose” JE Fonseca

“Lesões osteocartilaginosas e inflamassoma reumatóide” JE Fonseca

Fonseca JE coordinated the discussion of the case report contest.

Canhão H. Workshop: Introduction to Clinical Research. Harvard Medical School Program Faculdade de Ciências Médicas, Universidade Nova de Lisboa, May 14-15, 2011

Perpétuo I. Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis. ECTS PhD Training Course, Ljubljana, Slovenia September 1-4, 2011

Perpétuo I. Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis. V PhD Students Meeting IMM/CAML, Lisbon, Portugal, October 17-18, 2011 (Poster presentation)

Cascão R. Celastrol: a potential new drug for RA. V PhD Students Meeting IMM/CAML, Lisbon, Portugal, October 17-18, 2011 (Oral presentation)

Moura RA chair the Oral Presentation Session II in V PhD Students Meeting IMM/CAML, Lisbon, Portugal, October 17-18, 2011

Perpétuo I. Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis- a project overview, Pizza Seminar, IMM November, 2011(Oral presentation)

Canhão H, Ducla Soares JL, Luz-Rodrigues H. “Curso de Terapêutica de Osteoporose” Seminários de Terapêutica para alunos 6º ano FMUL. Faculdade de Medicina de Lisboa, Lisboa, Portugal, December 14, 2011

Saba Abdulghani Oliveira da Silva and João Eurico Fonseca. Tutors in “Mini-Projecto”. Disciplina de Introdução à Engenharia Biomédica. Instituto Superior Técnico, Lisbon, Portugal, 2011

Fonseca JE. Participation in module Inflammation and immune mediated inflammatory diseases. “Inflammatory joint disease, Lecture to student” and “Journal Club, student presentations of selected papers and discussion”.3rd Edition Programme for Advanced Medical Education, Lisbon, Portugal, January 31 – March 4, 2011

Fonseca JE. Participation in module Preparing for Research. “Finding research funding from a medical doctor’s perspective”. 3rd Edition Programme for Advanced Medical Education, Lisbon, Portugal, February, 24 – 25, 2011

Science and Society

The Duchess of Cornwall, Camilla Parker-Bowles and The Portuguese First Lady, Maria Cavaco Silva, visited IMM and RRU in March 29, mediated by APOROS (National Association against Osteoporosis).

This visit was referred in several TV channels, journals and magazines with CARAS, LUX, Jornal Publico e Diário de Notícias.

João Eurico Fonseca participated, in March 2011, in TV program, Edição da Manhã- SIC and Bom dia Portugal- RTP-1 to talk about rheumatic disease.

João Eurico Fonseca participated, in April 2011, in TV program, Sociedade Civil- RTP 2 to discuss diagnostic the rheumatic diseases.

João Eurico Fonseca and Helena Canhão participated in the TV program, Serviço Saúde – RTP-1 ,to talk about the burden of rheumatic diseases.

Helena Canhão, João Eurico Fonseca and Ana Filipa Mourão participated, in 2011, in TSF- Radio Program, to divulgate he scientific contents of Harvard Medical School Portugal Program. They have written texts about different diseases, such as osteoporosis, osteoarthritis, rheumatoid arthritis and their early diagnosis. This information was published in Official TSF Facebook.

João Eurico Fonseca validated different texts for Harvard Medical School Portugal Program - in translational research and information.

Helena Canhão participated, in October 2011, in TV program, Sic Noticias -Edição da Manhã for divulgation of the Project Reuma Census.

João Eurico Fonseca participated in November 2011, in the TV program, Sociedade Civil- RTP-2 to talk about rheumatic diseases.

Helena Canhão participated in November 2011, in a TV program, Sic Notícias -Edição da manhã to talk about osteoarthritis.

Rita Cascão and João Eurico Fonseca represented the RRU in Health Innovation & Technology Transfer Showcase/ Workshop "Investigação de translação e transferência de tecnologia na área da Saúde", Universidade do Minho, Braga, Portugal September 27,2011

Master and PhD thesis completed

Master Thesis

Nina Carvalho Fernandes (2011) Assessment and Management of Cardiovascular Risk Factors in Patients with Rheumatoid Arthritis Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Maria José Santos

Vasco Neves Evangelista (2011) “Casuística de terapêutica biotecnológica em doentes com Artrite Reumatóide seguidos em Centro de Reumatologia Privado” Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Helena Canhão

Sara Nunes Pires Nabais (2011) Analysis of a Systemic Lupus Erythematosus population registered on BioGeral Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Filipa Ramos

Sofia Costa Corado (2011) Rheumatoid Arthritis therapeutic approach and outcomes in a private practice setting. Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Joaquim Polido-Pereira

Nélia Martins da Cunha (2011) Are We Undertreating Rheumatoid Arthritis. Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Joaquim Polido-Pereira

Pedro Pereira Neves (2011) A case of Mycobacterium avium infection complicating long-term Rheumatoid Arthritis treatment with infliximab. Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Joaquim Polido-Pereira

Carina Lopes Teixeira (2011) “Tuberculose Miliar em Doente com Artrite Psoriática” Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Maria João Saavedra

Gisela Sofia dos Santos Eugénio (2011) “ Segurança da Terapêutica Biotecnológica em doentes com Espondilite Anquilosante: estudo prospetivo português com base na BioReportEA” Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Joaquim Polido-Pereira

Vanessa da Silva Mourato Henriques (2011) A case of fatal refractory Neuro-Behçet Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Joaquim Polido-Pereira

Rita Costal Ralha (2011) Spondyloarthritis a comparison of patients on conventional and anti-TNF biologic therapies, Mestrado Integrado em Medicina Medicine, Faculdade de Medicina de Lisboa. Supervisor: Elsa Sousa

Frederico Canas Ribeiro (2011) Computational Modeling of Long Bone Fracture Healing. Mestrado em Engenharia Biomédica, Instituto Superior Técnico e Faculdade de Medicina de Lisboa. Co.Supervisor: JE Fonseca

Jennifer Santos Faustino (2011) Caracterização Estrutural e Mecânica do Osso. Biomedical Enginnering master thesis. Co.Supervisor JE Fonseca and Saba Abdulghani

PhD Thesis

Joana Ribeiro Caetano Lopes (2011) Effect of inflammation on bone biological, structural and mechanical behavior. Biomedical Sciences PhD Thesis. Faculdade de Medicina de Lisboa. Supervisors JE Fonseca and Y Konttinen

Rita Aguiar de Moura (2011) The role of B cells in the early of rheumatoid arthritis. Biomedical Sciences PhD Thesis. Faculdade de Medicina de Lisboa. Supervisors JE Fonseca and Luis Graça

Viral Pathogenesis Unit

Major interests / Objectives

The overall aim of the Viral Pathogenesis Unit is to gain an understanding of the basic molecular mechanisms involved in the modulation of cellular function by herpesviruses. Herpesviruses are a major cause of disease worldwide and are amongst the most successful human pathogens, with specific viruses infecting more than 90% of the world's population. The main biological feature of these viruses is their ability to persist and reactivate in a primed immunocompetent host. The control of herpesviruses infections thus represents an important clinical goal. To achieve this we must first understand the basic mechanisms of viral pathogenesis. We use a laboratory animal model of infection with murine gamma-herpesvirus-68 (MHV-68), which establishes latent infection in B-lymphocytes. The ability to genetically manipulate both the virus and the host allows the dissection of the molecular mechanisms involved in the virus/host interaction.

Head of Unit

Pedro Simas, PhD—Associate Professor, FMUL

Research Team

Marta Miranda, PhD	Post Doc, IMM
Sofia Marques, PhD	Post Doc, IMM
Lénia Rodrigues, PhD	Post Doc Fellowship, FCT
Marta Alenquer, PhD	Post Doc Fellowship, FCT
Cristina Silva	PhD Fellowship, FCT
Diana Fontinha	PhD Fellowship, FCT
Sofia Cerqueira	PhD Fellowship, FCT

Keywords/Research Areas

Viral Pathogenesis

Recent Most Relevant Publications

Stevenson PG, Simas JP, Efstathiou S (2009) Immune control of mammalian gamma-herpesviruses: lessons from murid herpesvirus-4. *J Gen Virol.***90** (Pt 10), 2317-30. (Journal IF: 3.260, Citations: 4)

Rodrigues L, Filipe J, Seldon MP, Fonseca L, Anrather J, Soares MP, Simas JP (2009) Termination of NF-kappaB activity through a gammaherpesvirus protein that assembles an EC5S ubiquitin-ligase. *EMBO J.* **28** (9), 1283-95. (Journal IF: 8.993, Citations: 8)

Milho R, Smith CM, Marques S, Alenquer M, May JS, Gillet L, Gaspar M, Efstathiou S, Simas

JP, Stevenson PG (2009) In vivo imaging of murid herpesvirus-4 infection. *J Gen Virol* **90** (Pt 1), 21-32. (Journal IF: 3.241, Citations: 11)

Marques S, Alenquer M, Stevenson PG, Simas JP (2008) A single CD8+ T cell epitope sets the long-term latent load of a murid herpesvirus. *PLoS Pathog* **4** (10), e1000177. (Journal IF: 8.978 , Citations: 3)

Pires de Miranda M, Alenquer M, Marques S, Rodrigues L, Lopes F, Bustelo XR, Simas JP (2008) The Gammaherpesvirus m2 protein manipulates the Fyn/Vav pathway through a multidocking mechanism of assembly. *PLoS One*. **3** (2):e1654. (Journal IF: 4.351, Citations: 8)

Ongoing Research Projects

2010/12, Gammaherpesvirus latent infection: immunological synapse modulation, FCT, Principal Investigator: Pedro Simas, PTDC/SAU-MII/099314/2008, € 200 000

2011/13, Patogénese de gamma-herpesvírus: modulação dos factores de transcrição celulares NF-kB e MYC, FCT, Principal Investigator: Pedro Simas, PTDC/SAU-MIC/110887/2009, € 200 000

2011/13, Pathogenesis of Kaposi's Sarcoma herpesvirus LANA, FCT, Coordinator: Pedro Simas (HMSP-ICT/0021/2010), € 300 000 (€1 200 000)

Internationalization

Collaboration with Keneth Kay, Harvard Medical School , USA.

Collaboration with Hide Ploegh MIT, USA

Pedro Simas is Academic editor for PLoS-ONE

Master Thesis completed

Sofia Cerqueira, 2011, MSc, Faculdade de Ciências, Universidade de Lisboa, Supervised by Pedro Simas

Mycobacteria-Host Interactions Unit

External Unit

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 and inflammasome activation 2) Mtb PAMPS activates distinct inflammasomes 3) trafficking host factors are involved in Mtb uptake by macrophages, phagosome maturation and exosome secretion and finally 4) micro RNAs controls actin dynamics during early steps of Mtb phagocytosis.

Head of Unit

Elsa Anes, (PharmD. PhD), Associate Professor, FFUL

Research Team

Paulo Bettencourt	PhD Fellowship, FCT
Nuno Baltazar Carmo	PhD Fellowship, FCT
David Pires	PhD Fellowship, FCT
Leonor Freire Santos	Training Fellowship, FCT (left Nov 2011)
Joana Marques	Master student
Joana Bogalhão	Master student
Pedro Timóteo	Master student

Keywords/Research Areas

Innate immunity; Intracellular trafficking; Host-pathogen interactions; Tuberculosis

Major scientific achievements

- 1) We found that Mtb activates the over-expression and down-regulation of a set of miRNAs during macrophage phagocytosis and that some are involved in controlling actin dynamics.
- 2) We studied the distribution of key cathepsins (catB, cat L and cat S) inside human macrophages and dendritic cells infected with *M.tuberculosis complex*. It was found that the enzymatic containment and function is distinct in both cells.
- 3) We evaluated the antimycobacterial effect of extracts from medicinal plants from Mozambique. Indeed chemical compounds prodrugs derived with activity against PZA resistance mycobacteria strains and species were characterized (patent application submitted).
- 4) A Systematic Identification of NLR and CARD-domain containing proteins involved in IL-1 β response to Mtb was performed and CARD9 was common to several conditions (Keystone

selected OC and Melinda Gates award).

5) 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, Hacoheh 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 21)

Kuehnelt 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 10)

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 18)

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 25)

Anes, E., Kuehnelt, 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 117)

Ongoing Research Projects

2009/2012. Interference of *Mycobacterium tuberculosis* with the endocytic/ antigen presentation pathways on macrophages and dendritic cells from healthy and immuno-compromised donors. FCT Coordinator Elsa Anes (PIC/IC/82859/2007), €135000.

2010/2013. Role of *M. tuberculosis* in microRNA controlling of actin assembly and other pro-inflammatory signals in infected macrophages. FCT. Coordinator Elsa Anes (PTDC/BIA-BCM/102123/2008) €198.830, 00.

2010/2013. Dissecting the intracellular trafficking factors involved in *M. tuberculosis* killing/survival within human macrophages using RNA interference. FCT Coordinator Elsa Anes (PTDC/SAU-MII/098024/2008) €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. FCT. Coordinator Miguel Viveiros (PTDC/SAU-FCF/102807/2008) €25 000(total € 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. FCT. Coordinator Luis Constantino (PTDC/SAU-FCF/101950/2008) €25 000 (total €192.882,00).

Publications in peer review Journals

1. Luo X*. , **Pires D***, Ainsa J.A., Mulhovo S., Duarte A, **Anes E.**, Ferreira M.J.U. 2011. Antimycobacterial evaluation and preliminary phytochemical investigation of selected medicinal plants traditionally used in Mozambique. □Journal of Ethnopharmacology, 137(1):114-120, *Joined first authors.
2. Luo X*. , **Pires D***, Ainsa J.A., Mulhovo S., Duarte A, **Anes E.**, Ferreira M.J.U. 2011. Phytochemical characterization of antimycobacterial crude extracts from medicinal plants traditionally used in Mozambique. PLANTA MEDICA, 77(12):1318*Joined first authors.

Other publications International

Elsa Anes. 2011. For host factors weddings and a Koch's bacillus funeral: actin, lipids, phagosome maturation and inflammasome activation. " Understanding Tuberculosis - Analyzing the Origin of *Mycobacterium tuberculosis* Pathogenicity/ Book 3" Pere-Joan Cardona (Eds) Autonomous University of Barcelona, Pub: INTECH, Vol.3.ISBN 978-953-307-942-4.

Invited Lectures and Seminars

1. Elsa Anes. 2011. Innate immunity mechanisms for bacterial infections. Módulo Microbiologia e Saúde do mestrado de Microbiologia Aplicada UL.
2. Elsa Anes 2011. Cellular assays for Phagolysosome maturation. Mestrado/doutoramento em Ciências Biofarmacêuticas Março 21.
3. Elsa Anes 2011. Cellular assays for Phagolysosome maturation. Mestrado Biologia Molecular em Saúde ICSS April 29.
4. Elsa Anes 2011. Innate Immunity in tuberculosis. Mestrado Biologia Molecular em Saúde ICSS April 30.
5. Elsa Anes. 2011. Endocytic Pathways: new avenues for drug delivery and targeting. Lessons from pathogens. Mestrado em Farmacotecnia Avançada: Farmacotecnia avançada III. April
6. Elsa Anes. 2011. Immunity to tuberculosis. Imunologia, Integrated master in Pharmaceutical Sciences FFUL

Communications in International Conferences

1. Bettencourt P, Marion S, Pires D, Santos L, Pardal J, Blake J, Benes V, Griffiths G and Anes E. 2011. MicroRNA Reduces N-Wasp and Controls Phagocytosis of *Mycobacterium tuberculosis*. Tuberculosis: Immunology, Cell Biology and Novel Vaccination Strategies (J3), Keystone Symposia, January 15 – 20, Vancouver, British Columbia, Canada (poster)
2. Moura-Alves, P., Mishra, BB , Kaufmann, SH , Moita, L.F. ,Anes, E. 2011. Systematic

Identification of NLR and CARD-domain containing proteins involved in IL-1b response to Mtb” 2 Tuberculosis: Immunology, Cell Biology and Novel Vaccination Strategies (J3), Keystone Symposia, January 15 - 20, Vancouver, British Columbia, Canada (selected oral presentation)

3. Anes E.2011. Discovering, validating and exploiting novel host target-based treatments for tuberculosis.Amsterdam. Amsterdam Meeting on New combinatorial Medicine for Tuberculosis: for a SME-targeted Collaborative Project, July 19 (Invited Oral communication)
4. Luo X*. , Pires D*. , Ainsa J.A., Mulhovo S., Duarte A, Anes E., Ferreira M.J.U. 2011. Phytochemical characterization of antimycobacterial crude extracts from medicinal plants traditionally used in Mozambique. *Joined first authors. 59th International Congress and Annual Meeting of the Society-for-Medicinal-Plant-and-Natural-Product-Research Antalya, TURKEY,SEP 04-09, Soc Med Plant & Nat Prod Res

Communications in National Conferences

1. Anes E 2011 *Mycobacterium tuberculosis* protein ESAT-6 is a potent activator of the NLRP3/ASC inflammasome Workshop Phage Biology and Mycobacteria June 21 Fac. Pharmacy Univ. Of Lisbon.(CO)
2. Anes E. 2011. Molecular mechanisms for immunomodulation and immunoresistance in *Mycobacterium* spp infection . V Congresso da Sociedade Portuguesa de Ciências Veterinárias, Oct 13-15, Vale de Santarém (Invited Oral communication)

Organisation of Conferences

Anes, E. Organized the FFUL/URIA/ Cell Microbiology seminar *Mycobacterium tuberculosis* interactions with host cells. **Olivier Neyrolles**, Institute of Pharmacology & Structural Biology (IPBS) CNRS, University of Toulouse France, March 21, 2011

Anes, E. Organized the FFUL/URIA/ Cell Microbiology seminar “Bioinformatics and the Biologist” **Jonathon Blake** *Gene Core Facility, EMBL, HD*, March 22, 2011.

Anes, E. Organized the FFUL/URIA/ Cell Microbiology seminar “Microarray’s and Gene expression” **Jonathon Blake** *Gene Core Facility, EMBL, HD*, March 22, 2011.

Anes, E. Organized the FFUL/URIA/ Cell Microbiology seminar” Burkholderia cepacia complex: a group of pathogens endowed with a wide range of virulence determinants **Jorge Leitão**, Instituto Superior Técnico, March 25.

Anes, E. Organized the URJA/IMM seminar ”Next Generation Sequencing, from Sequence Production towards Human Genetics **Jonathon Blake** *Gene Core Facility, EMBL, HD*, March 24.

Carmo, N and Pires, D. organized the URJA seminar/workshop “Guava: Flow Cytometry Introductory Seminar”. **Oscar Marin** Merk Milipore Spain, June 22.

Carmo, N and Pires, D. organized the URIA workshop “Flow Cytometry” **Marleen Maras** Field Application Specialist Life Sciences - Cytometry Merck Millipore Belgica, December 13.

Internationalization

Collaborative Research:

Gareth Griffiths (Oslo University, Norway)

Olivier Neyrolles (CNRS, Toulouse , Fr)

Tina Bergant (Josef Stefan Inst, Ljubljana, Slov)

Maximiliano Gutierrez (Helmholtz Centre for Infection Research, Braunschweig, Ger)

Michael Niederweis (Univ. Alabama at Birmingham, USA)

Prizes, honours and awards

Award to Moura-Alves, Mishra to participate on "Tuberculosis: Immunology, Cell Biology and Novel Vaccination Strategies (J3)", Keystone Symposia, Bill and Melinda Gates Foundation Vancouver, British Columbia, Canadá, Jan 15-20.

Advanced teaching

Elsa Anes organized the Course Cellular Microbiology as part of the Master/PhD program on Biopharmaceutical Sciences at FFUL .

Elsa Anes. 2011. Endocytic Pathways: new avenues for drug delivery and targeting. Lessons from pathogens. Mestrado em Farmacotecnia Avançada: Farmacotecnia avançada III. April

Elsa Anes. 2011. Innate immunity mechanisms for bacterial infections. Módulo Microbiologia e Saúde do mestrado de Microbiologia Aplicada UL.

Elsa Anes 2011. Cellular assays for Phagolysosome maturation. Mestrado/doutoramento em Ciências Biofarmacêuticas Março 21.

Elsa Anes 2011. Cellular assays for Phagolysosome maturation. Mestrado Biologia Molecular em Saúde ICSS April 29.

Elsa Anes 2011. Innate Immunity in tuberculosis. Mestrado Biologia Molecular em Saúde ICSS April 30.

Elsa Anes 2011. Biologia Celular. Co-ordinator. Integrated Master in Pharmaceutical Sciences FFUL

Elsa Anes. 2011. Immunity to tuberculosis. Imunologia, Integrated Master in Pharmaceutical Sciences FFUL

Retroviruses Research Unit External Unit

Major interests / Objectives

We are interested in identifying cellular proteins and pathways involved in the process of HIV-1 latency and restriction to infection that may result in the discovery of strategies to eradicate the virus. By manipulating the transcription of genes controlling the HIV-1 life-cycle, specifically using zinc-finger library screening we aim to answer questions related to the mechanism of APOBEC3G expression/regulation and discovery of HIV restriction factors. To eradicate HIV-1 or inhibit viral infectivity we are developing strategies based on the platform of small antibody scaffolds and design of zinc-fingers that recognize specific regions of HIV-1 sequence.

Head of Unit

João Gonçalves, PhD – Associate Professor, Faculdade de Farmácia da Universidade de Lisboa.

Principal Investigators

Mariana Santa Marta, PhD
Paula Brito, PhD

Research Team

Mariana Santa-Marta, PhD	Ciência 2009
Paula Brito, PhD	Post Doc Fellowship, FCT
Cátia Cantante	PhD Fellowship, FCT
Soraia Oliveira	PhD Fellowship, FCT
Acilino Freitas Vieira	PhD student
Luis Ferreira	PhD Fellowship, FCT
Pedro Perdigão	PhD Fellowship, FCT
Ana Catarina Godinho Santos	PhD Fellowship, FCT
Ana Catarina Cunha Santos	PhD Fellowship, FCT

Keywords/Research Areas

HIV-1; latency; recombinant antibodies; zinc-fingers; lentiviral vectors

Major scientific achievements

- A) We identified novel restriction pathways deleterious for HIV-1 replication in T lymphocytes. This study brings new insights for the complex interplay of HIV-1/host cell and opens new possibilities for antiviral strategies.

- B) We designed new synthetic small domain antibodies that are able to target gp41 and gp120 that are capable to inhibit HIV-1 and HIV-2 infection. We have submitted a patent that addresses HIV-1 fusion inhibition using bacterial derived peptides. In addition, to address the issue of increasing the half-life of small antibody domains we submitted a patent application concerning the invention of an albumin-binding domain to improve the pharmacokinetic of therapeutic proteins.
- C) We demonstrated the applicability of protein complementation assay to quantitatively study the interaction between HIV-1 Vif and APOBEC proteins.

Recent Most Relevant Publications

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 Jun;6(2):296-307. (Journal IF: 3.6).

Ana I. S. Esteves, Marisa Nicolai, Madalena Humanes and Joao Goncalves. Sulfated Polysaccharides in Marine Sponges: Extraction Methods and Anti-HIV Activity. *Mar. Drugs* 2011, 9(1), 139-153; doi:10.3390/md9010139 - published online 24 January 2011. (Journal IF: 3.4).

Soraia S. Oliveira, Frederico Aires da Silva, Sara Lourenco, Acilino Freitas-Vieira, Ana Catarina Santos, Joao Goncalves. Assessing combinatorial strategies to multimerize libraries of single-domain antibodies. *Biotechnology and Applied Biochemistry* (2012) (Accepted for publication).

Ongoing Research Projects

2008/2011. A Novel Lentiviral Target-Specific Strategy for Molecular and Gene Therapy. FCT Coordinator: Joao Goncalves. PTDC/BIA-BCM/64275/2006. €125 000.

2008/2011. Screening the role of kinases/phosphatases in early stages of HIV-1 infection using shRNA-encoded lentiviral libraries. PTDC/SAU-MII/65346/2006. €142 000.

2008/2011. Genome-wide screening with libraries of synthetic zinc-finger proteins capable to modulate host gene expression: Application in HIV-1 infection. PTDC/SAU-GMG/71599/2006. €130 000.

2011/2013. Albumin binding-domain fusions to improve protein pharmacokinetics. PTDC/SAU-FAR/115846/2009. €130 000.

2011/2012. Nanotechnology against viral latency: Sensor strategies to eliminate HIV-1 infected cells. Bill and Melinda Gates Foundation. \$100 000.

Publications in peer review Journals

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 Jun;6(2):296-307. (Journal IF: 3.6).

Ana I. S. Esteves, Marisa Nicolai, Madalena Humanes and Joao Goncalves. Sulfated Polysaccharides in Marine Sponges: Extraction Methods and Anti-HIV Activity. *Mar. Drugs* 2011, 9(1), 139-153; doi:10.3390/md9010139 - published online 24 January 2011. (Journal IF: 3.4).

Santos AC, Oliveira S, Goncalves J (2010) Synthetic small domain antibodies targeting HR1 on gp41 are capable to inhibit both HIV-1 and HIV-2. *PLoSOne* (In press).

Other publications International

Sofia Corte-Real, Frederico Aires da Silva, and Joao Goncalves. Development of Antibody Fragments for Therapeutic Applications. *Peptide Drug Discovery and Development: Translational Research in Academia and Industry*. 2011 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Invited Lectures and Seminars

Insights in HIV-2 interaction with the cell: Differences and similarities to HIV-1. New York University, March 25, 2011.

Research and Development of Biologics. Merck, New York, May 18, 2011.

Qualidade dos medicamentos biológicos. Hospitais da Universidade de Coimbra. December 2, 2011.

Course of Biologic Medicines, APFH, Coimbra, May 13-14, 2011.

Molecular Biology of HIV, Ordem Farmacêuticos, FFUL. November 18, 2011.

Communications in International Conferences

Goncalves, J. Intracellular immunity to HIV-1 by APOBEC3G. 2011 CSHL Meeting on Retroviruses, Cold Spring Harbor Laboratory, New York, USA, May 18-23. (Oral Presentation)

Oliveira, S, Aires da Silva, F, Goncalves J. Accessing combinatorial strategies to multimerize libraries of single-domain antibodies. PEGS 2011. Hannover, October 23-25. (Poster presentation).

Fonseca, L, Martins, L, Aires da Silva, F, Barata J, Barbas III, C, Goncalves, J. Cell-specific targeting using a Sindbis-pseudotyped lentiviral vector expressing anti-FITC single-chain antibody. ESGCT meeting, Frankfurt (Poster presentation).

Oliveira, S, Aires da Silva, F, Goncalves J. The potential use of combinatorial single-domain antibodies. Antibody Engineering 2011, San Diego, USA. December 4-9.

Prizes and Awards

Grand Challenges from Bill and Melinda Gates Foundation.

Patents/prototypes

Albumin-binding Domain-fusions and use thereof to improve protein pharmacokinetics. USPTO 61104594.

Methods and Compositions to Treat HIV Infections by a Bacterial Protein. USPTO 987372643.

Master thesis completed

Pedro Perdigão (2011) “Eradication of HIV-1 latent infected cells with therapeutic plasmids”. Mestrado em Microbiologia e Genética Molecular, Faculdade de Ciências da Universidade de Lisboa. Supervisor: João Gonçalves.

Neurosciences

Programme Coordinator: Ana Sebastião and Mamede de Carvalho

Heads of Unit:

Tiago Fleming Outeiro, PhD

José Ferro, MD, PhD

Mamede de Carvalho, MD, PhD

Ana Sebastião, PhD

Principal Investigators:

Tiago Fleming Outeiro, Teresa Pais, Ana Dulce Correia

José Ferro, Alexandre Castro Caldas, Alexandre de Mendonça, Isabel Pavão Martins, José Pimentel, Cristina Sampaio, Teresa Paiva, Sofia A. Oliveira, Patrícia Canhão, Joaquim Ferreira

Mamede de Carvalho, Isabel Rocha

Ana Sebastião Joaquim Alexandre Ribeiro, Alexandre de Mendonça, Luísa Lopes, Maria José Diógenes, Cláudia Valente de Castro

Cell and Molecular Neuroscience Unit

Description and Objectives

UNCM (Unidade de Neurociência Celular e Molecular) was 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 Fleming Outeiro, Ph.D., Auxiliar Professor, FMUL (IMM Associate Investigator)

Principal Investigators

Teresa Pais, Ph.D., Staff Scientist

Ana Dulce Correia, Ph.D, Auxiliary Researcher, FMUL

Research Team

Sandra Tenreiro	Postdoc, FCT
Rita Oliveira	Postdoc, FCT
Federico Herrera	Postdoc, FCT
Hugo Miranda	Postdoc, FCT
Zrinka Marjjanovic	Postdoc, FCT (left in October 2011)
Leonor Fleming	Ph.D. Student, FCT
Susana Gonçalves	Ph.D. Student, AXA Research Fund
Oldriska Marques	Ph.D. Student, FCT
Patrícia Guerreiro	Ph.D. Student, FCT
Elisa Basso	Ph.D. Student, Marie Curie ITN
Sueli Marques	Ph.D. Student, PDBEB, FCT
Tomás Fonseca	Ph.D. Student, FCT
Andreia Peixoto	Technician
Dina Hernandez	Technician (left in September 2011)

Keywords/Research Areas

- Protein misfolding, oligomerization and aggregation
- Yeast models for Parkinson's and Huntington's disease

- Neuroinflammation
- Modulators of protein aggregation and toxicity
- Microscopy-based methods for investigating the molecular nature of the toxic proteinaceous species in Parkinson's disease

Major scientific achievements

Describe the major achievements of the unit in 2011. You may use text or bulleted topics or both. Major achievements should highlight scientific publications AND also include reference to relevant activity such as, for example, patents, technology transfer, prizes, honours and awards, public engagement, training and organization of national and international conferences.

We are unraveling the molecular mechanisms underlying neurodegeneration through the use of a variety of model organisms and molecular approaches. The first yeast model of Parkinson's disease was a major scientific achievement which we continue to build upon, while translating our findings in mammalian systems.

We have developed powerful imaging tools to investigate the nature of the toxic species leading to neuronal cell loss and dysfunction.

Recent Most Relevant Publications

Herrera F, Outeiro TF. α -Synuclein modifies huntingtin aggregation in living cells. FEBS Lett. 2012 Jan 2;586(1):7-12. (Journal IF: 3,601)

Näsström T, Gonçalves S, Sahlin C, Nordström E, Screpanti Sundquist V, Lannfelt L, Bergström J, **Outeiro TF**, Ingelsson M. Antibodies against alpha-synuclein reduce oligomerization in living cells. PLoS One. 2011;6(10):e27230. Epub 2011 Oct 31. (Journal IF: Times cited 1)

Outeiro TF, Putcha P, Tetzlaff JE, Spoelgen R, Koker M, Carvalho F, Hyman BT, McLean PJ. Formation of toxic oligomeric alpha-synuclein species in living cells. PLoS One. 2008 Apr 2;3(4):e1867. Erratum in: PLoS One. 2008;3(5). (Journal IF:4,351, Times cited: 51)

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. Sirtuin 2 inhibitors rescue alpha-synuclein-mediated toxicity in models of Parkinson's disease. Science. 2007 Jul 27;317(5837):516-9. (Journal IF:30,631, Times cited: 202)

Outeiro TF, Lindquist S. Yeast cells provide insight into alpha-synuclein biology and pathobiology. Science. 2003 Dec 5;302(5651):1772-5. (Journal IF:30,631, Times cited: 216)

Ongoing Research Projects

2011/2014 Identification of molecules to treat Parkinson's Disease (PD) using a novel zebrafish model, European Union, programme Eurostars. co-PI. E!5553-PARK, 200 530€ (total 1.357600€)

2010/2013 Polyphenols as protective agents in cellular models of alpha-synucleinopathies, in particular Parkinson's disease. Coordinator: Ricardo M.S. Boavida Ferreira. PTDC/BIA-BCM/111617/2009, € 52 280 (total € 180,068)

2011/2014 Molecular determinants of microglial activation and neuronal dysfunction in in vivo models of Parkinson's disease, FCT. Coordinator: Teresa Faria Pais. PTDC/SAU-ORG/114083/2009, € 115,664

2008/2011. NEUROFOLD, Uncovering the Molecular Basis of Neurodegenerative Disorders - funded by Marie Curie Program, European Commission. 48 months. €100,000.

2009/2011. PTDC/SAU-GMG/099655/2008, Slow and Rapid Progression Parkinson's Disease: Molecular Determinants and Biomarkers. FCT, Portugal. PI: Tiago Outeiro. 36 months. €195,000

2010-2012. PDS-UK. Deciphering the Molecular Role of DJ-1 in the Etiology of Parkinson's Disease. Co-PI: Tiago Outeiro. €70,000.

2010/2013. MEFOPA, Mendelian forms of Parkinson's disease €226,800 (Total €5,759,478)

2010/2013 Neurasync, Co-PI: Tiago Outeiro. €143,000(Total €2,384,412)

2010/2012. PTDC/SAU-GMG/099655/2008, Renal tubular dysgenesis associated with ACE misfolding: the molecular effects of the new ACE mutation – Q1069R, PI: Tiago Outeiro. €130,000.

2010/2012. PTDC/SAU-NEU/105215/2008. From phosphorylation to cleavage: switching on alpha-synuclein aggregation and toxicity. PI: Tiago Outeiro. €160,000.

2010/2012. PTDC/SAU-NEU/101928/2008. Deciphering the molecular mechanisms linking alpha-synuclein dysfunction and cytotoxicity in Parkinson's disease – the role of GDNF. Co-PI: Tiago Outeiro. €32,000 (Total €167,000).

Publications in Peer Review Journals

Kemppainen S, Rantamäki T, Jerónimo-Santos A, Lavasseur G, Autio H, Karpovab N, Kärkkäinen E, Stavén S, Vicente Miranda H, Outeiro TF, Diógenes MJ, Laroched S, Davis S, Sebastião AM, Castrén E, Tanila H (2011) Impaired TrkB receptor signaling contributes to memory impairment in APP/PS1 mice, *Neurobiology of ageing*, 2011, in press.

Vicente Miranda H, Ribeiro Morais G, Santos IC, Santos I, Paulo A, Outeiro TF (2011) Synthesis and in vitro evaluation of fluorinated styryl benzazoles as amyloid-probes, *Bioorg Med Chem*. **19**:7698-710. Epub 2011 Oct 18.

Marques S, Batalha VL, Lopes LV, Outeiro TF (2011) Modulating Alzheimer's disease through caffeine: a putative link to epigenetics. *J Alzheimers Dis* **24** Suppl 2: 161-71 (Journal IF: 4.261; Citations: 1).

Hansen C, Angot E, Bergström AL, Steiner JA, Pieri L, Paul G, Outeiro TF, Melki R, Kallunki P, Fog K, Li JY, Brundin P. α -Synuclein propagates from mouse brain to grafted dopaminergic neurons and seeds aggregation in cultured human cells. *J Clin Invest*. 2011 Feb 1;121(2):715-25. (Journal IF: 14,152 Times cited 26)

Marques SC, Oliveira CR, Pereira CM, Outeiro TF (2011) Epigenetics in neurodegeneration: a new layer of complexity. *Prog Neuropsychopharmacol Biol Psychiatry* **35** (2): 348-55 (Journal IF: 2.877; Citations: 5).

de Oliveira RM, Marijanovic Z, La Fuente Carvalho F, Miltenberger-Miltényi G, Matos JE, Tenreiro S, Oliveira S, Enguita FJ, Stone R, and Outeiro TF (2011) Proteostasis modulation in a novel ACE mutation: insights into the molecular basis of RTD. *PLoS One*. **6**(6):e20854. (Journal IF: 4.411)

Correia AD, Cunha S, Sholze M and Stevens ED (2011) A novel behavioral fish model of nociception for testing analgesics. *Pharmaceuticals* **4**,665-680.

Kopecka-Pilarczyk J and Correia AD (2011) Effects of Exposure to PAHs on brain AChE in Gilthead Seabream, *Sparus aurata* L., under laboratory conditions. *Bull Environ Cont Toxicol* **86**, 379-383. (Journal IF 1.139)

Ribeiro M, Pinto A, Pinto M, Heras M, Correia A, Bardaji E, Tavares I and Castanho M. (2011) Inhibition of nociceptive responses after systemic administration of amidated Kyotorphin. *BJP* **163**,964-973. (Journal IF:4.925)

Outeiro TF. Amyloidogenesis: FIAsh illuminates A β aggregation. *Nat Chem Biol*. 2011 Aug 17;7(9):581-2. doi: 10.1038/nchembio.636. (Journal IF: 15,808).

