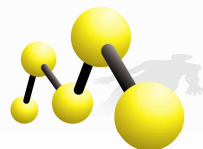


INSTITUTO DE MEDICINA MOLECULAR



2010 Activity Report



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

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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.

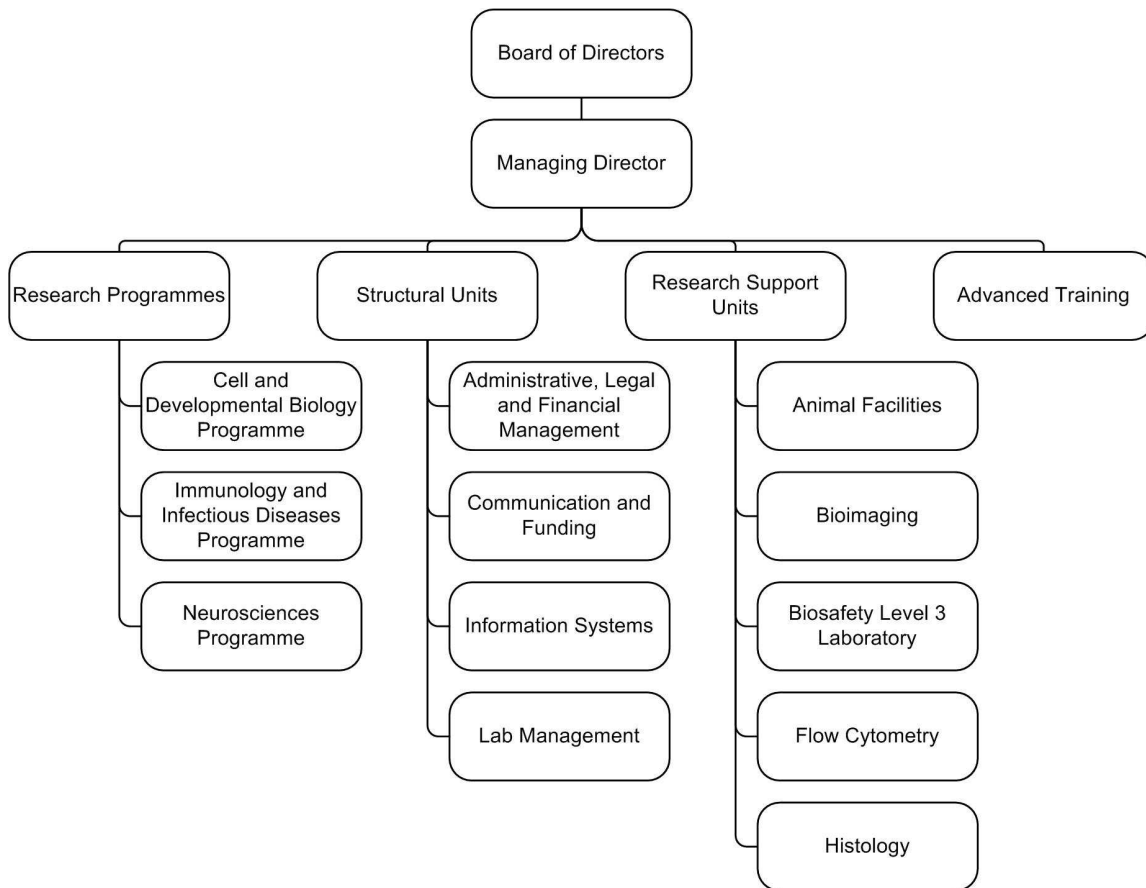
João Lobo Antunes, MD, PhD (President)
 Maria Carmo-Fonseca, MD, PhD (Executive Director)
 Joaquim Alexandre Ribeiro, MD, PhD (Vice-President)
 Patrícia da Cunha (Secretary)

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 2010

1. Summary of the evaluation of the *Instituto de Medicina Molecular as Laboratório Associado* of the Ministry of Science, Technology and Higher Education (LA)

Period of evaluation: 2003-07

Evaluation Panel:

Colin Berry, British Academy of Forensic Science, London, UK

Michael Spyer, University College London, UK

Steve Oliver, University of Cambridge, UK

Hugo Lagercrantz, Karolinska Institute, Sweden

Fernando Lopes da Silva (Chair), University of Amsterdam

Summary of the Panel's Report

The total budget of the IMM for the period was analyzed, in particular regarding the contribution from the FCT, the international funds and the contributions from the private sector. The panel considered that IMM displays a good balance between international and national, FCT and other national, funding and highlighted the fact that FCT projects amounted only to 38% of the FCT basic funding of the Laboratório Associado (LA). The panel stressed the need to know how much of the international funding originated from the EU Seventh Framework Program as an indicator of how successful the institute is in this international competition.

An important asset of IMM has been a successful policy of recruitment of young scientists, specially post-docs working abroad. The number of new group leaders and postdoctoral staff was analyzed in detail and considered remarkable. The panel highlighted the fact that the start up package for attracting group leader positions was not sufficiently competitive due to budgetary limitations. On their opinion, these hurdles should be clearly acknowledged by the responsible institutions, in particular by FCT, to put creative solutions in practice in order to open up the possibility of research institutes such as the IMM to compete for talented scientists with top biomedical institutes worldwide. (Underlined in the report; underline text refers to the recommendations of the panel).

The panel has acknowledged the international prestige gained by the IMM due to the fact that two of the new recruits, António Jacinto and Henrique Veiga Fernandes, were awarded the European Research Council Starting Grants and that Maria Manuel Mota received the prestigious EURYI award of the European Science Foundation in 2004. The role of the director Maria do Carmo Fonseca in keeping the recruitment standards very high was described as continually inspiring and an important driving force to IMM's reputation.

A note for thought was left regarding the policy of hiring investigators with no teaching obligations, which was the case for all IMM group leaders hired between 2004 and 2006.

The panel questions whether this is the best long-term policy considering that research can be stimulated by teaching, if kept within acceptable limits? A reference was made to teaching at the graduate level as an incentive for innovative and creative research and an inspiring school for young scientists.

The research outputs of the research program and of each research unit were carefully analyzed. This analysis included the quantification of total publications and those that reached at least an average of 10 citations / year. The evaluators also referred that the analysis of objectives and performance of the different groups was not carried out in detail. This would have been possible only if a site visit has been included in the evaluation round. In addition, they noted some insufficiencies on the report in terms of presentation of the relevant information (e.g. time dedicated to research of individual researchers, duration of their participation in the group's

activities, level of contribution of IMM researchers in papers carried out in collaboration). This information should be made more explicit in future reports of this kind.

Overall, the panel found that most research groups carry out high level research and have been very productive. They found some heterogeneity in research performance which, on their opinion, it is not surprising due to the large assembly of groups working and variety of themes. They highly encourage the scheduling of internal evaluations in depth for the different scientific programs.

Regarding the IMM core facilities, it was found necessary to invest regularly on novel microscopic systems in order to be able to carry out competitive research. In particular, the need for a confocal microscope with faster data collection (e.g. spinning disks) and 2-photon light microscope for investigations in live animals was acknowledged, whereas increased funding for updating IMM's equipment and infrastructures was considered priority.

Regarding research training, it was considered of most importance that IMM will be able to strengthen its International PhD Programme and to offer extended collaboration in advanced training projects for medical doctors/clinical scientists (MD/PhD Programme).

IMM should also have the necessary facilities to develop an international post-doctoral training program.

The level of internationalization was considered high, as evident from the percentage of international funding, and the involvement into outreach activities appropriate. In conclusion, the IMM should continue to pursue its objectives, with some adjustments.

The panel recommended the automatic renovation of the percentage year contract of the LA. The panel's specific recommendations are underlined throughout the text.

2. Summary of Review Report of the Scientific Advisory Board for the Immunology & Infectious Diseases Program

Period of evaluation: 2005-2009

Scientific Advisory Board members:

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

Alain Fischer, Hôpital Necker-Enfants Malades, Paris, France

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

Philippe Sansonetti, Institut Pasteur, Paris

Antonio Freitas (Chair), Institut Pasteur, Paris

Summary of the panel's overview:

The panel was of the opinion that research in the IMM was at a very good level. The IMM is clearly making an excellent use of its "limited resources". In the Program Immunology & Infectious Diseases major scientific accomplishments have been achieved. This was shown by a number of publications in some of the leading international journals.

It was also clear that research units at the IMM can only be competitive if able to develop new original projects within niches not occupied by highly competitive international laboratories that have greater access to technical resources. Thus, it was consensual that decisions on recruitment of new leaders should be always based on scientific excellence and originality.

The committee noted clear asymmetries between units. These asymmetries are due to historical or structural reasons and should be corrected in the next years.

The panel acknowledged that the leadership of the IMM is aware that it has the responsibility to provide its research groups with the resources they need to succeed. These groups represent a

major investment that should not be wasted by lack of support. Thus, the infrastructure requirements to support top-level research need to be discussed. While some can be dealt with at the institutional level, others require intervention at a national level.

There were two major infrastructure requirements in need of intervention, possibly at first an institute level and subsequently a national level, which are the animal facility and the link to the faculty and hospital.

The panel recommended that the new IMM animal facility starts running as soon as possible.

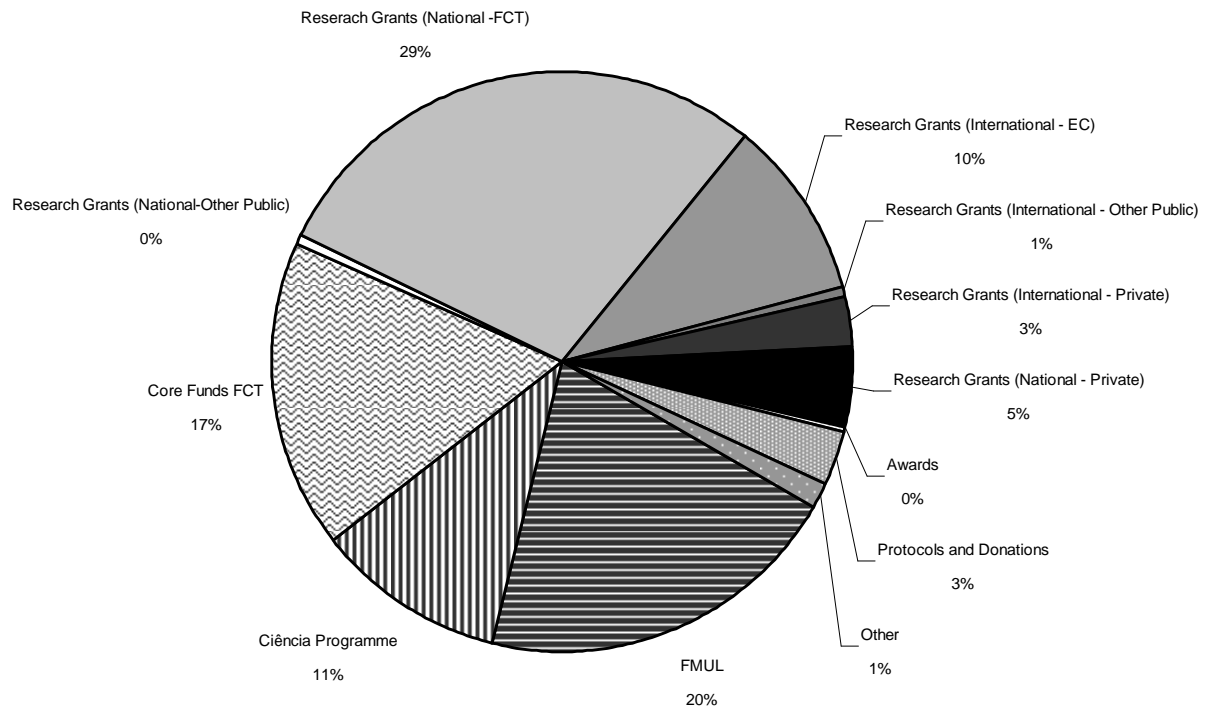
However, the panel has also acknowledged that the current facilities will be insufficient to cover all demands of the scientific staff. Ideally, the current animal facilities should be used for maintenance of experimental mice only. It is the opinion of the panel that the expenses associated with the personnel and the running costs required for the maintenance of this type of facilities are of strategic national importance and thus cannot be supported by the IMM alone, whereas other Portuguese institutions may have similar requirements. In this sense, the panel calls for a solution at a national level. This would imply the establishment of a collaborative program between intervening institutions and the commitment of the FCT to support the running costs and personnel for the operation of such an animal facility. Part of the running costs could be covered by fees charged to the users.

The connection with the Medical Faculty and the Hospital was considered crucial for the development of both IMM and the university hospital. The panel suggested the setting up of a translational program bridging basic research and clinically oriented groups, by granting a few proposals with a financial incentive. In addition, the panel has stressed the need to make sure that MDs enrolled in the IMM PhD program work full time (>90%) in the laboratory during their training. Furthermore, they would like to suggest the creation of a new MD/PhD program where students start their research training while still in the faculty. Another remark concerned ways to compensate the hospital (or the faculty) for protected time from patients' care or teaching duties for the few MDs enrolled in scientific training to pursue research activity. The panel acknowledges that part of these actions require interventions at the national level. They believe that MSc or PhD degrees should be critical for the heads of clinical departments in central hospitals, if clinical research is to be developed to a satisfactory level in Portugal's long-term future.

Research Funding

Expenditure in 2010 by funding source

Total expenditure: 9,209,736 €

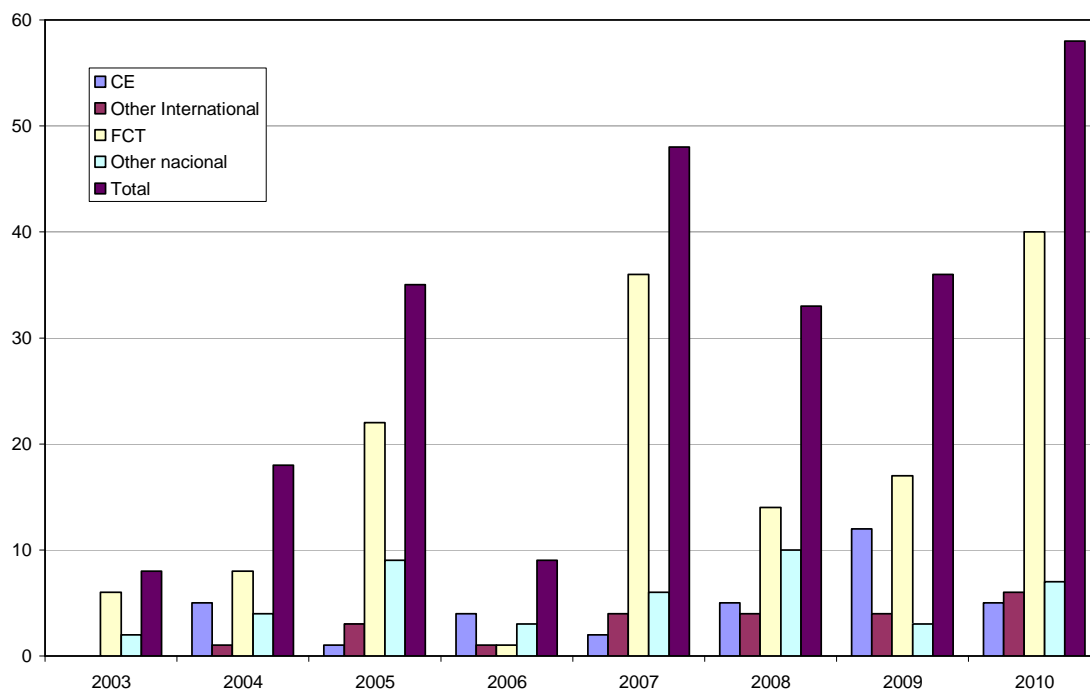


Number of ongoing research grants in 2010

154 Research Grants

- 93 Public National
- 23 Public European Commission
- 1 Public Other International
- 21 Private National
- 16 Private International

Number of research grants by start date



Research Funding that started in 2010

58 Research Grants

- 5 European Commission; 6 Other International

- 40 FCT; 7 Other National

21 Protocols/Donations/Awards

Research Grants (58)

Funding Agency	Reference	Title	PI at IMM	Duration	IMM Budget
EC	PIRG-GA-2009-256299-HistoneH1Tryp	Chomatin and Antigenic variation: The role of histone H1 in gene regulation in African trypanosomes	L. Figueiredo	48	100.000,00
EC	PIRSSES-247513-MEMPEPACROSS	Membrane-Active Peptides across disciplines and continents: an integrated approach to find news strategies to fight bacteria, dengue virus and neurodegeneration	N. Santos	48	73.800,00

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EC	PIEF-2009-25557	The role of EGF/ERK signaling pathway during the wound healing response in <i>Drosophila</i> and zebrafish epithelia	A. Jacinto	24	146.783,00
EC	ERC_260352_BSS	Differentiation of pro-inflammatory T cell subsets in vivo	B. Silva Santos	60	1.500.000,00
EC	HEALTH-single-stage-241791-MEFOPA	European Project on Mendelian Forms of Parkinson's Disease	T. Outeiro	36	226.800,00
EMBO	Short Term Fellowship	Support to Cellular Biology project	J. Desterro	12	1.900,00
EMBO	Practical course PC11/02	<i>Drosophila</i> Techniques	S. Prag	5	30.000,00
EMBO	Small Grant	Support to Molecular Immunology project	B. Silva Santos	10	10.000,00
Bill & Melinda Gates Found.	GATES	A new Whole-Organism Vaccine Against Malaria	M. Prudêncio	18	72.030,00
Michael J Fox Foundation	MJFF Alpha-synuclein	Deciphering the molecular effects of alpha-synuclein in the nucleus: DNA binding and transcriptional dysregulation	T. Outeiro	12	30.534,35
SOS Ataque Cerebral	TIA Registry	An International, prospective, TIA-clinic based, Web-based registry with long-term follow-up	P. Canhão	60	200/patient
FCT	PTDC/SAU-MII/108578/2008	Infecções do tracto respiratório e malária	M. Mota	36	190.850,00
FCT	PTDC/SAU-OSM/100878/2008	Prevalência e gravidade do fígado gordo na obesidade mórbida: correlações e mecanismos relacionados com o papel da gordura ectópica na resistência à insulina	H. Cortez Pinto	36	46.000,00
FCT	PTDC/SAU-MII/100780/2008	Regulação da secreção de IL-1 β pelos factores de splicing ASF/SF2 e SRp20	L. Moita	36	198.591,00
FCT	PTDC/SAU-GMG/103307/2008	Papel do metabolismo do ferro na progressão da hepatite C viral e na resposta à terapêutica	F. Serejo Leal Silva	36	45.545,00
FCT	PTDC/SAU-ESA/104947/2008	Caracterização e genotipagem de estirpes portuguesas de <i>Francisella tularensis</i>	T. Hanscheid	36	12.600,00
FCT	PTDC/SAU-OBD/104816/2008	Sinais intracelulares e microambientais entrecruzados: novos alvos para intervenção terapêutica em leucemia linfoblástica aguda?	J. Barata	36	190.000,00
FCT	PTDC/SAU-GMG/099655/2008	Disgenesia tubular renal associada a misfolding da ACE: efeitos moleculares da nova mutação Q1069R	T. Outeiro	36	162.422,00
FCT	PTDC/SAU-GMG/104392/2008	ARN não codificando em parasita de malária	C. Carret	36	103.581,00

FCT	PTDC/SAU-OSM/108267/2008	Indução de tolerância a factores de coagulação recombinantes num modelo animal de hemofilia	V. Oliveira Martins	36	200.000,00
FCT	PTDC/SAU-OBD/101259/2008	Função das integrinas na migração celular de hemócitos de <i>Drosophila</i>	S. Prag	36	120.000,00
FCT	PTDC/SAU-OBD/100200/2008	O papel da reinervação na regeneração de tecidos	A. Jacinto	36	140.000,00
FCT	PTDC/SAU-GMG/101537/2008	Genética da Fenda Lábio-Palatina não-sindrómica	A. Jacinto	36	196.176,00
FCT	PTDC/BIA-BCM/101575/2008	Mecanismos de regulação genética associados à transcrição	Carmo Fonseca	36	199.350,00
FCT	PTDC/SAU-GMG/098937/2008	BEDGET: decifrar a genética da doença de Behçet	S. Oliveira	36	180.708,00
FCT	PTDC/SAU-MII/104158/2008	Regulação da diferenciação tímica e activação periférica de linfócitos T pelo receptor CD27 e seu ligando CD70	B. Silva Santos	24	184.237,00
FCT	PTDC/SAU-NEU/105215/2008	Da fosforilação à clivagem: um "switch" para a agregação e a toxicidade da alfa-sinucleína	T. Outeiro	36	130.000,00
FCT	PTDC/SAU-OBD/100664/2008	Células estaminais: dialéctica, biologia e matemática	D. Henrique	36	140.000,00
FCT	PTDC/SAU-OSM/109081/2008	Modificação genética das células do núcleo paraventricular do hipotálamo (PVN) e medula rostral ventrolateral (RVLM) para controlar cronicamente a hipertensão.	I. Rocha	36	126.034,00
FCT	PTDC/EEA-ELC/109083/2008	Construção de um Pacemaker Diafragmático a ser testado em rato com vista a ser aplicado no ser humano com insuficiência respiratória	I. Rocha	36	147.456,00
FCT	PTDC/SAU-MII/104931/2008	Papel da tirosina cinase RET na hematopoiese fetal e adulta	H. Veiga Fernandes	36	182.000,00
FCT	PTDC/SAU-MII/100016/2008	Identificação do papel de subpopulações hematopoiéticas na organogénese linfóide	H. Veiga Fernandes	36	197.802,00
FCT	PTDC/QUI-BIQ/104787/2008	Papel dos componentes da membrana celular na entrada do HIV e sua inibição	N. Santos	36	174.130,00
FCT	PTDC/SAU-BEB/099142/2008	Actividade bactericida inerente a hidrogéis de péptidos para regeneração de tecidos	S. Veiga	36	199.350,00
FCT	PTDC/QUI-QUI/102049/2008	Derivados de Benzazolo Marcados com Fluor-18 e Tecnécio-99m para Visualização In Vivo de Depósitos de Amilóide	T. Outeiro	36	51.050,00

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FCT	PTDC/SAU- OBD/100202/2008	Estudo sobre a importância dos cílios como estruturas de sinalização na regeneração	L. Saúde	36	170.000,00
FCT	PTDC/SAU- OSM/099724/2008	Relevância de uma dieta rica em colesterol na protecção da malária cerebral experimental	A. Pamplona Santos	36	148.246,00
FCT	PTDC/SAU- GMG/100313/2008	Revelando os segredos do infecção hepática por Plasmodium: uma aproximação multidireccional.	M. Mota	36	199.943,00
FCT	PTDC/BIA- BCM/105610/2008	Regulacao da transcricao no Plasmodium durante a transmissao entre o hospedeiro e vector	G. Mair	36	191.710,00
FCT	PTDC/SAU- MII/099314/2008	Infecção latente por gammaherpesvírus: modulação da sinapse imunológica.	J. P. Simas	36	199.458,00
FCT	PTDC/BIA- BCM/101282/2008	Identificação dos reguladores de RNA do relógio da segmentação	L. Saúde	36	188.743,00
FCT	PTDC/SAU- NEU/101752/2008	Interacção entre receptores dos factores neurotróficos (TrkB) e receptores A2A da adenosina: implicações para a Esclerose Lateral Amiotrófica	J. A. Ribeiro	36	111.000,00
FCT	PTDC/SAU- NEU/099853/2008	Papel dos receptores A2A de adenosina no stress crónico - implicações na aprendizagem e memória	L. V. Lopes	36	120.000,00
FCT	PTDC/SAU- NEU/103639/2008	Papel dos receptores para o VIP na aprendizagem e plasticidade sináptica dependente do hipocampo: avaliação do potencial terapeutico de antagonistas dos receptores VPAC1 para mitigar as deficiências cognitivas em na ELT.	D. Reis	36	120.000,00
FCT	PTDC/SAU- MII/099118/2008	A influência dos ácidos biliares na infecção do fígado por malária	M. Prudêncio	36	171.482,00
FCT	PTDC/SAU- OBD/103981/2008	A investigação de uma nova via de sinalização entre DeltaD e ciliogénese e o seu impacto no desenvolvimento da identidade esquerda-direita	S. Lopes	12	77.778,00
FCT	PTDC/SAU- NEU/102710/2008	Alteração do tráfego intracelular mediado pela mitocôndria na doença de Parkinson	T. Outeiro	36	26.950,00
FCT	PTDC/SAU- NEU/101928/2008	Análise dos mecanismos moleculares que determinam disfunção da alfa-sinucleína e a citotoxicidade na doença de Parkinson - o papel do GDNF	T. Outeiro	36	25.600,00

FCT	PTDC/MAR/105313/2008	Desenvolvimento e caracterização de células estaminais de peixe zebra: implicações para o desenvolvimento de transgénicos - FishCell	A. Jacinto	36	18.739,00
FCT	HMSP-ICS/SAU-ICT/0002/2010	Preditores de resposta à terapêutica com antagonistas do TNF na Artrite Reumatoide	H. Canhão	36	398.618,00
FCT	HMSP-CT/SAU-ICT/0068/2009	Novas drogas para tratamento e erradicação de malária	M. Mota	36	300.000,00
Soc. Port. Nefrologia	Studies in MCKD	Phenotype-Genotype association studies in medullary cystic kidney disease - investigation of a new candidate genes	G. Miltényi	21	19.970,00
Núcleo Regional do Sul	MI-RNAs Terry Fox	Regulação recíproca entre expressão de TAL1 e de miRNAs em leucemias de células T	J. Barata	24	15.000,00
FLAD	B-A.V-109-09/07 - FLAD	Malaria drug-resistance:development of a novel, clinically useful drug-sensitivity assay for Plasmodium species	T. Hanscheid	12	18.000,00
Fund. Calouste Gulbenkian	Gulbenkian-UBM	Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease	N. Santos	12	10.000,00
Laboratórios Pfizer, Lda	Inflammasome	The role of inflammasome in the initiation and perpetuation of Rheumatoid Arthritis. Contribution for new targeted therapies	J. Eurico Fonseca	26	21.000,00
Merck Sharp & Dohme	OssO-Merck	Support to Rheumatology research project	J. Eurico Fonseca	11	10.000,00
Centro Empresarial de Aveiro	BLOOD	Devices and Protocols for blood processing and analysis	H. Rosário	24	6.000,00

Protocols, Donations & Awards (21)

Funding Agency	Reference	PI at IMM	Duration	IMM Budget
University of Glasgow	Inflammatory Arthritis Fellowship Program	J. Eurico Fonseca	8	29.902,67
Fund. das Universidades	Acção Integrada Luso-Alemã CRUP A-1/10	T. Outeiro	12	2.500,00
FLAD	Intership at Rush University Medical Center, Chicago	M. Trindade	4	1.700,00
Fund. EDP	Support to workshop "Ciência, Política e os Media"	M. Agostinho	4	3.075,00
Novartis Pharma	Support to seminars on Neuroses	T. Outeiro	10	4.000,00
FENS	Support to Brain Awareness Week outreach activity "What goes on in your mind?"	L. V. Lopes	11	1.000,00
Meeting Point	Services on project on multiple sclerosis	J. Ferro	10	9.750,00
Roche Farmaceutica Quimica	Support to meeting on Rheumatology	J. Eurico Fonseca	8	15.787,00
Zagreb Medical School	Location analysis of alpha-synuclein in patients with Parkinson's Disease (Grant 24/08)	T. Outeiro	12	5.000,00
Fund. das Universidades	Acção Integrada Luso-Britânica - CRUP B-4/10	T. Outeiro	12	1.500,00
FCT	Pessoa Programme 441: O papel da sinalização Notch na diferenciação das células -C durante a embriogénese	H. Neves	8	3.200,00
EMBO	Support to meeting on Neurosciences	T. Outeiro	12	800,00
Grunenthal S.A.	Support to course on botulinic toxin	J. Ferreira	2	15.000,00
ECTS Ltd	European Calcified Tissue Society / Servier Research Fellowship	J. Eurico Fonseca	24	40.000,00
Angelini Farmacêutica, Lda	Support to research project on neuromuscular diseases	M. Carvalho	9	3.500,00
Roche Farmaceutica Quimica	Support to meeting on Rheumatology	J. Eurico Fonseca	12	13.000,00
Astrazeneca	Support to meeting on Cellular Biology	Carmo Fonseca	7	1.250,00
Merck, S.A.	Support to research project on Molecular Genetics	Carmo Fonseca	6	25.025,00
Roche Farmaceutica Quimica	Support to meeting on Rheumatology	J. Eurico Fonseca	8	5.000,00
Fundação Amadeu Dias	Fellowship to project "Nutrição e Oncologia: a investigação e seu impacto na clínica e ensino"	P. Ravasco	12	800,00
Fund. Calouste Gulbenkian	Award Frontiers in Life Sciences - The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation	I. Martins	12	50.000,00

2010 IMM Activities Highlights

People in 2010

PhD Holders: 179

Total: 421

Productivity at a glance

Publications International Journals	263
...in journals with an impact factor higher than 10	19
...in journals with an impact factor between 5 – 10	57
Book/Book Chapters International	16
Communications in International Conferences	406
Communications in National Conferences	261
Seminars and Invited Lectures	328
Organization of Conferences	54
Prizes	65
PhD Thesis	18
Master Thesis	71

The number of citations for IMM papers (according to the Web of Science) has been increasing and IMM now has an average of **11.6** citations per paper.

Year	Publications JIF > 10	Publications JIF 5-10
2005	1	11
2006	8	20
2007	6	19
2008	3	20
2009	13	36
2010	19	57

Prizes and Awards

Pessoa Award 2010

Maria Carmo-Fonseca

Crioestaminal Award 2010

Luísa Figueiredo

Young Investigator EMBO 2010

Bruno Silva-Santos

Instalation Grant EMBO 2010

18 | 2010 IMM Activity Report

Luísa Figueiredo

Michael J. Fox *Rapid Response Innovation Award 2010*

Tiago F. Outeiro

Bill & Melinda Gates Foundation, Grand Challenges Exploration. Programme 2010

Miguel Prudêncio

BES Innovation Award in Health Technology 2010

Luís Graça, Marta Monteiro, David Cristina

Calouste Gulbenkian Foundation Award on the Frontiers in Life Sciences 2009

Ivo Martins

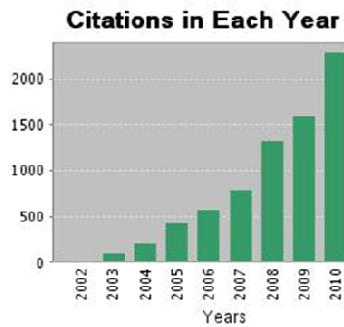
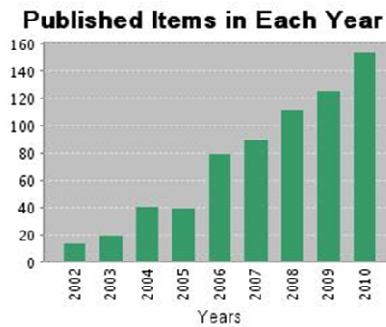
Pulido Valente Science Award 2009

Ana Silva

IMM Publications in International Journals

Citation Report

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



154 papers in 2010

677 since 2001

Sum of the Times Cited: **7,854**

Average Citations per Item: **11.60**

h-index : **41**

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=(PROCEEDINGS PAPER OR MEETING ABSTRACT)

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

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

10 Most Cited Articles 2001-2010

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? *Nat Med.* **8**, 319-321 (**Times cited: 243**)(Journal IF: 27.553)

Di Fonzo A, Rohe CF, Ferreira RJ, Chien HF, Vacca L, Stocchi F, Guedes L, Fabrizio E, Manfredi M, Vanacore N, Goldwurm S, Breedveld G, Sampaio C, Meco G, Barbosa E, Oostra BA and Bonifati V (2005) A frequent LRRK2 gene mutation associated with autosomal dominant Parkinson's disease. *Lancet* **365**, 412-415 (**Times cited: 209**)(Journal IF: 28.409)

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 (**Times cited: 204**)(Journal IF: 6.000)

Ribeiro JA, Sebastião AM and De Mendonça A (2002) Adenosine receptors in the nervous system: pathophysiological implications. *Prog Neurobiol.* **68**, 377-392 (**Times cited: 186**)(Journal IF: 9.130)

Emre M, Aarsland D, Brown R, Bum DJ, Duyckaerts C, Mizuno Y, Broe GA, Cummings J, Dickson DW, Gauthier S, Goldman J, Goetz C, Korczyn A, Lees A, Levy R, Litvan I, McKeith I, Olanow W, Poewe W, Quinn N, Sampaio C, Tolosa E and Dubois B (2007) Clinical diagnostic criteria for dementia associated with Parkinson's disease. *Movement Dis.* **22**, 1689-1707 (**Times cited: 169**)(Journal IF: 3.898)

Duarte A, Hirashima M, Benedito R, Trindade A, Diniz P, Bekman E, Costa L, Henrique D and Rossant J (2004) Dosage-sensitive requirement for mouse D114 in artery development. *Gene Dev.* **18**, 2474-2478 (**Times cited: 163**)(Journal IF: 13.623)

Carmo-Fonseca M (2002) The contribution of nuclear compartmentalization to gene regulation. *Cell* **108**,1-20 (**Times cited: 123**)(Journal IF: 31.253)

Stamm S, Riethoven JJ, Le Texier V, Gopalakrishnan C, Kumanduri V, Tang YS, Barbosa-Morais NL and Thanaraj TA (2006) ASD: a bioinformatics resource on alternative splicing *Nucleic Acids Res.* **34** (Special Issue), D46-D55 (**Times cited: 109**)(Journal IF: 6.878)

Santos NC, Figueira-Coelho J, Martins-Silva J and Saldanha C (2003) Multidisciplinary utilization of dimethyl sulfoxide: pharmacological, cellular, and molecular aspect. *Biochem. Pharmacol.* **65**, 1035-1041 (**Times cited: 107**)(Journal IF: 4.838)

Healy DG, Falchi M, O'Sullivan SS, Bonifati V, Durr A, Bressman S, Brice A, Aasly J, Zabetian CP, Goldwurm S, Ferreira JJ, Tolosa E, Kay DM, Klein C, Williams DR, Marras C, Lang AE, Wszolek ZK, Berciano J, Schapira AH, Lynch T, Bhatia KP, Gasser T, Lees AJ, Wood NW; International LRRK2 Consortium (2008) Phenotype, genotype, and worldwide genetic penetrance of LRRK2-associated Parkinson's disease: a case-control study. *Lancet Neurol.* **7**, 583-590. (**Times cited: 106**)(Journal IF: 18.126)

List of Publications in International Journals

Mair GR, Lasonder E, Garver LS, Franke-Fayard BM, Carret CK, Wiegant JC, Dirks RW, Dimopoulos G, Janse CJ, Waters AP (2010) Universal features of post-transcriptional gene regulation are critical for Plasmodium zygote development. *PLoS Pathog.* **6** (2), e1000767. (Journal IF: 8.978)

Aapro M, Saad F, Costa L (2010) Optimizing Clinical Benefits of Bisphosphonates in Cancer Patients With Bone Metastases. *The Oncologist* **15** (11), 1147-1158. (Journal IF: N.A.)

Aartsma-Rus A, Atkinson L, Brasseur D, Braun S, Buccella F, Bushby, K, Campion G, Catlin N, Connor E, Cwick V, Eagle M, Ellis JA, Florence J, Furlong P, Goemans N, Griggs R, Heslop E, Hoffman E, Hofmeister S, Kayadjanian N, Kirshner J, Levin A, Lynn S, McCormack P, McNeil E, Muntoni F, Narayanan G, Popat D, Porter J, Rose M, Saint-Raymond A, Sampaio C, Shrewsbury S, Straub V, Vamvakas S, Voit T, Vroom E, Wells D, Westermarck K, Wilks M, Woods S (2010) The development of antisense oligonucleotide therapies for Duchenne muscular dystrophy: report on a TREAT-NMD workshop hosted by the European Medicines Agency (EMA). *Neuromuscul Disord* **20**, 355-362. (Journal IF 2.807)

Afonso P, Brissos S, Figueira ML, Paiva T (2010) Discrepant nocturnal melatonin levels in monozygotic twins discordant for schizophrenia and its impact on sleep. *Schizophr Res* **120** (1-3), 227-228 (Journal IF: 4.458)

Aguiar SI, Brito MJ, Gonçalo-Marques J, Melo-Cristino J and Ramirez M (2010) Serotypes 1, 7F and 19A became the leading causes of pediatric invasive pneumococcal infections in Portugal after 7 years of heptavalent conjugate vaccine use. *Vaccine* **28**, 5167-73 (Journal IF: 3.616)

Aguiar SI, Pinto FR, Nunes S, Serrano I, Melo-Cristino J, Sá-Leão R, Ramirez M and de Lencastre H (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. (Journal IF: 4.162)

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. *Neurology* Epub ahead of print December 22 (Journal IF: 8.172)

Almeida AR, Ciernik IF, Sallusto F, Lanzavecchia A (2010). CD4+ CD25+ Treg regulate the contribution of CD8+ T-cell subsets in repopulation of the lymphopenic environment. *Eur J Immunol* **40**(12), 3478-88.(Journal IF : 5.179)

Almeida V, Mestre T, de Carvalho M (2010) Pseudobulbar syndrome in two patients with Human Immunodeficiency virus infection. *Amyotr Lat Scler* **11**, 220-222. (Journal IF: 2.963)

Almeida V, de Carvalho M (2010) Lesion of the Deep Palmar Branch of the Ulnar Nerve: causes and clinical outcome. *Neurophysiol Clin* **36**, 219-226. (Journal IF: 1.169)

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardají E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX and Castanho MARB (2010) Escherichia coli cell surface perturbation and disruption induced by antimicrobial peptides, BP100 and pepR. *J Biol Chem* **285**, 27536-27544. (Journal IF: 5.328)

Amaral P, Miguel R, Mehdad A, Cruz C, Monteiro Grillo I, Camilo M, Ravasco P (2010) Body fat and poor diet in breast cancer women. *Nutricion Hospitalaria* **25**, 456-461 (Journal IF: 1.065)

Anand PK, Anand E, Bleck CK, Anes E, Griffiths G (2010) Exosomal Hsp70 induces a pro-inflammatory response to foreign particles including mycobacteria. *PLoS One* **5** (4), e10136. (Journal IF: 4.5)

Antunes J, Filipe P, André M, Fraga A, Miltenberger-Miltenyi G and Marques Gomes M (2010) Livedoid Vasculopathy Associated with Plasminogen Activator Inhibitor-1 Promoter Homozygosity (4G/4G) and Prothrombin G20210A Heterozygosity: Response to t-PA Therapy. *Acta Derm Venereol* **90** (1), 91-2. (Journal IF: 3.007)

Antunes MI, Bujor L, Monteiro Grillo I (2010) Anal canal plasmacytoma - An uncommon presentation site. *Reports of Practical Oncology & Radiotherapy*, Online Publication, December 2010 (Journal IF: N/A)

Ardila A, Bertolucci P, Braga LW, Castro-Caldas A, Judd T, Kosmidis M, Matute E, Nitrini R, Ostrosky F, Rosselli M (2010) Illiteracy: The Neuropsychology of Cognition Without Reading. *Arch Clin Neuropsychol* **25**, 689-712 (Journal IF: 2.497)

Assaife-Lopes N, Sousa VC, Pereira DB, Ribeiro JA, Chao MV, Sebastião AM (2010) Activation of adenosine A2A receptors induces TrkB translocation and increases BDNF-mediated phospho-TrkB localization in lipid rafts: implications for neuromodulation. *J Neurosci* **30**, 8468-8480. (Journal IF: 7.178)

Baptista FG, Pamplona A, Pena AC, Mota MM, Pied S, Vigário AM (2010) Accumulation of Plasmodium-infected red blood cells in the brain is crucial for the development of cerebral malaria in mice. *Infect Immunity* **78** (9), 4033-4039. (Journal IF: 4.205)

Baptista MV, Ferreira S, Pinho-E-Melo T, Carvalho M, Cruz VT, Carmona C, Silva FA, Tuna A, Rodrigues M, Ferreira C, Pinto AA, Leitão A, Gabriel JP, Calado S, Oliveira JP, Ferro JM and PORTuguese Young STROKE Investigators (2010) Mutations of the GLA gene in young patients with stroke: the PORTYSTROKE study--screening genetic conditions in Portuguese young stroke patients. *Stroke* **41**, 431-436. (Journal IF: 7.041)

Bentes C, Costa J, Pires J, et al (2010) AM recall and seizures in patients with temporal lobe epilepsy. *Epilepsia* **51**, 100- (Journal IF: 4.052)

Bogas M, Machado P, Mourão AF, Costa L, Santos MJ, Fonseca JE, Silva JA, Canhão H (2010) Methotrexate treatment in rheumatoid arthritis: management in clinical remission, common infection and tuberculosis. Results from a systematic literature review. *Clin Rheumatol* **29** (6), 629-635 (Journal IF: 1.668)

Branco JC, Zachrisson O, Perrot S, Mainguy Y (2010) Multinational Coordinator Study Group. A European multicenter randomized double-blind placebo-controlled monotherapy

clinical trial of milnacipran in treatment of fibromyalgia. *J Rheumatol* **37** (4), 851-859. (Journal IF: 2.225)

Brilha S, Proença H, Cristino JM and Hänscheid T (2010) Use of flow cytometry (Sysmex) UF-100) to screen for positive urine cultures: in search for the ideal cut-off. *Clin Chem Lab Med* **48**, 289-292. (Journal IF: 1.886)

Bronzova J, Sampaio C, Hauser RA, Lang AE, Rascol O, Theeuwes A, van de Witte SV, van Scharrenburg G; Bruegel Study Group (2010) Double-Blind Study of Pardoprunox, a New Partial Dopamine Agonist, in Early Parkinson's Disease, *Mov Disord* **25**, 638-746 (Journal IF: 4.014)

Brown JE, Cook RJ, Lipton A, Costa L, Coleman RE (2010) Prognostic Factors for Skeletal Complications From Metastatic Bone Disease in Breast Cancer. *Breast Cancer Res Treat* **123**, 767-779. (Journal IF: 4.696)

Büttner S, Delay C, Franssens V, Bammens T, Ruli D, Zaunschirm S, de Oliveira RM, Outeiro TF, Madeo F, Buée L, Galas MC, Winderickx J (2010) Synphilin-1 enhances α -synuclein aggregation in yeast and contributes to cellular stress and cell death in a Sir2-dependent manner. *PLoS One*. **5** (10), e13700. (Journal IF: 4.351)

Caetano-Lopes J, Nery AM, Canhão H, Duarte J, Cascão R, Rodrigues A, Perpétuo IP, Abdulghani S, Amaral PM, Sakaguchi S, Kontinen YT, Graça L, Vaz MF, Fonseca JE (2010) Chronic arthritis leads to disturbances in the bone collagen network. *Arthritis Res Ther* **12**, R9 (IF 2009: 4.271)

Caldeira D, David C, Sampaio C (2010) Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis *J Hosp Infect*. Epub December 30. (Journal IF:3.016)

Campanilho-Marques R, Polido-Pereira J, Rodrigues A, Ramos F, Saavedra MJ, Costa M, Martins F, Pereira da Silva JA, Canhão H, Fonseca JE (2010) BioRePortAP, an electronic clinical record coupled with a database: an example of its use in a single centre. *Acta Reumatol Port* **35**(2), 176-183 (Journal IF: 0.726)

Campbell NR, Fernandes CC, Halff AW, Berg DK (2010) Endogenous signaling through alpha7-containing nicotinic receptors promotes maturation and integration of adult-born neurons in the hippocampus. *J Neurosci* **30**, 8734-8744. (Journal IF: 7.178)

Campuzano-Zuluaga G, Hanscheid T and Grobusch MP (2010) Automated haematology analysis to diagnose malaria. *Malar J* **9**, 346. (Journal IF: 2.995)

Canas N, Breiac P, Soares P, Saraiva P, Calado S, Jordão C and Vale J (2010). The electroclinical-imagiological spectrum and long-term outcome of transient periictal MRI abnormalities. *Epilepsy Res* **91**, 240-252. (Journal IF: 2.479)

Canas N, Soares P, Calado S, Calado S, Pestana R, Ribeiro C, Vale J (2010) Pathophysiology and Long-Term Outcome of Reversible Tumor-Like Lesions Induced by Presenting Status Epilepticus. *J Neuroimaging* **20**, 169-174. (Journal IF: 1.719)

Candeias C, Vaz Luís I, Ribeiro J, Costa L, Soares de Almeida L, Gomes MM, Barreto L, Brito-Avô L, Ducla-Soares JL (2010) Extended remission of metastatic epithelioid angiosarcoma of the heart with liposomal doxorubicin. *BMJ Case Reports* (doi:10.1136/bcr.08.2009.2157) (Journal IF: N.A.)

Candid M, Vicario CM, Abreu AM and Aglioti SM, (2010) Competing Mechanisms for Mapping Action-Related Categorical Knowledge and Observed Actions, *Cerebral Cortex Advance* **20** (12), 2832-41 (Journal IF: 6.979)

Canhão H (2010) Mudar e Evoluir. *Acta Reumatol Port.* **35**, 293 (Journal IF: 0.726)

Cardim N, Toste J, Carvalho V, Nunes I, Ferreira D, Carmelo V, Oliveira ASN, Ferro JM, Mariana S, Almeida A, Machado FP, Roquette J (2010) Playing games with a thrombus: a dangerous match. Paradoxical embolism from a huge central venous catheter thrombus: a case report. *Cardiovasc Ultrasound* **8**, 6. (Journal IF: 1.22)

Cardoso BM, Castanhinha S, Dupont J, Albuquerque M, Pereira SV, Miltenberger-Miltenyi G and Oliveira G (2010) Cleidocranial Dysplasia with Severe Parietal Bone Dysplasia: a new (p.Val124Serfs) RUNX2 mutation. *Clin Dysmorphol* **19** (3), 150-152 (IF: 0.468)

Carmo-Fonseca M (2010) Follow that messenger: live-imaging a journey out of the nucleus. *Dev Cell* **18**, 880-882. (Journal IF: 13.363)

Carrolo M, Frias MJ, Pinto FR, Melo-Cristino J and Ramirez M (2010) Prophage spontaneous activation promotes DNA release enhancing biofilm formation in *Streptococcus pneumoniae*. *PLoS ONE* **5**, e15678. (Journal IF: 4.351)

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS and Santos NC (2010) Atomic Force Microscopy-Based Molecular Recognition of a Fibrinogen Receptor on Human Erythrocytes. *ACS Nano* **4** (8), 4609-4620. (IF : 7.493)

Cascão R*, Moura RA*, Perpétuo I, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2010) Identification of cytokine network sustaining neutrophils and Th17 activation in early Rheumatoid Arthritis. *Arthritis Res Ther* **12**, R196 *Both authors contributed equally to this work. (Journal IF: 4.271)

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE (2010) Neutrophils in Rheumatoid Arthritis: more than simple final effectors. *Autoimmun Rev* **9** (8), 531-535 (Journal IF: 6.368)

Castro R, Barroso M, Rocha M, Esse R, Ramos R, Ravasco P, Rivera I, de Almeida IT (2010) The TCN2 776C> G polymorphism correlates with vitamin B-12 cellular delivery in healthy adult populations. *Clin Biochem* **43**, 645-649 (Journal IF: 2.019)

Cavaco S, Anderson SW, Correia M., Magalhães M, Pereira C, Tuna A, Taipa R, Pinto P, Pinto C, Cruz R, Lima AB, Castro-Caldas A, da Silva AM and Damásio H (2010) Task-specific contribution of the human striatum to perceptual-motor skill learning, *J Clin Exp Neuropsychol* **5**, 1-12. (Journal IF: 1.885)

Chaves MR, Boléo-Tomé C, Monteiro-Grillo I, Camilo M, Ravasco P (2010) The Diversity of Nutritional Status in Cancer: New Insights. *The Oncologist* **15**, 523-530 (Journal IF: 6.701)

Coelho M, Marti MJ, Tolosa E, Ferreira JJ, Valldeoriola F, Rosa M, Sampaio C (2010) Late-stage Parkinson's disease: the Barcelona and Lisbon cohort, *J Neurol* **257**, 1524-1532 (Journal IF: 2.903)

Colaço D, Mineiro A, Leal G and Castro-Caldas A (2010) Revisiting "The influence of literacy in paraphasias of aphasic speakers". *Clin Linguist Phon* **24**, 890-905. (Journal IF: 3.020)

Colosimo C, Martinez-Martin P, Fabbrini G, Hauser RA, Merello M, Miyasaki J, Poewe W, Sampaio C, Rascol O, Stebbins GT, Schrag A, Goetz CG (2010) Task Force Report on Scales to Assess Dyskinesia in Parkinson's Disease: Critique and Recommendations, *Mov Disord* **25**, 1131-1142. (Journal IF: 4.014)

Colvin RA, Means TK, Diefenbach TJ, Moita LF, Friday RP, Sever S, Campanella GSV, Abrazinski T, Manice LA, Moita C, Andrews NW, Wu D, Hacoen N and Luster AD (2010) Synaptotagmin mediated vesicle fusion regulates cell migration. *Nat Immunol* **11** (6), 495-502. (Journal IF: 26.000)

Conceição I, Evangelista T, Castro J, Pereira P, Silvestre A, Coutinho CA, Carvalho M (2010) Acquired amyloid neuropathy in a portuguese patient after domino liver transplantation. *Muscle Nerve* **42**, 836-839 (Journal IF: 2.287)

Correia Guedes L, Ferreira JJ, Rosa MM, Coelho M, Bonifati V, Sampaio C (2010) Worldwide frequency of G2019S LRRK2 mutation in Parkinson's disease: A systematic review. *Parkinsonism Relat Disord*. **16**, 237-242. (Journal IF: 2.406)

Cortez-Pinto H, Gouveia M, Pinheiro LD, Costa J, Borges M, Carneiro AV (2010) The burden of disease and the cost of illness attributable to alcohol drinking – results of a national study. *Alcohol Clin Exp Res*. **34**, 1442-1449 (Journal IF: 3.392)

Costa J, Gomes C, de Carvalho M (2010) Diagnosis, Pathogenesis and Therapeutic Targets in Amyotrophic Lateral Sclerosis. *CNS Neurol Disord Drug Targets*. **9**, 764-778 (Journal IF: 3.571)

Costa J, Gonzalez HA, Valldeoriola F, Gaig C, Tolosa E, Valle Sole J (2010) Nonlinear Dynamic Analysis of Oscillatory Repetitive Movements in Parkinson's Disease and Essential Tremor. *Mov Disord*. **25**, 2577-2586 (Journal IF: 4.014)

Costenla AR, Cunha RA, de Mendonça A (2010) Caffeine, adenosine receptors and synaptic plasticity. *J Alzheim Dis*. **20**, 25-34. (Journal IF: 3.832)

Coutinho JM, Ferro JM, Canhão P, Barinagarrementeria F, Bousser MG, Stam J and ISCVT Investigators (2010) Unfractionated or low-molecular weight heparin for the treatment of cerebral venous thrombosis. *Stroke* **41**, 2575-2580 (Journal IF: 7.041)

Cravo M, Sousa Guerreiro C, Moura dos Santos P, Brito M, Paula P, Fidalgo C, Tavares L, Dias Pereira A (2010) Risk factors for metabolic bone disease in Crohn's disease patients. *Inflamm Bowel Dis*. **16**, 2217-24 (Journal IF: 4.643)

Cudkowicz ME, Swash M (2010) CSF markers in amyotrophic lateral sclerosis. Has the time come? *Neurology* **24**, 949-950. (Journal IF: 8.172)

Curotto de Lafaille MA, Lafaille JJ, Graca L (2010) Mechanisms of tolerance and allergic sensitization in the airways and the lungs. *Curr Opin Immunol.* **22**, 616-622 (IF: 10.881)

da Costa G, Guerreiro A, Correia CF, Gomes RJ, Freire A, Monteiro E, Barroso E, Coelho AV, Outeiro TF, Freire AP, Cordeiro C (2010) A non-invasive method based on saliva to characterize transthyretin in familial amyloidotic polyneuropathy patients using FT-ICR high-resolution MS. *Proteomics Clin Appl* **4** (6-7), 674-678 (Journal IF: 1.875)

de Almeida JPL, Saldanha C (2010) Nonneuronal cholinergic system in human erythrocytes: biological role and clinical relevance. *J Membrane Biol.* **234** (3), 227-234. (Journal IF: 2.189)

de Almeida JPL, Pinto AC, Pereira J, Pinto S, de Carvalho M (2010) Implementation of a wireless device for real-time telemedical assistance of home-ventilated ALS patients - A feasibility study. *Telemed J E Health* **16**, 883-888. (Journal IF: 0.967)

de Almeida JPL, Saldanha C (2010) Dithiothreitol revisited in red cells: a new head for an old hat. *Clin Hemorheol Microcirc* **46**, 51-56. (Journal IF: 1.780)

de Almeida SF, Carmo-Fonseca M (2010) Cotranscriptional RNA checkpoints. *Epigenomics* **2**, 449-455. (Journal IF: N/A)

de Almeida SF, García-Sacristan A, Custódio N, Carmo-Fonseca M (2010) A link between nuclear RNA surveillance, the human exosome and RNA polymerase II transcriptional termination. *Nucleic Acids Res.* **38** (22), 8015-26. (Journal IF: 7.479)

de Carvalho M (2010) Olfactory ensheathing cells for human spinal cord injury. *Neurorehabil Neural Repair* **24**, 772. (Journal IF: 5.398)

de Carvalho M, Marcelino E, de Mendonça A (2010). Electrophysiological studies in healthy subjects involving caffeine. *J Alzh Dis.* **20** (suppl 1), S63-S69. (Journal IF: 3.832)

de Carvalho M, Pinto S, Costa J, Evangelista T, Ohana B, Pinto A (2010). A randomised, placebo-controlled trial of Memantine for Functional Disability in Amyotrophic Lateral Sclerosis. *Amyotr Lat Scler* **11**, 456-460 (Journal IF: 2.963).

de Carvalho M, Pinto S, Swash M (2010) Association between paraspinal muscles and diaphragm denervation in ALS *Amyotr Lat Scler* **11**, 63-66. (Journal IF: 2.963)

de Carvalho M, Swash M (2010). Sensitivity of electrophysiological tests for upper and lower motor neuron dysfunction in ALS: A six-month longitudinal study. *Muscle Nerve* **40**, 318. (Journal IF: 2.287)

de Carvalho M, Swash M (2010). The Onset of ALS? *Clin Neurophysiol.* **121**, 1709-1710. (Journal IF: 3.122)

de Carvalho M, Swash M (2010) Fasciculation-cramp syndrome preceding anterior horn cell disease: an intermediate syndrome? *J Neurol Neurosurg Psychiatry* Epub June 28 (Journal IF: 4.869).

- de la Torre I, Moura RA, Leandro MJ, Edwards J, Cambridge G (2010) B-cell-activating factor receptor expression on naive and memory B cells: relationship with relapse in patients with rheumatoid arthritis following B-cell depletion therapy. *Ann Rheum Dis* **69** (12), 2181-2188. (Journal IF: 8.111)
- de Mendonça A, Cunha RA (2010) Therapeutic opportunities for caffeine in Alzheimer's disease and other neurodegenerative disorders. *J Alzheim Dis* **20** (suppl 1), S1-S2, S249-S252. (Journal IF: 5.101)
- de Oliveira RM, Pais TF, Outeiro TF (2010) Sirtuins: common targets in aging and in neurodegeneration. *Curr Drug Targets* **11**(10), 1270-1280. (Journal IF: 3.932)
- de Oliveira S, Saldanha C (2010) An overview about erythrocyte membrane. *Clin Hemorheol Microcirc.* **44**, 63-74. (Journal IF: 1.780).
- Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L. (2010). Amlodipine effects on vasomotion in rabbit external ophthalmic artery. *Graefes Arch Clin Exp Ophthalmol.* **248** (2), 213-221. (Journal IF: 2.102)
- Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L (2010) Endothelin-1 effects on spontaneous oscillations in choroidal arterioles. *Acta Ophthalmol.* **88** (7), 742-747. (Journal IF: 2.441)
- Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L. (2010) L-arginine and L-nitroarginine methylester effects on vasomotion in isolated rabbit eyes. *Ophthalmic Res.* **43** (3), 113-121 (Journal IF: 2.441)
- Dias R, Ribeiro JA and Sebastião AM (2010) Enhancement of AMPA currents and GluR1 membrane expression through PKA-coupled adenosine A2A receptors. *Hippocampus*. Epub November 15. (Journal IF: 3.913)
- Diogenes MJ, Outeiro TF (2010) Neurotrophic Factors as a Protective Strategy in Parkinson's Disease. *CNS Neurol Disord Drug Targets.* **9**, 754-763. (Journal IF: 3.571)
- Diogo ELF; Santos JM; Phillips AJL (2010) Phylogeny, morphology and pathogenicity of *Diaporthe* and *Phomopsis* species on almond in Portugal. *Fungal Diversity* **44** (1), 107-115 (Journal IF: 3.803)
- 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 and 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**, 528-537. (Journal IF: 3.538)
- Duarte J, Agua-Doce A, Oliveira VG, Fonseca JE, Graca L (2010) Modulation of IL-17 and Foxp3 Expression in the Prevention of Autoimmune Arthritis in Mice. *PLoS One* **10**, (5), e10558. (Journal IF: 4.351)

Einhäupl K, Stam J, Bousser MG, De Bruijn SF, Ferro JM, Martinelli I and Masuhr F (2010) EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. *Eur J Neurol* **17**, 1229-1235. (Journal IF: 2.510)

Epiphanio S*, Campos MG*, Pamplona A*, Carapau D, Pena AC, Ataíde R, Monteiro CA, Félix N, Costa-Silva A, Marinho CRF, Dias S, Mota MM (2010) VEGF Promotes Malaria-associated Acute Lung Injury in Mice. *PLoS Pathogen*, **6** (5), e1000916 (*co-first authors). (Journal IF: 8.906)

Esteves T, Xavier C, Gama S, Mendes F, Raposinho PD, Marques F, Paulo A, Pessoa JC, Rino J, Viola G, Santos I (2010) Tricarbonyl M(I) (M = Re, (99m)Tc) complexes bearing acridine fluorophores: synthesis, characterization, DNA interaction studies and nuclear targeting. *Org Biomol Chem* **8** (18), 4104-4116. (Journal IF: 3.762)

Faria C, Miguéns J, Antunes JL, Salgado D, Nunes S, Barroso C, Martins Mdo C, Nunes VM, Roque L (2010) Pediatric brain tumors: genetics and clinical outcome. *J Neurosurg Pediatr.* **5**, 263-70. (Journal IF: 0.171)

Feldman-Stewart D, Caprici C, Brennenstuhl S, Tong C, Abacioglu U, Gawkowska-Suwinska M, Van Gils F, Heyda A, Igdem S, Macias V, Monteiro Grillo I, Moynihan C, Pijls-Johannesma M, Parker C, Pimentel N, Wordehoff H (2010) Information needs of early-stage prostate cancer patients: A comparison of nine countries. *Radiotherapy and Oncology* **94**, 328-333 (Journal IF: 4.343)

Ferencova J, Krajnak S, Chaves M, Cruz C, Grillo IM, Camilo ME, Ravasco P (2010) International exchange program between medical schools: the relevance of a clinical research training in nutrition. *Nutr Hosp.* **25**, 869-870. (Journal IF: 1.065)

Fernandes CC, Berg DK, Gómez-Varela D (2010) Lateral mobility of nicotinic acetylcholine receptors on neurons is determined by receptor composition, local domain, and cell type. *J Neurosci.*, **30**, 8841-8851. (Journal IF: 7.178).

Fernandes I, Borges da Costa J, Rego F, Quintela A, Soares de Almeida L, Costa L, Marques Gomes M. (2010) The importance of early diagnosis in Cowden syndrome. *Skin Cancer* **25**(2). (Journal IF: N.A.)

Ferreira AR, Santos MJ, Canas da Silva J, Fonseca JE, Gil V (2010) Avaliação não invasiva da função endotelial em doentes com Lúpus Eritematoso Sistémico. *Rev Port Cardiol*; **29** (Supl 1), 69

Ferreira JJ, Lew MF (2010) Immunogenicity analysis from an extension of a randomised, double-blind trial comparing botulinum neurotoxin type B vs. type A in previously toxin-naive patients with cervical dystonia: study 402CD-EU. *J Neur Transm.* **117**, 1234-1234. (Journal IF: 2.259)

Ferreira JJ, Neutel D, Mestre T, Coelho M, Rosa MM, Rascol O, Sampaio C (2010), Skin Cancer and Parkinson's Disease. *Mov Disord.* **25**, 139-148 (Journal IF: 4.014)

Ferreira JJ, Rascol O, Poewe W, Sampaio C, Rocha JF, Nunes T, Almeida L, Soares da Silva P (2010) A Double-Blind, Randomized, Placebo and Active-Controlled Study of Nebicapone

for the Treatment of Motor Fluctuations in Parkinson's Disease. *CNS Neurosci Ther.* **16**, 337-347. (Journal IF 2.690)

Ferreira P, Cravo M, Guerreiro CS, Tavares L, Santos PM, Brito M (2010) Fat intake interacts with polymorphisms of Caspase9, FasLigand and PPARgamma apoptotic genes in modulating Crohn's disease activity. *Clin Nutr.* **29**, 819-823. (Journal IF: 3.274)

Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F, Stolz E; ISCVT Investigators (2010) Cerebral venous thrombosis with nonhemorrhagic lesions: clinical correlates and prognosis. *Cerebrovasc Dis* **29**, 440-445 (Journal IF: 3.535)

Ferro JM, Massaro AR and Mas JL (2010) Aetiological diagnosis of ischaemic stroke in young adults. *Lancet Neurol.* **9**, 1085-1096. (Journal IF: 18.126)

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: 3.806)

Fonseca AC, Geraldês R, Reimão S, Pinho e Melo T and Ferro JM (2010) Neck hematoma after intravenous thrombolysis for stroke treatment. *Cerebrovasc Dis.* **30**, 101-102. (Journal IF: 3.535)

Fonseca JE, Brandi ML (2010) Mechanism of action of strontium ranelate: what are the facts? *Clin Cases Miner Bone Metab.* **7**, 17-18 (Journal IF: N/A)

Fonseca JE, Canhão H, Reis P, Santos MJ, Branco J, Quintal A, Malcata A, Araújo D, Ventura F, Figueiredo G, da Silva JC, Pato JV, de Queiroz MV, Santos RA, Neto AJ, de Matos A, Rodrigues A, Mourão AF, Ribeiro AS, Cravo AR, Barcelos A, Cardoso A, Vilar A, Braña A, Faustino A, Silva C, Godinho F, Cunha I, Costa JA, Gomes JA, Pinto JA, da Silva JA, Miranda LC, Inês L, Santos LM, Cruz M, Salvador MJ, Ferreira MJ, Rial M, Bernardes M, Bogas M, Araújo P, Machado P, Pinto P, de Melo RG, Cortes S, Alcino S, Capela S, Grupo de Estudos de Artrite Reumatóide da Sociedade Portuguesa de Reumatologia (2010) Portuguese guidelines for the use of biological agents in rheumatoid arthritis - March 2010 update. *Acta Reumatol Port.* **35** (1), 95-8. (Journal IF: 0.726)

Fonseca JE, Santos MJ, da Silva JA, Coelho P, Tavares V, Marques A, Branco J, da Silva JR, Queiroz MV, Figueirinhas J, Martins R, Canhão H (2010) Acta Reumatologica Portuguesa: impact factor attributed in June 2010 *Acta Reumatol Port* **35** (2), 129-130. (Journal IF: 0.726)

Foreid H, Barroso C, Evangelista T, Campos A, Pimentel J (2010) Intracerebral amyloidoma: case report and review of the literature. *Clin Neuropathol.* **29**, 217-222. (Journal IF: 1.037)

Foreid H, Bentes C, Pimentel J (2010) The use of placebo as a provocative test in the diagnosis of psychogenic non epileptic seizures. *Neuroethics* **3**, 95-98. (Journal IF: 12.79)

Foster KE, Gordon J, Cardenas K, Veiga-Fernandes H, Makinen T, Grigorieva E, Wilkinson DG, Blackburn CC, Richie E, Manley NR, Adams RH, Kioussis D, Coles MC (2010) EphB-ephrin-B2 interactions are required for thymus migration during organogenesis. *Proc Natl Acad Sci USA.* **107**, 13414-13419. (Journal IF: 9.43)

Franquelim HG, Veiga AS, Weissmüller G, Santos NC and Castanho MARB (2010) Unravelling the molecular basis of the selectivity of the HIV-1 fusion inhibitor sifuvirtide towards phosphatidylcholine-rich rigid membranes. *Biochim Biophys Acta*. **1798**, 1234-1243. (Journal IF: 4.396)

Friedman JH, Alves G, Hagell P, Marinus J, Marsh L, Martinez-Martin P, Goetz CG, Poewe W, Rascol O, Sampaio C, Stebbins G, Schrag A (2010) Fatigue Rating Scales Critique and Recommendations by the Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. *Mov Disord*. **25**, 805-822 (Journal IF 4.014)

Geraldes R, de Carvalho M (2010) Transcranial magnetic stimulation is a useful diagnostic test in psychogenic paralysis. *J Neurol Neurosurg Psychiatry* (Journal IF: 4.869).

Gil-Gouveia R, Martins IP (2010) Validation of the Portuguese Version of ID-Migraine. *Headache* **50**, 396-402 (Journal IF: 2.896)

Ginó S, Mendes T, Maroco J, Ribeiro F, Schmand BA, de Mendonça A, Guerreiro M (2010) Memory complaints are frequent but qualitatively different in young and old healthy people. *Gerontology* **56**, 272-277. (Journal IF: 1.69)

Gomes AQ*, Correia DV*, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, 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), 1397-1404. (Journal IF: 6.416) (* co-first authors)

Gomes AQ*, Martins DS* and Silva-Santos B (2010) Targeting $\gamma\delta$ T-lymphocytes for cancer immunotherapy: from novel mechanistic insight to clinical application. *Cancer Res* **70** (24), 10024-10027. (Journal IF: 7.543) (* co-first authors)

Gonçalves SA, Matos JE, Outeiro TF (2010) Zooming into protein oligomerization in neurodegeneration using BiFC. *Trends Biochem Sci*. **35** (11), 643-651. (Journal IF: 12.374)

Gonçalves-Sousa N, Ribot JC, deBarros A, Correia DV, Caramalho I and Silva-Santos B (2010) Inhibition of murine $\gamma\delta$ lymphocyte expansion and effector function by regulatory $\alpha\beta$ T-cells is cell-contact dependent and sensitive to GITR modulation. *Eur J Immunol* **40** (1), 61-70. (Journal IF: 5.179)

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 (2010) Dissemination and evaluation of the 3E initiative recommendations for use of methotrexate in rheumatic disorders: results of a study among 2,233 rheumatologists. *Ann Rheum Dis*. Epub May 14 (Journal IF: 8.111)

Gouveia LO and Canhão P (2010) MTHFR and the risk for cerebral venous thrombosis- a meta-analysis. *Thromb Res*. **125**, e153-158. (Journal IF: 2.449)

HÃagl B, Arnulf I, Comella C, Ferreira J, Iranzo A, Tilley B, Trenkwalder C, Poewe W, Rascol O, Sampaio C, Stebbins GT, Schrag A, Goetz CG (2010) Scales to assess sleep impairment in Parkinson's disease: critique and recommendations, *Mov Disord*. **25**, 2704-2716. (Journal IF 4.014)

Hampel H, Wilcock G, Andrieu S, Aisen P, Blennow K, Broich K, Carrillo M, Fox NC, Frisoni GB, Isaac M, Lovestone S, Nordberg A, Prvulovic D, Sampaio C, Scheltens P, Weiner M, Winblad B, Coley N, Vellas B; for the Oxford Task Force Group. (2010) Biomarkers for Alzheimer's disease therapeutic trials, 2010 Dec 2. *Prog Neurobiol* Epub December 2. (Journal IF: 11.554)

Hänscheid T and Grobusch MP (2010) Biosafety and tuberculosis laboratories in Africa. *Lancet Infect Dis* **10**, 582-583. (Journal IF: 15.583)

Henrique D, Bally-Cuif L (2010) A cross-disciplinary approach to understanding neural stem cell in development and disease. *Development* **137** (12), 1933-1938 (Journal IF: 7.194)

Henriques CM, Rino J, Nibbs RJ, Graham GG, Barata JT (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R α in T cells. *Blood* **115** (16): 3269-3277. (Journal IF: 10.555)

Henriques R, Lelek M, Fornasiero EF, Valtorta F, Zimmer C, Mhlanga MM (2010) QuickPALM: 3D real-time photoactivation nanoscopy image processing in Image. *J Nature Methods* **7** (5), 339-340. (Journal IF: 16.874)

Henriques ST and Castanho MARB (2010) Is PrP(106-126) fragment involved in the membrane activity of the prion protein? *Curr Protein Pept Sci.* **11**, 326-333. (Journal IF: 3.854)

Henriques ST and Craik DJ (2010) Cyclotides as templates in drug design. *Drug Discov Today.* **15**, 57-64. (Journal IF: 6.630)

Henriques ST, Pattenden LK, Aguilar MI and Castanho MARB (2010) Fast membrane association is a crucial factor in the peptide pep-1 translocation mechanism: A kinetic study followed by surface plasmon resonance. *Biopolymers* **94**, 314-322. (Journal IF: 2.605)

Henriques ST, Tan CC, Craik DJ and Clark RJ (2010) Structural and Functional Analysis of Human Liver-Expresses Antimicrobial Peptide 2. *ChemBioChem* **11**, 2148-2157. (Journal IF: 3.824)

Jónsdóttir T, Gunnarsson I, Mourão AF, Lu TY, van Vollenhoven RF, Isenberg D. (2010) Clinical improvements in proliferative vs membranous lupus nephritis following B-cell depletion: pooled data from two cohorts. *Rheumatology (Oxford)* **49** (8), 1502-1504. (Journal IF: 4.236)

Jorge Z, Carvalho MR, Guerra AS, Alves N, de Almeida JM, Fagundes MJ, Cortez-Pinto H, do Carmo I (2010) Malnutrition in morbid nutrition. *Acta Médica Portuguesa* **23**, 273-276 (Journal IF: NA)

Jotta PY, Ganazza MA, Silva A, Viana MB, da Silva MJ, Zambaldi LJG, Barata JT, Brandalise SR, Yunes JA (2010). Negative prognostic impact of PTEN mutation in pediatric T-cell acute lymphoblastic leukemia. *Leukemia* **24** (1), 239-42. (Journal IF: 8.296)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010) Life without geminin. *Cell Cycle* **16**, 3181-3185. (Journal IF: 4.8)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010) Differential geminin requirement for proliferation of thymocytes and mature T cells. *J Immunol.* **184**(5), 2432-2441. (Journal IF: 5.6)

Kazantsev AG, Outeiro TF (2010) Drug discovery for CNS disorders: from bench to bedside. *CNS Neurol Disord Drug Targets* **9** (6), 668 (Journal IF: 3.571)

Kollensperger M, Geser F, Ndayisaba JP, Boesch S, Seppi K, Ostergaard K, Dupont E, , Cardozo A, , Tolosa E, Abele M, Klockgether T, Yekhelef F, Tison F, Daniels C, Deuschl G, Coelho M, Sampaio C, Bozi M, Quinn N, Schrag A., Mathias CJ, Fowler C, Nilsson CF, Widner H, Schimke N, Oertel W, del Sorbo F, Albanese A, Pellecchia MT, Barone P, Djaldetti R Colosimo C, Meco G, Gonzalez-Mandly A, Berciano J, Gurevich T, Giladi N, Galitzky M, Rascol, O, Kamm, C, Gasser T, Siebert, U, Poewe W, Wenning, GK (2010) Presentation, Diagnosis, and Management of Multiple System Atrophy in Europe: Final Analysis of the European Multiple System Atrophy Registry. *Mov Disord.* **25**, 2604-2612 (Journal IF: 4.014)

Krug T, Manso H, Gouveia L, Sobral J, Xavier JM, Albergaria I, Gaspar G, Correia M, Viana-Baptista M, Simões RM, Pinto AN, Taipa R, Ferreira C, Fontes JR, Silva MR, Gabriel JP, Matos I, Lopes G, Ferro JM, Vicente AM, Oliveira SA (2010) Kalirin: A novel genetic risk factor for ischemic stroke. *Human Genetics* **127**, 513-523. (Journal IF: 4.042)

Kuperstein I, Broersen K, Benilova I, Rozenski J, Jonckheere W, Debulpaep M, Vandersteen A, Segers-nolten I, Van Der Werf K, Subramaniam V, Braeken D, Calewaert G, Bartic C, D'Hooge R, Martins IC, Rousseau F, Schymkowitz J and De Strooper B (2010) Neurotoxicity of Alzheimer disease A β -peptides is induced by small changes in the A β 42 to A β 40 ratio. *EMBO J.* **29**, 3408-3420. (Journal IF: 8.993)

Lança T, Correia DV, Moita CF, Raquel H, Ferreira C, Ramalho JS, Barata JT, Moita LF, Gomes AQ and Silva-Santos B (2010) The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. *Blood.* **115** (12), 2407-2411. (Journal IF: 10.555)

Liehl P, França A.R, Prudêncio M, Latz E, Zaidman-Rémy A, Mota MM (2010). Phosphothioate Oligodeoxynucleotides inhibit Plasmodium sporozoite gliding motility, *Cell. Microbiol.*, **12**, 506-515 (Journal IF: 5.725)

Lopes de Almeida JP, Saldanha C (2010) Dithiothreitol revisited in red cells: a new head for an old hat. *Clin Hemorheol Microcirc.* **46**, 51-56. (Journal IF: 1.780)

Lopes SS, 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: 7.194)

Louis ED, Ferreira JJ (2010) How Common Is the Most Common Adult Movement Disorder? Update on the Worldwide Prevalence, Essential Tremor. *Mov Disord.* **25**, 534-541. (Journal IF: 4.014)

Lourenço R, Lopes SS and Saúde L (2010) Left-right function of dmr2 genes is not conserved between zebrafish and mouse. *PlosONE.* **5** (12), e14438. (Journal IF: 4.351)

- Lourenço R and Saúde L (2010) Symmetry OUT, Asymmetry IN. *Symmetry*. **2**, 1033-1054.
- 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.)
- Machado MV, Cortez-Pinto H (2010) Osteopontin: A Missing Link between Hedgehog Signaling and Fibrosis in Nonalcoholic Steatohepatitis. Editorial. *Hepatology* **53**, online Dec 21 (Journal IF: 10.840)
- Machado MV, Oliveira AG, Cortez-Pinto H (2010) Hepatic steatosis in patients coinfectd with human immunodeficiency virus/hepatitis C virus: A meta-analysis of the risk factors. *Hepatology* **52**, 71-78 (Journal IF: 10.840)
- Machado P, Castrejon I, Katchamart W, Koevoets R, Kuriya B, Schoels M, Silva-Fernández L, Thevissen K, Vercoutere 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, Martinez-Osuna P, Montecucco C, Müller-Ladner U, Ostergaard M, Sheane B, Xavier RM, Zochling J, Bombardier C (2010) 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*. Epub August 19. (Journal IF: 8.111)
- Madureira S, Verdelho A, Moleiro C, Ferro JM, Erkinjuntti T, Jokinen H, Pantoni L, Fazekas F, Van der Flier W, Visser M, Waldemar G, Wallin A, Hennerici M and Inzitari D (2010) Neuropsychological predictors of dementia in a three-year follow-up period: data from the LADIS study. *Dement Geriatr Cogn Disord* **29**, 325-334. (Journal IF: 2.578)
- Manso H, Krug T, Sobral J, Albergaria I, Gaspar G, Ferro JM, Oliveira SA, Vicente AM (2010) Variants of the Matrix Metalloproteinase-2 but not the Matrix Metalloproteinase-9 genes significantly influence functional outcome after stroke. *BMC Med Genet* **11**, 40. (Journal IF: 2.76)
- Marcelino G, Oliveira JM, Ravasco P, Marques-Vidal P (2010) Body image, weight concerns and related practices by Portuguese adolescents. *Nutritional Therapy and Metabolism* **27**, 189-192 (no IF yet, cited on medline)
- 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 (2010) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of two cases. *Blood* Epub October 26. (Journal IF: 10.555).
- Marques SC, Oliveira CR, Outeiro TF, Pereira CM (2010) Alzheimer's disease: the quest to understand complexity. *J Alzheimers Dis*. **21** (2), 373-383. (Journal IF: 3.832)
- Marques SC, Oliveira CR, Pereira CM, Outeiro TF (2010) Epigenetics in neurodegeneration: A new layer of complexity. *Prog Neuropsychopharmacol Biol Psychiatry* Epub August 22 (Journal IF: 2.823)

Martin Martins J, Vale S, Ferreira F, Fagundes MJ, Carmo I, Saldanha C, Martins e Silva J (2010) Plasma corticotropin releasing hormone during the feeling of induced emotions. *Neuro Endocrinol Lett.* **31**, 250-255. (Journal IF: 1.047)

Martins AP, Lopes PA, Martins SV, Madeira A, Santos NC, Prates JAM, Moura TF and Soveral G (2010) Conjugated linoleic acid reduces permeability and fluidity of adipose plasma membranes from obese Zucker rats. *Biochem Biophys Res Commun.* **398**, 199-204. (Journal IF: 2.720)

Martins ER, Melo-Cristino J and Ramirez M (2010). Evidence for rare capsular switching in *Streptococcus agalactiae*. *J Bacteriol* **192**, 1361-1369 (Journal IF: 3.940)

Martins IP, Loureiro C, Rodrigues S, Dias B, Slade P (2010) Factors affecting the retrieval of famous names. *Neurol Sci.* **31**, 269–276. (Journal IF: 1.236)

Martins LR, Lúcio P, Silva MC, Gameiro P, Silva MG, Barata JT (2010) Targeting CK2 overexpression and hyperactivation as a novel therapeutic tool in Chronic Lymphocytic Leukemia. *Blood* **116** (15), 2724-2731. (Journal IF: 10.555)

Martins M, Martins IP (2010) Memory malingerer: Evaluating WMT criteria. *Applied Neuropsychol.* **17**, 177-182. (Journal IF: 1.027)

Maruta C, Guerreiro M, de Mendonça A, Hort J, Scheltens P (2010) The use of neuropsychological tests across Europe: The need for a consensus in the use of assessment tools for dementia. *Eur J Neurol* Epub June 27. (Journal IF: 2.732)

Matos PM, Castanho MARB and Santos NC (2010) HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes. *PLoS ONE* **5**, e9830. (Journal IF: 4.351)

Matos PM, Franquelim HG, Castanho MARB and Santos NC (2010) Quantitative assessment of peptide–lipid interactions. Ubiquitous fluorescence methodologies. *Biochim Biophys Acta.* **1798**, 1999-2012. (Journal IF: 4.396)

Matos PM, Freitas T, Castanho MARB and Santos NC (2010) Sifuvirtide interaction with blood cell membranes denotes the conjugation of different lipid preferences. *Biochem Biophys Res Commun.* **403**, 270-274. (Journal IF: 2.720)

Maurer-Stroh S, Debulpaep M, De La Paz ML, Martins IC, Reumers J, Copland A, Serpell L, Serrano L, Schymkowitz J, Morris K and Rousseau F (2010) Exploring the sequence determinants of amyloid structure using position-specific scoring matrices. *Nat Methods* **7**, 237-2342. (Journal IF: 16.874)

McMillan DJ, Bessen DE, Pinho M, Ford C, Hall GS, Melo-Cristino J and Ramirez M (2010) Population genetics of *Streptococcus dysgalactiae* subspecies *equisimilis* reveals widely dispersed clones and extensive recombination. *PLoS ONE* **5**, e11741. (Journal IF: 4.351)

Mehdad A, McBride E, Monteiro Grillo I, Camilo M, Ravasco P (2010) Nutritional status and eating pattern in prostate cancer patients. *Nutr Hosp* **25**, 422-427 (Journal IF: 1.065)

Melo-Cristino J, Santos L, Silva-Costa C, Friães A, Pinho MD and Ramirez M (2010) The Viriato Study: Update on antimicrobial resistance of microbial pathogens responsible for community-acquired respiratory tract infections in Portugal. *Paediatr. Drugs* **12**, 11-17. (Journal IF: NA)

Mendonça V, Jorge M, Monteiro Grillo I, Palhano MJ, Feijó S (2010) Tracheal chondrosarcoma. *Clin Transl Oncol.* **12**, 576-580 (Journal IF: 1.146)

Menzel U, Ktistaki E, Tolaini M, Veiga-Fernandes H, Kioussis D (2010). Replication allows inactivation of a knocked-in locus control region in inappropriate cell lineages. *Proc Natl Acad Sci USA* **107**:16928-16933. (Journal IF: 9.43)

Mestre T, Ferreira JJ (2010) Pharmacotherapy in Parkinson's disease: case studies. *Adv Neurol Disord* **3**, 117-126. (Journal IF: N/A)

Mestre T, Lang AE (2010) The Grasp Reflex: A Symptom in Need of Treatment, *Mov Disord.* **25**, 2479-2485. (Journal IF: 4.014)

Miranda B, Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, Scoditti U and ISCVT Investigators (2010) Venous thromboembolic events after cerebral vein thrombosis. *Stroke* **41**, 1901-1906. (Journal IF: 7.041)

Mishra BB, Moura-Alves P, Sonawane A, Hacoheh N, Griffiths G, Moita LF*, Anes E* (2010) Mycobacterium tuberculosis Protein ESAT-6 is a Potent Activator of the NLRP3/ASC Inflammasome. *Cell Microbiol.* **12**, 1046-1063. *Corresponding Authors. (Journal IF: 5.725)

Moidunny S, Dias RA, Wesseling E, Sekino Y, Boddeke HWGM, Sebastiao AM, Biber K (2010). Interleukin (IL)-6-type cytokines in Neuroprotection and Neuromodulation: OSM, but not LIF, requires neuronal Adenosine A₁ Receptor function. *J Neurochem* **114**, 1667-1677. (Journal IF: 3.999)

Mollet IG, Ben-Dov C, Felício-Silva D, Grosso AR, Eleutério P, Alves R, Staller R, Silva TS and Carmo-Fonseca M (2010) Unconstrained mining of transcript data reveals increased alternative splicing complexity in the human transcriptome. *Nucleic Acids Res.* **38** (14), 4740-4754. (Journal IF: 7.479)

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: 5.646)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Água-Doce A, Wollenberg I, Silva-Santos B and Graça L (2010) Identification of regulatory Foxp3+ invariant Natural Killer T cells induced by TGF-beta. *J Immunol* **185** (4), 2157-2163. (Journal IF: 5.646)

Morgado J, Rocha CS, Maruta C, Guerreiro M, Martins IP (2010) Cut-off scores in MMSE: a moving target? *Eur J Neurol.* **17** (5), 692-695. (Journal IF: 3.020)

Moura RA*, Cascão R*, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2010) Cytokine pattern in very early Rheumatoid arthritis favours B-cell activation and survival. *Rheumatology*

(Oxford) Epub November 2. *Both authors contributed equally to this work. (Journal IF: 4.236)

Moura RA, Weinmann P, Pereira PA, Caetano-Lopes J, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Graça L, Fonseca JE (2010) Alterations on peripheral blood B cell subpopulations in very early arthritis patients. *Rheumatology (Oxford)* **49** (6), 1082-92 (Journal IF: 4.236)

Mourão AF, Canhão H, Sousa E, Cascão R, Costa JB, Almeida LS, Oliveira ME, Gomes MM, Queiroz MV, Fonseca JE (2010) From a neutrophilic synovial tissue infiltrate to a challenging case of rheumatoid arthritis. *Acta Reumatol Port.* **35** (2), 228-231. (Journal IF: 0.726)

Mourão AF, Rustin MHA, Isenberg D (2010) Exacerbation of psoriatic skin lesions in 3 patients with psoriatic arthritis receiving anti-tumour necrosis factor-alpha therapy. *Clin Exp Rheumatol* **28** (3), 408-410. (Journal IF: 2.396)

Nakhjavani M, Morteza A, Khajeali L, Esteghamati A, Khalilzadeh O, Asgarani F, Outeiro TF (2010) Increased serum HSP70 levels are associated with the duration of diabetes. *Cell Stress Chaperones* **15** (6), 959-964. (Journal IF: 2.167)

Nielsen TR, Vogel A, Riepe MW, de Mendonça A, Rodriguez G, Nobili F, Gade A, Waldemar G (2010) Assessment of dementia in ethnic minority patients in Europe – A European Alzheimer’s Disease Consortium survey. *Int Psychogeriatr.* Epub December 30. (Journal IF: 2.21)

Nunes T, Fragata I, Ribeiro F, Palma T, Maroco J, Cannas J, Secca M, Menezes C, Carmo I, Cunha G, Castelo Branco M, Guerreiro M, de Mendonça A (2010) The outcome of elderly patients with cognitive complaints but normal neuropsychological tests. *J Alzheimers Dis.* **19**, 137-145. (Journal IF: 5.101)

Nunes-Cabaço H, Ribot JC, Caramalho I, Serra-Caetano A, Silva-Santos B* and Sousa AE* (2010) Foxp3 induction in human and murine thymus precedes the CD4⁺ CD8⁺ stage but requires early T cell receptor expression. *Immunol Cell Bio* **88** (5), 523-8. (Journal IF: 4.200) (* Co-senior authors)

Oliveira M, da Silva MN, Geraldés V, Xavier R, Laranjo S, Silva V, Postolache G, Ferreira R, Rocha I (2010) Acute vagal modulation of electrophysiology of the atrial and pulmonary veins increases vulnerability to atrial fibrillation. *Exp Physiol* Epub October 15. (Journal IF: 3.168)

Oliveira M, da Silva N, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R (2010) Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation. *Int J Cardiol.* Epub March 16. (Journal IF: 3.469)

Oliveira M, da Silva N, Geraldés V, Postolache G, Xavier R, Laranjo S, Rocha I, Ferreira R, Silva Carvalho (2010) Effect of vagal stimulation on the initiation and termination of atrial fibrillation in the anaesthetized rabbit. *Rev.Port Cardiol.* **29** (3), 375-89. (Journal IF: N/A)

Orge L, Oliveira A, Machado C, Lima C, Ochoa C, Silva J, Carvalho R, Tavares P, Almeida P, Ramos M, Pinto MJ, Simas JP (2010) Putative emergence of classical scrapie in a background of enzootic atypical scrapie. *J Gen Virol* **91** (Pt 6), 1646-1650. (Journal IF: 3.241)

Ostrowski M, Carmo NB, Krumeich S, Fanget I, Raposo G, Savina A, Moita CF, Schauer K, Hume AN, Freitas RP, Goud B, Benaroch P, Hacohen N, Fukuda M, Desnos C, Seabra MC, Darchen F, Amigorena S, Moita LF* Thery C*. (2010) Rab27a and Rab27b control different steps of the exosome secretion pathway. *Nat Cell Biol* **12** (1), 19-30. *Corresponding authors. (Journal IF: 19.527)

Pato MP, Santos NJG, Areias P, Pires EB, de Carvalho M, Pinto S, Lopes DS (2010). Finite element studies of the mechanical behavior of the diaphragm in normal and pathological cases. *Comput Methods Biomech Biomed Engin* Epub November 15 (Journal IF: 1.454).

Pedrosa H, de Sá A, Guerreiro M, Maroco J, Simões MR, Galasko D, de Mendonça A (2010) Functional Evaluation distinguishes MCI patients from healthy elderly people - the ADCS/MCI/ADL scale. *J Nutr Health Aging* **14**, 703-709. (Journal IF: 2.321)

Petros P, Swash M (2010) Sacrocolpopexy may cause difficult defecation by inhibiting the external opening out mechanism. *Int Urogynecol J Pelvic Floor Dysfunct* Epub October 22.

Pimentel J, Bentes C, Campos A, Gonçalves Ferreira A, and the Epilepsy Surgery Group (2010) Long-term and late seizure outcome after surgery for temporal lobe epilepsy. *Epileptic Disord* **12**(1), 54-58. (Journal IF: 1.198)

Pinho MD, Melo-Cristino J and Ramirez M (2010) Fluoroquinolone resistance in *Streptococcus dysgalactiae* subsp. *equisimilis* and evidence for a shared global gene pool with *Streptococcus pyogenes*. *Antimicrob Agents Chemother.* **54**, 1769-1777. (Journal IF: 4.802)

Pinto A, Almeida JP, Pinto S, Pereira J, Oliveira AG, de Carvalho, M (2010). Home telemonitoring of non invasive ventilation decreases healthcare utilization in a prospective controlled trial of ALS patients. *J Neurol Neurosurg Psychiatry* **81**, 1238-1242 (Journal IF: 4.869).

Pinto S, de Carvalho M (2010) Is a 4-hour use of non-invasive ventilation enough to define compliance? *Amyotr Lat Scler* **11**, 250-252 (Journal IF: 2.963).

Pinto S, de Carvalho M (2010). Symmetry of phrenic nerve motor response in amyotrophic lateral sclerosis. *Muscle Nerve* **42**, 882-884 (Journal IF: 2.287)

Pires R, Ardanuy C, Rolo D, Morais A, Brito-Avô A, Marques JG, Liñares J and Santos-Sanches I (2010) Emergence of ciprofloxacin-nonsusceptible *Streptococcus pyogenes* isolates from healthy children and pediatric patients in Portugal. *Antimicrob Agents Chemother* **54**, 2677-2680. (Journal IF: 4.802).

Pousinha PA, Correia AM, Sebastião AM and Ribeiro JA (2010) Predominance of adenosine excitatory over inhibitory effects on transmission at the neuromuscular junction of infant rats. *J Pharmacol Exp Ther* **332**, 153-163. (Journal IF: 4.093).

Prakash H, Lüth A, Grinkina N, Holzer D, Wadgaonkar R, Gonzalez AP, Anes E, Kleuser B (2010) Sphingosine kinase-1 (SphK-1) regulates *Mycobacterium smegmatis* infection in macrophages. *PLoS One* **5** (5), e10657. (Journal IF 4.5)

Pugdahl K, Fuglsang-Frederiksen A, Johnsen B, Tankisi H, de Carvalho; Fawcett P, Labarre-Vila A, Liguori R, Nix W, Schofield I (2010). Variation in the neurophysiological examination of Amyotrophic Lateral Sclerosis in Europe. *Amyotr Lat Scler* **11**, 443-448 (Journal IF: 2.963).

Ramirez M and Melo-Cristino J (2010) Expanding the diagnosis of pediatric bacteremic pneumococcal pneumonia from blood cultures to molecular methods: advantages and caveats. *Clin Infect Dis.* **51**, 1050-1052. (Journal IF: 8.195)

Ramiro S, Canhão H, Branco JC. (2010) EpiReumaPt Protocol- Portuguese epidemiologic Study of the Rheumatic diseases. *Acta Reumatol Port.* **35**, 384-390 (Journal IF: 0.726)

Ramos C, Rocha S, Gaspar C, Henrique D (2010) Two Notch ligands, Dll1 and Jag1, are differentially restricted in their range of action to control neurogenesis in the mammalian spinal cord. *PLoS ONE* **5** (12): e15515. (Journal IF: 4.351)

Raposo BR, Rodrigues-Santos P, Carvalheiro H, Agua-Doce AM, Carvalho L, Pereira da Silva JA, Graça L, Souto-Carneiro MM (2010) Monoclonal anti-CD8 therapy induces disease amelioration in the K/BxN mouse model of spontaneous chronic polyarthritis. *Arthritis Rheum.* **62**, 2953-2962 (Journal IF : 7.332)

Rato S, Maia S, Brito PM, Resende L, Pereira CF, Moita C, Freitas RP, Moniz-Pereira J, Hacoen N, Moita LF, Goncalves J (2010) Novel HIV-1 knockdown targets identified by an enriched kinases/phosphatases shRNA library using a long-term iterative cscreen in jurkat T-cells. *PLoS One.* **17**, 5(2):e9276. (Journal IF: 4.351)

Ratziu V, Bellentani S, Cortez-Pinto H, Day C, Marchesini G (2010) A position statement on NAFLD/NASH based on the EASL 2009 special conference. *J Hepatol* **53**, 372-384 (Journal IF: 7.818)

Ravasco P, Anderson H, Mardones F (2010). Métodos de valoración del estado nutricional. *Nutr Hospital.* **25** (Supl. 3), 57-66. (Journal IF: 1.065)

Ravasco P, Aranha MM, Borralho PM, da Silva IBM, Correia L, Fernandes A, Rodrigues CMP, Camilo M (2010) Colorectal cancer: Can nutrients modulate NF-kappa B and apoptosis? *Clin Nutr.* **29**, 42-46 (Journal IF: 3.274)

Ribeiro JA, Machado P, Ramiro S, Duarte C, Mourão AF, Bogas M, Costa L, Bernardes M, Santos MJ, Fonseca JE, Canhão H (2010) Portuguese Recommendations «How to diagnose, monitor and treat undifferentiated peripheral inflammatory arthritis»: systematic literature review and expert opinion. *Acta Reumatol Port* **35**, 475-496 (Journal IF: 0.726)

Ribeiro JA and Sebastiao AM (2010) Caffeine and adenosine. *J Alzheim Dis.* **20**, 3-13. (Journal IF: 3.832).

Ribeiro JA and Sebastião AM (2010) Modulation and metamodulation of synapses by adenosine. *Acta Physiol.* **199**, 161-169. (Journal IF: 2.455)

Ribeiro MMB, Castanho MARB and Serrano I (2010) *In vitro* blood-brain barrier models – latest advances and therapeutic applications in a chronological perspective. *Mini Rev Med Chem.* **10**, 262-270. (Journal IF: 2.971)

Ribeiro MMB, Melo MN, Serrano I, Santos NC and Castanho MARB (2010) Drug-lipid interaction evaluation: Why a 19th century solution? *Trends Pharmacol Sci.* **31**, 449-454. (Journal IF: 9.064)

Ribot JC, Chaves-Ferreira M, d'Orey F, Wencker M, Gonçalves-Sousa N, Decalf J, Simas JP, Hayday AC 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)

Rolando M, Stefani C, Flatau G, Auberger P, Mettouchi A, Musa M, Ulf Rapp, Antoine Galmiche and Emmanuel Lemichez. (2010) Transcriptome dysregulation by anthrax lethal toxin plays a key role in induction of human endothelial cell cytotoxicity. *Cellular Microbiology* **12**, 1462-5822 (Journal IF: 5.725)

Rosa MM, Ferreira JJ, Coelho M, Freire R, Sampaio C (2010) Prescribing Patterns of Antiparkinsonian Agents in Europe. *Mov Disord* **8**, 1053-1060. (Journal IF: 4.014)

Saldanha C, de Almeida JPL, Freitas T, Oliveira S, Silva-Herdade AS (2010). Erythrocyte deformability responses to shear stress under external and internal stimuli influences. *Series on Biomechanics* **25**, 54-60. (Journal IF: N/A)

Sampaio C, Ferreira JJ (2010) Parkinson disease adagio trial hints that rasagiline slows disease progression. *Nat Rev Neurol.* **6**, 126-128. (Journal IF: N/A)

Sampaio C, Ferreira JJ (2010) Parkinson disease Adjunctive entacapone therapy increases risk of dyskinesia. *Nat Rev Neurol.* **6**, 590-591 (Journal IF: N/A)

Santiago PS, Carvalho FAO, Domingues MM, Carvalho JWP, Santos NC and Tabak M (2010) Isoelectric point determination for *Glossoscolex paulistus* extracellular hemoglobin: Oligomeric stability in acidic pH and relevance to protein-surfactant interactions. *Langmuir* **26**, 9794-9801. (Journal IF: 4.363)

Santiago PS, Carvalho JWP, Domingues MM, Santos NC and Tabak M (2010) Thermal stability of extracellular hemoglobin of *Glossoscolex paulistus*: Determination of activation parameters by optical spectroscopic and differential scanning calorimetric studies. *Biophys Chem.* **152**, 128-138. (Journal IF: 2.276)

Santos A, Duarte A, Fedorov A, Martinho J and Moura I (2010) Rubredoxin mutant A51C unfolding dynamics: a Förster Resonance Energy Transfer study. *Biophys Chem.* **148**, 131-137. (Journal IF: 2.276)

Santos C, Lunet N, Azevedo A, de Mendonça A, Ritchie K, Barros H (2010) Caffeine intake is associated with a lower risk of cognitive decline: a cohort study from Portugal. *J Alzheim Dis* **20** (suppl 1), S175-S185. (Journal IF: 5.101)

Santos L, Romeu JC, Canhão H, Fonseca JE, Fernandes PR.(2010) A quantitative comparison of a bone remodeling model with dual-energy X-ray absorptiometry and analysis of the inter-individual biological variability of femoral neck T-score. *J Biomech* **43** (16), 3150-3155. (Journal IF: 2.567)

Santos MJ, Fernandes D, Capela S, da Silva JC, Fonseca JE (2010) Interleukin-6 promoter polymorphism -174 G/C is associated with nephritis in Portuguese Caucasian systemic lupus erythematosus patients. *Clin Rheumatol*. Epub December 14. (Journal IF: 1.668)

Santos MJ, Vinagre F, Canas da Silva J, Gil V, Fonseca JE. (2010) Cardiovascular risk profile in systemic lupus erythematosus and rheumatoid arthritis: a comparative study of female patients. *Acta Reumatol Port* **35**, 325-332 (Journal IF: 0.726)

Santos NC (2010) In and out – biochemical and biophysical mechanisms of viral fusion and assembly. *TheScientificWorldJournal* **10**, 419-421. (Journal IF: 1.658)

Santos NC, Martins e Silva J, Freitas T, Doroana M, Duarte N, Tavares L, Antunes F and Saldanha C (2010) Blood cell membrane fluidity and intracellular Ca²⁺ changes in antiretroviral-naïve and -treated HIV-1-infected patients. *TheScientificWorldJournal* **10**, 350-355. (Journal IF: 1.658)

Santos R, Oliveira J, Vieira E, Coelho T, Carneiro AL, Evangelista T, Dias C, Fortuna A, Geraldo A, Negrão L, Guimarães A, Bronze-da-Rocha E (2010). Private dysferlin exon skipping mutation (c.5492G>A) with a founder effect reveals further alternative splicing involving exons 49-51. *J Hum Genet.* **55**, 546-549 (Journal IF: 2.431).