Herrera F and Outeiro TF (2011) α -Synuclein modifies huntingtin aggregation in living cells. *FEBS Lett*. Jan 2;**586**:7-12. (Journal IF: 3.601)

Swinnen E, Büttner S, Outeiro TF, Galas MC, Madeo F, Winderickx J, Franssens V. Aggresome formation and segregation of inclusions influence toxicity of α -synuclein and synphilin-1 in yeast. *Biochem Soc Trans*. 2011 Oct;39(5):1476-81.

Martins M, Rosa A, Guedes LC, Fonseca BV, Gotovac K, Violante S, Mestre T, Coelho M, Rosa MM, Martin ER, Vance JM, Outeiro TF, Wang L, Borovecki F, Ferreira JJ, Oliveira SA. Convergence of miRNA expression profiling, α -synuclein interacton and GWAS in Parkinson's disease. *PLoS One*. 2011;6(10):e25443. (Journal IF: 4.411)

Badiola N, de Oliveira RM, Herrera F, Guardia-Laguarta C, Gonçalves SA, Pera M, Suárez-Calvet M, Clarimon J, Outeiro TF and Lleó A (2011) Tau enhances α -synuclein aggregation and toxicity in a cellular models of synucleinopathy. *PLoS One* **6**:e26609. (Journal IF: 4.411)

Näsström T, Gonçalves S, Sahlin C, Nordström E, Screpanti Sundquist V, Lannfelt L, Bergström J, Outeiro TF, Ingelsson M. Antibodies against alpha-synuclein reduce oligomerization in living cells. *PLoS One*. 2011;6(10):e27230. (Journal IF: 4.411)

Herrera F, Tenreiro S, Miller-Fleming L and Outeiro TF (2011). Visualization of cell-to-cell transmission of mutant huntingtin oligomers. *PLoS Curr*. Feb 11; **3**:RRN1210. (Journal IF: not available yet)

Other publications International

Gonçalves SA, Miranda VM, Outeiro TF (2011) Human Molecular Therapeutics, Novel Molecular Therapeutics in Parkinson's Disease. John Wiley & Sons, in press.

Marques S and Outeiro TF (2011) Epigenetics: Development and Disease– Chapter- Epigenetics in Parkinson's and Alzheimer's diseases. Springer.

Marques S, Pereira CMF and Outeiro TF (2011) Epigenetics in Human Disease-Chapter in Subject area "Aging and disease: the epigenetic bridge " - Bridging aging and neurodegeneration through epigenetics. Elsevier.

Marques S, Pereira CMF and Outeiro TF (2011) Epigenetics: Mechanisms, Functions and Human Effects . Chapter 10 - Epigenetics and Neurodegeneration: A Connection Overlooked. Series: Genetics - Research and Issues. Nova Publishers. Editors: Balázs Pintér and Zolt Mészáros Pub. Date: 2011 - 2nd quarter. ISBN: 978-1-60741-454-4.

Invited Lectures and Seminars

Outeiro, TF, From the bakery to the bedside: the molecular basis of Parkinson's disease, Novartis, Switzerland, December 2011.

Outeiro, TF, Unraveling the molecular basis of Parkinson's disease, Nestle Institutes for Health Sciences, Switzerland, December 2011.

Outeiro, TF, Intra and extracellular effects of a-synuclein oligomers, Cold Spring Harbor Banbury Meeting on Transmissible Amyloidosis, USA, November 2011

Outeiro, TF, Modulation of a-synuclein oligomerization in living cells, International Society for Neurochemistry Satellite meeting on a-synuclein, Greece, September 2011.

Outeiro, TF, Yeast as a model to study Parkinson's disease, Sociedade Brasileira de Bioquímica, Brasil, May 2011.

Tenreiro, S. Simple is good: Yeast as a model to study Parkinson's disease, Lisbon Area of Neuroscience Meeting, May 18, 2011.

Tenreiro, S. Simple is good: Yeast as a model to study neurodegenerative diseases. Jornadas Engenharia Química Biológica 2011, Instituto superior Técnico, Lisbon, Portugal, March 24, 2011.

Correia, AD. Zebrafish: a model to study Parkinson's Disease. Ciclo de Seminários em Neurociências. Molecular/FMUL, Universidade de Lisboa, October 24, 2011.

Herrera, F. Genetic and pharmacological modifiers of huntingtin oligomerization *and* toxicity. Pizza Seminar, Instituto de Medicina Molecular, October 4, 2011.

Correia, AD. A novel model to study acute pain and Parkinson's Disease. CFTC, Ciclo de Conferências. Complexo Interdisciplinar, Universidade de Lisboa, Lisboa, Portugal, December, 13, 2011.

Gonçalves, S. PCR-RFLP, Bioimaging techniques, Immunocytochemistry: unraveling the molecular basis of alpha-synuclein dysfunction, Gene Therapy. Genética Humana, Universidade do Algarve, Portugal, January 2011.

Gonçalves, S. Unraveling the genetic basis for alpha-synuclein oligomerization in living cells using BiFC, Universidade do Algarve, Portugal, January 2011.

Herrera, F. Phosphorylation pathways involved in astroglialogenesis. Centro Biomedicina Molecular Estrutural, University of Algarve, Faro, Portugal, January 28, 2011.

Communications in International Conferences

Guerreiro P and Outeiro TF. Immunoprecipitation (IP) and Co-IP: tools to identify protein-protein interactions, EMBO YIP PhD Course, Heidelberg, October 2011 (Poster Presentation).

Pais TF, Miller-Fleming L, Marques O, Guerreiro P, de Oliveira R and Outeiro TF. Sirtuins: a novel link between neuroinflammation and neurodegeneration, 10th European Meeting on Glial Cells in Health and Disease, Prague, Czech Republic, September 13-17, 2011 (Poster presentation).

Basso E, Tenreiro S, Marijanovic Z and Outeiro TF. Dissecting the role of alpha-synuclein phosphorylation in Parkinson's disease, Satellite meeting of the ISN: Synucleinopathies: From genes to pathogenesis, Naxos, Greece, September 3-4, 2011 (Poster presentation).

Miller-Fleming L, Smalley JL, Gant TW, Giorgini F and Outeiro TF. A yeast model of Parkinson's disease: deciphering the cellular roles of the DJ-1 protein family, Satellite Meeting of the ISN: From genes to pathogenesis: The evolving spectrum of synucleinopathies, Naxos, Greece, September 3-4, 2011 (Poster presentation).

Herrera F, Tenreiro S, Miller-Fleming L and Outeiro TF. Live imaging of mutant huntingtin oligomerization in cell cultures. Gordon Conference on CAG-triplet repeat disorders, Barga, Italy, June 5-10, 2011 (Poster presentation).

Gonçalves S and Outeiro TF. Modifying alpha synuclein dimerization in living cells, AXA Talent Day on Longevity and Life Risks meeting, Paris, France, March 2011 (Poster presentation).

Gonçalves S. Modifying alpha synuclein dimerization in living cells, 9th Göttingen Meeting of the German Neuroscience Society, Göttingen, Germany, March 2011 (Poster presentation).

Gonçalves S. Modifying alpha synuclein dimerization in living cells, The 10th International Conference on Alzheimer's & Parkinson's Diseases, Barcelona, Spain, March 2011 (Poster presentation).

Fonseca T, Correia AD, Willemsen R and Outeiro TF. Zebrafish: a new model of Parkinson's Disease. 2011. In: 9th Göttingen Meeting of the German Neuroscience Society, Göttingen, Germany, March 23-26, 2011 (Poster presentation).

Communications in National Conferences

Jorge CD, Faria C, Borges, N, Tenreiro S, Outeiro TF and Santos H. Mannosylglycerate, a compatible solute widespread in hyperthermophiles, inhibits α -synuclein aggregation in the cytoplasm of yeast cells. Microbiotec'11. University of Minho, Braga, December 1-3, 2011.

Macedo, D, Tenreiro, S, Ferreira, RB, Outeiro, TF and Santos, CN. Protective effects of novel phytochemicals in a yeast *model of* Parkinson's disease Champalimaud Neuroscience Symposium. Lisbon, September 18-21, 2011 (Poster presentation).

Basso E, Tenreiro S, Marijanovic Z and Outeiro TF. Dissecting the role of alpha-synuclein phosphorylation in Parkinson's disease. XII Meeting of the Portuguese Neuroscience Society, Lisbon, May 26-28, 2011 (Poster presentation).

Gonçalves S, Moita L and Outeiro TF. Modifying alpha synuclein dimerization in living cells, V IMM PhD Student Meeting, Lisbon, October 2011 (Oral presentation).

Herrera F, Tenreiro S, Miller-Fleming L and Outeiro TF. Visualization of cell-to-cell transmission of mutant huntingtin oligomers. XII Meeting of the Portuguese society for Neuroscience, Lisbon, May 26-28, 2011 (Oral presentation).

Herrera F and Schubert D. C-Jun N-terminal kinase controls a negative loop in the regulation of glial fibrillary acidic protein expression. Sinal 2011, University of Coimbra, Coimbra, April 28-30, 2011 (Oral presentation).

Marques SC, Pereira CMF and Outeiro TF. An epigenetic perspective into Alzheimer's disease. XII Meeting of the Portuguese society for Neuroscience (SPN), Lisbon, May 26-28, 2011 (Poster presentation).

Vicente Miranda H, Oliveira RM, Simões T, Penque D and Outeiro TF. A method for rapid enrichment and characterization of post-translational modifications of the Parkinson's associate protein alpha-synuclein, XII Meeting Portuguese Society for Neurosciences, Lisbon, May 26-28, 2011 (Poster presentation).

Oliveira R, Guerreiro P, Vicente Miranda H, Marijanovic Z, Pais TF and Outeiro TF. SIRT2: Crossing the bridge between ageing and neurodegeneration, XII Meeting Portuguese Society for Neurosciences, Lisbon, May 26-28, 2011 (Poster presentation).

Marques O, Vicente Miranda H, Pais TF and Outeiro TF. The role of alfa-synuclein secretion in microglia activation and neurodegeneration in Parkinson's disease, XII Meeting Portuguese Society for Neurosciences, Lisbon, May 26-28, 2011 (Poster presentation).

Organisation of Conferences

Herrera F co-organized the 4th season of the Lisbon Area of Neuroscience Meetings. Instituto de Medicina Molecular, Lisbon, Portugal, 2011.

Basso E co-organized the 4th season of the Lisbon Area of Neuroscience Meetings. Instituto de Medicina Molecular, Lisbon, Portugal, 2011.

Herrera F designed the logos and illustrations of the XII meeting of the Portuguese Society for Neuroscience 2011. Instituto de Medicina Molecular, Lisbon, Portugal, May 26-28, 2011.

Marques SC co-organized the XII Meeting of the Portuguese society for Neuroscience (SPN), Lisbon, May 26-28, 2011.

Internationalization

Basso E. Attended EC Framework 7 Marie Curie Fellowship Training Network Grant (NEURASYNC) Summer School: “Advance techniques of neurobiology: Grant Proposal Writing”, Naxos, Greece, 6-8 September 2011 .

2009-2013. COST European Network: “Fish Biomedical Models (EuFishBioMed)- a community resource to enable effective zebrafish partnering in projects targeting human diseases”: <http://www.cost.esf.org/>

Advanced teaching

Outeiro, TF, PENS Summer School in Metabolic Aspects of Neurodegeneration, Reims, Germany, July 2011.

Outeiro, TF, PhD Program in Neuroscience, University of Zagreb, Croatia, June 2011.

Herrera, F. Lectured the class “Protein quality control systems in health and disease”. M.Sc. and PhD Neuroscience Program, School of Medicine, University of Lisbon, Lisbon, Portugal, December 6, 2011.

Tenreiro, S. Lectured the class “Multidrug resistance in yeast”, PhD Programme from the NEURASYNC Initial Training Network funded through the people programme of FP7 of the European Union –Annual meeting and Training, IMM, Lisbon, Portugal, April 14, 2011.

Pais, TF. Lectured the class “Neuroinflammation”. Master of Neurochemistry, Faculty of Sciences, University of Lisbon, Portugal, March 15, 2011.

Outeiro, TF. “Neurodegenerative disorders”, PGFMA and IMM PhD Program, IMM, Lisbon, February 2011.

Science and Society

de Oliveira, RM. “Sir2: o elixir da juventude” presented to L’Oréal selling assistants.

Vicente Miranda, H. Coordinator of the Parkinson's disease corner for secondary school students during the Brain awareness week organized by Portuguese Society for Neurosciences.

Outeiro, TF “Neurodegenerative disorders”, Brain Awareness Week, Lisbon, March 2011.

Outeiro, TF “Novos avanços na investigação na doença de Parkinson”, Associação Portuguesa de Doentes de Parkinson, Faro, November 2011.

Outeiro, TF “A investigação do cérebro em Portugal”, Academia VVV, Odivelas, November 2011.

Neurological Clinical Research Unit

Major interests / Objectives

The general objective of UNIC is to increase the knowledge and foster the prevention and treatment of major prevalent and disabling disorders involving the brain, such as stroke, dementia, and Parkinson's disease. The main advantage of the unit is the strong collaboration among the 10 experienced Principal Investigators, based on common clinical investigation methodologies and particular features of research expertise. This teamwork has progressively become more coherent and fruitful, as reflected in shared interests between areas, joint meetings, and common authorship of projects and articles. The UNIC proficiency is expanded by the multiple collaborations developed by the Principal Investigators, both at the 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. The researchers of UNIC 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 M. Ferro, MD, PhD

Full Professor, FMUL/HSM

Principal Investigators

Alexandre Castro Caldas, MD, PhD	Full Professor, Catholic University of Portugal
Alexandre de Mendonça, MD, PhD	Principal Investigator, FMUL and IMM
Cristina Sampaio MD, PhD,	Associated Professor, FMUL
Isabel Pavão Martins, MD, PhD	Associated Professor, FMUL
Joaquim Ferreira, MD, PhD	Assistant Professor, FMUL:
José M. Ferro, MD, PhD	Full Professor, FMUL/HSM
José Pimentel, MD, PhD	Associated Professor, FMUL
Patrícia Canhão, MD, PhD	Assistant Professor, FMUL / HSM
Sofia A. Oliveira, PhD	Invited Assistant Professor, FMUL
Teresa Paiva, MD, PhD	Associated Professor

Research Team

<i>full time researchers</i>	
Antonina Pereira, PsyD, PhD	Post-doc fellowship, IMM
Inês Sousa, PhD	Post-doc Fellowship FCT, IMM
Madalena Martins, PhD	Post-doc Fellowship, FCT, IMM
Manuela Guerreiro, PsyD, PhD	Investigator, FMUL

<i>part time researchers</i>	
Ana Mineiro, PhD	Auxiliary Professor, ICS-UCP

Ana Marta Teixeira Anes	Pharmacist
Ana Rita Peralta, MD, MSc	Neurologist, Assistant, FMUL, HSM
João Costa, MD, PhD	Assistant Professor, FMUL
Leonor Correia Guedes, MD	Neurologist, HSM
Mário Miguel Rosa, MD	Neurologist, HSM
Martin Lauterbach, MD, PhD	Neurologist, Research Fellow
Miguel Coelho, MD	Neurologist, HSM
Maria Vânia Nunes, PhD	Auxiliary Professor, ICS-UCP

<i>occasional collaboration</i>	
Anabela Valadas, MD	Neurologist
Clara Loureiro, MSc	Psychologist, FMUL
Dulce Neutel, MD	Training Fellowship
Filipa Ribeiro, PhD	Psychologist, PhD degree, FMUL
Helena Pedrosa, PsyD	Psychologist, Master degree, FMUL
Luísa Albuquerque, MD	Neurologist, HSM
Maria Carolona Pires, MD	Training Fellowship
Patrícia Lobo, MD	Training Fellowship
Ruth Gerales, MD	Neurologist, HSM
Sandra Ginó, PsyD	Psychologist, Master Degree, ULHT, volunteer
Teresa Pinho e Melo, MD	Neurologist, Assistant, FMUL / HSM
Tiago Mendes, MSc	Psychologist, HSM
Tiago Teodoro	Training Fellowship
Vítor Oliveira, MD, PhD	Neurologist, Auxiliary Professor, FMUL / HSM

<i>PhD students</i>	
Ana Catarina Fonseca, MD	HSM, PhD student, Harvard Program, FMUL
Ana Verdelho, MD	Neurologist, HSM, PhD student
Bruno Miranda, MD	PhD student Champalimau Foundation, FMUL, HSM
Carla Bentes, MD	Neurologist, Assistant, FMUL / HSM
Carolina Maruta, MSc	Psychologist, PhD student research fellow
Catarina Santos, PsyD	PhD student, FMUL
Dina Silva, PsyD	Psychologist, PhD student, FMUL
Frederico Simões do Couto, MD	Psychiatrist, PhD student, FMUL
Graça Melo, MSc	Nurse, PhD student, UL
Joana Xavier, MSc	PhD student, FMUL
José Fonseca	PhD student, FMUL
Lara Caeiro, PsyD	PhD student, FMUL
Manuela Lopes	Artist, PhD student, FMUL
Maurício Martins, MD	PhD student
Patrícia Abrantes	PhD student
Raquel Gil-Gouveia, MD	Neurologist, PhD student, FMUL
Sara Fernandes	PhD Fellowship, FCT
Sofia Madureira, PsyD	PhD student, FMUL
Tiago Krug, MSc	PhD student, FMUL

<i>Master students</i>	
Bernardo Moura	Master in Medicine student
Catarina Chester	Master in Neurosciences, FMUL
Helena Bárrios	Master in Palliative Care, FMUL
Inês Mares	Master in Neurosciences, FMUL
Rita Gameiro	Master in Medicine student
Sandra Cardoso	Master in Cognitive Sciences, FMUL
Sara Câmara	Master student
Sofia Narciso	Master student, FMUL
Vanda Freitas	Master in Neurosciences, FMUL

<i>Technicians</i>	
Ana Noronha, Biology Degree	Study Coordinator
Ana Rita Silvestre, MSc	Technician, HSM
Andreza Viegas, Biochemical degree	Study Coordinator
Carla Firmo, MSc	Technician, HSM
Ema Roque, Management Degree	Study Coordinator
Fátima Soares	Technician, HSM
Gabriela Leal	Speech Therapist, HSM
Joana Pires, MSc	EEG Technician, HSM
João Sobral	Research technician, FCT
Lígia Ferreira	EEG Technician, HSM
Luisa Farrajota	Speech Therapist, HSM
Maria Finisterra	Study Coordinator
Nádia Rei, MSc	Research technician, FCT
Paulo Batista	Technician, HSM
Rosa Santos	EEG Technician, HSM
Vânia Francisco	Research technician, FCT

Keywords/Research Areas

Stroke

Vascular cognitive impairment ; Neuropsychiatry of stroke; Cerebral venous thrombosis; Cardioembolic stroke; Transient ischemic attacks

Cognition

Mild Cognitive Impairment; Prevention of cognitive decline; Illiteracy ; Portuguese sign language; Neuroplasticity for language recovery; Cognitive disturbance of migraine

Movement disorders

Parkinson's disease; Clinical trials; Systematic reviewsGuidelines; Cochrane collaboration; Regulatory science; Pharmacoepidemiology

Genetics and genomics of complex neurological diseases

Stroke; Behçet's disease; Parkinson's disease

Sleep

Dreams; Neurophysiology of Sleep

Neuropathology

Neuropathology of human prion diseases; Epilepsy surgery

Major scientific achievements

The researchers of UNIC made in 2011 significant scientific contributions expressed in as much as **69 full papers published in international peer-reviewed journals**, as listed below. It is just possible to highlight a few of these contributions. In cerebral venous thrombosis, the description was made of the risk factors for venous thrombotic events, and identification of the patients who benefit most from prolonged anticoagulation and from decompressive surgery. Regarding vascular white matter changes, the risk of specific subtypes of dementia and identification of its clinical, imagiological and neuropsychological predictors was accomplished. Advances were made on the understanding of memory complaints in healthy young and elderly adults, and the determination of the prognosis of elderly people with cognitive complaints who do not fulfill criteria for Mild Cognitive Impairment. New data were published on the relationship of genetic risk factors and mitochondrial genome polymorphisms with susceptibility to Behçet's Disease. Significant progresses were done on the study of language recovery after early brain lesions and the development of new assessment tools and normative data for language and cognitive evaluation. Concerning the study of dreams, preliminary but promising novel data were presented. The analysis of the impact of illiteracy on neuropsychological test performance, as an approach to understand human cognition and its brain organization under normal and abnormal conditions, was also accomplished.

Recent Most Relevant Publications

Vellas B, Andrieu S, Sampaio C, Coley N, Wilcock G; European Task Force Group. Endpoints for trials in Alzheimer's disease: a European task force consensus (April 2011) *Lancet Neurol* (Journal IF: 24.659)

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). *Ann Rheum Dis* **70**, 1514-16. (Journal IF: 9.082)

Aisen PS, Andrieu S, Sampaio C, Carrillo M, Khachaturian ZS, Dubois B, Feldman HH, Petersen RC, Siemers E, Doody RS, Hendrix SB, Grundman M, Schneider LS, Schindler RJ, Salmon E, Potter WZ, Thomas RG, Salmon D, Donohue M, Bednar MM, Touchon J, Vellas B. Report of the task force on designing clinical trials in early (predementia) AD: (Jan 2011) *Neurology* (Journal IF:8.017)

Jokinen H, Gouw AA, Madureira S, Ylikoski R, van Straaten EC, van der Flier WM, Barkhof F, Scheltens P, Fazekas F, Schmidt R, Verdelho A, Ferro JM, Pantoni L, Inzitari D and Erkinjuntti T; LADIS Study Group (2011) Incident lacunes influence cognitive decline: the LADIS study. *Neurology* **76**, 1872-1878. (Journal IF: 8.017)

Moreno-López C, Santamaría J, Salamero M, Del Sorbo F, Albanese A, Pellecchia MT, Barone P, Overeem S, Bloem B, Aarden W, Canesi M, Antonini A, Duerr S, Wenning GK, Poewe W, Rubino A, Meco G, Schneider SA, Bhatia KP, Djaldetti R, Coelho M, Sampaio C, Cochen V,

Hellriegel H, Deuschl G, Colosimo C, Marsili L, Gasser T, Tolosa E. Excessive Daytime Sleepiness in Multiple System Atrophy (SLEEMSA Study) (Feb 2011) *Arch Neurol* (Journal IF: 7.108)

Ongoing Research Projects

1998/ Impact of Age-related brain white matter changes on transition to disability in the elderly. Leukoaraiosis And DISability. Fifth (EC) Framework Programme 1998-2002 – “Quality of life and management of living resources”: QLK6-2000-00446. Co-Coordinator: JM Ferro

2004/ Caracterização de Perfis de Envelhecimento na População Portuguesa Normal - Fundação Calouste Gulbenkian

2004/ Prospective registry of patients with transient neurological attacks (TNA). Classification of (TNA) in a consecutive cohort of patients referred to a TIA Clinic. Prognosis of TIA and non-ischemic TNA patients. Coordinator: Patrícia Canhão

2004/2011 - Intensive speech therapy for patients with aphasia after stroke: a single-masked, parallel randomised controlled trial in aphasic stroke patients. Joint project: LEL/Cerebrovascular disease' group of UNIC and the Centro de Medicina de Reabilitação de Alcoitão. Coordinator: I. P. Martins (not funded)

2005-2008, extended to 2011 - Cognitive Impairment in the Aged - A prospective clinical, neuropsychological, NMR and biochemical study (A. de Mendonça, principal investigator; collaboration with Faculdade de Ciências e Tecnologia of Lisbon and Departamento de Biologia da Universidade de Aveiro; Fundação Calouste Gulbenkian).

2006/2010 Apatia na fase aguda do AVC e alteração da personalidade após o AVC. FCT, SFRH/BD/2282/2005 PhD scholarship, Coordinator: José M. Ferro

2008/ Turma Piloto em Língua Gestual Portuguesa” - Fundação Calouste Gulbenkian

2009/2011 Lising in 3D images. Project inserted in Mestrado integrado de Engenharia Electrotécnica e de Computadores. Coordinator: Yves Rybarczyk, Co-Coordinator: José Fonseca (not funded)

2009/2011 Bateria Montreal de Avaliação da Comunicação – MAC. Joint project: LEL/Associação Nacional de Afásicos/Faculty of Medicine, University of Montreal. Coordinator: José Fonseca (not funded)

2009/2011 Contribuição da resposta imunitária para a associação de doenças do sono (hipersonolência) e cardiovasculares, FCT. Coordinator: L Moita: Co-Coordinator: T Paiva, A Bugalho de Almeida, R Staats, S Moreira, J Valença, A Rodrigues, C Bentes, R Gerales - PIC/IC/82991/2007.

2009/2015 An international, Prospective, TIA-clinic based, Web-based registry with long-term follow-up. Principal Investigator: Patrícia Canhão (€20 000)

2009-2011, extended 2012 - Neuropsychological predictors of the outcome in non-demented subjects with cognitive complaints (A de Mendonça, principal investigator; FCT).

2010 - 2011 – Caracterização neurofisiológica dos fusos de sono e complexos K em doentes com AVC agudo de alteração cerebral média e correlação com o prognóstico – GAPIC Coordinator: Ana Rita Peralta Student: Joana Isaac Teixeira.

2010/ Dicionários Terminológicos de LGP - Fundação PT

2010/2012 - Frontal lobe dysfunction during migraine attacks. Tecnifar Grant for Headache Research of Sociedade Portuguesa de Cefaleias. Raquel Gil-Gouveia, Isabel Pavão Martins, P. Vilela.

2010/2012 RAPS. Reading Analysis with neuroPhysiological Signs, FCT. Coordinator: N. Guimarães. PTDC/EIA-EIA/113660/2009, (total € 82 000)

2010/2012 VITHEA. Virtual Therapist for Aphasia treatment, FCT. Coordinator: Alberto Abad Gareta. RIPD/ADA/109646/2009, € 6 180 (total € 58 00)

2010/2012 BEDGET: deciphering BEhçet's Disease GEneTics, FCT. Coordinator: Oliveira SA. PTDC/SAU-GMG/098937/2008, €180 708 (total €199 908)

2010/2012 Genetics of Nonsyndromic Cleft Lip and Palate, FCT. Participant PI: Oliveira SA. PTDC/SAU-GMG/101537/2008 (€196 176).

2010/2013 Mindful aging. Avoiding age related cognitive decline, Bial Fundation and Nunes Vicente Grant (SPN). Coordinator: I.P Martins, (€ 84 000)

2010-2012 - Detection of brain microstates in Fibromyalgia, FCT. Coordinator: J Sanches. (IST).

2010-2012 - Estudo Genético de Famílias com Demência sem Mutações Reconhecidas (A. de Mendonça, principal investigator; collaboration with Gabriel Miltenberger, GenoMed; Grunenthal).

2010-2012 – Reading analysis with neurophysiological signals, FCT. Coordinator: Nuno Guimarães. Participant: Carla Bentes. PTDC/EIA-EIA/113666/2009 (€82.000)

2010-2012 Estudo necrópsico de doentes com formas familiares ou atípicas de demência (Ana Verdelho, principal investigator; Bial).

2010-2014 – AQUI_LGP: Corpus longitudinal da Aquisição da Língua Gestual Portuguesa (Refª: PTDC/CLE-LIN/111889/2009) - FCT

2011 – Estados dissociados na Fibromialgia: Caracterização clínica e neurofisiológica e desenvolvimento de estratégias terapêuticas com neurofeedback. (Co-investigador/Master Thesis) Ferreira L. (funding project)

2011 – Estudo de CAPs pré e pós-terapia com dispositivos orais. Meira e Cruz, Rebocho S, Ferreira L.

2011/2013 N-terminal do Peptideo Natriuretico Cerebral como marcador de acidente vascular cerebral isquémico de etiologia cardioembolica. FCT, HMSP-ICJ/0003/2010 Ana Catarina Gaspar Fonseca, (€126.540)

2011-2012: The perception of illness in acute stroke patients (no funding) Lara Caeiro

2011-2014 NEUROCLINOMICS - Understanding NEUROdegenerative diseases throught CLINical and OMICS data integration (Sara Madeira, principal investigator, collaboration involving Instituto de Engenharia de Sistemas e Computadores, Investigação e Desenvolvimento em Lisboa, IMM and Katholieke Universiteit Leuven; FCT).

2012- 2015 BIOMARKAPD – Joint Programming in Neurodegenerative Disorders (Alexandre de Mendonça, principal investigator)

2012-2015 - Partners in the FP7 funded project: SENSE-PARK: Supporting and Empowering Parkinson patients in their home environment using a Novel Sensory information system that monitors dailylife- relevant parameters of PARKinson disease and their change. Responsables for the workpackage 7: Scenario-based multicentre study

BMBS COST Action BM1101 European network for the study of dystonia syndromes
Cochrane Collaboration Movement Disorders Group

Publications in peer review Journals

Afonso P, Figueira L, Paiva T (2011) Schizophrenia patients with predominant positive symptoms have more disturbed sleep-wake cycles measured by actigraphy. *Psychiatry Res* **189**;62-66 (Journal IF: 2.344)

Afonso P, Figueira ML, Paiva T. (2011) Sleep-promoting action of the endogenous melatonin in schizophrenia compared to healthy controls. *Int J Psychiatry Clin Pract.* Nov;**15**(4):311-5. Epub. (Journal IF: 0.5)

Aguiar de Sousa D, Mestre T and Ferro JM (2011) Cerebral venous thrombosis in Behçet's disease: a systematic review. *J Neurol* **258**, 719-27 (Journal IF: 3.853)

Aisen PS, Andrieu S, Sampaio C, Carrillo M, Khachaturian ZS, Dubois B, Feldman HH, Petersen RC, Siemers E, Doody RS, Hendrix SB, Grundman M, Schneider LS, Schindler RJ, Salmon E, Potter WZ, Thomas RG, Salmon D, Donohue M, Bednar MM, Touchon J, Vellas B. Report of the task force on designing clinical trials in early (predementia) AD (Jan 2011) *Neurology* (Journal IF:8.017)

Bentes C, Costa J, Peralta R, Pires J, Sousa P Paiva T. (2011) Dream recall frequency and content in patients with temporal lobe epilepsy. *Epilepsia* **52**(11):2022-2077 (Journal IF: 3.955)

Caeiro L, Santos CO, Ferro JM and Figueira ML (2011) Neuropsychiatric disturbances in acute subarachnoid haemorrhage. *Eur J Neurol* **18**, 857-864 (Journal IF: 3.765)

Caldeira D, Amaral T, David C, Sampaio C. Educational strategies to reduce serum phosphorus in hyperphosphatemic patients with chronic kidney disease: systematic review with meta-analysis. (July 2011) *J Ren Nutr* (Journal IF:1.480)

Caldeira D, David C, Sampaio C. Rate vs rhythm control in patients with a trial fibrillation and heart failure: A systematic review and meta-analysis of randomised controlled trials. (Oct 2011) *Eur J Int Med* (Journal IF: 1.657)

Caldeira D, David C, Sampaio C. Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis. (March 2011) *J Hosp Infect* (Journal IF: 3.078)

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Conceição Pereira M, Loureiro JL, Pinto-Basto J, Brandão E, Margarida Lopes A, Neves G, Dias P, Geraldes R, Martins IP, Cruz VT, Kamsteeg EJ, Brunner HG, Coutinho P, Sequeiros J, Alonso I. Alu elements mediate large SPG11 gene rearrangements: further spatacsin mutations. *Genet Med (in press)*. (Journal IF: 5.280)

Costa J, Fareleira F, Ascensão R, Borges M, Sampaio C, Vaz Carneiro A, Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis, (Sep 2011) *Eur J Neurol* (Journal IF: 3.765)

Costa J, Is neurophysiology a valuable marker of pre-clinical stages of Lewy Body Disorders? (Dec 2011) *Clin Neurophysiol* (official journal of the International Federation of Clinical Neurophysiology) (Journal IF:2.786)

Costenla AR, Diógenes MJ, Canas PM, Rodrigues RJ, Nogueira C, Ribeiro JA, Maroco J, Agostinho PM, Cunha RA, de Mendonça A. Enhanced role of adenosine A_{2A} receptors in the modulation of LTP in the rat hippocampus upon aging. *Eur J Neurosci* 2011 34:12-21 (Journal IF: 3.658)

Coutinho JM, Seelig R, Boussier MG, Canhão P, Ferro JM and Stam J (2011) Treatment variations in cerebral venous thrombosis: an international survey. *Cerebrovasc Dis* **32**, 298-300. (Journal IF: 2.987)

Domingues-Montanari S, Fernández-Cadenas I, Del Rio-Espinola A, Corbeto N, Krug T, Manso H, Gouveia L, Sobral J, Mendioroz M, Fernández-Morales J, Alvarez-Sabin J, Ribó M, Rubiera M, Obach V, Martí-Fàbregas J, Freijo M, Serena J, Ferro JM, Vicente AM, Oliveira SA, Montaner J (2010) Association of a genetic variant in the ALOX5AP with higher risk of ischemic stroke: a case-control, meta-analysis and functional study. *Cerebrovasc Dis* **29**, 528-37 (Journal IF: 2.987)

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Goetz CG, Stebbins GT, Theeuwes A, Stocchi F, Ferreira JJ, van de Witte S, Bronzova J. Temporal stability of the Unified Dyskinesia Rating Scale. *Mov Disord*. 2011 Dec 26(14):2556-9. doi: 10.1002/mds.23931. Epub 2011 Sep 13 (Journal IF:4.480)

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Martins IP, Maruta C, Silva C, Rodrigues P, chester C, Ginó S, Freitas V, Freitas S, Oliveira AG. The effect of education on age related changes in three cognitive domains: A cross-sectional study in primary care. *Appl Neuropsychol* (in press) (Journal IF: 1.027)

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Martins, M, Moura, B L, Martins, IP, Figueira, ML, Prkachin, KP (2011) Sensitivity to expressions of pain in Schizophrenia patients. *Psychiatry Res* **30**; 189 (2),180-184 (Journal IF: 2.803)

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Moreno-López C, Santamaría J, Salamero M, Del Sorbo F, Albanese A, Pellecchia MT, Barone P, Overeem S, Bloem B, Aarden W, Canesi M, Antonini A, Duerr S, Wenning GK, Poewe W, Rubino A, Meco G, Schneider SA, Bhatia KP, Djaldetti R, Coelho M, Sampaio C, Cochen V, Hellriegel H, Deuschl G, Colosimo C, Marsili L, Gasser T, Tolosa E. Excessive Daytime Sleepiness in Multiple System Atrophy (SLEEMSA Study) (Feb 2011) *Arch Neurol* (Journal IF: 7.108)

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Invited Lectures and Seminars

Castro-Caldas A, Ciclo de Conferências Saber mais sobre, “Acidentes Vasculares Cerebrais”, Lisbon, June 8th, 2011

Castro-Caldas A, Ciclo de Conferências Saber mais sobre, “Envelhecimento Saudável”, Lisbon, April 13th, 2011

Castro-Caldas A, Plano Nacional de Leitura, Fundação Calouste Gulbenkian (moderador), Lisbon, September 13th - 14th, 2011

Castro-Caldas A. “A Neuroplasticidade”, Faculdade de Engenharia, Sintra, April 28th, 2011

Castro-Caldas A. “A Neuroplasticidade”, Sessão Solene da Sociedade Científica da Universidade Católica Portuguesa, Lisbon, October 14th, 2011

Castro-Caldas A. “A plasticidade cerebral no idoso”, Dia da Escola Superior de Enfermagem de S. João de Deus, Évora, March 14th, 2011

Castro-Caldas A. “A Viagem ao Cérebro e a algumas das suas competências”, Semana da Ciência e da Tecnologia, Arcos de Valdevez, March 24th, 2011

Castro-Caldas A. “As neurociências cognitivas”, II Congresso de Medicina AEICBAS-UP, Porto, March 19th, 2011

Castro-Caldas A. “As neurociências”, Conferência de Valorização 2011 – Mobilidade: Factor de Aprendizagem, Agência Nacional PROALV, Lisbon, November 30th, 2011

Castro-Caldas A. “Brain plasticity”, The Borders of Reason - ICS Conference 2011, Lisbon, November 29th, 2011

Castro-Caldas A. “Clinical Studies” (moderator), 48th Inner Ear Biology Workshop (IEB 2011)., Lisbon, September 21st, 2011

Castro-Caldas A. “Consciência e os Cuidados Intensivos”, Jornadas da Primavera de Medicina Intensiva., Hospital de Santo António, Porto, April 14th, 2011

Castro-Caldas A. “Envelhecimento saudável”, Comemorações do 63º Aniversário da Escola Superior de Saúde Dr. Lopes Dias, Castelo Branco, June 7th, 2011

Castro-Caldas A. “Formação em Controlo de Infecção”, Colóquio de Controlo de Infecção em Portugal, Porto, October 7th, 2011

Castro-Caldas A. “Linguagem e Memória na Aprendizagem”, VII Seminário de Pediatria do Neurodesenvolvimento” Porto, January 28th, 2011

Castro-Caldas A. “Neurociências”, Os Sinais do Tempo, Faculdade de Teologia UCP, Lisboa, February 17th, 2011

Castro-Caldas A. “Neurologia e Envelhecimento: O estado actual da investigação”, IV Congresso Internacional sobre Envelhecimento e Qualidade de Vida, Universidade dos Açores, November 5th, 2011

Castro-Caldas A. “Neuroplasticidade”, Jornadas Ibéricas de Reabilitação, Instituto Politécnico de Viana do Castelo, March 4th, 2011

Castro-Caldas A. “O Cérebro depois dos 60”, Residências Espírito Santo Saúde, Oeiras, February 9th, 2011

Castro-Caldas A. “O Cérebro que aprende”, Unidade de Ensino de Enfermagem de Lisboa” Sintra, February 3rd, 2011

Castro-Caldas A. “O Idoso e a Saúde Mental”, VII Colóquio da Associação de Apoio a Profissionais do Hospital de Santa Maria (AAP_HSM), Lisboa, March 10th, 2011

Castro-Caldas A. “O que aprendemos com o cérebro de quem não aprende”, Cem Lições Comemorações dos 100 Anos da Universidade de Lisboa, Lisbon, March 29th, 2011

Coelho M, Neck: BonT indications and injection techniques, Second Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 8, 2011 (oral communication)

Coelho M, Other localizations: BonT indications and injection techniques, Second Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 8, 2011 (oral communication)

Coelho M, Patient consultation: Atypical Parkinsonism, III Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Coelho M, Patient consultation: Dystonia, III Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Coelho M, Stage Parkinson’s Disease: a missed phenotype, XII meeting of the Portuguese Society for Neurosciences, Faculdade de Medicina de Lisboa, Lisbon, May 26-28, 2011

Costa J, Comparação de diferentes métodos para avaliação da adesão à terapêutica anti-retrovírica, 14º workshop Educação pela Ciência, Projectos de investigação científica de alunos da FMUL, Faculdade de Medicina de Lisboa, December 12, 2011

de Mendonça A. Approach to the Patient with Memory Impairment. 4th European Neurological Conference on Clinical Practice, Lisbon, January 2011.

de Mendonça A. Estratégias Terapêuticas para a Cura da Doença de Alzheimer. III Jornadas Ibéricas sobre a Doença de Alzheimer, Lisboa, October 2011.

de Mendonça A. Perspectiva do Neurologista: O Princípio da Doença de Alzheimer. VII Congresso da Sociedade Portuguesa de Neuroradiologia, Lisboa, May 2011

Fernandes R. Aspectos farmacológicos da terapêutica pediátrica. UCF – Saúde da Criança e da Família, Lisboa, December 16, 2011.