Santos JM, Correia VG, Phillips AJL (2010) Primers for mating-type diagnosis in *Diaporthe* and *Phomopsis*: their use in teleomorph induction in vitro and biological species definition. *Fungal Biology*. **114** (2-3), 255-270 (Journal IF: 2.921)

Schmidt R, Ropele S, Ferro J, Madureira S, Verdelho A, Petrovic K, Gouw A, van der Flier WM, Enzinger C, Pantoni L, Inzitari D, Erkinjuntti T, Scheltens P, Wahlund LO, Waldemar G, Rostrup E, Wallin A, Barkhof F, Fazekas F and LADIS study group (2010) Diffusion-weighted imaging and cognition in the leukoarosis and disability in the elderly study. *Stroke* **41**, e402-408. (Journal IF: 7.041)

Sebastião AM (2010) Adenosine and epilepsy-thinking beyond A(1) receptors. *Purinergic Signal* **6**, 1-2. (Journal IF: 2.870)

Sebastião AM, Assaife-Lopes N, Diógenes MJ, Vaz S, Ribeiro JA (2010) Modulation of brain-derived neurotrophic factor (BDNF) actions in the nervous system by adenosine A(2A) receptors and the role of lipid rafts.. *BBA Biomembranes*, Epub ahead of print (Journal IF: 4.180).

Silva A, Jotta PY, AB Silveira, Ribeiro D, Brandalise SR, Yunes JA, Barata JT (2010). Regulation of PTEN by CK2 and Notch1 in primary T-cell acute lymphoblastic leukemia: rationale for combined use of CK2- and gamma-secretase inhibitors. *Haematologica* **95** (4), 674-678. (Journal IF: 6.416)

Silva-Santos B (2010) Promoting angiogenesis within the tumor microenvironment: the secret life of IL-17-producing $\gamma\delta$ T cells. *Eur J Immunol.* **40** (7), 1873-1876. (Journal IF: 5.179)

Simões AS, Sá-Leão R, Eleveld MJ, Tavares DA, Carriço JA, Bootsma HJ and Hermans PWM (2010) Highly penicillin-resistant multidrug-resistant pneumococcus-like strains colonizing children in Oeiras, Portugal: genomic characteristics and implications for surveillance. *J Clin Microbiol.* **48**, 238-46 (Journal IF: 4.162)

Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, Combe B, Cutolo M, de Wit M, Dougados M, Emery P, Gibofsky A, Gomez-Reino JJ, Haraoui B, Kalden J, Keystone EC, Kvien TK, McInnes I, Martin-Mola E, Montecucco C, Schoels M, van der Heijde D, T2T Expert Committee (2010) Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis.* **69** (4), 631-637. (Journal IF: 8.111)

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. (2010) Cell-associated viral burden provides evidence of ongoing viral replication in aviremic HIV-2 infected patients. *J Virol.* E-pub December 15. (Journal IF: 5.150).

Sofia Vala I, Martins LR, Imaizumi N, Nunes RJ, Rino J, Kuonen F, Carvalho LM, Rüegg C, Grillo IM, Barata JT, Mareel M, Santos SC (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *PLoS One.* **5** (6), e11222 (Journal IF: 4.351)

Sousa, VC, Assaife-Lopes N, Brett RR, Ribeiro JA, Pratt JA, Sebastião AM. (2010) Regulation of hippocampal cannabinoid CB1 receptor actions by adenosine A1 receptors and chronic caffeine administration: implications for the effects of tetrahydrocannabinol on spatial memory. *Neuropsychopharmacology* Epub October 6 (Journal IF: 6.993).

Su LJ, Auluck PK, Outeiro TF, Yeger-Lotem E, Kritzer JA, Tardiff DF, Strathearn KE, Liu F, Cao S, Hamamichi S, Hill KJ, Caldwell KA, Bell GW, Fraenkel E, Cooper AA, Caldwell GA, McCaffery JM, Rochet JC, Lindquist S (2010) Compounds from an unbiased chemical screen reverse both ER-to-Golgi trafficking defects and mitochondrial dysfunction in Parkinson's disease models. *Dis Model Mech.* **3** (3-4), 194-208 (Journal IF: 3.304)

Swash M (2010) Apraxia contributes to the motor deficit in Parkinson's disease and multiple system atrophy. *Eur J Neurol.* **17**, 346-347 (Journal IF: 2.510).

Swash M (2010) Coping with motor neuron disease: how do people adapt to the devastating news? *J Neurol Neurosurg Psychiatry* **81**, 826 (Journal IF: 4.869).

Swash M (2010) Internet facilitated management improves home ventilation in amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry* **81**, 1180 (Journal IF: 4.869).

Swash M (2010) Lithium time-to-event trial in amyotrophic lateral sclerosis stops early for futility. *Lancet Neurol.* **9**, 449-451 (Journal IF: 18.126).

Tauber E, Miller-Fleming L, Mason RP, Kwan W, Clapp J, Butler NJ, Outeiro TF, Muchowski PJ, Giorgini F. (2010) Functional gene expression profiling in yeast implicates

translational dysfunction in mutant huntingtin toxicity. *J Biol Chem*. Epub November 2 (Journal IF: 5.328)

Teixeira MC, Cabrito TR, Hanif ZM, Vargas RC, Tenreiro S, Sá-Correia I Yeast response and tolerance to polyamine toxicity involving the drug: H⁺ antiporter Qdr3 and the transcription factors Yap1 and Gcn4, *SGM Microbiology*, Epub December 9. (Journal IF: N/A)

Tenreiro S, Outeiro TF (2010) Simple is good: yeast models of neurodegeneration. *FEMS Yeast Res* **10** (8), 970-979 (Journal IF: 1.785)

Teodorczuk A, Firbank MJ, Pantoni L, Poggesi A, Erkinjuntti T, Wallin A, Wahlund LO, Scheltens P, Waldemar G, Schrotter G, Ferro JM, Chabriat H, Bazner H, Visser M, Inzitari D, O'Brien JT and LADIS Group (2010) Relationship between baseline white-matter changes and development of late-life depressive symptoms: 3-year results from the LADIS study. *Psychol Med* **40**, 603-610. (Journal IF: 5.012)

Truelle JL, Koskinen S, Hawthorne G, Sarajuuri J, Formisano R, Von Wild K, Neugebauer E, Wilson L, Gibbons H, Powell J, Bullinger M, Höfer S, Maas A, Zitnay G, Von Steinbuechel N; Qolibri Task Force (2010) Quality of life after traumatic brain injury: the clinical use of the QOLIBRI, a novel disease-specific instrument. *Brain Inj*. **24**, 1272-1291. (Journal IF: 1.533)

Turner M, Swash M, Ebers G (2010). Lockhart Clarke's contribution to the description of amyotrophic lateral sclerosis. *Brain* **133**, 3470-3479 (Journal IF: 9.490)

Veiga-Fernandes H, Kioussis D, Coles M (2010). Natural killer receptors: the burden of a name. *J Exp Med*. **207** (2), 269-272. (Journal IF: 14.5)

Verdelho A, Madureira S, Moleiro C, Ferro JM, Santos CO, Erkinjuntti T, Pantoni L, Fazekas F, Visser M, Waldemar G, Wallin A, Hennerici M, Inzitari D and LADIS Study (2010) White matter changes and diabetes predict cognitive decline in the elderly: the LADIS study. *Neurology* **75**, 160-167. (Journal IF: 8.172)

Vicente MI, Costa PF, Lima PA (2010) Galantamine inhibits slowly inactivating K⁺ currents with a dual dose-response relationship in differentiated N1E-115 cells and in CA1 neurones. *Eur J Pharmacol*. **634** (1-3), 16-25 (Journal IF: 2.585)

Vicente Miranda H, Outeiro TF (2010) The sour side of neurodegenerative disorders: the effects of protein glycation. *J Pathol*. **221** (1), 13-25. (Journal IF: 6.466)

Vilas-Boas F, Henrique D (2010) HES6-1 and HES6-2 function through different mechanisms during neuronal differentiation, *PLoS ONE* **5** (12): e15459 (Journal IF: 4.351)

von Campenhausen S, Winter Y, Silva AR, Sampaio C, Ruzicka E, Barone P, Poewe W, Guekht A, Mateus C, Pfeiffer KP, Berger K, Skoupa J, BÄtzel K, Geiger-Gritsch S, Siebert U, Balzer-Geldsetzer M, Oertel WH, Dodel R, Reese JP (2010) Costs of illness and care in Parkinson's Disease: An evaluation in six countries. *Eur Neuropsychopharmacol*. Epub October 2. (Journal IF: 3.68)

Wanden-berghe C, Camilo ME, Culebras J (2010) Conceptos y definiciones de la desnutrición iberoamericana. *Nutr. Hospit.* **25**(Supl. 3), 1-9 (Journal IF: 1.065)

Seminars and Workshops

IMM Seminars

11-01-2010

Musa Mhlanga, Gene Expression and Biophysics Unit, IMM, Portugal

Decrypting gene expression & RNA biology: from genome-wide screens to single molecule interactions

15-01-2010

Paul J. Coffer, Utrecht University Medical Center, Netherlands

Divide, differentiate or die? A novel PKB/Akt-FOXO node coordinating regulation of metabolism and autophagy

18-01-2010

Margarida Bastos, Faculdade de Ciências da Universidade do Porto, Portugal

Antimicrobial peptides as new antibiotic paradigm - What can model membrane studies reveal?

21-01-2010

Eric F. Wieschaus, Howard Hughes Medical Institute/Princeton University

The mechanics of shape change in the Drosophila embryo

26-01-2010

Carlos Ramos, Baylor College of Medicine, Houston, Texas, USA

Redirected T cell therapy for B cell Non-Hodgkin lymphoma

27-01-2010

Dominique Baten, Amsterdam Academic Center

Modulation of humoral responses by TNF blockade

27-01-2010

Jean-Pierre Montani, University of Fribourg, Switzerland

Role of sympathetic nerve activity in the pathogenesis of obesity-induced hypertension

29-01-2010

David Baker, Barts and The London School of Medicine and Dentistry

Understanding animals for the treatment of Multiple Sclerosis: Useful tools or a confusing side issue?

01-02-2010

Carmo-Fonseca, IMM, Portugal

From mRNA biogenesis to human disease

09-02-2010

Sjoerd Repping, Centre for Reproductive Medicine, Academic Medical Centre, University of Amsterdam

Reproductive fitness of the human Y chromosome

15-02-2010 12:00 - 13:00

Paul Martin, Departments of Physiology & Biochemistry School of Medical Sciences, UK

Wound healing and inflammation in mice, fish and flies

22-02-2010

Monika Marx, Carl Zeiss MicroImaging

Practical Superresolution Microscopy: Theory and Applications of SR-SIM and PAL-M

25-02-2010

Jan Willem Koten Jr, Aachen University, Germany.

Genetic Contribution to Variation in Cognitive Function

01-03-2010

David Withmore, Research Department of Cell and Developmental Biology; University College London - UK

Why do cells contain clocks? Lessons from zebrafish cell culture

02-03-2010

Sandra Caldeira, Editor of EMBO Molecular Medicine

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Hazel Pinheiro, Exiqon

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08-03-2010

João Eurico Fonseca, UIR, IMM, Portugal

Cytokines, bone and biomechanics

09-03-2010

Joelle Hillion, Johns Hopkins University, School of Medicine, Baltimore

The High Mobility Group A1 protein and target genes in neoplastic transformation

15-03-2010

Margarida Saraiva, Universidade do Minho, Portugal

The impact of the innate on the acquired immune response to Mycobacterium tuberculosis: from the study of basic molecular events to their in vivo role

18-03-2010

Gerry J. Graham, Glasgow Biomedical Research Centre, University of Glasgow

Coordination of the innate and adaptive immune response by the D6 chemokine scavenging receptor

22-03-2010

David Aanansen, Imperial College, London, Division of Epidemiology, Public Health and Primary Care

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Matthew Harris, Department of Genetics, Tuebingen, Germany

Genetic basis of Postembryonic Development and Morphological Variation

30-03-2010

Mario Roederer, Vaccine Research Center, NIAID, NIH, USA

Design and implementation of multicolor flow cytometry experiments

05-04-2010

Carlos Penha Gonçalves, IGC, Portugal

Host Genetic Factors in Murine and Human Malaria

07-04-2010

David Pina, Marie Curie Actions

Marie Curie Fellowships: Funding opportunities for mobile researchers

07-04-2010

Marc Cruts, University of Antwerp

Genética das Demências

08-04-2010

Marc Cruts, University of Antwerp, Belgium

Molecular genetics and genomics of neurodegenerative dementias

09-04-2010

Olivier Neyrolles, CNRS - University of Toulouse, France

Mycobacterium tuberculosis interactions with host cells

15-04-2010

Patrick Hollender, Invitrogen

RNA world: not so small

19-04-2010

Eugenia Carvalho, Center for Neurosciences and Cell Biology, Coimbra, Portugal

Diabetes and Wound Healing

26-04-2010

Sergio Filipe, ITQB, Portugal

Building a bacterial peptidoglycan undetectable by the host

30-04-2010

Ted Strom, Memphis VA Medical Center, USA.

The Wiskott-Aldrich Syndrome: How can impaired phagocytosis lead to increased autoimmunity?

06-05-2010

Herwig Turk, IMM, Portugal

One cannot say where the organ ends and the processing begins!

10-05-2010

Gareth Jones, King's College London, UK

Podosomes: adhesive structures regulating leukocyte migration

14-05-2010

Alexandra Rosa, IMM, Portugal

The Angiogenic Factor Angiopoietin-1 Is a Proneurogenic Peptide on Subventricular Zone Stem/Progenitor Cells

17-05-2010

David Gillespie, Beatson Institute, Univ Glasgow, UK.

Keeping DNA Damage and Replication in Chk

17-05-2010

Thomas Gasser, Hertie-Institute for Clinical Brain Research University of Tübingen, Germany

Genetics of Parkinson's disease

18-05-2010

Peter Daniel, Charité & MDC, Germany.

Novel aspects of cell death resistance in cancer: regulation of the Bak pathway

24-05-2010

Peter Jordan, Instituto Nacional de Saúde Dr. Ricardo Jorge, Portugal

Dissecting the role of alternative spliced Rac1b in colorectal cancer

31-05-2010

Nilabh Shastri, UC Berkeley, USA

Revealing the hidden self: Peptide presentation by MHC molecules

31-05-2010

Andrzej Górski, Polish Academy of Sciences, Wrocław, Poland

The past, present and future of phage therapy

07-06-2010

Paula Ravasco, UNM, IMM, Portugal

Nutrition modulates disease activity, expression and prognosis: cancer and more

14-06-2010

Lawrence Rajendran, Systems & Cell Biology of Neurodegeneration, University of Zurich

Membrane trafficking and Targeting in Alzheimer's disease

18-06-2010

Roberto Cattaneo, Mayo Clinic College of Medicine, USA

Viruses as cancer therapeutics: three points of attack

18-06-2010

Victor Nussenzweig, New York University School of Medicine, USA.

Malaria vaccines

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22-06-2010

Victoriano Mulero, University of Murcia

TNF receptor signaling and vascular development in the zebrafish

28-06-2010

James S. Huston, Boston Biomedical Research Institute

Immunoglobulin Domain Engineering: from the Single-Chain Fv to SEEDbodies

28-06-2010

Luisa Figueiredo, UPAR, IMM, Portugal

The role of chromatin in antigenic variation of African Trypanosomes

30-06-2010

Bruno Frenguelli, University of Warwick

New players in homeostatic synaptic plasticity

05-07-2010

Margarida Gama-Carvalho, Functional and Integrative Genomics (BioFIG), Centre for Biodiversity, Faculty of Sciences, Lisbon, University of Lisbon, Portugal

Post-transcriptional control of SMN2 gene expression - novel leads for treating Spinal Muscular Atrophy

12-07-2010

Antonella Viola, Humanitas Institute, Milan, Italy

Improving cancer immunotherapy by preventing chemokine nitration

19-07-2010

Elsa Anes, FFUL

Why phagocytosis need not be a degrading experience for Mycobacterium?

26-07-2010

Olivier Bensaude, École Normale Supérieure Paris, France

Non-coding RNAs that regulate transcription

03-09-2010

Paula Alexandre, MRC Centre for Developmental Neurobiology, King's College London, UK

Live imaging reveals novel aspects to asymmetric divisions and neural differentiation in the vertebrate neural tube

06-09-2010

Frederico Soares Regateiro, Sir William Dunn School of Pathology, University of Oxford, UK

Adenosine generation by CD73 to control immune responses and inflammation?

06-09-2010

João Ferreira, UBCr, IMM, Portugal

Soy beans and Cancer treatment: what in common?

09-09-2010

Beth Seaton, Director of Sponsored Projects, Western Illinois University, USA

Science Management at Western Illinois University

13-09-2010

Rui Martinho, IGC, Portugal

Constraints to and from mitosis during development

20-09-2010

David W. Raible, University of Washington, Seattle, USA

Sensory Neurogenesis in Zebrafish

20-09-2010

Ricardo Gutiérrez Gallego, Bioanalysis Group, Neuropsychopharmacology Program, IMIM-Hospital del Mar Department of Experimental and Health Sciences, University Pompeu Fabra (UPF) Barcelona, Spain

Studying biomolecular interactions - tales of an evanescent wave

23-09-2010

Gennaro Schettini, Professor of Pharmacology, Faculty of Medicine University of Genova

Tyrosine Phosphorylation of APP-CTFs in Alzheimer Disease Brain: New insight into APP Processing. Relevance for Alzheimer Disease Pathology and Therapy

28-09-2010

Bert Poolman, Groningen Biomolecular and Biotechnology Institute, The Netherlands

The molecular basis for anti-microbial activity of pore-forming peptides

29-09-2010

Alexandre Potocnik, National Institute for Medical Research (NIMR), Mill Hill, London, UK

How pathogens reprogram their host: re-wiring of hematopoietic development during malaria

04-10-2010

Jules Hoffmann, Strasbourg, France

The Antimicrobial Defense of Drosophila: A Paradigm for Innate Immunity

06-10-2010

Dulce Veloso, University of Texas Health Science Center, Houston

Monoclonal antibodies to human plasma prekallikrein and their application to biochemical studies and detection of biomarkers of health and disease associated with the kallikrein-kinin system

11-10-2010

Rita Fior, UDEV, IMM, Portugal

Mesogenin throws the switch that converts progenitors into paraxial mesoderm

Susana Lopes, UDEV, IMM, Portugal

Cilia length control in zebrafish

15-10-2010

Xavier Busquets, Institute for Bioengineering of Catalonia, and Barcelona Centre for International Health Research

Nanotechnology against malaria: Strategies for the identification of new drugs and their targeted delivery

15-10-2010

Christian Muchardt, Institut Pasteur, CNRS, Paris, France

Chromatin and Splicing decisions

18-10-2010

Rossana Henriques, Laboratory of Plant Molecular Biology, The Rockefeller University, New York

Arabidopsis S6 Kinase, a cell growth regulator involved in repression of cell proliferation

25-10-2010

Nicolai Siegel, Pasteur Institute, Paris, France

Peaks and valleys: High-throughput sequencing paves the way for studying chromatin structure in parasites

04-11-2010

Paul MacPherson, Ottawa Hospital Research Institute

The IL-7 Receptor: A key factor in HIV pathogenesis

15-11-2010

Vasco Barreto, IGC, Portugal

Clonal Analysis of V(D)J rearrangement in immunoglobulin genes: implications for allelic exclusion of the Ig loci and beyond

16-11-2010

Egdar Gomes, Inserm, Univ Paris 06, Institut Myologie, France

Mechanisms of nuclear positioning during cell migration and muscle formation

22-11-2010

Philippe Benaroch, Institute Curie, Paris, France

A dynamic journey into HIV assembly in primary macrophages

06-12-2010 12:00 - 13:00

Rui Costa, IGC

Learning and Organizing Novel Action Sequences

10-12-2010

Fotis Kafatos, Imperial College London

The major challenges to global health: from insect vectors of Malaria (& other parasitic or viral diseases)

13-12-2010

Paula Duque, IGC, Portugal

Plant SR proteins and their functions in abiotic stress response

20-12-2010

Justin Boddey, Division of Infection and Immunity, The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia

Export of malaria virulence proteins into parasitized human erythrocytes

Oncology Series

09-02-2010

Miguel Martín, Chairman of the Spanish Breast Cancer Research Group

Tailored adjuvant chemotherapy for early breast cancer

29-04-2010

Rodolfo Capanna, Orthopaedic Oncology Department, University Hospital of Florence, Italy

Xavier Garcia del Muro, Institut Català d'Oncologia L'Hospitalet, Barcelona, Spain

Robert Maki, Memorial Sloan-Kettering Cancer Center, New York, USA

Soft Tissue Sarcomas

17-06-2010

Robert Coleman, Yorkshire Cancer Research, Professor of Medical Oncology, University of Sheffield, UK

Improving cancer care with bone targeted treatments

E-PI Seminars

13-01-2010

José Bessa, CABD-Centro Andaluz de Biología del Desarrollo Univ. Pablo de Olavide Sevilla

The Enhancer Disruption (ED) screen in zebrafish

27-01-2010

Adriano Henrique, ITQB/UNL, Portugal

Bacterial cell morphogenesis: control of cell shape and elongation by a novel core component of the actin cytoskeleton

10-02-2010

Lars Jansen, IGC, Portugal

The centromere: A showcase for epigenetic inheritance

24-02-2010

Rui Malhó, FCUL, Portugal

Studying cell signalling with live microscopy tools

10-03-2010

Ana Cristina Rego, CNC, Portugal

Protective strategies in Huntington's disease

24-03-2010

João Malva, CNC, Portugal

Proneurogenic effect of histamine in subventricular zone neural stem cell cultures

07-04-2010

Florence Janody, IGC, Portugal

The actin cytoskeleton: A Tumor suppressor organelle

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21-04-2010

Moises Mallo, IGC, Portugal

The instruction manual for building the vertebral column in HOX language

19-05-2010

Mónica Dias, IGC, Portugal

Centrosome biogenesis and function in development and human disease

16-06-2010

Solveig Thorstein

The extracellular matrix dimension of myogenesis

30-06-2010

Sérgio Simões, Developmental Biology Program, Sloan-Kettering Institute, NY, USA

Rho kinase directs Bazooka/Par3 planar polarity in the early Drosophila embryo

14-07-2010

José Pereira Leal, IGC, Portugal

From Evolutionary Cell Biology to Translational Research

13-10-2010

Rasmus Larsen, IGC, Portugal

A Central Role for Free Heme in The Pathogenesis of Severe Sepsis

25-11-2010

Cláudio Soares, ITQB, Portugal

Life at the molecular level: contributions from biomolecular modelling / structural bioinformatics

Pizza Seminars

12-01-2010

Mariana Simões, UMO, IMM, Portugal

The role of nerves during fin regeneration

Marco Domingues, UBM, IMM, Portugal

Testing AMP bactericidal activity in Escherichia coli and Staphylococcus aureus: an inglorious effort

26-01-2010

Patrícia Inácio, UMA, IMM, Portugal

ER stress and Plasmodium infection in liver stage

Irina Alho, UIAOC, IMM, Portugal

What is the mechanism behind LWM-PTP activity in bone metastasis?

09-02-2010

Aida Costa, UBD, IMM, Portugal

From Embryonic Stem Cells to Sensory Hair Cells: Cell therapy for deafness

Ana Água-Doce, UNICEL, IMM, Portugal

Enhancing tolerogenic antibodies to prevent Factor VIII inhibitors

23-02-2010

Raquel Lourenço, UDEV, IMM, Portugal

Symmetry-Out asymmetry-In: the role of Terra

Margarida Carrolo, UMMI, IMM, Portugal

*Studying competence in *Streptococcus pneumoniae**

09-03-2010

Luísa Figueiredo, UPAR, IMM, Portugal

Epigenetics and antigenic variation in trypanosomes

23-03-2010

Marta Caridade, UNICEL, IMM, Portugal

Defining the quantitative aspects of dominant tolerance induction and maintenance

Telma Lança, UNIMOL, IMM, Portugal

The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/lymphoma susceptibility to gd T-cell cytotoxicity

06-04-2010

Margarida Rodrigues, UBM, IMM, Portugal

Snake venom as a potential drug carrier: lipid model systems approach

Ana de Barros, UNIMOL, IMM, Portugal

The role of CD27-CD70 interactions in the activation of human peripheral blood gd T cells

04-05-2010

Sílvia Portugal, UMA, IMM, Portugal

Interactions of Plasmodium blood and liver stages within a single host

Paula Pousinha, UNF, IMM, Portugal

Neuromuscular junction and ageing: the role of adenosine

18-05-2010

Anna Zaidman-Rémy, UMO, IMM, Portugal

Drosophila hemocytes: the right place at the right moment

01-06-2010

Diogo Fonseca Pereira, UIB, IMM, Portugal

Role of the proto-oncogene Ret in foetal haematopoiesis

Maria João Frias, UMMI, IMM, Portugal

Bacterial Autolysin LytA in Streptococcus pneumoniae Phage Release

15-06-2010

Pedro Matos, UBM, IMM, Portugal

Evaluating membranotropism of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 in blood cells

Rita Tendeiro, UIC, IMM, Portugal

Naïve CD4 T-cell turnover and telomere length in HIV/AIDS

29-06-2010

Carina Santos, UMA, IMM, Portugal

Plasmodium Fitness: The importance of being prepared...PUF!!!

Raquel Mendes, UDEV, IMM, Portugal

N-cadherin is asymmetrically expressed in the chicken Hensen's node. What for?

07-09-2010

Sofia Azevedo, UDEV, IMM, Portugal

Patterning a regenerating caudal fin

Joana Lopes, UIR, IMM, Portugal

What happens to genes when a bone breaks?

21-09-2010

Leonor Fleming, UNCM, IMM, Portugal

Using yeast as a model to decipher the role of DJ-1 in the etiology of Parkinson's Disease

12-10-2010

Leila Martins, UBCa, IMM, Portugal

Targeting CK2 Overexpression and Hyperactivation as a Novel Therapeutic Tool in Chronic Lymphocytic Leukemia

Filomena Carvalho, UBM, IMM, Portugal

Recognizing fibrinogen human erythrocyte receptor via an atomic force microscopy approach

26-10-2010

Ivonne Wollenberg, UNICEL, Portugal

Regulatory T cells in B cell business

Ana Rita Barbosa, UIC, IMM, Portugal

Evidence for a link between human IL-17-producing CD4 T cells and B-cell differentiation

09-11-2010

Ana Pamplona, UNIMOL, IMM, Portugal

VEGF Promotes Malaria-associated Acute Lung Injury in Mice

07-12-2010

Sara Sousa, UMO, IMM, Portugal

Bone repair v.s. Bone regeneration in zebrafish caudal fin

Oldriska Marques, UNCM, IMM, Portugal

Investigating the role of extracellular alpha-synuclein in Parkinson's disease

21-12-2010

Rosângela Frita, UMMI, IMM, Portugal

Role of hemozoin in Malaria and Tuberculosis interactions

Marta Amaral, UNCM, IMM, Portugal

Towards crystallization of human kynurenine 3-monooxygenase, a candidate Huntington's disease drug target

Chromatin Club

19-10-2010

Dani Bodor, IGC, Portugal

Determining the Human Centromeric CENP-A Copy Number

14-12-2010

Joana Cardoso, UBCr, IMM, Portugal
Molecular Puzzles of Aging and Senescence

Immunology Club

04-02-2010

Ângelo Chora, UBCSI, IMM, Portugal
Role of new regulators of cross-presentation in anti-tumor immunity

11-02-2010

Andreia Amaral, UIC, IMM, Portugal
Application of massive parallel sequencing in population genomics and in miRNA profiling during HIV infection

25-02-2010

Bruno Cardoso, UBCA, IMM, Portugal
Targeting Tal1/Scl in T-ALL: The role of HDAC inhibitors

04-03-2010

Etienne Joly, IPBS, Toulouse
Trogocytosis: Why, and how, do lymphocytes nibble the membrane of other cells?

11-03-2010

Florian Kreppel, Department of Gene Therapy, University of Ulm, Germany
Adenovirus Vectors for Genetic Vaccination - Limitations and Perspectives: a Genetic and Chemical view

18-03-2010

Bruno Silva-Santos, UNIMOL, IMM, Portugal
Conference Report

25-03-2010

Afonso Almeida, UIB, IMM, Portugal
From T Cell Homeostasis to the role of the proto-oncogene /Ret/ in T cell biology

08-04-2010

Ana Isabel Lopes, UIC, IMM, Portugal
Clinical and immunopathological aspects of Helicobacter pylori infection at paediatric age

22-04-2010

Rita Cascão, UIR, IMM, Portugal
Cytokine network in the first 6 weeks of Rheumatoid Arthritis onset
Rita Moura, UIR, IMM, Portugal
Cytokine profile in serum and synovial fluid of established Rheumatoid Arthritis patients
Inês Perpétuo, UIR, IMM, Portugal
TNF antagonists and tocilizumab have a higher impact on Rheumatoid Arthritis osteoclastogenic stimuli than methotrexate

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20-05-2010

António Peixoto, Harvard Medical School, Boston, MA, USA

LFA1 integrin, a key modulator of T cell crawling on HEVs, T-DC interactions and effector/memory commitment during LCMV infection

17-06-2010

Leila Martins, UBCA, IMM, Portugal

CK2 as a novel therapeutic target in Chronic Lymphocytic Leukemia

15-07-2010

Francisca Ferreira de Almeida, UIB, Portugal

Retinoic acid in enteric lymphoid organogenesis

07-10-2010

UNIMOL delegates

Report on the International Congress of Immunology 2010 (Kobe)

14-10-2010

Íris Couto, UBCSI, IMM, Portugal

In vivo role of the splicing factor SRp20 in the regulation of mouse immune responses

21-10-2010

Joana Duarte, UNICEL, IMM, Portugal

Reprogramming the immune system with anti-CD4 monoclonal antibodies

28-10-2010

Rita Cascão, UIR, IMM, Portugal

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

04-11-2010

Rita Tendeiro, UIC, IMM, Portugal

CD4 naive T-cell disturbances and HIV/AIDS

02-12-2010

Daniel Ribeiro e Milene Silva, UBCA, IMM, Portugal

Involvement of IL-7R in T-ALL

09-12-2010

Daniel Correia, UNIMOL, IMM, Portugal

Generation of Natural Cytotoxicity Receptor-expressing gamma delta T lymphocytes with enhanced killing activity against leukemia

16-12-2010

Karine Serre, MRC Centre for Immune Regulation, University of Birmingham, UK

Molecular mechanisms that control CD4 T helper 2 and follicular T helper cell differentiation in vivo

Neuroscience Seminars

04-01-2010

Claudia Valente de Castro, UNF, IMM, Portugal

An in vitro model of seizures

08-01-2010

Rodrigo Cunha, CNC/FMUC, Portugal

Control of memory impairment by caffeine and adenosine A2A receptor antagonists

11-01-2010

Ana Cristina Osório de Oliveira, UNCM, IMM, Portugal

Interactions between autonomic dysfunction and motor changes in rat-parkinson like model

18-01-2010

Pedro A. Lima, Fac. Sciences, Univ. Lisbon, Portugal

The other side of insulin: role in neuronal function

25-01-2010

Rita Oliveira, UNCM, IMM, Portugal

Spotlight on ACE: from bedside to the bench

01-02-2010

Paula Pousinha, UNF, IMM, Portugal

Net Modulation of adenosine A1/A2A receptors of the neuromuscular transmission upon ageing

08-02-2010

Patrícia Guerreiro, UNCM, IMM, Portugal

The role of LRRK2 in Parkinson's disease: from function to dysfunction

22-02-2010

Frederico Simões do Couto, UNF, IMM, Portugal

Depression as a risk factor for dementia

01-03-2010

Antonina Simão Pereira, UNF, IMM, Portugal

Enactment and relatedness in Prospective Remembering

15-03-2010

Mamede de Carvalho, UN, IMM and Clin. Univ. Neurologia, FML, Portugal

Les uns e les autres

22-03-2010

Elisa Basso, UNCM, IMM, Portugal

Alpha-synuclein phosphorylation: role and regulation

12-04-2010

Raquel Dias, UNF, IMM, Portugal

AMPA receptors and adenosine: together in sickness and in health

19-04-2010

Patricia Canhão, Departamento de Neurociências (Neurologia), HSM, Portugal
Cerebral venous thrombosis: clinical investigation of a rare disease

26-04-2010

Natália Lopes, UNF, IMM, Portugal
The role of lipid rafts in the cross-talk between adenosine A2A and TrkB receptors

10-05-2010

Sofia Ferreira, UNF, IMM, Portugal
Striatal circuits and movement control

24-05-2010

Sandra Tenreiro, UNCM, Portugal
Deciphering the role of α -synuclein phosphorylation in Parkinson's Disease

31-05-2010

André Santos, UNF, IMM, Portugal
Amyloid-beta induces changes on TrkB receptors levels: a contribution for neuronal death?

07-06-2010

Oldriska Marques, UNCM, IMM, Portugal
Striatal Neuroinflammation Promotes Parkinsonism in Rats

14-06-2010

Francesca Maiolino, UNCM, IMM, Portugal
Study of GABAA Receptor Functionality in Neuronal Pathologies: from humans to animal models

21-06-2010

Maria José Diógenes, UNF, IMM, Portugal
Increased LTP: friend or enemy?

28-06-2010

Diogo Rombo, UNF, IMM, Portugal
Adenosine as a modulator of inhibitory transmission in the hippocampus: from neurons to interneurons

05-07-2010

Oldriska Marques, UNCM, IMM, Portugal
Striatal Neuroinflammation Promotes Parkinsonism in Rats

12-07-2010

Armando Cruz, IFN
The Influence of epilepsy in synaptic plasticity in the hippocampus: Neuroprotective role of VIP and its receptors

19-07-2010

Sandra Henriques Vaz, Instituto de Farmacologia e Neurociências, Portugal
GABA uptake-dependent Ca²⁺ signaling in developing olfactory bulb astrocytes.

26-07-2010

Ana Filipa Ribeiro, Instituto de Farmacologia e Neurociências, Portugal

Modulation of Neuronal Maturation: Influence of Neurotrophic Factors and Neuromodulators

06-09-2010

Vânia Batalha, UNF, IMM, Portugal

Involvement of Adenosine A2A receptors in the stress induced impairments of rat hippocampal function

13-09-2010

Mariana Rocha, UNF, IMM, Portugal

The synaptic transmission and its modulation by adenosine in the SOD1G93A transgenic mice model of amyotrophic lateral sclerosis

20-09-2010

Luísa Lopes, UNF, IMM, Portugal

Adenosine A2A receptors in the hippocampus: implications in ageing and stress

27-09-2010

Leonor Fleming, UNCM, IMM, Portugal

Deciphering the role of DJ-1 in the etiology of Parkinson's Disease

Raquel Dias, UNF, IMM, Portugal

Course report: Microelectrode techniques for Cell Physiology

11-10-2010

Juan Carlos Martín, Institute of Neurosciences Castilla y Leon, University of Salamanca

A retention factor modulates AMPA receptor function

18-10-2010

Roberto Paes de Carvalho, Instituto de Biologia, Universidade Federal Fluminense do Rio de Janeiro

Regulation of adenosine receptor expression in the retina

25-10-2010

Raquel Dias, UNF, IMM, Portugal

Course report: Microelectrode techniques for Cell Physiology

08-11-2010

Catarina Luís, UNF, IMM, Portugal

Characterization of glycinergic transmission in primary cultures of hippocampus: potential role in epilepsy

15-11-2010

Andreia Silva, UNF, IMM, Portugal

Calcium signalling modulation in astrocytes by adenosine receptors

22-11-2010

Daniela Calçada, UNF, IMM, Portugal

The role of lithium on apoptotic cell death induced by amyloid-beta peptide

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29-11-2010

Jorge Valadas, UNF, IMM, Portugal

Role of adenosine A2A receptors in the neuroprotective effect of corticotrophin release hormone (CRH)

06-12-2010

Federico Herrera, UNCM, IMM, Portugal

Visualization of huntingtin oligomerization in living mammalian cells

13-12-2010

Sueli Marques, UNCM, IMM, Portugal

Epigenetics in Alzheimer's disease

20-12-2010

Tomás da Fonseca, UNCM, IMM, Portugal

Zebrafish: A new model of Parkinson's disease

Lisbon Area Neuroscience Meetings

20-01-2010

Federico Herrera, UNCM, IMM, Portugal

Retinoic acid receptor alpha links major astroglial pathways

Epigenetic regulation of BDNF in the rat medial prefrontal cortex alters the reinforcing efficacy of cocaine

Ghazaleh Sadri-Vakili, Instructor of Neurology at Harvard Medical School

Assistant in Neuroscience at Massachusetts General Hospital/MassGeneral Institute for Neurodegenerative Disease

17-02-2010

Hugo Miranda, UNCM, IMM, Portugal

Protein glycation in yeast novel insights into the molecular basis of Parkinson's disease

Pedro Lima, Centro de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa, Portugal

Insulin and metabolic cycles: effects in neuronal activity

17-03-2010

Adelaide Fernandes, Neuron-Glia Biology in Health and Disease, CPM-iMed.UL Faculdade de Farmácia, University of Lisbon, Portugal

Neonatal jaundice as a potential effector of neurodevelopmental deficits: from morphological changes to cytoskeleton defects

Mário Miguel Rosa, Neurological Clinical Research Unit, Clinical Neuropharmacology Group, IMM, Portugal

Prescription pattern of antiparkinsonian agents: How have clinicians been prescribing?

21-04-2010

Thomas Näsström, Molecular Geriatrics Department of Public Health and Caring Sciences, Rudbeck laboratory, Uppsala University, Sweden

The role of protein misfolding in neurodegenerative diseases

Luís Oliveira, Molecular Pathology Laboratory, Instituto Superior de Ciências da Saúde Egas Moniz and Enzymology Group, Faculdade de Ciências da Universidade de Lisboa, Portugal
Methylglyoxal effects on protein aggregation and amyloid formation

19-05-2010

Andreia Cunha, Inflammation Unit, IGC, Portugal
Regulation of autoimmune neuroinflammation by Nrf-dependent cytoprotective genes expressed in oligodendrocytes

Isabel Fragata, Unidade de Neuroradiologia, Serviço de Radiologia, Hospital de S. José, CHLC, Portugal

MRI and Neurosciences: picturing molecules and brain function

16-06-2010

Mamede de Carvalho, Department of Neurology, Hospital de Santa Maria and Neuromuscular Unit, IMM, Portugal

Testing transsynaptic degeneration in ALS

Elsa Rodrigues, Molecular and Cell Biology of Eukaryotic Systems iMed.UL, Faculty of Pharmacy, Portugal

Epigenetic regulation of CYP46A1, a key player in brain cholesterol elimination

20-10-2010

Patrícia Calado, Drug Discovery and Development Director, BIOALVO

Bugs and Brain – a joint path to drug discovery

Raquel Dias, Institute of Pharmacology and Neurosciences, FML; Neurosciences Unit, IMM, Portugal

Postsynaptic modulation of AMPA receptors by Gs-coupled adenosine A2A receptors: implications for synaptic plasticity

17-11-2010

Diana Macedo, Disease & Stress Biology Laboratory, ITQB; Cell and Molecular Neuroscience Unit, IMM, Portugal

Polyphenols as antioxidants in Parkinson's Disease: protein aggregates in cellular models

Dora Maria Tuna de Oliveira Brites, Faculty of Pharmacy, University of Lisbon, Portugal

Microglia dynamics in bilirubin-induced neurodegeneration

15-12-2010

Francesca Maiolino, UNCM, IMM, Portugal

Functional effects of alpha-synuclein on hippocampal synaptic activity: involvement of NMDA receptors

Ana Raquel Esteves, Center for Neuroscience & Cell Biology, University of Coimbra, Portugal

Mitochondrial dysfunction: the road to alpha-synuclein oligomerization

15-12-2010

Francesca Maiolino, UNCM, IMM, Portugal

Functional effects of alpha-synuclein on hippocampal synaptic activity: involvement of NMDA receptors

Ana Raquel Esteves, Center for Neuroscience & Cell Biology, University of Coimbra, Portugal

Mitochondrial dysfunction: the road to alpha-synuclein oligomerization

Tissue Regeneration and Stem Cells Forum

14-01-2010

Sofia Azevedo, UDEV, IMM, Portugal

Circadian clock ticking cell division

11-02-2010

Ana Cristina Silva, UMO, IMM, Portugal

Xenopus as a Model to study Regeneration

18-03-2010

Inês Tenente, UMO, IMM, Portugal

Telomeres and telomerase on stem cell behaviour

08-04-2010

Evguenia Bekman, UBD, IMM, Portugal

Neural stem cell systems: physiological players or in vitro entities?

22-04-2010

Joana Lima, UDEV, IMM, Portugal

What can we get from studying regeneration in larvae?

IMM NeuroSeS

29-03-2010

David Blum, INSERM, Jean-Pierre Aubert Research Centre, Lille, France

A unique transgenic model to study synaptic dysfunctions associated with Tau pathology

04-10-2010

Michael Schwarzschild, Harvard Medical School, MassGeneral Institute for Neurodegenerative Disease Boston, USA

Urate in Parkinson's: From Apes to Antioxidant Trials

Courses and Workshops

03-05-02-2010

Dolores Bonaparte, IMM, Portugal

Rodents and fish in research - IMM practical course

10-04-2010

Joaquim Ferreira, IMM, Portugal

I Parkinson's Disease course for caregivers and family members

14-04-2010

José Rino, IMM, , Portugal and **Tom Kirchhausen**, HMS - USA

Workshop: Quantitative Light Microscopy in Living Cells

15-04-2010

Marta Agostinho, Cheila Almeida, Inês Domingues, IMM, Portugal and **José Xavier**, IMAR, Portugal

Workshop Ciência Política e Media: Como traduzir conhecimento em decisões políticas

24-04-2010

De Novo Parkinson's Disease: Diagnosis and Treatment

29-05-2010

II Teaching Course in Movement Disorders

27-10-2010

Miguel Prudêncio, IMM BSL3 Facility Supervisor, Portugal

Course: IMM BSL3 Facility

Meetings

22,23-01-2010

HIV/AIDS: Closing the Gap between Basic Research and Clinical Practice

10-02-2010

XII EPI – Encontro Peptídico Ibérico

14-05-2010

Rheumatoid arthritis: from practical issues to cutting edge translational research

IMM Advanced Training

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.

In the summer of 2010 we launched 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 was inspired by the IMM practices, the goal being to have a programme focused on the excellence of the research proposals, which features a flexible and modular training component. The CAML PhD Programme, seeks to promote clinicians to ask new questions at the bedside and take them to the lab. And reciprocally bridge questions from the lab to the clinic. By bringing together clinic and non-clinic researchers the program fosters new collaborative approaches and a more effective communication among fundamental and clinical investigators. The three institutions, FMUL, IMM and HSM-CHLN, actively participated in the design of the CAML PhD Program, using the existing resources and synergies to create a attractive and stimulating environment for doctors and researchers to develop their doctoral thesis. The program is managed by a Direction and Scientific Commission both composed by representatives of the three institutions.

Advanced Training in numbers

114 Students

60 Students registered in the CAML Doctoral Programme

89 Students with fellowships from *Fundação para a Ciência e Tecnologia*

Other PhD fellowships: 1 Axa Research Fund, 2 Marie Curie Initial Training Network, 3 MD Resident (PFMA - FCG/FCT/FC), 2 IMM.

16 Medical Doctors

New PhD Students

Alice Melão, Ana Filipa Mourão, Ana Osório, Ana Silva Herdade, André Santos, Diogo Rombo, Elisa Basso, Jorge Santos, Margarida Rei, Marta Tiago Gória, Mauricio Martins, Nina Schmolka, Patricia Guerreiro, Raquel Gil-Gouveia, Rita Aroeira, Sofia de Oliveira, Susana Mendes Fernandes, Teresa Nazareth, Vânia Batalha. (Total: 19)

Nanocourses

*The 2010 Nanocourses were co-funded by Bayer
A total of 10 nanocourses were organized*

Biostatistics

Organizer: João Maroco, ISPA

Date: Jan 6 – Feb 10 (Wednesdays 16h – 19h)

Nº of Participants: 15 (27 applications)

In this course, the main descriptive, graphical and inferential statistical techniques used in the analysis of biological and health sciences data were presented. The coursework was supported by a statistical analysis software: PASW Statistics.

Get the best from your sequences

Organizer: Francisco Enguita, IMM

Date: Feb 11-12 (Mornings 10h – 13h)

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.

Bioinformatics: What? When? How?

Organizer: João Carriço, IMM

Date: Mar 22-24

Nº of Participants: 14

This course aimed to answer three major questions about Bioinformatics: What is Bioinformatics? When should we consider a Bioinformatics approach? And how can Bioinformatics help us in a specific field of molecular biology?.

Flow Cytometry Workshop - From Basic Concepts to multicolor analysis

Organizer: Maria Soares, IMM

Date: Mar 29-31

Nº of Participants: 12 (33 applications)

This course introduced participants to the basic concepts in flow cytometry as well as addressing its potential applications. The course had a strong component addressing instrument setup and calibration including "hands on" calibration on the FACSCalibur and FACSCanto.

Biology of Cancer

Organizer: João Barata, IMM

Date: Apr 19-22

Nº of Participants: 20

The course covered different aspects of cancer research and therapeutics, from the basics, to the bench, to the bedside. Also there was a focus on actual therapeutic achievements that originated from the rational identification of molecular targets and a better knowledge of fundamental oncogenic mechanisms.

Advanced Course on Protein Expression and Purification: Tips and Tricks

Organizer: Francisco Enguita, IMM

Date: Apr 28-30

Nº of Participants: 20 (46 applications)

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

Cell Adhesion and Migration in Health and Disease

Organizer: Soren Prag, IMM

Date: May 10-12

Nº of Participants: 8

This course covered the fundamental mechanisms in cell behaviour during adhesion and migration both during normal development and in diseases.

Technology Transfer and Intellectual Property in Biomedicine

(In collaboration with Health Cluster Portugal)

Organizer: Nuno Afonso, IMM

Date: June 14-15

Nº of Participants: 20 (31 applications)

This course aimed to show the importance of Technology transfer from Universities to Industry to researchers, as well as to stimulate the identification of opportunities for technology transfer in the scope of their biomedical research.

Interacting with different publics

Organizer: Marta Agostinho, IMM

Date: Sep 28-29

Nº of participants: 9

Discussion on the most usual formats to interact with different publics, from writing to designing science communication events with the general public.

Presenting your research: from bench to peers

Organizer: Inês Crisóstomo, IMM

Date: Oct 28-29

Nº of participants: 18

The motto of this nanocourse was from bench to peers - it aims to teach techniques and tools for an effective presentation of your data to different scientific publics.

Courses under PFMA – “Programa de Formação Médica Avançada”

Under the IMM partnership with the Doctoral Program for Physicians (PFMA) IMM students attended the following courses:

Pathogen & Hosts (Jan 4-8); Neurocognitive Disorders (Jan 18-22); Inflammation (Jan 25 - Feb 5); Regeneration (Feb 15-19); Scientific Integrity (Feb 22-23); Epidemiology (Nov 8-12); Computational Biology (Nov 15-19).

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 IMM PhD Students Meeting”. In 2010 the students' commission remodel the “Onboard Talks” to the “Pizza Seminars”.

2010 PhD Students commission

Carolina Moreira; Henri Franquelim; Irina Alho; Joana Tato; Margarida Rodrigues; Maurice Itoe; Pedro Matos; Raquel Mendes; Rita Mateus; Telma Lança.

2010 PhD Students representatives

Inês Domingues and Marta Ribeiro

Pizza Seminars

In 2010, the student's refashioned their bi-weekly seminar series, and launched the 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)

III IMM PhD Students Retreat

Date: May 7-9

Place: Herdade dos Cadouços, Abrantes

Participants: 50, PhD students, post-docs, master students and technicians

Programme:

- Guess who? (Game activity to get to introduce participants)
- Benefits of a PhD: what competences do you gain? (Group discussion)
- Hiking
- IMM Trivia! (Game activity to present IMM units, functioning and people)
- Trip to Almourol

IV IMM PhD Students Annual Meeting

Date: November 22-23

Place: IMM

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

November 22

Opening Session

Inês Domingues and Marta Ribeiro; Miguel Carneiro de Moura; Inês Crisóstomo

Oral Presentation Session I

Moderators: Rui Freitas and Sérgio Almeida

Rita Cascão; Marta Caridade; Patrícia Inácio; Marta Ribeiro; Marco Antunes

Poster Presentation Session I

Vânia Batalha; André Santos; Jorge Santos; Diogo Rombo; Carolina Moreira; Rita Mateus; Nádia Correia; Pedro Pereira; Marta Amaral; Joana Tato-Costa; Telma Lança; Joana Monteiro; Nuno Figueiredo; Raquel Mendes; Joana Xavier; Leonor Miller-Fleming; Vera Geraldés

Oral Presentation Session II

Moderators: Julie Ribot and José Rino

Speakers: Marco Domingues; Leila Martins; Raquel Dias; Margarida Rodrigues; Sofia Ferreira

November 23

Oral Presentation Session III

Moderators: Sandra Aguiar and Jérémie Decalf

Speakers: Rita Tendeiro; Henri Franquelim; Ana de Barros; Maria João Frias; Paula Pousinha

Oral Presentation Session IV

Moderators: Filipe Vilas-Boas and Soren Prag

Speakers: Filomena Carvalho; Ana Sofia Azevedo; Daniel Correia; Aida Costa; Pedro Matos

Keynote Lecture

“How are cell membranes organized?”

Speaker: Prof. Kai Simons (Max Planck Institute of Cell Biology and Genetics, Dresden, Germany)

Poster Presentation Session II

Sofia de Oliveira; Ana Silva-Herdade; Elisa Basso; Patrícia Guerreiro; Rosângela Frita; Susana Gonçalves; Oldriska Marques; Maurice Itoe; Cristina Silva; Angelica Vittori; Rita Barbosa; Ana Água-Doce; Irina Alho; Diogo Fonseca Pereira; Daniel Felício-Silva; Rita I. Aroeira; Ricardo Fernandes

Oral Presentation Session V

Moderators: Rita Fior and Inês Domingues (UAG)

Speakers: Rita Moura; Sara Sousa; Ivonne Wollenberg; Sandra Vaz; Elisabete Martins

Crioestaminal Award Presentation

The 2010 Crioestaminal award was to Luísa Figueiredo

Awards Ceremony and Closing Remarks

Jury: Afonso Almeida, Francisco Enguita, Miguel Carneiro de Moura, and Teresa Pais

Awardees: Vânia Batalha (Best Poster Presentation) and Sara Sousa (Best Oral Presentation)

Meeting Dinner

Other events

IMM Open Day for PhD Candidates

Organizer: Inês Crisóstomo, with Advanced Training Team and PhD Students Commission.

Date: May 14, 2010

Participants: 29

IMM Open its doors for potential candidates for a PhD at IMM. The Advanced Training Team gave an overview of IMM and the PhD Programme and there were talks from Principal Investigators. The PhD Students Commission organized a guided tour followed by a light lunch where the candidates could ask questions and talk to IMM researchers in an informal context (Speakers: I. Crisóstomo, A. Jacinto, A. Sebastião, João Carriço, Luísa Figueiredo, Francisco Enguita and Inês Domingues).

PhD thesis

Catarina Alexandra Gomes (January 8, 2010) Neurotrophic Factors Modulation by Adenosine Receptors and Dopamine Release in the Rat Striatum. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.A. Ribeiro

Ana Silva (January 15, 2010) IL-7- and PI3K-Mediated Signaling in T-Cell Leukemia: The Role of External and Cell-Autonomous Signals in Tumorigenesis. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata, Co-supervisor: L. Parreira

Hugo Miranda (January 20, 2010) Protein glycation and methylglyoxal metabolism in Parkinson's Disease. Faculdade de Ciências da Universidade de Lisboa. Supervisors: T. Outeiro, Co-Supervisors: A. Quintas and C. Cordeiro.

Jennifer Ann Geiger (February 2, 2010) Wound healing: a genetic approach in *Drosophila*. Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa. Supervisor: A. Jacinto

Paulo Navarro Costa (February 8, 2010) (EPI) Genetic Characterization of the AZFc Region of the Y Chromosome: New Links to Male Fertility. Faculdade de Medicina da Universidade de Lisboa. Supervisor: C. Plancha, Co-Supervisor: J. Gonçalves

Ana Rita Fialho Grosso (February 26, 2010) New insights into alternative splicing using microarray technology. Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Carmo-Fonseca

Marta Bebiano Alenquer (March 2, 2010) Molecular Pathogenesis of Murid Herpesvirus-4 Latent Infection. Faculdade de Medicina da Universidade de Lisboa. Supervisor: P. Simas

Catarina Henriques (March 18, 2010) The regulation of interleukin 7 receptor alpha internalization, recycling and degradation by IL-7 – possible implications in T-cell homeostasis, migration and leukaemogenesis. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata, Co-supervisors: L. Parreira and G. Graham

Sílvia Portugal (June 18, 2010) Interactions of Plasmodium blood and liver stages within a single host. Faculdade de Medicina da Universidade de Lisboa. Supervisors: M. Mota

Catarina Moita (September 17, 2010) Genetic Dissection of Antigen Presentation Pathways. Faculdade de Medicina da Universidade de Lisboa. Supervisor: L.F. Moita

Manuel Melo (September 28, 2010) A study on the mode of action of clinically relevant antimicrobial peptides. PhD in Biochemistry, Molecular Biophysics specialty. Faculdade de Ciências da Universidade de Lisboa. Co-Supervisor: M.A.R.B. Castanho

Natália Assaife-Lopes (October 11, 2010). Molecular Interactions Between Neurotrophins and Adenosine Receptors at Neuronal Plasma Membranes. Faculdade de Medicina da Universidade de Lisboa. Supervisor: A.M. Sebastião

Pedro Moura-Alves (October 25, 2010) Identification of Splicing Factors with a role in IL-1b Secretion. Faculdade de Medicina da Universidade de Lisboa. Supervisor: L.F. Moita

Adriana Silva de Albuquerque (November 18, 2010) Strategies for T-cell reconstitution: insights from human clinical models. Faculdade de Medicina da Universidade de Lisboa. Supervisor: A.E. Sousa

Helena Cabaço (November 19, 2010) Development of regulatory T cells in the human thymus: one step beyond. Faculdade de Medicina da Universidade de Lisboa. Supervisor: A. E. Sousa

Carina Santos (November 26, 2010) Plasmodium Fitness: The Importance of being Prepared Plasmodium sporozoites post-transcriptional regulation of gene expression and host cell cytoskeleton dynamics during Plasmodium intra-hepatic development. Faculdade de Ciências e Tecnologia da Universidade de Coimbra. Supervisors: M. Mota, Co-Supervisor: A.L. Carvalho (FCT-UC)

Rui Freitas (December 15, 2010) Synthetic Pathogens for Integrated Biophysical and Genetic Dissection of Antigen Cross-Presentation. Faculdade de Medicina da Universidade de Lisboa. Supervisor: L.F. Moita

Mario Martins Oliveira (July 27, 2010) The role of autonomic nervous system on the initiation, maintenance and termination of paroxysmal atrial fibrillation. Faculdade de Medicina da Universidade de Lisboa. Supervisor: I. Rocha

(Total: 18)

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 a newly formed 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/FML), 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 will build 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** and **Technophage** (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 2010, IMM hosted 31 research units.

Of these:

- 28 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

João Ferreira, MD, PhD

Luis 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, Nina Matova

João Ferreira

Luis Costa

Domingos Henrique

Leonor Saúde

Musa Mhlanga

Carlota Sadanha, Ângelo Calado

Miguel Castanho

António Jacinto, Soren Prag

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 investigate the molecular mechanisms by which nuclear VEGFR-2 may amplify the angiogenic response; 2) to study the effects of low doses of ionizing radiation on tumor angiogenesis, growth and metastasis; 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, FML

Principal Investigators

Susana Constantino Rosa Santos, PhD - Auxiliary Professor, FML

Research Team

Raquel Sampaio, PhD	Post Doc Fellowship, FCT
Augusto Ministro, MD	Researcher
Ana Inês Domingues	PhD Fellowship, FCT
Inês Sofia Vala	PhD Fellowship, FCT
Paula Oliveira	IEFP/IMM fellowship
Filipa Cunha	IEFP/IMM fellowship (left in June 2010)
André Rocha	Md Student, FML
Joana Simões	Mst Student
Teresa Freitas	Technician, FML

Keywords/Research Areas

Angiogenesis
Vascular Biology
Metastasis
VEGF/VEGFR-2 signaling

Major scientific achievements

1. Nuclear VEGFR-2

We found that nuclear VEGFR-2 may act as a transcription factor by binding to and activating its own promoter. By this mechanism nuclear VEGFR-2 could amplify the angiogenic response. This work was submitted for publication.

2. Low doses of Ionizing Radiation (IR)

During radiotherapy the tissues surrounding the tumor area are exposed to low doses of IR. Our results show that some of these low doses promote tumor growth and metastasis by enhancing angiogenesis. These findings demonstrate a new mechanism relevant to the understanding of the potential pro-metastatic effect of IR and may provide a new rational basis to the improvement of current radiotherapy protocols. This work was published in *PLoS ONE*

3. Transthyretin

We are investigating the effect of the wild-type or mutated Transthyretin in the differential response of the hepatic vasculature. This work will be important to understand why FAP patients have more hepatic artery thrombosis incidence after transplantation.

Recent Most Relevant Publications

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: 13)

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: 23)

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: 10.5, Citations: 77)

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. €50000

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

2009/2011 The differential effect of WT and V30M Transthyretin in the hepatic microenvironment and vasculature response, FCT. Coordinator: Susana Constantino and Rui Perdigo. PIC/IC/83062/2007, €190 000.

Publications in peer review Journals

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)

Invited Lectures and Seminars

Constantino Rosa Santos, S. Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. ESTRO 2010 on Contribution of the tumor microenvironment to radiation responses, Barcelona, Spain, September 12-16, 2010.

Constantino Rosa Santos, S. Radiotherapy- Ionizing radiation in angiogenesis and tumor metastasis. Ciência 2010 – Encontro com a Ciência e a Tecnologia em Portugal, Lisbon, Portugal, July 4-7, 2010.

Communications in International Conferences

Vala I. et al. Low doses of Ionizing Radiation promote tumor growth and metastasis by enhancing angiogenesis, Young European Scientist (YES) Meeting, Porto, September 24-26, 2010 (Oral presentation).

Vala I. et al. Low doses of Ionizing Radiation promote tumor growth and metastasis by enhancing angiogenesis, 21st European Students' Conference (ESC) on Dimensions of Cancer- from micro to macro, Berlin, Germany, October 13-17, 2010 (Oral presentation).

Internationalization

Collaborative Publication:

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.

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.

Prizes, honours and awards

Prize in the Oncology and Molecular Biology Area to André Rocha for the First Best Oral Presentation at the Young European Scientist (YES) Meeting, Porto, Portugal.

First Prize for the work “Low doses of IR promote tumor growth and metastasis by enhancing angiogenesis” in the 21st European Conference (ESC) “Dimensions of Cancer-from micro to macro”, Berlin, Germany.

Advanced teaching

Constantino, S. Tumoral Angiogenesis lecture for the Master in Neurosciences - Pathology of the Nervous System, FML, Lisbon. February 9, 2010

Constantino, S. Angiogenesis lecture for the Pós-Graduação em Genética Clínica e Laboratorial, Universidade Lusófona de Humanidades e Tecnologia, Lisbon. April 24, 2010

Science and Society

Inês Dominges. Co-organizer of Workshop Ciência Política e Media at Fundação Calouste Gulbenkian, April 15, 2010

Media appearances:

Susana Constantino. Doses baixas de radioterapia em tecidos que rodeiam o tumor podem potenciá-lo. Jornal Público, June 25, 2010.

Susana Constantino. Estudo português esclarece efeitos da radiação nos tecidos à volta do tumor. TSF Rádio Notícias, June 25, 2010

Susana Constantino. Crescimento de vasos sanguíneos nos tecidos à volta do tumor. Jornal Notícias Médicas, October 27, 2010.

Biomembranes Unit

Major interests / Objectives

Biological membranes serve not only as biological boundaries but also as dynamic structures essential for several cellular events, both on health and disease. The scope of the Unit is the study of biochemical and biophysical processes occurring at the level of the membranes of human cells and of their viral and bacterial pathogens, even without the involvement of membrane receptors. The Unit is mainly focused on the two steps of the life cycle of enveloped viruses (mainly HIV and dengue virus) that involve biomembranes: the entry of the virus in a target cell and the release of new virus. The questions that we try to answer are related to specific lipid recruitment during viral assembly, virus-target cell interactions conditioning by viral lipid composition and, the role of lipid rafts (heterogeneous membrane areas enriched in specific components) on the virus life cycle and on the action of some anti-HIV drugs. The answering of some of these questions may reveal specific interactions, show how they can be modulated and, hopefully, identify new targets for antiretroviral therapy. Adding to this main focus, we are also involved in collaborative projects on: i) the evaluation of the activity of microbicides that bind to specific component of the membranes of some bacteria; ii) the study of the binding of fibrinogen to platelets and erythrocytes and its relevance as cardiovascular risk factor; and, iii) on the Nanomedicine / Nanotechnology area, the structural characterization of metal nanoparticles conjugated with proteins for biomedical applications (e.g., biosensors).

Head of Unit

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

Principal Investigators

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

Research Team

Sónia Gonçalves, PhD	Researcher, FMUL
Ivo Martins, PhD	Post-doc Fellowship, Marie Curie (European Union)
Andrea Santos, PhD	Post-doc Fellowship, FCT
Fabiana Carneiro, PhD	Assistant Professor, UFRJ
Filomena Carvalho	Assistant, FMUL
Marco Domingues	PhD Fellowship, FCT
Pedro Matos	PhD Fellowship, FCT
Margarida Rodrigues	PhD Fellowship, FCT
André Faustino	Master Student
Teresa Santos	Technician, FMUL

Keywords/Research Areas

Membranes
HIV
Antimicrobial peptide
AFM
Fibrinogen
Nanomedicine

Major scientific achievements

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS and Santos NC (2010) Atomic force microscopy-based molecular recognition of a fibrinogen receptor on human erythrocytes. *ACS Nano* **4**, 4609-4620.

The established hypothesis for the increase on erythrocyte aggregation associated with a higher incidence of cardiovascular pathologies is based on an increase on plasma adhesion proteins concentration, particularly fibrinogen. Fibrinogen-induced erythrocyte aggregation has been considered to be caused by its nonspecific binding to erythrocyte membranes. In contrast, platelets are known to have a fibrinogen integrin receptor expressed on the membrane surface (the membrane glycoprotein complex $\alpha_{IIb}\beta_3$). We demonstrate, by force spectroscopy measurements using an atomic force microscope (AFM), the existence of a single molecule interaction between fibrinogen and an unknown receptor on the erythrocyte membrane, with a lower but comparable affinity relative to platelet binding (average fibrinogen-erythrocyte and -platelet average (un)binding forces were 79 and 97 pN, respectively). This receptor is not as strongly influenced by calcium and eptifibatide (an $\alpha_{IIb}\beta_3$ specific inhibitor) as the platelet receptor. However, its inhibition by eptifibatide indicates that it is an $\alpha_{IIb}\beta_3$ -related integrin. Results obtained for a Glanzmann thrombastenia (a rare hereditary bleeding disease caused by $\alpha_{IIb}\beta_3$ deficiency) patient show (for the first time) an impaired fibrinogen-erythrocyte binding. Correlation with genetic sequencing data demonstrates that one of the units of the fibrinogen receptor on erythrocytes is a product of the expression of the β_3 gene, found to be mutated in this patient. This work demonstrates and validates the applicability of AFM-based force spectroscopy as a highly sensitive, rapid and low operation cost nanotool for the diagnostic of genetic mutations resulting in hematological diseases, with an unbiased functional evaluation of their severity.

Matos PM, Castanho MARB and Santos NC (2010) HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes. *PLoS ONE* **5**, e9830.

Enfuvirtide and T-1249 are two HIV-1 fusion inhibitor peptides that bind to gp41 and prevent its fusogenic conformation, inhibiting viral entry into host cells. Previous studies established the relative preferences of these peptides for membrane model systems of defined lipid compositions. We aimed to understand the interaction of these peptides with the membranes of erythrocytes and peripheral blood mononuclear cells. The peptide behavior toward cell membranes was followed by di-8-ANEPPS fluorescence, a lipophilic probe sensitive to the changes in membrane dipole potential. We observed a fusion inhibitor concentration-dependent decrease on the membrane dipole potential. Quantitative analysis showed that T-1249 has an approximately eight-fold higher affinity towards cells, when compared with enfuvirtide. We also compared the binding towards di-8-ANEPPS labeled lipid vesicles that model cell membranes and obtained concordant results. We demonstrated the distinct enfuvirtide and T-1249 membranotropism for circulating blood cells, which can be translated to a feasible in vivo scenario. The enhanced interaction of T-1249

with cell membranes correlates with its higher efficacy, as it can increase and accelerate the drug binding to gp41 in its pre-fusion state.

Recent Most Relevant Publications

Domingues MM, Castanho MARB and 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: 4.351, Citations: 2)

Franquelim HG, Loura LMS, Santos NC and Castanho MARB (2008) Sifuvirtide screens rigid membrane surfaces. Establishment of a correlation between efficacy and membrane domain selectivity among HIV fusion inhibitor peptides. *J. Am. Chem. Soc.* **130**, 6215-6223. (Journal IF: 8.580, Citations: 5)

Santiago PS, Moura F, Moreira LM, Domingues MM, Santos NC and Tabak M (2008) Dynamic light scattering and optical absorption spectroscopy study of pH and temperature stabilities of the extracellular hemoglobin of *Glossoscolex paulistus*. *Biophys. J.* **94**, 2228-2240. (Journal IF: 4.764, Citations: 7)

Santos NC, Prieto M, Castanho MARB (2003) Quantifying molecular partition into model systems of biomembranes: an emphasis on optical spectroscopic methods. *Biochim. Biophys. Acta* **1612**, 123-135. (Journal IF: 4.396, Citations: 83)

Santos NC, Figueira-Coelho J, Martins-Silva J, Saldanha C (2003) Multidisciplinary utilization of dimethyl sulfoxide: pharmacological, cellular, and molecular aspect. *Biochem. Pharmacol.* **65**, 1035-1041. (Journal IF: 4.254, Citations: 106)

Ongoing Research Projects

2007/11 Fibrinogen-dependent signalling in microvascular blood cell function – implications of inflammation and cardiovascular disease. Coordinator: C. Saldanha. FCT - PTDC/SAU-OSM/73449/2006.

2007/10 The role of lipid membranes in the dengue virus cell infection. Coordinator: M. Castanho. FCT - PTDC/QUI/69937/2006.

2007/10 Metal- and magnetic nanoparticles functionalized with biological molecules: towards bio-nanoprobes. Coordinator: E. Pereira. FCT - PTDC/QUI/64484/2006.

2009/11 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.

2010/13 Cell membrane features in HIV entry and its inhibition. Coordinator: N.C. Santos. FCT - PTDC/QUI-BIQ/104787/2008.

2010/13 Inherent antibacterial activity in peptide-based hydrogels for tissue regeneration. Coordinator: A.S. Veiga. FCT - PTDC/SAU-BEB/099142/2008.

2010/13 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.

2010/13 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.

2010/13 The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly and encapsidation. Coordinator: I.C. Martins. Calouste Gulbenkian Foundation.

2011/4 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.

FCT Base

Publications in peer review Journals

Matos PM, Freitas T, Castanho MARB and Santos NC (2010) Sifuvirtide interaction with blood cell membranes denotes the conjugation of different lipid preferences. *Biochem. Biophys. Res. Commun.* **403**, 270-274. (Journal IF: 2.720, Citations: 0)

Ribeiro MM, Melo MN, Serrano I, Santos NC and Castanho MARB (2010) Drug-lipid interaction evaluation: Why a 19th century solution? *Trends Pharmacol. Sci.* **31**, 449-454. (Journal IF: 9.064, Citations: 0)

Santiago PS, Carvalho JWP, Domingues MM, Santos NC and Tabak M (2010) Thermal stability of extracellular hemoglobin of *Glossoscolex paulistus*: Determination of activation parameters by optical spectroscopic and differential scanning calorimetric studies. *Biophys. Chem.* **152**, 128-138. (Journal IF: 2.276, Citations: 0)

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardají E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX and Castanho MARB (2010) *Escherichia coli* cell surface perturbation and disruption induced by antimicrobial peptides, BP100 and pepR. *J. Biol. Chem.* **285**, 27536-27544. (Journal IF: 5.328, Citations: 0)

Matos PM, Franquelim HG, Castanho MARB and Santos NC (2010) Quantitative assessment of peptide–lipid interactions. Ubiquitous fluorescence methodologies. *Biochim. Biophys. Acta* **1798**, 1999-2012. (Journal IF: 4.396, Citations: 0)

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS and Santos NC (2010) Atomic force microscopy-based molecular recognition of a fibrinogen receptor on human erythrocytes. *ACS Nano* **4**, 4609-4620. (Journal IF: 7.493, Citations: 0)

Kuperstein I, Broersen K, Benilova I, Rozenski J, Jonckheere W, Debulpaep M, Vandersteen A, Segers-nolten I, Van Der Werf K, Subramaniam V, Braeken D, Calewaert G, Bartic C, D’Hooge R, Martins IC, Rousseau F, Schymkowitz J and De Strooper B (2010) Neurotoxicity of

Alzheimer disease A β -peptides is induced by small changes in the A β 42 to A β 40 ratio. *EMBO J.* **29**, 3408-3420. (Journal IF: 8.993, Citations: 0)

Martins AP, Lopes PA, Martins SV, Madeira A, Santos NC, Prates JAM, Moura TF and Soveral G (2010) Conjugated linoleic acid reduces permeability and fluidity of adipose plasma membranes from obese Zucker rats. *Biochem. Biophys. Res. Commun.* **398**, 199-204. (Journal IF: 2.720, Citations: 0)

Santiago PS, Carvalho FAO, Domingues MM, Carvalho JWP, Santos NC and Tabak M (2010) Isoelectric point determination for *Glossoscolex paulistus* extracellular hemoglobin: Oligomeric stability in acidic pH and relevance to protein-surfactant interactions. *Langmuir* **26**, 9794-9801. (Journal IF: 4.363, Citations: 1)

Santos A, Duarte A, Fedorov A, Martinho J and Moura I (2010) Rubredoxin mutant A51C unfolding dynamics: a Förster Resonance Energy Transfer study. *Biophys. Chem.* **148**, 131-137. (Journal IF: 2.276, Citations: 0)

Franquelim HG, Veiga AS, Weissmüller G, Santos NC and Castanho MARB (2010) Unravelling the molecular basis of the selectivity of the HIV-1 fusion inhibitor sifuvirtide towards phosphatidylcholine-rich rigid membranes. *Biochim. Biophys Acta* **1798**, 1234-1243. (Journal IF: 4.396, Citations: 0)

Santos NC (2010) In and out – biochemical and biophysical mechanisms of viral fusion and assembly [editorial]. *TheScientificWorldJournal* **10**, 419-421. (Journal IF: 1.658, Citations: 0)

Santos NC, Martins e Silva J, Freitas T, Doroana M, Duarte N, Tavares L, Antunes F and Saldanha C (2010) Blood cell membrane fluidity and intracellular Ca²⁺ changes in antiretroviral-naïve and -treated HIV-1-infected patients. *TheScientificWorldJournal* **10**, 350-355. (Journal IF: 1.658, Citations: 1)

Matos PM, Castanho MARB and Santos NC (2010) HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes. *PLoS ONE* **5**, e9830. (Journal IF: 4.351, Citations: 1)

Maurer-Stroh S, Debulpaep M, De La Paz ML, Martins IC, Reumers J, Copland A, Serpell L, Serrano L, Schymkowitz J, Morris K and Rousseau F (2010) Exploring the sequence determinants of amyloid structure using position-specific scoring matrices. *Nature Methods* **7**, 237-2342. (Journal IF: 16.874, Citations: 12)

Other publications International

Domingues MM and Santos NC (2010) Laser-light-scattering approach to peptide-membrane interaction. In *Membrane Active Peptides – Methods and Results on Structure and Function*. Castanho M (ed.), International University Line (IUL), La Jolla, USA, pp. 145-168.

Rodrigues M, Rádis-Baptista G, de la Torre BG, Castanho M, Andreu D and Santos NC (2010) Selective Membrane Interactions of Nucleolar-Targeting Peptides. In *Peptides 2010 – Tales of Peptides. Proceedings of the 31st European Peptide Symposium*. Lebl M, Meldal M, Jensen KJ and Hoeg-Jensen T (eds.), European Peptide Society, San Diego, USA, pp. 408-409.

Freire JM, Domingues MM, Matos J, Melo MN, Veiga AS, Santos NC and Castanho MARB (2010) Quantifying Molecular Partition of Charged Molecules by Zeta-Potential Measurements. em Peptides 2010 – Tales of Peptides. Proceedings of the 31st European Peptide Symposium, Michal Lebl, Morten Meldal, Knud J. Jensen, Thomas Hoeg-Jensen (eds.), European Peptide Society, San Diego, pp. 564-565.

Invited Lectures and Seminars

Santos NC. MEMPEPACROSS – A experiência de submissão de uma candidatura. Sessão de Divulgação Accções Marie Curie IRSES (International Research Staff Exchange Scheme), Lisbon, Portugal, January 26, 2010.

Santos NC. Interações proteína-membrana como alvos terapêuticos. Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, May 14, 2010.

Martins IC. The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly. Award ceremony of the Calouste Gulbenkian Foundation “Frontiers Life Sciences Research” prize, Lisbon, Portugal, May 26, 2010.

Santos NC. Antiviral drugs preventing HIV-1 entrance into human blood cells: a mechanistic approach with implications for drug design. Ciência 2010 – Encontro com a Ciência e Tecnologia em Portugal, Lisbon, Portugal, July 4-7, 2010.

Franquelim HG, Matos PM, Castanho M, Santos NC. Biomembranes play a role on Sifuvirtide’s mechanism of action. Symposium on Sifuvirtide & Phase IIb Clinical Summary, Beijing, China, August 1, 2010.

Santos NC. Interações proteína-membrana como alvos terapêuticos. Instituto de Ciências do Mar (Labomar), Universidade Federal do Ceará, Fortaleza, Brazil, August 17, 2010.

Santos NC. Protein-Biomembrane interactions as therapeutic targets. 1st ITQB PhD Students’ Meeting (Keynote Lecture), Oeiras, October 21-22, 2010.

Santos NC. Nanomedicine – Science, Technology and Education. XI Seminário Nacional do CNECV – Conselho Nacional de Ética para as Ciências da Vida – Nanotecnologias e O.G.M. Ciência, Ética, Sociedade, Lisbon, November 26-27, 2010.

Communications in International Conferences

Domingues MM, Castanho M, Santos NC. rBPI₂₁ aggregates lipopolysaccharide and induces both (hemi)fusion and leakage of negatively charged membranes, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Oral presentation).

Carvalho FA, Santos NC. Inhibition of the binding of fibrinogen to a specific erythrocyte membrane receptor by eptifibatide. A force spectroscopy study., XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Oral presentation).

Matos PM, Castanho MARB, Santos NC. Evaluating membranotropism of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 in blood cells. Implications for mode of action, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Oral presentation).

Franquelim HG, Veiga AS, Weissmüller G, Santos NC, Castanho MARB. Decoding the HIV-1 fusion inhibitor sifuvirtide selectivity towards phosphatidylcholine rigid membranes, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Oral presentation).

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardaji E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX, Castanho MARB. Relation between E. coli killing and charge neutralization by the antimicrobial peptides BP100 and DAMP, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Oral presentation).

Rodrigues M, Rádis-Baptista G, de la Torre BG, Castanho M, Andreu D, Santos NC. Selective membrane interactions of nucleolar-targeting peptides, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Poster presentation).

Matos JC, Veiga AS, Santos NC, Kowalczyk W, Andreu D, Castanho M. Characterization of the interaction of two Dengue virus C protein-derived peptides with lipid membranes, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Poster presentation).

Freire J, Veiga AS, Santos NC, Kowalczyk W, Andreu D, Castanho M. Dengue Virus Infection and Encapsidation – Unravelling the Role of the Capsid Protein, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Poster presentation).

Gonçalves S, Abade J, de Medeiros LN, Barreto-Bergter E, Kurtenbach E, Santos NC. Lipid selectivity basis of the microbicide action of the plant defensin Psd1, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Poster presentation).

Sousa D, Veiga A, Santos N, Castanho M. The role of lipid membranes in dengue virus assembly, XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010 (Poster presentation).

Santiago PS, Carvalho JWP, Poli AL, Domingues MM, Santos NC, Tabak M. On the thermal stability of extracellular hemoglobin of *Glossoscolex paulistus*: optical spectroscopic studies, Biophysical Society's 54th Annual Meeting, San Francisco, USA, February 20-24, 2010 (Poster presentation).

Franquelim HG, Veiga AS, Santos NC, Castanho MARB. Unraveling the molecular basis of the selectivity of the HIV-1 fusion inhibitor sifuvirtide towards phosphatidylcholine-rich rigid membranes, Biophysical Society's 54th Annual Meeting, San Francisco, USA, February 20-24, 2010 (Poster presentation).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC. Atomic force microscopy-based molecular recognition of fibrinogen receptor in human erythrocytes, AFM BioMed Conference, Red Island, Croatia, May 12-15, 2010 (Oral presentation).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC. Atomic force microscopy-based molecular recognition of fibrinogen receptor on human erythrocytes, 39th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, May 18-21, 2010 (Poster presentation).

Domingues MM, Castanho MARB, Santos NC. rBPI₂₁ acts by (hemi)fusion and permeabilization of bacterial membrane model systems and promotes massive lipopolysaccharide aggregation, 39th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, May 18-21, 2010 (Poster presentation).

Santiago PS, Carvalho JWP, Domingues MM, Santos NC, Tabak M. Dynamic light scattering studies of thermal stability of the extracellular hemoglobin of *Glossoscolex paulistus* in the presence of surfactants, 39th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, May 18-21, 2010 (Poster presentation).

Carneiro FA, Carvalho FA, Martins IC, Mohana-Borges R, Da Poian AT, Santos NC. Characterization of the interaction of the dengue virus C protein with lipid droplets, 39th Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, Brazil, May 18-21, 2010 (Poster presentation).

Rodrigues M, Rádis-Baptista G, de la Torre BG, Castanho M, Andreu D, Santos NC. Selective membrane interactions of nucleolar-targeting peptides, EBSA Biophysics Course – Membrane Biophysics and Lipid-Protein Interaction, Arcachon, France, June 6-11, 2010 (Poster presentation).

Matos PM, Castanho MARB, Santos NC. Evaluating membranotropism of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 in blood cells. Implications for mode of action., 10th Young Scientist Forum – Life of Molecules, Gothenburg, Sweden, June 23-26, 2010 (Poster presentation).

Matos PM, Castanho MARB, Santos NC. Evaluating membranotropism of HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 in blood cells. Implications for mode of action., 35th FEBS Congress – Molecules of Life, Gothenburg, Sweden, June 26 - July 1, 2010 (Poster presentation).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC. Atomic force microscopy-based molecular recognition of fibrinogen receptor on human erythrocytes, 4th Spanish-Portuguese Biophysical Congress, Zaragoza, Spain, July 7-10, 2010 (Poster presentation).

Martins AP, Lopes PA, Martins SV, Madeira A, Santos NC, Prates JAM, Moura TF, Soveral G. Conjugated linoleic acid impairs adipose plasma membranes permeability and fluidity, 4th Spanish-Portuguese Biophysical Congress, Zaragoza, Spain, July 7-10, 2010 (Oral and Poster presentation).

Gonçalves S, Teixeira AG, Abade J, de Medeiros LN, Barreto-Bergterc E, Kurtenbach E, Santos NC. Antimicrobial peptides Psd1 and HNP1: a comparison of their lipid selectivity, Australia-Croatia Workshop on Antimicrobial Peptides, Split, Croatia, August 8-14, 2010 (Poster presentation).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC. Recognizing fibrinogen human erythrocyte receptor via an atomic force microscopy approach, XXIst International Fibrinogen Workshop, Rotterdam and Amsterdam, Holland, August 23-25, 2010 (Oral presentation).

Rodrigues M, Rádis-Baptista G, de la Torre BG, Castanho M, Andreu D, Santos NC. Selective Membrane Interactions of Nucleolar-Targeting Peptides, 31st European Peptide Symposium, Copenhagen, Denmark, September 5-9, 2010 (Poster presentation).

Rodrigues M, Rádis-Baptista G, de la Torre BG, Castanho M, Andreu D, Santos NC. Selective Membrane Interactions of Nucleolar-Targeting Peptides, Cell Penetrating Peptides - 31st EPS CPP satellite meeting, Denmark, September 10-11, 2010 (Poster presentation).

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MARB. Distinct HIV-1 membrane-proximal external region lipid bilayer interactions of broad neutralizing mAbs 2F5 and 4E10 detected by combined AFM and confocal microscopy, OzBio 2010 Young Scientist Forum, Yarra Valley, Australia, September 23-26, 2010 (Oral presentation).

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MARB. Distinct HIV-1 membrane-proximal external region lipid bilayer interactions of broad neutralizing mAbs 2F5 and 4E10 detected by combined AFM and confocal microscopy, OzBio 2010 – The Molecules of Life: from Discovery to Biotechnology (12th IUBMB Conference, 21st FAOBMB Conference and ComBio2010 Meeting), Melbourne, Australia, September 26 - October 1, 2010 (Oral presentation).

Matos PM, Castanho MARB, Santos NC. Evaluating membranotropism of HIV-1 fusion inhibitor peptides enfuvirtide and T 1249 in blood cells. Implications for mode of action., EuroPrise Network Annual Conference – Rational Design of HIV Vaccines and Microbicides, Lisbon, Portugal, November 15-18, 2010 (Poster presentation).

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MARB. Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes, EuroPrise Network Annual Conference – Rational Design of HIV Vaccines and Microbicides, Lisbon, Portugal, November 15-18, 2010 (Oral presentation).

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MARB. Interaction of anti-HIV-1 antibodies with gp41 MPER peptide at the lipid membrane level – Mode of action unravelled by combined microscopy approaches, 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010 (Oral presentation).

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D, Castanho MARB. New insights on dengue virus infection and assembly – The role of the capsid protein, 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010 (Poster presentation).

Communications in National Conferences

Castanho M, Santos NC, Veiga AS, Franquelim H, Matos P. Developing HIV fusion inhibitor peptides: do lipids play a role?, HIV & AIDS – Closing the Gap between Basic Research and Clinical Practice, Lisbon, January 22-23, 2010 (Oral presentation).

Domingues MM, Carvalho FA, Santos NC. Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease. Sessão de entrega dos Prémios do Programa de Estímulo à Investigação da Fundação Calouste Gulbenkian, Lisbon, March 2, 2010 (Oral presentation).

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Tavares A, Ariëns RAS, Santos NC. Atomic force microscopy-based molecular recognition of fibrinogen receptor on human erythrocytes, Protein – Protein interactions and Protein folding, Monte da Caparica, March 29-31, 2010 (Oral presentation).

Nunes P, Silva H, Santos C, Domingues MM, Santos NC, Lyubartsev A, Eaton P, Caldeira J. Protein electrostatic assembly with matrix magnetic alignment, Protein – Protein interactions and Protein folding, Monte da Caparica, March 29-31, 2010 (Oral presentation).

Martins IC, Mohana-Borges R, Almeida F, Carneiro FA, Castanho M, Santos NC, Da Poian AT. Conformational changes of Dengue virus capsid protein upon lipids interaction, 2PYCheM – 2nd Portuguese Young Chemists Meeting, Aveiro, April 21-23, 2010 (Poster presentation).

Inácio RG, Domingues MM, Santos NC. Avaliação da interacção da polimixina B com LPS e modelos de biomembranas por potencial zeta, Ciência 2010 – Encontro com a Ciência e Tecnologia em Portugal, Lisbon, July 4-7, 2010 (Poster presentation).

Fernandes L, Carvalho FA, Santos NC. Estudo da interacção fibrinogénio-eritrócito por espectroscopia de força utilizando um microscópio de força atómica, Ciência 2010 – Encontro com a Ciência e Tecnologia em Portugal, Lisbon, July 4-7, 2010 (Poster presentation).

Castanho M, Santos NC, Veiga AS, Franquelim H, Matos P. Developing HIV fusion inhibitor peptides: the unexpected role of lipids, II Jornadas de Bioengenharia, Porto, November 26-27, 2010 (Oral presentation).

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MARB. Lipid membrane modulation in the interaction of anti-HIV-1 antibodies 2F5 and 4E10 with their respective epitopes on gp41 membrane proximal external region, XVII Congresso Nacional de Bioquímica, Porto, December 15-17, 2010 (Oral presentation).

Faustino A, Martins IC, Carneiro FA, Mohana-Borges R, Pereira RM, Carvalho FA, Castanho M, Almeida F, Da Poian AT, Santos NC. Characterization of the Interaction of the Dengue Virus Capsid Protein with Lipid Droplets, XVII Congresso Nacional de Bioquímica, Porto, December 15-17, 2010 (Poster presentation).

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D, Castanho MARB. A new perspective on Dengue Virus infection and assembly – a biophysical study of the capsid protein, XVII Congresso Nacional de Bioquímica, Porto, December 15-17, 2010 (Poster presentation).

Organisation of Conferences

Carvalho FA, Domingues MM, Gonçalves S, Matos PM, Rodrigues M, Santos NC. Members of the Organizing Committee of the XII EPI – Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010.

Santos NC. Co-organizer of the Workshop Nanoscale imaging and force measurements in Life Sciences, Lisbon, Portugal, April 29, 2010.

Santos NC. Member of the Scientific Committee of the 4th Spanish-Portuguese Biophysical Congress, Zaragoza, Spain, July 7-10, 2010.

Santos NC. Member of the Organizing Committee of the 9th Short Course of the Portuguese Biophysical Society – Protein folding, misfolding and disease, Santarém, Portugal, October 8-10, 2010.

Santos NC. Member of the Scientific Committee of the XVII Congresso Nacional de Bioquímica, Porto, Portugal, December 15-17, 2010.

Internationalization

Collaborative publications and funded projects with groups from the University of Leeds (UK), Federal University of Rio de Janeiro (Brazil), University of São Paulo (São Carlos, Brazil), Pompeu Fabra University (Barcelona, Spain), Federal University of Ceará (Fortaleza, Brazil), University of Girona (Spain), Macfarlane Burnet Institute for Medical Research and Public Health (Melbourne, Austrália), Oswaldo Cruz Foundation (Rio de Janeiro, Brazil), Catholic University of Leuven (Belgium), Free University of Brussels (Belgium), University of Twente (Enschede, The Netherlands), Agency for Science, Technology and Research (Singapore), European Molecular Biology Laboratory (EMBL, Heidelberg, Germany), University of Sussex (Brighton, UK) and Centre for Genomic Regulation (Barcelona, Spain), as well as with Biotech companies from the United States, Belgium 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.

Ivo C. Martins and Sónia Gonçalves received and oriented research students from the Charles University (Pilsen, Czech Republic) and from the University of Belgrade (Serbia), respectively.

Nuno C. Santos participated in foreign PhD juries from the University of Queensland (Brisbane, Australia) and University of Girona (Spain).

Prizes, honours and awards

“Frontiers Life Sciences Research” prize awarded by the Calouste Gulbenkian Foundation to Ivo C. Martins for the project “The interplay between lipid droplets, RNA and the capsid protein during dengue virus assembly”.

“Programa Gulbenkian de Estímulo à Investigação” prize awarded by the Calouste Gulbenkian Foundation to Marco M. Domingues and Filomena A. Carvalho for the project “Atomic force microscopy-based molecular recognition of fibrinogen receptors in platelets and erythrocytes. Applications in health and disease”.

Advanced teaching

Santos, N.C. lectured “Force spectroscopy”, Master in Biological Engineering, Master in Chemical Engineering and PhD Program, Instituto Superior Técnico, Universidade Técnica de Lisboa, Lisbon, April 28, 2010.

Santos, N.C lectured. “Light scattering techniques and their Biochemical applications”, Master in Biotechnology, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica, May 10, 2010.

Santos, N.C. lectured “Light scattering techniques and their Biochemical applications”, Master in Structural and Functional Biochemistry, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica, October 25, 2010.

Domingues, M.M. lectured Dynamic light scattering and zeta-potential practical sessions, Master in Structural and Functional Biochemistry, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte da Caparica, October 25, 2010.

Science and Society

During 2010, the Research work of the Biomembranes Unit of IMM was addressed at several mass media news and interviews (TV, radio, journals, magazines and on-line news); namely, on SIC on-line (March 22, 2010), Jornal de Notícias (March 23, 2010, pp. 1, 5 and 30), Público (March 23, 2010, pp. 8), Rádio Renascença (March 23, 2010), Antena 1 (March 23, 2010), CiênciaHoje (March 23, 2010), Metro (March 23, 2010, pp. 1 and 4), RTP (ComCiência, March 23, 2010), Diário de Notícias on-line (March 23, 2010), i on-line (March 23, 2010), Lux on-line (March 23, 2010), Tribuna Médica Press (March 23, 2010), cienciapt.net (March 23, 2010), Boas Notícias.pt (March 24, 2010), Visão (March 25, 2010, p. 76), Jornal de Leiria (March 25, 2010, pp. 1, 2 e 3), Notícia Aberta (April 5, 2010), RTP 1 (“Bom Dia Portugal”, April 6, 2010), Tribuna Médica Press (May 21, 2010), CiênciaHoje (May 26, 2010), Destak (May 26, 2010), SIC on-line (May 26, 2010), RCM Pharma (May 26, 2010), TVI 24 on-line (May 26, 2010), Jornal de Notícias (May 27, 2010, p. 34), Tribuna Médica Press (May 27, 2010), 24 Horas (May 29, 2010, p. 74), Correio da Manhã (May 30, 2010, Revista Domingo p. 71), Tempo Medicina (June 7, 2010, p. 10) and Destak (June 22, 2010, p.7).

Santos, N.C. Seminar “Membranas biológicas como alvos terapêuticos”. Colégio Sagrado Coração de Maria, Lisbon, March 26, 2010.

Carvalho FA, Domingues MM, Faustino A, Freitas T, Gonçalves S, Martins IC, Matos PM, Rodrigues M, Santos A, Santos NC. Visit of Escola Secundária Júlio Dantas (Lagos) to the Biomembranes Unit, including presentation and “speed-dating” style contact with the different components the Unit’s Research work, Lisbon, December 9, 2010.

Santos, N.C. Seminar “Membranas biológicas como alvos terapêuticos”. Semana da Ciência e Tecnologia 2010, Escola Secundária Ferreira Dias, Agualva-Cacém, December 10, 2010.

Santos NC. Collaborated with the “Bioquímica de Portas Abertas” initiative, targeted at High School students from the entire Country (organized by the IMM’s Communication and Training Unit and by the Fundação Oswaldo Cruz, Rio de Janeiro, Brazil), which took place at the XVII Congresso Nacional de Bioquímica, Porto, December 15-17, 2010.

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, FML
Inês Antunes	Post-Doc Fellowship, FCT
Catarina Henriques	PhD Fellowship, FCT (left in March 2010)
Bruno Cardoso	PhD Fellowship, FCT
Leila Martins	PhD Fellowship, FCT
Nádia Correia	PhD Fellowship, FCT
Alice Melão	PhD Fellowship, FCT
Milene Silva	BI Fellowship, FCT
Daniel Ribeiro	BI Fellowship, FCT
Maureen Spit	Short-term trainee, Erasmus MSc student (March-Aug)

Keywords/Research Areas

Oncobiology
Leukemia
Signal transduction
Cellular and molecular biology

Major scientific achievements

To characterize the impact of IL-7 in T-cell acute lymphoblastic leukemia (T-ALL) is one of the specific goals in the lab. We have recently shown that IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R α in T cells, an observation that might

have important implications in diseases such as leukemia or AIDS, where the IL-7/IL-7R axis plays a role (Blood 115:3269).

In 2008, we showed that PI3K/Akt pathway is hyperactivated in most T-ALL cases, mainly due to posttranslational inactivation of PTEN by high ROS and CK2 levels (J Clin Invest 118:3762). Notch activating mutations are very common in T-ALL and lead to PTEN transcriptional downregulation. Therefore, we reasoned that CK2 inhibitors and γ -secretase inhibitors (GSIs), which block Notch, should cooperate in reactivating PTEN in leukemia cells. Indeed, combined inhibition of CK2 and Notch leads to cooperative blockade of proliferation and viability of T-ALL cells (Haematologica 95:674). Interestingly, our collaboration with Centro Infantil Boldrini, Brazil, revealed that the relatively few T-ALL patients harboring exon 7 PTEN mutations may be at increased risk of relapse (Leukemia 24:239).

We found that the critical role of CK2 for leukemia cell viability extends to chronic lymphocytic leukemia (CLL), the most common form of leukemia in the Western world. We showed that CK2 is overexpressed and hyperactivated in CLL, constituting a potential major therapeutic target (Blood 116:2724).

Finally, we collaborated with other IMM Units, participating in studies that regard the characterization of the effects of low dose ionizing irradiation in promotion of angiogenesis and tumor growth (PLoS ONE 5:e11222) or the immunotargeting of hematological cancers by $\gamma\delta$ T cells (Haematologica 95:1397, Blood 115:2407).

Recent Most Relevant Publications

Silva A, Yunes JA, Cardoso BA, Martins LR, Jotta PY, Abecasis M, Nowill AE, Leslie NR, Cardoso AA and Barata JT (2008) PTEN Posttranslational Inactivation and Hyperactivation of the PI3K/Akt Pathway Sustain Primary T Cell Leukemia Viability. *J. Clin. Invest.* **118**, 3762-3774 (Journal IF: 15.387, Citations: 24)

Barata JT, Silva A, Brandão JG, Nadler LM, Cardoso AA, Boussiotis VA (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. (Journal IF: 14.505, Citations: 61)

Barata JT, Cardoso AA, Nadler LM, Boussiotis VA (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. (Journal IF: 10.555, Citations: 68)

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-OBD/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

2007/10 Overexpression of Oncogenes in Normal Human Hematopoietic Stem Cells: Impact on T-cell Leukemia. FCT. Coordinator: J.T. Barata. PTDC/SAU-OB/69974, € 174 800

2007/10 Grant into Causes and Prevention of Childhood Leukaemia. Children with Leukaemia Charity, UK. Coordinator: J.T. Barata, € 140 000

Publications in Peer Reviewed International Journals 2010

Martins LR, Lúcio P, Silva MC, Gameiro P, Silva MG, Barata JT (2010) Targeting CK2 Overexpression and Hyperactivation as a Novel Therapeutic Tool in Chronic Lymphocytic Leukemia. *Blood* **116** (15), 2724-2731. (Journal IF: 10.555)

Vala IS, Martins LR, Imaizumi N, Nunes RJ, Rino J, Kuonen F, Carvalho LM, Ruegg C, Monteiro Grillo I, Barata JT, Mareel M, Santos SCR (2010). Low Doses of Ionizing Radiation Promote Tumor Growth and Metastasis by Enhancing Angiogenesis. *PLoS ONE* **5** (6), e11222. (Journal IF: 4.351)

Gomes AQ, Correia DV, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, da Silva MG, Silva-Santos B (2010) Identification of a panel of ten cell surface protein antigens associated with immunotargeting of leukemias and lymphomas by peripheral blood $\gamma\delta$ T cells. *Haematologica* **95** (8), 1397-1404. (Journal IF: 6.416)

Henriques CM, Rino J, Nibbs RJ, Graham GG, Barata JT (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R α in T cells. *Blood* **115** (16): 3269-3277. (Journal IF: 10.555)

Lança T, Correia DV, Moita CF, Raquel H, Neves-Costa A, Ferreira C, Ramalho JS, Barata JT, Moita LF, Gomes AQ, Silva-Santos B (2010). The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to gamma-delta T cell. *Blood* **115** (12), 2407-2411. (Journal IF: 10.555)

Jotta PY, Ganazza MA, Silva A, Viana MB, da Silva MJ, Zambaldi LJG, Barata JT, Brandalise SR, Yunes JA (2010). Negative prognostic impact of PTEN mutation in pediatric T-cell acute lymphoblastic leukemia. *Leukemia* **24** (1), 239-42. (Journal IF: 8.296)

Silva A, Jotta PY, AB Silveira, Ribeiro D, Brandalise SR, Yunes JA, Barata JT (2010). Regulation of PTEN by CK2 and Notch1 in primary T-cell acute lymphoblastic leukemia: rationale for combined use of CK2- and gamma-secretase inhibitors. *Haematologica* **95** (4), 674-678. (Journal IF: 6.416)

Other publications International

J.T. Barata (2010). The impact of PTEN regulation by CK2 on PI3K-dependent signaling and leukemia cell survival, *Advances in Enzyme Regulation*, doi:10.1016/j.advenzreg.2010.09.012.

Invited Lectures and Seminars

J.T. Barata. *The ins and outs of T-cell leukemia: CK2, PTEN-PI3K and IL-7*. Centro de Biomedicina Molecular e Estrutural (CBME), University of Algarve, Faro, Portugal, December 10, 2010.

J.T. Barata. *The ins and outs of T-cell leukemia signaling: PTEN, PI3K/Akt and IL-7*. Instituto de Investigação em Ciências da Vida e Saúde (ICVS), University of Minho, Braga, Portugal, October 13, 2010.

J.T. Barata. *The Impact of PTEN Regulation by CK2 on PI3K-Dependent Signaling and Leukemia Cell Survival*. *Advances in Enzyme Regulation – 51st International Symposium on “Regulation of Enzyme Activity and Synthesis in Normal and Neoplastic Tissues”*, University of Bologna, Italy, October 4-5, 2010.