Ferreira JJ, Abordagem Terapêutica das complicações motoras, Congresso de Neurologia 2011, Lisboa, November 3-5, 2011 (oral communication)

Ferreira JJ, Basic Movement Disorders Course, Chorea, atetosis and ballism, Toronto, Canada, June 3, 2011

Ferreira JJ, Centro único vs rede de centros como modelo de investigação em doenças do movimento, Ciência e Ensino, 100 anos da FMUL, Faculdade e Medicina de Lisboa, Lisbon, May 6-7, 2011

Ferreira JJ, Clinical progression of Parkinson’s disease, Jahrestagung der Österreichischen Parkinson Gesellschaft, Congress Center Villach 2011 13.-15. October 2011.

Ferreira JJ, Diagnostic Procedures in Distonias, The Movement Disorder Society Section, Diagnosis and Treatment of Dystonia Syndromes, Milan Italy, September 22-23, 2011

Ferreira JJ, How to manage a botulinum toxin clinic, Second Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 8, 2011 (oral communication)

Ferreira JJ, Huntington’s disease world congress 2011, Are we ready to conduct clinical trials in pre-symptomatic gene carriers in Huntington’s disease, Melbourne, Australia, September 11-14, 2011

Ferreira JJ, Latin America Huntington’s Disease workshop, EHDN as a network Model to support translational research, Santiago, Chile, October 17-19, 2011

Ferreira JJ, Lower Limb BonT indications and injection techniques, Second Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 8, 2011 (oral communication)

Ferreira JJ, Markers, diagnosis and progression in early Parkinson’s disease, Global Parkinson’s disease Expert Meeting, The Vatican, Vatican City, April 3-4, 2011

Ferreira JJ, O estudo epidemiológico sobre a Doença de Parkinson, Encerramento das Comemorações de Abril, Dia Mundial do Doente de Parkinson, April 11, 2011

Ferreira JJ, Parkinson’s disease look-alike – what is it? Teaching Course 1, Movement disorders – basic clinical knowledge, 15th Congress of the European Federation of Neurological Societies, Budapest, Hungary, September 10-13, 2011

Ferreira JJ, Parkinson’s Disease progression, XII meeting of the Portuguese Society for Neurosciences, Lisbon, Faculdade de Medicina de Lisboa, May 26-28, 2011

Ferreira JJ, Parkinsonian syndromes (PSP, MSA, vascular, post-neuroleptics): is DAT over or under used? Dopamine Transporter Imaging Workshop Paris, France _ December 10, 2010

Ferreira JJ, Patient consultation, Chorea, III Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Ferreira JJ, Patient consultation: Parkinsonism, III Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Ferreira JJ, Tics and Tourette, MDS-ES Movement Disorders Summer Scholl, Naples, Italy, July 1-3, 2011

Ferreira JJ, Use of Botulinum Toxins in Dystonia Syndromes, The Movement Disorder Society Section, Diagnosis and Treatment of Dystonia Syndromes, Milan Italy, September 22-23, 2011

Ferreira JJ; Secondary Parkinsonisms, MDS-ES Movement Disorders Summer Scholl, Naples, Italy, July 1-3, 2011

Ferreira L. Estudos do Sono: na doença vascular - Sessão Científica: Estudos do Sono. 17º Congresso Português de Cardiopneumologia, 25 – 27 de Março, Hotel Meliã, Braga (invited lecture).

Ferro JM. A epidemia da fibrilhação auricular e AVC. Inibição do factor X na prevenção do AVC. 5º Congresso Português do AVC, Porto, Portugal, February 3-5, 2011.

Ferro JM. Deterioração cognitiva vascular. 4º Curso Médico-Cirúrgico em Neurociências, Porto, Portugal, February 12, 2011.

Ferro JM. Doença Cerebrovascular. Destaques do ano na prevenção cardiovascular. Reunião do GERC – 2011. Lisboa, March 26, 2011.

Ferro JM. Etiologic diagnosis: an effective approach. XX World Congress of Neurology, Marrakesh, Marrocco, November 13, 2011.

Ferro JM. Prevention of cardioembolic stroke. XX World Congress of Neurology, Marrakesh, Marrocco, November 13, 2011.

Ferro JM. Stroke in the young. 21st Meeting of the European Neurological Society, Lisboa, Portugal. May 28-31, 2011

Ferro JM. The burden of cerebral vein thrombosis in cerebrovascular diseases. Old and new concepts. 20th European Stroke Conference, Hamburg, Germany. May 24-27, 2011.

Fonseca, J. A gaguez e a investigação científica (Gaguez adquirida por lesão). 5ª Edição das Jornadas sobre a Gaguez. Associação Portuguesa de Gagos, ISCAC, Escola Superior Agrária de Coimbra, Coimbra, October, 22, 2011.

Guedes LC, Patient consultation, genetic Movement Disorders, II Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Lauterbach, M. Neuroplastizität bei kindlicher Aphasie - eine fMRI Studie. Hospital de Dia de Reabilitação Cognitiva da Universidade de Leipzig. May 19, 2011.

Lauterbach, M. Recuperação da afasia - 20 anos de evolução. Sessão clínica do Serviço de Neurologia. Anfiteatro Almeida Lima, Serviço de Neurologia do Hospital de Santa Maria, March 3, 2011.

Leal, G. Revisitando a apraxia do discurso. Sessão clínica do Serviço de Neurologia. Anfiteatro Almeida Lima, Serviço de Neurologia do Hospital de Santa Maria, April 28, 2011.

Martins, IP. Cefaleias. XV Jornadas Nacionais Patient Care. Centro de Congressos de Lisboa, February 17-18, 2011.

Martins, IP. Migraine: the contribution of clinical symptoms to clarify the pathogenesis. 4th European Neurological Conference on Clinical Practices, Lisbon Marriott Hotel Lisbon, Portugal, January 28-30, 2011.

Martins, IP. Sintomas Paroxísticos na Enxaqueca. prelector. Reunião da Primavera da Sociedade Portuguesa de Cefaleias. Hotel Olissipo Oriente. Lisboa, May 6, 2011.

Maruta, C. Os seniores, o cérebro e a memória. Centro de Convívio dos Serviços Sociais da Administração Pública, Lisboa, July 8, 2011.

Melo TP. Medidas gerais. Tratamento do AVC na fase aguda, aquém e além da fibrinólise. 5º Congresso Português do AVC, Porto, Portugal, February 3-5, 2011.

Pimentel, J. A terapêutica actual da epilepsia. 2º Fórum “Boas Práticas na Saúde Mental, Coimbra, October 3-4, 2011 (Oral presentation).

Pimentel, J. Anatomia das vias vestibulares. Congresso de Neurologia 2011, Lisboa, November 3-5, 2011.

Pimentel, J. Epilepsias refractárias: quando a cirurgia não é possível – “estado da arte”. VII Reunião Luso-Espanhola de Epilepsia, Málaga, October 22, 2011

Pimentel, J. Politerapia na epilepsia. 23º Encontro Nacional de Epileptologia, Lisboa, March 18-19, 2011.

Pimentel, J. Politerapia: quando e como? 23º Encontro Nacional de Epileptologia, Lisboa, March 18-19, 2011.

Pimentel, J. Situações agudas no tratamento da epilepsia. Jornadas de Medicina Intensiva da Primavera, Porto, April 14-15, 2011.

Rosa M, Botulinum toxin's history, mechanisms of action and formulations, Second Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 8, 2011 (oral communication)

Rosa MM, Patient consultation, Metabolic Movement Disorders, II Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Sampaio C, 10th International Conference Alzheimer's Disease and Parkinson's disease, Biomarkers and their predictive values in AD and PD, Barcelone, Spain, March 10, 2011

Sampaio C, 9th Nordic Meeting on advanced Parkinson's disease with motor fluctuations, New pharmacological options, Stockholm, April 7-8, 2011

Sampaio C, CHDI challenges of Clinical Research, EHDN as a network Model to support translational research, Santiago, Chile, October 17-19, 2011

Sampaio C, Impact XIV, Improving Understanding and Interpretation of Analgesic Clinical Trial Results, The initiative on methods, measurement and pain assessment in clinical trials, Arlington, USA, June 16-17 2011

Sampaio C, The principles of evidence based medicine and the Cochrane collaboration: how to use evidence to treat an individual patient, 15th International Congress of Parkinson's disease and Movement disorders, Toronto, Canada, June 5-9, 2011

Valadas A, Patient consultation: Psychogenic Movement Disorders, II Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Valadas A, Sousa A, Face and platysma: BotT indications and injections techniques, Second Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 8, 2011 (oral communication)

Verdelho A. Age-related white matter changes and cognition. 20th European Stroke Conference, Hamburg, Germany. May 24-27, 2011.

Verdelho A. Headache in stroke. 20th European Stroke Conference, Hamburg, Germany. May 24-27, 2011.

Communications in International Conferences

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Albuquerque, L., Maruta, C., Coelho, M., Martins, I.P.. Visual recognition and memory of faces in non-demented late Parkinson's disease patients with visual hallucinations. 21st Meeting of the European Neurological Society, Lisbon, May 28-31, 2011 (Poster presentation)

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Organisation of Conferences

Bentes C. Cientific comission of the 23º Encontro Nacional de Epilepsia. Lisboa Hotel Sana, Lisboa, 18th and 19th of March 2011

Castro-Caldas A, Debate ICS "Saber Estudar - Saberão os alunos aprender?", Universidade Católica Portuguesa, Lisbon, January 20th 2011

Castro-Caldas A, I Conferência Internacional sobre Enfermagem Geriátrica (CIEG), Fundação D. Pedro IV - Universidade Católica Portuguesa, Lisbon, October 28th, 2011

Castro-Caldas A, II International Symposium on Neuropsychology and Rehabilitation, CRPG – Gaia, November 24th and 25th, 2011

Castro-Caldas A, III Jornadas Ibéricas sobre a Doença de Alzheimer, Alzheimer Portugal, UCP, October 20th and 21st, 2011

Castro-Caldas A, International Conferences on Neuropsychology, Dr. Katja Wiech, "Neral Mechanisms of Cognitive-affective Pain Modulation", UCP, March 23th 2011

Castro-Caldas A, International Conferences on Neuropsychology, Dr. Usha Goswami, "Brain, Science and Education", UCP, February 23th 2011

Castro-Caldas A, International Conferences on Neuropsychology, Professor Michael Corballis, "The Origins of Language", UCP, November 28th, 2011

de Mendonça, A. Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demências, Tomar, Junho 2011.

Ferreira JJ, Course Director of the course III Teaching Course in Movements Disorders of the Neurological Clinical Research Unit, Lisbon, Instituto de Medicina Molecular, May 21, 2011

Ferreira JJ, Course Director of the course: "Second Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 8, 2011.

Ferro JM. Chaiperson. 21st Meeting of the European Neurological Society, Lisboa, Portugal. May 28-31, 2011.

Fonseca, J. Encontro dos Técnicos de Diagnóstico e Terapêutica. Edifício Egas Moniz, Faculdade de Medicina de Lisboa, Universidade de Lisboa. Lisboa, November 12, 2011.

Lauterbach, M. Encontro anual da Secção de Neurologia de Comportamento no âmbito da Sociedade Portuguesa de Neurologia. Congresso de Neurologia 2011. Sana Lisboa Hotel. Lisboa, November 3-5, 2011.

Oliveira V. Congresso de Neurologia 2011. Lisboa, Portugal. November 3-5, 2011.

Oliveira, S. Co-organizer of the ESF-ITQB Workshop “Basic Experimental Techniques in Biological Dynamics”, at ITQB, Oeiras, Portugal (5-9 September 2011), sponsored by European Science Foundation.

Internationalization

Bousser MG, Amarenco P, Chamorro A, Fisher M, Ford I, Fox KM, Hennerici MG, Mattle HP, Rothwell PM, de Cordoue A and Fratacci MD; PERFORM Study Investigators (2011) Terutroban versus aspirin in patients with cerebral ischaemic events (PERFORM): a randomised, double-blind, parallel-group trial. *Lancet* **377**, 2013-2022. (Journal IF: 33.633)

de Mendonça A. is coordinator of the EADC – European Alzheimer’s Disease Consortium - centre in Lisbon.

de Mendonça A. is national representative in the Dementia Panel of the EFNS – European Federation of Neurological Societies.

Dennis M, Mordi N, Graham C and Sandercock P; Clots Trials Collaboration (2011) The timing, extent, progression and regression of deep vein thrombosis in immobile stroke patients: observational data from the CLOTS multicenter randomized trials. *J Thromb Haemost* **9**, 2193-2200. (Journal IF: 5.349)

Dennis M, Sandercock P, Reid J, Graham C, Murray G, Venables G, Rudd A and Bowler G; CLOTS Trials Collaboration (2011) Can clinical features distinguish between immobile patients with stroke at high and low risk of deep vein thrombosis? Statistical modelling based on the CLOTS trials cohorts. *J Neurol Neurosurg Psychiatry* **82**, 1067-1073. (Journal IF: 4.791)

Ferreira JJ Co-chair of the Membership and Public relations Committee of MDS

Ferreira JJ is the Science Director of the European Huntington Disease Network.

Ferreira JJ, Member of European Cooperation in the field of Scientific and Technical Research - COST

Ferreira JJ, Member of the Movement Disorders Society Task Force on Tremor

López-Sendón JL, Royuela A, Trigo P, Orth M, Lange H, Reilmann R, Keylock J, Rickards H, Piacentini S, Squitieri F, Landwehrmeyer B, Witjes-Ane MN, Jurgens CK, Roos RA, Abaira V, de Yébenes JG; and the European HD Network. What is the impact of education on Huntington's disease? *Mov Disord.* 2011 Jul;26(8):1489-95. doi: 10.1002/mds.23385. Epub 2011 Mar 22. (Journal IF:4.480)

Mishra NK, Ahmed N, Davalos A, Iversen HK, Melo T, Soinne L, Wahlgren N and Lees KR; SITS Collaborator; VISTA Collaborator (2011) Thrombolysis outcomes in acute ischemic stroke

patients with prior stroke and diabetes mellitus. *Neurology* **77**, 1866-1872. (Journal IF: 8.017, Citations: 0)

Orth M; European Huntington's Disease Network, Handley OJ, Schwenke C, Dunnett S, Wild EJ, Tabrizi SJ, Landwehrmeyer GB. Observing Huntington's disease: the European Huntington's Disease Network's REGISTRY. *J Neurol Neurosurg Psychiatry* 2011 Dec;82(12):1409-12. Epub 2010 Nov 19. (Journal IF: 4.791)

Rickards H, De Souza J, van Walsem M, van Duijn E, Simpson SA, Squitieri F, Landwehrmeyer B; European Huntington's Disease Network. Factor analysis of behavioural symptoms in Huntington's disease. *J Neurol Neurosurg Psychiatry*. 2011 Apr;82(4):411-2. (Journal IF: 4.791)

Rickards H, Souza JD, Crooks J, van Walsem MR, van Duijn E, Landwehrmeyer B, Squitieri F, Simpson SA. Discriminant Analysis of Beck Depression Inventory and Hamilton Rating Scale for Depression in Huntington's Disease. *J Neuropsychiatry Clin Neurosci*. 2011 Sep 1;23(4):399-402. (Journal IF:2.34)

Saft C, Epplen JT, Wieczorek S, Landwehrmeyer GB, Roos RA, de Yebenes JG, Dose M, Tabrizi SJ, Craufurd D; REGISTRY Investigators of the European Huntington's Disease Network, Arning L. NMDA receptor gene variations as modifiers in Huntington disease: a replication study. *PLoS Curr*. 2011 Oct 4;3 (Journal IF:4.411)

Sampaio C, Ferreira JJ - Cochrane collaboration- the group host one of the movement disorders review groups

Sampaio C, Ferreira JJ - Movement Disorders Society – hold leading positions in the Society and are heads of lines of work with the society at a worldwide level.

Vaccarino AL, Anderson K, Borowsky B, Duff K, Giuliano J, Guttman M, Ho AK, Orth M, Paulsen JS, Sills T, van Kammen DP, Evans KR; PREDICT-HD and REGISTRY Investigators Coordinators. An item response analysis of the motor and behavioral subscales of the unified Huntington's disease rating scale in Huntington disease gene expansion carriers. *Mov Disord*. 2011 Apr;26(5):877-84. (Journal IF:4.480)

Prizes, honours and awards

“Best oral presentation” of the “5º Congresso Português do AVC” to Fonseca M, Canhão P. Risco precoce de AVC em consulta de AIT diária versus semanal.

“Junior Clinical Research/ Career Development Award 2011” of the “Harvard Medical School-Portugal Program” to Ana Catarina Fonseca

“Prémio João Alfredo Lobo Antunes” of the “Sociedade Portuguesa de Neurologia” to Bruno Miranda.

2º Prize – Prize Florbela Espanca: Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T. “Dream recall frequency and content in patients with Temporal Lobe Epilepsy”.

Basic Research Prize 2011 awarded by the Portuguese Society of Human Genetics (2011) for the work entitled “Convergence of miRNA Expression Profiling, α -synuclein Interacton and GWAS in Parkinson's Disease” by Martins M, Rosa A, Guedes LC, Fonseca BV, Gotovac K, Violante S,

Mestre T, Coelho M, Rosa MM, Martin ER, Vance JM, Outeiro TF, Wang L, Borovecki F, Ferreira JJ, Oliveira SA.

First prize from Liga Portuguesa Contra a Epilepsia, 2011, Costa J, Fareleira F, Ascensão R, Borges M, Sampaio C, Vaz Carneiro A, Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis,

Prize for best oral communication on the session - Diálogos em Epilepsia – Neutel D, Coelho M, Bentes C, Barroso C, Pimentel J. “Perturbação da Consciência por hiperamonemia secundária à terapêutica com Valproato de Sódio” – Hotel Viva Marinha - Cascais, September 2011.

Prize of LPCE to best poster presentation: Almeida V, Campos A, Bentes C, Morgado C, Loureiro C, Pimentel J, “Encefalite auto-imune “tratada” por cirurgia da epilepsia” on the 23º Encontro Nacional de Epileptologia. Lisboa Hotel Sana, 18th and 19th of March 2011.

Industry contract research

Clinical trials

2007/ - PERFORM- Principal Investigator - Patrícia Canhão, Servier

2008/ - ICTUS Principal Investigator - Teresa Pinho e Melo, Ferrer International

2008/ - A randomized, double-blind, placebo-controlled, parallel-group study to investigate efficacy and security of Bapineuzumab (AAB-001, ELN115727) in Subjects with severe, moderate and mild Alzheimer Disease who are not Apolipoprotein E ϵ 4. Phase III. (Pfizer 3133K1-3000-WW) National Coordinator A. Mendonça

2008/ - A randomized, double-blind, placebo-controlled, parallel-group study to investigate efficacy and security of Bapineuzumab (AAB-001, ELN115727) in Subjects with severe, moderate and mild Alzheimer Disease who are Apolipoprotein E ϵ 4. Phase III. (Pfizer 3133K1-3001-WW) National Coordinator A. Mendonça

2009/ - A Phase 3 Extension, Multicenter, Double-blind, Parallel-Group, Long-term Safety and Tolerability Trial of Bapineuzumab (AAB-001, ELN115727) in Subjects With Alzheimer Disease Who Are Apolipoprotein E ϵ 4 Noncarriers and Participated in Study 3133K1-3000-WW" (3133K1 – 3002-WW) National Coordinator A. Mendonça

2009/ - A Phase 3 Extension, Multicenter, Double-blind, Parallel-Group, Long-term Safety and Tolerability Trial of Bapineuzumab (AAB-001, ELN115727) in Subjects With Alzheimer Disease Who Are not Apolipoprotein E ϵ 4 Noncarriers and Participated in Study 3133K1-3001-WW, (3133K1-3003-WW) National Coordinator A. Mendonça

2009/2013 - TIMI - Principal Investigator - Patrícia Canhão, Icon

2010/ A randomized of phase III, double-blind, placebo-controlled and multicenter study, to investigate bevacizumab, temozolomida and radiotherapy, followed by bevacizumab and temozolomida versus placebo, temozolomida and radiotherapy followed by placebo and temozolomida in patients with recent diagnosis of glioblastoma. Coordinator: L. Albuquerque (clinical trial AVAGLIO –BO21990)

2010/ Clinical trial in AD with the histamine H₃ receptor antagonist, SAR110894D, Sanofi. National Coordinator A. Mendonça

Government/Organization contract research

Alexandre de Mendonça is scientific coordinator of the Direcção Geral de Saúde (DGS) guideline on Cognitive Decline and Dementia.

Saposnik G, Barinagarrementeria F, Brown RD Jr, Bushnell CD, Cucchiara B, Cushman M, deVeber G, Ferro JM, Tsai FY; American Heart Association Stroke Council and the Council on Epidemiology and Prevention (2011) Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* **42**,1158-1192. (Journal IF: 5.756)

Advanced teaching

Bentes C. Chairman of the meeting Hypersomnias and Parasomnias of the Master Course in Sleep Medicine, Lisbon, November 18, 2011.

Bentes C. Lecture the session “Arousal Parasomnias” in the meeting Hypersomnias and Parasomnias at the Master Course in Sleep Medicine, FMUL, 2011, November 18, 2011.

Bentes C. Participated at the Master Course in Neurosciences, FMUL, 2011.

Caeiro L. Diagnostic traps in post-stroke dementia, depression, apathy, etc. European Master in Stroke Medicine. Danube University Krems, Krems, Abril 14, 2011.

Caeiro L. How to evaluate cognition in the follow-up of stroke patients? European Master in Stroke Medicine. Danube University Krems, Krems, Abril 14, 2011.

Caeiro L. Metodologia da descrição de um caso neuropsicológico. Master in Neurosciences, University of Lisbon, Lisbon, May 4, 2011

Caeiro L. Presentation of a neuropsychological case. European Master in Stroke Medicine. Danube University Krems, Krems, Abril 14, 2011.

Canhão P. Estudos de coorte. Factores de risco e factores de prognóstico. XII Master in Neurosciences, University of Lisbon, Lisbon, May, 2011

Canhão P. Investigação clínica em neurociências- Tipos de estudos. XI Master in Neurosciences, University of Lisbon, Lisbon, May, 2011

Farrajota, L. “Reabilitação da afasia (APP)”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, March 25, 2011.

Ferreira JJ, aula em Programa de Doutoramento – Fundação Champalimaud

Ferreira JJ, Evidence based medicine, Training programme in Pharmaceutical Medicine, Pharmacoeconomics and healthcare economics, Universidade de Aveiro, Aveiro, April 29-30, 2011

Ferreira JJ, Masters in Neurosciences – Responsible for the Module Therapeutic Research in Neurosciences, Faculdade de Medicina de Lisboa, 2011-2012

Ferreira JJ, Métodos de Investigação II, Instituto de Ciências da Saúde da Universidade Católica de Lisboa, December 15, 2011

Ferreira L. Lectured the practical teaching Neurologia – Electroencefalograma e Monitorização Vídeo – EEG. Clinical Girassol Luanda. May 17-27; 2011.

Ferreira L. Practical Session of PSG, at the Master Course in Sleep Medicine, FMUL, 2011

Ferro JM. Anxiety and disorders of emotional control. European Master in Stroke Medicine. Danube University Krems, Krems, October 19, 2011.

Ferro JM. Delirium and related disorders. European Master in Stroke Medicine. Danube University Krems, Krems, October 19, 2011.

Ferro JM. Estado vegetativo. XI Master in Neurosciences, University of Lisbon, Lisbon, January 26, 2011.

Ferro JM. Estudos casos-controlo. XI Master in Neurosciences, University of Lisbon, Lisbon, May, 2011

Ferro JM. Executive deficits. European Master in Stroke Medicine. Danube University Krems, Krems, October 19, 2011.

Ferro JM. Mood disorders. European Master in Stroke Medicine. Danube University Krems, Krems, October 19, 2011.

Ferro JM. Visual agnosias. European Master in Stroke Medicine. Danube University Krems, Krems, October 19, 2011.

Guerreiro, M. "Cognitive rehabilitation" Master in Neurosciences. FM da UL, Lisboa, March 24, 2011.

Guerreiro, M. "Episodic memory." Master in Neurosciences. FM da UL, Lisboa, March 10, 2011.

Lauterbach, M. "Avaliação da linguagem". Master in Clinical Linguistic, Universidade Católica Portuguesa, April, 29, 2011.

Lauterbach, M. "Functional image for the study of language organization". Master in Neurosciences. FM da UL, Lisboa, March 22, 2011.

Lauterbach, M. "Imagem funcional (RMf) para o estudo da linguagem". Master in Clinical Linguistic, Universidade Católica Portuguesa, July 2, 2011.

Lauterbach, M. "Neuroplasticidade". Master in Clinical Linguistic, Universidade Católica Portuguesa, July 14, 2011.

Lauterbach, M. "Plasticidade cerebral para a linguagem". Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, March 25, 2011.

Martins, I.P. "Neglect". European Master in Stroke Medicine, Krems, Austria, October 19, 2011.

Martins, I.P. "Semantic memory – proper names". Master in Neurosciences. FM da UL, Lisboa, March 15, 2011.

Martins, I.P. "General Introduction Aphasia". European Master in Stroke Medicine, Krems, Austria, October 19, 2011.

Martins, I.P. "Memory disorders". European Master in Stroke Medicine, Krems, Austria, October 19, 2011.

Martins, I.P. "Reading Disorders". European Master in Stroke Medicine, Krems, Austria, October 19, 2011.

Martins, I.P. Plasticidade das lesões do hemisfério direito na neuroreabilitação. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, March 18, 2011

Martins, I.P., Ximenes, M.J., Tavares, D. “Perturbações da Linguagem e da Aprendizagem Académica” Curso de Pós – Graduação em Neurodesenvolvimento em Pediatria no Módulo 5 , Universidade Católica, May, 20, 2011.

Maruta, C. “Afasiologia: Afasia Primária Progressiva – Um quadro particular dentro das doenças neurodegenerativas”. Master in Clinical Linguistic, Universidade Católica Portuguesa. May 14, 2011.

Maruta, C., Loureiro, C. “Avaliação invasiva da linguagem”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, February 17, 2011.

Oliveira SA. Co-organized and lectured in the ESF-ITQB Workshop “Basic Experimental Techniques in Biological Dynamics”, at ITQB, Oeiras, Portugal. September 5-9, 2011.

Oliveira SA. Lectured in Genetics Course of the 2011 Programme for Advanced Medical Education. December 1, 2011.

Oliveira SA. Lecturer in the “Stroke - Molecular Neuropathology and Neurorecovery” module of the GABBA PhD program 2011, Institute for Molecular and Cell Biology - IBMC, Porto, Portugal. June 1, 2011.

Oliveira SA. Lecturer in the Mestrado de Neurociências, FMUL, May 11, 2011.

Oliveira SA. Lecturer in the Mestrado em Doenças Metabólicas, January 22 and 29, 2011.

Peralta A. Participated at the Master Course in Neurosciences, FMUL 2011.

Peralta R. Lecture the session “Methodology of Dream Analysis” in the meeting Presentations and Roundtable Discussions of the Master Course in Sleep Medicine, Lisbon, May 21, 2011.

Pimentel, J. Master on Biopharmacy – Glial tumors.(April 2011)

Pimentel, J. Master/PhD on Neurosciences (coordinator of the NS Pathology – February 2011

Silvestre, A.R. “Patologia neuromuscular: aplicação das biópsias musculares” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, February 8-17, 2011.

Silvestre, A.R. “Patologia neuromuscular: aplicação das biópsias de nervo” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, February 8-17, 2011.

Science and Society

Ferreira L. Orientação do Estágio Curricular dos Alunos de Neurofisiologia da Escola Superior de Saúde do Vale do Ave: 2011 – 540 h (35h/semana)

Ferreira L. Professora Assistente e Co-Responsável das componentes Teórica e Prática da componente de Estudo do Sistema Nervoso, do curso de Cardiopneumologia, da Escola Superior de Saúde de Lisboa, IPL (1º Semestre – 2º Ano). Ano lectivo 2010/11 e 2011/12.

Ferro JM. (2011) Acidente Vascular Cerebral. Programa Harvard Medical School – Portugal Program

Oliveira V. (2011) Organizer of the “Stroke day”. Sociedade Portuguesa do AVC. Lisboa, March 31.

Peralta R. (2011) Sonolência ao volante – Dia Mundial do Sono. com a criação de “spot” de rádio, televisão e panfletos informativos e Workshops.

Pires J. Professora Assistente e Co-Responsável das componentes Teórica e Prática da componente de Estudo do Sistema Nervoso, do curso de Cardiopneumologia, da Escola Superior de Saúde de Lisboa, IPL (1º Semestre – 2º Ano). Ano lectivo 2010/11 e 2011/12.

Santos R. Professora Assistente e Co-Responsável das componentes Teórica e Prática da componente de Estudo do Sistema Nervoso, do curso de Cardiopneumologia, da Escola Superior de Saúde de Lisboa, IPL (1º Semestre – 2º Ano). Ano lectivo 2010/11 e 2011/12.

Master and PhD thesis completed

Ana Catarina Gaspar Fonseca (2011). “Determination of the best time window to measure NT-proBNP – a biomarker of cardioembolic stroke”. European Master in Stroke Medicine, Danube University Krems, Austria. Supervisor: José M. Ferro.

Ana Margarida dos Santos Ferreira (2011) Caracterização quantitativa do núcleo basolateral da amígdala na esclerose mesial. Integrated Master on Medicine. Faculdade de Medicina de Lisboa. Supervisor: José Pimentel

Bernardo Moura (2011) “A case-control analysis between two elderly non-disabled populations: the effect of White Matter Changes in neuropsychological outcomes”. Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão Martins.

Filipa Batista dos Santos (2011) Proteína C-Reactiva e recorrência vascular após o Acidente Isquémico Transitório Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: Patricia Canhão

Joana Luísa Pereira Estrela Gameiro (2011) “Is the prognosis of cerebral vein thrombosis presenting as early or late isolated headache similar? Results of the International Study on Cerebral Vein and Dural Sinus Thrombosis. Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: José Ferro

Licínia Lara Rodrigues Araújo, “Cuidados Paliativos: Estágio Observacional no Hospital Élisabeth Bruyère”, Universidade Católica Portuguesa, May 17th

Nuno Martins (2011) Amígdala na epilepsia do lobo temporal. Integrated Master on Medicine. Faculdade de Medicina de Lisboa. Supervisor: José Pimentel

Renato Jorge Coelho Monteiro dos Santos, “Adaptação Cultural e Validação da “*Pain Assessment Checklist for Senior with Limited Ability to Communicate*” (PACSLAC) para a População Portuguesa, Universidade Católica Portuguesa, January 19th

Rita Gameiro (2011) “Autonomia no Envelhecimento”. Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão Martins.

Ruben Duarte Ferreira (2011) Estudo do padrão circadiano das crises em doentes com epilepsia temporal mesial refractária, em ambulatório. Master Thesis FMUL. Supervisor: Bentes C.

Sara Lobo (2011) Colocação de shunt no tratamento da doença trombótica das veias e seios venosos cerebrais. Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: José Ferro

Sérgio Manuel Ribeiro de Figueiredo, “Aprendizagem das Competências Nucleares na Área das Neurociências Clínicas”, Universidade Católica Portuguesa, September 19th

Tiago Krug Coelho (2011) “Stroke Genetics and Genomics”. PhD in Biomedical Sciences, Specialization in Neurosciences, Faculdade de Medicina da Universidade de Lisboa. Supervisors: Sofia A. Oliveira, José M. Ferro

Vanda Freitas (2011) “Contributo de dois testes de funções executivas no diagnóstico neuropsicológico”. Mestrado de Neurociências. Faculdade de Medicina de Lisboa. Universidade de Lisboa. Supervisor: Isabel Pavão Martins.

Vanessa Cristina Sobral Fonseca, “Contributo para a adaptação e validação da Walking Index for Spinal Cord Injury II para a população portuguesa”, Universidade Católica Portuguesa, June 29th

Bruno Miranda (2011). Thrombotic recurrent events after cerebral vein thrombosis. Mestrado de Neurociências. Faculdade de Medicina de Lisboa. Supervisor: José M. Ferro.

Translational and Clinical Physiology Unit

Description and Objectives

This Unit was formed by the merging of the Neuromuscular and Autonomic Nervous System Units in order to establish a larger Unit concerned with animal and human research on Physiology, taking advantage of many members being related to the Physiology Institute of the Faculty of Medicine-University of Lisbon. The investigation focus will be the autonomic nervous system, cardiovascular function, muscle, peripheral nerve physiology, motor neurons, as well as the central nervous system, including behaviour and imaging-neurocomputational models of brain dysfunction. Studies involve both animal models and humans. Physiological homeostatic mechanisms and diseases are targeted in our activities. We plan to implement a translational, multi-methodological approach to neuromuscular and brain diseases, using animal models, clinical neurophysiology, neurocomputational models, brain imaging and neuropsychological experimentation.