J.T. Barata. *PTEN non-deleting posttranslational inactivation in human T-cell leukemia*. Instituto Gulbenkian de Ciência, Oeiras, Portugal, September 24, 2010.

J.T. Barata. *T-ALL signals: translating posttranslational alterations into therapy?* European Hematology Association and European School of Haematology Joint Scientific Workshop “T-cell Acute Lymphoblastic Leukemia (T-ALL) Meets Normal T-cell Development”, Mandelieu, France, May 7-9, 2010.

Communications in International Conferences

L.R. Martins, P. Lúcio, M.C. Silva, P. Gameiro, M.G. Silva, J.T. Barata. *CK2 as a novel therapeutic target in chronic lymphocytic leukemia*. 6th International Conference on Protein Kinase CK2, University of Cologne, Germany, September 7-10, 2010 (Oral presentation).

A.B. Silveira, B. Nogueira, B.A. Cardoso, P. Leal, R.A. Yunes, J.T. Barata, N.I.T. Zanchin, J.A. Yunes. *Inhibition of PI3K sensitizes T-ALL cells to prednisolone and methotrexate*. European Hematology Association and European School of Haematology Joint Scientific Workshop “T-cell Acute Lymphoblastic Leukemia (T-ALL) Meets Normal T-cell Development”, Mandelieu, France, May 7-9, 2010 (Poster presentation).

Communications in National Conferences

B.A. Cardoso, S. de Almeida, A. Larangeira, M. Carmo-Fonseca, J.A. Yunes, P.J. Coffey, J.T. Barata. *The oncogene TALI/SCL is downregulated by Histone Deacetylase inhibitors in human T-cell leukemia*. XVII National Congress of Biochemistry, Porto, Portugal, December 15-17, 2010 (Oral presentation).

L.R. Martins, P. Lúcio, M.C. Silva, P. Gameiro, M.G. Silva, J.T. Barata. *CK2-mediated signaling as a novel therapeutic target in chronic lymphocytic leukemia*. SINAL 2010 – 4th National Meeting on Signal Transduction, University of Algarve, Portugal, May 21-22, 2010 (Oral presentation).

L.R. Martins, M.C. Silva, P. Gameiro, M.G. Silva, P. Lúcio, J.T. Barata. *CK2 is overexpressed in B-cell chronic lymphocytic leukemia cells and promotes leukemia cell viability*. XI Technical Congress of Patho-anatomy, Évora, Portugal, May 7-9, 2010. (Oral presentation)

A. Gírio, N. Correia, A.R. Grosso, B.A. Cardoso, J.T. Barata. *Identification of three novel TALI target genes with potential relevance in T-cell acute lymphoblastic leukemia*. SINAL 2010 – 4th National Meeting on Signal Transduction, University of Algarve, Portugal, May 21-22, 2010 (Poster presentation)

B.A. Cardoso, S. Almeida, P.J. Coffey, J.T. Barata. *TALI/SCL is downregulated upon histone deacetylase inhibition in human T-cell leukemia*. SINAL 2010 – 4th National Meeting on Signal Transduction, University of Algarve, Portugal, May 21-22, 2010 (Poster presentation).

Organisation of Conferences

J.T. Barata was a Member of the Scientific Committee and Chair of Session 4, SINAL 2010 – 4th National Meeting on Signal Transduction, University of Algarve, Portugal, May 21-22, 2010.

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 2010 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), Dr. Maria Toribio (CBM “Severo Ochoa”, Madrid, Spain), Prof. Gerry Graham (Glasgow University, UK), and Dr. Nick Leslie (Dundee University, UK).

During 2010, the Cancer Biology Unit lab head, Dr. J.T. Barata, was invited to give two talks at international meetings (The 51st International Symposium on “Regulation of Enzyme Activity and Synthesis in Normal and Neoplastic Tissues” and the European Hematology Association and European School of Haematology Joint Scientific Workshop “T-cell Acute Lymphoblastic Leukemia (T-ALL) Meets Normal T-cell Development”). Furthermore, Dr. Barata was asked to review international grants (e.g. from the Health Research Board, Ireland), and to act as referee for prestigious international journals (including The Journal of Clinical Investigation, Blood, Leukemia, etc).

In addition, the lab welcomes regularly foreign students (e.g. undergrad Erasmus students).

Prizes, honours and awards

Liga Portuguesa Contra o Cancro – “TERRY FOX” 2010 Grant/Prize for Research in Oncology to J.T. Barata for the project *Reciprocal regulation between TAL1 and miRNA expression in T-cell leukemia*.

Roche “Best oral presentation” award to M.C. Silva for the presentation *CK2 is overexpressed in B-cell chronic lymphocytic leukemia cells and promotes leukemia cell viability* at the XI Technical Congress of Patho-anatomy, Évora, Portugal, May 7-9, 2010.

Advanced teaching

J.T. Barata lectured the topic “Signal Transduction in Cancer” at the Masters in Biomedical Sciences, University of Algarve, Faro, Portugal, December 10, 2010.

J.T. Barata taught at the Advanced Course on “Fundamentals of Genetics, Development and Neoplasia”, International Postgraduate Programme, School of Health Sciences, University of Minho, Braga, Portugal, October 14, 2010.

J.T. Barata taught at the Module of Cancer Immunotherapy (July 2-3), Curricular unit of Immunological Therapies, Masters in Molecular Therapies, CESPU, Gandra, Portugal, July 2-3, 2010.

J.T. Barata organized the Biology of Cancer Course for the IMM International PhD Program and lectured the topic “Signal Transduction in Cancer”, IMM, Lisbon, Portugal, 19-21 April and May 17-18, 2010.

J.T. Barata lectured the topics “Signal Transduction Aberrations in Cancer” and “Novel Concepts in Cancer Signal Transduction” at the Advanced Course on Oncobiology, BEB PhD Program of the Center for Neuroscience and Cell Biology (CNC), University of Coimbra, March 9, 2010.

Science and Society

J.T. Barata, Seminar “Novel molecular therapeutic targets in leukemia”, Encontro com a Ciência e a Tecnologia em Portugal 2010, Lisbon, Portugal, July 4-7, 2010.

Master and Ph.D. thesis completed

PhD Thesis

Ana Silva (2010) “IL-7- and PI3K-Mediated Signaling in T-Cell Leukemia: The Role of External and Cell-Autonomous Signals in Tumorigenesis”. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata. Co-supervisor: L. Parreira.

Catarina Henriques (2010) “The regulation of interleukin 7 receptor alpha internalization, recycling and degradation by IL-7 – possible implications in T-cell homeostasis, migration and

leukaemogenesis”. Faculdade de Medicina da Universidade de Lisboa. Supervisor: J.T. Barata.
Co-supervisors: L. Parreira and G. Graham.

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, FML

Principal Investigators

Francisco Enguita, PhD - Auxiliary Professor, FML

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

Research Team

Teresa Carvalho, MD, PhD	Auxiliary Professor, FML
Joana Desterro, PhD	Auxiliary Professor, FML
Célia Carvalho, PhD	Auxiliary Professor, FML
Noélia Custódio, PhD	Auxiliary Professor, FML
Sandra Martins, PhD	Auxiliary Professor, FML
José Rino, PhD	Investigator, IMM
Rute Marcelino, M.Sc.	Invited Investigator, IMM
Natalia Kozlova, PhD	Post Doc Fellowship, FCT (left in 2010)
Marco Campinho, PhD	Post Doc Fellowship, FCT (left in 2010)
Houda Hallay, PhD	Post Doc Fellowship, MCTN (left in 2010)
Robert Manfred Martin, PhD	Post Doc Fellowship, FCT
Ana Rita Grosso, PhD	Post Doc Fellowship, FCT
Jorge Andrade	PhD Fellowship, FCT
Ana Cláudia Raposo	Masters Student, FCUL
Jasmin Klose	ERASMUS, University Duisburg Essen, Germany
Marisa Cabrita	Technician, FML
Sérgio Marinho	Technician, FML
Sílvia Carvalho	Technician, IMM

Research Areas

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

Major scientific achievements

Using fluorescence in situ hybridization (FISH) and confocal microscopy, our group showed that mRNA processing defects induce an accumulation of β -globin transcripts in discrete nuclear foci localized in close proximity to the site of transcription. The group has since been interested in further dissecting the molecular mechanisms involved in this RNA surveillance process. In parallel, we have developed methodologies to study how splicing factors are recruited to nascent transcripts in the living cell nucleus, and we are currently developing live-cell microscopy tools to visualize the dynamics of transcription, spliceosome assembly and splicing. We have also established and further developed computational approaches to analyze genome-wide EST, microarray, ChIP-Seq and RNA-Seq datasets in order to better understand the splicing code and mechanisms of co-transcriptional splicing regulation.

ExonMine: a novel method to mine EST and mRNA transcript alignments to genomic sequence.

Mining massive amounts of transcript data for alternative splicing information is paramount to help understand how the maturation of RNA regulates gene expression. We developed an algorithm to cluster transcript data to annotated genes to detect unannotated splice variants. A higher number of alternatively spliced genes and isoforms were found compared to other alternative splicing databases. Comparison of human and mouse data reveals a marked increase, in human, of splice variants incorporating novel exons and retained introns. Previously unannotated exons were validated by tiling array expression data and shown to correspond preferentially to novel first exons. Retained introns were validated by tiling array and deep sequencing data. The majority of retained introns are shorter than 500 nucleotides and have weak polypyrimidine tracts. A subset of retained introns matching small RNAs were found to be enriched in GC content, suggesting a possible coordination between splicing regulation and production of non-coding RNAs. Conservation of unannotated exons and retained introns was found to be higher in horse, dog and cow than in rodents, however 40% of exon sequences were only found in primates. This analysis highlights previously bypassed alternative splicing variants which may be crucial to deciphering more complex pathways of gene regulation in human (*Mollet et al., 2010*).

A novel role for the human exosome in RNA polymerase II transcriptional termination.

In eukaryotes, the production of mature messenger RNA that exits the nucleus to be translated into protein in the cytoplasm requires precise and extensive modification of the nascent transcript. Any failure that compromises the integrity of an mRNA may cause its retention in the nucleus and trigger its degradation. Multiple studies indicate that mRNAs with processing defects accumulate in nuclear foci or “dots” located near the site of transcription, but how exactly are defective RNAs recognized and tethered is still unknown. We found evidence suggesting that unprocessed β -globin transcripts render RNA polymerase II (Pol II) incompetent for termination and that this quality control process requires the integrity of the nuclear exosome. Our results show that unprocessed pre-mRNAs remain tethered to the DNA template in association with Pol

II, in an Rrp6-dependent manner. This reveals an unprecedented link between nuclear RNA surveillance, the exosome and Pol II transcriptional termination (*de Almeida et al. 2010*).

Recent Most Relevant Publications

Braga J, Desterro JM, Carmo-Fonseca M (2004) Intracellular macromolecular mobility measured by fluorescence recovery after photobleaching with confocal laser scanning microscopes. *Mol. Biol. Cell* **15**, 4749-4760. (Journal IF: 7.454, Citations: 85)

Desterro J, Keegan L, Lafarga M, Berciano MT, O'Connell M and Carmo-Fonseca M (2003) Dynamic association of RNA editing enzymes with the nucleolus. *J. Cell Sci.* **116**, 1805-1818. (Journal IF: 6.954, Citations: 63)

Calapez A, Pereira HM, Calado A, Braga J, Rino J, Carvalho C, Tavanez JP, Wahle E, Rosa AC 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 (Journal IF: 12.915, Citations: 78)

Calado A, Tomé FMS, Brais B, Rouleau GA, 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. (Journal IF: 9.048, Citations: 118)

Custódio N, Carmo-Fonseca M, Geraghty F, Pereira HS, Grosveld F and Antoniou M (1999) Inefficient processing impairs release of RNA from the site of transcription. *EMBO J.* **18**, 2855-2866. (Journal IF: 13.999, Citations: 145)

Ongoing Research Projects

2006/2010 EURASNET: European Alternative Splicing Network of Excellence (FP6-LSHG-CT-2005-518238) Participant: M. Carmo-Fonseca, € 180.000,00.

2006/2010 Chromatin Plasticity (FP6- Marie Curie Training Network)
Participant: M. Carmo-Fonseca, € 314.716,00.

2009/2012 Transcription-coupled mechanisms of gene regulation (FCT- PTDC/BIA-BCM/101575/2008)
PI: M. Carmo-Fonseca, € 199.350,00.

Publications in peer review Journals

Mollet IG, Ben-Dov C, Felício-Silva D, Grosso AR, Eleutério P, Alves R, Staller R, Silva TS and Carmo-Fonseca M (2010) Unconstrained mining of transcript data reveals increased alternative splicing complexity in the human transcriptome. *Nucleic Acids Research* **38** (14), 4740-54. (Journal IF: 7.479)

de Almeida SF, García-Sacristan A, Custódio N, Carmo-Fonseca M (2010) A link between nuclear RNA surveillance, the human exosome and RNA polymerase II transcriptional termination. *Nucleic Acids Research* **38** (22), 8015-26. (Journal IF: 7.479)

de Almeida SF, Carmo-Fonseca M (2010) Cotranscriptional RNA checkpoints. *Epigenomics* **2**, 449-55. (Journal IF: N/A)

Carmo-Fonseca M (2010) Follow that messenger: live-imaging a journey out of the nucleus. *Dev Cell* **18**: 880-882. (Journal IF: 13.363)

Other Publications International

Carmo-Fonseca M, Berciano MT, Lafarga M (2010) Orphan nuclear bodies. *Cold Spring Harbor Perspect. Biol.* **2**(9), a000703.

Invited Lectures and Seminars

Carmo-Fonseca, M. *The anticancer compound Spliceostatin A inhibits splicing and alters RNA polymerase II dynamics*. International Symposium on Alternative Splicing in Neurodegenerative Disease and Cancer. Tel Aviv, February 7-9, 2010.

Carmo-Fonseca, M. *Live-cell imaging of co-transcriptional pre-mRNA splicing*. TriRhenia Chromatin and Transcription meeting. IGBMC, Strasbourg, February 10, 2010.

Carmo-Fonseca, M. *Live-cell imaging of co-transcriptional pre-mRNA splicing*. Janelia Farm Conference "Imaging Transcription in Living Cells: A Systems and Computational Approach". Janelia Farm Research Campus, VA, March 11-14, 2010.

Carmo-Fonseca, M. *Real-time dynamics of pre-mRNA splicing*. EMBO Workshop Advanced Light Microscopy. EMBL, Heidelberg, May 18-21, 2010.

Carmo-Fonseca, M. *Live-cell imaging of co-transcriptional splicing*. Mini-Symposium "Mechanisms of gene expression". IBMC, Porto, September 10, 2010.

Carmo-Fonseca, M. *Real-time dynamics of transcription and pre-mRNA splicing*. EURASNET interdisciplinary focus meeting "Splicing regulation: from molecules to organisms". Berlin, September 20-21, 2010.

Carmo-Fonseca, M. *Chromatin modification by trimethylation of H3K36 is splicing-dependent*. Cold Spring Harbor Asia Conference "RNA Biology". China, November 1-5, 2010.

Carmo-Fonseca, M. *Live-cell imaging reveals coordination between splicing, RNA polymerase II dynamics and RNA surveillance at the transcription site*. EMBO Workshop "RNA Control of Cell Dynamics". Ein Gedi, Israel, November 15-18, 2010.

Enguita, F.J. *Upregulated miRNAs and putative pathway control in a cellular model of human aging*. Eurotides meeting, Barcelona, November 17-18, 2010.

Communications in International Conferences

Carmo-Fonseca et al. *Pre-mRNA splicing enhances co-transcriptional H3K36 trimethylation*. Platform presentation at RNA 2010 (Annual Meeting of the RNA Society). Seattle, Washington, June 22-26, 2010.

Hallay, H. et al. *Splicing regulation and human cell aging*. Poster presentation at RNA 2010 (Annual Meeting of the RNA Society). Seattle, Washington, June 22-26, 2010.

Martins, S., et al. *The splicing inhibitor Spliceostatin A induces accumulation of unspliced transcripts in nuclear speckles*. Poster presentation at “Nuclear Organization and Function” meeting, Cold Spring Harbor, New York, June 2-7, 2010.

Carvalho, T., et al. *An assay to study in vivo splicing*. Poster presentation at “Nuclear Organization and Function” meeting, Cold Spring Harbor, New York, June 2-7, 2010.

Organisation of National and International Conferences

M. Carmo-Fonseca organized the EURASNET annual meeting (European Network of Excellence on Alternative Splicing). Lisboa, March 1-4, 2010.

M. Carmo-Fonseca and Francisco Enguita organized a Workshop on RNA Therapeutics. Lisboa, March 4-5, 2010.

Internationalization

The group participates in an European Network of Excellence and in a Marie Curie Training Network (both supported by the European Commission FP6).

Prizes, honours and awards

Prémio Pessoa 2010 awarded to M. Carmo-Fonseca

Advanced teaching

Enguita, F.J. lectured *miRNAs: the cell biology “maestros”*. Gulbenkian Program for Advanced Medical Education, Instituto de Medicina Molecular, October 10, 2010.

Enguita, F.J. lectured *Protein Structure*. Gulbenkian Program for Advanced Medical Education, Instituto Gulbenkian de Ciência, October 18, 2010.

Enguita, F.J. lectured *RNA structure*. Gulbenkian Program for Advanced Medical Education, Instituto Gulbenkian de Ciência, October 19, 2010.

Enguita, F.J. lectured *Get the best from your sequences*. IMM PhD. Programme nanocourse, February 11-12, 2010.

Enguita, F.J. Organized *Advanced course on Protein Expression and Purification: tips and tricks*. IMM PhD. Programme nanocourse, April 28-30, 2010

Science and Society

Carmo-Fonseca, M. Lectured *A variabilidade do genoma humano*. Escola Secundária de Águeda, January 13, 2010

Carmo-Fonseca, M. Lectured *Doenças sexualmente transmitidas e cancro*. Escola Secundária de Reguengos de Monsarraz, June 1, 2010

Master and PhD thesis completed

PhD thesis

Ana Rita Fialho Grosso (2010) “New insights into alternative splicing using microarray technology” Faculdade de Medicina da Universidade de Lisboa. Supervisor: M. Carmo-Fonseca.

Ana Toste Rêgo (2010) “Molecular studies on the PapC usher domains and MrkD adhesin, protein of two distinct chaperone-usher systems”. Birkbeck College, London, UK. Co-supervisor: Francisco J. Enguita.

Sofia Caria (2010) “Biochemical and structural studies on the PhoR-PhoB two-component regulatory system from *Deinococcus radiodurans*”. Faculdade de Farmácia, Universidade de Lisboa. Supervisor: Francisco J. Enguita.

Master thesis

André Melo (2010) “Identificação de redes metabólicas controladas por miRNAs e envolvidas no envelhecimento celular”. Faculdade de Ciências e Tecnologia, Universidade de Coimbra. 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

Luis Ferreira Moita, M.D., Ph.D. Assistant Professor at FML

Principal Investigators

Nina Matova, Ph.D.

Staff Scientist

Research Team

Maria Helena Raquel	Post Doc Fellowship, FCT
Raquel Rodrigues	Post Doc Fellowship, FCT
Ana Neves-Costa	Post Doc Fellowship, FCT
Angelo Chora	Post Doc Fellowship, FCT
Catarina Moita	Post Doc Fellowship, FCT
Iris Cadima- Couto	Post Doc Fellowship, FCT
Patricia Rodrigues	Technician Fellowship, FCT (Left in September 2010)
Nuno Figueiredo	MD, PGFMA
Richard Staats	MD, Lung Specialist at HSM
Susana Moreira	MD, Lung Specialist at HSM

Keywords/Research Areas

Innate Immunity
Antigen Cross-Presentation
Sepsis and Sleep

Major scientific achievements

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.***, They, C.*. Rab27 controls constitutive exosome secretion. *Nat Cell Biol.* 2010 Jan;12(1):19-30. *Corresponding authors. (Journal IF: 19.527, Citations: 13)

Recent Most Relevant Publications

Colvin RA, Means TK, Diefenbach TJ, Moita LF, Friday RP, Sever S, Campanella GSV, Abrazinski T, Manice LA, Moita C, Andrews NW, Wu D, Hacoheh N and Luster AD (2010) Synaptotagmin mediated vesicle fusion regulates cell migration. *Nature Immunology* **11** (6), 495-502. (Journal IF: 26.000 , Citations: 3)

Ostrowski M, Carmo NB, Krumeich S, Fanget I, Raposo G, Savina A, Moita CF, Schauer K, Hume AN, Freitas RP, Goud B, Benaroch P, Hacoheh N, Fukuda M, Desnos C, Seabra MC, Darchen F, Amigorena S, Moita LF* (January 2010) Thery C*. Rab27a and Rab27b control different steps of the exosome secretion pathway.. *Nat Cell Biol* **12** (1), 19-30. (Journal IF: 19.527 , Citations: 13) *Corresponding authors.

Robinson M, Osorio F, Rosas R, Freitas R, Schweighoffer E, Groß O, Verbeek JS, Ruland J, Tybulewicz V, Brown GD, Moita LF, Taylor PR and Sousa CR (August 2009) Dectin-2 is a Syk-coupled pattern recognition receptor crucial for Th17 responses to fungal infection. *J Exp Med* **206** (9), 2037-51 (Journal IF: 15.463, Citations: 33)

Savina A, Peres A, Cebrian I, Carmo N, Moita C, Hacoheh N, Moita LF and Amigorena S (April 2009) The Small GTPase Rac2 Controls Phagosomal Alkalinization and Antigen Crosspresentation Selectively in CD8(+) Dendritic Cells. *Immunity* **30** (4), 544-55. (Journal IF: 20.579 , Citations: 20)

Oberdoerffer S, Moita LF, Neems D, Freitas RP, Hacoheh N, Rao A (August 2008) Regulation of CD45 alternative splicing by heterogeneous ribonucleoprotein, hnRNPLL. *Science* **1**, 321(5889), 686-91. . (Journal IF: 26.372, Citations: 31)

Ongoing Research Projects

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

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

2007 – 2010 Genetic dissection of innate immune processes using RNA interference, **FCT**. Coordinator: Luis Ferreira Moita (PTDC/SAU-MII/78333/2006) - €90.482

2007 – 2010 Synthetic pathogens for integrated biophysical and genetic dissection of antigen presentation, **FCT**. Coordinator: Luis Ferreira Moita (PTDC/SAU-MII/69280/2006) - €117.716

2006 – 2010: Synthetic pathogens for the integrated biophysical and genetic dissection of antigen presentation. Human Frontier Science Program. Coordinator: Luis Ferreira Moita (HFSP - RGY0058/2006-C). (IMM: USD400.000 / Consortium: USD750.000)

Publications in peer review Journals

Colvin RA, Means TK, Diefenbach TJ, Moita LF, Friday RP, Sever S, Campanella GSV, Abrazinski T, Manice LA, Moita C, Andrews NW, Wu D, Hacoheh N and Luster AD (Jun 2010)

Synaptotagmin mediated vesicle fusion regulates cell migration. *Nature Immunology* **11** (6), 495-502. (Journal IF: 26.000 , Citations: 3)

Rato S, Maia S, Brito PM, Resende L, Pereira CF, Moita C, Freitas RP, Moniz-Pereira J, Hacoheh N, Moita LF, Goncalves J (February 2010) Novel HIV-1 Knockdown Targets Identified by an Enriched Kinases/Phosphatases shRNA Library Using a Long-Term Iterative Screen in Jurkat T-Cells. *PLoS One*. **17**, 5(2):e9276. (Journal IF: 4.351, Citations: 1)

Mishra BB, Moura-Alves P, Sonawane A, Hacoheh N, Griffiths G, Moita LF*, Anes E* (2010) Mycobacterium tuberculosis Protein ESAT-6 is a Potent Activator of the NLRP3/ASC Inflammasome. *Cell Microbiol*. **12**, 1046-1063. *Corresponding Authors. (Journal IF: 5.725, Citations: 4)

Lança T, Correia DV, **Moita CF**, **Raquel H**, **Neves-Costa A**, Ferreira C, Ramalho JS, Barata JT, **Moita LF**, Gomes AQ and Silva-Santos B (2010) The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\{\gamma\}\{\delta\}$ T-cell cytotoxicity. *Blood*. **12**, 2407-2411. (Journal IF: 10.555, Citations: 3)

Ostrowski M, Carmo NB, Krumeich S, Fanget I, Raposo G, Savina A, Moita CF, Schauer K, Hume AN, Freitas RP, Goud B, Benaroch P, Hacoheh N, Fukuda M, Desnos C, Seabra MC, Darchen F, Amigorena S, Moita LF* (January 2010) Thery C*. Rab27a and Rab27b control different steps of the exosome secretion pathway.. *Nat Cell Biol* **12** (1), 19-30. (Journal IF: 19.527, Citations: 13) *Corresponding authors.

Invited Lectures and Seminars

Luis Ferreira Moita, “shRNA-based Dissection of Innate Immune Responses”. Division of Psychiatry Research, University of Zurich, Switzerland. Host: Lawrence Rajendran. September 27, 2010.

Luis Ferreira Moita, “shRNA-based Dissection of Innate Immune Responses”. Netherlands Cancer Institute, Amsterdam, Netherlands. Host: Jacques Neefjes. October 7, 2010.

Luis Ferreira Moita, “shRNA-based Dissection of Innate Immune Responses”. At Mechanisms of Gene Expression, IBMC Mini-Symposium, Porto, Portugal. Organizer and Host: Alexandra Moreira. September 10, 2010.

Communications in International Conferences

Moita LF. “shRNA Dissection of Antigen Cross-Presentation Pathways”. 6th International Antigen Processing and Presentation Workshop Cargèse, Corsica, France March 29th to April 2nd 2010. March 31, 2010. (Oral communication)

Moita C, Hacoheh N and Moita LF. shRNA Dissection of Antigen Cross-Presentation Pathways DC2010: Forum on Vaccine Science. 11th International Symposium on Dendritic Cells in Fundamental and Clinical Immunology. Lugano, Switzerland. 26-30 September 2010 (Poster presentation)

Raquel H, Moita C, Figueiredo N, Hacoheh N, Moita L . Identification Of Genes Involved In

Unconventional Protein Secretion Pathways.. Presented at the Cell Symposia on Inflammation and Disease. Sheraton Lisboa Hotel, Lisbon, Portugal. 26-28 September 2010 (Poster presentation)

Neves-Costa A, Raquel H and Moita LF. TET1 is a negative regulator of cytokine, adhesion and co-stimulator molecule expression in the THP-1 cell line. Presented at the Cell Symposia on Inflammation and Disease., Sheraton Lisboa Hotel, Lisbon, Portugal. 26-28 September 2010. (Poster presentation)

Susana Moreira, Comparison between two measures of excessive daytime sleepiness: Stanford Sleepiness Scale versus Pupillography, **2010 ATS International Conference in New Orleans, Louisiana May 14-19, 2010**. New Orleans, Louisiana, USA., May 18, 2010. (Poster presentation)

Susana Moreira, Diurnal objective evaluation of sleepiness after a night of work in health care professionals, **2010 ATS International Conference in New Orleans, Louisiana May 14-19, 2010**. New Orleans, Louisiana, USA., May 19, 2010, Poster.

European Respiratory Society – Annual Congress 2010

R. Staats, S. Moreira, J. Valença, D. Escalera, P. Rodrigues, M. Aguiar, I. Claro, L. Moita, T. Paiva, A. Bugalho de Almeida. Effect of obstructive sleep apneas/hypopneas on hemodynamic parameters during a short period of stable sleep. **European Respiratory Society – Annual Congress 2010**, Santa Maria Hospital, Lisbon, Portugal. (Poster presentation)

S. Moreira, R. Staats, J. Valença, N. Marçal, P. Rodrigues, A. Colaço, D. Grencho, L. Moita, T. Paiva, A. Bugalho de Almeida. Objective evaluation of daytime sleepiness in health care professionals after a nightshift. **European Respiratory Society – Annual Congress 2010**, Santa Maria Hospital, Lisbon, Portugal. (Poster presentation)

S. Moreira, R. Staats, J. Valença, F. Caeiro, N. Marçal, P. Rodrigues, D. Correia, L. Moita, T. Paiva, A. Bugalho de Almeida. Comparison between measures of excessive daytime sleepiness: Pupillography versus Sleepiness Scales, **European Respiratory Society – Annual Congress 2010**, Santa Maria Hospital, Lisbon, Portugal. (Poster presentation)

L. Oliveira, S. Moreira, R. Staats, J. Valença, F. Caeiro, N. Marçal, A. Colaço, D. Grencho, D. Correia, P. Rodrigues, L. Moita, A. Bugalho de Almeida. Relation between pupillography and polysomnographic parameters, Santa Maria Hospital, Lisbon, Portugal. (Poster presentation)

S. Moreira, R. Staats, J. Valença, F. Caeiro, P. Rodrigues, A. Colaço, L. Moita, A. Bugalho de Almeida. Diurnal objective evaluation of sleepiness after a night of work in health care professionals, Santa Maria Hospital, Lisbon, Portugal. (Poster presentation).

Organisation of Conferences

Moita LF, Coordinator of IMM external seminars. January 2009 – Present
Personally hosted the following talks: Sebastian Amigorena, Miguel Soares, Carlos Penha Gonçalves, Sergio Filipe, Peter Jordan, Nilabh Shastri, Lawrence Rajendran, Jules Hoffmann, Vasco Barreto, Philippe Benaroch, Rui Costa e Paula Duque.

Moita LF, Co-organizer of the 2010 edition of the IMM retreat. May 27-29th

Internationalization

Colvin RA, Means TK, Diefenbach TJ, Moita LF, Friday RP, Sever S, Campanella GSV, Abrazinski T, Manice LA, Moita C, Andrews NW, Wu D, Hacoheh N and Luster AD (Jun 2010) Synaptotagmin mediated vesicle fusion regulates cell migration. *Nature Immunology* **11** (6), 495-502. (Journal IF: 26.000 , Citations: 3)

Ostrowski M, Carmo NB, Krumeich S, Fanget I, Raposo G, Savina A, Moita CF, Schauer K, Hume AN, Freitas RP, Goud B, Benaroch P, Hacoheh N, Fukuda M, Desnos C, Seabra MC, Darchen F, Amigorena S, Moita LF* (January 2010) They C*. Rab27a and Rab27b control different steps of the exosome secretion pathway.. *Nat Cell Biol* **12** (1), 19-30. (Journal IF: 19.527, Citations: 13) *Corresponding authors.

Advanced teaching

PhD Programs

Moita LF. *Regulation of gene expression by RNAs* Programa Gulbenkian de Formação Médica Avançada (PGFMA)

Moita LF. “Dissection of the Role of Phagocytosis in Innate Immunity”. GABBA, May 19th, 2010

Moita LF. Lecture (“Genetic Dissection of Immune Response Signaling Pathways”), Journal Club discussion (Oberdoerffer S, Moita LF, Neems D, Freitas RP, Hacoheh N, Rao A. (2008) “Regulation of CD45 alternative splicing by heterogeneous ribonucleoprotein, hnRNPLL.” *Science* . 2008 Aug 1;321(5889):686-91.) and a Tutorial on the use of RNAi. March 9, 2010

Moita LF. “RNAi-based Dissection of Immune Response Signaling Pathways”, PhD Program for Medical Doctors from Universidade Nova de Lisboa

Masters Programs

Moita LF. “Basic and translational research bioethics”, Master in Bioethics

Ph.D. thesis completed

Catarina Moita (September 17, 2010), Genetic Dissection of Antigen Presentation Pathways. University of Lisbon. Supervisor: Luis Ferreira Moita.

Pedro Moura-Alves (October 25, 2010), Identification of Splicing Factors with a role in IL-1b Secretion. University of Lisbon. Supervisor: Luis Ferreira Moita.

Rui Freitas (December 15, 2010), Synthetic Pathogens for Integrated Biophysical and Genetic Dissection of Antigen Cross-Presentation. University of Lisbon. Supervisor: Luis Ferreira Moita.

Chromatin Biology Unit

Major interests / Objectives

The main objective of our research unit is to understand how human cells repair DNA damage introduced by cellular topoisomerases. We are currently focusing our research on identifying regulators of chromatin structure that influence cellular responses to topoisomerase 2-mediated DNA damage and cell fate decisions (apoptosis, accelerated senescence) in cancer cells. To this end we are utilizing a combination of approaches both in the small and the large-scale (expression microarray analysis, siRNA screens). Results originating from this research shall unravel chromatin structure regulators that may become targets for the chemotherapy of cancer.

Head of Unit

João Ferreira (MD, PhD) – (Associate Professor, Faculty of Medicine, Lisbon/FML)

Research Team

Joana Cardoso, PhD	Post-Doc Fellowship, FCT
Pedro Pereira	PhD Fellowship, FCT

Keywords/Research Areas

Topoisomerases
Chromatin
DNA damage
Cellular senescence

Major scientific achievements

We have contributed to establish how chromosomes organize inside the cell nucleus and, more recently, how topoisomerase 2- α participates in the organization and separation of human mitotic chromosomes via conjugation with SUMO peptides. We have also characterized the axis of mitotic chromosomes as both sumoylation centres for topoisomerase 2 and as targets for topoisomerase 2-specific anticancer drugs. Our data and views on the organization of interphase and mitotic chromosomes has been highlighted in international cell biology textbooks. Finally, in collaboration with the group of Dr. Patrick Varga-Weisz (Babraham Institute, Cambridge, UK), we contributed to establish WSTF as the first known chromatin remodeling factor operating in S phase to epigenetically propagate specific chromatin states.

Recent Most Relevant Publications

Agostinho M, Santos V, Ferreira F, Costa R, Cardoso J, Pinheiro I, Rino J, Jaffray E, Hay RT and Ferreira J (2008) Conjugation of human topoisomerase 2 α with small ubiquitin-like modifiers

2/3 in response to topoisomerase inhibitors: cell cycle and chromosome domain specificity. *Cancer Research* **68**, 2409-2418. (Journal IF: 7.514; Citations: 5)

Poot RA, Bozhenok L, van denBerg DLC, Steffensen S, Ferreira F, Grimaldi M, Gilbert N, Ferreira J and Varga-Weisz PD (2004) The Williams syndrome transcription factor interacts with PCNA to target ISWI chromatin remodeling to replication foci. *Nature Cell Biology* **6**, 1236-1244. (Journal IF: 17.774; Citations: 45)

Agostinho M, Rino J, Braga J, Ferreira F, Steffensen S and Ferreira J (2004) Human topoisomerase II α : targeting to subchromosomal sites of activity during interphase and mitosis. *Mol. Biol. Cell* **15**, 2388-2400. (Journal IF: 5.558; Citations:14)

Ongoing Research Projects

2009 Feb/2012 Mar. Novel therapeutic targets for the treatment of Acute Myeloid Leukemia, Gulbenkian Foundation-Portugal. Coordinator: J. Ferreira (Project: 96526/2008) €50.000. FCT Base (plurianual), €10.000

2009/2010 Characterization of two novel anti-cancer drugs, collaborative project with “ELARA Pharmaceuticals GmbH, Heidelberg, Germany (based at the European Molecular Biology Laboratory/EMBL, Heidelberg). Coordinators: J.D. Lewis and J. Ferreira.

Communications in International Conferences

Cardoso J, Grosso AR, Carmo-Fonseca M, Ferreira J. “Molecular Crossroads of Aging and Senescence”. EMBO Conference Series - From Functional Genomics to Systems Biology, Heidelberg, Germany, November 13-16, 2010 (Poster presentation).

Internationalization

Chromatin Plasticity Network (EU FP6; Research training network. Andreas Ladurner, Network coordinator). Participation in collaboration with Maria Carmo-Fonseca.

Advanced teaching

Ferreira J. Organized and lectured in the Gene Expression module of the “Gulbenkian Programme for Advanced Medical Education (with collaboration of the Champalimaud Foundation)” held at the Instituto de Medicina Molecular/IMM, Lisbon, October 2-15, 2010.

Cardoso J. Lecture “Large-scale approaches to the study of gene expression”, Gene expression Module, “Gulbenkian Programme for Advanced Medical Education” Lisbon, October 12, 2010.

Science and Society

Ferreira J. A Biologia Molecular e o moderno *quadrivium*. Lecture at “Conferências do Equinócio”, IPATIMUP, Porto (Org. M. Sobrinho-Simões; co-Org. A. Lobo Antunes), November 4, 2010.

Ferreira J. Participated as member of the juri for selection of best scientific presentations by students of FML, during the ENJOYMed meeting (organized by students of FML). Faculty of Medicine, Lisbon, December 11-12.

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 metastization; 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 metastization. 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

Luis Costa, MD, PhD – Director of the Oncology Division, HSM; Auxiliary Professor, FML

Research Team

Teresa Raquel Pacheco, PhD	Auxiliary Professor, FML
Ana Cristina Santos, PhD	Auxiliary Investigator, FML
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
Sofia Ribeiro	Undergrad. Student (left in December 2010)

Keywords/Research Areas

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

Major scientific achievements

In 2010 our project on the significance of RANK/RANKL/MMP1 in bone metastases reached major conclusions. RANKL up-regulates MMP1 in RANK+ cells. *In vivo*, MMP-1 KD

significantly decreases osteolysis. RANK/RANKL are expressed in the tumor compartment of bone metastases, a potential anti-tumoral advantage for RANKL-targeting therapies. In the context of our projects we successfully implemented a 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 2010, three new projects were implemented. The diffusion of hot topics in translation oncobiology is also one of our priorities. The Oncology Series organized in 2010 was a success, gathering together basic researchers and clinicians in a same audience.

Recent Most Relevant Publications

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)

Brown JE, Cook RJ, Lipton A, Costa L, Coleman RE (2010) Prognostic Factors for Skeletal Complications From Metastatic Bone Disease in Breast Cancer. *Breast Cancer Res Treat* **123**, 767-779. (Journal IF:4.696, Citations: 1)

Aapro M, Saad F, Costa L (2010) Optimizing Clinical Benefits of Bisphosphonates in Cancer Patients With Bone Metastases. *The Oncologist* **15** (11), 1147-1158. (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: **3.221**, citations: **5**)

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: **8.075**, citations: **15**)

Ongoing Research Projects

2008/2010 Analysis of RANK/RANKL and MMPs in clinical samples of solid tumors bone metastases, Amgen. Coordinator: Sandra Casimiro & Luis Costa, €46 800

2007/2011 Molecular Markers of Bone Metastasis, Novartis. Coordinator: Luis Costa, €79 571

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

2009/2010 Detection of Aromatase in Breast Cancer Metastases in Humans, AstraZeneca. Coordinators: Luis Costa & Joana Ribeiro, €3 450

2008/2011 Mechanisms of invasion and progression of cancer in bone: Molecular profiling of matrix and adhesion-related molecules in metastatic disease, LPCC/NRS. Coordinator: Sandra Casimiro, €15 000

2010 Plurianual, FCT. Coordinator: Luis Costa, €7 21,61

Publications in peer review Journals

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)

Candeias C, Vaz Luís I, Ribeiro J, Costa L, Soares de Almeida L, Gomes MM, Barreto L, Brito-Avô L, Ducla-Soares JL (2010) Extended remission of metastatic epithelioid angiosarcoma of the heart with liposomal doxorubicin. *BMJ Case Reports* (doi:10.1136/bcr.08.2009.2157) (Journal IF: N.A., Citations: 0)

Brown JE, Cook RJ, Lipton A, Costa L, Coleman RE (2010) Prognostic Factors for Skeletal Complications From Metastatic Bone Disease in Breast Cancer. *Breast Cancer Res Treat* **123**, 767-779. (Journal IF:4.696, Citations: 1)

Aapro M, Saad F, Costa L (2010) Optimizing Clinical Benefits of Bisphosphonates in Cancer Patients With Bone Metastases. *The Oncologist* **15** (11), 1147-1158. (Journal IF: N.A., Citations: 0)

Fernandes I, Borges da Costa J, Rego F, Quintela A, Soares de Almeida L, Costa L, Marques Gomes M. (2010) The importance of early diagnosis in Cowden syndrome. *Skin Cancer* **25**(2). (Journal IF: N.A., Citations: 0)

Other publications National

Vaz Luís I, Nunes da Silva MJ, Monteiro PH, Pinheiro LS, Nolasco T, Dutschman R, Gaspar T; Ribeiro J, Dias P, Duarte AF, Matias JS, Lucas M, Victorino RMM (2010) Uso de Marcadores Tumorais num Serviço de Medicina Interna - Um Estudo Basal e Pós-intervenção. *Medicina Interna* **17**(1), 5-12.

Vaz Luís I, Macedo R, Teixeira E, Sotto-Mayor R, Bugalho de Almeida A (2010) Clinical characteristics of patients with lung cancer and metachronous tumours with other locations. *Rev Port Pneumol*. **16**(3), 391-405.

Fernandes I, Borges da Costa J, Moitinho M, Fraga A, Amaral T, Fernandes A, Ribeiro J, Luís I, Semedo M, Matias M, Peres M, Lopes J, Soares de Almeida L, Sacramento-Marques M, Filipe P, Quintela A, Marques Gomes A, Costa L. Angiossarcoma do couro cabeludo - caso clínico de doente com metastização pulmonar fatal. *Revista da Sociedade Portuguesa de Oncologia*. Maio, 2010.

Invited Lectures and Seminars

Magalhães, A., Ledo, L., Monteiro, P.H., Vaz Luís, I., Gaspar, T., Pinheiro, L., Nunes Silva, M.J., Lourenço, E., Lucas, M., Metrass, M.J., Victorino, R.M.M. Racionalização de exames complementares e terapêutica: dois contributos da investigação clínica. Sessão Clínica HSM/FML, Lisbon, Portugal, November 16, 2010.

Vaz Luís, I., Matias, M., Quintela, A., Ribeiro, L., Cortes, P., Lourenço, C., Ribeiro, J., Casanova, M., Semedo, M., Cruz, J., Campos, P., Pignatelli, A., Mendes, A.C., Costa, L. Adenopatias

mediastínicas no doente oncológico - Estratégia no diagnóstico. Sessão Clínica HSM/FML, Lisbon, Portugal, October 28, 2010.

Costa, L. Terapêutica alternada com inibidores VEGF e mTOR no cancro do Rim. XIV Workshop de Urologia Oncológica. Carvoeiro, Portugal, October 23, 2010.

Costa, L. Antitumor effect of bisphosphonates: myth or reality? Encontros da Primavera. Encontros da Primavera - Oncologia 2010. Évora, April 9, 2010.

Costa, L. Terapêutica Médica Adjuvante no Cancro da Mama: quando, como e porquê. 9ª Reunião Internacional de Cirurgia. Lisbon, Portugal, January 29, 2010.

Communications in International Conferences

Luís, I., Bridgewater, C.H., Coleman, R.E. Brain metastases from breast cancer. Management of Adult Central Nervous System Tumours- British Institute of Radiology, London, UK, November, 2010 (Oral presentation)

Ribeiro, S., Casimiro, S. and Costa, L. Effect of RANK-RANKL signalling pathway on MMP1, MMP9, OPG and PTHrP gene expression of breast and prostate cancer cell lines in vitro. European Students Conference, Berlin, Germany, October 15, 2010 (Oral presentation)

Caiado, J., Ribeiro, J., Vaz Luís, I., Barbosa, M.B., Costa, L. Desensitization to different chemotherapy agents: a successful collaboration between Oncology and Immunoallergy. 35th ESMO Multidisciplinary Congress. Milan, Italy, October 8-12, 2010 (Poster presentation)

Costa, L., Luís, I., Alho, I., Fernandes, A., Casimiro, S., Lee, B.H., Gangolli, E.A., Motwani, M., Wang, L., Modur, V. Expression of Matrix Metalloproteinase 1 (MMP1), Dickkopf-1 (Dkk1) and Macrophage Colony Stimulating Factor Receptor 1 (MCSFR1) in bone metastatic tissue (BMT) and in serum of patients with bone metastases (BM) from different solid tumors". 35th ESMO Congress, Milan, Italy, October 8-12, 2010 (Poster presentation)

Fernandes, I., Pacheco, T., Costa, A., Santos, A.C., Oliveira, A.G., Casimiro, S., Quintela, A., Fernandes, A. and Costa, L. mTOR Activation in Advanced Neuroendocrine Tumors in Treatment with Somatostatin Analogues – a Single Center Study. 35th ESMO Congress, Milan, Italy, October 8-12, 2010 (Poster presentation)

Costa, L., Luís, I., Alho, I., Fernandes, A., Casimiro, S., Lee, B.H., Gangolli, E.A., Motwani, M., Wang, L., Modur, V. Expression of Matrix Metalloproteinase 1 (MMP1) and Dickkopf-1 (Dkk1) in bone metastatic tissue (BMT) and in serum of patients with bone metastases (BM) from different solid tumors". X international Conference Cancer-Induced Bone Disease, Sheffield, UK, September 22-25, 2010 (Poster presentation)

Ribeiro, J., Vaz Luís, I., Costa, C., Correia, L., Semedo, M., Lourenço, C., Cortes, P., Quintela, A., Costa, L. Correlation between hormonal receptors and HER2 status of primary and metastatic breast cancer according to the metastatic organ involved. 7th European Breast Cancer Conference. Barcelona, Spain, March 24-27, 2010 (Poster presentation)

Luis, I. A rare case of prolonged survival in a HER2 positive breast cancer patient with CNS disease. 9th ESMO Masterclass in Clinical Oncology-European School. Ermatingen, Switzerland, March 13-18, 2010 (Oral presentation)

Communications in National Conferences

Ribeiro, S., Casimiro, S. and Costa, L. Effect of RANK-RANKL signalling pathway on MMP1, MMP9, OPG and PTHrP gene expression of breast and prostate cancer cell lines in vitro. 13^o Workshop “Educação pela Ciência”, Lisbon, December 14, 2010 (Poster presentation)

Ribeiro, S., Casimiro, S. and Costa, L. Effect of RANK-RANKL signalling pathway on MMP1, MMP9, OPG and PTHrP gene expression of breast and prostate cancer cell lines in vitro. Oral presentation at EnjoyMed Conference, Lisbon, December 11, 2010. (Oral presentation)

Alho, I., Coelho, C., Bicho, M. and Costa, L. The importance of LMW-PTP on the tumour progression: an update. IV IMM PhD Students Meeting, Lisbon, November 22-23, 2010 (Poster presentation)

Tato-Costa, J., Casimiro, S. and Costa, L. A new method for detection of senescent cells in formalin-fixed paraffin-embedded tissues. IV IMM PhD Students Meeting, Lisbon, November 22-23, 2010 (Poster presentation)

Teixeira, R.L., Carvalho, A., Casimiro, S., Costa, L. Effect of RANK-RANKL signalling pathway and MMP1 expression in the invasive ability of breast and prostate cancer cell lines in vitro. Young European Scientist Meeting. Porto, September 25, 2010 (Poster presentation)

Di Meglio, A., Ribeiro, J., Vaz Luís, I., Matias, M., Cortes, P., Costa, L. Linfoma MALT e Adenocarcinoma do pâncreas síncronos: Um desafio oncológico. 8^o Congresso Nacional das Unidades de Oncologia. Vilamoura, September 24-26, 2010 (Poster presentation)

Vaz Luís, I. Eficácia e segurança dos Bisfosfonatos nos doentes oncológicos com patologia óssea. VI Jornadas Hospitalares de Estomatologia e III Congresso do Internato Médico de Estomatologia. Lisbon, April 16-17, 2010 (Oral presentation)

Caiado, J., Matias, M., Fernandes, I., Faria, M., Cortes, P., Barbosa, M.B., Costa, L. Dessensibilização a diferentes citostáticos: experiência de um Serviço. Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Oral presentation)

Ribeiro, J., Vaz Luís, I., Semedo, M., Campos, A., Albuquerque, L., Costa, L. Gliosarcoma secundário - A propósito de um caso clínico. Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Poster presentation)

Ribeiro, J., Vaz Luís, I., Caiado, J., Matias, M., Fernandes, I., Faria, M., Barbosa, M.B., Costa, L. Dessensibilização a diferentes citostáticos: a experiência de um serviço. Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Oral presentation)

Vaz Luís, I., Ribeiro, J., Faria, M., Matias, M., Ribeiro, L., Cortes, P., Santos, J.M., Ivo, M., Gonzalez, O., Pina, F., Fernandes, A., Presa, D.L., Costa, L. Pecoma irresecável peri-uterino: descrição de um caso e revisão da literatura. Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Poster presentation)

Vaz Luís, I., Ribeiro, J., Faria, M., Matias, Fernandes, I., Casa-Nova, M., Cortes, P., Pereira, S.V., Miltenberger- Milteny, G., Costa, L. Impacto do estado mutacional do KRAS nos tempos de sobrevivência global- análise retrospectiva: Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Poster presentation)

Matias, M., Faria, M., Peres, M., Semedo, M., Ribeiro, J., Luís, I., Fernandes, I., Costa, J., Ribeiro, L., Costa, L. Sarcoma de Kaposi em doente imunodeprimido após transplante renal. Encontros da Primavera - Oncologia 2010. Évora, April 8-11, 2010 (Poster presentation)

Organisation of Conferences

Costa, L. organized the Oncology Series 2010, Instituto de Medicina Molecular, Lisbon, Portugal. Invited speakers and title of Conferences:

- Miguel Martin (Chairman of the Spanish Breast Cancer Research Group), "Tailored adjuvant chemotherapy for early breast cancer", 9 February, 2010
- Soft Tissue Sarcomas, 29 April, 2010
 - o Rodolfo Capanna (Orthopaedic Oncology Department, University Hospital of Florence, Italy), "Surgery in soft tissue sarcomas: rules and expectations"
 - o Xavier Garcia del Muro (Institut Català d'Oncologia L'Hospitalet, Barcelona, Spain), "Systemic therapy in Soft Tissue Sarcoma: Current status and cooperative research"
 - o Robert Maki (Memorial Sloan-Kettering Cancer Center, New York, USA), "New clinical trial designs and new drugs for patients with sarcomas"
- Robert Coleman (Yorkshire Cancer Research, Professor of Medical Oncology, University of Sheffield), "Improving cancer care with bone targeted treatments", 17 June, 2010.