Head of the Unit

Mamede de Carvalho, MD, PhD – Associated Professor, FMUL

Principal Investigator

Isabel Rocha, PhD – Associated Professor, FMUL

Research Team

Michael Swash, MD, PhD	Invited Full Professor, FMUL
Alberto Escalda, MD, PhD	Assistant Professor, FMUL
Anabela Pinto, MD, PhD	Assistant Professor, FMUL
Conceição Azevedo Coutinho, MD, PhD	Assistant Professor, FMUL
João Costa, MD, PhD	Assistant Professor, FMUL
Mario Oliveira, MD, PhD	Assistant Professor, FMUL
Tiago Maia, PhD	Assistant Professor, FMUL
Victor Gonçalves, MD, PhD	Assistant Professor, FMUL
Ana Londral, MSc	PhD student
Anna Caroline Braga, MSc	PhD student
José Pedro Almeida, MD	PhD student
Fernando Domingos, MD	PhD student
Pedro Pereira, BSc	PhD student
Sergio Laranjo, MD	PhD student
Susana Pinto, MD	PhD student
Teresa Moreno, MD	PhD student
Vera Geraldès, BSc, Biotech eng	PhD student
Bruno Gil Rosa, MSc, Biomedical eng	PhD student

Isabel Casanova, Biotech eng	Master student
José Castro, BSc	Master student
Sofia Catarino, BSc	Master student
Sofia Xavier, DMV	Master student
Ana Vieira, BSc	Master student
Sofia Santos, BSc	Master student
Diana Reis, PhD, Postdoctoral Fellow	Investigator
Andreia Borges, BSc	Technician
Angela Leal, BSc biochemistry	Investigator
Benjamim Ohana, MD	Investigator
Cristiano Tavares, MSc, Biomedical Eng	Investigator
Eduardo Infante, MD	Investigator
Gabriela Postoloache, PhD	Investigator
Isabel Conceição, MD	Investigator
Luz Rocha, BSc	Investigator
Mafalda Carvalho, BSc, Biologist	Investigator
Mariana Bento, MD	Investigator
Mario Gomes Marques, MD	Investigator
Nataniel Rosa, DMV, MSc	Investigator
Teresinha Evangelista, MD	Investigator
Vânia Almeida, MD	Investigator

Research areas

Amyotrophic Lateral Sclerosis; Autonomic nervous system; Biological signal processing; Clinical Neurophysiology; Familial Amyloid Polyneuropathy; Integrated neuroimaging and neurocomputational modelling of brain disorders

Major scientific achievements

This is a new Unit formed by the merging of the previous Neuromuscular Unit and Autonomic Nervous System Unit. In addition, Prof Tiago Maia has joined our team, including behaviour and imaging-neurocomputational models of brain dysfunction as a new area of scientific development in our Unit. The Neuromuscular Unit has mostly developed scientific research on Amyotrophic Lateral Sclerosis (wireless control of home-ventilation, trial on respiratory exercise in ALS, genetic abnormalities, biomarkers of disease progression) and in Familial Amyloid Polyneuropathy (early markers of disease progression). The Autonomic Nervous System Unit reached major achievements on the clarification of the inner mechanisms regulating choroidal circulation; on the elucidation of the autonomic interference in the genesis and maintenance of atrial fibrillation and its relationship to molecular expression of ion channels, connexins and cardiac purinergic system; on demonstrating the role central sympathetic areas hyperexcitability on neurogenic hypertension; on showing that autonomic remodelling is on the basis of life quality improvement in patients with neurocardiogenic syncope; on the mathematical development and software validation applied to autonomic evaluation (mod HHT, coherence, forecasting, FISIOSINAL); development of a prototype to evaluate urinary bladder volume non-invasively and a LED sensor to detect non invasively blood gases. Professor Tiago Maia has driven significant advances on dysfunctional emotional processing, behavioural changes, the neural

circuits that generate tics in Tourette's syndrome and conflict adaptation. The main target is to join all these different approaches in a common strategy.

Recent Most Relevant Publications

- Maia, TV, Frank M J (2011) **From reinforcement learning models to psychiatric and neurological disorders**. Nat Neuroscience 14: 154-162 (JIF: 14.191).
- Lee T, Li YR, Ingre C, Weber M, Grehl T, Gredal O, de Carvalho M, Meyer T, Tysnes OB, Auburger G, Gispert S, Bonini NM, Andersen PM, Gitler AD, (2011) **“Ataxin-2 intermediate-length polyglutamine expansions in European ALS patients”**. Hum Mol Genet; **20**, 1697-1700. (Journal IF 8.058).
- Oliveira M, da Silva N, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R (2011) **“Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation”**. Int Journal Cardiol **149**: 290-295. (JIF: 6.802).
- Oliveira M, Silva N, Matos L, Xavier R, Gerales V, Ferreira R, Silva-Carvalho L, Rocha I (2011) **“Effect of vagal stimulation on atrial refractoriness and vulnerability to induce atrial fibrillation in the anaesthetized rabbit”**. Exp Physiol. **96**: 125-33. (JIF: 3.333).
- Pinto S, de Carvalho M, Swash M (in press) **“Respiratory exercise in amyotrophic lateral sclerosis”**. Amyotr Lat Scler **13**, 33-43 (Journal IF: 3.397)

Ongoing Research Projects

- 2007-2011 – **Respiratory Rehabilitation in Amyotrophic Lateral Sclerosis: Clinical and Biochemical Impact**. FCT., Coordinator: M. de Carvalho. (PIC/IC/82765/2007). Total: 193.000; IMM: 100.632,00 [Instituições Participantes: ITQB – 86.968,00 euros; Univ. Aveiro – 5.400,00 euros]
2008/2012 - **Prevalence and severity of fatty liver in morbid obesity: correlation and mechanisms related to the role of ectopic fat in insulin resistance**, FCT, Coordinator: H. Cortez-Pinto. (PTDC/SAU- OSM/100878/2008). 46.000,00 euros
- 2008/2018 - **Transthyretin-associated amyloidoses outcomes survey (THAOS). A Global, Multi-Center, Longitudinal, Observational Survey of Patients with Documented Transthyretin (TTR) Mutations or Wild-Type TTR Amyloidosis**, Pfizer/FoldRx Pharmaceuticals, Inc. – Scientific Board Member, Coordinator: I Conceição
2009/2011 – **Autonomic nervous system influences on renal stone disease**. FCT, Coordinator: I.Rocha, PIC/IC/83243/2007. Total: 50.000,00 euros
IMM: 45.000,00 euros
Faculdade de Ciências Médicas: 5.000,00 euros
2009/2011 – **Correlation of molecular misfolding and autonomic influences on heart rate and blood pressure of an animal model of parkinson disease**. FCT, Coordinator: T. Outeiro, PIC/IC/82760/2007. 195.000,00 euros
- 2009/2011 - **Complement polymorphism analyses in FAP type I populations**. To test for correlation between polymorphisms in C1QA, with age of onset in Portuguese, Greek and further Cypriot patients with FAP type I, Coordinator: M.J Saraiva
- 2009/2011 - **Caracterização Clínica e Diagnóstica de Doentes com Patologia Neuromuscular – Estudo Epidemiológico em Portugal (ENDOMUS)**. (Sociedade

- Portuguesa de Estudos de Doenças Neuromusculares (SPEDNM). Coordinator: T. Evangelista
- 2009/2012- **MUNIX – Multicentric International study to evaluate a new method for motor unit number estimation.** Coordinator: M. Weber
 - 2009-2012 – **Awaji criteria validation. This is an international project to test sensitivity and specificity of Awaji criteria for ALS.** Coordinator: M. de Carvalho (no current funding).
 - 2010/2011- **Open-Label Safety Evaluation of Fx-1006A in Patients with Transthyretin Amyloidosis.** Pfizer/FoldRx Pharmaceuticals, Inc., Coordinator: I. Conceição.
 - 2010/2013 **Wi-CardioResp, Sistema Integrado para Monitorização em Ambulatório de Parâmetros Cardio-Respiratórios.** Entidade financiadora PLUX e Co-Promoção do QREN, aviso nº 16/SI/2009, Coordinator: H. Gamboa.
2010/2013- Construção de um Pacemaker Diafragmático a ser testado em rato com vista a ser aplicado no ser humano com insuficiência respiratória. FCT, Coordinator: I. Rocha , PTDC/EEA-ELC/109083/2008. 147.456,00 euros
2010/2013- Modificação genética das células do núcleo paraventricular do hipotálamo (PVN) e medula rostroventrolateral (RVLM) para controlar cronicamente a hipertensão. FCT, Coordinator: I. Rocha , PTDC/SAU-OSM/109081/2008. 126.034,00 euros
2010/2012 – **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.** FCT, Coordinator: Diana Cunha Reis, PTDC/SAU-NEU/103639/2008. 120.000,00 euros
2011/2012- Autorregulação no acidente vascular cerebral agudo. FCT, Coordinator: I. Rocha , PTDC/SAU-ORG/113329/2009. Total: 140.000,00 euros
IMM: 54.982,00 euros
Faculdade de Medicina da UP: 85.018,00 euros
 - 2011/2012 – **Estudo do Cito-Esqueleto Neuronal em Neuropatias de Pequenas Fibras: Reconstrução Tridimensional de Imagens de Alta Resolução com a Utilização de Quantum Dots.** Coordinator: M. de Carvalho.
 - 2011/2012 – **Fx1A-303 – Open-Label Safety and Efficacy Evaluation os Fx-1006^a in Patients with Transthyretin Amyloidosis.** Pfizer/FoldRx Pharmaceuticals, Inc., Coordinator: I. Conceição.
 - 2011-2013 – **Estudo do impacto das Tecnologias de Apoio à Comunicação nos Doentes com ela e respectivos cuidadores,** FCG Fundação Calouste-Gulbenkian, Coordinator: M. de Carvalho.
 - 2011/2014 – **Understanding Neurodegenerative Diseases Through Clinical and OMICS data Integration-Neuroclinomics – Neuroclinomics,** FCT, Coordinator: S. Madeira (PTDC/EIA-EIA/111239/2009). Total: 130.472,00 euros
IMM: 39.067,00 euros (Participantes)
INESC ID: 91.405,00 euros
 - 2011/2013 – **Reinforcement learning and motor biases in children with Tourette syndrome.** Tourette Syndrome Association. Coordinator: T. V. Maia.

Publications in International Journals

- Pato MP, Santos NJG, Areias P, Pires, EB, de Carvalho M, Pinto, S, Lopes, DS (2011) “Finiteelement studies of the mechanical behavior of the diaphragm in normal and

- pathological cases**". Comput Methods Biomech Biomed Engin; **14**, 505-513 (Journal IF: 1.566).
- de Carvalho M (2011) **"The needle goes deeper in ALS"**. Clin Neurophysiol (Editorial); **122**, 414-422 (Journal IF: 2.786).
 - de Carvalho M, Pinto S, Swash M (2011) **"Does the motor cortex influence denervation in ALS? EMG studies of muscles with both contralateral and bilateral corticospinal innervations"**. Clin Neurophysiol; **122**, 629-635 (Journal IF: 2.786, Citations: 2).
 - de Carvalho M, (2011) **"Deep Thoughts in ALS"**. Clin Neurophysiol (Editorial); **122**, 845-846 (Journal IF: 2.786).
 - de Carvalho M, Swash M (2011) **"Fasciculation-cramp syndrome preceding anterior horn cell disease: an intermediate syndrome?"** J Neurol Neurosurg Psychiatry; **82**, 459-461. (Journal IF: 4.791 Citations: 3).
 - Lee T, Li YR, Ingre C, Weber M, Grehl T, Gredal O, de Carvalho M, Meyer T, Tysnes OB, Auburger G, Gispert S, Bonini NM, Andersen PM, Gitler AD, (2011) **"Ataxin-2 intermediate-length polyglutamine expansions in European ALS patients"**. Hum Mol Genet; **20**, 1697-1700. (Journal IF 8.058).
 - de Carvalho M, (2011) **"Why is ALS so excited?"** Clin Neurophysiol (Editorial); **122**, 1689-1690. (Journal IF: 2.786).
 - Neuwirth C, Nandedkar S, Stalberg E, Barkhaus PE, de Carvalho M, Furtula J, van Dijk JP, Baldinger R, Castro J, Costa J, Otto M, Sandberg A, Weber M (2011) **"Motor Unit Number Index (MUNIX): A novel neurophysiological marker for neuromuscular disorders; test-retest reliability in healthy volunteers in a multicentre study"**. Clin Neurophysiol; **122**, 1867-1872. (Journal IF: 2.786 Citations: 3).
 - Neuwirth C, Nandedkar S, Stalberg E, Barkhaus PE, de Carvalho M, Furtula J, van Dijk JP, Baldinger R, Castro J, Costa J, Otto M, Sandberg A, Weber M (2011) **"Motor Unit Number Index (MUNIX): Reference values of five different muscles in healthy subjects from a multi-centre study"**. Clin Neurophysiol; **122**, 1895-1896 (Journal IF: 2.786)
 - Almeida V, Ohana B, de Carvalho M, Swash M (in press) (2011) **"Patrikios syndrome: two patients with treatable flail-leg weakness"**. J Clin Neurosci (Journal IF: 1.165).
 - de Carvalho M, Swash M (2011) **"Amyotrophic Lateral Sclerosis: an update"**. Curr Opin Neurol; **24**: 497-503. (Journal IF: 5.021 Citations: 1)
 - Pereira AF, Silva MT, Martins JM, de Carvalho M (2011) **"Implementation of an efficient muscle fatigue model in the framework of multibody systems dynamics for analysis of human movements"**. J Multi-body Dynamics **225**: 359-370 (Journal IF: 0.346)
 - Swash M, de Carvalho M, (2011) **"Muscle ultrasound detects fasciculations and facilitates diagnosis in ALS"**. Neurology (Editorial) **77**, 1508-1509 (Journal IF: 8.017)
 - Pugdahl K, Fuglsang-Frederiksen A, Tankisi H, Johnsen B, de Carvalho; Fawcett P, Labarre-Vila A, Liguori R, Nix W, Schofield I, (2011) **"Impact of medical audit on electrodiagnostic medicine in polyneuropathy"**. Clin Neurophysiol **122**, 2523-2529 (Journal IF: 2.786)
 - Peter P, Sharon A, Borasio GD, de Carvalho M, Chio A, Van Damme P, Hardiman O, Karen M, Petri S, Pradat P-F, Silani V, Barbara T, Wasner M, Markus W (in press) **"EFNS guidelines on the clinical management of Amyotrophic Lateral Sclerosis (MALS) - revised report of an EFNS task force"**. Eur J Neurol (Journal IF: 3.765)

- de Carvalho M, Dengler R, Eisen A, England JD, Kaji R, Kimura R, Mills K, Mitsumoto H, Nodera H, Shefner J, Swash M (2011) **“The Awaji criteria for diagnosis of ALS”** (letter) *Muscle Nerve* **44**, 456-7 (Journal IF: 2.320)
- Neutel D, Miltenberger-Miltenyi G, Silva I, de Carvalho M (in press) (2011) **Chorea-acanthocytosis presenting as motor neuron disease**. *Muscle Nerve* (Journal IF: 2.320)
- Pinto S, de Carvalho M, Swash M (in press) **“Respiratory exercise in amyotrophic lateral sclerosis”**. *Amyotr Lat Scler* **13**, 33-43 (Journal IF: 3.397)
- Ostrowska M, de Carvalho M (in press) (2011) **“Prognosis of phrenic nerve injury following thoracic interventions: 4 new cases and a review”**. *Clin Neurol Neurosurg* (Journal IF: 1.303)
- Lopes de Almeida JP, Silvestre R, Pinto AC, de Carvalho M (in press) (2011) **“Exercise and amyotrophic lateral sclerosis – a review”**. *Neurol Sci* (Journal IF: 1.220)
- Miguel C, Sousa M, Castro J, Gonçalves I, Costa J, de Carvalho M (in press) (2011) **“Validity, reliability and tolerability of ultrasound in the diagnosis of carpal tunnel syndrome”**. *Acta Reumat Port* (Journal IF: 0.726)
- Pinto S, Pinto A, de Carvalho M (in press) (2011) **“Decreased heart variability predicts death in amyotrophic lateral sclerosis”**. *Muscle Nerve* (Journal IF: 2.320)
- Swash M (in press) (2011). **“Survey of non-invasive ventilation use in ALS in Britain”** (Editorial). *J Neurol Neurosurg Psychiatry* (JIF: 4.791).
- Ratilal BO, Costa J, Sampaio C, Pappamikail L, (2011) **“Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures”**. *Cochrane Database Syst Review*. **8**: CD004884.
- Saldanha C, de Almeida JP (2011) **“Erythrocyte as a link between basic and clinical research.”** *Clin Hemorheol Microcirc*; **49**:463-72. (JIF: 2.838).
- Mariano, Cibelle; Silva, Sandra; Pereira Pedro; Fernandes, Adelaide; Brites, Dora; Brito, Maria (2011). **“Evidence of tricellulin expression by immune cells, particularly microglia”**. *Biochem Biophys Res Commun*; **409**: 799-802. (JIF: 2.720).
- Maria A Brito, Emanuele Zurolo, Pedro Pereira, Cândida Barroso, Dora Brites, Eleonora Aronica, (in press) **“Cerebellar axon/myelin loss, angiogenic sprouting and neuronal increase of vascular endothelial growth factor in a preterm infant with kernicterus”**. *J Child Neurol* (JIF: 1.668).
- de Carvalho M, Pinto S (2011) **“Lithium treatment in amyotrophic lateral sclerosis: do we have enough?”** *Expert Rev Neurother*; **11**, 1693-1698.
- Duarte ST, Oliveira J, Santos R, Pereira P, Barroso C, Conceição I, Evangelista T.
 - (2011) **“Dominant and recessive RYR1 mutations in adults with core lesions and mild muscle symptoms”** *Muscle Nerve* **44**; 102-108. (JIF: 2.320).
- Ferreira M, Evangelista T, Almeida LS, Martins J, Macario MC, Martins E, Moleirinho A, Azevedo L, Vilarinho L, Santorelli FM (2011) **“Relative frequency of known causes of multiple mtDNA deletions: two novel POLG mutations”**. *Neuromuscul Disord* **21**: 483-8. (JIF: 2.764).
- Pereira JP, Barroso C, Evangelista T, Fonseca JE, Pereira da Silva JA (2011) **“Macrophagic myofasciitis: a case report of autoimmune/inflammatory syndrome induced by adjuvants (ASIA)”**. *Acta Reumatol Port*. **36**: 75-6. (JIF: 0.726).
- Ferreira DM, Castro RE, Machado MV, Evangelista T, Silvestre A, Costa A, Coutinho J, Carepa F, Cortez-Pinto H, Rodrigues CM (2011) **“Apoptosis and insulin resistance in liver and peripheral tissues of morbidly obese patients is associated with different stages of non-alcoholic fatty liver disease”**. *Diabetologia* **54**: 1788-98. (JIF: 6.973).
- Swash M (2011) **Nitric oxide and muscle weakness**. (Editorial) *Neurology* **76**: 940-941. (JIF: 8.017).

- Valls-Sole J, Castillo CD, Casanova-Molla J, Costa J. (2011) **Clinical consequences of reinnervation disorders after focal peripheral nerve lesions**. Clin Neurophysiol.; **122**: 219-28. (JIF: 2.786).
- de Carvalho M and Swash M_ (2011) **Fasciculation potentials: still mysterious** Clin Neurophysiol (Editorial); **123**: 399-401. (JIF: 2.786).
- Costa J, Fareleira F, Ascensão R, Borges M, Sampaio C, Vaz-Carneiro A (2011) **Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: A systematic review and meta-analysis**. Epilepsia **52**: 1280-91. (JIF: 3.955).
- Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T (2011) **Dream recall frequency and content in patients with temporal lobe epilepsy**. Epilepsia; **52**: 2022-7. (JIF: 3.955).
- Costa J (2011) **Is neurophysiology a valuable marker of pre-clinical stages of Lewy Body Disorders?** Clin Neurophysiol **122**: 2330-1. (JIF: 2.786).
- Costa J, Guzmán J, Valdeoriola F, Rumià J, Tolosa E, Casanova-Molla J, Valls-Solé J (2011) **Modulation of the soleus H reflex by electrical subcortical stimuli in humans**. Exp Brain Res **112**: 439-48. (JIF: 2.296).
- de Almeida JP, Freitas-Santos T, Saldanha C, (2011) **Evidence that the degree of band 3 phosphorylation modulates human erythrocytes nitric oxide efflux - in vitro model of hyperfibrinogenemia**. Clin Hemorheol Microcirc. **49**: 407-16. (JIF: 2.838).
- Oliveira M, Silva N, Matos L, Xavier R, Geraldés V, Ferreira R, Silva-Carvalho L, Rocha I (2011) **“Effect of vagal stimulation on atrial refractoriness and vulnerability to induce atrial fibrillation in the anaesthetized rabbit”**. Exp Physiol. **96**: 125-33. (JIF: 3.333).
- Guimarães D, de M Carvalho; L, Geraldés V, Rocha I, Santos JP (2011) **“Study of lead accumulation in bones of Wistar rats by X-ray fluorescence analysis: aging effect”**. Metallomics. **4**: 66 – 71. (JIF: 3.359).
- Oliveira M, da Silva N, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R (2011) **“Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation”**. Int Journal Cardiol **149**: 290-295. (JIF: 6.802).
- Guimarães D, JP Santos, ML Carvalho, G Vale, HM Santos, Geraldés, V, Rocha, I, JL Capelo (2011) **“Ultrasonic energy as a tool to overcome some drawbacks in the determination of lead in brain tissue and urine of rats.”**. Talanta **86**: 442–446. (JIF: 3.722).
- Guimarães D, ML Carvalho , Geraldés, V, Rocha I, JP Santos (in press) **“Lead concentration in feces and urine of exposed rats by X-ray Fluorescence and Electrothermal Atomic Absorption Spectrometry”** XRay Spectroscopy (JIF: 1.661).
- Delgado, E; Marques-Neves, C; Rocha, I ; Sales-Luís, J ; Silva-Carvalho, L (in press) **“Modulation of Vasomotive Activity in Rabbit External Ophthalmic Artery by Neuropeptides”**. J Ophthalmology.
- Domingos F, Escalda A (in press) **“Causes of autonomic dysfunction in idiopathic recurrent kidney stone formers”**. Int Urol Nephrol. (JIF: 1.567).
- Guimarães D, JP Santos, ML Carvalho, G Vale, HM Santos, Geraldés V, Rocha I, JL Capelo, Domingos F, Serra A (2011) **“Nephrolithiasis is associated with an increased prevalence of cardiovascular disease”** Nephrol Dial Transplant. **26**: 864-8 (JIF: 3.564).
- Fonseca AC, Geraldés R, Almeida V, Pinho e Melo T (2011) **“Treatment with rtPA of stroke associated with intravenous immunoglobulins perfusion”** J Neurol Sci. **308**, 180-1.
- Maia, TV, Frank M J (2011) **From reinforcement learning models to psychiatric and neurological disorders**. Nat Neuroscience **14**: 154-162 (JIF: 14.191).

- Horga G, Maia TV, Wang P, Wang Z, Marsh R, Peterson, BS (2011) **Adaptation to conflict via context-driven anticipatory signals in the dorsomedial prefrontal cortex.** J Neuroscience 31: 16208–16216. (JIF: 7.270).
- Posner J, Maia TV, Fair D, Peterson BS, Sonuga-Barke EJ, Nagel BJ (2011) **The attenuation of dysfunctional emotional processing with stimulant medication: An fMRI study of adolescents with ADHD.** Psychiatry Research: Neuroimaging 193:151-160. (JIF: 2.064).
- Posner J, Nagel B J, Maia TV, Mechlin, A, Oh M, Wang Z, Peterson BS (2011) **Abnormal amygdalar activation and connectivity in adolescents with attention-deficit/hyperactivity disorder.** J Am Acad Child Adolescent Psychiatry 50: 828-837. (JIF: 5.148).
- Wang Z, Maia TV, Marsh R, Colibazzi T, Gerber, A, Peterson, BS (in press) **The neural circuits that generate tics in Gilles de la Tourette syndrome.** American Journal of Psychiatry. (JIF: 12.759).
- Maia TV, McClelland JL (in press). **A neurocomputational approach to obsessive-compulsive disorder.** Trends in Cognitive Sciences. (JIF: 9.686).

Other publications International

- de Carvalho M, Swash M (in press) (2011) **“Neurologic Complications of Atlanto-Axial Dislocation”.** In Handbook of Clinical Neurology – Neurologic Aspect of Systemic Diseases. Ed. Biller J, Ferro JM. Elsevier.
- The EFNS Task Force on Diagnosis and Management of ALS: Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P, Hardiman O, Kollewe K, Morrison KE, Petri S, Padrat PF, Silani V, Tomik B, Masner M, Weber M (2011) **Managment of Amyotrophic Lateral Sclerosis.** In European Handbook of Neurological Management, Vol 1. Ed- Gilhus NE, Barnes M, Brainin M, 2nd Ed. Wiley-Blackwell, pp. 283-310.
- Pinto A, Lopes de Almeida JP, Pinto S, de Carvalho, M (2011) **Avaliação da sincronização do paciente com VNI.** In Princípios da Ventilação Mecânica Não-Invasiva - do Hospital ao Domicílio. Ed. Esquinas AM. Gasin Médica, pp. 150-164.
- Maia TV (in press). **Avoidance learning.** In N. M. Seel (ed.), Encyclopedia of the Sciences of Learning. Springer.
- Carmo AJ, Cunha-Reis D (2011) **”Evidence of Emergent patterns in GluR1 phosphorylation in theta-burst LTP experiments with data mining tools”** Proceedings of the “12th forum of Amino Acid, Peptide and Protein Research”, 1st-5T August, Beijing, China. Amino Acids **41**(supp1) S442.
- Cunha-Reis D, Carmo AJ (2011) **“Correlation of VIP VPAC1 modulation of GluR1 phosphorylation and inhibition of protein kinases in theta-burst LTP experiments with data mining tools.** Proceedings of the 12th forum of “Amino Acid, Peptide and Protein Research”, 1st-5T August, Beijing, China. Amino Acids **41**(supp1) S43.

Invited Lectures and Seminars

- de Carvalho M, **“Intravenous Immunoglobulin for the treatment of neuromuscular disorders”.** 4th Edition of European Neurological Conference on Clinical Practices, Lisbon, Janeiro 2011.

- de Carvalho M, **“Electromyography in the Early Diagnosis of ALS, Master en Electrodiagnóstico Neurológico”**. Barcelona, Março, 2011.
- de Carvalho M, **“Estudos Neurofisiológicos, modelação e simulação do diafragma”**, Celebração dos 100 Anos da FMUL da UL, Lisboa. Maio, 2011.
- de Carvalho M, **“The Typical Features that can indicate Early ALS “**, 21st Meeting of the European Neurological Society, Lisboa, Maio, 2011.
- de Carvalho M, **“ANS dysfunction and Clinical Neurophysiology”**, European Federation of Autonomic Societies School, Lisboa. Maio, 2011.
- de Carvalho M, **“Motor Neuron Diseases, Evaluati6n Neurofisiol6gica do Nervio Frénico, Biomarcadores, Diagn6stico Temprano de ELA”** - X Congresso Colombiano de Neurologia. Bogota. Agosto, 2011.
- de Carvalho M, **“Polineuropatia Amiloid6tica Familiar: avanços clínicos e neurofisiológicos. Avaliaç6o Neurofisiol6gica do Envolvimento Respirat6rio na Esclerose Lateral Amiotr6fica”**. VI Congreso del CLA-IFCN/XXIII Congreso da SBNC. Punta del Leste. Outubro, 2011.
- Pinto A **“Critérios de adaptaç6o da VNI nas doenças neuromusculares”**, Ao X Congresso de Neurologia da sociedad Colombiana de Neurologia, Bogotá, Agosto de 2011-08-28. (Palestra a convite da Sociedade Colombiana e Neurologia)
- Pinto A, **“Os Porquês, o quando e o como da VNI na ELA”**, Ao X Congresso de Neurologia da sociedad Colombiana de Neurologia. Bogotá, Agosto de 2011-08-28. (Palestra a convite da Sociedade Colombiana e Neurologia)
- Pinto A, **“Telemonitoring - A new perspective for ventilation at home”**, Ao 13th Capital City Conference of the DGAI Congress of Anesthesiology and Intensive Care Medicine - HAI 2011 , Berlim 10 -14- Setembro 2011 (Conferência a convite da Sociedade Alemã de Anestesiologia e de Cuidados Intensivos)
- De Carvalho M, **“Evaluati6n Neurofisiol6gica do Nervio Frénico; Biomarcadores; Diagn6stico Temprano de ELA”**. X Congresso Colombiano de Neurologia Bogota. Agosto, 2011.
- Azevedo Coutinho MC, **Impacto da Imagem na Insuficiênci Cardíaca**. Intervenção no Painel de Discuss6o da Mesa Redonda do Congresso Novas Fronteiras em Cardiologia. Ericeira, 11 a 13 de Fevereiro de 2011.
- Azevedo Coutinho MC, **Desenvolvimentos Recentes em Cardiologia Nuclear** Intervenção como moderadora da Mesa Redonda na Reuni6o Anual do Grupo de Estudo de Cardiologia Nuclear, Ressonância Magnética e Tomografia Computorizada da Sociedade Portuguesa de Cardiologia. Lisboa, 25 e 26 de Fevereiro de 2011.
- Azevedo Coutinho MC, **Reabilitaç6o Cardíaca e Reabilitaç6o Respirat6ria: Como Mudar Atitudes de Médicos e Doentes?”** Intervenção no Painel de Discuss6o da Mesa Redonda da Reuni6o Conjunta de Reabilitaç6o Cardíaca e Respirat6ria da Sociedade Portuguesa de Cardiologia. Tr6ia, 25 e 26 de Março de 2011.
- Azevedo Coutinho MC, **Estamos a Chegar ao Fim da Era das Técnicas Nucleares?** Intervenção como palestrante na Mesa Redonda intitulada “Multimodalidade de Imagem na Doença Coronária Isquémica” no XXXII Congresso Português de Cardiologia. Lisboa, 8 a 10 de Abril de 2011.
- Evangelista, T, **Doença de Pompe**. 17º Congresso Nacional de Medicina Interna, Porto, May 18-21, 2011.
- Evangelista, T, **Doenças neurológicas genéticas**. Jornadas de Medicina Intensiva da Primavera, Porto, April 14-15, 2011.

Communications in International Conferences

- Pinto A, Braga ACM, Almeida JP, Ferrão C, Coelho A, Pinto S, de Carvalho M **Does rigorous control of exercise intensity affects survival and functional outcomes in ALS?** 22nd INTERNATIONAL SYMPOSIUM ON ALS/MND. Sydney, November, 2011. Apresentação oral
- Braga ACM, Pinto A, de Carvalho M, Jesus de C, **“Assessment of Caregivers Burden applying the Zarit Burden Interview (ZBI): correlation with functionality, QoL, mood disorders and technical aids”**. 22nd INTERNATIONAL SYMPOSIUM ON ALS/MND. Sydney, November, 2011. Apresentação em “poster”
- Azevedo Coutinho MC, Dias N Cortez, Conceição I, Cantinho G, A Bordalo E Sá, Almeida AG, M de Carvalho, Diogo A Nunes. **Reduced myocardial iodine-123-metaiodobenzylguanidine uptake: a strong prognostic marker in familial amyloidotic polyneuropathy**. Eur. Heart J. **32** (suppl 1), ESC Congress, Agosto de 2011, em Paris. Apresentação oral.
- Evangelista, T. **Diagnostic outcomes of patients presenting with LGMW + elevated CK**. Neuromuscular Differential Diagnosis Advisory Board Meeting, Amsterdam, June 24, 2011. Apresentação oral.
- Coelho T, Maia L, Martins da Silva A, Waddington-Cruz M, Planté-Bordeneuve, Lozeron P, Suhr O, Campistol J, Conceição I, Schmidt H, Trigo P, Packman J, Grogan RD. **“A Comprehensive Evaluation of the Disease-modifying Effects of Tafamidis in Patients with Transthyretin Type Familial Amyloid Polyneuropathy”**. American Academy of Neurology (AAN) 2011, Honolulu, April 2011. Apresentação oral.
- Coelho T, Maia L, Martins da Silva A, Waddington-Cruz M, Planté-Bordeneuve, Lozeron P, Suhr O, Campistol J, Conceição I, Schmidt H, Trigo P, Packman J, Grogan RD **“The Long-term Effects of Tafamidis for the Treatment of Transthyretin Type Familial Amyloid Polyneuropathy”**. American Academy of Neurology (AAN) 2011, Honolulu, April 2011. Apresentação em “poster”.
- Conceição I, Coelho T, Planté-Bordeneuve, Waddington-Cruz M, Erickson B-G; Rodney F, Ikeda S, Maurer M, Suhr O, Ando Y, Mazzeo A, Grogan RD. **“Baseline Neurologic Function in Symptomatic Patients in the Transthyretin Amyloidosis Outcomes Survey (THAOS)”**. American Academy of Neurology (AAN) 2011, Honolulu, April 2011 (poster); 16th World Muscle Society Congress. Algarve 18-22 Oct 2011. Apresentação em “poster”.
- Conceição I, Coelho T, Planté-Bordeneuve, Waddington-Cruz M, Erickson B-G; Rodney F, Ikeda S, Maurer M, Suhr O, Ando Y, Mazzeo A, Grogan RD. **“An Evaluation of the Quality of Life in Symptomatic Patients in the Transthyretin Amyloidosis Outcomes Survey (THAOS)”**. Twenty-first Meeting of the European Neurological Society, Lisbon, May 2011. Apresentação oral.
- Pita Lobo P, Evangelista T, Silvestre R, Conceição I. **“Vasculitic neuropathy after Hansen disease: coincidence or cause?”** Twenty-first Meeting of the European Neurological Society, Lisbon, May 2011. Apresentação em “poster”
- Waddington-Cruz M, Coelho T, Conceição I, Planté-Bordeneuve, Erickson B-G; Rodney F, Ikeda S, Maurer M, Suhr O, Ando Y, Mazzeo A, Grogan RD. **“Demographics and Neurologic Function in Early- and Late-onset Symptomatic Patients in the Transthyretin Amyloidosis Outcomes Survey (THAOS)”**. Peripheral Neuropathy Society (PNS) June 2011, Potomac. Apresentação em “poster”
- Waddington-Cruz M, Coelho T, Conceição I, Planté-Bordeneuve, Erickson B-G; Rodney F, Ikeda S, Maurer M, Suhr O, Ando Y, Mazzeo A, Grogan RD. **“Baseline Nutritional**

- Status in Symptomatic Patients in the” “Transthyretin Amyloidosis Outcomes Survey”**. 15th EFNS Congress. Budapest Sept 2011. Apresentação oral.
- Waddington-Cruz M, Coelho T, Conceição I, Planté-Bordeneuve, Erickson B-G; Rodney F, Ikeda S, Maurer M, Suhr O, Ando Y, Mazzeo A, Grogan RD. **“Nerve Conduction in Symptomatic Patients in the Transthyretin Amyloidosis Outcomes Survey (THAOS)”** . American Association of Neuromuscular & Electrodiagnostic Medicine Annual Meeting; September 14-17, 2011; San Francisco, CA. Apresentação em “poster”
 - Pires, MC, Ferreira, M, Silvestre, R, Vilarinho, L, Evangelista, T, **Mitochondrial myopathy and associated inflammatory changes in an adult patient with a m.4317A>G**. Twenty-first Meeting of the European Neurological Society, Lisboa, May 28-31, 2011. Apresentação em “poster”
 - Evangelista, T, Lacerda, L, Santos, R. **ENDOMUS: Clinical and diagnostic characterization of patients with neuromuscular disorders – epidemiologic study**. 16th International Congress of the World Muscle Society, Almancil, October 18-22, 2011. Apresentação em “poster”.
 - Pires, C, Silvestre, AR, Vilarinho, L, Evangelista, T, **Autosomal dominant chronic progressive ophthalmoplegia (adPEO) and lung adenocarcinoma showing compound heterozygous POLG1 mutations**. 16th International Congress of the World Muscle Society, Almancil, October 18-22, 2011. Apresentação em “poster”
 - Antunes, AP, Nogueira, C, Rocha, H, Vilarinho, L, Evangelista, T, **Adult onset intermittent rhabdomyolysis**. 16th International Congress of the World Muscle Society, Almancil, October 18-22, 2011. Apresentação em “poster”
 - Silvestre, AR, Machado, M, Vilarinho, L, Cortez-Pinto, H, Evangelista, T , **Effect of morbid obesity in skeletal muscle and its association with insulin resistance**. 16th International Congress of the World Muscle Society, Almancil, October 18-22, 2011 Apresentação em “poster” Swash M, Address to New South Wales Clinical Neurophysiological Society, 2011, Sydney Australia. Apresentação oral.
 - Swash M, Panel Discussion on Current Status of Research in ALS, 2011, Sydney, Australia. Apresentação oral.
 - Geraldes V, Gonçalves-Rosa N, Paton JFR, Rocha I. **“Genetic modification of the neural sympathetic regions to control hypertension chronically”**. Federation of European Physiological Societies 2011 Congress Abstracts book, pp. Apresentação em “poster”
 - Geraldes V, Gonçalves-Rosa N, Paton JFR, Rocha I. **“Modification of Brain Sympathetic Regions in Long Standing Hypertension”**, 64th High Blood Pressure Research 2011, Congress Abstracts book pp207. Apresentação em “poster”
 - Oliveira M, Laranjo S, Tavares C, Xavier R, Geraldes V, Silva N, Ferreira R, Rocha I. **“Autonomic outflow during provocative maneuvers in paroxysmal lone atrial fibrillation”**. ICPES 2011. Apresentação oral.
 - Conceição I. **“Joint ENS-PNS Symposium Familial amyloid polyneuropathy. In memory of Corino Andrade**. Clinical aspects and management”. Twenty-first Meeting of the European Neurological Society, Lisbon, May 2011, Apresentação oral.
 - Conceição I. **“TTR - FAP Meet the expert”**. Pfizer Satellite Symposium. Twenty-first Meeting of the European Neurological Society, Lisbon, May 2011. Apresentação oral.
 - Conceição I. **“Advancing the Management of TTR FAP”**. Pfizer Satellite Symposium. 15th EFNS Congress. Budapest 2011. Apresentação oral.
 - Conceição I. **“Clinical features of FAP in Portugal”**. VII International Symposium on Familial Amyloidotic Polyneuropathy, Kumamoto, Japan Nov 2011. Apresentação oral.

Communications in National Conferences

- Swash M, 6th **Course of Clinical Neurophysiology** - Portugal , From Neuropathology to Neurophysiology. Neurophysiology of the pelvic floor May 6-8, 2011- Lisbon. Apresentação oral.
- Swash M, Hughlings Jackson Symposium, National Hospital for Neurology and Neurosurgery, 2011, London,. Apresentação oral.
- Swash M, Association of British Neurologists Annual Meeting, invited speaker (Hughlings Jackson) 2011. Apresentação oral.
- Swash M, History of Neuroscience, introductory lecture for science students, Queen Mary University of London, 2011
- Pinto A, Uma Clínica de ELA, 2^a Comemoração do dia Internacional da ELA promovida pela Associação Portuguesa de doentes de ELA (APELA) Lisboa, 21 de Junho de 2011, Apresentação oral.
- Pinto A, A importância da telemonitorização do doente neuromuscular. Ao II Forum da Fundação Portuguesa do Pulmão, Lisboa, 6-7 de junho de 2011, Apresentação oral.
- Almeida V, Lobo PP, Barroso C, Conceição I, Pinho e Melo T. Miopatia dos cuidados intensivos numa Unidade de AVC. 5^o Congresso Português do AVC. Porto, 2011, Sinapse. 2011;11:87-8. Apresentação oral.
- Fonseca V.R. Azevedo Coutinho C, Cantinho G, Correia MJ, Parreira B, Diogo AN Estudo da neuropatia autonómica cardíaca e da isquémia miocárdica silenciosa em doentes diabéticos. Rev. Port. Cardiol.; 30 (Supl 1), 65 (apresentado sob a forma de poster no XXXII Congresso Português de Cardiologia, Abril 2011. Apresentação “poster”.
- Gerales, Vera; Gonçalves-Rosa, Nataniel; Lopes-Gonçalves, Rafael; Paton, Julian F R; Rocha, Isabel. **“Importância do Núcleo Paraventricular do Hipotálamo no Controlo Crónico da indução de alterações genéticas simpato-depressoras”**. XXXIII Congresso Português de Cardiologia, 2011. Apresentação oral.
- Carvalho, Mafalda; Laranjo, Sérgio Oliveira, Mário Martins; Rocha, Isabel; **“Loss of Atrial A1/ A2A receptors cross-talk during autonomic stimulation”**- XXXIII Congresso Português de Cardiologia, 2011. Apresentação oral.
- Tavares C, R Carneiro Martins, S Laranjo, I Rocha. **“Computational Tools for Assessing Cardiovascular Variability”**. XXXIII Congresso Português de Cardiologia, 2011. Apresentação oral.
- Gerales V, Gonçalves-Rosa N, Hewinson J, Kasparov S, Paton JFR, Rocha I (2011). **Genetic modification of the Paraventricular Nucleus of the Hypothalamus (PVN) cells to control hypertension chronically**. Abstract book of XII Portuguese Society for Neurosciences Meeting 2011, pp222. Apresentação oral.
- Gerales V, Gonçalves-Rosa N, Paton JFR, Rocha I. **“Genetic modification of the neural sympathetic regions to control hypertension chronically”**. V Congresso da Sociedade Portuguesa de Ciências Veterinárias / Portuguese Veterinary Sciences Congress 2011, October 13-25, 2011, Congress Abstracts book pp153. Apresentação oral.
- Gonçalves-Rosa N, Gerales V, Tavares C, Amaro-Leal A, Cunha-Reis D, Carvalho M, Rocha I **“Comparação dos ritmos circadianos de pressão arterial e de frequência cardíaca em Rattus norvegicus normotensos e espontaneamente hipertensos utilizando telemetria: influências autonómicas em repouso”**. V Congresso da Sociedade Portuguesa de Ciências Veterinárias / Portuguese Veterinary Sciences Congress, 2011 Abstracts book pp152. Apresentação oral.

- Gonçalves-Rosa N, Geraldês V, Tavares C, Amaro-Leal A, Cunha-Reis D, Carvalho M, Rocha I. **“Alterações das influências simpática e parassimpática sobre os ritmos circadianos de pressão arterial e de frequência cardíaca em ratos hipertensos”**. Lisboa, 2011, Abstracts book do I Encontro de Técnicos de Diagnóstico e Terapêutica da FMUL, pp19. Apresentação oral.
- Oliveira AC, Geraldês V, Rocha I, Outeiro T, **“ Baroreflex sensitivity and reduced sympathetic activity in hemiparkinsonism rat model”**. XII Portuguese Society for Neurosciences Meeting 2011 / XII Reunião da Sociedade Portuguesa de Neurociências, May 26, 2011, Faculdade de Medicina de Lisboa, Lisboa, Portugal, pp 143, poster 55. Apresentação oral.
- Conceição I. **“Sympathetic Skin Response – workshop”**. VI Course of Clinical Neurophysiology, Carcavelos, May 2011. Apresentação oral.
- Conceição I. **“Acquired Amyloid Neuropathy after Domino Liver Transplantation”** Dia Nacional da Paramiloidose. Porto, 16 Junho 2011. Apresentação oral.
- Dias, S, Tornada, A, Faria, M, Evangelista, T, Quelhas, D, Gomes, M J, **Doença de Mc’Ardle – Uma nova mutação na miofosforilase**. 17º Congresso Nacional de Medicina Interna, Porto, May 18-21, 2011. Apresentação oral.
- Pires, C, Ferreira, M, Silvestre, AR, Vilarinho, L, Evangelista, T, **Miopatia mitocondrial associada a alterações inflamatórias num adulto com a mutação m.4317A>G**. Sociedade Portuguesa de Estudos de Doenças Neuromusculares (Reunião de Primavera), Coimbra, May 26, 2011. Apresentação oral.
- Moreno, T, Evangelista, T, **Miopatia não classificada – como prosseguir?** Sociedade Portuguesa de Estudos de Doenças Neuromusculares (Reunião de Primavera), Coimbra, May 26, 2011. Apresentação oral.
- Moreno, T, Pinto, S, Evangelista, T, **“Hemi-miopatia”? Caso clínico sem diagnóstico**. Sociedade Portuguesa de Estudos de Doenças Neuromusculares (Reunião de Primavera), Coimbra, May 26, 2011. Apresentação oral.
- Sousa, P, Geraldês, R, Evangelista, T, Pinho e Melo, T, **Terapêutica com rt-PA intravenoso em grávida com acidente vascular cerebral**. Congresso de Neurologia 2011, Lisboa, November 3-5, 2011. Apresentação em “poster”.

Organisation of Conferences

- de Carvalho M, Organizador do Program Committee e Co-Organizador do **6º Curso de Neurofisiologia Clínica**, da **Associação Portuguesa de EEG e Neurofisiologia Clínica**. Lisboa, Abril de 2011.
- de Carvalho M Membro do Comité Local de Organização do **21st Meeting of the European Neurological Society**. Lisboa, Maio de 2011.
- de Carvalho M, Organizador e moderador do **Workshop em Estimulação Magnética Transcraniana**, promovido pela Unidade de Neuromusculares do IMM. Lisboa, Outubro de 2011.
- de Carvalho M, Membro do Comité Local de Organização do **16th International World Muscle Society Congress**. Almancil, Outubro de 2011.
- de Carvalho M, Co-Organizador do **1º. Seminário Luso-Afro-Brasileiro sobre Poliomielite e Síndrome Pós-Poliomielite**. Lisboa, Novembro de 2011.
- de Carvalho M, Moderador do **1º. Seminário Luso-Afro-Brasileiro sobre Poliomielite e Síndrome Pós-Poliomielite**. Lisboa, Novembro de 2011
- de Carvalho M, Chairman no **6º Curso de Neurofisiologia Clínica**”, da **Associação Portuguesa de EEG e Neurofisiologia Clínica**, Lisboa, 2011

- de Carvalho M, Chairman do “Teaching Course” “**Peripheral Neuropathies, ALS and Mimicks**” no **21st Meeting of the European Neurological Society**, Lisboa, 2011
- de Carvalho M, Moderador da “**Sessão de Neuromusculares**” do Congresso de Neurologia 2011 da SPN, Lisboa, 2011
- Evangelista, T, **Organizer of Pre-Congress Teaching Course**, 16th Congress of the World Muscle Society – October 17 – 18, de 2011, Lisbon, Portugal
- Evangelista, T, co-organized the 16th Congress of the World Muscle Society. October 19-22, 2011, Almancil, Portugal.
- Evangelista, T, co-organized the Spring meeting of SPEDNM. March, 26, 2011, Coimbra, Portugal.

Moderador e Membro de Painel de discussão

- Pinto A “**Technology & Medicine – What is the trend? (Talents and Sustainability)**” (Chairman)
- de Carvalho M, Chairman da Sessão de posters “**Motor Neuron Disease**” no 14th European Congress of Clinical Neurophysiology (Roma, 2011).
- de Carvalho M, Chairman do Workshop “**Motor Neuron Diseases**” no 14th European Congress of Clinical Neurophysiology (Roma, 2011).
- De Carvalho M, ALS- what is the consensus? Fort Denilson, Sydney, Novembro de 2011

Prizes, homours and awards

- Prémio da Melhor Comunicação do Lisbon Arrhythmia Meeting com o trabalho intitulado “**Changes in connexin and ion channel gene expression induced by autonomic stimulation: potential interactions with atrial remodeling?**” e os Prémios Jorge Quininha para as seguintes publicações de que é autor: “**Acute Vagal Modulation of Electrophysiology of the atrial and pulmonary veins increase vulnerability to atrial fibrillation**”, “**Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation**” e “**Defining left bundle branch block in the era of cardiac resynchronization therapy**” Mário Oliveira
- **Bolsa de Investigação Clínica em Doenças Neuromusculares** atribuída pela *Sociedade Portuguesa de Neurologia* ao trabalho "Estudo do Cito-esqueleto Neuronal em Neuropatias de Pequenas Fibras - Reconstrução Tridimensional de imagens de alta resolução com a utilização de Quantum Dots", de Pedro Pereira e Mamede de Carvalho, 2011.

Advanced Teaching

Mamede de Carvalho

*Professor Associado Convidado e Regente de Fisiologia.

*Professor Catedrático Convidado de Fisiologia, desde Outubro 2011.

Member of the Council of the Neurosciences Master/Doctoral Thesis Program.

Professor of Biomechanics – Biomedical Engineering – IST-FMUL

MC Azevedo Coutinho

Mestrado Integrado em Engenharia Biomédica, IST em Colaboração com a Faculdade de Medicina De Lisboa.

Leccionou os seguintes módulos: Doenças Circulatórias e da Coagulação e Falência dos principais sistemas II.

Licenciatura em Ciências da Saúde - Disciplina de Mecanismos Gerais da Doença
Leccionou as seguintes Aulas Teóricas: Insuficiência Coronária e Insuficiência Cardíaca.

T Evangelista

Evangelista, T. co organized and lectured the Neuropathology course of the masters/PhD Neurosciences Programme (12th edition) IMM, Lisbon, February, 2010-2011/02/2011.

I Rocha

Seminar and Lessons in Master Degree and Doctoral Program on Neurosciences. Anabela Pinto

Seminar ad Lessons in Master degree on Physical Medicine and Rehabilitation. Anabela Pinto

Seminar and Lessons on Orthopedic Rehabilitation. Anabela Pinto

Seminar and Lessons in Master Degree and Doctoral Program on Neurosciences. Isabel Conceição

Seminar and Lessons in Master Degree and Doctoral Program on Pain. Isabel Conceição

Lessons in Biomechanics - Biomedical Engineering integrated master degree. Isabel Conceição

Master and Ph.D. thesis completed

Mamede de Carvalho

Orientador de Tese de Mestrado de Reabilitação Neurológica da Universidade Católica Portuguesa do terapeuta Carlos Fernando Leite Martins, com o título “*Imaginação Motora de Actividade da Vida Diária? Alterações na Excitabilidade Cortical*”. Aprovado com a classificação de 18 valores, em 2011.

Orientador de Tese de Mestrado de Reabilitação Neurológica da Universidade Católica Portuguesa do terapeuta Carlos Fernando Leite Martins, com o título “*Imaginação Motora de Actividade da Vida Diária? Alterações na Excitabilidade Cortical*”. Aprovado com a classificação de 18 valores, em 2011.

T Evangelista

Tese de mestrado integrado em medicina “Quality of life in Mild Cognitive Impairment patients” da discente Sofia Silva Narciso

MC Azevedo Coutinho

Orientou os seguintes Trabalhos de Mestrado:

“Biomarcadores na Insuficiência Cardíaca” da aluna Sofia Alexandra Gomes Rosas de Azevedo Fernandes (2011);

“Qual a Estratégia Antitrombótica mais Adequada na Fibrilhação Auricular Permanente na Ausência de Doença Valvular?” do aluno José Carlos Mendes (2011);

“Miocardiopatia de Tako-Tsubo” da aluna Teresa Mendonça (2011).

Isabel Rocha

“Bases Autonómicas e Hemodinâmicas da Resposta Terapêutica ao Treino de Ortostatismo na Síncope Neurocardiogénica Reflexa”. Aluno de Mestrado: Sofia Santos. Instituto Politécnico de Lisboa - Universidade de Lisboa, Escola Superior de Tecnologia da Saúde de Lisboa - Faculdade de Medicina.

“Análise de Custo-Efectividade da Terapêutica de Ressincronização Cardíaca na Insuficiência Cardíaca. Impacto da selecção baseada na dessincronia mecânica”. Aluno de Mestrado: Maria João Ferreira. Escola Nacional de Saúde Pública – Universidade Nova de Lisboa.

“Benefícios da Monitorização Remota no Follow-Up de Doentes com Insuficiência Cardíaca Portadores de Cardioversor-Desfibrilhador Implantável”. Aluno de Mestrado: Carla Rocha. Instituto Politécnico de Lisboa - Universidade de Lisboa, Escola Superior de Tecnologia da Saúde de Lisboa - Faculdade de Medicina.

Neurosciences Unit

Major interests / Objectives

The unit aims the elucidation of cellular and molecular mechanisms involved in tuning and fine-tuning neuronal communication at synaptic level, including receptor mobility, pre- and post-synaptic receptor activation and the transducing systems operated by receptors as well as the systems involved in neurotransmitter/neuromodulator inactivation including membrane transporters. The impact for nervous system function and dysfunction is also evaluated in the context of behaviour, memory and learning. The unit is now composed by six independent groups. Each group has its own research team and ongoing financed research projects. Therefore, in this report groups will be identified independently. Due to the tight interaction between the groups within the Unit the major scientific achievements and publications are pooled together.

The specific research objectives of each group in the Unit are:

Neuroprotection Group - To investigate mechanisms involved in neuronal protection, focusing on the control of a delicate balance between neuronal inhibition/excitability. We have been focusing on adenosine (for a review by the group leader see e.g., Sebastião et al., 1996, *Prog Neurobiol*, 48, 167-189 - Journal IF: 9.966, Citations: 194), which besides acting itself as an endogenous neuroprotective agent, interacts with other substances, including cannabinoids and neurotrophic factors, also relevant for cell survival. Our aim is to evaluate the interplay between different neuroprotective substances and, therefore, to contribute for the understanding of how neurones can be helped to survive and recover from insults.

Neuromodulation and Plasticity Group -To elucidate fine tune regulation of the chemical synapses by neuromodulators (e.g. purines, neuropeptides). We aim to recognize the way neurotransmitters are controlled at the synaptic level and the implications for plasticity and in neuronal dysfunctions (for a review by the group leader see e.g., Ribeiro et al., 2002, *Prog Neurobiol*, 68, 377-392 - Journal IF: 9.966, Citations: 199). A project aiming to identify a role for adenosine in transgenic animal models of amyotrophic lateral sclerosis (ALS) has been initiated.

Receptor Biology and Cognition group - To understand how brain structures involved in memory are affected in situations of cognitive decline, in particular on changes occurring with ageing and whether these changes are hastened or exacerbated by several pathological conditions, namely depression and anxiety. By the use of experimental models (for the chronic stress model used by the group leader see Lopes et al., 2008 *J. Proteomics* 71, 80-88, Journal IF: 5.074), mimicking these situations, we investigate the impact on cognition both at neuronal and behavioural levels. We are mainly focused into exploring the role of adenosine A_{2A} receptors as potential cognitive modulators both *in vitro* and *in vivo*.

Regulation of Neuronal Death group - To understand neuronal death mechanisms induced by noxious conditions. We are particularly interested in understanding how loss of endogenous neuronal trophic support occurs in Alzheimer's disease patients. We are particularly interested on the potential involvement of A β aggregates in that loss. The age-related changes of neurotrophins-mediated control of synaptic transmission (for a recent publication by the group leader see Diógenes et al., 2007, *Hippocampus*, 17: 577-585 - Times cited: 28, Journal IF: 4.609) are also a focus of the group.

Inhibitory Synapses Group – To understand the molecular mechanisms of inhibitory synapses, focussing upon glycinergic ones, and their modulation in the brain. The group aims to elucidate the glycinergic neurotransmission in the hippocampus, both at molecular and functional levels, and to clarify the role of glycine-mediated inhibition within the context of neuronal

hyperexcitability, as it occurs in epilepsy (for a recent publication by the group leader see Aroeira et al., 2011, *J Neurochem*, **118**: 339-35, Times cited: 1 Journal IF: 4.337).

Head of Unit

Ana Maria Ferreira de Sousa Sebastião, PhD – Associate Professor, FMUL

Principal Investigators

Ana Maria Ferreira de Sousa Sebastião, PhD	Associate Professor, FMUL
Joaquim Alexandre Ribeiro, MD, PhD	Full Professor, FMUL
Alexandre Valério de Mendonça, MD, PhD	Principal Investigator, FMUL
Luisa V. Lopes PhD	Staff Scientist, IMM
Maria José Diógenes, PhD	Assistant Professor, FMUL
Claudia Alexandra Valente de Castro, PhD	Research Fellow, FMUL

Research Teams

Neuroprotection Group

Principal Investigator: Ana Maria Sebastião, PhD, Associate Professor (c/agregação), FMUL

Fábio Marques Simões de Sousa, Basic Degree in Biology	Post Doc Fellowship, FCT
Raquel Dias, Basic Degree in Biology; PhD in Neurosciences	Post Doc Fellowship, FCT
Sandra Vaz, Basic Degree in Biochemistry; PhD in Neurosciences	Post Doc Fellowship, FCT
Sara Xapelli, Basic Degree in Biology; PhD in Cell Biology	Post Doc Fellowship, FCT
Catarina Fernandes, Basic Degree in Biology	Ph.D. Fellowship, FCT (finished December 2011) left in December 2011
Sofia Cristóvão-Ferreira, Basic Degree in Biochemistry	Ph.D Fellowship, FCT
Diogo Rombo, Degree in Biology	Ph.D Fellowship, FCT
Ana Filipa Ribeiro, Degree in Biochemistry	Ph.D Fellowship, FCT
Mariana Colino de Oliveira	Ph.D. Fellowship, FCT
Joaquim Jacob, Degree in Biology	MSc Student (Neurosciences); (finished December 2011)
Ruben Gonçalves, Basic Degree in Cell Biology	MSc Student (Neurosciences); start September 2010 (co-supervised by João Ferreira, Chromatin Biology Unit)
Andreia Cruz Silva, Basic degree in Biochemistry	MSc Student (Biochemistry); (finished December 2011)
Francisco Mouro, Basic Degree in Psychology	Master student (start Nov 2011)
Afonso Felix de Oliveira, Medical Student	GAPIC fellow (start September 2010)

Victor Câmera Pimentel, Degree in Biological Sciences	PhD student at Univ Federal Santa Maria, Brasil (6 month short stay at IMM, start Dec 2011)
João Baião	Technician, FMUL

Neuromodulation and Plasticity Group

Principal Investigator: Joaquim Alexandre Ribeiro, MD, PhD, Full Professor, FMUL

Alexandre Valério de Mendonça, MD, PhD	Principal Investigator, FMUL (also in the Neurological Clinical Research Unit)
Fernando Martins do Vale	Assistant Professor, FMUL
Alexandra Marçal, PhD	Investigator, MNHNC/UL
Rui Gomes, PhD	Assistant Professor, FCUL
António Pinto Duarte – MSc	PhD. Fellowship, FCT (collaborative project on cell calcium imaging with San Diego, California)
Paula I. Pousinha, MSc	PhD. Fellowship, FCT
Ana Rita Gagean de Sousa Guerra Costenla, Degree in Biology	PhD. Fellowship, FCT
Frederico Simões do Couto, MD	Assistant, FMUL
Nuno Canas, MD, MSc	Assistant, FMUL
Luís Abegão Pinto, MD	Assistant, FMUL
Gonçalo Ramos, Degree in Biology	MSc Student, FCUL
Mariana Rocha, Degree in Biology	MSc Student (started September 2010)
Joao Baião	Technician, FMUL

Receptor Biology and Cognition group

Principal Investigator: Luisa Vaqueiro Lopes, PhD, IMM Staff Scientist

Joana E. Coelho	Postdoc, Fellowship NESTEC
Vânia Batalha, MSc	PhD Fellowship, FCT
Diana Ferreira, Degree in Pharmacy	PhD student, FMUP
Jorge Valadas, Degree in Biochemistry	BI fellowship, FCT
João Baião	Technician, FMUL

Regulation of Neuronal Death group

Principal Investigator: Maria José Diógenes, PhD, Auxiliary Professor, FMUL

André Jerónimo Santos, Basic degree in Biochemistry	PhD Fellowship, FCT
Daniela Calçada, Basic degree in Biochemistry	MSc Neuroscience Student (finished January, 2011)
Júlia Pinho, Basic degree in Biology	MSc Neuroscience Student (finished December 2011)
António Caetano, Medical Student	Medical student, Fellowship, BAYER

Rúben Duque do Vale, Medical Student	GAPIC Fellow
Sofia Lérias, Medical Student	GAPIC Fellow (co-supervised by S Vaz)
Sara Parreira, Medical Student	GAPIC Fellow (co-supervised by S Vaz)
Carla Leão, Medical Student	GAPIC Fellow (co-supervised by S Vaz)
Carla Nunes, Medical Student	GAPIC Fellow (co-supervised by S Vaz)

Inhibitory Synapses Group

Principal Investigator: Cláudia Valente, PhD Research Assistant, FMUL

Research Team

Rita Aroeira, MSc in Biochemistry	PhD fellowship, FCT (co-supervised by Ana M Sebastião)
Catarina Luís, Basic Degree in Cell Biology	MSc Neurosciences Student
Renato Nogueira, Medical Student	GAPIC fellow
David Correia, Medical Student	GAPIC fellow
Inês Figueiredo, Medical Student	GAPIC fellow

Keywords/Research Areas

Tripartite synapse mechanisms; Neuronal Excitation/Inhibition balance; Chronic stress; Ageing
Neurodegenerative mechanisms; Brain dysfunctions

Major Scientific Achievements of the Unit

Following the broad objective of the Unit – to understand how neurons are finely tuned, or in other words, how neuronal activity is metamodulated (to better understand the concept see Ribeiro & Sebastião, 2010 – *Acta Physiol* 199, 161-169), by adenosine – major scientific achievements during 2011 include the following findings:

- 1) **Modulation of excitatory and inhibitory transmission** - We found that GABA transporters (GATs) in astrocytes are under control by BDNF, which by operating a truncated form of the TrkB receptor, facilitates the insertion of GAT molecules in the astrocytic membrane (Vaz et al., 2011, *J Biol Chem.*, 286,40464-4076, Journal IF: 5.328). Furthermore, GATs in astrocytes are under tight control by adenosine receptors, which, as identified by the Unit, form tetramers composed by two homodimers of A1 and A2A receptors; these tetramers coupled to two G proteins, Gs and Gi and in this way exert a dual control of GABAergic function (Cristovão-Ferreira et al., 2011, *J Neurosci.*, 31,15629-15639, Journal IF: 7.271). Heteromerization between dopamine and galanin receptors to control cholinergic transmission and hippocampal excitability was also found (Moreno et al., 2011, *J Neurosci.*, 31,7412-742, Journal IF: 7.271). In addition, a close interaction between cannabinoid CB1 and adenosine A1 receptors to control GABA release and memory function has been identified (Sousa et al., 2011, *Neuropsychopharmacology*, 36, 472-487, Journal IF: 6.685).
- 2) **Synaptic and plasticity changes upon ageing**. By analysing age-dependent changes in adenosine modulation of neuromuscular transmission we identified that, at least at the

- neuromuscular junction, tonic activation of A_{2A} receptors predominates over A₁ receptor activation in very young animals, challenging an old paradigm that in young animals inhibition by adenosine predominates over excitation (Pousinha et al, *Neurobiol Aging*, in the press, Journal IF: 6.634). At the aged hippocampus, there is an enhanced A_{2A} receptor mediated adenosinergic tone and as we showed, this allows a role of endogenous BDNF upon ageing leading to enhanced synaptic plasticity (Diógenes et al., 2011, *Neuropsychopharmacology*, 36,1823-1836, Journal IF: 6.685).
- 3) **Neuronal dysfunction induced by amyloid-beta peptide (A β -peptide).** The Unit clearly identified that A β -peptide, a hallmark of Alzheimers' disease, leads to impaired TrkB receptor signalling, and as shown in a collaboration with a group of the Univ Helsinki, this can be related to memory impairment in a mice model (APP/PS1 mice) of Alzheimers's disease (Kemppainen et al., 2011, *Neurobiol Aging*, Epub ahead of print, Dec 29, Journal IF: 6.634).
 - 4) **Stress.** Sustained enhancement of glucocorticoid levels by chronic stress leads to synaptic dysfunction and as the Unit clearly showed, blockade of adenosine A_{2A} receptors can revert this dysfunction, highlighting the therapeutic interest of adenosine A_{2A} receptor antagonists in stress-induced memory impairment (Batalha et al, *Molecular Psychiatry*, in the press, Journal IF: 15.470).
 - 5) **Glycinergic transmission.** The unit clearly showed that glycinergic receptors are widely expressed in hippocampus and that their subcellular localization and subunit composition change over development, peaking at postnatal day 7, but being still evident in adulthood (Aroeira et al., 2011, *J Neurochem*, 118,339-353, Journal IF: 4.337).

Another major achievement was that clinical research lines, namely those in neuro-ophthalmology and psychiatry, have been opened by Unit members in 2011 (; Couto et al., *Actas Espan Psiqu* 39, 147-154, Journal IF: 0.695; Pinto et al., *Arch Clin Exp Ophthalmol*, in the press, Journal IF: 2.158).

Recent Most Relevant Publications

- 1-Assaife-Lopes, N., Sousa V. C., Pereira D. B, Ribeiro J. A., Chao M. V. and Sebastião A. M. (2010). Activation of adenosine A_{2A} receptors induces TrkB translocation and increases BDNF-mediated phospho-TrkB localization in lipid rafts: implications for neuromodulation. *J Neurosci*, 30: 8468–8480. (Journal IF: 7.271, Citations: 11)
- 2-Sebastião AM and Ribeiro J A (2009). Adenosine Receptors and the Central Nervous System, *Handbook Exp Pharmacol*, 193: 471-534. (Google Scholar Citations: 40)
- 3-Diógenes, M.J., Fernandes, C.C., Sebastião, A.M., Ribeiro, J.A. (2004) Activation of adenosine A_{2A} receptor facilitates BDNF modulation of synaptic transmission in hippocampal slices. *Journal of Neuroscience*, 24, 2905-2913. (Journal IF: 7.271, Citations: 60)
- 4-Lopes LV, Cunha RA, Kull B, Fredholm BB, Ribeiro JA (2002) Adenosine A_{2A} receptor facilitation of hippocampal synaptic transmission is dependent on tonic A₁ receptor inhibition. *Neuroscience*, 112, 319-329. (IF: 3.215, Citations: 79)
- 5-Sebastião, A.M., Ribeiro, J.A. (2000). Fine tuning neuromodulation by adenosine. *Trends in Pharmacological Sciences (TIPS)*, 21, 341-346. (Journal IF: 11.050, Citations: 145)

Ongoing Research Projects

Neuroprotection Group

National:

2011/2014 - Modulation of GABAergic transmission in the hippocampus by adenosine. FCT, Coordinator: Ana M Sebastião. PTDC/SAU-NMC/110838/2009. 156 000€

International:

2009/2011 –Control of GABA transport in astrocytes. Collaborations with Rafael Franco, University of Pamplona, Carmen Dias, University of Barcelona, Spain, Ulrik Gether, University of Copenhagen, and with F Conti, Univ Ancona, Italy. Co-ordinator: Ana M Sebastião (no funding).

2008/2011 – Modulation by adenosine of the BDNF synaptic influences. Collaboration with Detlev Boisson (Oregon), Bruno Frenguelli (Warwick University, UK), Regeneron Pharmaceuticals (USA). Co-ordinator: Ana M Sebastião (no funding).

2007/2011 – Memory impairments caused by cannabinoids: interplay with adenosine A1 receptors. Collaboration with Judith Pratt and Rose Brett (Strathclyde Univ, Glasgow). Project Coordinator: Ana M Sebastião (no funding).

2011/2012 - Consequences of perinatal hypoxia/ischaemia upon TrkB, A2A and A1 receptor expression in the hippocampus. PI: Maria Rosa Chitolina, Universidade Federal de Santa Maria, Brasil (no funding).

2011/2012 - Modulation of tonic GABAergic currents in the hippocampus. Collaboration with Enrico Cherubini, Univ Trieste. Project Coordinator: Ana M Sebastião (no funding).

2011/2012 - Modulation of AMPA receptor trafficking. Collaboration with Jeremy Henley, Univ Bristol. Project Coordinator: Ana M Sebastião (no funding).

Neuromodulation and Plasticity Group

National:

2011/2014 – Are Microglia a New Potential Pharmacological Target in Amyotrophic Lateral Sclerosis (ALS)? FCT, Coordinator: D Brites FFUL, Partners at IMM: Alexandra Marçal, Member of the research team, Consultant: J.A. Ribeiro. PTDC/SAU-FAR/118787/2010. IMM budget: 22.000€

2010/2013 – Cross talk between neurotrophic factor receptors (TrkB) and adenosine A2A receptors: implications for amyotrophic lateral sclerosis (ALS). FCT, Coordinator: J.A. Ribeiro PTDC/SAU-NEU/101752/2008. 159 760€

2008/2011 – Membrane receptors and mediators involved in plastic changes induced by neuronal insults: implications for neuroprotection.). FCT, Coordinator: J.A. Ribeiro. PTDC SAU-FCF/68607/2006. 160 000€

International:

2008/2011. Modulation of transmission at the hippocampus by receptor heteromerization. Coordinators: S. Ferre (NIH, Bethesda, USA) and J.A. Ribeiro (IMM), also involving R Franco (Univ Pamplona) and Carmen Lluís (Univ Barcelona). Coordinator at IMM: J.A. Ribeiro. “(no funding)”.

Receptor Biology and Cognition group

National:

2010/2013 - Role of the adenosine A2A receptors in chronic stress - implications for learning and memory. Collaboration with Christa Müller (Bonn University). FCT, Coordinator: Luísa V Lopes. PTDC/SAU-NEU/099853/2008. 130 000€

2010-2012– “Psychological indicators of stress reactivity and disease adaptation” – BIAL Foundation Fellowship 38 000 EUR. Coordinator at IMM: Luísa V Lopes. IMM budget: 38 000€

International:

2011-2012 - Adenosine A2A receptors and glucocorticoids in age-related hippocampal dysfunctions, Égide/Pessoa (PI in France David Blum). Coordinator at IMM: Luísa Lopes. Funding (mobility): 6 400€

2008-2011- Brain-gut interaction. In collaboration with Kussmann M (Lausanne). Coordinator: Luísa Lopes - Project financed by Nestlé Research Center (Nestec/IMM/474/2008) 190 000€.

2010-2014 – Functional consequences of A2A receptor overexpression. Project leadered at IMM, in collaboration with Michael Bader for the supply of tg CAMKII-hA2AR rats (no funding).

Regulation of Neuronal Death group

National:

2008/present- Deciphering the role of A β toxicity in the loss of endogenous neuroprotection. FCT funding for the PhD fellowship of André Jerónimo Santos. Coordinator: Maria José Diógenes (no funding)

2008/present – Dysfunctional or compensatory enhanced plasticity upon ageing? Collaboration with Merz Pharma. Coordinator: Maria José Diógenes (no funding).

International:

Collaboration with Eero Castren (Univ Helsinki) and Heikki Tanila (Univ Kuopio) to evaluate A β toxicity at the cellular level and how toxicity hallmarks can be related to memory impairment in a mice model (APP/PS1 mice) of Alzheimers’s disease (no funding).

Inhibitory Synapses Group

National:

2009/2013 - Characterization of glicinergeric neurotransmission in the hippocampus FCT funding for the PhD fellowship of Rita Aroeira. Coordinator: Cláudia Valente (no funding).

International:

2011- Collaboration with Uwe Heinemann (Univ Charité, Berlin) for setting up an in vitro model of drug resistant epilepsy. Supported by NENS (Network of European Neuroscience Schools) (no funding).

2011-2012 – Collaboration with Manuel Miranda (Univ Texas at El Paso) for the supply of glycine transporter antibodies (no funding)

Publications in peer review Journals

Batalha VI, Pego JM, Fontinha B, Costenla AR, Valadas J, Baqi Y, Radjainia H, Müller CE, Sebastião AM and Lopes LV (2012). Adenosine A2A receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. *Molecular Psychiatry* (in the press) (Journal IF: 15.470).

Pousinha PA, Correia AM, Sebastião AM and Ribeiro JA (2012). Neuromuscular transmission modulation by adenosine upon aging. *Neurobiol Aging* (in the press) (Journal IF: 6.634).

Freitas PP, Cardoso FA, Martins VC, Martins SA, Loureiro J, Amaral J, Chaves RC, Cardoso S, Fonseca LP, Sebastião AM, Pannetier-Lecoeur M, Fermon C. (2012) Spintronic platforms for biomedical applications. *Lab Chip*. **12**:546-557 (Journal IF: 6.260)

Pinto LA, Vandewalle E and Stalmans I (2012) Disturbed correlation between arterial resistance and pulsatility in glaucoma patients”. *Acta Ophthalmologica*. (in the press) (Journal IF: 2.809)

Kempainen S, Rantamäki T, Jerónimo-Santos A, Lavasseur G, Autio H, Karpova N, Kärkkäinen E, Stavén S, Miranda HV, Outeiro TF, Diógenes MJ, Laroche S, Davis S, Sebastião AM, Castrén E and Tanila H. (2011). Impaired TrkB receptor signaling contributes to memory impairment in APP/PS1 mice. *Neurobiol Aging*. Dec 29. [Epub ahead of print] (Journal IF: 6.634).