Internationalization

During 2010 we continued a collaborative research project involving Luis Costa, Sandra Casimiro and Theresa Guise. We established this collaboration in 2009, with Theresa Guise's Lab at the University of Virginia, USA, which moved to the University of Indiana, USA, in the past year. This collaboration allowed Sandra Casimiro to conduct the experiments in animal models, and to acquire skills that will allow her to establish the model in our own laboratory. Theresa Guise's Lab has a long history of research in metastases and train many international investigators to study bone metastases.

Prizes, honours and awards

Best Presented Work Award to Joana Ribeiro at the Encontros da Primavera - Oncologia 2010. Évora, Portugal, 2010.

2nd Prize for Oral Presentations to Sofia Ribeiro at the European Students Conference, Berlin, Germany, 2010.

3rd Prize for Oral Presentations to Sofia Ribeiro at the EnjoyMed Conference, Lisbon, Portugal, 2010.

Advanced teaching

In 2010, 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 FML. The main goal of this course is to highlight the clinical impact of understanding molecular and cellular mechanisms operating in cancer, and to learn on cancer diagnosis, prognosis and therapeutics, always connecting with the biological viewpoints.

Science and Society

Casimiro, S., Pires, R. and Costa L. Participation in the TV programme “Repórter TV” - “Podia ser eu”, TVI, 27 December, 2010.

Costa L. Participation in the TV programme “sociedade Civil” - “Cancro da mama: rastreio é a solução?”, RTP2, 29 October, 2010.

Casimiro, S. Organizer of “A week in the Lab” for High School students. Number of participants: 2, July 2010.

Developmental Biology Unit

Description and Objectives

The research work being developed at the Developmental Biology Unit aims to elucidate the molecular mechanisms that regulate the genesis of neurons in vertebrate embryos. In vertebrates, neurogenesis starts very early during embryonic life and the majority of neurons is produced before birth. A conserved genetic circuitry, comprising the action of both proneural and neurogenic genes, is employed to regulate the production of neurons during embryonic development. Our goal is to understand how this circuitry functions to regulate the establishment of neural precursors 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 pre-requisite 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 stemness properties in embryonic stem cells, focusing on the central role of *Nanog* in these molecular networks.

Head of Unit

Domingos Henrique, PhD – Investigator, FML

Research Team

Elsa Abranches, PhD	Post-Doctoral Fellow, FCT
Catarina Ramos, PhD	Post-Doctoral Fellow, FCT
Cláudia Gaspar, PhD	Post-Doctoral Fellow, FCT
Evguenia Bekman, PhD	Post-Doctoral Fellow, FCT
Filipe Vilas Boas	PhD Student, FCT
Aida Costa	PhD Student, FCT
Sara Ferreira	Technician/Lab Manager, Fellowship FCT
Ana Margarida Cristóvão	Technician, Fellowship FC (left in October 2010)

Keywords/Research Areas

Developmental Biology
Cell and Molecular Biology of Notch signalling
Neural Stem cell biology

Major scientific achievements

Our recent work has focused on two main areas, namely, i) the function of the Delta/Notch signalling pathway during neurogenesis and ii) the genetic circuitry underlying the “stemness” state in Embryonic Stem (ES) cells.

Concerning the first area, our work has contributed to elucidate some molecular mechanisms that control cell fate determination in the vertebrate nervous system, and this will continue to be the main research area in our group. We have recently shown how two Notch ligands, Dll1 and Jag1, contribute to regulate neurogenesis in the developing vertebrate spinal cord. Analysis of mouse embryos carrying mutations in both *Dll1* and *Jag1* revealed that Dll1 is able to signal to neighbouring Jag1-expressing domains and control spinal cord neurogenesis in the absence of *Jag1*. Moreover, analysis of neurogenesis in specific spinal cord domains revealed that either one copy of *Dll1* or *Jag1* is enough to restore normal neurogenesis, showing that the two ligands are functionally equivalent in controlling neuronal production. Furthermore, our work shows that neuronal type specification is independent of the type of Notch ligand that is active.

We have also addressed the role of two *hes6* genes in the chick spinal cord and how they modulate Notch signaling to allow progression of neuronal differentiation. We established an assay for the two *hes6* genes in the developing chick spinal cord and analysed various mutants of these two highly related HES proteins. Our results indicate that they work through different molecular mechanisms: while HES6-1 acts primarily by protein sequestration, forming inactive heterodimers with other HES proteins, HES6-2 acts as a transcriptional repressor. Together, the two chick HES6 proteins regulate neurogenesis by releasing differentiating neurons from Notch signalling.

We have also generated a novel reporter to monitor Notch signalling in neural progenitors at the single-cell level. A correlation was observed between the timing of Notch activation and the cell cycle of neural progenitors: when the pathway is active during mitosis, progenitor-generating divisions are favoured, whereas absence of Notch activity in mitotic progenitors might lead to different daughter cell fates.

Altogether, our work provides new insights into the role of Notch signalling in neural progenitors during vertebrate nervous system development, and how differentiating neurons terminate Notch activity. This knowledge is important to design novel strategies to control neural differentiation and might lead to future applications in regenerative medicine of the adult nervous system.

Concerning the second research topic of the lab, our main goal is to investigate how the Nanog/Oct4/Sox2 (NOS) regulatory network functions to generate and sustain the self-renewal and pluripotency characteristics of ES cells. Although this network has been extensively dissected in terms of interacting partners, downstream targets and auto/cross-regulations, little is known about the network's dynamic behaviour and how it regulates the "stemness" properties of cultured ES cells. The challenge is therefore to understand how "stemness" emerges from the inner workings of the NOS regulatory network and we have been building tools to address this question. We have generated lines of ES cells carrying a short-lived fluorescent reporter inserted into the nanog locus, allowing the selection of ES cells according to the levels of nanog expression. We are trying to correlate these levels with stemness potential, using mathematical models to explain, analyze and further predict the network's behaviour during stem cell growth and differentiation. We expect that this project will provide a new molecular framework to understand the genetic circuitry underlying "stemness" and facilitate the development of rational and more efficient methods to achieve full reprogramming of somatic cells, leading to better perspectives for the clinical use of iPS cells.

Recent Most Relevant Publications

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: N.A., Citations: 7)

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Rocha SF, Lopes SS, 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: 4.416, Citations:5)

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: 7.194, Citations: 181)

Afonso C, Henrique D (2006) “PAR3 acts as a molecular organizer to define the apical domain of chick neuroepithelial cells”, *J. Cell Science* **119**, 4294-4304. (Journal IF: 6.543, Citations: 20)

Fior R, Henrique D (2005) “A novel *hes5/hes6* circuitry of negative regulation controls Notch activity during neurogenesis”, *Dev. Biology* **281**, 318-333. (Journal IF: 5.432, Citations: 36)

Ongoing Research Projects

2007-2010 - “Stem cell based therapy for inner ear hair cell regeneration” (PTDC/SAU-NEU/71310)

2007-2010 - “Notch signaling and regulatory mechanisms during mammalian neurogenesis” (PTDC/SAU-OBD/75106)

2007-2010 - “NEURAL TALK - Scaffold-driven stem-cell regenerative therapy for spinal cord injury. Biomimetic neurogenesis in the CNS” (PTDC/SAU-BEB/65328). Joint Project with INEB, Porto (Project Leader -Ana Paula Pêgo)

2010-2012 - “The dialectics of “Stemness”: from biology to mathematics”, (PTDC/SAUOBD/100664/2008)

Publications in International Journals (2010)

Vilas-Boas F, Henrique D (2010) HES6-1 and HES6-2 function through different mechanisms during neuronal differentiation, *PLoS ONE* **5** (12):e15459 (Journal IF: 4.351)

Ramos C, Rocha S, Gaspar C, Henrique D (2010) Two Notch ligands, *Dll1* and *Jag1*, are differentially restricted in their range of action to control neurogenesis in the mammalian spinal cord, *PLoS ONE* **5** (12):e15515 (Journal IF: 4.351)

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: 7.194:)

Communications in International Conferences

Abranches, E., Henrique, D., “From ES cells to Neurons: The role of Notch in Neural Progenitors”, ESTOOLS scientific symposium - Stem Cells in Biology and Disease, Lisbon, Portugal. May 2010 (**1st Prize for Best Poster**)

Costa, A., Bekman, E., Henrique, D. "From Embryonic Stem Cells to Sensory Hair Cells: A Cell Reprogramming Approach" ESTOOLS scientific symposium - Stem Cells in Biology and Disease. Lisbon, Portugal, May 2010 (Poster Presentation)

Vilas-Boas, F., Fior, R., Henrique, D, "Two *hes6* genes in the chick with different functions during embryonic development", 18th Biennial Meeting of the International Society for Developmental Neuroscience - Understanding basic mechanisms of neurodevelopmental disorders", June 2010 (Poster Presentation)

Gaspar, C., Ramos, C., Henrique, D., "Dll1 and Dll4 Notch ligands have non-redundant functions in the development of the retina", 18th Biennial Meeting of the International Society for Developmental Neuroscience - Understanding basic mechanisms of neurodevelopmental disorders", June 2010 (Poster Presentation)

Bekman, E., Costa, A., Cristóvão, A., Henrique, D., "Stem cell based therapies for inner ear hair cell regeneration", 18th Biennial Meeting of the International Society for Developmental Neuroscience - Understanding basic mechanisms of neurodevelopmental disorders", June 2010 (Poster Presentation)

Ramos, C., Gaspar, C., Henrique, D., "The role of Notch ligands during spinal cord neurogenesis", 18th Biennial Meeting of the International Society for Developmental Neuroscience - Understanding basic mechanisms of neurodevelopmental disorders", June 2010. (Poster Presentation)

Ramos, C., Rocha, S., Gaspar, C., Henrique, D. "Two Notch ligands, Dll1 and Jag1, are restricted in their range of action to control neurogenesis in the mammalian spinal cord ", Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain November 10-12, 2010 (Poster Presentation)

Gaspar, C., Ramos, C., Henrique, D., "Dll1 and Dll4 Notch ligands have non-redundant functions in the development of the retina", Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 10-12, 2010 (Poster Presentation)

Costa, A., Bekman, E., Henrique, D. "From Embryonic Stem Cells to Sensory Hair Cells: A Cell Reprogramming Approach", BSDB Autumn Meeting 20 Development of Sensory Systems. Oxford, UK, September 7-9, 2010 (Poster Presentation)

Communications in National Conferences

Vilas-Boas, F., Fior, R., Henrique, D, "Notch reporters in chicken embryos", IV IMM PhD Students Meeting, November 2011 (Oral Communication- 1st prize for Best Student presentation)

Costa, A., Henrique, D. "Tweety-1 is a novel target of the Notch pathway", IV IMM PhD Students Meeting, November 2011 (Oral Communication)

Abranches, E., Henrique, D., "Da célula estaminal ao neurónio: um mapa para a neurogénese no embrião", Jornadas de Engenharia Química e Biológica 2010, Lisbon, Portugal, April 2010 (Oral Communication)

Invited Lectures and Seminars

Henrique, D., “*From ES cells to Neurons*”, Seminar at ESTOOLS scientific symposium - Stem Cells in Biology and Disease, Lisbon, Portugal, May 2010.

Henrique, D., “*Notch, Neural Progenitors and Neurons*”, Seminar at the Company of Biologists Workshop “Neural Stem Cells in development and Disease”, Winton Park U.K, February 7-10, 2010.

Henrique, D., “*Notch Ligands and Neurogenesis*”, Seminar at IGBMC, Strasbourg, France, June 3, 2010.

Henrique, D., “*New data on Notch and its role in regulating vertebrate neurogenesis*”, Seminar at PRBB, Barcelona, Spain, November 2, 2010.

Organisation of National and International Conferences

Domingos Henrique was a Co-organizer of the ESTOOLS Scientific Symposium - Stem Cells in Biology and Disease, Fundação Calouste Gulbenkian, Lisbon, Portugal, May 26-30, 2010.

Domingos Henrique was a Co-organizer of the 18th Biennial Meeting of the International Society for Developmental Neuroscience – “Understanding basic mechanisms of neurodevelopmental disorders”, Estoril, June 6-9, 2010.

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 15-19.
Henrique, D. – Lectures on “Development of the nervous system” – Masters Program on Neuroscience, Faculdade Medicina Lisboa

Abranches, E., Bekman, E. – Lectures on “From Neurons to Stem Cells”, PhD course about “Neural Stem Cell Environment” at the CNC-Coimbra.

Abranches, E., Bekman, E. – Course on Stem Cell Biology, Mestrado em Ciências Biológicas, Univ. Algarve, Faro, October 28-29.

Abranches, E., Lectures on “Neural differentiation in vitro and in vivo”, FCUL Mestrado Biologia e Tecn. das Células Estaminais, October 2010.

Science and Society

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

Filipe Vilas-Boas, Catarina Ramos, Elsa Abranches and Cláudia Gaspar participated at the Brain Awareness Week, March 19, IMM.

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, FML/“Ciência 2007”, FCT

Research Team

Susana Lopes, PhD	Post Doc Fellowship, FCT
Susana Pascoal, PhD	Post Doc Fellowship, FCT
Rita Fior, PhD	Post Doc Fellowship, FCT
Raquel Lourenço	PhD Fellowship, FCT
Raquel Mendes	PhD Fellowship, FCT
Sofia Azevedo	PhD Fellowship, FCT
Patrícia Matos	Technician, FML (left in September 2010)
Margarida Cristovão	Technician, FML
Joana Lima	Master student, FCUL
João Gonçalves	Visitor PhD Fellowship, FCT

Keywords/Research Areas

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

Major scientific achievements

1. Notch signalling promotes left-right asymmetry through ciliary length control.

We have identified Notch signalling as a major regulator of cilia length in the laterality organ of zebrafish and therefore of organ laterality in this vertebrate. This work was published in *Development*.

2. A non-conserved role for Dmrt2 in left-right establishment in vertebrates

In clear contrast to what we described in zebrafish, we showed that there are no LR defects, neither at the lateral plate mesoderm nor at the presomitic mesoderm in *dmrt2* homozygous mutant mice. In addition, we also found that the expression of *dmrt2* has not been conserved during evolution underlying the different functions that this gene plays between the zebrafish and the mouse. This work was published in *PlosOne*.

3. The regenerative capacity of zebrafish caudal fin is not affected by repeated amputations

We show that consecutive repeated amputations of zebrafish caudal fin do not limit its regeneration capacity and do not compromise any of the successive regeneration steps: wound healing, blastema formation and regenerative outgrowth. Using a heat-shock inducible transgenic zebrafish line we were able to inhibit Wnt/ β -catenin signalling in a time-controlled manner and therefore regeneration. Notably, if these fins were re-amputated, regeneration was resumed even after several rounds of consecutive Wnt/ β -catenin signalling inhibition and re-amputation. This suggests that blastema formation does not depend on a pool of stem/progenitor cells that require Wnt/ β -catenin signalling for their survival. **This work is being prepared for publication.**

4. Mesogenin switches mesodermal progenitors into presomitic mesoderm cells by negative feed back into the Wnt/Ntl loop and coordination of cell movement

We investigated the role of mesogenin (*msgn*) in the transition from mesodermal progenitors into presomitic mesoderm in the zebrafish embryo. Our results show that *msgn* is important for the switch from tailbud progenitors to PSM, by a negative feedback into the WNT/Ntl loop. In addition, we show that *msgn* is important for the internalization movement of tailbud cells into PSM, controlling in this way axis elongation and as a consequence somite size. **This work is being prepared for publication.**

5. 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. We are now investigating the reason behind this phenotype.

6. 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.

Recent Most Relevant Publications

Lourenço R, Lopes SS 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: 7.194, Citations: 0)

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-OBD/100202/2008, €170.000,00

2009/2011 Investigation of a new signalling pathway linking deltaD to ciliogenesis and its impact on left-right development, FCT. Coordinator: Susana Lopes. PTDC/SAU-OBD/103981/2008, €140.000,00

2007/2010 Functional study of the molecular clock during vertebrate limb development, FCT. Coordinator: Leonor Saúde. PTDC/SAU-OBD/64628/2006, €129.700,00

2009 UDEV Plurianual, FCT. Coordinator: Leonor Saúde. €11. 000,00

Publications in peer review Journals

Lourenço R, Lopes SS 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 SS, 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: 7.194, Citations: 0)

Lourenço, R and Saúde, L (2010) Symmetry OUT, Asymmetry IN. *Symmetry* **2**, 1033-1054.

Invited Lectures and Seminars

Saúde, L. Symmetry versus Asymmetry decisions in the vertebrate embryo. CEDOC, Lisboa, Portugal, January 15, 2010.

Communications in International Conferences

Pascoal S. The role of Shh signaling during larvae caudal fin regeneration. Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 11, 2010 (Oral presentation).

Lopes, S. Notch signalling regulates left-right asymmetry through ciliary length control. Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 12, 2010 (Oral presentation).

Saúde, L. The role of mesogenin during mesoderm formation. Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 11, 2010 (Oral presentation).

Azevedo S. and Saúde L. Effect of repeated amputations in the zebrafish caudal fin regeneration. Joint Meeting of the Portuguese and Spanish Societies of Developmental Biology, Badajoz, Spain, November 10-12, 2010 (Poster presentation).

Lourenço R. and Saúde L. Role of Terra in vertebrates. Joint Meeting of the Portuguese and Spanish Societies of Developmental Biology, Badajoz, Spain, November 10-12, 2010 (Poster presentation).

Mendes R. and Saúde L. N-cadherin is asymmetrically expressed in the Hensen's node. What for? Joint Meeting of the Portuguese and Spanish Societies of Developmental Biology, Badajoz, Spain, November 10-12, 2010 (Poster presentation).

Azevedo S. and Saúde L. Effect of repeated amputations in the zebrafish caudal fin regeneration. EMBO-Molecular and Cellular Basis of Tissue Repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Pascoal S., Lima J. and Saúde L. The role of Shh signaling during larvae caudal fin regeneration. EMBO-Molecular and Cellular Basis of Tissue Repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Mendes R. and Saúde L. N-cadherin is asymmetrically expressed in the Hensen's node. What for? The Embo meeting 2010, Barcelona, Spain, September 4-7, 2010 (Poster presentation).

Fior R., Lewis J. and Saúde L. The role of mesogenin in mesoderm formation. 9th International Zebrafish Meeting on Development and Genetics, Madison, USA, June 16-20, 2010 (Poster presentation).

Saúde, L. The role of mesogenin during mesoderm formation. 1st European Zebrafish PI meeting, Padova, Italy, March 18, 2010 (Oral presentation).

Internationalization

Collaborative publication with Jill Kreiling from Brown University, USA and Nuno Moreno from Instituto Gulbenkian de Ciência, Portugal.

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.

Collaborative project (manuscript in preparation) with Julian Lewis from CRUK, UK and Sharon Amacher from University of California at Berkeley, USA.

Fior R., Maxwell A., Lewis J. and Saúde L. Mesogenin throws the switch that converts mesodermal progenitors into paraxial mesoderm.

Collaborative project (manuscript in preparation) with Gilbert Weidinger from Center for Regenerative Therapies University of Technology Dresden, Germany and António Jacinto from IMM, Portugal.

Azevedo S., Grotek B., Jacinto A., Weidinger G. and Saúde L. The regenerative capacity of zebrafish caudal fin is not affected by repeated amputations.

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 Carl-Philipp Heisenberg from IST, Austria on “Defining the molecular profile of the Kupffers vesicle in zebrafish”.

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

Advanced teaching

Fior, R. lectured "Notch talking" PhD Programme in Integrative Biomedical Sciences, IGC, Oeiras, October 20, 2010.

Lopes, S. lectured "Left-right determination in vertebrates" PhD Programme in Integrative Biomedical Sciences, IGC, Oeiras, October 20, 2010.

Saúde, L. lectured “Cell synchronization in development” PhD Programme in Integrative Biomedical Sciences, IGC, Oeiras, October 20, 2010.

Saúde, L. lectured “Interpersonal relationships: Mentoring” Nanocourse. IMM, Lisbon, October 28, 2010.

Saúde, L. lectured “Scientific reasoning” Programa Gulbenkian de Formação Médica Avançada. IMM, Lisbon, October 15, 2010.

Fior, R. Laboratory training for 2 students from the Development and Evolution Master FCUL Course, Faculdade de Ciências da Universidade de Lisboa. March 15-26, 2010.

Fior, R. lectured on the Development and Evolution Master FCUL Course, Faculdade de Ciências da Universidade de Lisboa. March 23, 2010.

Master thesis completed

Joana Lima (2010) O papel dos cílios e da sinalização Hedgehog (Hh) na regeneração da barbatana caudal de larvas de peixe-zebra. Faculdade de Ciências da Universidade de Lisboa. Supervisor : Susana Pascoal

Gene Expression & Biophysics Unit

Major interests / Objectives

In biology several important processes occur at spatial dimensions currently beyond the reaches of conventional light microscopy. Our laboratory is concerned with biological questions at this scale as they are related to gene expression. As such the study of RNA transcription, metabolism and transport are active areas of study in the lab, 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 most optical microscopy techniques. The direct observation of these events at the single molecule level, is currently the subject of intense research. Intrinsic to RNA transcription are modifications to the nuclear architecture and the dynamic repositioning of chromosomal loci, as well as the interplay of several ribonucleic proteins (RNPs). These events remain opaque at the single RNA transcript level, and questions such as the timing and spatial position of interactions of these RNPs with RNA, the number of genes targeted in the transcriptional process at a single spatial location, the splicing and the export of RNA, remain unresolved. Further how the stochastic nature gene expression is affected by nuclear architecture are also important questions we are interested in our lab. Understanding and visualizing these processes has implications not only for our understanding of basic biology, but extends to mechanisms in development and disease.

Attempts have been made, with mixed results, to decipher gene expression and relate it to biological noise and stochasticity, while simultaneously accounting for cell-to-cell variation. Thus far none have been able to do so whilst including gene organization and transcription. Such experiments are hindered by the technical difficulties in observing and quantifying gene expression in live cells. Currently the only way to achieve an approximation of RNA numbers, is to use FISH and take snap shots of transcription. These approaches are inadequate, lacking the high spatiotemporal resolution necessary to take accurate measurements and construct models of these processes. Highly reduced our objectives are: Determining whether transcription factories form during this process or are they pre-existing; if chromosomal kissing nucleates the formation these factories. Are such contacts stabilized under certain conditions between co-regulated genes? Are the RNA species and spatial position of these factories conserved? Why does transcriptional potency of a gene appear correlated with a nuclear subdomains? What within the subdomain confers repressive or inductive properties?

Questions abound as to how in mRNA spatial regulation of translation is mechanistically controlled. Two important themes have emerged the first is the spatial control of translation, the second is the role of 'nuclear history' i.e. How nuclear factors loaded on mRNA affect its biogenesis and cytoplasmic fate. Using different cellular and animal models, our objective is to decipher these processes in areas where long range mRNA transport is essential to function such as in neurons. We tackle all these questions by using tools that enable us to go from the single molecule to the genome-wide scale.

Head of Unit

Musa M. Mhlanga Ph.D – Research Group Leader, New York University School of Medicine

Research Team

Ricardo Henriques	PhD Fellowship, FCT
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Research Areas

RNA transport
 Super-resolution
 Nuclear Architecture
 Gene Expression
 Genome-wide screening
 Host pathogen Interactions

Major scientific achievements

Our group over the past 12 months has focused on two major aspects: On the one hand we have developed tools for super-resolution microscopy using the techniques of PALM & STORM. These have resulted in three publications (two reviews and one original research paper). The latter publication was done in collaboration with the group of Christophe Zimmer Ph.D. The second area of focus of our research has been in the development of high-content genome-wide screening approaches. This has primarily focused on developing high density arrays of siRNA on glass slides that can be used for rapid genome-wide screening. This work has been carried out in collaboration with the group of Neil Emans Ph.D. We are currently in the process of submitting an original research publication on this work. Below we provide a more in-depth look at the specific major scientific achievements of the PALM/STORM work we have published.

We have recently developed an algorithm for extremely rapid analysis of PALM/STORM data that achieves a resolution similar to that reached by the leading groups in the field (Zhuang, Hess, Betzig... etc), which we have shared with the community. This algorithm is open source and termed QuickPALM. The most significant advantages it has over the prior art are:

- 3D super-resolution:** QuickPALM is able to do both 2D and 3D STORM/PALM (using astigmatism).
- Drift correction:** Drift is a major challenge in PALM/STORM microscopy and in most cases the limiting factor for resolution. Since the acquisition can take from several minutes to hours, drifts of even a few tens of nanometers can drastically deteriorate resolution, or worse, create anomalies in reconstructed images (e.g. artifactual doubling of filamentary structures). We provide a full drift correction method based on tracking beads or other visual landmarks.
- Multi-color:** the algorithm is able to handle multi-color super-resolution imaging, allowing users to take advantage of the increasing number of fluorophores compatible with PALM/STORM
- Availability, ease of use and open-source:** The software and its sources codes are freely available as an ImageJ plugin. This allows maximal dissemination of the software in the biological research community, optimal usability, and offers users the ability to modify and improve the software at will. To date, there is no PALM/STORM software that is freely available with the exception of that of U. Nienhaus and colleagues that requires Matlab and cannot be modified and lacks the substantial number of features we provide.

Integrated software for parallel acquisition & processing: The plugin can be used in conjunction with the Micro-Manager software (open-source, freely available) providing a full system ready for PALM/STORM acquisition and analysis.

Speed: Our algorithm is very fast (<100 ms CPU time per frame), allowing direct visualization of 2D/3D or 4D super-resolution images during acquisition - 4D in this case stands for 3D+time as the algorithm allows to visualize super-resolution movies in live imaging.

Finally we summarize the work/major achievements on genome-wide screening that we have submitted for publication recently:

We have developed a printing method that permits the simultaneous printing of thousands of siRNAs onto glass cover slips far surpassing the prior art (Nature Methods 3, 5, 385, 2006, Nat Methods 2, 392, 2007). In a procedure akin to the Gutenberg's printer, like a moveable type press, all the individual siRNAs –2870 distinct sequences- are printed as an array onto a single cover slip at once. The arrays of siRNA are mass-produced at a scale of over 1000 individual glass cover slips (each with 2870 genes) in the space of a few hours. Repeating this process over an entire siRNA library covering a human genome (~18,157 genes) uses 7 cover slips per genome. This leads to the production of over 1000 complete siRNA genome libraries, which are ready for screening after desiccation in just over 6 days.

Recent Most Relevant Publications

Henriques R, Mhlanga MM (2009) PALM and STORM: What hides beyond the Rayleigh limit?, *Biotechnol J.* **4**, 846 – 857. (Journal IF: 2.1 Citations: 8)

Mhlanga MM, Bratu DP, Genovesio A, Rybarska A, Chenouard N, Nehrbass U and Olivo-Marin JC (2009) In vivo Colocalisation of oskar mRNA and Trans-Acting Proteins Revealed by Quantitative Imaging of the Drosophila Oocyte, *PLoSOne* **4** (7), e6241. (Journal IF: 4.351 Citations: 2)

Mhlanga MM, Vargas DY, Fung CW, Kramer FR and Tyagi S (2005) tRNA-linked molecular beacons for imaging mRNAs in the cytoplasm of living cells. *Nucleic Acids Research* **33**, 1902-1912. (Journal IF: 7.48 Citations: 56)

Bratu DP, Cha BJ, Mhlanga MM, Kramer FR and Tyagi S (2003) Visualizing the distribution and transport of mRNAs in living cells. *Proceedings of the National Academy of Sciences of the U.S.A* **100**, 13308- 13313. (Journal IF: 9.432 Citations: 148)

Ghislain C, Jost Enninga and Musa MM (2007) Single molecule tracking of mRNA and proteins. Book Chapter in 'Imaging Cellular and Molecular Biological Function' (Springer).

Ongoing Research Projects

2008/2012: Development of Super-resolution microscopy hardware and software tools for use in PALM/STORM. Andor. Coordinator: M Mhlanga

2009/2013: Genome-wide siRNA screens in TB, HIV & factors implicated in the long-range transport of RNA.

Publications in Peer Review International Journals 2010

Rolando M, Stefani C, Flatau G, Auburger P, Mettouchi A, Musa M, Ulf Rapp, Antoine Galmiche and Emmanuel Lemichez. (2010) Transcriptome dysregulation by anthrax lethal toxin plays a key role in induction of human endothelial cell cytotoxicity. *Cellular Microbiology* **12**, 1462-5822 (Journal IF: 5.725, Citations 1)

Henriques R, Lelek M, Fornasiero EF, Valtorta F, Zimmer C, Mhlanga MM (2010) QuickPALM: 3D real-time photoactivation nanoscopy image processing in Image. *J Nature Methods* **7** (5), 339-340 (Journal IF: 16.874, Citations: 5)

Invited Lectures and Seminars

Mhlanga, MM, lectured at Biotechnology Conference, Beijing, China.
Mhlanga, MM, lectured at Beijing Genomics Institute, Beijing, China.
Mhlanga, MM, lectured at International Genomics Conference, Shenzhen, China.
Mhlanga, MM, lectured at ICS-UNIDO, Trieste, Italy.
Mhlanga, MM, lectured at Witswatersrand Univ, Johannesburg South Africa.
Mhlanga, MM, lectured at Univ. of KZN, Durban, South Africa.
Mhlanga, MM, lectured at Johns Hopkins Univ. Baltimore MD, USA.
Mhlanga, MM, lectured at Public Health Research Institue, Newark, NJ USA.
Mhlanga, MM, lectured at Harvard Medical School, Boston, USA.
Mhlanga, MM, lectured at Institut Pasteur, Paris, France.
Mhlanga, MM, lectured at Institut Pasteur-Korea, Seoul, Korea.
Mhlanga, MM, lectured at RNAi Global Meeting, London, UK.
Mhlanga, MM, lectured at Chinese National Academy of Science – Nanocenter Beijing, China

Patents

PCT/EP2008/062204 WO2009/065635 A1 SINGLE CELL BASED REPORTER ASSAY TO MONITOR GENE EXPRESSION PATTERNS WITH HIGH SPATIO-TEMPORAL RESOLUTION. APPLICANT: INSTITUT PASTEUR [FR/FR]; INVENTORS: MHLANGA, MUSA [US/FR]; ENNINGA, Jost [DE/FR]; SANSONETTI, Philippe [FR/FR]; NEHRBASS, Ulf [DE/FR];

Advanced teaching

Mhlanga, MM, Organized and lectured at the EMBO microscopy course “Microscopy: from genome scale to the single molecule” held at CSIR, Pretoria, South Africa. May 31- June 12, 2010.

Microvascular Biology and Inflammation Unit

Major interests / Objectives

Inflammation aims the elimination of a noxious agent so as to regain cellular homeostasis. It involves the interplay between inflammatory cells, vascular cells and various inflammatory mediators. These players are involved in either pro- or anti-inflammatory mechanisms that appropriately balanced conduct the inflammatory process onto resolution.

In this inflammatory context, we study: (1) the function of fibrinogen in modulating blood-vessel wall interaction, (2) the action of non-neuronal cholinergic systems, (3) the development of simulation models at the level of leukocyte-vascular wall interaction in the microvascular network and (4) the relation with hemorheological biomarkers and more recently, (5) the mechanisms that ensure the concerted action of chemoattractants in driving leukocyte migration.

Head of Unit

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

Principal Investigators

Ângelo Calado, PhD – Auxiliary Professor, FMUL

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
Paula Oliveira, Master Degree	BI Fellowship, FCT (left in June 2010)
Teresa Freitas	Lab Technician, FMUL

Keywords/Research Areas

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

Major scientific achievements

Fibrinogen (Fib) plays an important role in inflammation by interacting with distinct cellular players, such as neutrophils. In this respect, we have shown that under physiological concentrations, this protein is able in vitro to modulate: (1) neutrophil activation and (2) neutrophil-endothelium interaction. Moreover, we are currently evaluating the pattern of neutrophil activation in patients of Sickle Cell Disease, so as to correlate it with the occurrence of characteristic episodes of vasoocclusion.

High Fib plasma concentration is also considered an independent risk factor for cardiovascular diseases, possibly by increasing erythrocyte aggregation. We have shown that fibrinogen interacts specifically with the erythrocyte membrane in dependence of the cellular age. Importantly, this interaction decreases in the presence of anti-CD47 antibody suggesting this surface protein as a potential target for fibrinogen binding. Additionally, we have shown that Fib increases erythrocyte GSNO.

Recent Most Relevant Publications

de Almeida JP, Saldanha C (2010) Nonneuronal cholinergic system in human erythrocytes: biological role and clinical relevance. *J Membr Biol* **234** (3), 227-34. (Journal IF: 2.482, 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: 2.657, Citations: 4).

Lund E, Guttinger S, Calado A, Dahlberg JE, Kutay U (2004) Nuclear export of microRNA precursors. *Science* **303**, 95-98. (Journal IF: 29,747, Citations: 577).

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: 5.673, Citations: 23)

Waldo SW, Rosario HS, Penn AH, Schmid-Schönbein GW (2003) Pancreatic digestive enzymes are potent generators of mediators for leukocyte activation and mortality. *Shock* **20**, 138-43. (Journal IF: 2.871, Citations: 20)

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).

2007/2010 Multiscale Mathematical Modelling in Biomedicine, FCT. Coordinator: Adélia Sequeira, IST, UTL. PTDC/MAT/68166/2006, € 6330 (IMM), € 78000 (total).

2009/2011 Cardiovascular risk and inflammation- contribution to the etiopathogenesis of atherosclerosis and cardiovascular disease, FCT. Coordinator: João Eurico, IMM, FML, 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).

Publications in peer review Journals

Saldanha C, Lopes de Almeida JP, Freitas T, Oliveira S, Silva-Herdade AS (2010) Erythrocyte deformability responses to shear stress under external and internal stimuli influences. *Series on Biomechanics* **25**, 54-60. (Journal IF: N/A)

Lopes de Almeida JP, Saldanha C (2010) Dithiothreitol revisited in red cells: a new head for an old hat. *Clin Hemorheol Microcirc.* **46**, 51-56. (Journal IF: 1.780)

Martin Martins J, Vale S, Ferreira F, Fagundes MJ, Carmo I, Saldanha C, Martins e Silva J (2010) Plasma corticotropin releasing hormone during the feeling of induced emotions. *Neuro Endocrinol Lett.* **31**, 250-5. (Journal IF: 1.047)

de Almeida JP, Saldanha C (2010) Nonneuronal cholinergic system in human erythrocytes: biological role and clinical relevance. *J Membr Biol.* **234**(3), 227-34. (Journal IF: 2.482)

Santos NC, Silva JM, Freitas T, Doroana M, Duarte N, Tavares L, Antunes F, Saldanha C (2010) Blood cell membrane fluidity and intracellular Ca²⁺ changes in antiretroviral-naïve and -treated HIV-1-infected patients. *The Scientific World Journal.* **10**, 350-5. (Journal IF: 1.658).

de Oliveira S, Saldanha C (2010) An overview about erythrocyte membrane. *Clin Hemorheol Microcirc.* **44**, 63-74. (Journal IF: 1.780).

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 (2010) Cytokine pattern in very early rheumatoid arthritis favours B-cell activation and survival. *Rheumatology*, [Epub ahead of print]. (Journal IF: 4.236).

Cascão R, Moura RA, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graca L, Fonseca JE (2010) Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early rheumatoid arthritis. *Arthritis Res Ther* **12**, R196. (Journal IF: 4.271).

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE. Neutrophils in rheumatoid arthritis: More than simple final effectors (2010) *Autoimmun Rev* **2010** **9**, 531-535. (Journal IF: 6.368).

Other publications National

Martins e Silva J, Saldanha C, (editors) (2010) *Bioquímica em Medicina Vol I- Análises e Perspectivas. Pages (9-265) Vol II Metodologias e Programas de Estudo, Pages (9-593), Vol III - Temes e Mapas Metabólicos de Bioquímica Fisiológica, Page (9-741)*

Communications in International Conferences

Cascão R, Moura RA, Perpétuo I, Canhão H, Vieira de Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Viana Queiroz M, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early Rheumatoid Arthritis, 5th European Workshop on Immune Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010. (Poster).

Moura RA, Cascão R, Perpétuo I, Canhão H, Vieira de Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Viana Queiroz M, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine pattern in very early Rheumatoid arthritis favours B cell activation and survival, 5th European Workshop on Immune Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010. (Poster).

Moura RA, Cascão R, Perpétuo I, Canhão H, Vieira de Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Pereira da Silva JA, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Spondyloarthropathy and Rheumatoid arthritis: Two different diseases, a similar cytokine network, 5th European Workshop on Immune Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010. (Poster).

Sequeira, A., Artoli, A.M., Silva-Herdade, A.S., Vitorino de Almeida, V., Saldanha, C. Numerical simulation as an experimental model – Role of shear stress in leukocyte recruitment, Joint FEBS/EFIS Workshop: Inflammatory Diseases and Immune Response: Basic Aspects, Novel Approaches and Experimental Models, Vienna, Austria, September 28-October 1, 2010. (Poster presentation).

Vitorino de Almeida, V., Rosário, H.S., Saldanha, C. Modulation of neutrophil recruitment by fibrinogen, Joint FEBS/EFIS Workshop: Inflammatory Diseases and Immune Response: Basic Aspects, Novel Approaches and Experimental Models, Vienna, Austria, September 28-October 1, 2010. (Poster presentation).

Saldanha, C. “Interaction study at molecular level of the hemorheological parameters fibrinogen and erythrocyte”. 9th World Congress for Microcirculation, Paris, France, September 26-28, 2010. (Poster presentation).

Saldanha, C. “Erythrocyte membrane binding fibrinogen” 9th World Congress for Microcirculation, Paris, France, September 26-28, 2010. (Oral presentation).

Almeida, J., Saldanha, C. “Fibrinogen-dependent signaling in microvascular erythrocyte function – implications on nitric oxide”. 9th World Congress for Microcirculation, Paris, France, September 26-28, 2010. (Poster presentation).

Oliveira, P., Saldanha, C. and Calado, A. “Inflammation controls Acetylcholinesterase gene expression”. Cell Symposia on Inflammation and Disease, Lisbon, September 26-28, 2010. (Poster presentation).

De Oliveira, S., Vitorino de Almeida, V., Calado, A., Rosário, H.S., Saldanha, C. “Fibrinogen binding to erythrocyte membrane: CD47 a possible molecular target”. 21st International Fibrinogen Workshop, Rotterdam/Amsterdam, The Netherlands, August 23-25, 2010. (Poster presentation).

Motacarmo, M., Napoleão, P., Andrade, S., Selas, M., Freixo, C., Turkman, A., Andreozzi, V., Viegas-Crespo, A.M., Pinheiro, T., Motacarmo, M., Ferreira, R.C. High oxidized LDL associate to low T lymphocytes in acute myocardial infarction, World Congress of Cardiology, Beijing, China, June 16 – 19, 2010. (Poster presentation).

Moura RA, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Viana Queiroz M, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine profile in serum and synovial fluid of established rheumatoid arthritis patients, 11th European League against Rheumatism Congress / 30th European Workshop on Rheumatology Research, Rome, Italy, June 16-19, 2010. (Poster).

Cascão R, Moura RA, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine network in the first 6 weeks of rheumatoid arthritis onset. 11th European League against Rheumatism Congress / 30th European Workshop on Rheumatology Research, Rome, Italy, June 16-20, 2010. (Poster).

De Oliveira, S. Rosário, H.S., Saldanha, C. Binding of fibrinogen with RBCs of different biological ages: CD47, a possible molecular target. 8th World Congress on Trauma, Shock, Inflammation and Trauma – TSIS 2010, Munich, Germany, March 9-13, 2010. (Oral communication).

Communications in National Conferences

De Oliveira, S., Mulero, V. and Calado, A. “CXCL8: a player in zebrafish inflammatory process?” IV IMM PhD Students Meeting, Lisbon, November 22-23, 2010. (Poster presentation).

Silva-Herdade, A.S., Saldanha, C., Calado, A. Liver ischemia-reperfusion: studying inflammation resolution. IV IMM PhD Students Meeting, Lisbon, November 22-23, 2010 (Poster presentation).

Napoleão, P., Selas, M., Freixo, C., Motacarmo, M., Viegas-Crespo, A., Pinheiro, T., Cruz Ferreira, R. T lymphocytes associate to oxidized low-density lipoprotein, C-reactive protein and troponin T in acute myocardial infarction Inflammatory markers variations in acute myocardial infarction: a longitudinal study, XXXI Congresso Português de Cardiologia, Lisbon, Portugal, April 9–12, 2010 (Oral Presentation).

Napoleão, P., Cabral, L.B.P., Criado, M.B., Monteiro, M.C., Selas, M., Toste, A., Viegas-Crespo, A.M., Pinheiro, T., Motacarmo, M., Ferreira, R.C. Differentiation of patients with ST-elevation myocardial infarction based on soluble CD40 ligand forty days after initial coronary intervention, XXXI Congresso Português de Cardiologia, Lisbon, Portugal, April 9–12, 2010 (Oral presentation).

Napoleão, P., Toste, A., Selas, M., Cabral, L.B.P., Criado, M.B., Monteiro, M.C., Viegas-Crespo, A.M., Pinheiro, T., Motacarmo, M., Ferreira, R.C. Association of the serial changes of inflammatory markers with adverse clinical outcomes in patients with acute myocardial infarction based on soluble CD40 ligand forty days after initial coronary intervention, XXXI Congresso Português de Cardiologia, Lisbon, Portugal, April 9–12, 2010 (Oral presentation).

Napoleão, P., Monteiro, M.C., Toste, A., Selas, M., Viegas-Crespo, A.M., Pinheiro, T., Motacarmo, M., Ferreira, R.C. Endothelial microparticles correlate to the expression of CD40 ligand on platelets and T lymphocytes in acute myocardial infarction, XXXI Congresso Português de Cardiologia, Lisbon, Portugal, April 9–12, 2010 (Oral presentation).

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.

De Oliveira, S. Participation as a student at the EMBO Practical Course “Animal Models for Physiology and Disease”, Sheffield, UK, 19th-30th July 2010.

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).

Advanced teaching

Rosário, HS. Lectured at the Immunology Module of the Doctoral Programme in Experimental Biology and Biomedicine 2009/10 (Centro de Neurociências e Biologia Celular – Universidade de Coimbra): “Neutrophils – At the onset of immune response”. Coimbra, January 5, 2010.

Rosário, HS. Co-Advisor for a Master Thesis in Biomedical Engineering (Instituto Superior Técnico). Candidate: Diana Catarina da Fonseca Madeira Nunes, “Mathematical and Numerical Modelling of Angiogenesis”. Lisbon, December 7, 2010.

Saldanha C. organized and lectured the Biochemistry Module of the 8th Pos-Graduate Course in Sports Medicine, Sports Medical Center, Lisbon, November 27, 2010.

Saldanha C lectured “Haemostasis and Inflammation” at the Continuum Formation “Wet Lab – Haemostáticos” Ethicon Biosurgery, Johnson & Johnson Medical, and Surgery Department Centro Hospitalar Lisboa Norte

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. “Evaluation disclosure of the educational quality” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2010: 25 (1) :3-4

Saldanha, C. “Erythrocyte signalling” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2010: 25 (2) :3-4

Saldanha, C. “Interlinked Information” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2010: 25 (3) :3-4

Saldanha, C. “Red Cell and Physical Exercise” editorial in the Bulletin of the Portuguese Society of Hemorheology and Microcirculation , 2010: 25 (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 interest not only in drug targets and drug discovery itself, but also in the molecular-level mechanism of action of drugs that are known for their therapeutic efficacy and safety. 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
Isa Domingues Serrano, PhD	Post Doc Fellowship, FCT
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
Henri Girão Franquelim	PhD Fellowship, FCT
Manuel Nuno Melo	PhD Fellowship, FCT (left September 2010)
Marta Maria B. Ribeiro	PhD Fellowship, FCT
Sara Matos Santos, MD	PhD Researcher
João M Freire	Research Student (masters)
Inês Torcato	Research Student (masters)
Joana Matos	Research Student (left September 2010)
David Sousa	Undergraduate Research Student (FMUL)
Filipa Fernandes	Undergraduate Research Student (FMUL)
Mafalda Neves	Undergraduate Research Student (FMUL)
Miguel Vasques	Undergraduate Research Student (FMUL)
Catarina Laborinho	Technician, FMUL

Keywords/Research Areas

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

Major scientific achievements

UBqF:

- Proved that a previously designed kyotorphin derivative (analgesic dipeptide) with improved lipophilicity is effective, finding its mechanism of action;
- Demonstrated a correlation between the efficacy of both HIV fusion inhibitors and anti-HIV antibodies with their membrane-interaction properties;
- Imaged the local action of antimicrobial peptides (AMP's) using Atomic Force Microscopy, which brought significant advancements both to imaging of bacteria and the mechanism of action of AMP's;
- Engaged in technology transfer activities, having collaborations with Bioalvo (patent in international phase), Synovo (under a FP7 project framework) and Technoantibodies (FP7/QREN DoIT project);
- Ranked first in the "I2P-Ideas to products" 2010 national competition. In the European competition UBqF ranked 2nd;
- Co-organized the XII EPI-Iberian Peptide Meeting, IMM-FMUL, Lisbon, Portugal, February 10-12.

Recent Most Relevant Publications

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardaji E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX and Castanho MARB (2010) Escherichia coli cell surface perturbation and disruption induced by antimicrobial peptides, BP100 and pepR. *J Biol Chem* **285**, 27536-27544. (Journal IF: 5.328, Citations: 0)

Ribeiro MMB, Melo MN, Serrano ID, Santos NC and Castanho MARB (2010) Drug-lipid interaction evaluation: why a 19th century solution? *Trends Pharmacol Sci.* **31**, 449-454. (Journal IF: 9.064; Citations: 0)

Melo MN, Ferre R and Castanho MARB (2009) Antimicrobial peptides: linking partition, activity and high membrane-bound concentrations. *Nat Rev Microbiol* **7**, 245-250. (Journal IF: 17.644, Citations: 31)

Franquelim HG, Loura LMS, Santos NC and Castanho MARB (2008) Sifuvirtide screens rigid membrane surfaces. Establishment of a correlation between efficacy and membrane domain selectivity among HIV fusion inhibitor peptides. *J Am Chem Soc* **130**, 6215-6223. (Journal IF: 8.091, Citations: 5)

Henriques ST, Melo MN and Castanho MARB (2006) Cell-penetrating peptides and antimicrobial peptides: how different are they? *Biochem J* **399**, 1-7. (Journal IF: 4.365, Citations: 66)

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

2008/2010 Unravelling the mechanism of action of membrane-active peptides combining NMR and optical spectroscopies, CRUP-DAAD. Portuguese Coordinator: Miguel Castanho. Portuguese-German Joint Action Project A-6/08, €5 000 (total: €15 000)

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. Portuguese Coordinator: Miguel Castanho. PEOF-GA-2008-220318 (joint project with the Institute for Molecular Biosciences, The University of Queensland, Australia), € 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. FP7-PEOPLE-IOF-2008-235154, €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

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

2010 FCT “Financiamento base”, €11 250

Publications in peer review Journals

Aguiar SI, Pinto FR, Nunes S, Serrano I, Melo-Cristino J, Sá-Leão R, Ramirez M, de Lencastre H (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. (Journal IF 4.162, Citations: 4)

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardaji E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX and Castanho MARB (2010) Escherichia coli cell surface

perturbation and disruption induced by antimicrobial peptides, BP100 and pepR. *J Biol Chem* **285**, 27536-27544. (Journal IF: 5.328, Citations 0)

Franquelim HG, Veiga AS, Weissmüller G, Santos NC and Castanho MARB (2010) Unravelling the molecular basis of the selectivity of the HIV-1 fusion inhibitor sifuvirtide towards phosphatidylcholine-rich rigid membranes. *Biochim Biophys Acta* **1798**, 1234-1243. (Journal IF: 3.998, Citations 0)

Henriques ST and Castanho MARB (2010) Is PrP(106-126) fragment involved in the membrane activity of the prion protein? *Curr Protein Pept Sci* **11**, 326-333. (Journal IF: 3.854, Citations: 0)

Henriques ST and Craik DJ (2010) Cyclotides as templates in drug design. *Drug Discov Today* **15**, 57-64. (Journal IF: 6.630, Citations: 3)

Henriques ST, Pattenden LK, Aguilar MI and Castanho MARB (2010) Fast membrane association is a crucial factor in the peptide pep-1 translocation mechanism: A kinetic study followed by surface plasmon resonance. *Biopolymers* **94**, 314-322. (Journal IF: 2.605, Citations 1)

Henriques ST, Tan CC, Craik DJ and Clark RJ (2010) Structural and Functional Analysis of Human Liver-Expresses Antimicrobial Peptide 2. *ChemBioChem* **11**, 2148-2157. (**Cover picture**, Journal IF: 3.824, Citations: 0)

Matos PM, Castanho MARB and Santos NC (2010) HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes. *PLoS One* **5**, e9830. (Journal IF: 4.351, Citations:1)

Matos PM, Franquelim HG, Castanho MARB and Santos NC (2010) Quantitative assessment of peptide-lipid interactions. Ubiquitous fluorescence methodologies. *Biochim Biophys Acta* **1798**, 1999-2012. (Journal IF: 3.998, Citations: 0)

Ribeiro MMB, Castanho MARB and Serrano I (2010) *In vitro* blood-brain barrier models – latest advances and therapeutic applications in a chronological perspective. *Mini Rev Med Chem* **10**, 262-270. (Journal IF: 2.971, Citations: 0)

Ribeiro MMB, Melo MN, Serrano ID, Santos NC and Castanho MARB (2010) Drug-lipid interaction evaluation: why a 19th century solution? *Trends Pharmacol Sci* **31**, 449-454. (Journal IF: 9.064, Citations: 0)

Other publications International

Books – International (as invited editor)

Miguel ARB Castanho, Book: “Membrane Active Peptides: Methods and Results on Structure and Function”, IUL Publishers (La Jolla, CA, USA), ISBN: 978-0-9720774-5-3.