Dias R, Ribeiro JA and Sebastião AM. (2012) Enhancement of AMPA currents and GluR1 membrane expression through PKA-coupled adenosine A2A receptors (*Hippocampus*, **22**, 276-291 (Journal IF: 4.609)

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. (2011). Modulation of GABA Transport by Adenosine A1R-A2AR Heteromers, Which Are Coupled to Both Gs- and Gi/o-Proteins. *J Neurosci*. **31**:15629-15639. (Journal IF: 7.271)

Lopes LV and Kussmann M. (2011). Proteomics at the interface of psychology, gut physiology and dysfunction: an underexploited approach that deserves expansion. *Expert Rev Proteomics* **8**: 605-614 (Journal IF: 4.406)

- Vaz S. H., Jørgensen T. N., Cristóvão-Ferreira S, Dufлот S, Ribeiro J A, Gether U. and Sebastião A. M. (2011). Brain-derived neurotrophic factor (BDNF) enhances GABA transport by modulating the trafficking of GABA transporter-1 (GAT-1) to the plasma membrane of rat cortical astrocytes *J Biol Chem*, 286: 40464-40476 (**Journal IF: 5.328**).
- Marques S, Batalha VL, Lopes LV, Outeiro TF.(2011). Modulating Alzheimer's disease through caffeine: a putative link to epigenetics. *J Alzheimers Dis*. **24**:161-171 (Journal IF: 4.261)
- Costenla AR, Diógenes MJ, Canas PM, Rodrigues RJ, Nogueira C, Maroco J, Agostinho PM, Ribeiro JA, Cunha RA, de Mendonça A (2011). Enhanced role of adenosine A(2A) receptors in the modulation of LTP in the rat hippocampus upon ageing. *Eur J Neurosci*. **34**:12-21. (Journal IF: 3.658)
- Moreno E, Vaz SH, Cai NS, Ferrada C, Quiroz C, Barodia SK, Kabbani N, Canela EI, McCormick PJ, Lluís C, Franco R, Ribeiro JA, Sebastião AM and Ferré S. (2011) Dopamine-galanin receptor heteromers modulate cholinergic neurotransmission in the rat ventral hippocampus. *J Neurosci*, **31**:7412–7423. (Journal IF: 7.271, Citations: 2)
- Diógenes MJ, Costenla AR, Lopes LV, Jerónimo AS, Sousa VC, Fontinha BM, Ribeiro JA and Sebastião AM. (2011) Enhancement of LTP in aged rats is dependent on endogenous BDNF. *Neuropsychopharmacology*, **36**:1823-1836. (Journal IF: 6.685)
- Aroeira RI, Ribeiro JA, Sebastião AM and Valente CA (2011). Age-related changes of glycine receptor at the rat hippocampus: from the embryo to the adult. *J Neurochem*, **118**: 339-353. (Journal IF: 4.337, Citations:1)
- Lopes LV, Sebastião AM, and Ribeiro JA. (2011) Adenosine and related drugs in brain diseases: present and future in clinical trials *Curr Topics Med Chem* **11**:1087-1101. (Journal IF: 4.112, Citations:1)
- Sebastião AM, Assaife-Lopes N, Diógenes MJ, Vaz S and Ribeiro JA (2011) Modulation of brain-derived neurotrophic factor (BDNF) actions in the nervous system by adenosine A2A receptors and the role of lipid rafts *BBA Biomembranes Biochimica et Biophysica Acta*, **1808**, 1340–1349. (Journal IF: 4.647)
- Sousa VC, Assaife-Lopes N, Brett RR, Ribeiro JA, Pratt JA and Sebastião AM. (2011) Regulation of hippocampal cannabinoid CB1 receptor actions by adenosine A1 receptors and chronic caffeine administration: implications for the effects of Δ^9 -tetrahydrocannabinol on spatial memory. *Neuropsychopharmacology*, **36**: 472-487. (Journal IF: 6.685)
- Sebastião AM. (2011) Neuronal ENT1 takes up synaptic adenosine even under hypoxia/ischemia *J Neurochem* **118** 1-3. (Journal IF: 4.337)
- do Couto FS, Queiroz C, Barbosa T, Ferreira L, Firmino H, Viseu M, Ramos L, Romero J and Figuera M. (2011). Clinical and therapeutic characterization of a portuguese sample of patients with schizophrenia *Actas Espan Psiqu* **39**, 147-154 (Journal IF: 0.695)
- Pinto LA, Vandewalle E, Pronk A and Graefes IS. (2011) Intraocular pressure correlates with optic nerve sheath diameter in patients with normal tension glaucoma” *Arch Clin Exp Ophthalmol*. DOI 10.1007/s00417-011-1878-3 (Journal IF: 2.158)

Other publications International

- Sebastião AM, Cristóvão-Ferreira S and Ribeiro JA (2012) Downstream pathways of adenosine. Springer Books in “Adenosine: a key link between metabolism and central nervous system activity” ed. Susan Masino, Springer Books, USA, (in press).

- Blum D, Sandau, U, Laurent, C, Batalha, V, Leboucher, A, Hamdane, M, Pasquier F, Detlev Boison, Buée L, LV (2012) “Adenosine receptors and Alzheimer’s Disease” Springer Books in “Adenosine: a key link between metabolism and central nervous system activity” ed. Susan Masino, Springer Books, USA, (in press).
- Blum D, Martire A, Burnouf S, Sablonnière B, Krystkowiak P, Ledent C, Lopes LV, Popoli P (2012) “Adenosine receptors in Huntington’s Disease” in “Adenosine: a key link between metabolism and central nervous system activity” ed. Susan Masino, Springer Books, USA, (in press).
- Amaral J, Cardoso S, Freitas PP and Sebastiao AM. (2012) Toward a system to measure action potential on mice brain slices with local magnetoresistive probes *J Appl Phys* **109**, 07B308 - 07B308-3 (Journal IF: 2.079)
- Barroso S and Sebastião AM (2012) Research Possibilities for Pre-graduate Students In: The Researching, Teaching, and Learning Triangle Mentoring in Academia and Industry, 2012, Volume 10, Part 1, 17-25, DOI: 10.1007/978-1-4614-0568-9_2
- Pinto, L:A: and Stalmans I (2011). A Vascular Approach to Glaucoma, Glaucoma - Basic and Clinical Concepts, Shimon Rumelt (Ed.), ISBN: 978-953-307-591-4, In Tech, Available from: <http://www.intechopen.com/articles/show/title/a-vascular-approach-to-glaucoma>
- Canas N and Soares, P (2011). MRI Abnormalities Induced by Seizures Em “Neuroimaging/ 2”, Intech publishing (Editor Peter Bright), (in the press)
- Martins do Vale, F. (2011). The noxious mechanism of pain after intravenous injections. online <http://www.bmj.com/rapid-response/2011/11/03/noxious-mechanism-pain-after-intravenous-injections>.
- Martins do Vale, F. (2011). The replacement of medical prescription undermines pharmacological vigilance and may encourage corruption. online 15 Novembro BMJ .com “Rapid Response”: <http://www.bmj.com/rapid-response/2011/11/15/re-pharmacists-may-be-allowed-change-prescriptions-without-consulting-pres>
- Martins do Vale, F. (2011). Specialization may also bias diagnosis. online 11 November BMJ .com “Rapid Response”: <http://www.bmj.com/rapid-response/2011/11/11/re-keeping-open-mind>

Other Publications National

- Pinto LA, Ferreira J, Patrício M, Rios C, Cunha JP, Marques-Neves C. Impacto do diâmetro do nervo óptico na amplitude de pulso ocular no glaucoma primário de ângulo aberto”. Revista da Sociedade Portuguesa de Oftalmologia (2011), 1: 27-31. (Prémio Borges de Sousa)
- Pinto LA, Ferreira J, Fernandes F, Patrício M, Brás A, Rios C. Correlação entre morfologia da bolha de filtração e eficácia hipotensora dos dispositivos de drenagem. Aceite para publicação na Revista da Sociedade Portuguesa de Oftalmologia.
- Pinto LA, Vandewalle E., Zeyen T, Stalmans I. Avaliação da regulação vascular da circulação retrobulbar por Color Doppler Imaging. Aceite para publicação na Revista da Sociedade Portuguesa de Oftalmologia. (prémio MSD)
- Pinto LA, Vandewalle E, Zeyen T, Stalmans I. Ausência de pulsatilidade venosa espontânea como factor de risco no glaucoma normotensional. Aceite para publicação na Revista da Sociedade Portuguesa de Oftalmologia

Invited Lectures and Seminars

- Sebastião, AM. Modulation of hippocampal synaptic plasticity by adenosine A2A receptors. Physiology 2011, The Physiological Society, Oxford, UK, July 11-14, 2011
- Lopes, LV. 1st Annual MIND Symposium Molecular Mechanisms of Neurodegeneration, “Adenosine A2A receptors in the brain: sensor or triggering signal?”, Harvard Medical School, MIND symposium, Boston – USA, November 2011.
- Lopes, LV. "Adenosine receptors as therapeutic targets in brain disorders" Chair of symposium in the European Brain and Behaviour Society Meeting, Seville, Spain, September 2011
- Lopes, LV. Time for a coffee-break? – Exploring caffeine-like properties in brain disorders. Nestlé Institute for Health Sciences, Lausanne – Switzerland, December 2011
- Lopes, LV., Adenosine A2A receptors in the brain: implications in ageing and stress, INSERM Lille, June 2011.
- Lopes, LV. European Winter Conference on Brain Research – "Caffeine control of brain function – role of adenosine receptors" Les Alpes, France, March 2011
- Pinto, LA “Stress and Glaucoma – link or myth?” Reunião Annual da Merck Foundation Belgium, Bruxelas, Belgium, May 25, 2011
- Sebastião, AM., Cristóvão-Ferreira, S., Navarro, G., Brugarolas, M., Pérez-Capote, K., Vaz, SH., Lluís, C., Casadó, V., Franco, R., Ribeiro, JA. G protein coupling of A1/A2A heteromers in astrocytes. SINAL 2011 – 5th National Meeting on Signal Transduction, Coimbra, April 28-30, 2011.
- Sebastião, AM. Reinforcement of excitatory signaling at the tripartite synapse by adenosine A2A receptors. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011.
- Aroeira, RI. Temporal characterization of glycine receptor in rat hippocampus. Lisbon Area Neuroscience Meetings, Institute of Molecular Medicine, Lisboa, Portugal, April 2011
- Rombo, DM, Dias, RA, Ribeiro, JA, Sebastião, AM. Tuning inhibition with adenosine – synaptic vs extrasynaptic responses. Lisbon Area Neuroscience Meeting, Institute of Molecular Medicine, Lisbon, December 14, 2011.
- Pinto LA “Venous circulation in Glaucoma” – Lecture da European Ophthalmology Society no congresso anual da Sociedade Portuguesa Oftalmologia, Vilamoura 2011. (Indigitado para apresentar a 1^a Edição em Portugal desta iniciativa da Sociedade Europeia, que visa promover um jovem oftalmologista com menos de 40 anos)

Communications in International Conferences

- Aroeira, R.I., Ribeiro, J.A., Sebastião, A.M., Valente, C.A. Expression and function of glycine transporters, GlyT1 and GlyT2, in rat astrocytes. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Batalha, V.L., Valadas, J.S., Hockmeyer, J., Müller, C.E., Sebastião, A.M., Lopes, L.V. Adenosine A_{2A} receptors regulate the hypothalamic pituitary adrenal-axis function. 41st Annual Meeting of the Society for Neuroscience, Washington DC, USA, November 12-16, 2011 (Poster presentation).

- Batalha, V.L., Sebastião, A.M., Lopes, L.V. The synaptic responses of adenosine receptors in the rat hippocampus are modified by chronic stress: the aging hypothesis. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Brites, D., Silva, S.L., Oliveira, A., Vaz, A.R., Diógenes, M.J., van Rooijen, N., Sebastião, A.M., Fernandes, A., Gomes, C., Falcão, A.S., Silva, R.F.M. Microglia faces featuring a potential pathological neural/glial behavior highly common in neonatal life. 10th European meeting on Glial cells in health and disease, Prague, Czech Republic, September 13-17, 2011: GLIA Volume: 59 Supplement: 1 Pages: S101-S101 Published: OCT 2011 (Poster presentation).
- Costenla, A.R., Diógenes, M.J., Agostinho, P.M., de Mendonça, A., Cunha, R.A. Enhanced role of adenosine A_{2A} receptors in the modulation of LTP in the rat hippocampus upon aging. European Winter Conference on Brain Research, Les Alpes, France, March 14-18, 2011. (Poster presentation).
- Cristóvão-Ferreira, S., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. A₁-A_{2A} heteromer is coupled to both G_{i/o} and G_s proteins. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Do Vale, R.D., Pinho, J., Lopes, L.V., Ribeiro, J.A., Sebastião, A.M., de Mendonça, A., Diógenes, M.J. Blockade of NMDA receptors by memantine decreases the augmented LTP in old rats hippocampus to “physiologic” values. Berlin Brain Days 2011, Berlin, Germany, December 7-9, 2011 (Poster presentation).
- Jerónimo-Santos, A., Batalha, V.L., Müller, C., Hockemeyer, J., Sebastião, A.M., Lopes, L.V., Diógenes, M.J. Chronic blockade of adenosine A_{2A} receptors abolish BDNF effect on hippocampal LTP. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Ribeiro, F.F., Neves-Tomé, R., Assaife-Lopes, N., Silva, R., Brites, D., Ribeiro, J.A., Sebastião, A.M. The mechanisms underlying the role of adenosine A_{2A} and BDNF TrkB receptors upon neuronal maturation. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Rocha, M.C., Pousinha, P.A., Sebastião, A.M., Ribeiro, J.A., Correia, A.M. Changes in neuromuscular transmission in both pre- and symptomatic phases of the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis. 41st Annual Meeting of the Society for Neuroscience, Washington DC, USA, November 12-16, 2011 (Poster presentation).
- Sebastião, A.M., Sousa, V.C., Assaife-Lopes, N., Ribeiro, J. A., Pratt, J. A., Brett, R. Chronic caffeine-induced upregulation of adenosine A₁ receptors exacerbates spatial memory deficits induced by cannabinoids. 41st Annual Meeting of the Society for Neuroscience, Washington DC, USA, November 12-16, 2011 (Poster presentation).
- Valente, C.A., Aroeira, R.I., Ribeiro, J.A., Sebastião, A.M. Expression of glycine receptor subunits in cortical cultured astrocytes”. 41st Annual Meeting of the Society for Neuroscience, Washington DC, USA, November 12-16, 2011 (Poster presentation).
- Vaz, S.H., Cristóvão-Ferreira, S., Ribeiro, J.A., Sebastião, A.M. Modulation of GAT-1 transporter in astrocytes by BDNF involves the truncated form of TrkB receptors coupled to a non-classic PLC- γ /PKC- δ and Erk/MAP kinase pathway. 8th IBRO World Congress of Neuroscience, Florence, Italy, July 14-18, 2011 (Poster presentation).
- Pimentel J., Canas N., Almeida V. et al. (2011) Proposal To Study The Immune-Mediated Epilepsies In Adults Conference: 29th International Epilepsy Congress Location: Rome,

ITALY Date: AUG 28-SEP 01, 2011 *Epilepsia* Volume: 52 Special Issue: SI Supplement: 6 Pages: 31-31 Published: Aug 2011

- Pinto, L.A., Vandewalle, E., Pronk, A & Stalmans, I. Retrobulbar flow velocities reveal different responses to changes in resistance index between glaucomatous and healthy subjects. Meeting of Association for Research in Vision and Ophthalmology, Ft Lauderdale 2011.
- Pinto, L.A., Vandewalle, E., Pronk, A & Stalmans, I. "Intraocular pressure correlates with optic nerve sheath diameter in patients with normal tension glaucoma" World Glaucoma Congress, Paris, France, June 29 – July 2, 2011.
- Pinto, L.A., Vandewalle, E., & Stalmans, I. Lack of spontaneous venous pulsation as a risk factor for normal tension glaucoma. Basel Glaucoma Meeting 2011. (Poster presentation). (Prémio melhor poster da reunião)

Communications in National Conferences

- Aroeira, R.I., Ribeiro, J.A., Sebastião, A.M., Valente, C.A. Molecular and functional evidences for the occurrence of glycine transporters in rat cortical astrocytes. 5th IMM PhD Students Meeting, Lisboa, October 17-18, 2011. (Poster presentation).
- Aroeira, R.I., Ribeiro, J.A., Sebastião, A.M., Valente, C.A. Developmental changes of glycine receptors in rat hippocampus. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Batalha, V.L., Hamdane, M., Sebastião, A.M., Buée, L., Blum, D., Lopes, L.V. Adenosine A_{2A} receptors decrease glucocorticoid receptor transcriptional activity impacting in the stress response system. 5th IMM PhD Students Meeting, Lisboa, October 17-18, 2011. (Poster presentation).
- Batalha, V.L., Hamdane, M., Sebastião, A.M., Buée, L., Blum, D., Lopes, L.V. Modulation of glucocorticoid receptor transcriptional activity by adenosine A_{2A} receptors: consequences for stress response. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Batalha, V.L., Valadas, J.S., Hockemeyer, J., Müller, C.E., Sebastião, A.M., Lopes, L.V. Involvement of adenosine A_{2A} receptors in the hypothalamic pituitary adrenal-axis regulation. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Batalha, V.L., Valadas, J.S., Hockemeyer, J., Müller, C.E., Sebastião, A.M., Lopes, L.V. *In vivo* Adenosine A_{2A} receptor blockade reverts early life stress-induced impairments in the rat hippocampus and reestablishes the stress response system. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Calçada, D., Ribeiro, J.A., Sebastião, A.M., Diógenes, M.J. The role of lithium on apoptotic cell death induced by amyloid - β peptide. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Coelho, D., Figueiredo, I., Sebastião, A.M., Valente, C.A. Mapping glycine receptor (GlyR) and glycine transporters (GlyT1 and GlyT2) in primary cortical astrocytes. VI Young European Scientist Meeting (YES Meeting), Porto, September 16-18, 2011 (Oral presentation)
- Cristóvão-Ferreira, S., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. A1-A_{2A} heteromers are coupled to both G_{i/o} and G_s and modulate GABA uptake through PKA activity. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).

- Cristóvão-Ferreira, S., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. A1-A2A heteromer is coupled to both $G_{i/o}$ and G_s proteins. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Cruz-Silva, A., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. Calcium signaling modulation by adenosine receptors in astrocytes. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Dias, R.B., Ribeiro, J.A., Sebastião, A.M. Ischemia-induced plasticity requires activation of A_{2A} adenosine receptors and signalling through calcium-permeable AMPA receptors: echoing physiological LTP? 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation)
- Dias, R.B., Ribeiro, J.A., Sebastião, A.M. Activation of A_{2A} receptors is required for ischemia-induced facilitation of hippocampal synaptic transmission. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Diógenes, M.J., Costenla, A.R., Lopes, L.V., Jerónimo-Santos, A., Sousa, V.C., Fontinha, B.M., Ribeiro, J.A., Sebastião, A.M. Enhanced LTP in ageing is dependent on endogenous BDNF. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Diógenes, M.J., Costenla, A.R., Lopes, L.V., Jerónimo-Santos, A., Sousa, V.C., Fontinha, B.M., Ribeiro, J.A., Sebastião, A.M. Enhancement of LTP in aged rats is dependent on endogenous BDNF. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Duque do Vale, R., Lopes, L.V., Ribeiro, J.A., Sebastião, A.M., de Mendonça, A., Diógenes, M.J. Detailing the age-related effects of memantine on long-term potentiation. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Jerónimo-Santos, A., Batalha, V.L., Muller, C., Hockemeyer, J., Sebastião, A.M., Lopes, L.V., Diógenes, M.J. Chronic blockade of adenosine A_{2A} receptors prevents BDNF effect on hippocampal LTP. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Jacob, J.P., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. Modulation of GABA uptake by P2Y1 metabotropic receptor in rat cortical astrocytes. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Jacob, J.P., Vaz, S.H., Ribeiro, J.A., Sebastião, A.M. Modulation of γ -aminobutyric acid (GABA) uptake by P2Y1 metabotropic purinergic receptor in rat cortical astrocytes. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 2011 (Poster presentation).
- Guerreiro, C.*, Ferreira, C.*, Vaz, S.H., Diógenes, M.J., Ribeiro, J.A., Sebastião, A.M. Influence of the protein amyloid- β in glutamate release from pre-synaptic terminals from rat hippocampus. Workshop GAPIC 2011, FMUL, December 12, 2011 (Poster presentation).
*co-first author
- Guerreiro, C.*, Ferreira, C.*, Vaz, S.H., Diógenes, M.J., Ribeiro, J.A., Sebastião, A.M. Modulation of BDNF effect on glutamate release in synaptosomes by amyloid peptide. VI Young European Scientist Meeting (YES Meeting), Porto, September 16-18, 2011 (Poster presentation). *co-first author

- Luís, C., Ribeiro, J.A., Sebastião, A.M., Valente, C.A. Characterization of glycinergic transmission in an *in vitro* epilepsy model. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Parreira, S.*, Lérias, S.R.*, Vaz, S.H., Diógenes, M.J., Ribeiro, J.A., Sebastião, A.M. Effect of the amyloid- β peptide in GABA release from hippocampal synaptosomes of rat. Workshop GAPIC 2011, FMUL, December 12, 2011 (Poster presentation) *co-first author
- Parreira, S.*, Lérias, S.R.*, Vaz, S.H., Diógenes, M.J., Ribeiro, J.A., Sebastião, A.M. Effect of the amyloid- β peptide in GABA release from hippocampal synaptosomes: modulation by BDNF. VI Young European Scientist Meeting (YES Meeting), Porto, September 16-18, 2011 (Oral presentation). *co-first author
- Pinho, J.S., Batalha, V.L., Valadas, J., Constela, A.R., Sebastião, A.M., Lopes, L.V., de Mendonça, A., Diógenes, M.J. Chronic administration of memantine in aged rats: impact on hippocampal dependent memory. Grupo de estudos de envelhecimento cerebral e demências, Tomar, June 3-4, 2011. (Poster presentation).
- Pinho, J.S., Batalha, V.L., Valadas, J., Constela, A.R., Sebastião, A.M., Lopes, L.V., de Mendonça, A., Diógenes, M.J. NMDA receptor blockade in ageing: impact on hippocampal dependent memory. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Pinho, J.S., Batalha, V.L., Valadas, J., Constela, A.R., Sebastião, A.M., Lopes, L.V., de Mendonça, A., Diógenes, M.J. Effect of memantine upon ageing: impact on hippocampal dependent memory. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Oliveira, A.F., Ribeiro, J.A., Sebastião, A.M. Brain Derived Neurotrophic Factor (BDNF) impairs recovery of synaptic transmission after hypoxia, by a mechanism dependent on glutamate NMDA receptors. VI Young European Scientist Meeting (YES Meeting), Porto, September 16-18, 2011
- Oliveira, M.C., Sebastião, A.M. Molecular mechanisms underlying A_{2A}/TrkB crosstalk. 5th IMM PhD Students Meeting, Lisboa, October 17-18, 2011 (Poster presentation).
- Ribeiro, F.F., Silva, R., Fernandes, A., Brites, D., Ribeiro, J.A., Sebastião, A.R. Adenosine A_{2A} receptor and the axon elongation. 5th IMM PhD Students Meeting, Lisboa, October 17-18, 2011 (Poster presentation).
- Ribeiro, F.F., Silva, R., Fernandes, A., Brites, D., Ribeiro, J.A., Sebastião, A.R. The role of adenosine A_{2A} receptor on neuronal outgrowth. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Ribeiro, F.F., Assaife-Lopes, N., Silva, R., Fernandes, A., Brites, D., Ribeiro, J.A., Sebastião, A.R. Neuronal Maturation: Roles of Adenosine A_{2A} and BDNF TrkB receptors. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Ribeiro, F.F., Neves-Tomé, R., Assaife-Lopes, N., Silva, R., Brites, D., Ribeiro, J.A., Sebastião, A.M. Influence of Adenosine A_{2A} and BDNF TrkB receptors upon neuronal maturation. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Rocha, M.C., Pousinha, P.A., Sebastião, A.M., Ribeiro, J.A., Correia, A.M. Is the neuromuscular transmission of the SOD1G93A mouse, a model of Amyotrophic Lateral Sclerosis, compromised? 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).

- Rocha, M.C., Pousinha, P.A., Sebastião, A.M., Ribeiro, J.A., Correia, A.M. Neuromuscular transmission of the SODG93A mouse model of Amyotrophic Lateral Sclerosis. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Rombo, D.M., Dias, R.A., Ribeiro, J.A., Sebastião, A.M. A.M Cell-type specific A1 receptor modulation of perisynaptic/extrasynaptic GABAA receptors in the hippocampus. 5th IMM PhD Students Meeting, Lisboa, October 17-18, 2011 (Poster presentation).
- Rombo, D.M., Dias, R.A., Ribeiro, J.A., Sebastião, A.M. Cell-type specific adenosinergic modulation of perisynaptic/extrasynaptic GABA_A receptors in the hippocampus. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Rombo, D.M., Dias, R.A., Ribeiro, J.A., Sebastião, A.M. Cell-specific modulation of extarsynaptic GABAA receptors in the hippocampus. 12th Reunion of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Rombo, D.M., Dias, R.A., Ribeiro, J.A., Sebastião, A.M. Synapse-specific purinergic signaling in the hippocampus. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Rombo, D.M., Dias, R.A., Maiolino, F., Guerreiro, P., Miranda, H.V., Sebastião, A.M., Diógenes, M.J., Lopes, L.V., Outeiro, T.F. Changes in NMDA and AMPA receptor-mediated glutamatergic transmission by alpha-synuclein. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Rombo, D.M., Dias, R.A., Ribeiro, J.A., Sebastião, A.M. Synapse-specific modulation of inhibitory signaling in the hippocampus. Pizza Seminars, Institute of Molecular Medicine, Lisbon, Portugal, May 24, 2011 (Oral presentation).
- Sebastião, A.M., Ribeiro, J.A. Fine-tuning of plasticity by adenosine A2A receptors at the tripartite synapse. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Vasco C Sousa, V.C., Assaife-Lopes, N., Ribeiro, J.A., Pratt, J.A., Brett, R., Sebastião, A.M. Spatial memory deficits induced by cannabinoids are exacerbated by chronic caffeine-dependent upregulation of adenosine A₁ receptors. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Valadas, J.S., Batalha, V.L., Comin, C.M., Sebastião, A.M., Bader, M., Lopes, L.V. Memory and motor impairments in rats overexpressing adenosine A_{2A} receptors in the forebrain. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Valadas, J.S., Batalha, V.L., Diógenes, M.J., Sebastião, A.M., Lopes, L.V. Corticotrophin-Releasing Factor (CRF) receptors differentially influence the neuroprotective effect of A_{2A} receptor blockade. 12th Reunion of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Valadas, J.S., Batalha, V.L., Diógenes, M.J., Sebastião, A.M., Lopes, L.V. Protective interaction between adenosine A_{2A} receptors and Corticotrophin-Releasing Factor (CRF) in rat cortical neurons. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation).
- Valente, C.A., Aroeira, R.I., Ribeiro, J.A., Sebastião, A.M. Mapping glycine receptor and transporters in cultured rat cortical astrocytes. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).

- Vaz, S.H., Ferré, S., Franco, R., Ribeiro, J.A., Sebastião, A.M. Functional interactions between galanin and dopamine receptors: role of D-5 and GAL-1 receptor on acetylcholine release and synaptic transmission. 1st Champalimaud Neuroscience Symposium, Lisboa, September 18-21, 2011 (Poster presentation).
- Vaz, S.H., Jørgensen, T.N., Cristóvão-Ferreira, S., Ribeiro, J.A., Gether, U., Sebastião, A.M. BDNF modulates GAT-1 transporter in astrocytes through the TrkB-t receptor coupled to non-classic PLC/PCK and ERK/MAP Kinase pathway. 12th Meeting of the Portuguese Neuroscience Society, Lisboa, May 26-28, 2011 (Poster presentation).
- Vaz, S.H., Ferré, S., Franco, R., Ribeiro, J.A., Sebastião, A.M. Modulation of cholinergic neurotransmission by dopamine-galanin receptors in the rat ventral hippocampus: role of D5 and Gal1 receptor on acetylcholine release and synaptic transmission. 41st Annual Meeting of the Portuguese Pharmacological Society, Coimbra, February 2-4, 2011 (Oral presentation)
- Pinto, L.A., Fernandes, F., Lopes, T. Avaliação oftalmológica em doentes com síndrome de apneia obstrutiva de sono. Reunião Anual da Sociedade Portuguesa de Oftalmologia, Vilamoura 2011.
- Pinto, LA, Vandewalle, E., Stalmans, I. Estudo da waveform da curva Doppler da Artéria Oftálmica em doentes com Glaucoma. Reunião Anual da Sociedade Portuguesa de Oftalmologia, Vilamoura 2011.
- Pinto, LA, Ferreira, J., Lisboa M., Duarte, A., Fernandes, F., Lisboa, J., Vandewalle, E., Stalmans, I. Recobrimento de tubos de dispositivos de drenagem com enxertos de córnea/esclera. Reunião Anual da Sociedade Portuguesa de Oftalmologia, Vilamoura 2011.

Organization of Conferences

May 2011 – Organizing Committee (LV Lopes) of the XII Portuguese Society for Neuroscience Meeting

Internationalization

1. As can be concluded from the above description of the research projects, there are several **international collaborations** running in the Unit, with joint manuscripts published or under preparation. A list of the group leaders with whom the Unit presently has active collaborations, can be found in great detail in the Projects section. A list of those with joint papers published in 2011 follows; for details on the publications, see Publication list:

Collaboration with Judith Pratt and Rose Brett (Strathclyde Univ, Glasgow). 1st and senior authorship from the Lisbon group

Collaboration with Sergi Ferre (NIH, Bethesda, USA) and Rafael Franco (Univ Pamplona) and Carmen Lluís (Univ Barcelona) – Both 1st and senior authorship co-shared between Bethesda and Lisbon

Collaboration with Francisco Conti (Ancona, Italy), Rafael Franco (Univ Pamplona) and Carmen Lluís (Univ Barcelona). First and senior authors from the Lisbon group

Collaboration with Eero Castrén (Helsinki Univ) and H. Tanila (Univ Kuopio) – 1st and senior authorship from Kuopio.

Collaboration with Müller CE (Univ Bonn). First and senior authors from the Lisbon group

Collaboration with Ulrik Gether (Univ. Copenhagen). 1st and senior authorship from the Lisbon group

Collaboration with Stalmans I (Univ Livre Bruxelles). First author from the Lisbon group, senior author from Bruxelles

Collaboration with Gether U (Univ Copenhagen). First and senior authors from the Lisbon group

Collaboration with Kussmann M (Nestle Research Center). Review paper with two senior authors, one from the Lisbon group and another from Nestle.

Collaboration with Blum D (Univ INSERM, Lille). Two review papers, involving several senior authors, one as last author.

2. The Unit often **invites foreign speakers** to give seminars/discuss projects/scientific achievements. A list of those invited in 2011 follows:

Christine Gall, Gillespie Neurosci. Res. Facility, University of California Irvine
“Synaptic modulators, actin remodeling, and memory consolidation

Judith Pratt, Strathclyde Institute of Pharmacy and Biomedical Sci, University Strathclyde
”Glutamate dysfunction in schizophrenia: from prefrontal cortex to disrupted networks”

Michael Swash, The Royal London Hospital
“How should we approach ALS?”

Gisele Dias, Universidade Geral do Rio de Janeiro
“Behavioral and neurogenic aspects of an animal model for studying the biological basis of Generalized Anxiety Disorder”

Angela Wyse, Universidade Federal do Rio Grande do Sul, Brasil
“Toxicidade da homocisteína e possíveis estratégias de proteção”

Rosa Chitolina Schetinger, Universidade Federal de Santa Maria, Brasil
“Diabetes and ectonucleotidases in humans and experimental models”

Cecilia Gotti, Institute of Neuroscience, National Research Council of Italy, Milano
“New tools to study the role of native brain alpha6-containing nicotinic receptor subtypes”

Detlev Boison, Legacy Research Institute, Portland, USA
“Homeostatic bioenergetic network regulation: towards a new philosophy to understand and to treat neurological disorders”

3. PIs of the Unit quite often go abroad to **give seminars/discuss projects/scientific achievements**, namely:

A.M. Sebastião to Univ Pamplona and Univ Oxford

LV Lopes to Nestlé Research Center (Lausanne) and to INSERM, Lille

4. It is policy of the Unit to motivate the **PhDs and even Master students to stay abroad** for short periods to learn/use approaches/techniques not available or not routinely implemented at the Unit, and required for their research projects. With this policy the Unit also aims to promote international training of its students. A list of the students short stays abroad during 2011 follows:

Sofia Cristovão-Ferreira to Univ. Trieste, Italy for studies on tonic GABAergic currents (collab with Enrico Cherubini)

Raquel A Dias to Bristol, UK, for studies on AMPA receptor trafficking (collab Jeremy Henley).

Vânia Batalha to INSERM, Lille, for studies on modulation of glucocorticoid receptor expression (collab David Blum)

5. It is policy of the Unit to receive students from other Institutions for collaborative international projects. A list of the students short stays abroad during 2011 follows:

Cyril Laurent and Antoine Leboucher from INSERM, Lille to learn electrophysiological techniques (field recordings of synaptic potentials from hippocampal slices)

Victor Pimentel from Univ Santa Maria, Brasil, to evaluate changes in receptor expression using Western Blot assays

6. The Master and PhD project in Neurosciences, co-coordinated by Unit members, belongs to the **European Network of Neuroscience Schools**.

7. Team members **belong to several Boards**, as follows:

Ribeiro, J.A.- Member of the Editorial Board of the scientific journals:

- Autonomic Neuroscience*
- Pharmacology & Toxicology*
- Purinergic Signalling*
- An R. Acad. Nac. Farm*
- J Caffeine Res*
- Pharmacologia*

Sebastião, A.M.- Member of the Editorial Board of the scientific journals:

- *Journal of Neurochemistry* (Handling Editor)
- *European Journal of Pharmacology*
- *Purinergic Signalling*

Advanced Teaching

Sebastião AM – Co-coordinator and Member of the Scientific Council of the Master and PhD Programmes in Neurosciences, FMUL; organizer of the blocks: ‘Cellular and Molecular Neurosciences’, ‘Neuronal Networks’, ‘Neurodegeneration and Regeneration’,

Ribeiro JA – Organizer of the block ‘Neuroethics’ in the Master and PhD Programmes in Neurosciences, FMUL.