Book Chapters

Kaas Q, Westermann JC, Henriques ST and Craik DJ (2010) Antimicrobial Peptides in Plants. In “Antimicrobial peptides, Discovery, Design and Novel Therapeutic Strategies” (Wang G, Ed.) CABI (Oxfordshire, UK), pp 40-70. ISBN: 978-1-84593-657-0.

Henriques ST (2010) Biophysics and the way out of the endosomal versus non-endosomal dilemma for cell-penetrating peptides pep-1. In "Membrane Active Peptides: Methods and Results on Structure and Function" (Castanho M, Ed.) IUL Publishers (La Jolla, CA, USA), pp 377-414. ISBN: 978-0-9720774-5-3.

Veiga AS, Franquelim HG, HIV-1 Fusion Inhibitor Peptides: A Cross Correlation between Efficacy and Membrane-Level Activity, In "Membrane Active Peptides: Methods and Results on Structure and Function" (Castanho M, Ed.) IUL Publishers (La Jolla, CA, USA), pp 495-528. ISBN: 978-0-9720774-5-3.

Conference Proceedings

Freire JM, Domingues MM, Matos J, Melo MN, Veiga AS, Santos NS and Castanho MARB (2010) Quantifying Molecular Partition of Charged Molecules by Zeta-Potential Measurements. *Proceedings of the 31st European Peptide Symposium* (Lebl M, Meldal M, Jensen KJ and Hoeg-Jensen T, Eds.) European Peptide Society, pp 564-565.

Others

"Diabetes", www.beon.biomedicalmovies.com (interactive multimedia production)

Showreel: www.youtube.com/watch?v=ZmuPI5bj-zs (2010)

Scientific consultants: Ambrósio F; **Castanho M**; Grazina MM; Laranjinha J; Quintas, A. Directed and edited by: Take the Wind (www.takethewind.com)

Invited Lectures and Seminars

Castanho MARB. Developing HIV fusion inhibitor peptides: do lipids play a role? Symposium "HIV/AIDS: Closing the Gap between Basic Research and Clinical Practice", IMM-FMUL, Lisbon, Portugal, January 23, 2010.

Castanho MARB. "Ciência, consciência e paciência", Instituto Superior de Línguas de Santarém, Invited Lecture in the solemn opening ceremony of the academic year 2010/11, January 2010.

Castanho MARB. MICs go molecular with antimicrobial peptides: linking partition, activity and high-membrane-bound concentrations. Keynote talk at 455th WE-Heraeus seminar "Biophysics of Membrane-Active Peptides", Bad Honnef, Germany, April 12, 2010.

Castanho MARB. Beating the BBB. (S)low (but effective) throughput screening in the quest for a new analgesic drug, Invited Seminar at FMP, Berlin, Germany, April 16, 2010.

Castanho MARB. Biochemistry in Portugal: Where from? Where to? What to learn? XXXIX Annual Meeting of the Brazilian Biochemistry and Molecular Biology Society (SBBq), Foz do Iguaçu, Paraná, Brazil, May 20, 2010.

Castanho MARB. "(Cons)ciência e Modernidade", UTIS - Universidade da Terceira Idade de Santarém, Keynote Lecture in the solemn opening ceremony of the academic year 2010/11, October 27, 2010.

Castanho MARB. Molecular biophysics goes live in biomedicine: turning peptides into drugs – the case of Kyotorphin. António Xavier's seminar, ITQB-UNL, Oeiras. November 4, 2010.

Castanho MARB. Developing HIV fusion inhibitors: the unexpected role of lipids. II Jornadas de Bioengenharia, Porto, Portugal, November 27, 2010.

Communications in International Conferences

Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardaji E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX and Castanho MARB. Relation between E.coli killing and charge neutralization by the antimicrobial peptides BP100 and DAMP. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal February 10-12, 2010. (Oral presentation)

Franquelim HG, Veiga AS, Weissmüller G, Santos NC and Castanho MARB. Decoding the HIV-1 fusion inhibitor sifuvirtide selectivity towards phosphatidylcholine rigid membranes. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal February 10-12, 2010. (Oral presentation)

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D and Castanho MARB. Dengue Virus Infection and Encapsidation – Unravelling the Role of the Capsid Protein. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Poster presentation)

Henriques ST, Huang YH, Daly NL and Craik DJ. The bioactivity of cyclotides is modulated by peptide-lipid interactions. As revealed by kalata B1 and its analogues. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Poster presentation)

Matos JC, Veiga AS, Santos NC, Kowalczyk W, Andreu D and Castanho MARB. Characterization of the interaction of two Dengue virus C protein-derived peptides with lipid membranes. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Poster presentation)

Melo MN, Ferre R and Castanho MARB. Relating molecular-level events with AMP-mediated bacterial death. XII Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Oral presentation).

Ribeiro MMB, Heras M, Bardaji E, Pinto A, Pinto M, Tavares I and Castanho MARB. A new brain-targeted analgesic peptide: from Biophysics to *in vivo* proof-of-concept. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Oral presentation)

Serrano I and Castanho MARB. An *in vitro* BBB model to evaluate drugs penetration to the brain. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Poster presentation)

Sousa D, Veiga AS, Santos NC and Castanho MARB. The role of lipid membranes in dengue virus assembly. XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. (Poster presentation)

Franquelim HG, Veiga AS, Santos NC and Castanho MARB. Unraveling the molecular basis of the selectivity of the HIV-1 fusion inhibitor sifuvirtide towards phosphatidylcholine-rich rigid membranes. Biophysical Society 54th Annual Meeting, San Francisco, USA, February 20-24, 2010. (Poster presentation)

Henriques ST, Huang Y-H, Daly NL and Craik DJ. The bioactivity of cyclotides is modulated by peptide-lipid interactions. Gordon Research Conference on the Chemistry & Biology of peptides, Ventura, CA, USA, February 28 - March 5, 2010. (Poster presentation)

Melo MN, Alves CS, Franquelim HG, Ferre R and Castanho MARB. Relating molecular-level events with AMP-mediated bacterial death. 455th WE-Heraeus-Seminar: Biophysics of Membrane Active Peptides, Bad Honnef, Germany, April 11-14, 2010. (Poster presentation).

Henriques ST, Huang Y-H, Daly NL and Craik DJ. The bioactivity of cyclotides is dependent on their affinity for the lipid bilayer. "Australia-Croatia workshop on antimicrobial peptides", Split, Croatia, August 9-13, 2010. (Oral presentation)

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D and Castanho MARB. Dengue Virus Infection and Assembly – Unravelling the Role of the Capsid Protein. 31st European Peptide Symposium, Copenhagen, Denmark, September 5-9, 2010. (Poster presentation)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Distinct HIV-1 membrane-proximal external region lipid bilayer interactions of broad neutralizing mAbs 2F5 and 4E10 detected by combined AFM and confocal microscopy. Young Scientist Forum OzBio2010 IUBMB Conference, Melbourne, Australia, September 23-26, 2010. (Oral presentation)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Distinct HIV-1 membrane-proximal external region lipid bilayer interactions of broad neutralizing mAbs 2F5 and 4E10 detected by combined AFM and confocal microscopy. OzBio2010 IUBMB Conference, Melbourne, Australia, September 26 - October 1, 2010. (Oral presentation)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes. Europrise 2010 - Rational Design of HIV Vaccines and Microbicides Network Annual Conference, Lisbon, Portugal, November 15-18, 2010. (Oral presentation)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Interaction of anti-HIV-1 antibodies with gp41 MPER peptide at the lipid membrane level: Mode of actions unravelled by combined microscopy approaches. 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010. (Oral presentation)

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D and Castanho MARB. New Insights on Dengue Virus Infection and Assembly – The Role of the Capsid Protein. 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010. (Poster presentation)

Ribeiro MMB, Heras M, Bardaji E, Pinto A, Pinto M, Tavares I and Castanho MARB. New brain-targeted analgesic Kyotorphin derivatives: linking peptide-membrane interaction with *in vivo* efficacy. 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010. (Poster presentation)

Sá Santos S, Ribeiro MMR, Sousa DSC and Castanho MARB. New Kyotorphin derivatives: comparative study of side-effects with opioids used in clinical practice. 5th International Peptide Symposium, Kyoto, Japan. December 4-9, 2010. (Poster presentation)

Schneider, JP, Sinthuvanich, C and **Veiga AS**. Design and application of material forming peptides: from antibacterials to mammalian cell delivery. 5th International Peptide Symposium, Kyoto, Japan. December 4-9, 2010. (Oral presentation)

Communications in National Conferences

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Mode of action of anti-HIV-1 antibodies 2F5 and 4E10 with their respective epitopes at the lipid membrane level decoded by combined microscopy approaches. 4th IMM PhD Students Meeting, Lisbon, Portugal, November 22-23, 2010. (Oral presentation)

Ribeiro MMB, Heras M, Bardaji E, Pinto A, Pinto M, Tavares I and Castanho MARB. Characterization of new analgesic Kyotorphin derivatives: from Biophysics to *in vivo* proof-of-concept. 4th IMM PhD Students Meeting, Lisbon, Portugal, November 22-23, 2010. (Oral presentation)

Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P and Castanho MARB. Lipid membrane modulation in the interaction of anti-HIV-1 antibodies with their epitopes on gp41 membrane proximal external domain. 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. (Oral presentation)

Freire JM, Veiga AS, Santos NC, Kowalczyk W, Andreu D and Castanho MARB. A New Perspective on Dengue Virus Infection and Assembly – A Biophysical Study of the Capsid Protein. 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. (Poster presentation)

Ribeiro MMB, Heras M, Bardaji E, Pinto A, Tavares I and Castanho MARB. Ibuprofen-Kyotorphin conjugate targeting to the brain: linking peptide-membrane interaction with *in vivo* efficacy. 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. (Poster presentation)

Sá Santos S, Ribeiro MMR, Sousa DSC and Castanho MARB. “*In vivo* side-effects evaluation of two novel analgesic drugs, Kyotorphin derivatives: a comparative study with opioids morphine and tramadol. 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. (Poster presentation)

Santos SP, **Franquelim HG**, Pierpaolo C, **Castanho MARB**, Chiancone E and Romão CV. Biochemical Characterization of *Deinococcus radiodurans* Dps1 and Dps2. 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. (Poster presentation)

Organisation of Conferences

Castanho MARB, Franquelim HG, Henriques ST, Melo MN, Ribeiro MMB, Serrano I and Veiga AS, co-organized the XII EPI-Iberian Peptide Meeting, Lisbon, Portugal, February 10-12, 2010. Chairman: Miguel ARB Castanho.

Castanho MARB, co-chair and co-organizer of the Symposium "The researching, teaching and learning triangle at universities: Unite or divide?" at the 35th FEBS Congress - Molecules of life, Gothenburg, Sweden, June 26 - July 1, 2010.

Castanho MARB. Member of the Scientific Committee of ICAR2010 - I International Conference on Antimicrobial Research, Valladolid, Spain, November 3-5, 2010.

17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010. Organized by the Sociedade Portuguesa de Bioquímica (SPB). President of the Directive Committee of SPB: Miguel ARB Castanho.

Castanho MARB chairman of the Symposium "New drugs and Improved therapies" at the 17th National Biochemistry Congress, Porto, Portugal, December 15-17, 2010.

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 (i.e. transfer of knowledge and training). S 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".

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

Marta MB Ribeiro, Henri G Franquelim, Isa Serrano, Miguel ARB Castanho ("M-GATE team"), Winners of the "I2P – Ideas to products" Portugal – COTEC, Portugal, April 9-10, 2010.

Marta MB Ribeiro, Henri G Franquelim, Isa Serrano, Miguel ARB Castanho ("M-GATE team"), Ranked 2nd place in the "I2P – Ideas to products" Europe – RWTH Aachen, Germany, June 16-17, 2010.

Travel Award to Sónia T Henriques to participate in Gordon Research Conference on the Chemistry & Biology of Peptides, Ventura, CA, USA, February 28 - March 5, 2010.

Poster prize to Sónia T Henriques at the Gordon Research Conference on the Chemistry & Biology of peptides, Ventura, CA, USA, February 28 - March 5, 2010.

Best YSF Oral Presentation to Henri G Franquelim at the Young Scientist Forum OzBio2010 IUBMB Conference, Melbourne, Australia, September 23-26, 2010

Travel Awards and Fellowships for conference participation to Henri G Franquelim by the:

- Biophysical Society 54th Annual Meeting, San Francisco, USA, February 20-24, 2010;
- YSF OzBio2010 IUBMB Conference, Melbourne, Australia, September 23-26, 2010;
- 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010.

Travel Awards and Fellowships for conference participation to João Freire by the 31st European Peptide Symposium, Copenhagen, Denmark, September 5-9, 2010.

Best Poster Award to João Freire at the 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010.

Best Poster Award to Marta Ribeiro at the 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010.

Advanced teaching

Castanho MARB. "Atomic force Microscopy: touching proteins brings new insights". Lecture in the Post-graduate teaching program for first year PhD students PhD program, Instituto de Engenharia Química e Biológica, Universidade Nova de Lisboa, Oeiras, Portugal, February 2010.

Castanho MARB. "Atomic Force Microscopy: the power of touch". Lecture in Masters Course on Biologic Engineering, Instituto Superior Técnico, Lisbon, Portugal, March 2010.

Castanho MARB tutor at the "I European Biophysical Societies Association summer course - Membrane biophysics & lipid/protein interaction". Lecture: "Peptide drugs: CPP vs. AMP". Practical workshop: "Optimization of Biological Activity – the antimicrobial peptide BP100", Arcachon, France, June 6-11, 2010.

Castanho MARB. "A success case of collaboration between industry and academia in biomedical science". IMM PhD Program - course on "Technology Transfer and Intellectual Property in Biomedicine", June 14-15, 2010.

Castanho MARB invited tutor of the course "Peptide-lipid interactions in biomedicine":
Lecture 1: "Developing HIV fusion inhibitor peptides. Do lipids play a role?"
Lecture 2: "AMPs – bridging the gap between microbiology and molecular biophysics."
Lecture 3: "Kyotorphin and its derivatives. (S)low (but effective) throughput screening in the quest for a new analgesic drug." University of Girona, Spain, July 2010.

Workshops/Courses Attended

Franquelim HG, Freire JM and Sá Santos S participated in the Symposium "HIV/AIDS: Closing the Gap between Basic Research and Clinical Practice", IMM-FMUL, Lisbon, Portugal, January 22-23, 2010.

Sá Santos S also participated in:

- 1st RNEM Course on Protein Identification by Mass Spectrometry, ITQB-UNL, Oeiras, Portugal, January 27-28, 2010;
- “Rodents and fish in research - IMM practical course”, IMM-FMUL, Lisbon, Portugal, February 3-5, 2010;
- Workshop “Novel Experimental Therapies for Diseases of The Nervous System” organized by Harvard Medical School- Portugal, Lisbon, Portugal, May 29-30, 2010.

Freire JM also attended the 1st EBSA Biophysics Course on: Membrane Biophysics and Lipid-Protein Interaction, Bordeaux-Arcachon, France, 6-11 June, 2010.

Franquelim HG and Freire JM participated in the IMM Nanocourse "Presenting your research - From bench to peers", Lisbon, Portugal October 28-29, 2010.

Science and Society

Castanho MARB. "Ciência: a bela está adormeSIDA?", Lecture at Escola Profissional da Paiã, Lisbon, Portugal, March 2010.

Castanho MARB. "Novos medicamentos... Para uma vida nova?", Lecture at Escola Secundária Ginestal Machado, Santarém, Portugal, April 2010.

Castanho MARB. Jury member for the Prizes "Medalha Vicente Seabra" and "Prémio Ferreira da Silva", Sociedade Portuguesa de Química, October 2010.

Freire JM. “Biomoléculas: da Bioquímica à Ciência Aplicada”, Lecture at Escola EB2,3/S Octávio Duarte Ferreira (10th to 12th grades), Tramagal, Portugal, October 22, 2010.

Freire JM. “Moléculas – Factos e Curiosidades”, Workshop at the elementary School (4th grade) Externato Maria Teresa (Alvalade), Lisbon, Portugal, November 18, 2010.

Master and Ph.D. thesis completed

Ph.D. Thesis

Manuel Nuno de Sousa Pereira Simões de Melo (2010) A study on the mode of action of clinically relevant antimicrobial peptides. PhD in Biochemistry, Molecular Biophysics specialty, Faculdade de Ciências da Universidade de Lisboa. Co-Supervisor: Miguel ARB Castanho.

Master Thesis

João M Freire (2010) Dengue Virus Infection and Assembly. A Biophysical study for unravelling the role of the capsid protein, Master in Biochemistry, Faculdade de Ciências da Universidade de Lisboa. Co-Supervisor: Miguel ARB Castanho.

Henrique Nemésio (2010) Dengue virus structural proteins - Characterization of the membrane-active regions of proteins C and E, Masters in Biomedical Engineering, Instituto, Superior Técnico e Faculdade de Medicina da Universidade de Lisboa. Supervisor: Miguel ARB Castanho.

Morphogenesis and Tissue Repair Unit

Major interests / Objectives

Epithelia have the essential role of acting as a barrier that protects living organisms and its organs from the surrounding environment. It is crucial for epithelial tissues to have robust ways of maintaining their integrity despite the frequent damage caused by injury, inflammation and normal cell turnover. One of our objectives is to understand molecular and cellular basis of re-epithelialization, a conserved repair mechanism that acts in several types of simple epithelia, across species. The organism of choice has been the fruit fly (*Drosophila melanogaster*), due to its amenability to genetic manipulation and live imaging analysis. We are also using flies to investigate the mechanisms that control the recruitment of macrophage-like blood cells to wound sites to clear damaged cells. Recently we have started using Zebrafish to translate our *Drosophila* findings to a vertebrate model and to explore more complex tissue repair mechanisms, such as epimorphic regeneration.

Head of Unit

António Jacinto, PhD – Principal Investigator, IMM / Assistant Professor, FMUL

Principal Investigators

Soren Prag, PhD – Staff Scientist, IMM

Research Team

Isabel Campos, PhD	Post Doc Fellowship, FCT
Dulce Azevedo, PhD	Post Doc Fellowship, FCT
Ana Cristina Silva, PhD	Post Doc Fellowship, FCT
Anna Zaidman, PhD	Post Doc Fellowship, FCT
Joao Cordeiro, PhD	Post Doc Fellowship, FCT
Jenny Regan, PhD	Post Doc Fellowship, EMBO
Lara Carvalho, PhD	Post Doc Fellowship, Marie Curie
Marta Carapuço, PhD	Post Doc Fellowship, ERC-FP7
Mariana Simões	PhD Fellowship, FCT
Marco Antunes	PhD Fellowship, FCT
Sara Sousa	PhD Fellowship, FCT
Rita Mateus	PhD Fellowship, FCT
Carolina Moreira	PhD Fellowship, FCT
Telmo Pereira	PhD Fellowship, FCT
Angela Dias	Technician, ERC-FP7
Ana Sofia Brandão	Master Student, FCUL
Gonçalo Brito	Master Student, FCUL

Keywords/Research Areas

Cell and Developmental Biology
Drosophila Genetics
Cell Migration
Cell Adhesion
Tissue Repair
Regeneration

Major scientific achievements

The detailed analysis of novel genes involved in re-epithelisation, which we have identified through a *Drosophila* genetic screen, has revealed that EGF signaling is involved in this process.

We have developed a new wound healing assay using the *Drosophila* pupa that allows us to analyse the tissue movements with unprecedented spatial and temporal resolution and to manipulate the system with the full range of fly genetic tools.

Our study of *Drosophila* dorsal closure, a natural occurring morphogenetic movement that has striking similarities to wound repair, has shown that the pulsations of the amnioserosa, which drive the tissue movements, are regulated by RhoGEF2 and Rho signalling.

We have demonstrated that during zebrafish fin regeneration the bone tissue de-differentiates and contributes to the blastema, which is a mass of cells that gives rise to the regenerated tissues. In addition we have demonstrated that, similarly to amphibians, re-innervation is essential for fin regeneration in zebrafish.

We have participated in the organization of the main European annual meeting on our research field: EMBO Conference - Molecular and cellular basis of regeneration and tissue repair, 26-30 September 2010, Sesimbra, Portugal.

Recent Most Relevant Publications

Campos I, Geiger JA, Santos AC, Carlos V. and Jacinto A (2010) Genetic screen in *Drosophila melanogaster* uncovers a novel set of genes required for embryonic epithelial repair. *Genetics* **184**, 129-140. (Journal IF: 3.889, Citations: 1)

Brodland GW, Conte V, Cranston PG, Veldhuis J, Narasimhan S, Hutson MS, Jacinto A, Ulrich F, Baum B and Miodownik M (2010). Video force microscopy reveals the mechanics of ventral furrow invagination in *Drosophila*. *PNAS* **107**, 22111-22116. (Journal IF: 9.432, Citations: 0)

Wood W, Jacinto A (2007) *Drosophila melanogaster* embryonic haemocytes: masters of multitasking. *Nat Rev Mol Cell Biol* **8**, 542-551. (Journal IF: 42.198, Citations: 29)

Simoes S, Denholm B, Azevedo D, Sotillos S, Martin, P, Skaer H, Castelli-Gair Hombria J and Jacinto A (2006) Compartmentalization of Rho regulators directs cell invagination during tissue morphogenesis. *Development* **133**, 4257-4267. (Journal IF: 7.194, Citations: 29)

Wood W, Faria C and Jacinto A (2006) Distinct mechanisms regulate hemocyte chemotaxis during development and wound healing in *Drosophila*. *J. Cell Biol* **174**, 405-416. (Journal IF: 9.575, Citations: 41)

Ongoing Research Projects

2008/2010 Embryonic wound healing: a genetic approach, FCT. Coordinator: A. Jacinto. PTDC/BIA-BCM/65872/2006, €150 000.

2007/2011 Integrating the genetics, mechanics and phenomenology of embryonic wound healing, HFSP. Participant: A. Jacinto. RGP21/2007, €250 000 (total \$1 050 000).

2010/2013 Genetics of nonsyndromic cleft lip and palate, FCT. Coordinator: A. Jacinto. PTDC/SAU-GMG/101537/2008, €196 176.

2010/2013 The role of re-innervation in tissue regeneration, FCT. Coordinator: A. Jacinto. PTDC/SAU-OB/100200/2008, €140 000.

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

2008/2013 Epithelial Resealing, European Commission. Coordinator: A. Jacinto. ERC-2007-StG-208631-RESEAL, €1 150 000.

Publications in peer review Journals

Brodland GW, Conte V, Cranston PG, Veldhuis J, Narasimhan S, Hutson MS, Jacinto A, Ulrich F, Baum B and Miodownik M. (2010). Video force microscopy reveals the mechanics of ventral furrow invagination in *Drosophila*. *PNAS* **107**, 22111-22116 (Journal IF: 9.432).

Campos I, Geiger JA, Santos AC, Carlos V, and Jacinto A. (2010). Genetic Screen in *Drosophila melanogaster* Uncovers a Novel Set of Genes Required for Embryonic Epithelial Repair. *Genetics* **184**, 129-140. (Journal IF: 3.889, Citations: 1)

Invited Lectures and Seminars

Jacinto A. 2nd Institut Curie course on cytoskeleton - Cytoskeleton in cell division and migration, Institut Curie, Paris, France, June 7-11, 2010.

Communications in International Conferences

Jacinto A. Pupal Wound Healing, *Drosophila* wound healing (Workshop), Max Plank Institute for Biology and Ageing, Cologne, Germany, November 20, 2010 (Oral presentation).

Jacinto A. Genetic analysis of epithelial repair in *Drosophila*. EMBO Conference series - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010 (Oral presentation).

Jacinto A. Epithelial Resealing. EMBO Conference Series - The molecular and developmental biology of *Drosophila*, Kolymbari, Crete, Greece, June 20-26, 2010 (Oral presentation).

Jacinto A. Epithelial Resealing. Mathematical modeling and biomechanics of wound healing and morphogenesis (Workshop), Nice, France, May 25-27, 2010 (Oral presentation).

Sousa S, Afonso N, Benismon-Brito A, Fonseca M, Leon J, Rohel H, Cancela ML and Jacinto A. Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 10-12, 2010 (Poster presentation).

Carvalho L, Geiger J, Campos I and Jacinto A. Studying epithelial wound healing in *Drosophila*. Joint Meeting of the Portuguese and Spanish Developmental Biology Societies, Badajoz, Spain, November 10-12, 2010 (Poster presentation).

Sousa S, Afonso N, Fonseca M and Jacinto A. Osteoblast differentiation during bone regeneration in zebrafish caudal fin. EMBO Conference series - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Simões M and Jacinto A. Zebrafish - A model to study the role of nerves in regenerating appendages. EMBO Conference series - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Mateus R and Jacinto A. Size-control regulation during regeneration: How to stop growth?. EMBO Conference series - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Antunes M, Cordeiro J, Pereira T, Hutson S, Brodland W and Jacinto A. Integrating the genetics, mechanics and phenomenology of embryonic wound healing. EMBO Conference series - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010 (Poster presentation).

Communications in National Conferences

Mateus R, Pereira T and Jacinto A. Tissue and cell movements underlying zebrafish fin fold regeneration. 4th IMM PhD Student Meeting, IMM, Lisbon, Portugal, November 22-23, 2010 (Poster presentation).

Moreira CGA, Regan JC, Zaidman A. *Drosophila* Hemocyte Migration - an in vivo Assay for Directional Cell Migration, 4th IMM PhD Student Meeting, IMM, Lisbon, Portugal, November 22-23, 2010 (Poster presentation).

Sousa S, Afonso ND, Bensimon-Brito A, Fonseca M, Leon J, Rohel H, Cancela ML and Jacinto A. Differentiated scleroblasts contribute to blastema formation during zebrafish fin regeneration, 4th IMM PhD Student Meeting, IMM, Lisbon, Portugal, November 22-23, 2010 (Oral presentation).

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Antunes M, Cordeiro JV, Pereira T and Hutson S, Brodland W and Jacinto A, Integrating the genetics, mechanics and phenomenology of wound healing. 4th IMM PhD Student Meeting, IMM, Lisbon, Portugal, November 22-23, 2010 (Oral presentation).

Jacinto, A. Epithelial repair in *Drosophila*. Porto Cancer Meeting 2010, Porto, Portugal, April 22-23, 2010 (Oral presentation).

Jacinto, A. Tissue repair in *Drosophila*. Ciência 2010, Lisbon, Portugal, July 4-7, 2010 (Oral presentation).

Organisation of Conferences

Jacinto A co-organized the EMBO Conference - Molecular and cellular basis of regeneration and tissue repair, Sesimbra, Portugal, September 26-30, 2010.

Internationalization

Integrating the genetics, mechanics and phenomenology of embryonic wound. Collaborative grant funded by Human Frontiers Science Program with Shane Hutson, Vanderbilt University, Nashville USA, and Wayne Brodland, University of Waterloo, Canada. A collaborative paper has been published and a second one has been submitted in 2010.

Quantitative models of cellular and developmental biology. Collaborative grant submitted to the European Science Foundation Research Networking Programme, including 14 groups from 9 different European countries.

Differentiated skeletal cells contribute to blastema formation during zebrafish fin regeneration. Collaboration that is a follow up from the previously funded Network of Excellence – Cells into Organs, with Henry Roehl, MRC Centre for Developmental and Biomedical Genetics, University of Sheffield. A collaborative paper has been submitted in 2010.

Mathematical and Physical Modeling of Regenerative Repair. Collaboration including several groups based in France: Françoise Giroud and Luis Almeida from the Laboratoire Techniques de l'Ingénierie Médicale et de la Complexité, Informatique, Mathématiques et Applications de Grenoble, and Nadine Peyrieras from the Neurobiologie et Développement et Plateforme BioEmergences, Gif sur Yvette. Application for a collaborative grant has been submitted to the Agence Nationale de la Recherche, France.

Prizes, honours and awards

First Prize for Oral Presentation in the 4th IMM PhD Student Meeting 2010, to Sara Sousa for the presentation “Differentiated scleroblasts contribute to blastema formation during zebrafish fin regeneration”.

Advanced teaching

Jacinto A organized the Between Cells module of the Gulbenkian PhD Programme in Biomedical Integrative Sciences, Instituto Gulbenkian de Ciência, Oeiras, 18-22 October 2010.

Jacinto A was lecturer in the EMBO Practical Course Animal Models for Development, Physiology and Disease, University of Sheffield, Sheffield, UK, 19-30 July 2010.

Science and Society

A Jacinto was elected president of the Portuguese Society for Developmental Biology in November 2010.

Master and Ph.D. thesis completed

Ph.D. thesis

Jennifer Ann Geiger (2010) "Wound healing: a genetic approach in *Drosophila*", PhD, ITQB, Universidade Nova de Lisboa. Supervisor: António Jacinto.

Master thesis

Inês Moreira Tenente (2010) "The role of telomerase on cell proliferation in zebrafish (*Danio rerio*): characterization of a tert mutant", Master in Biologia Evolutiva e do Desenvolvimento, Faculdade de Ciências da Universidade de Lisboa. Supervisors: Miguel Godinho Ferreira (IGC) e António Jacinto.

Immunology & Infectious Diseases Programme

Programme Coordinators: Mário Ramirez, José Moniz Pereira, Rui Victorino

Heads of Unit:

Luis Graca, 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 Graca

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, Celine Carret

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, Inês Soeiro

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.

We have been researching new methods to induce tolerance in allergic asthma, food allergy, and an animal model of rheumatoid arthritis using antibodies or cells from the immune system able to regulate excessive immune responses.

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 Graca, MD, DPhil – Assistant Professor, FML

Research Team

Ana Água-Doce	PhD Fellowship, FCT
Catarina Almeida	MSc Student, IEFP
Ivonne Wollenberg	PhD Fellowship, FCT
Joana Duarte	PhD student, FCT
Marta Caridade, MSc	PhD student, FCT
Marta Monteiro, PhD	Post-doctoral Fellowship, FCT
Patricia Santos, PhD	Post-doctoral Fellowship, FCT
Vanessa Oliveira, DPhil	Post-doctoral Fellowship, FCT

Research Areas

Immune tolerance
Regulatory T cells
Natural Killer T cells (NKT)
Follicular helper T cells
Allergy, Autoimmunity
Transplantation

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.

We have shown CD4 blockade at the time of allergen exposure induces antigen-specific tolerance in mice, sparing immune competence to unrelated antigens. Tolerance can be induced to a model antigen (OVA) or clinically relevant allergens (house dust mite, HDM, or crude peanut extract).

3. Natural Killer T cells can be polarized *in vitro* towards different functional fates, namely regulatory (characterized by Foxp3 expression) and effector (producing IL-17 or IL-9).

Functional plasticity in response to cytokines has been considered a characteristic of conventional T lymphocytes. We have shown that iNKT-cell activation in presence of appropriate cytokines can lead to a functional polarization similar to what has been described for T cells. Induced Foxp3⁺iNKT cells displayed a phenotype similar to Treg cells, suppressing through a contact-dependent, GITR-mediated mechanism.

Recent Most Relevant Publications

Curotto de Lafaille MA, Lafaille JJ, Graca L (2010) Mechanisms of tolerance and allergic sensitization in the airways and the lungs. *Curr Opin Immunol.* **22**, 616-622 (Journal IF 2009: 10.881; Citations: 0)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Agua-Doce A, Wollenberg I, Silva-Santos B, Graca L (2010) Identification of Regulatory Foxp3⁺ Invariant NKT Cells Induced by TGF- β . *J Immunol.* **185**, 2157-2163 (Journal IF 2009: 5.646; Citations: 1)

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: 56)

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: 288)

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: 91)

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

2009/2011 Improving Immunotherapy. European Commission. Participant: L. Graça. FP7/SUDOE/Immunonet, €117 000 (total).

Publications in Peer Review International Journals

Moura RA, Weinmann P, Pereira PA, Caetano-Lopes J, Canhão, H, Sousa E, Mourão AF, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Graça L, Fonseca JE (2010) Alterations on peripheral blood B-cell subpopulations in very early arthritis patients. *Rheumatology*. **49**, 1082-1092. (IF 2009: 4.236, Citations: 1)

Caetano-Lopes J, Nery AM, Canhão H, Duarte J, Cascão R, Rodrigues A, Perpétuo IP, Abdulghani S, Amaral PM, Sakaguchi S, Kontinen YT, Graça L, Vaz MF, Fonseca JE (2010) Chronic arthritis leads to disturbances in the bone collagen network. *Arthritis Research and Therapy*. **12**, R9 (IF 2009: 4.271, Citations: 2)

Duarte J, Agua-Doce A, Fonseca JE, Graça L (2010) Modulation of synovial IL-17 and Foxp3 expression in the prevention of autoimmune arthritis in mice. *PLoS ONE*. **5**, e10558 (IF 2009: 4.351, Citations: 2)

Raposo BR, Rodrigues-Santos P, Carvalheiro H, Agua-Doce AM, Carvalho L, Pereira da Silva JA, **Graça L**, Souto-Carneiro MM (2010) Monoclonal anti-CD8 therapy induces disease amelioration in the K/BxN mouse model of spontaneous chronic polyarthritis. *Arthritis and Rheumatism*. **62**, 2953-2962 (IF 2009: 7.332, Citations: 0)

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 (IF 2009: 5.646, Citations: 1)

Curotto de Lafaille MA, Lafaille JJ, Graça L (2010) Mechanisms of tolerance and allergic sensitization in the airways and the lungs. *Curr Opin Immunol*. **22**, 616-622 (IF 2009: 10.881, Citations: 0)

Cascão R, Moura RA, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosario HS, Souto-Carneiro MM, Graça L*, Fonseca JE* (2010) Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early rheumatoid arthritis. *Arthritis Research and Therapy*. **12**, R196 (IF 2009: 4.271, Citations: 0)
*JOINT SENIOR AUTHOR

Moura RA, Cascão R, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosario HS, Souto-Carneiro MM, Graça L, Fonseca JE (2010) Cytokine pattern in very early rheumatoid arthritis favours B-cell activation and survival. *Rheumatology*. Epub 2010 Nov 2. (IF 2009: 4.236, Citations: 0) *JOINT SENIOR AUTHOR

Communications in International Conferences

Caridade M, Agua-Doce A, Duarte J, Oliveira VG, Ribeiro RM, and Graça L. The Role of Microenvironment in Tolerance Induction to Foreign Antigens. Cell Symposia: Inflammation and Disease, Lisbon, Portugal. September 26-28, 2010. (Poster presentation)

Agua-Doce A, Caridade M, Oliveira VG, Curotto de Lafaille M, Lafaille JJ, and Graca L, Prevention of house dust mite induced allergic airways disease in mice through immune tolerance, FOCIS 2010, Boston, Massachusetts, USA. June 24-27, 2010. (Poster presentation)

Monteiro M, Almeida C, Caridade M, Ribot JC, Agua-Doce A, Silva-Santos B, and Graca L. Plasticity of invariant Natural Killer T cells in response to TGF- β leads to the generation of distinct functional subsets expressing Foxp3, IL-9 and IL-17. IV Immune Regulation Meeting, Davos, Switzerland. 29 March – 1 April 2010. (Poster presentation)

Monteiro M, Almeida C, Caridade M, Ribot JC, Duarte J, Agua-Doce A, Silva-Santos B, and Graca L. Plasticity of invariant Natural Killer T cells in response to TGF- β leads to the generation of distinct functional subsets expressing Foxp3, IL-9 and IL-17. China Tregs 2010. Shanghai, China, July 16-22, 2010. (Oral presentation)

Oliveira VG, Caridade M, and Graca L. Suboptimal CD4 T cell activation triggers conversion to Foxp3+ regulatory T cells. China Tregs 2010. Shanghai, China, July 16-22, 2010. (Poster presentation)

Wollenberg I, Agua-Doce A, Faro J, and Graca L. T cell regulation of germinal center dynamics. International Conference of Immunology. Kobe, Japan, August 21-29, 2010. (Poster Presentation).

Communications in National Conferences

Monteiro M, Almeida C, Caridade M, Ribot J, Água-Doce A, Silva-Santos B, and Graca L. The plasticity of invariant Natural Killer T cells, XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga, Portugal, September 20-22, 2010. (Poster presentation)

Invited Lectures and Seminars

Graça L. *Tolerance induction to recombinant clotting factors in Hemophilia*. CSL Behring – Prof. Heimburger Award Symposium 2010. Marburg, Germany, March 26, 2010.

Graça L. *As bases imunitárias das doenças reumáticas*. Congress of the Portuguese Society of Rheumatology, Funchal, April 7, 2010.

Graça L. *Immune tolerance and unique regulatory cells*. Institute Pasteur Shanghai, Shanghai, China, July 21, 2010.

Internationalization

Collaborative research with Dr. José Faro (University of Vigo, Spain) – co-supervision of PhD student. Support from Programa Bilateral Luso-Espanhol.

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

BES National Innovation Award for Health Technologies, 2010, to M. Monteiro D. Cristina and L. Graca.

Honorary mention in the ISCTE-IUL MIT-Portugal Venture Competition, 2010, to M. Monteiro D. Cristina and L. Graca.

Young Entrepreneur Award, from ANJE, to M. Monteiro D. Cristina and L. Graca.

Travel Award from the Portuguese Society of Immunology to Marta Monteiro to attend IV Immune Regulation Meeting, Davos, Switzerland. 29 March – 1 April 2010.

Travel Award to Ivonne Wollenberg.

Travel Award to Vanessa G. Oliveira.

Industry contract research

The research output from this unit has led to the creation of a start-up company – Acellera Therapeutics (www.acellera.com) – with the objective to further develop the technology towards its clinical use.

Government/Organization contract research

Report for the Conselho Nacional de Ética para as Ciências da Vida on Animal Experimentation in Biomedical Sciences. L. Graça and M. Monteiro. Presented on 15 March 2010.

Advanced teaching

Coordinator of the Immunology module for the Programa Gulbenkian de Formação Médica Avançada – Programa Doutoral para Médicos. Held at IMM in January 2010.

Science and Society

During 2010 the research output of this unit received extensive attention from national and international media (Portuguese television networks, national newspaper and newsmagazines, New Scientist, etc...). In addition members of the unit participated in several events related to the development of public awareness of science:

Participation in Science Communication event organized by Instituto Gulbenkian de Ciência at Festival Optimus Alive!10, Oeiras, Portugal, 8-10 July 2010. Catarina Almeida, and Marta Caridade.

Participation in Science Communication event organized by Instituto Gulbenkian de Ciência at Mundo Mix2010, Castelo de S. Jorge, Lisbon, 14-16 May 2010. C. Almeida.

Lecture in Oeiras Biotech “*Investigação Básica e Medicina*”, Taguspark, Oeiras, 5 March 2010. L. 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, 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 – Staff Scientist, IMM (Head of the Flow Cytometry Unit)

Research Team

Russell B Foxall, PhD	Post Doc Fellowship, FCT
Andreia Fonseca, PhD	Post Doc Fellowship, EMBO
Adriana S. Albuquerque, PhD	Research Fellowship, FCT
Helena Nunes Cabaço, PhD	Research Fellowship, FCG
Rui Soares, MSc	PhD Fellowship, FCT
Rita Tendeiro, BSc	PhD Fellowship, FCT
Ana Rita Barbosa, BSc	PhD Fellowship, FCT
Rita Azevedo, BSc	PhD Fellowship, FCT
Susana Mendes Fernandes, MD	PhD Fellowship, FCT (since October 2010)
Paula Matoso, MSc	Research Fellowship, FCT
Susana Lopes da Silva, MD, MSc	Immunoallergologist, HSM, Lecturer, FMUL
José Gonçalo 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
Carlos Ferreira, MD, PhD	Auxiliary Professor, FMUL, Consultant Internist, HSM
Ana Margarida Amaral Gomes, BSc	Traning Fellowship, FCT
Filipa Sousa, MD	Resident in Immunoallergology, Hospital Central do Funchal (from June to October 2010)

Marta Calado, BSc	Traning Fellowship, FCT (left in August 2010)
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Keywords/Research Areas

Human T cell homeostasis
 Immune regulation
 HIV/AIDS immunopathogenesis
 HIV-2 infection.
 Primary immunodeficiencies
 Immunological reconstitution.

Major scientific achievements

- *Human T cell homeostasis / Immune regulation*
 T cells are crucial players in the immune system. A central theme of UIC's research is focused on T cell homeostasis and regulatory mechanisms in health and in differing clinical settings. There are very limited data on the development of a CD4+ T cell subset devoted to immune regulation, namely regulatory T cells, in the human thymus. Taking advantage of the access to thymic tissue removed under the current standard protocols of reconstructive cardiac surgery in children we contributed to the definition of the steps involved in regulatory T cell development.
- *Primary immunodeficiencies*
 The UIC pursued the work on the development of a centre dedicated to the diagnosis, treatment and investigation of congenital immunodeficiencies that formally integrates the related clinical departments of the Hospital de Santa Maria and the Clinical Immunology Unit at the IMM/FMUL. Studies of the cohort of patients with Common Variable Immunodeficiencies, and of individual cases, have been pursued as illustrated by the first report of thymic transplantation in FOXP1 deficiency published in the "Blood" journal.
- *HIV/AIDS immunopathogenesis / HIV-2 infection*
 HIV-2 infection is characterized by low to undetectable levels of circulating virus (viremia) despite a significant number of infected cells as assessed by the proviral DNA integrated in the cell genome. In order to investigate this apparent paradox UIC developed assays to quantify HIV-2 spliced and unspliced RNA transcripts in order to estimate the amount of ongoing viral replication. Our data, published in the Journal of Virology, provided for the first time evidence of ongoing viral replication in HIV-2 infection despite the low to undetectable viremia, and of its association with CD4 and CD8 T cell activation. These data have implications for the understanding of the relationship between viremia and cell-associated viral burden in HIV pathogenesis with impact on our ongoing studies on HIV-2 immunopathogenesis.
- *Organization of the meeting "HIV-AIDS: Closing the Gap between Basic Research and Clinical Practice" at the IMM*
 UIC organized this meeting aiming at promoting the dialogue between researchers and clinicians on the most recent advances in the area of HIV/AIDS, focusing on aspects such as novel therapeutic approaches, vaccines, HIV pathogenesis and epidemiology, viral and immunologic aspects of the infection. We believe that this meeting was a very relevant event in HIV/AIDS research in Portugal that fostered novel scientific and medical

collaborative approaches. This meeting gathered international researchers including Françoise Barré-Sinoussi, Medicine Nobel Prize in 2008, with the Portuguese scientific and medical communities, as well as society opinion leaders in this area (see <http://imm.fm.ul.pt/web/imm/hivmeeting>).

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: 8.978, Citations: 2).

Azevedo RI, Soares MV, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE. (2009) IL-7 sustains CD31 expression in human naive CD4+ T cells and preferentially expands the CD31+ subset in a PI3K-dependent manner. *Blood* **113**, 2999-3007 (Journal IF: 10.555, Citations: 7).

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: 4.084, Citations: 19)

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: 5.646, Citations: 200)

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: 27.136, Citations: 241)

Ongoing Research Projects

- | | |
|---------|---|
| 2007/11 | HIV-2 infection and the thymus, FCT, PI: Ana E Sousa, FCT/PTDC/SAU-MII/66248/2006, €136.621 |
| 2007/11 | HIV/AIDS Program IMM-FCG, Fundação Calouste Gulbenkian, PI: Ana E Sousa, €150.000 |
| 2008/10 | Cellular and Molecular Response of HIV-2 and HIV-1 Infection to Integration Modulation, Merck & Co., Inc., PI: Ana E Sousa (Co-PI João Gonçalves), €100.000 |
| 2008/11 | Immune Reconstitution after Unrelated and Haplotype-Mismatched Stem Cell Transplantation, FCT, PI: Maria Soares, PTDC/SAU-MII/67662/2006, €122.986 |
| 2009/11 | Long-term impact of thymectomy performed in early infancy, FCT, PI: Rui MM Victorino, PIC/IC/83068/2007, €75.000 |

- 2009/12 Clinical implications of activation of PI3K/Akt signaling pathway in primary adult acute lymphoblastic leukemia, FCT, PI: João F. Lacerda, PIC/IC/83023/2007, €134.000
- 2009/12 Lymphoid Tissues in HIV-2 Infected patients, FCT, PI: Ana E Sousa, PIC/IC/82712/2007, €195.000

Publications in peer review Journals

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. (2010) Cell-associated viral burden provides evidence of ongoing viral replication in aviremic HIV-2 infected patients. *J Virol* Published online Dec 15; doi:10.1128/JVI.01921-10. (Journal IF: 5.150).

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 (2010) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of two cases. *Blood* Published online Oct 26; doi:10.1182/blood-2010-06-292490. (Journal IF: 10.555).

Gonçalves-Sousa N., Ribot J.C., Debarros A., Correia D.V., Caramalho I. and Silva-Santos B. (2009) Inhibition of murine gammadelta lymphocyte expansion and effector function by regulatory alphabeta T cells is cell-contact-dependent and sensitive to GITR modulation". *Eur J Immunol* **40**, 61-70 (Journal IF: 5.179).

Aguiar SI, Brito MJ, Gonçalo-Marques J, Melo-Cristino J, and Ramirez M. (2010) Serotypes 1, 7F and 19A became the leading causes of pediatric invasive pneumococcal infections in Portugal after 7 years of heptavalent conjugate vaccine use. *Vaccine* **28**, 5167-5173. (Journal IF: 3.616).

Gomes AQ, Correia DV, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, Silva MG, 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**, 1397-1404. (Journal IF: 6.416).

Pires R, Ardanuy C, Rolo D, Morais A, Brito-Avô A, Marques JG, Liñares J, and Santos-Sanches I. (2010) Emergence of Ciprofloxacin-Nonsusceptible *Streptococcus pyogenes* Isolates from Healthy Children and Pediatric Patients in Portugal. *Antimicrobial Agents and Chemotherapy* **54**, 2677-2680. (Journal IF: 4.802).

Nunes-Cabaço H, Ribot JC, Caramalho I, Serra-Caetano A, Silva-Santos B and Sousa AE (2010) Foxp3 induction in human and murine thymus precedes the CD4+ CD8+ stage but requires early T cell receptor expression. *Immunology and Cell Biology* **88**, 523-528. (Journal IF:4.200).

Other publications International

Crispim JN, Dâmaso C, Marques JG, Miguéns J and Valente P (2010) Burkholderia cepacia meningitis: A case report. *J Pediatr Infect Dis* **5**, 393-396.

Other publications National

Comissão de Vacinas da Sociedade Portuguesa de Pediatria: Cavaco A, Manso A, Rodrigues F, Marques JG, and Marques L (2010) Recomendações sobre vacinas. Sociedade Portuguesa de Pediatria, Lisboa.

Sousa AE, and Victorino RMM. Imunopatogénese e Resposta Imunológica. In: Manual sobre SIDA - Ed. F. Antunes - Permanyer Portugal, 4ª Edição, 2010.

Duarte FC, Costa AC, Silva SL, Lopes A, Santos AS, Pedro E and Barbosa MP (2010) Avaliação do tratamento com imunoglobulina na urticária crónica autoimune. *Revista Portuguesa de Imunoalergologia* **18**, 137-156.

Barbosa F, Ferreira C, Patrício P, Mota C, Alcântara C, and António Barbosa A (2010) Estilo de vinculação em doentes com Lúpus Eritematoso Sistémico. *Acta Médica Portuguesa* **23**, 51-62.

Sousa DA, Silva SL and Ferreira MB (2010) Síndrome hiper-IgE – Imunologia. *Revista Portuguesa de Imunoalergologia* **18**, 291-311.

Costa AC, Cabral Duarte F, Costa Trindade J, Bento ML, and Pereira Santos MC (2010) Aquisição de tolerância às proteínas do peixe: alteração do padrão de sensibilização identificado por immunoblotting. *Revista Portuguesa de Imunoalergologia* **18**, 353-371.