Sebastião AM – Member of the Scientific Council of the Master and PhD programmes in Cognitive Science, UL; organizer of the block: Neurosciences, October-December 2011

- Sebastião AM - Co-coordinator of the Neurochemistry course at the Medical Biochemistry Master, FCUL,
- Lopes LV- Co-coordinator of the Neurochemistry course at the Medical Biochemistry Master, FCUL
- Rita Aroeira, Unidade de Neurociências "Age-related changes of glycine receptor at the rat hippocampus: from the embryo to the adult" January 2011. IMM Neuroscience Seminars
- André Santos, Unidade de Neurociências "Chronic blockade of adenosine A2A receptor impairs the facilitatory effect of Brain-derived neurotrophic factor upon hippocampal LTP" January 2011. IMM Neuroscience Seminars
- Diogo Rombo, Unidade de Neurociências "Synapse-specific purinergic signalling in the hippocampus" February 2011. IMM Neuroscience Seminars
- Júlia Pinho, Unidade de Neurociências "Effect of memantine in aging: impact on hippocampus-dependent memory". IMM Neuroscience Seminars
- Raquel Dias, Unidade de Neurociências "Erythropoietin enhances hippocampal long-term potentiation and memory". IMM Neuroscience Seminars
- Sandra H Vaz, Unidade de Neurociências "Modulation of cholinergic neurotransmission by dopamine-galanin receptors in the rat ventral hippocampus". IMM Neuroscience Seminars
- Cláudia Valente, Unidade de Neurociências "Mapping glycine receptor and glycine transporters in cultured cortical astrocytes". IMM Neuroscience Seminars
- Vânia Batalha, Unidade de Neurociências "Stress and adenosine neuromodulation: from the aging hypothesis to the molecular interaction with GR". IMM Neuroscience Seminars
- Mariana Rocha, Unidade de Neurociências "Is the neuromuscular transmission in the SOD1G93A mice, a model of Amyotrophic Lateral Sclerosis, compromised? What is the role of adenosine in those mice?"
- Joaquim Jacob, Unidade de Neurociências "GABA Uptake and Calcium Signaling in Primary Cultures of Astrocytes: The Role of P2Y Receptors" IMM Neuroscience Seminars
- Andreia Silva, Unidade de Neurociências (UNF), "Calcium signalling modulation in astrocytes by adenosine receptors" October 2011. IMM Neuroscience Seminars
- Ana Filipa Ribeiro, Unidade de Neurociências "The role of adenosine A2A receptor on neuronal outgrowth.". IMM Neuroscience Seminars
- Jorge Valadas, Unidade de Neurociências "Adenosine A2A receptors overexpression in rats: effects on memory. IMM Neuroscience Seminars.
- Sebastião AM – Neuronal organization and neuronal excitability, Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences,
- Sebastião AM – Main molecules involved in neuronal excitability, Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October, 2011
- Sebastião AM – Inhibitory and excitatory synaptic transmission. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October, 2011
- Sebastião AM – Synaptic plasticity, Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October, 2011
- Diogenes MJ – Maintenance of neuronal survival by Neurotrophic factors. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Science, November, 2011
- Rombo D. Evaluation of synaptic activity through electrophysiological recording techniques; modulation of GABAergic currents. Master and PhD Programmes in Neurosciences, October, 2011
- Ana Filipa Ribeiro - Imaging modulation of neuronal outgrowth in cultured neurons. Master and PhD Programmes in Neurosciences, October, 2011
- Cristovão-Ferreira S - GABA transport modulation in nerve terminals and astrocytes. Master and PhD Programmes in Neurosciences, October, 2011

- Ribeiro JA - Cell and molecular mechanisms of drug dependence. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Science, November, 2011
- Lopes LV - Corticoids, stress axis, alterations in synaptic plasticity and in behavior. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Science, November, 2011
- Batalha V - Corticoids, stress and neuromodulation by adenosine. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Science, November, 2011
- Sebastião AM - Major neurotransmitter pathways and their role in the brain function. Master and PhD Programmes in Neurosciences, November, 2011
- Ribeiro JA - Models and main circuits affected in neurodegenerative diseases. Master and PhD Programmes in Neurosciences, November, 2011
- Vaz S - Calcium signalling in astrocytes; implications for neuronal communication. Master and PhD Programmes in Neurosciences, November, 2011
- Valente C – Imaging of single molecules by immunofluorescence. Master and PhD Programmes in Neurosciences, October, 2011
- Jerónimo-Santos A - Beta-Amyloid peptide, neurotrophins and neuronal death. Master and PhD Programmes in Neurosciences, December, 2011
- Aroeira R -Glycine receptors and glycinergic synapses during synapse maturation Master and PhD Programmes in Neurosciences, December, 2011
- Sebastião AM. Neuron and glial cells. Master in Medical Biochemistry, FCUL, February 2011.
- Sebastião AM. Basic rules for the interaction between ligands and receptors Master in Medical Biochemistry, FCUL, February 2011.
- Sebastião AM. Principles of neuronal excitability. Master in Medical Biochemistry, FCUL, March 2011.
- Valente C. Fluorescence microscopy techniques for nervous system research. Master in Medical Biochemistry, FCUL, March 2011.
- Dias RA. Microelectrophysiological Techniques. Master in Medical Biochemistry, FCUL, March 2011.
- Lopes LV. Synaptic transmission, main neurotransmitters and their receptors. Master in Medical Biochemistry, FCUL, April 2011.
- Lopes LV - Signalling pathways, Master in Medical Biochemistry, FCUL, April 2011.
- Dias RA. Synaptic Plasticity. Master in Medical Biochemistry, FCUL, April 2011.
- Sebastião A. Neuromodulation and co-transmission. Master in Medical Biochemistry, FCUL, April 2011.
- Ribeiro. JA. Mechanisms of Drug Addiction. Master in Medical Biochemistry, FCUL, April 2011.
- Diogenes MJ. Neurotrophic Factors Factores neurotróficos. Master in Medical Biochemistry, FCUL, April 2011.
- Cristovão-Ferreira S. Modulation of neurotransmitter transporters by adenosine. Master in Medical Biochemistry, FCUL, April 2011.
- Lopes, LV - Stress, HPA axis and cognition. Master in Medical Biochemistry, FCUL, April 2011.
- Mendonça A. Neurodegenerative Diseases. Master in Medical Biochemistry, FCUL, May 2011.
- Lopes LV. Stem cells, neurogenesis and neuronal repair. Master in Medical Biochemistry, FCUL, May 2011.
- Jerónimo Santos A – Neurotrophic Factors. Master in Medical Biochemistry, FCUL, May 2011.
- Ribeiro JA. Neuroethics. Master in Medical Biochemistry, FCUL, June 2011.
- Lopes LV. Animal models in brain research. Master Programme in Bioethics, FMUL
- Lopes LV. Stem Cells, neurogenesis and neuronal repair. Master in Medical Biochemistry, FCUL, June 2011
- Sebastião AM. Electrophysiological Techniques. Master in Physics, Instituto Superior Técnico, March 2011.

- Diógenes, M. J. Synaptic Plasticity, School of Sciences and Technology; Master on Cell Biology, New University of Lisbon.
- Ribeiro JA. Pharmacotherapy. Master in Cardiovascular Techniques, Escola Superior de Tecnologias da Saúde, January 2011
- Sebastião AM. Pharmacodynamics. Master in Cardiovascular Techniques, Escola Superior de Tecnologias da Saúde, January 2011
- Diogenes MJ. Pharmacokinetics. Master in Cardiovascular Techniques, Escola Superior de Tecnologias da Saúde, January 2011
- Ribeiro, J.A. Lecture on The Toxic effects of Psychopharmacological Agents in the Mastercourse in Legal Medicine and Forensic Sciences, March 2011
- Dias RA Postsynaptic modulation of AMPA receptors by Gs-coupled adenosine A2A receptors: implications for synaptic plasticity. Clinical Neurology Meeting, July, 2011

Science and Society

(1) public lectures or discussions;

- Public lecture and Theatre debate "Blame my Brain" - 18th March - 380 high school students from 7 different schools.
- 9 lectures in public high schools

(2) TV/Radio or Online interviews + date and programme;

TV interview: 9th March - Sic Radical - Curto Circuito

(<http://sic.sapo.pt/sicradical/programas/curto-circuito/videos?videoId={7257DCBF-5E16-46F3-BFBB-757AF949BAAF}>)

TV interview: 16th March - Sic Notícias - Falar Global

(http://www.falarglobal.com/final/videos.htm?cat=corpo_humano&id=232&tipologia=reportagem)

TV interview and IMM report activities - 6th April - RTP2 - Com Ciência

(<http://ww1.rtp.pt/icmblogs/rtp/comciencia/?k=1-parte-do-Com-Ciencia-de-2011-04-06.rtp&post=32377>)

(3) Activities Description

The IMM joined the International Brain Week, promoted in Portugal by the Portuguese Society of Neuroscience and Ciência Viva, and organized several activities during March, as the Facebook initiative *Brain 2.0*, the Open Day to high school students, under the theme *Blame my brain*.

How does the brain work? What is the relation between brain and art?

From February 22 to March 18, *Brain 2.0* challenged people from all ages to share an image related to the brain on the Facebook page of IMM and follow the online comments of researchers and resident artists.

Hands-on activities, brain challenges, live neurons, biological models, theater-debate, were the activities that were waiting for the visitors on the IMM Open Day on March 18, 14h-18h. The aim was to promote the interaction between high school students, teachers and neuroscientists, to motivate young people for the role of neurobiology in behavior and provide a forum for sharing knowledge.

The theater-debate *Blame my brain* was created by high school students and also had the participation of neuroscientists, teachers, health professionals. In addition, all students who developed school projects on neuroscience were invited to propose their presentation.

Thesis completed

PhD Thesis

Sousa VC (2011). Cross-talk mechanisms between adenosine and cannabinoid implications for the effects of Δ^9 -tetrahydrocannabinol on spatial memory. Faculdade Medicina da Universidade de Lisboa. Supervisors: Ana M. Sebastião and Rose Brett.

Dias RA (2011). Modulation of glutamate AMPA receptors by adenosine, in physiology and hypoxic/ischemic conditions. Faculdade Medicina da Universidade de Lisboa. Supervisor: Ana M. Sebastião.

Vaz SH (2011). Regulation of GABA transporter in neuronal cells: role of Brain-Derived Neurotrophic Factor. Faculdade Medicina da Universidade de Lisboa. Supervisor: Ana M. Sebastião.

Fernandes CA (2011). Dynamics and function of nicotinic acetylcholine receptors in the nervous system. Faculdade Medicina da Universidade de Lisboa. Supervisors: A. M. Sebastião and Darwin K. Berg.

Master Thesis

Calçada D (Master in Neurosciences, FMUL). The role of lithium on apoptotic cell death induced by amyloid-Beta peptide. Supervisor: Diogenes MJ, January 2011

Jacob JP (Master in Neurosciences, FMUL). Modulation of γ -aminobutyric acid (GABA) uptake by P2Y1 metabotropic purinergic receptor in rat cortical astrocytes. Supervisors: A. M. Sebastião, December 2011

Pinho J (Master in Neurosciences, FMUL). Effect of Memantine in Aging: the Impact on Hippocampal Dependent Memory. Supervisors: Maria J. Diogenes and Luísa V Lopes, December 2011

Cruz-Silva A (Medical Biochemistry MSc). Calcium signalling modulation in astrocytes by adenosine receptors. Faculty of Sciences, University of Lisbon. Supervisors: Ana M. Sebastião, December 2011

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 & Training and Lab Management. 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 House and Fish, 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.

Management	Margarida Pinto Gago
Lab Management	Alexandra Maralhas
Information Systems	Maria do Carmo-Fonseca
Communication and Training	Marta Agostinho
Bioimaging	José Rino
BioSafety Level Laboratory 3	Miguel Prudêncio
Flow Cytometry	Maria Soares
Animal House	Joana Marques
Zebrafish Facility	Leonor Saúde
Histology Service	Sandra Casimiro
Biobank	João Eurico Fonseca

Management Unit

Major Objectives

The Management Unit is responsible for the overall IMM legal, human resources, administrative, and financial issues. The main areas:

- ✓ Accounts – general accounting and preparation of IMM statutory accounts and tax returns; cost accounting per project/activity;
- ✓ 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 submission to termination;
- ✓ Human resources - new appointments/contracts, individual files, with current issues and registrations.
- ✓ 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 other matters - organizational issues, inter-institutional collaborations, financial and budget management strategy.

Head of Unit

Margarida Pinto Gago, Degree in Management , ISEG-UTL

Team

André Fialho	Lawyer
Cláudia Soeiro	Front desk
Patrícia Cúcio	Board of Directors Secretary
Sandra Duarte	Chief Accountant
Ana Marcelino	Accounts
Joana Filipe dos Reis	Accounts (joined in December)
Ricardo Pereira	Accounts (left in August)
Vera Rego	Accounts
Isabel Roque	Accounts
Diogo Miguel de Sousa Henriques	Accounts
Andreia Vaz	Projects manager
Maria José Antunes	Projects officer
Mónica Vieira	Projects officer
Fábio Joel Andrade de Oliveira	Projects officer
Fernanda Maria Duarte Barbosa	Projects officer

Keywords/Areas

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 the Accounts, responsible for the registrations, wages processing and payments to the staff, social security and tax authorities.

Andreia Vaz was appointed as Project Manager and this fact had a positive impact in the interaction between the two main areas – accounts and projects. The changes in the accounting processes were also a very good contribution to the performance improvement of both areas.

Quality Management System – the first internal audit was carried out in last September and the official internal audit is scheduled for May 2012. The certification audits will follow, aiming to obtain the certification before the end of 2012. This process would not have been possible without the collaboration and pro-activity of the Lab Management Team.

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.

Laboratory Management Unit

Major interests / Objectives

The Laboratory Management Unit is divided in three distinct sections, each with a very specific mission, but all with a common goal: to enhance the *backoffice* work and improve the support to research.

The Washing Room is responsible for the supply of clean and sterilized common material, along with the cleaning and preparation of specific material for the research units, and for the sterilization of solutions, as requested by researchers.

The Purchasing Office is responsible for the Internal Storehouse, reducing the waiting time for the most common materials and for External Orders, centralizing all the Institute acquisitions, either products, services (including import/export) or equipments. Thanks to this centralization, it also provides updated information on prices, ongoing promotions, new products and delivery conditions.

The Lab Management works as advisor and authority regarding safety with products, equipments and installations. 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. The Unit is also responsible for the adequate selection, acquisition and installation of new equipment and the design of (re) new laboratory infrastructures, applying the health and safety practices according to National and International Legislation.

Head of Unit

Alexandra Maralhas - Degree in Biotechnology Engineering, Occupational Health and Safety Technician (Category VI)

Research Team

Rita Soares	Lab Manager Assistant
Alexandre Jesus	Lab Manager Assistant
Sandra Lopes	Purchasing Office
Ana Rita Vicente	Purchasing Office
Fernanda Vila-Chã	Washing Room technician, FMUL
Edna Gomes	Washing Room technician, FMUL
Aida Barros	Washing Room technician (ended Oct 31, 2011)
Carlos Curado	Washing Room technician
Henrique Wesley Camargo	Washing Room technician (started Nov 1, 2011)

Keywords/Research Areas

Infrastructure and equipments maintenance; Health and Safety in Work; Laboratory Design; Purchases

Major scientific achievements

In order to increase the efficiency, while maintaining the high number of deliveries to the research units, the Purchasing Office has changed, in May 2011, the schedule and replaced the existing ordering and delivery system by a digital one.

The preventive maintenance policy that has been followed in the latest years is now giving its rewards, with a faster response time and less downtime of equipments and a greater engagement of all users in the report of situations. This directly relates to an increased optimization of resources and the notion of a major reliability in the equipment of IMM and a better communication with LMN.

We are applying the Health and Safety practices necessary for the Institute with a better awareness of all the research that is being developed. We started training sessions regarding Health and Safety matters, directly focused on the work developed in research laboratories. Also in the Lab Management Meetings we give special importance to information about new equipments, products and technical information concerning daily issues and all sorts of queries.

This year was marked by a strong evolution in the communication between the research support units of IMM and LMN. The Unit was actively involved in all the activities regarding the new Biobank Facility, the move and expansion of the Rodent Facility and the technical assistance to other units, such as, the Bioimaging and Flow Cytometry Units.

Information Systems Unit

Description and Objectives

The Information Systems Unit provides, manages and develops Information Technology Resources in order to facilitate the work of IMM researchers increasing their productivity. It also enforces process compliance with international and internal norms and procedures. The Information Systems Unit is designing and implementing several projects that aim to pursue its main goals. These projects intervene in the areas of 1) Information System Design; 2) Integration of Existing and New Information Systems; 3) Web Site (in collaboration with the Communication and Training Unit); 4) Documentation and Information Workflow; 5) Physical Support (Backups, Storage, Network Reliability, Network Performance, Security); 6) Knowledge Management. Support to IMM researchers includes the provision of a help-desk support service. A help-desk team is scheduled in order to respond all working days of the year. This help-desk team receives all help requests from the users, and acts as their only contact. If necessary, the help-desk team works in cooperation with the Information Technology Unit of the Medicine Faculty of Lisbon. In 2012, the projects will mainly focus on IMM Infra-Structure, and on Enterprise Solutions for IMM Information Systems.

Head of Unit

Maria do Carmo Fonseca, PhD – Full Professor, FMUL

Research Team

Tito Santos Silva, PhD	IT Consultant
Daniel Silva	PhD Fellowship, IMM
Pedro Eleutério	IT Technician, IMM
Daniel Guerreiro	Training Fellowship, IMM
Emanuela Simões	Training Fellowship, IMM

Keywords/Service Areas

Information Systems, Databases, Computer Network maintenance, Helpdesk

Major achievements

A high-performance bioinformatics computing server was implemented for Morphogenesis Unit. Another high performance computing server, for Deep Base Sequencing, was configured and deployed at Hospital de Santa Maria Data center.

Ongoing Projects

Web-based Human Resources maintenance page. This project aims to substantially decrease paper with registration of new IMM members, as well as with annual revision of IMM member's information. It also aims to automate these processes, standardise data, prevent data loss, potentiate fast search for IMM staff data, and feed IMM webpage with people's data. (no funding)

Communication and Training Unit

The Communication and Training Unit (UCOM) is a transversal unit that aims to work with the IMM community as a whole to help establish the IMM as a leading biomedical research institute in Europe. UCOM is based in three main areas – Communication, Funding and Advanced Training.

We act at three different levels. We aim at meeting the needs of IMM researchers by providing support in different areas, from communication to funding, training, and other. We are active players in the strategic mission of the institute. For that, we work closely with IMM Direction and with external and internal stakeholders. Finally, we aim at becoming a reference in each of our areas of action, producing new knowledge, creating standards and best practices.

Head of Unit

Marta Agostinho, PhD – University of Lisbon, Staff Scientist 2008

Team

Margarida Trindade, PhD	Pre-award Funding Coordinator, Staff Scientist Ciência 2007
Inês Crisóstomo, PhD	Advanced Training Coordinator, Staff Scientist Ciência 2008
Joana Costa, PhD	Pre-award Funding Assistant, BGCT Fellowship , FCT
Ana Catarina Rebelo	Communication Assistant, IMM Fellowship
Sandra Moreira	Communication Assistant, IMM Fellowship

Keywords

Institutional Communication, Science Communication, Advanced Training, Pre-award Funding

Major achievements

Communication

We produced materials that promote the corporate image of IMM (leaflet, bookmarks, brochures, media portfolio, folders), and consolidated IMM presence in the social networks and the national press. We started placing releases at international settings in a regular basis and diversified formats for IMM researchers' media training.

We focused in fostering collaborations with decision makers and media (TRIOS project); patients associations (proposal to HMS-PT with Rarissimas); and clinicians (Oncobiology project).

We pursued an active role in science policy by participating in national and international initiatives (e.g. FEBS Science & Society/Science Policy Committee, European public consultations, opinion articles at IN IMM) and by launching a FCT-funded research-action project to develop the professional relationships between the scientific, political and media communities in Portugal (TRIOS project), in collaboration with CES/UC and IBMC/UP.

Funding

We provided funding information through the weekly newsletter (Tip of the Week), on-line resources (12), information sessions (3), workshops (2) and individual or group meetings (40). We have resized our funding opportunities database according to UCOM's human resources availability.

Of the 203 IMM applications registered, we provided support to 37 international and 150 national grant applications, a substantial increase from the previous year. We have intensified the support to international applications (ERC, Marie Curie, other European) and researchers responded positively. We concluded 11 international and 34 national funding contracts.

We registered the IMM at relevant platforms (NIH, Fit for Health); we submitted and successfully obtained an accreditation for the IMM to supply R&D services in QREN funded projects.

According to our internal monitoring, the number of IMM international applications increased constantly since 2008, whereas IMM researchers applied to a progressively larger range of international funding sources.

Advanced Training

A major achievement was the establishment of the CAML PhD programme, which is fully running in close articulation with FMUL. We are responsible for the executive coordination of the program.

We started to develop knowledge in biomedical education for clinical and non-clinical professionals: we secured funding from the Harvard Medical School Portugal Programme for a medical e-training project in Oncology to develop educational tools for physicians; and coordinated and submitted an application for a Master in Oncology, under the CAML.

Recent Most Relevant Publications

Xavier, J. Nelson, S., Agostinho, M., Almeida, C. and Domingues, I. "Jornalismo de ciência em Portugal: esperança para o futuro?", *Jornalismo e Jornalistas*, nº45 Jan/Mar 2011 (opinion article)

Ongoing Projects

2010/2014 MEMPEPACROSS - Membrane-active peptides across disciplines and continents: An integrated approach to find new strategies to fight bacteria, dengue virus and neurodegeneration, European Commission. PI: Nuno Santos, IMM; Participants: Marta Agostinho and Margarida Trindade. FP7-PEOPLE-2009-IRSES, €73800 for IMM (total €181800)

2011/2013 Oncobiology: developing educational tools for a new generation of physician-scientists, Harvard Medical School – Portugal Program. PI: Inês Crisóstomo; Participant: Marta Agostinho HMSP-PCM/0007/2010, €99000

TRIOS Project: Individual pos doc fellowship FCT - DFRH - Bolsa SFRH/BPD/80627/2011. PI: Marta Agostinho

Invited Lectures and Seminars

Agostinho, M. invited *rapporteur* at the panel “Media” at the science communication meeting SciCom Portugal, Lisbon, April 8, 2011

Agostinho, M. invited lecturer at the session/workshop for preparation of proposal for the FP7 health and Science in Society, Lisbon, June 3, 2011

Agostinho, M. “Comunicação de ciência a partir de um instituto de investigação: desafios e oportunidades”, September 20, Instituto de Física da Universidade de S. Paulo, Brazil, 2011

Agostinho, M. “Comunicação de ciência a partir de um instituto biomédico: o exemplo do Instituto de Medicina Molecular”, September 20, Instituto de Ciências Biomédicas da Universidade de S. Paulo, Brazil, 2011

Agostinho, M. “Comunicação de ciência em Portugal: o exemplo de um instituto de investigação”, September 20, UNESP – Universidade Adventista de S. Paulo, Brazil, 2011

Agostinho, M. invited speaker on the “1º Encontro Nacional de Bioquímicos” organized by ANBIOQ, “Bioquímica e Sociedade: promoção ou comunicação?”, Leiria, November 27, 2011

Trindade, M., “Meeting the requirements of external agencies: bottlenecks in research management”, European Parliament, Room Jazsef Antall, Brussels, June 15, 2011

Trindade, M., “Captação de fundos externos – perspectiva de um instituto biomédico em Portugal”, Instituto Isrealita de Pesquisa Albert Einstein, September 21, São Paulo, Brazil, 2011

Trindade, M., panel member on session on “Science Networks”, Gammeets 2011 Meeting, Instituto Gulbenkian Ciência, December 27, Oeiras, Portugal

Communications in International Conferences

Trindade, M., Professional Training in Research Management, 17th EARMA Conference, June 22-24, 2011, Bragança (oral presentation)

Organisation of Conferences

Crisóstomo, I., organization of V PhD Meeting IMM/CAML, Lisboa, October 17-18, 2011

Trindade, M., Vidal, S., organizers of the session on Professional Development of Research Managers at the 17th EARMA Conference “Grand Challenges in Research Management and Administration in Europe”, Bragança, June 22-24, 2011

Trindade, M., organization of session “Research of Excellence at the European Parliament – a day with IMM” at the European Parliament on, June 15, 2011 (host: Maria Graça Carvalho, MEP)

Trindade, M., Costa, J., logistic organization of the workshop “Emerging tools in quantitative fluorescence microscopy for systems biology” in collaboration with Inserm, IMM, September 4-10, 2011

Internationalization

Marta Agostinho is involved in outreach initiatives from FEBS (the Federation of the Societies of Biochemistry), where she is an elected member of the Science and Society Committee. M. Agostinho has acted as an evaluator of FP7 call in Science Communication (FP7-KBBE-2011-5 Activity 2.4), in March-April

In 2011, as part of an on-going collaboration with Mauricio Luz under the MEMPEPACROSS project (FP7-PEOPLE-2009-IRSES) M. Agostinho and M. Trindade hosted Mauricio Luz at IMM in June 2011 and visited several research institutions in Rio de Janeiro and S. Paulo in September-October 2011. There, they delivered training, as an extension to a complementary skills training programme that was recently developed by UCOM, and gave several institutional lectures. As a result of this collaboration, Agostinho, M. supervised the internship of a PhD student (Carlos Teixeira) from Universidade de S. Paulo at IMM (Dec 16, 2011- Jan 26, 2012).

Agostinho, M. hosted H. Peter Peters IMM seminar, on Societal contextualization of neuroscience by public communication: a research agenda and first results, May, 3

M. Trindade attended the 17th EARMA Conference “*Grand Challenges in Research Management and Administration in Europe*” in **Bragança**, June 22-24, 2011, where she co-organized a session on Professional Development of Research Managers. She is also currently a member of this association.

Advanced Teaching

Agostinho, M., lecturer of “Science Communication in Portugal” and “Media Training session” at the course “Ethics, Science & Society”, GABBA - Graduate Program in Areas of Basic and Applied Biology, January 12, Porto

Agostinho, M., lecture “Comunicar ciência para diferentes públicos”, Pos-graduation programme in Public Health, Faculdade de Saúde Pública, Universidade de S. Paulo, September 21, São Paulo, Brazil

Agostinho, M., lecture “Comunicação de ciência e saúde pública: pontes entre investigação e acção”, Pos-graduation programme in Public Health, Faculdade de Saúde Pública, Universidade de S. Paulo, September 21, São Paulo, Brazil

Agostinho, M. organizer and lecturer at course “Comunicar ciência para diferentes públicos”, Instituto Oswaldo Cruz, September 26-30, Rio de Janeiro, Brazil

Agostinho, M. organizer and lecturer at course “Curso de preparação para os média para pos docs e *PIs*”, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, November, 17-18, Lisbon

Agostinho, M. establishment of a collaboration agreement with Universidade Nova de Lisboa to receive Master Students in the UNL Masters in Science Communication (starting in 2012)

Agostinho, M. coordinated the FincaPé Meetings, a series of science communication and science management meetings for professionals of the Lisbon metropolitan area, held every two month since April 2010

Crisóstomo, I. coordinated and submitted an application to the Agency for the Evaluation and Accreditation of Higher Education (A3ES) for a *Master in Oncology*

Crisóstomo, I. organized the recruitment of IMM candidate (Sara Gonçalves) and coached her during the application for a Poste d'Accueil

Crisóstomo, I. prepared a proposal to Fundação Oriente for a joint PhD Programme between IMM and a Chinese University (Macau, Cantão)

Crisóstomo, I. coached PhD students of the CAML PhD Programme, including recruitment of prospective candidates, organization of thesis committees, annual renewals, thesis submission (imprimaturs), solving issues with FCT fellowships and conflict management

Crisóstomo, I., co-organization of student's Seminar Series (Pizza Seminars), IMM

Crisóstomo, I., logistic co-organization of Advanced Courses of the CAML PhD Programme

Crisóstomo, I. organization of *Summer internships (Bes-up)*: IMM hosted 1 student in the summer of 2011

Moreira, S. lecture "O Online e a comunicação não mediada" at course "Curso de preparação para os média para pos docs e *PIs*", Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, November, 17-18, Lisbon

Trindade, M. co-organizer of course and lecturer of "Preparing for Research" at the Doctoral Programme for Physicians of Fundação Calouste Gulbenkian (PMFA), February 24-25, IMM

Trindade, M., Agostinho, M., Crisóstomo, I. organizers and lecturers of course "Launching your research career", PhD Programme of the Centro Académico de Medicina de Lisboa, May 30-June 1, IMM

Trindade, M., Vidal, S. organizers and lecturers of course "Getting funded in biomedical research", PhD Programme of the Faculdade de Ciências Médicas da Universidade Nova de Lisboa, June, 3-4, 17-18 Lisbon

Trindade, M. lecturer of "Applying for grants", Instituto Isrealita de Pesquisa Albert Einstein, September 21, São Paulo, Brazil

Trindade, M. organizer and lecturer of course "Perspectivas de financiamento em pesquisa biomédica", Instituto Oswaldo Cruz, September 26-30, Rio de Janeiro, Brazil

Trindade, M., Caldeira, S., Vidal, S. organizers and lecturers at course "Writing up your research to get funded and publish", Master on Clinical Research of the Faculdade de Ciências Médicas da Universidade Nova de Lisboa, October 21-22, 28-29, November 4-5, Lisbon

Science and Society

Agostinho, M., issued 4 international and 12 national press releases, plus 4 specific contacts; diversified media coaching to researchers (courses, one-to-one, press kits)

Agostinho, M., Moreira, S., supported more than 80 press visits, maintained media contacts, *negotiated* contract for clipping service; maintained clipping data base and archives (>760 entries and documents)

Agostinho, M., Moreira, S., followed up institutional contacts by email: deliver and reply to contacts through external IMM email (uncountable) and website contact us (> 66 conversations)

Agostinho, M., supervised the artistic residency of Herwig Turk (video and installation), IMM, 2011

Agostinho, M., organized the visit of the Duchess of Cornwall with APOROS, IMM, March 29, 2011

Agostinho, M., participated at the organization of the event 100 years of FMUL, IMM, 2011

Agostinho, M. undertook a communication/education expertise exchange in IRSES FP7 project: follow up of Bioquímica de Portas abertas; establishment of the partnership “Células Adentro” for Secondary schools, hosting Mauricio Luz at IMM, June 2011

Agostinho, M., hosted the visit of the Secretary of State of Angola to FMUL and IMM, November, 2011

Costa, J., organized the visit of Raríssimas Association, IMM, September 26, 2011

Moreira, S., Rebelo, A.C. supported the artistic residency of Maria Manuela Lopes (video and installation), IMM, 2011 and organized 2 *work in progress* exhibitions, IMM, 2011

Moreira, S. setup *Web 2.0 – Social networks Facebook and Twitter* platforms (design graphic elements, programming in HTML), research and content production (until Nov 15: Twitter 108 posts; Facebook 142 posts; develop new features (e.g. IMM papers @ facebook)); continuous management of interactions

Moreira, S., Agostinho, M. delivered the campaign *Pedalar contra o cancro*: conception of the communication campaign (partnership with Liga Portuguesa Contra o Cancro), content and image production, media management; March-May 2011

Moreira, S., Agostinho, M., delivered the campaign *Cérebro 2.0*: see Science education programme March 2011

Moreira, S., Agostinho, M., delivered the *IMM School visits programme* (total 88 students + 4 teachers), 2011

Moreira, S., Agostinho, M., co-organized the day at IMM with neurosciences units (hands-on, debates and theatre) and coordination of *Cérebro 2.0* (2 week online activity), as part of the *Brain awareness week*: at IMM total 120 students.

Moreira, S., organized the *Summer internships Ciência Viva*: internal dissemination, budget and proposal preparation, follow up reports for 5 internships

Moreira, S., Rebelo, A.C. produced materials and delivered stand representation for the Semana das inscrições FMUL, IMM, September 2011

Moreira, S., Agostinho, M., organized the training session for L’Oreal on biology of the skin, September 5, 2011

Moreira, S., Rebelo, A.C. supported researcher participating at Health Cluster Portugal Meeting, September, 2011 and started IMM content management at the HCP web platform.

Rebelo, A.C. performed website updates (640 pages produced); trained and supported editor-users (40 editors)

Rebelo, A. C.Agostinho, M., managed 12 mailing lists with over 3800 contacts. Until Nov 15: 270 external email disseminations, internal Emailing (252 emails), production of 46 internal newsletter IN IMM and posters, Monitoring of In IMM Newsletter (questionnaire to IMM collaborators) and reformulation of IN IMM, Jun-July

Rebelo, A.C., participated in the organization of the “Dia do candidato FMUL”, IMM, April 2011

Trindade, M., hosted the session “Ensaaios Clínicos: da Molécula ao Medicamento” for patients associations, promoted by Apifarma, Bayer and Merck Sharp & Dome, IMM, April 19, 2011

Trindade, M., organization meetings with researchers and Rob Pinnock, Licensing Officer from Merck Sharp & Dome, March 21

Trindade, M., organized and hosted visit of Clive Wood, Senior Vice President and Head, Global Biologics at Bayer HealthCare AG, May 13

Other

UCOM participated in a series of institutional processes such as the production of annual reports (activity report IMM, FCT report, FCT projecto estratégico), preparation of institutional texts and profiles, the support to the preparation of Scientific Advisory Committees, the organization of PI and student Retreats and contributed to the IMM *Quality Certification System*. We have also concluded a series of monitoring processes such as on IMM funding applications, IMM presence in the media, consultation of IMM website and social networks, PhD Programme, Advanced Courses, IMM programme of school visits/educational activities.

Rodent Facility

Major interests / Objectives

The IMM Rodent Facility has two main units: one **conventional facility** and one **SPF facility**. The **conventional facility** started in 2003 as a small set of 4 rooms with the total capacity to house 1200 animals. During the autumn of 2011 this unit has been remodelled and has the capacity to house 7500 mice and rats.

The **SPF facility** has the capacity to host 10000 mice and rats, and includes two different housing areas: Production area and Experimental area. In the experimental area, there are three rooms for experimental work with animals: two procedure room and one surgical suite.

All husbandry and manipulation procedures 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, training, and guidance** for researchers, according to the Portuguese and international laws/recommendations for good practices and animal welfare.

Head of Unit

Joana Marques, PhD

Research Team

Dolores Bonaparte	Veterinarian, IMM
Iolanda Moreira	Technician / colony manager, IMM
Alina Costa	Manager (left in July 2011)
Joel Filipe	Technician (left in September 2011)
Raquel Matos	Technician (left in August 2011)
Carlos Barata Silva	Technician / colony manager, IMM
Cecília Simão	Animal caretaker, IMM
Felícia Ramos	Animal caretaker, IMM
José Vila Chã	Animal caretaker, IMM
Nuno Inácio	Animal caretaker, IMM
Olena Pinho	Animal caretaker, IMM
Wilma Zovo	Animal Caretaker, IMM

Keywords/Research Areas

Rodent Facility, mice, rats,

Major scientific achievements

The conventional unit of the rodent facility started in 2003 as a set of 4 small rooms. It had the total capacity for housing 1200 animals and was located at the Sta Maria Hospital.

During the Autumn of 2011, this unit was transferred to the Egas Moniz Building, to a space that was remodelled to be able to accommodate it. With those changes, this conventional facility has now the capacity to house 7500 mice and rats. It also has an infection room, which allows researchers to carry out research with experimental infection, using biological agents that were not authorized in the other areas of the facility, due to the risk of contaminations.

The SPF unit, which started its activity during summer of 2010, was further equipped, with its production area now reaching about 70% occupation.

One of the major achievements of 2011 was the training of the facility staff. For the first time at IMM a course in Laboratory Animal Science specific for animal caretakers was organized, giving our team the adequate knowledge to perform a high quality work. A course for researchers was also organized, allowing a considerable amount of researchers to obtain their pending DGV licenses.

Invited Lectures and Seminars

Marques, JM, Animal experimentation. Scientific integrity and Ethics (MSc program in Bioethics) Faculdade de Medicina, Universidade de Lisboa. February 17, 2011

Marques, JM. Animal Welfare and Scientific validity. Theoretical course in laboratory animal science. Instituto Gulbenkian de Ciência. November 15, 2011.

Marques, JM. Rodent behavior and environment. I Congress of Animal Behaviour and welfare therapy. Lisboa. December 18, 2011.

Advanced teaching

Marques, JM. Organized and lectured the course in Laboratory Animal Science (cat. B). Instituto de Medicina Molecular, Lisboa. 28/03 – 01/04; 11 – 13 / 04 2011.

BioImaging Unit

Major interests / Objectives

The BioImaging Unit constitutes the core microscopy facility of the IMM, serving as a support structure to carry out and nurture research done with Light Microscopy inside the institute. We aim at providing IMM scientists and visitors with excellence in scientific know-how and expertise in using advanced light microscopy methods for their research. We assist in project planning, experiment design, provide advice and support on sample preparation, image analysis and processing and in writing research papers with microscopy data. Together with continuous training of new users, we organize regular courses and workshops on basic and advanced microscopy techniques. We research novel microscopy techniques for detecting protein-protein interactions and measuring protein dynamics in collaboration with research units with challenging biological problems.

Head of Unit

José Rino, PhD in Biophysics – Faculdade de Ciências da Universidade de Lisboa

Research Team

António Temudo	Research Technician, IMM
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Keywords/Research Areas

Fluorescence Microscopy; Laser Scanning Confocal Microscopy; Image Processing and Analysis; Quantification of protein dynamics and interactions

Major scientific achievements

José Rino organized the Phase 2 (technical workshop) of the INSERM *Atelier de formation 210* “Emerging tools in quantitative fluorescence microscopy for systems biology”, which took place at IMM from 7 to 10 September 2011. The four-day event included introductory lectures and hands-on laboratory exercises on image acquisition and image processing and was attended by 12 trainees from Portugal, France, the Netherlands and Switzerland, selected among Phase 1 participants.

Scientific collaboration with 2 IMM units and 1 research group from Instituto Tecnológico e Nuclear resulted in 3 publications where live imaging microscopy was used to study the coupling between spliceosome assembly and RNA Pol II transcription dynamics (*Martins SB, Rino J et al, Nat Struct Mol Biol, 2011*), nuclear targeting of (99m)Tc bioconjugates with potential therapeutic applications (*Esteves T et al, J Biol Inorg Chem, 2011*) and VEGFR2 nuclear translocation and self-regulated transcription (*Domingues I et al, PLoS One, 2011*).

In 2011 the BioImaging Unit services were used by 192 users from 36 different research units (8 of them from outside the IMM), which corresponds to an increase of 12 % in the total number of users relative to 2009. We trained 71 new users in different microscopy systems during the year.

Recent Most Relevant Publications

Martins SB*, Rino J*, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M. (2011) “Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3’ end of human genes”. *Nat Struct Mol Biol*, 18(10):1115-23. * These authors contributed equally to this work (Journal IF: 13.69)

Ongoing Research Projects

Participation in projects from other units:

2010/2012 Transcription-coupled mechanisms of gene regulation (FCT- PTDC/BIA-BCM/101575/2008) Team Member: J. Rino, PI: Maria Carmo-Fonseca, €199 350

2010/2012 Function of Integrins in Drosophila Haemocyte Migration (PTDC/SAU-OBD/101259/2008) Team Member: J. Rino, PI: Soren Prag, €120 000

2011/2014 Splicing-coupled mechanisms of chromatin remodelling and their global role in transcription (PTDC/BIA-BCM/111451/2009) Team Member: J. Rino, PI: Sérgio de Almeida, €141 967

Publications in peer review Journals

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(9):e25668 (Journal IF: 4.351)

Martins SB*, Rino J*, Carvalho T, Carvalho C, Yoshida M, Klose JM, de Almeida SF, Carmo-Fonseca M. (2011) “Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3’ end of human genes”. *Nat Struct Mol Biol*, 18(10):1115-23. * These authors contributed equally to this work (Journal IF: 13.69)

Esteves T, Marques F, Paulo A, Rino J, Nanda P, Smith CJ, Santos I. (2011) “Nuclear targeting with cell-specific multifunctional tricarbonyl M(I) (M is Re, (99m)Tc) complexes: synthesis, characterization, and cell studies”. *J Biol Inorg Chem* 16(8):1141-53 (Journal IF: 3.287)

Invited Lectures and Seminars

Rino J, Live-cell imaging of mRNA biogenesis reveals coupling between splicing and RNA Polymerase II dynamics at the transcription site, Microscopy at the Frontiers of Science 2011, 2nd Joint Congress of the Portuguese and Spanish Microscopy Societies, Aveiro, Portugal, October 19, 2011

Rino J, Quantificação de mobilidade e interações de proteínas dentro de células vivas por microscopia confocal, Seminar at Faculdade de Medicina Veterinária, Lisboa, Portugal, June 3, 2011

Rino J, Splicing e Microscopia, 1º Encontro de Biologia Molecular em Saúde, Escola Superior de Saúde Egas Moniz, Almada, Portugal, March 18, 2011

Communications in International Conferences

Rino J et al. “Live-cell imaging of pre-mRNA processing and RNA Polymerase II dynamics” Eurasnet Meeting on Alternative Splicing Granada, Spain. February 28-March3, 2011. Poster communication

Internationalization

José Rino organized the Phase 2 (technical workshop) of the INSERM *Atelier de formation 210* “Emerging tools in quantitative fluorescence microscopy for systems biology”, which took place at IMM from 7 to 10 September 2011. The four-day event included introductory lectures and hands-on laboratory exercises on image acquisition and image processing and was attended by 12 trainees from Portugal, France, the Netherlands and Switzerland, selected among Phase 1 participants.

Advanced teaching

Rino, J. lectured on “Quantitative Microscopy” at the Workshop “Introduction to Microscopy Fundamentals “, IGC, Oeiras, Portugal, December 13, 2011

Rino, J. lectured on “Cellular Protein Dynamics” at the PIBS Tech Week Workshop for the IGC PhD Programme in Integrative Biomedical Sciences, Oeiras, Portugal, December 8, 2011

Rino J organized and lectured at the BioImaging Nanocourse on Microscopy 2011, IMM, Lisboa, Portugal, December 5 – 6, 2011

Temudo, A. lectured at the BioImaging Nanocourse on Microscopy 2011, IMM, Lisboa, Portugal, December 5 – 6, 2011

Rino, J. organized and lectured at the INSERM Workshop Phase 2 - “Emerging tools in quantitative fluorescence microscopy for systems biology”, September 7 - 10, 2011, IMM, Lisboa, Portugal

Temudo, A. lectured the practical teaching for the INSERM Workshop Phase 2 - “Emerging tools in quantitative fluorescence microscopy for systems biology”, September 7 - 10, 2011, IMM, Lisboa, Portugal

Science and Society

Rino J, Um novo habitat para Físicos: o laboratório de Biologia Celular, Workshop Física iLimitada, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal, May 20, 2011

BioSafety Level 3 Facility

Major interests / Objectives

The IMM houses a 70 m² BSL3 Facility meeting the highest safety standards as defined by European and International guidelines. Work to be carried out in this Facility includes all experimental procedures biosafety level 3 pathogens. The Facility is available to IMM internal and affiliated researchers, as well as to external researchers from academia, pharma and biotech. The Facility provides education, training, and guidance for researchers and is constantly monitored by a fully dedicated technical supervisor. Applications to use the IMM's BSL3 laboratories are reviewed and must be approved by the Facility's supervisor and Scientific Commission before access is granted.

Head of Unit

Miguel Prudêncio, PhD – Principal Investigator, IMM

Research Team

Inês Matos	Technician, IMM
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Keywords/Research Areas

Mycobacterium tuberculosis, HIV, Biosafety Level 3, Containment, ABSL3

Major scientific achievements

The IMM BSL3 Facility is now fully operational, for work with both non-airborne and airborne pathogens, as well as for procedures involving animal models. Standard operation procedures were updated to meet the highest safety standards in accordance to users' suggestions. A 2-day course on level 3 biosafety practices and specific aspects of operations in the IMM BSL3 Facility was held for all new Facility users. The Facility was publicly advertised for use by non-IMM researchers. An occupational health protocol was established and implemented in collaboration with Hospital Santa Maria.

Invited Lectures and Seminars

M. Prudêncio participated as a session chair in the 14th Meeting of the European BioSafety Association, April 2011, Estoril, Portugal.

M. Prudêncio attended the Workshop "BSO BSL3" of the Curriculum Biosafety, October 2011, Mittelhausern, Switzerland.

M. Prudêncio participated in the Workshop “Biossegurança: Situação em Portugal”, held at Instituto Nacional de Saúde Dr. Ricardo Jorge, November 2011, Lisboa, Portugal.

M. Prudêncio lectured at the “Biossegurança em laboratórios de nível 2 e 3” held at Instituto Nacional de Saúde Dr. Ricardo Jorge, December 2011, Lisboa, Portugal

Advanced teaching

Prudêncio , M. organised the course “Biosafety training for use of the IMM BSL3 Facility”, 2-3 February 2011, Instituto de Medicina Molecular, Lisboa, Portugal

M. Prudêncio lectured at the “Biossegurança em laboratórios de nível 2 e 3” held at Instituto Nacional de Saúde Dr. Ricardo Jorge, Dez 2011, Lisboa, Portugal.

Flow Cytometry Unit

Objectives

The Flow Cytometry Unit provides support and training in flow cytometry to IMM and external users. This training takes place on an individual basis or through workshops. We provide support in experiment planning, instrument operation, data analysis and interpretation. In addition, the 2 High Speed Cell Sorters, operated by our staff, allow us to provide a cell purification service. In 2011 UCF users comprise a total of 31 Units, representing a total of 152 researchers. An additional component of our work is to ensure adequate quality control and maintenance on all instruments. As an IMM facility, UCF has been implementing the Quality Management System, according to ISO 900.

UCF staff are also involved in research projects that keep them up to date with new advances in the technology.

Head of Unit

Maria Soares, PhD, University College London, London, UK

Team

Maria Soares, PhD	Head of Unit
Ana Luísa Caetano	Technician, FMUL (left in September 2011)
Ana Isabel Pinto	Technician
Ana Isabel Vieira	Technician (since November 2011)

Keywords

Flow Cytometry, High Speed Cell Sorting

Major achievements

In 2011 UCF underwent a significant upgrade with the acquisition of the Cell Sorter FACSria III and two analysers, the LSR Fortessa. The new FACSria became fully operational in January 2011 and the number of hours of cell sorting increased by 75% as compared to 2010. This was substantial improvement to IMM researchers who can now benefit from more hours of sorting per day as well different laser configurations, allowing an increased level of flexibility in fluorochrome detection.

In 2010 the Unit was equipped with analysers that could detect either 4 colours or 6 colours. By detecting up to 8 colours, the new Fortessa have increased the quality of the work developed at the IMM and have the potential to be further upgraded through the addition of more lasers. The Fortessa became fully operational in February 2011 and analyser usage has increased by 12%,

with the LSR Fortessa overtaking the Calibur usage by 20%. During 2011 our staff trained a total of 107 users in instrument operation.

Ongoing Research Projects

2008/2011 Immune Reconstitution after Unrelated and Haplotype-Mismatched Stem Cell Transplantation, FCT. Coordinator: Maria Soares (PTDC/SAU-MII/67662/2006). €122.986

Participation in projects from other Units:

2007/2011, Maria Soares: participant in the project "HIV-2 infection and thymus", FCT. Coordinator: Ana E. Sousa (PTDC/SAU-MII/66248/2006) €136.621

2009/2012, Maria Soares: participant in the project "Long-term impact of thymectomy performed in early infancy", (PIC/IC/83068/2007) €75.000

2009/2012, Maria Soares and Ana Luísa Caetano participants in the project "Clinical implications of activation of PI3K/Akt signaling pathway in primary adult acute lymphoblastic leukemia", FCT. Coordinator: João F. Lacerda (PIC/IC/83023/2007) €134.000

2011/2014 Maria Soares: participant in the project HIV/AIDS: contribute of naïve CD4 T cell homeostasis FCT Coordinator: Ana E. Sousa (PTDC/SAU-MIC/109786/2009) €159.694,00.

Publications in peer review Journals

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. (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*. **132**(3):326-339. (Journal IF: 3.3 Citations: 4)

Di Mitri D, Azevedo RI, Henson SM, Libri V, Riddell NE, Macaulay R, Kipling D, Soares MV, Battistini L, Akbar AN. (2011) "Reversible senescence in human CD4+CD45RA+CD27- memory T cells". *J Immunol.*; **187**(5):2093-100. (Journal IF: 5.7)

Rodriguez-Nieto S, Cañada A, Pros E, Pinto AI, Torres-Lanzas J, Lopez-Rios F, Sanchez-Verde L, Pisano DG, Sanchez-Cespedes M. Source (2011) "Massive parallel DNA pyrosequencing analysis of the tumor suppressor BRG1/SMARCA4 in lung primary tumors." *Hum Mutat*. **32**(2):E1999-2017 (Journal IF: 5.9, Citations: 2)

Invited Lectures and Seminars

Soares, M. "A citometria de Fluxo aplicada á investigação", IX Congresso Anual de Análises Clínicas e Saúde Pública organizado pela Sociedade Portuguesa dos BioAnalistas Clínicos (SPBS), Almada, Lisboa, Portugal November 25 and 26 2011

Communications in National Conferences

Iris Caramalho, Vânia Nunes-Silva, Ana Rita Pires, Ana Isabel Pinto, Catarina Mota, Helena Nunes-Cabaço and Ana E. Sousa "Impact of common-gamma chain cytokines on human thymic regulatory T cell development" XXXVII SPI Annual Meeting Novembro de 2011, Instituto Gylbenkian de Ciência, Oeiras, Portugal (Poster Presentation)

Advanced teaching

Soares, M. lectured at the "8th Master Course in Infectious diseases, Lectures entitled "Immaturity and Senescence in the Immune System" and "An Introduction to basic concepts in Flow Cytometry" IMM Lisbon January 3rd 2011

The Flow cytometry Unit hosted a visit from students from Universidade Atlântida, 11th May 2011 where Ana Caetano introduced the technique, its applications and the instruments available at IMM UCF.

Between the 10th and the 27th of January 2011 UCF organized in conjunction with Enzifarma a series of training sessions for the new LSR Fortessa. These included theoretical modules on FACSDiva (the software) and practical modules on the instruments. A total of 9 mini courses were performed where users were divided according to their previous expertise. A total of 35 users were trained at this initial stage.

In addition, throughout the year of 2011 our staff trained 72 new users on one to one sessions.

February 8th 2011 Maria Soares hosted a FlowJo Training Course provided by H       Dujardin, Application Scientist, Celeza GmbH.

Ph.D. thesis completed

Rita Isabel Silva de Azevedo (2011) The role of IL-7 in the Homeostasis of Human Naive and Memory CD4⁺ T cell subsets. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Maria Soares

Histology Service

Major interests / Objectives

Starting on September 09, the Histology Service was implemented in IMM, resulting from collaboration with the Histology Institute of FMUL. The Histology Service has a permanent technician, and is located in the Histology facilities of the Histology Institute of FMUL.

The main objectives of the Histology Service are: processing tissue samples for routine histochemical procedures; processing and visualization of samples for Transmission Electron Microscopy (in collaboration with the Instituto Gulbenkian de Ciência); processing of samples for Laser Capture Microdissection; training new users in sample preparation and analysis with the available equipment in the laboratory; and provide tutorship in the design and implementation of immunostaining and other procedures not performed in the Service.

Head of Unit

Sandra Casimiro, PhD – Post-Doc Researcher, IMM

Research Team

Afonso Fernandes, MD, PhD	Medical Pathologist, IMM
Andreia Pinto	Technician, IMM

Keywords/Research Areas

Histopathology, immunohistochemistry, tissue processing, microscopy

Major scientific achievements

The implementation of the Histology Service (HS) represents a major achievement in IMM. A survey conducted in the beginning of 2009 indicated that most research Units considered necessary to have this facility available in-house. In fact, since the HS implementation a total of 22 IMM research Units have used the available services in a regular basis. The HS also provides services for five external users, including biotech companies and hospitals. Researcher's formation in standard procedures had also a high demand in previous years and training and tutorship maintained as one of our main goals in 2011. It is also our purpose to implement new services according to the needs of the IMM Research Units. In 2011 we upgraded our services in Transmission Electron Microscopy (TEM), by establishing a new collaboration with Hospital Amadora-Sintra for visualization of samples, and maintained our collaboration with Instituto Gulbenkian de Ciência, offering now two different equipments to our users. In the last year we also implemented processing of samples and tutorship on Laser Pressure Microdissection, serving the users of a new microdissection microscope acquired by several IMM Units.

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**, 155-164, published online in 2 December 2011. (Journal IF: 4.113, Citations: N.A.)

Publications in peer review Journals

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**, 155-164, published online in 2 December 2011. (Journal IF: 4.113, Citations: N.A.)

Zebrafish Facility

Major Objectives

To provide a fully functional facility to be used by several IMM research units.
To provide technical assistance to facilitate the use of zebrafish in a wide range of experimentation sets.

Head of Unit

Leonor Saúde, PhD Invited Assistant Professor, FMUL

Team

Lara Carvalho	Unit Manager
Fábio Valerio	Technician (left end May)
Susana Ponte	Technician (left end September)
Aida Barros	Technician

Major achievements

TECNOPHAGE SA is a Biotech company with labs located at the IMM, under a collaboration protocol signed by these two entities. The ZebraFish Facility/IMM was able to attract their new business unit called TECNOZeb that is operating inside our ZebraFish Facility since September 2011 with the contribution of our technical expertise.

Publications

The work done using the zebrafish of the IMM facility generated the following publications:

Cutty S.J., Fior F., Henriques P.M., Saúde L. and Wardle F.C. Identification and expression analysis of two novel members of the Mesp family in zebrafish. The International Journal of Developmental Biology *in press*.

Sousa S, Afonso N, Bensimon-Brito A, Fonseca M, Simões M, Leon J, Roehl H, Cancela ML, Jacinto A. Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. Development. 2011 Sep;138(18):3897-905.

Azevedo A.S., Grotok B., Jacinto A., Weidinger G. and Saúde L. (2011) The regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. PloS ONE Vol. 6(7); e22820.

Teaching/Training

Carvalho, L. lectured Laboratory Animal Science (basic level), Faculdade de Medicina Veterinária/SPCAL, Lisboa. February 2011

Carvalho, L. lectured Laboratory Animal Science (cat B), IMM, Lisboa. March 2011

Carvalho, L. lectured Laboratory Animal Science (cat A), IMM, Lisboa. October 2011

Science and Society

Leonor Saúde (2011) APIFARMA visit to the IMM. A guided-visit to the Fish Facility designed members of different Portuguese Patients Associations.

Leonor Saúde (2011) LÓreal visit to the IMM. A guided-visit to the Fish Facility to LÓreal collaborators.

Biobank

Major interests / Objectives

The aims of the IMM Biobank are to promote the study of the pathogenesis of diseases with significant impact on human health, contributing to the identification of new prognostic and diagnostic tests and novel therapeutic targets.

The IMM biobank will act as a catalytic factor for the cooperation between national and international academic researchers and between the academia and the pharmaceutical industry.

Head of Unit

João Eurico Fonseca, MD, PhD - Assistant Professor with habilitation (“agregação”) at the Faculdade de Medicina da Universidade de Lisboa

Research Team

Angela Afonso, Biochemist, Technical Responsible for the Biobank

Keywords/Research Areas

Biological Samples, Cryopreservation, Database

Major achievements

- 1- Dedicated space, acclimatized, with electronic surveillance, state of the art freezers, backup freezers, backup energy supply, and CO injection emergency rescue.
- 2- Collection of cryopreserved human biological samples (blood, serum, urine, cerebrospinal fluid, synovial fluid, DNA, RNA and various types of tissues).
- 3- Clinical information of individuals who donated samples managed by a tailored information system.
- 4- Approved by the FMUL/CHLN Ethics Committee and also by the Portuguese Data Protection Authority (Comissão Nacional de Proteção de Dados - CNPD). At the present, the IMM Biobank is under a quality certification process, which will ultimately lead to the certification by NP EN ISO 9001:2008.
- 5- Integrated in the European biobank network (BBMRI - Biobanking and Biomolecular Resource Research Infrastructure)

Ongoing Research Projects

2008/2011 Molecular Characterization of the Portuguese Population Affected by Neurodegenerative Disorders promoted by Alto Comissariado da Saúde (ACS). Coordinator: Tiago Outeiro, 11.000€

2011/2013 Epireuma.pt: Epidemiological Study of Rheumatic Diseases in Portugal, promoted by Sociedade Portuguesa de Reumatologia. Storage of data and samples. Coordinator: Jaime Branco, 12.400€

Invited Lectures and Seminars

Chalk Talk, IMM, 12th October 2011, The implementation of the IMM biobank

Communications in National Conferences

Afonso, A. Biobank-IMM an OverView. Oral presentation at the Workshop FCT-ISCIH Neurodegenerative Diseases Networks & Biobanks, Lisboa, July 4-5, 2011

Internationalization

The IMM Biobank has joined the European biobank network (BBMRI - Biobanking and Biomolecular Resource Research Infrastructure) in December 2011

Industry contract research

Novartis Farma, Donation of 6.000€
Amgen, Donation of 10.000

Companies

GenoMed – Diagnósticos de Medicina Molecular, SA

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 300 different tests that are used in diagnosis, prognosis and therapeutic follow up. The main medical areas covered include Oncology, Infectious Diseases, Genetic diseases and Pharmacogenetics. Additionally, GenoMed provides parental and ancestry DNA testing.

Head of Unit

Teresa Porta Nova, MSc (Director)

Team

GenoServices:

Genetic Diseases and Pharmacogenetics Unit:

Gabriel Miltenberger-Miltenyi, MD, PhD (IMM staff scientist, CIÊNCIA 2007) - Coordinator

Ana Coutinho, PhD - Technician

Sónia Pereira, Lic. Biochemistry - Technician

André Janeiro, Lic. Biochemistry - Technician

Catarina Silveira, Lic. Clinical Analysis and Public Health - Technician

Inês Silva, MSc - Technician

Marisa Silva, Lic. Pathology and Cytology – Technician (left in August 2011)

Diana Colom, Lic. Biology – Technician (left in April 2011)

Oncology Unit:

Sónia Santos, PhD – Citogenetics Unit Coordinator

Paula Costa, Lic. Biochemistry - Citogenetics Unit Technician

Ana Carla Sousa, Lic. Applied Chemistry/Biotechnology - Citogenetics Unit Technician

Susana Ramos, Lic. Pathology and Cytology - Citogenetics Unit Technician

Renata Casimiro, Lic. Marine Biology and Biotechnology - Citogenetics Unit Technician (left in September 2011)

Sónia Matos, MSc – Hemato-Oncology - Molecular Biology Unit Coordinator

Sara Malveiro, Lic. Cellular and Molecular Biology - Hemato-Oncology Unit Technician

Silvia Kakoo, Lic. Pathology and Cytology – Hemato - Oncology Unit Technician (left in February 2011)

Paula Mimoso, Lic. Applied Chemistry/Biotechnology - Technician

Hélia Guerreiro, Lic. Clinical Analysis and Public Health - Technician

Virology Unit:

Rute Marcelino, MSc – Coordinator

André Janeiro, Lic. Biochemistry - Technician

Management Unit:

Fabíola Rosa, Direction Assistant

Ana Flores, Management Assistant
 Rafaela Neto, Business Developer
 Tatiana Terreiro, Business Developer

GenoResearch:

Rute Marcelino, MSc

Gabriel Miltenberger-Miltenyi, MD, PhD (IMM staff scientist, CIÊNCIA 2007)

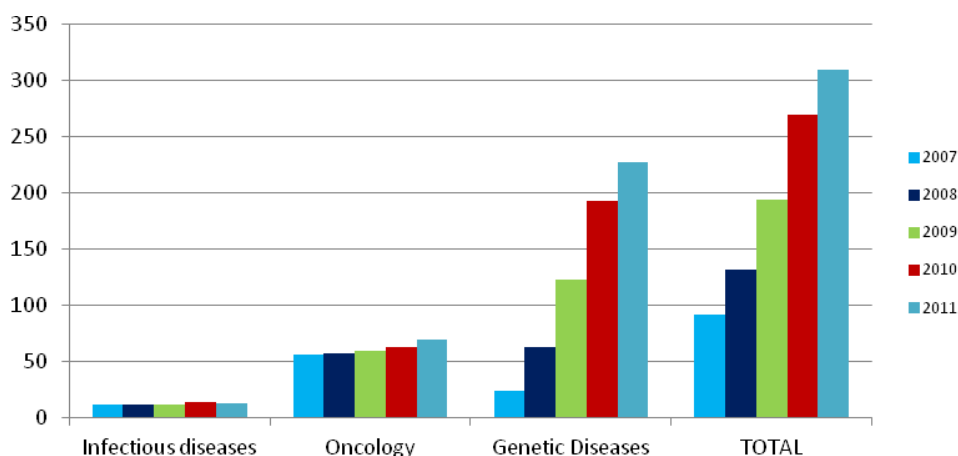
Research Areas

In vitro molecular diagnostics have established themselves as effective tools for all aspects of disease management, especially in areas of unmet clinical need. Such tests have been developed for screening and prognosis as well as for applications, such as determination of genetic predisposition to disease, detection of presymptomatic disease, and prediction of individual drug response. Molecular diagnostics are the basis of pharmacogenomics, enabling the evolution of personalized medicine.

Major scientific achievements

Increased number of tests available.

Total Number of tests available



Ongoing Research Projects

Biomarkers for Alzheimer's disease and Parkinson's disease (BIOMARKADP). European research projects for the optimisation of biomarkers and harmonisation of their use between clinical centres. Joint Programming in Neurodegenerative Disease (JPND). Portuguese coordinator: Alexandre de Mendonça. Participant: Gabriel Miltenberger-Miltenyi

starting in 2011: Investigação translacional em Alzheimer. Quadro de Referência Estratégico Nacional (QREN). Coordinator: Sofia Corte-Real. Participant: Gabriel Miltenberger-Miltényi

starting June 2011: Caracterização genética de doentes com enxaqueca hemiplégica familiar tipo 1. Gabinete de Apoio à Investigação Científica (GAPIC) – Medical Faculty, University of Lisbon -2010. Coordinator: Gabriel Miltenberger-Miltényi

starting June 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-Miltényi, 16000.- EUR

starting March 2011: Improving the quality of education through the development of science. TAMOP 4.1.2/B-09/1/KMR-2010-0001. Hungarian National Development Agency and Semmelweis University Budapest – external scientific collaborator. Coordinator: M.J. Molnar. Participant: Gabriel Miltenberger-Miltényi

2010/2013 Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease. Calouste Gulbenkian Foundation. Coordinator: N.C. Santos. Participant: Gabriel Miltenberger-Miltényi

starting July 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-Miltényi. 20000.- EUR

2009/2011, Development of a pyrosequencing method to detect resistance mutations to nucleosidic and non nucleosidic polimerase inhibitors and to protease inhibitors, in chronic infection of Hepatitis C Virus (HCV), Coordinator: Rute Marcelino, APEF/Roche, 5000€.

Publications in peer review Journals

de Oliveira RM, Marijanovic Z, Carvalho F, Miltényi GM, Matos JE, Tenreiro S, Oliveira S, Enguita FJ, Stone R, Outeiro TF. (2011) Impaired proteostasis contributes to renal tubular dysgenesis. PLoS One. 6(6):e20854 (IF [2009]: 4.411, cited: 0)

Jorge C, Marques JS, Veiga A, Nóbrega J, Cruz J, Peralta R, Correia MJ, de Sousa J, Miltenberger-Miltényi G, Nunes Diogo A. (2011) Novel mutation in long QT syndrome in a patient with prior diagnosis of epilepsy. Rev Port Cardiol. 2011 Nov 18.

Jorge C, Marques JS, Miltenberger-Miltényi G, Pinto FJ. (2011) Hypertrophic cardiomyopathy or non-compaction? How the first impression can be wrong. Int J Cardiol. 2011 Nov 10. **(IF [2010]: 6.802)**

Other publications National

Matos S (2011) LMC: Monitorização da Resposta e Mecanismos de Resistência. HematOncologia Especial, 14-15.

Invited Lectures and Seminars

Marcelino, R. HCV Resistance, Sharing Evolution2 Workshop - Delivering the Commitment, Miragem Hotel, Cascais, 12th of November, 2011

Miltenberger-Miltenyi, G: O estudo genético da demência. Curso de Demências. Congresso de Neurologia 2011, Lisboa, 06.11.2011.

Marcelino, R. IL28B genetic polymorphisms and Hepatitis C: portuguese data, Advanced Course on viral Hepatitis, Gastroenterology Service of Santa Maria Hospital, Lisbon, Portugal, 7th of October, 2011

Miltenberger-Miltenyi, G: Genetic basis of skeletal disease and pathological calcifications. Advanced Course: Human Genetics: from basic science to clinics and genetic counselling. University of Algarve, Faro, 21-22.07.2011,

Miltenberger-Miltenyi, G: Human genetics and bone diseases. Masters in Biomedical Sciences; University of Algarve, Faro, 01.04.2011

Communications in International Conferences

Miltenberger-Miltenyi Gábor, Reményi Viktória, Molnár Mária Judit, Kovács Tibor. Rare finding in dementia: description of a patient with a novel PSEN2 mutation. Xth Congress of the Hungarian Society of Clinical Neurogenetics, Budapest, 2-3.12.2011 (Oral presentation)

Dulce Brito, Gabriel Miltenberger-Miltenyi, Doroteia Silva, Nunes Diogo, Hugo Madeira. Hypertrophic cardiomyopathy: clinical aspects of 7 novel missense mutations in MYBPC3 gene. I European Congress on Myocardial and Pericardial Diseases. 13-15.10.2011, Lisbon (Oral presentation)

Han van Krieken, Jeroen Dijkstra, Felice Shieh, Gerald Hoefler, Susan Richman, Danielle Heidemann, Joachim Diebold, Etienne Rouleau, Evan Boers, Gabriel Miltenberger, Marjolein Ligtenberg, Sabine Tejpar, Jeffrey Lawrence. KRAS mutation analysis on low percentage of tumor cells: The importance of standardization and quality assurance. 23rd European Congress of Pathology (ECP 2011), 27 Aug - 1 Sept, 2011, Helsinki, Finland. (Oral presentation)

Gabriel Miltenberger-Miltenyi, Edgar Almeida, Joaquim Calado, Fernanda Carvalho, Catarina Teixeira, Sofia Jorge, Sonia Pereira, Helena Viana, António Gomes da Costa. Report on four novel UMOD mutations in medullary cystic kidney disease patients in Portugal. 48th Congress of European Renal Association – EDTA, 23-26.June, Prague (Poster presentation)

Miltenberger-Miltenyi Gábor, Sonia Vale Pereira, Bókay János, Balogh Lídia, Fekete György, Szőnyi László: Clinical and genetic testing of further three patients with GSD I from Hungary. European Human Genetics Conference, May 28-31, 2011 - Amsterdam, Netherlands (Poster presentation)

Communications in National Conferences

Santos, PS, Conceição, C, Silveira, MP, Gomes, AP, Afonso, C, Reichert, A, Pinto, M, Santos, S, Lima, F. Um Caso de Leucemia Mieloide Aguda com inv(3)(q21q26) e Trombocitose Sintomática. Reunião Anual da Sociedade Portuguesa de Hematologia. Centro de Congressos dos Salgados, Albufeira, November 10-12, 2011 (publication)

Miltenberger-Miltenyi, G, Pereira, SV, Timoteo, A, Costa, C. Uma família com doença de Parkinson sem mutações nos genes SNCA, LRRK2 e PARK2 – mais um exemplo de heterogeneidade genética. Congresso de Neurologia Lisboa 2011, 06.11.2011, (Oral presentation)

Miltenberger-Miltenyi, G, Verdelho, A, Pereira, SV, Barroso, C, de Mendonça, A. Variabilidade de expressão de uma nova mutação no gene GRN numa família com Degenerescência Lobar Frontotemporal. Congresso de Neurologia Lisboa 2011, 06.11.2011, (Oral presentation)

Miltenberger-Miltenyi, G, Pereira, SV, de Mendonça, A. Alzheimer's disease associated biomarkers in the cerebrospinal fluid of non-demented individuals – searching for laboratory specific normal values. 25^a Reunião do Grupo de Estudo de Envelhecimento Cerebral e Demências, Tomar 3 e 4 de Junho de 2011, (Oral presentation)

Miltenberger-Miltenyi, G, Almeida, E, Teixeira, C, Jorge, S, Carvalho, F, Gomes da Costa, A: Medullary cystic kidney disease in Portugal – genetic results of 14 families. Encontro renal – Congress of the Portuguese Society of Nephrology, Vilamoura 30.03.-02.04.2011, (Poster presentation)

Prizes, honours and awards

Best presentation: D Brito, G Miltenberger-Miltenyi, D Silva, N Diogo, H Madeira. Hypertrophic cardiomyopathy: clinical aspects of 7 novel missense mutations in MYBPC3 gene. I European Congress on Myocardial and Pericardial Diseases. 13-15.10.2011, Lisbon

Advanced teaching

Marcelino, R., Molecular Biology Module of Emergent Infectious Diseases Master Course, of Faculty of Medicine of Lisbon University, January 24th and 31th, 2011.

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 Garcia, PhD, PharmD, MBA – Associate Professor, Instituto de Ciências da Saúde Egas Moniz

Research Team

Sofia Corte-Real, PhD	Business Unit Manager, TechnoAntibodies
Nuno Afonso, PhD	Business Unit Manager, TechnoPhage, TechnoZeb
Frederico Silva, PhD	Business Unit Scientific Manager, TechnoAntibodies
Rui Freitas, PhD	Senior Scientist (left in December 2011)
Sara Sousa, MSc	Senior Scientist
Clara Leandro, MSc	Scientist
Sara Lourenço, MSc	Scientist
Raquel Barbosa, MSc	Junior Scientist
Daniela Proença, MSc	PhD student
João João Mendes, MD	PhD student
Rita Vaz	MSc student
Patrícia Pinto	Technician

Keywords/Research Areas

Antibodies, bacteriophages, zebrafish screening, Inflammation, Infection, Neurodegeneration

Major achievements

Technophage and UCB Pharma signed a collaborative protocol under which UCB is funding Technophage to develop new therapeutic agents using Technophage's small-domain antibody proprietary technology.

Technophage has began preclinical studies for TA-101 therapeutic agent against Rheumatoid arthritis, TP-102 therapeutic anti-infective agent against soft tissue ulcers.

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TechnoPhage was granted a Eurostars project (powered by EUREKA and the European Union) to deliver candidate-molecules for the treatment of Parkinson's Disease.

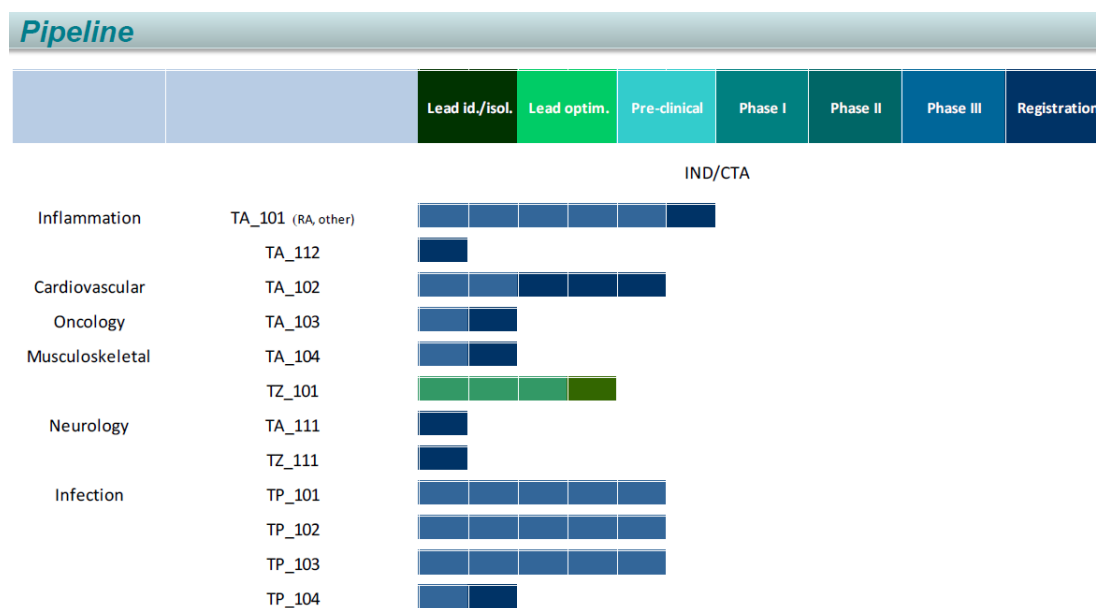
Ongoing Research Projects / Internationalization

TechnoPhage and UCB Pharma signed a collaborative protocol under which UCB is funding TechnoPhage to develop new therapeutic agents using TechnoPhage's small-domain antibody proprietary technology.

TechnoPhage was granted a Eurostars project (powered by EUREKA and the European Union) to deliver candidate-molecules for the treatment of Parkinson's Disease.

The project will run from 2011 to 2013, and will have TechnoPhage as the Project Leader and involves partners from several top European research centers from Portugal and the Netherlands (TechnoPhage, Instituto de Medicina Molecular, Erasmus University Medical Center Rotterdam, Faculdade de Engenharia da Universidade do Porto).

QREN Project- Projecto mobilizador Do IT – Desenvolvimento e Operacionalização de Translação. Participants include TechnoPhage, Instituto de Medicina Molecular and BIAL.



Other publications International

Sofia Corte-Real, Frederico Aires da Silva and João Goncalves. Chapter16- Development of Antibody Fragments for Therapeutic Applications, Castanho, M. / Santos, N., Peptide Drug Discovery and Development, Translational Research in Academia and Industry, Wiley-VCH Verlag GmbH & Co. KG (2011).

Master thesis completed

Sara Ferreira Llorente Grancho Lourenço, MSc thesis, 2011. Selecção e caracterização de anticorpos de domínio único específicos para a proteína gp41 de VIH-1. Faculdade de Medicina da Universidade de Lisboa. Co-Supervisor: Dr. Frederico Silva and Prof. Emilia Valadas.

Rita Leitão Landeiro Vaz, MSc thesis, 2011. Utilização do bacteriófago F44/10 na detecção de *Staphylococcus aureus* em feridas crónicas, Faculdade de Ciências da Universidade de Lisboa. Co-Supervisor: Prof. Madalena Pimentel, Prof .Mário Santos.

Thelial Technologies S.A.

Major interests / Objectives

Cancer is the second largest killer disease, affecting about 50% of people sometime in their lives. Thelial is a drug discovery company that applies its unique, proprietary *Drosophila* based technology to find new candidate compounds for the treatment of cancer.

Chief Executive Officer

Pedro Vilarinho, PhD

Founders

Rui Martinho, PhD

Richard Hampson, PhD

Research Team

Richard Hampson, PhD	General management and development
Virginia Oliveira Marques, PhD	Laboratory manager
Teresa Gomes, MSc	Technical staff

Keywords/Research Areas

Epithelium, carcinoma, drug discovery, early stage, *Drosophila*

Major achievements

In 2011 Thelial started up laboratory operations and met its ambitious plans in technology and intellectual property development.

Publications

Hampson RJ and Wyatt MD (2011) Whole organism based techniques and approaches in early stage oncology drug discovery-patents and trends. Recent Pat Endocr Metab Immune Drug Discov. 2011 Sep;5(3):183-91.