Spinilloa santos A, Cabral Duarte F, Lopes A, Sokolova A, Pereira Santos MC, Melo A, Branco Ferreira M, and Pereira Barbosa M (2010) Hipersensibilidade mediada por IgE ao paracetamol- Caso clínico. *Revista Portuguesa de Imunoalergologia* **18**, 459-466.

Lopes AI (2010) H. pylori na doença gastroduodenal da criança. *Gastrenterologia Pediátrica. Edição da Sociedade Portuguesa de Endoscopia Digestiva (SPED)*.

Invited Lectures and Seminars

Lopes AI. Epidemiology of hepatitis C in pediatric patients. Burden and Prevention of Viral Hepatitis in Portugal. Viral Hepatitis Prevention Board Meeting, Lisboa, November 18-19, 2010.

Pereira-Santos MC Alergénios recombinantes-vantagens e limitações. Portuguese Society for Immunoallergology and Clinical Immunology XXXI Annual Meeting, Funchal, October 14-17, 2010.

Ferreira C. Aterosclerose: uma doença auto-imune? 18º Congresso Nacional de Aterosclerose, Vilamoura, October 2010.

Sousa AE. Reversible and irreversible damage in HIV/AIDS. XXXVI Annual Meeting of the Portuguese Society for Immunology (SPI), Braga, September 20, 2010

Albuquerque AS, Human nude/SCID and thymic transplantation. CIPM, Instituto Português de Oncologia de Lisboa Francisco Gentil, E.P.E., Lisboa, Portugal, May 26, 2010.

Caramalho, I. Killing me softly: the Dynamics of CTL-mediated tumor cell death. Faculdade de Ciências da Universidade de Lisboa, March 29, 2010.

Lopes AI. Estudo epidemiológico da gastroenterite a rotavirus. Gastroenterite aguda por rotavirus. Reunião da SPP, Porto, March 6, 2010.

Sousa AE. Understanding AIDS pathogenesis through HIV-2 infection. Instituto de Higiene e Medicina Tropical. Lisboa, February 8, 2010.

Ferreira C. B-cell Targeted Therapies for Systemic Autoimmune Diseases 8th Medinterna International Meeting - "Systemic Autoimmune Diseases Revisited" January, 2010

Lopes AI. Úlcera péptica em Idade Pediátrica. Reunião Monotemática SPG. Úlcera Péptica: Passado, Presente e Futuro. Sociedade Portuguesa de Gastroenterologia, Lisboa, January 30, 2010.

Sousa AE. Lessons from HIV-2 infection. HIV/AIDS: Closing the Gap between Basic Research and Clinical Practice. Lisboa, January 23, 2010

Communications in International Conferences

Barbosa R, Silva SP, Silva SL, Tendeiro R, Melo A, Santos MC, Pedro E, Barbosa MP, Victorino RMM, Sousa AE. T-cell disturbances in B-cell immunodeficiencies, São Paulo Advanced School on Primary Immunodeficiencies: Unraveling Human Immuno-Physiology, São Paulo, Brazil, November 28-December 4, 2010 (Poster presentation)

Amaral AJ, Matoso P, Soares R, Gama-Carvalho M, Gonçalves J, Sousa AE. Profiling the effect of cell activation in the microRnome of human CD4+ T-cells, The Non Coding Genome Meeting, Heidelberg, Germany, October 10-13, 2010 (Poster presentation)

Barbosa R, Silva SP, Silva SL, Melo A, Santos MC, Pedro E, Barbosa MP, Victorino RMM, Sousa AE. IL-17 production by CD4 T cells is related to B-cell differentiation: evidence of a reduced Th17 pool in congenital agammaglobulinemia, 14th Meeting of the European Society for Immunodeficiencies (ESID), Istanbul, Turkey, October 6-9, 2010 (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, 14th Meeting of the European Society for Immunodeficiencies (ESID), Istanbul, Turkey, October 6-9, 2010 (Poster presentation)

Pinto MV, Marques JG, Silva SL, Palha AM, Lopes AI. Gastrointestinal manifestations in chronic granulomatous disease: a clinical case, Espghan Summer School, Greece, September, 2010 (Oral Presentation)

Amaral, AJ, Matoso, P, Soares R, Gama-Carvalho M, Gonçalves J, Sousa AE. Profiling microRNA expression during human CD4+ T-cell activation, ESF, Next Generation Sequencing Meeting, Leiden, Netherlands, August 29-September 1, 2010 (Poster Presentation)

Vitoriano I, Rocha-Gonçalves A, Calado C, Lopes AI, Oleastro M; Roxo-Rosa M. The protein signature of pediatric peptic ulcer-associated Helicobacter pylori strains, 9th International

Workshop on Pathogens and Host Response in Helicobacter infections, Helsingor, Denmark, July 7-10, 2010 (Oral Presentation)

Mascarenhas MI, Silva SL, Marques JG, Albuquerque A, Melo A, Ferreira MB, Santos MC, Sousa AE, Barbosa MP. Recurrent abscesses, XXIX Congress of the European Academy of Allergology and Clinical Immunology, London, UK, June 5-9, 2010 (Poster presentation)

Mascarenhas MI, Melo A, Silva SL, Mendes A, Pedro E, Barbosa MP, Santos MC. Immediate reaction to local anesthetics: contribution of in vitro methods, XXIX Congress of the European Academy of Allergology and Clinical Immunology, London, UK, June 5-9, 2010 (Poster presentation)

Sokolova A, Páris-Fernandes N, Lopes A, Pereira-Santos MC, Pereira-Barbosa M, Occupational asthma and anaphylaxis induced by cow's milk proteins, XXIX Congress of the European Academy of Allergy and Clinical Immunology, London, UK, June 5-9, 2010 (Poster presentation)

Morais-Silva P, Cabral-Duarte F, Costa A, Lopes-Silva S, Pedro E, Pereira-Santos MC, Barbosa M. An atypical presentation of common variable immunodeficiency, XXIX Congress of the European Academy of Allergy and Clinical Immunology, London, UK, June 5-9, 2010 (Poster presentation)

Luz S, Lopes A, Spinola Santos A, Costa A, Pereira-Barbosa M, Pereira-Santos MC, Tree nut allergy: LTP sensitization as a possible increasing risk factor for systemic symptoms, XXIX Congress of the European Academy of Allergy and Clinical Immunology, London, UK, June 5-9, 2010 (Poster presentation)

Cavaco A, Lopes AI, Rodrigues F, and the Rotavirus Study Group of the Portuguese Society of Paediatrics. Burden of Rotavirus Acute Gastroenteritis in Portugal: Multicenter Prospective Study 2008-2009, ESPID Annual Meeting, Nice, France, 4-8, 2010 (Poster Presentation)

Communications in National Conferences

Martins M, Ligeiro D, Caramalho I, Soares M, Trindade H, Sousa AE, Lacerda JF. Diversidade de perfis IgH na reconstituição imunológica pós-transplante haploidêntico de células progenitoras hematopoiéticas. 13º Simpósio pela Ciência. GAPIC, Faculdade de Medicina da Universidade de Lisboa, December 14, 2010 (Poster presentation)

Viveiros C, Raposo J, Neves M, Lopes C, Lacerda J, Gomez B, Costa MJ, Carmo JA. Associação de rituximab e metilprednisolona (RMP) como alternativa no tratamento de doentes com LLC refractária e/ou sem indicação para fludarabina, Sociedade Portuguesa de Hematologia, Tróia, November 11-13, 2010 (Oral presentation)

Santos-Sousa P, Lacerda JF, Martins C, Lourenço F, Juncal C, Carmo JA. Transplante de progenitores hematopoiéticos de dador não familiar com ajuste de dose de timoglobulina segundo com grau de compatibilidade entre dador e receptor. Sociedade Portuguesa de Hematologia, Tróia, November 11-13, 2010 (Oral presentation)

Gonçalves C, Palha A, Oliveira E, Lopes AI. Gastrite autoimune e anemia ferropénica refractária: contribuição de uma pequena série pediátrica. Congresso Nacional de Pediatria, Funchal, October 6-8, 2010 (Oral presentation)

Pinto MV, Gomes C, Silva SL, Palha A, Loreto H, Marques JG, Lopes AI. Colite na Doença Granulomatosa Crónica – manifestação frequente numa doença rara. XI Congresso Nacional de Pediatria. Funchal, October 6-8, 2010 (Poster presentation)

Russo T, Crujo C, Loreto H, Morato P, Sousa AE, Lopes AI. Doença de Menétrier associada a infecção por Citomegalovirus. Congresso Nacional de Pediatria, Funchal, October 6-8, 2010 (Poster presentation)

Silva SL, Silva SP, Pedro E, Barbosa MP. Imunodeficiências – humorais: experiência de uma consulta diferenciada, XXXI Reunião Anual da SPAIC/XIV Congresso Luso-Brasileiro de Alergologia e Imunologia Clínica. Funchal, October 14-17, 2010 (Oral presentation)

Costa AC, Morais-Silva P, Bartolomé B, Pereira-Santos MC, Pereira-Barbosa M. Anafilaxia após ingestão de bombom com caju numa doente com alergia ao pistáchio, Portuguese Society for Immunoallergology and Clinical Immunology XXXI Annual Meeting, Funchal, October 14-17, 2010 (Poster presentation)

Mascarenhas MI, Lopes da Silva S, Portigo I, Costa AC, Bento L, Pereira-Barbosa M, Martinez J, Pereira-Santos MC. Estudo da composição proteica das fórmulas lácteas da primeira infância, Portuguese Society for Immunoallergology and Clinical Immunology XXXI Annual Meeting, Funchal, October 14-17, 2010 (Oral presentation)

Amaral, AJ, Matoso, P, Soares R, Gama-Carvalho M, Gonçalves J, Sousa AE. Profiling the effect of cell activation in the microRnome of human naïve CD4+ T cells. XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga, September 20-22, 2010 (Oral Presentation)

Barbosa R, Silva SP, Silva SL, Tendeiro R, Melo A, Santos MC, Pedro E, Barbosa MP, Victorino RMM, Sousa AE. Common Variable Immunodeficiency: does circulating LPS contribute to chronic immune activation? XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga, September 20-22, 2010 (Poster presentation)

Fernandes SM, Tendeiro R, Paulo S, Costa A, Victorino R, Sousa AE. Inflammatory bowel disease in HIV 2 infection acquired early in life, XXXVI Annual meeting of the Portuguese Society for Immunology. Braga, September 20-22, 2010 (Poster 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, XXXVI Annual meeting of the Portuguese Society for Immunology. Braga, September 20-22, 2010 (Poster presentation)

Caramalho I, Melo A, Pedro E, Barbosa MP, Victorino RMM, Sousa AE and Santos MC. Investigating tools to increase the Human Regulatory T cell compartment, XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga, September 20-22, 2010 (Poster presentation)

Gonçalves C, Palha A, Oliveira E, Fernandes A, Ferrão A, Morais A, Lopes AI. Gastrite atrofica, gastrite autoimmune e anemia ferropénica: a ponta do iceberg? 23ª Reunião Anual da Secção de Gastroenterologia Pediatrica da SPP, Aveiro, March 18-20, 2010 (Oral presentation)

Barbosa R, Silva SP, Silva SL, Tendeiro R, Melo A, Santos MC, Pedro E, Barbosa MP, Victorino RMM, Sousa AE. Common Variable Immunodeficiency: does circulating LPS contribute to

chronic immune activation? IV Reunião de Imunodeficiências Primárias, Coimbra, February 5, 2010 (Oral presentation)

Barbosa R, Silva SP, Silva SL, Melo A, Santos MC, Pedro E, Barbosa MP, Victorino RMM, Sousa AE. Common variable immunodeficiency: relationship between IL-17 producing CD4 T cells and the imbalances of the B- and T-cell populations, IV Reunião de Imunodeficiências Primárias, Coimbra, February 5, 2010 (Poster presentation)

Albuquerque AS, Melo A, Silva S, Marques J, Ferrão A, Figueiredo A, Faria E, Neves J, Freitas O, Lemos S, Victorino RM, Sousa AE, Santos MC. Circulating levels of IL-10 and of Fas-L as useful markers for the diagnosis of Autoimmune Lymphoproliferative Syndrome, IV Reunião de Imunodeficiências Primárias, Coimbra, 5 February, 2010 (Oral presentation)

Organisation of Conferences

Ferreira C. Co-organized the 2^a Reunião do Núcleo de Doenças Auto-imunes do Hospital de Santa Maria/Faculdade de Medicina de Lisboa. Lisboa, November, 2010

Silva S. Co-organized and lectured in the Workshop “Imunodeficiências Primárias – como reconhecer e diagnosticar”, XXXI Anual Meeting da Sociedade Portuguesa de Alergologia e Imunologia Clínica, SPAIC/XIV Congresso Luso-Brasileiro de Alergologia e Imunologia Clínica, Funchal, October 15, 2010

Lopes AI. Symposium Co-organizer: Probióticos, Prebióticos e Simbióticos. Congresso Nacional de Pediatria, Funchal, October 6-8, 2010

Sousa AE and Foxall RB. Organized the Meeting “HIV-AIDS: Closing the Gap between Basic Research and Clinical Practice”. IMM, Lisboa, January 22-23, 2010.

Internationalization

Lopes AI. Member of the Pediatric Task Force of European Helicobacter Study Group: H pylori therapy in pediatrics – Multicenter study – sequential therapy protocol (Coordination: Megraud F, Koletzko S).

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 (2010) First use of thymus transplantation therapy for FOXP1 deficiency (nude/SCID): a report of two cases. *Blood* Published online Oct 26; doi:10.1182/blood-2010-06-292490. (Journal IF: 10.555).

Lopes AI. Editorial Board Member of the World Journal of Gastroenterology, the Journal of Pediatric Biochemistry, and the World Journal of Gastrointestinal Pharmacology and Therapeutics.

Prizes, honours and awards

Excellence Award in Immunology Mário Arala-Chaves 2010 to Iris Caramalho, Alcinda Melo, Elisa Pedro, Manuel P Barbosa, Rui MM Victorino, Ana E Sousa and M. Conceição Santos at the XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga, Portugal.

Portuguese Society for Immunology Prize “Best Image 2010” to Iris Caramalho, Braga, Portugal.

Prémio Astra-Zeneca / Revista Portuguesa de Imunoalergologia 2010 to Pereira da Silva S, Lopes da Silva S, Mascarenhas I, Pregal AL, Santos AS, Ferreira MB, Pedro E, Pereira Barbosa M. “Provocação com inibidores da cicloxigenase-2: percepção dos resultados e rentabilidade clínica”.

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

Ana E Sousa. Member of the Assessment Board for PhD and Post-Doc Fellowships, FCT

Ana E Sousa. President of the Sociedade Portuguesa de Imunologia

Advanced teaching

Marques JG. - *Staphylococcus aureus* metilino-resistente adquirido na comunidade - Abordagem e terapêutica. VIII Encontro de Infecçiology Pediátrica. Lisboa, December 10, 2010.

Lacerda JF. Transplante de Medula Óssea. II Simpósio de ciências da saúde. Transplantação: perspectiva imunológica. Lisboa, December 9, 2010

Sousa AE. Imunopatogénese da infecção VIH/SIDA. Mestrado em Análises Clínicas. Faculdade de Farmácia da Universidade de Lisboa. Lisboa, December 6, 2010.

Caramalho I. lectured at the Cell Imaging Module of the Programa Doutoral da Faculdade de Ciências Médicas, Lisboa. December 4, 2010.

Silva S. Lectured in the Course "Vacinas", Satellite to the XVII Jornadas de Pediatria, Departamento da Criança e da família do H.S.M. Lisboa, November 17, 2010

Marques JG. Vacinas – Princípios Gerais. Curso satélite das XVII jornadas de Pediatria “Vacinas”. Departamento da Criança e da família do HSM. Lisboa, November 17, 2010.

Marques JG. Vacinação em circunstâncias especiais. Curso satélite das XVII jornadas de Pediatria “Vacinas”. Departamento da Criança e da família do HSM. Lisboa, November 17, 2010.

Lacerda JF. Transplante de dador não familiar. Sessão plenária da Reunião Anual da Sociedade Portuguesa de Hematologia. Tróia, November 13, 2010

Pereira Santos MC Reacções adversas a fármacos. Curso Pós-graduado “Reacções adversas a fármacos: imunopatologia e clínica”, Universidade Lusófona, Lisboa, October-November, 2010
Marques JG. - Infecção VIH na Criança. Seminário do Instituto de Higiene e Medicina Tropical, Lisboa, September 28, 2010

Marques JG. - Crianças infectadas pelo VIH – a realidade portuguesa. Reunião do Grupo de Trabalho sobre Infecção VIH na Criança. Porto, September 24, 2010.

Caramalho I. Co-organized and lectured the course “Practical course on Image Acquisition in Immunology”, Instituto Gulbenkian Ciência, Oeiras, June 12-18, 2010.

Marques JG. Coordenação do II Curso de Formação da Sociedade de Infecçiology da Sociedade Portuguesa de Pediatria “Antimicrobianos em Pediatria”. Porto, May 27-28, 2010

Silva S. Lectured in the Course “Antimicrobianos em Pediatria”. Sociedade de Infecçiology da Sociedade Portuguesa de Pediatria. Porto, May 27-28, 2010.

Marques JG. Princípios e regras da terapêutica antibiótica. II Curso de Formação da Sociedade de Infecçiology da SPP – Antimicrobianos em Pediatria. Porto, May 27-28, 2010

Sousa AE. Imunodeficiência associada à infecção VIH. Instituto de Ciências Biomédicas Abel Salazar. Porto, May 20, 2010

Sousa AE. HIV Immunopathogenesis. GABBA Immunology Course 2010. Porto, May 21, 2010

Lopes AI. Organizer and lecturer of the Post-Graduate Pediatric Gastroenterology Course “Celiac disease in childhood”, Section of Pediatric Gastroenterology, President (Portuguese Society of Pediatrics) Lisboa, May 14-16, 2010

Marques JG. Infecção VIH – Panorama na Criança Portuguesa. IV Jornadas do Departamento de Pediatria, Hospital Fernando Fonseca, Amadora, April 22-23, 2010.

Lacerda JF. The clinic – Hematological tumours. Biology of Cancer Nanocourse. Programa de Doutoramento do Instituto de Medicina Molecular. Lisboa, April 20, 2010

Lacerda JF. Púrpura trombocitopénica imune – novas guidelines de tratamento. Simpósio HOPE – Hematologia e Oncologia Para Especialistas. Lisboa, April 17, 2010

Lacerda JF. Cell based therapy in oncology. Programa de Doutoramento em Ciências da Saúde. Faculdade de Medicina da Universidade de Coimbra. Coimbra, March 26, 2010

Sousa AE. Imunopatologia da infecção VIH/SIDA. VII Curso pós-graduado em tuberculose e infecção por VIH. FMUL, Lisboa, March 25, 2010

Lacerda JF. Transplante de progenitores hematopoiéticos. Encontro de doentes da Associação Portuguesa de Leucemias e Linfomas. Porto, March 13, 2010

Lacerda JF. Púrpura trombocitopénica imune – novas *guidelines* de tratamento. Simpósio LIFE - Liderança e Inovação com Farmacêuticos de Excelência. Torres Vedras, March 6, 2010

Marques JG. Infecções de repetição na infância: quando suspeitar de imunodeficiências primárias? II Conferência Moçambicana de Pediatria. MAPUTO. February 24-26, 2010

Marques JG. Infecções por Herpes simplex: quem e como tratar. 5º Curso de Infecçologia Pediátrica. Coimbra, January 28-29, 2010

Sousa AE. HIV Immunopathogenesis. Immunology Module, Doctoral Programme in Experimental Biology and Biomedicine 2009/10. Coimbra, January 8, 2010

Caramalho I. Lectured at the Immunology Module of the Doctoral Programme in Experimental Biology and Biomedicine, Coimbra. January 4, 2010.

Science and Society

Silva S. Co-organized a meeting with patients with Primary Immunodeficiencies and their families in collaboration with International Patient Organisation for Primary Immunodeficiencies (IPOPI) / Grupo Português de Imunodeficiências Primárias (GPIP) / Associação Portuguesa de Doentes com Imunodeficiências Primárias (APDIP). IMM, Lisboa, September 23, 2010.

Lopes AI, Investigação médica em Portugal. Oportunidades e constrangimentos. Sociedade de Ciências Médicas de Lisboa, Lisboa, June 21, 2010.

Sousa AE. “Collaborating with the hospital in the identification of new strategies for immunological reconstitution and targets for immune-based therapies”. Sessão: Novas Terapias Biomédicas. Ciência 2010: Ao Encontro da Ciência. July 5, 2010.

Master and Ph.D. thesis completed

PhD Thesis

Adriana Silva de Albuquerque (2010) “Strategies for T-cell reconstitution: insights from human clinical models”. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Ana Espada de Sousa.

Helena Isabel Marques Nunes Cabaço (2010) “Development of regulatory T cells in the human thymus: one step beyond”. 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)

Filipa Sousa, M.D. (2010) Supervisor: Maria Conceição Pereira-Santos.

Master Thesis

The UIC had a significant contribution for the supervision of the final “thesis” work of the MsC degree in Medicine at the FMUL.

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 rejection, 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.

Immune protection involves the generation of immunological memory, through which an individual acquires the capacity to respond better to the initial antigen on re-exposure. Immune and neuronal memory are characterized by obvious differences, but also striking parallels. Indeed, mounting evidence indicates that some of the most potent neurotrophic factors may act on or are produced by immune cells.

Our research projects are centred on the cellular and molecular mechanisms governing lymphoid organogenesis and on the role of neurotrophic factors in 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
Francisca Almeida	Master student
Silvia Madeira	Master student
Inês Barbosa	Technician
Lara dos Santos	Technician

Keywords/Research Areas

Lymphoid organogenesis
Haematopoiesis
Lymphocyte function
Lymphocyte development

Major scientific achievements

The Immunobiology unit (UIB) was created in October 2008 at the IMM. In 2010 we concentrated our efforts in consolidating our research by tackling the following projects:

Differential mechanisms for enteric organogenesis: We investigated which mechanisms empower cells from different embryonic origin, ie, nervous and haematopoietic cells, to use RET signalling but with such different enteric colonisation outcomes. We found that haematopoietic cells responded efficiently to all known RET ligands *in trans*, which was in great contrast to nervous cells that responded exclusively to the ligand GDNF *in cis*. This unique property relied on haematopoietic single cell expression signature. Indeed, conversely to nervous cells, haematopoietic cells expressed *Ret* but did not co-express *Ret* co-receptors. To further support this hypothesis, we reprogrammed haematopoietic cells to co-express *Gfra1 in cis* and showed that in this context they responded preferentially to GDNF, mimicking nervous cells responses. These data have recently been submitted for publication.

Role of neurotrophic factors during embryonic haematopoiesis: We found that *Ret* and its co-receptors *Gfra1* and *Gfra2* were expressed in embryonic Haematopoietic Stem Cells (HSCs). Using mice homozygous for a null mutation of *Ret* we found that the HSC compartment of *Ret* deficient embryos was profoundly reduced when compared to their WT littermate controls. Moreover, *Ret* null HSCs had a reduction of quiescent cells, which also correlated with a loss of reconstitution potential and poor competitive transplantation fitness. RET acted in a cell-intrinsic manner and through the anti-apoptotic genes *Bcl2* and *Bcl2l1*. These finding strongly implicate RET signalling involvement in early foetal haematopoiesis, suggesting that GFLs might be used to modulate haematopoietic differentiation.

Role of neurotrophic factors in T cell differentiation and function: We found that *Ret* is expressed by memory T cells but completely absent in naive T cells. *Ret* ablation had no impact on T cell development, proliferation and/or expansion. Conversely, we found that *Ret* play an important role in T cell differentiation into polarised conditions. Both *in vitro* and *ex vivo Ret* deficient T cells had impaired Th1 and Th17 polarising capacity, but differentiated very efficiently into a Th2 cytokine profile.

Generation of transgenic models for de-regulated *Ret* expression in lymphocytes: In the laboratory we have generated different transgenic constructs taking advantage of the human CD2 (*hCD2*) regulatory elements We have generated a *hCD2-Ret* construct that will enforce RET over-expression in lymphocytes, *hCD2-RetMEN2A* and *hCD2-RetMEN2B* that determine the expression of constitutively activated forms of RET. 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: RA has recently been involved in lymph node development through induction of CXCL13 expression. Contrary to lymph node development we found that Peyer's patch development was severely compromised when RA signalling was impaired. Importantly, similarly to RET signalling, RA induced haematopoietic cell clustering in explants organ cultures. However, haematopoietic clustering induced by RET ligands was only marginally affected by RA signalling block and absence of RET signalling did not impact on RA mediated clustering revealing that RA acts independently of RET signalling. Interestingly the chemokine CXCL13 was not modulated upon RA stimulation of gut samples neither affected clustering efficiency induced by RA. Genetic analysis revealed that RA signalling leads to a genetic signature that differs from what was previously described during LN development.

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: 14.5; Citations: 0)

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: 26.00; Citations: 19)

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: 34.48; Citations: 35)

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: 14.5; Citations: 26)

Veiga-Fernandes, H. and Rocha, B. (2004). High expression of active CDK6 in the cytoplasm of CD8 memory cells favors rapid division. *Nature Immunol* **5**, 31-37. (Journal IF: 26.00; Citations: 53)

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

Menzel U, Ktistaki E, Tolaini M, Veiga-Fernandes H, Kioussis D (2010). Replication allows inactivation of a knocked-in locus control region in inappropriate cell lineages. *Proc Natl Acad Sci U S A*. 2010 107(39):16928-33. (Journal IF: 9.43, Citations: 0)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010). Life without geminin. *Cell Cycle*. 16:3181-5. (Journal IF: 4.8, Citations: 0)

Foster KE, Gordon J, Cardenas K, Veiga-Fernandes H, Makinen T, Grigorieva E, Wilkinson DG, Blackburn CC, Richie E, Manley NR, Adams RH, Kioussis D, Coles MC (2010). EphB-ephrin-B2 interactions are required for thymus migration during organogenesis. *Proc Natl Acad Sci U S A*. 107:13414-9. (Journal IF: 9.43, Citations: 0)

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: 14.5; Citations: 0)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010). Differential geminin requirement for proliferation of thymocytes and mature T cells. *J Immunol.* 184(5):2432-41. (Journal IF: 5.6; Citations: 1)

Almeida AR, Ciernik IF, Sallusto F, Lanzavecchia A (2010). CD4+ CD25+ Treg regulate the contribution of CD8+ T-cell subsets in repopulation of the lymphopenic environment. *Eur J Immunol.* 2010 Dec;40(12):3478-88.

Other publications International

Coles M, Kioussis D, Veiga-Fernandes H (2010). Cellular and molecular requirements in lymph node and Peyer's patch development. *Prog Mol Biol Transl Sci.* 92:177-205.

Coles M, Kioussis D, Veiga-Fernandes H (2010). Commentary on "lymphoid tissue inducer cells and the evolution of CD4 dependent high-affinity antibody responses". *Prog Mol Biol Transl Sci.* 92:175-6.

Veiga-Fernandes H, Foster K, Patel A, Coles M, Kioussis D. (2010). Visualisation of lymphoid organ development. *Methods Mol Biol.* 616:161-79.

Cupedo T, Coles M, Veiga-Fernandes H. (2010). 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. (2010). Structure and development of Peyer's patches in humans and mice. In: *Developmental Biology of Peripheral Lymphoid Organs.* Springer (Heidelberg). P. 97-106.

Invited Lectures and Seminars

Veiga-Fernandes, H. Enteric Lymphoid organogenesis. IEO, Milan, Italy. January 2010

Veiga-Fernandes, H. Neurotrophic factors and Immune cell functions. YIP 2010 meeting. Heidelberg, Germany. May 2010.

Veiga-Fernandes, H. Neurotrophic factors and Immune cell functions. ICVS, Braga, Portugal. May 2010.

Veiga-Fernandes, H. Lymphoid organogenesis. ENII 2010. Cappelletti, Italy. May 2002.

Veiga-Fernandes, H. Enteric Lymphoid organogenesis. ICH, Milan, Italy. January 2010

Communications in International Conferences

Afonso Almeida. Role of proto-oncogene *Ret* during lymphocyte development and function. Interdisciplinary Group for Hirschsprung's Disease Meeting. National Institutes of Health, Bethesda, Maryland, USA. November 2010.

Communications in National Conferences

Fonseca-Pereira, D. Role of proto-oncogene *Ret* in foetal haematopoiesis. XXXVI Reunião annual da Sociedade Portuguesa de Imunologia. Braga, Portugal. September 2010.

Fonseca-Pereira, D. Role of proto-oncogene *Ret* in foetal haematopoiesis. IV IMM PhD Student Meeting. Lisboa, Portugal. November 2010.

Afonso Almeida. The role of the RET tyrosine kinase receptor in T cell function. XXXVI Reunião annual da Sociedade Portuguesa de Imunologia. Braga, Portugal. September 2010.

Francisca Almeida. Retinoic Acid in Enteric Lymphoid Organogenesis. XXXVI Reunião annual da Sociedade Portuguesa de Imunologia. Braga, Portugal. September 2010.

Internationalization

Menzel U, Ktistaki E, Tolaini M, Veiga-Fernandes H, Kioussis D (2010). Replication allows inactivation of a knocked-in locus control region in inappropriate cell lineages. *Proc Natl Acad Sci U S A*. 2010 107(39):16928-33. (Journal IF: 9.43, Citations: 0)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010). Life without geminin. *Cell Cycle*. 16:3181-5. (Journal IF: 4.8, Citations: 0)

Foster KE, Gordon J, Cardenas K, Veiga-Fernandes H, Makinen T, Grigorieva E, Wilkinson DG, Blackburn CC, Richie E, Manley NR, Adams RH, Kioussis D, Coles MC (2010). EphB-ephrin-B2 interactions are required for thymus migration during organogenesis. *Proc Natl Acad Sci U S A*. 107:13414-9. (Journal IF: 9.43, Citations: 0)

Karamitros D, Kotantaki P, Lygerou Z, Veiga-Fernandes H, Pachnis V, Kioussis D, Taraviras S (2010). Differential geminin requirement for proliferation of thymocytes and mature T cells. *J Immunol*. 184(5):2432-41. (Journal IF: 5.6; Citations: 1)

Advanced teaching

Veiga-Fernandes H. Lymphoid organogenesis. GABBA PhD programme. Universidade do Porto, Portugal. May 2010.

Almeida A. Lymphocyte homeostasis. GABBA PhD programme. Universidade do Porto, Portugal. May 2010.

Veiga-Fernandes H. Lymphoid organogenesis. ENII Summer School. Cappo Caccia. May 2010

Science and Society

Veiga-Fernandes, H. Migrações e memórias celulares. Café Ciência, Bragança, Portugal. April 9, 2010.

Master thesis completed

Silvia Madeira (2010) “Role of RET tyrosine kinase in foetal haematopoiesis.” Master thesis. Faculdade de Ciências e tecnologia. Universidade de Coimbra. Supervisor: Henrique Veiga-Fernandes.

Francisca Almeida (2010) “Retinoic Acid in Enteric Lymphoid Organogenesis” Master thesis. Faculdade de Ciências. Universidade de Lisboa. Supervisor: Henrique Veiga-Fernandes.

Malaria Unit

Major interests / Objectives

Plasmodium, the causative agent of malaria has a complex life cycle that oscillates between two hosts. In its mammalian host, *Plasmodium* infects very distinct cells types (hepatocytes and red blood cells) and while hepatocyte-*Plasmodium* interactions during liver stages constitute an ideal target for intervention strategies, the blood stages of infection constitute the ultimate goal for therapeutic strategies against the disease. The overall goal of the IMM's Malaria Unit is to elucidate the role of host components in the establishment of a malaria infection (liver stage) as well as in the development of pathology (blood stage). The laboratory is focused on understanding the biology of *Plasmodium* infection and on discovering and developing novel drugs or vaccines to treat and eradicate malaria.

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
Claúdia Cunha	PhD – Post-doc	FCT Fellowship
Daniel Carapau	PhD – Post-doc	FCT Fellowship
Eliana Real	PhD – Post-doc	EMBO Fellowship
Ghislain Cabal	PhD – Post-doc	Marie Curie Fellowship
Liliana Mancio	PhD – Post-doc	EMBO Fellowship
Kirsten Hanson	PhD – Post-doc	Marie Curie Fellowship
Peter Liehl	PhD – Post-doc	FCT Fellowship
Vanessa Luís	PhD – Post-doc	EMBO Fellowship
		Fellowship (from HHMI grant) until 31 st August
	PhD student	Fellowship (from FCT grant) between 1 st September to 31 st December
Carina Santos		
Maurice Itoe	PhD student	Marie Curie ITN Fellowship
Patricia Inácio	PhD Student	FCT Fellowship
Sílvia Portugal	PhD Student	FCT Fellowship
Teresa Nazareth	PhD Student	FCT Fellowship
		Fellowship (from FCT grant) between 1 st October to 31 st December
Patrícia Meireles	Researcher	
Catarina Marques	Msc student	-
Inês Albuquerque	Msc student	-
Joana Sales	Msc student	-
Joana Carrelha	Msc student	-

Mariana Almeida	Internship Laboratory and	- Fellowship (from HHMI grant) until 31 st August
Fernanda Baptista	Insectary manager Laboratory and	Fellowship (from EVIMALAR grant) since 1 st September
Ana Parreira	Insectary technician	Fellowship (from FCT grant) until 31 st December

Keywords/Research Areas

Cell and Molecular Biology
Plasmodium biology
 Microbiology
 Host-*Plasmodium* Cellular and Molecular Interactions
 Malaria Pathogenesis
 Anti-malarial intervention

Major scientific achievements

The Malaria Unit has contributed decisively to the identification of host factors that contribute to the establishment of a malaria infection (liver stage) and to malaria pathology (blood stage). We have exploited the post-genome knowledge of the host in order to understand the requirements that govern *Plasmodium* development inside the hepatocyte. We have not only revealed important modifications occurring in the host cell and liver throughout infection but also identified several crucial factors that govern *Plasmodium* infection of hepatocytes (Rodrigues et al., 2008; Prudêncio et al., 2008; Albuquerque et al., 2009; Prudêncio et al., 2009).

On the other hand, we have been able to establish the role of several host factors that dictate the susceptibility or resistance to the onset of severe disease and death, as well as to establish new animal models to study malaria-associated disease (Pamplona et al., 2007; Pamplona et al., 2009; Epiphany et al., 2010; Baptista et al., 2010).

Recent Most Relevant Publications

Ploemen IH, Prudêncio M, Douradinha BG, Ramesar J, Fonager J, van Gemert GJ, Luty AJ, Hermesen CC, Sauerwein RW, Baptista FG, Mota MM, Waters AP, Que I, Lowik CW, Khan SM, Janse CJ, Franke-Fayard BM. (2009). Visualisation and quantitative analysis of the rodent malaria liver stage by real time imaging. *PLoS One*. 4(11):e7881 (IF 4.351, Citations: 2)

Albuquerque SS, Carret C, Grosso AR, Tarun AS, Peng X, Kappe SH, Prudêncio M, Mota MM. (2009). Host cell transcriptional profiling during malaria liver stage infection reveals a coordinated and sequential set of biological events. *BMC Genomics*. 10:270. (IF: 3.759; Citations: 1)

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 9,125, Citations: 10)

Pamplona A, Ferreira A, Balla J, Jeney V, Balla G, Epiphanio 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. *Nat Med.* Jun;13(6):703-10. (IF 26.382, Citations: 82)

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: 15.845; Citations: 54)

Ongoing Research Projects

2010/2013 New drugs for treating and eradicating malaria. FCT. Coordinator: Maria Mota. HMSP-CT/SAU-ICT/0068/2009, 300.000,00 €

2010/2013 Respiratory tract infections & malaria: a new case of mutual interactions?. FCT. Coordinator: Maria Mota. PTDC/SAU-MII/108578/2008, 190.850,00 €

2010/2013 Unravelling the secrets of *Plasmodium* liver stage: a multi-directional approach. FCT. Coordinator: Maria Mota. PTDC/SAU-GMG/100313/2008, 199.943,00 €

2010/2013 The influence of bile acids on malaria liver infection. FCT. Coordinator: Miguel Prudêncio. PTDC/SAU-MII/099118/2008, 171.482,00 €

2010/2012 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 host cell kinases in *Plasmodium* development inside hepatocytes during the liver stage of malaria infections. FCT. Coordinator: Maria Mota. PTDC/BIA-MIC/72211/2006, 135.000,00 €

2008/2011 The role of SR-BI in malaria infection. FCT. Coordinator: Miguel Prudêncio. PTDC/BIA-BCM/71920/2006, 118.000,00 €

2005/2010 Functional genomics in malaria – which are the host cell molecules and pathways required for *Plasmodium* development inside hepatocytes? Howard Hughes Medical Institute. Coordinator: Maria M. Mota (HHMI#55005523, International Research Scholars Program. Infectious Diseases and Parasitology - 2005), 133106,33 €

Publications in peer review Journals

Baptista FG, Pamplona A, Pena AC, Mota MM, Pied S, Vigário AM. (2010). Accumulation of *Plasmodium berghei*-infected red blood cells in the brain is crucial for the development of cerebral malaria in mice. *Infect Immun* 78(9):4033-9 (IF -, Citation 0)

Epiphanio S, Campos MG, Pamplona A, Carapau D, Pena AC, Ataíde R, Monteiro CA, Félix N, Costa-Silva A, Marinho CR, Dias S, Mota MM. (2010). VEGF promotes malaria-associated acute lung injury in mice. *PLoS Pathog* 6(5):e1000916 (IF -, Citation 0)

Liehl P, França A.R, Prudêncio M, Latz E, Zaidman-Rémy A, Mota MM. (2010). "Phosphothioate Oligodeoxynucleotides inhibit Plasmodium sporozoite gliding motility", *Cell. Microbiol.*, **12**, 506-515

Invited Lectures and Seminars

Mota, M.M., Harvard School of Public Health. Invited Seminar. July 9, 2010, Boston, USA (Oral presentation: "*Approaching Malaria from Various Angles*").

Prudêncio, M. Workshop "Latest developments in malaria research towards eradication within Portugal and Spain", July 16, 2010, Madrid, Spain (Oral presentation: "Hybrid molecules to target the liver and blood stages of Plasmodium infection").

Mota, M.M. MIT-Portugal Program. Invited Seminar, August 31, 2010, Cambridge, USA (Oral presentation: "Approaching Malaria from the Host Side")

Mota, M.M. Johns Hopkins School of Public Health. Invited seminar. August, 2010, Baltimore, USA. (Oral presentation)

Mota, M. M. "Parasite to prevention: Advances in the understanding of malaria". October 20-22, 2010. Edinburgh, UK (Oral presentation: "Liver stage malaria")

Mota, M. M. EMBO Conference Series: At the joint edge of cellular microbiology & cell biology. Kraków, Poland (Oral presentation: "Host-*Plasmodium* interactions")

Communications in International Conferences

Mota, M. Crossroads in Biology 2010, Cologne, Germany, February 3-5 2010 (Oral presentation)

Mota, M. Keystone Malaria: New Approaches to Understanding Host-Parasite Interactions, April 11-16, 2010, Colorado, USA (Oral presentation)

Mota, M & Itoe, M. Sixth Annual BioMalPar Conference on Biology and Pathology of the Malaria Parasite, May 3-8, 2010, Heidelberg, Germany (Poster presentation)

Mota, M. CRIMALDDI Consortium Workshop N° 4 "Stage-specific screening methods", May 26, 2010, Geneva, Switzerland (Oral Presentation)

Hanson, K. Meeting "Intellectual Property Rights workshop for Marie Curie Fellows", June 21-23, 2010. Munique, Germany.

Santos, C. 2010 (21st) Annual Molecular Parasitology Meeting, September 12-16, 2010, Woods Hole, MA, USA (Poster presentation)

Cabal, G. EMBO Conference Series: At the joint edge of cellular microbiology and cell biology, October 9-14, 2010. Kraków, Poland (Poster presentation)

Mota, M. EMBO Conference Series: At the joint edge of cellular microbiology and cell biology, October 9-14, 2010. Kraków, Poland (Oral presentation)

Mota, M. “Parasite to prevention: Advances in the understanding of malaria”. October 20-22, 2010. Edinburgh, UK.(Oral presentation)

Liehl, P. “Parasite to prevention: Advances in the understanding of malaria”. October 20-22, 2010. Edinburgh, UK.(Poster presentation).

Itoe, M. Genes & Genomes in the Tropics: Advanced course, Nov 1-19, 2010, Kampala, Uganda (Oral Presentation)

Liehl, P. Meeting of Network EVImalaR - Cluster 1. December 14-18, 2010. Cambridge, UK (Oral Presentation)

Organisation of Conferences

Mota M. Organizer of EVImalaR Cluster II Meeting, November 4-6, 2010, Instituto de Medicina Molecular, Lisbon, Portugal

Advanced teaching

Prudêncio, M. organized the course “Biosafety training for use of the IMM BSL3 Facility”, October 27-28, 2010, Instituto de Medicina Molecular, Lisbon.

Master and Ph.D. thesis completed

Sílvia Portugal (2010) “Interactions of Plasmodium blood and liver stages within a single host”. Faculdade de Medicina da Universidade de Lisboa. Supervisors: Maria Mota, PhD degree

Carina Santos (2010) “Plasmodium Fitness: The Importance of being Prepared Plasmodium sporozoites post-transcriptional regulation of gene expression and host cell cytoskeleton dynamics during Plasmodium intra-hepatic development”. Faculdade de Ciências e Tecnologia da Universidade de Coimbra. Supervisors: Maria Mota (IMM) e Ana Luisa Carvalho (FCT-UC). PhD degree

Catarina Marques (2010) “The importance of apoptosis of Plasmodium-infected cells in the generation of immunity against malaria infection”. Faculdade de Ciências da Universidade de Lisboa. Supervisors: Miguel Prudêncio(IMM) e Rui Malhó (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
Liliana Mâncio, PhD	Post Doc Fellowship, EMBO
Daniel V. Correia	PhD Fellowship, FCT
Telma Lança	PhD Fellowship, FCT
Ana deBarros	PhD Fellowship, FCT
Nina Schmolka	PhD Fellowship, IMM
Natacha Gonçalves Sousa	Research grant, FCT

Keywords/Research Areas

T cell development/ differentiation
 T cell activation
 Tumour immunology
 Malaria immunity and pathogenesis

Major scientific achievements in 2010

- Our lab published 10 papers in peer-reviewed international journals, 8 of which with impact factor >5.
- We obtained a 1.5 million euro Starting Grant from the European Research Council.
- B. Silva-Santos was selected for the EMBO Young Investigator Programme.
- Our work was distinguished with the 2nd Prize of the CESPUI International Award, and with the best poster of the Annual Meeting of the Portuguese Society of Immunology.

Recent Most Relevant Publications

Ribot JC, deBarros A, Pang DJ, Neves JF, Peperzak V, Girardi M, Borst J, Hayday AC, Pennington DJ and Silva-Santos B (2009). CD27 is a thymic determinant of the balance between IFN- γ - and IL-17-producing $\gamma\delta$ T cell subsets. *Nature Immunology* **10**, 427-436. (Journal IF: 26.218, Citations: 35)

Correia DV, d'Orey F, Cardoso BA, Lança T, Grosso AR, deBarros A, Martins LR, Barata JT and Silva-Santos B (2009). Highly active microbial phosphoantigen induces rapid yet sustained MEK/ Erk- and PI-3K/ Akt-mediated signal transduction in anti-tumor human $\gamma\delta$ T cells. *PloS ONE*, e5657. (Journal IF: 4.415, Citations: 11)

Gomes AQ, Correia DV, and Silva-Santos B (2007). Non-classical MHC class Ib proteins as determinants of tumour immunosurveillance. *EMBO Rep* **11**, 1024-30. (Journal IF: 8.175, Citations: 3)

Pennington DJ, Silva-Santos B, Silberzahn T, Escorcio-Correia M, Dyson PJ and Hayday AC (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: 51)

Silva-Santos B, Pennington DJ and Hayday AC (2005). Lymphotoxin-mediated regulation of $\gamma\delta$ T cell differentiation by $\alpha\beta$ T cell progenitors. *Science* **307**, 925-928. (Journal IF: 31.853, Citations: 68)

Ongoing Research Projects

- | | |
|-----------|--|
| 2007/2011 | Innate Mechanisms of Tumor Immunossurveillance. European Molecular Biology Organization, Installation Grant, €250 000. PI: B.Silva-Santos. |
| 2008/2010 | Identification of ligands for $\gamma\delta$ T cell receptors: a genomics/ transcriptomics approach. Fundação para a Ciência e Tecnologia, PTDC/BIA-BCM/71663/2006, €115 000. 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

Gomes AQ*, Martins DS* and Silva-Santos B (2010) Targeting $\gamma\delta$ T-lymphocytes for cancer immunotherapy: from novel mechanistic insight to clinical application. *Cancer Res* **70** (24), 10024-7. (Journal IF: 7.543) (* co-first authors)

Ribot JC, Chaves-Ferreira M, d'Orey F, Wencker M, Gonçalves-Sousa N, Decalf J, Simas JP, Hayday AC 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)

Epiphany S*, Campos MG*, Pamplona A*, Carapau D, Pena AC, Ataíde R, Monteiro CA, Félix N, Costa-Silva A, Marinho CRF, Dias S, Mota MM (2010) VEGF Promotes Malaria-associated Acute Lung Injury in Mice. *PLoS Pathogen*, **6** (5), e1000916 (*co-first authors). (Journal IF: 8.906)

Gomes AQ*, Correia DV*, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, 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) (* co-first authors)

Lança T, Correia DV, Moita CF, Raquel H, Ferreira C, Ramalho JS, Barata JT, Moita LF, Gomes AQ and Silva-Santos B (2010) The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. *Blood*: **115** (12), 2407-11. (Journal IF: 10.555)

Baptista FG, Pamplona A, Pena AC, Mota MM, Pied S, Vigário AM (2010) Accumulation of Plasmodium-infected red blood cells in the brain is crucial for the development of cerebral malaria in mice. *Infect Immunity* **78** (9), 4033-9. (Journal IF: 4.205)

Monteiro M, Almeida CF, Caridade M, Ribot JC, Duarte J, Água-Doce A, Wollenberg I, Silva-Santos B and Graça L (2010) Identification of regulatory Foxp3+ invariant Natural Killer T cells induced by TGF-beta. *J Immunol* **185** (4), 2157-63. (Journal IF: 5.646)

Silva-Santos B (2010) Promoting angiogenesis within the tumor microenvironment: the secret life of IL-17-producing $\gamma\delta$ T cells. *Eur J Immunol* **40** (7), 1873-1876. (Journal IF: 5.179)

Nunes-Cabaço H, Ribot JC, Caramalho I, Serra-Caetano A, Silva-Santos B* and Sousa AE* (2010) Foxp3 induction in human and murine thymus precedes the CD4⁺ CD8⁺ stage but requires early T cell receptor expression. *Immunol Cell Bio* **88** (5), 523-8. (Journal IF: 4.200) (* Co-senior authors)

Gonçalves-Sousa N, Ribot JC, deBarros A, Correia DV, Caramalho I and Silva-Santos B (2010) Inhibition of murine $\gamma\delta$ lymphocyte expansion and effector function by regulatory $\alpha\beta$ T-cells is cell-contact dependent and sensitive to GITR modulation. *Eur J Immunol* **40** (1), 61-70. (Journal IF: 5.179)

Invited Lectures and Seminars

Silva-Santos B. Differentiation and activation of $\gamma\delta$ T lymphocytes. Instituto de Ciências da Vida e da Saúde, Universidade de Braga, Portugal, January 12, 2010.

Silva-Santos B. Immune responses to **Plasmodium** infection mediated by mouse T lymphocytes. Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Portugal, April 19, 2010.

Silva-Santos B. CD70-CD27 costimulation in $\gamma\delta$ T cell differentiation and activation. College of Life Sciences, University of Dundee, Scotland, July 1, 2010.

Communications in International Conferences

Ribot J. C., deBarros A., Lança T., Correia D. V., Chaves-Ferreira M., d'Orey F., Gomes A. Q. and Silva-Santos B. CD27, NKG2D and Toll-like receptors provide critical signals for the activation of $\gamma\delta$ T lymphocyte subsets. Keystone Symposium – Lymphocyte Activation and gene Expression. Breckenridge, Colorado, USA, 27 February-4 March 2010 (Oral Presentation).

Correia D.V., Gomes A.Q., Grosso A.R., Lança T., Ferreira C., Lacerda J.F., Barata J.T., Gomes da Silva M. and Silva-Santos B. Identification of a panel of ten cell surface protein antigens associated with immunotargeting of leukemias and lymphomas by peripheral blood gamma delta T cells. Gordon Research Conference - Immunochemistry & Immunobiology, Les Diablerets (Switzerland), May 16-21, 2010 (Poster Presentation).

Ribot J.C., Chaves-Ferreira M., d'Orey F., deBarros A., Neves J., Pang J., Decalf J., Peperzak V., Borst J, Hayday A.C., Simas P., and Silva-Santos B. CD27 controls the thymic differentiation and peripheral expansion of IFN- γ producing $\gamma\delta$ T cells. 4th International $\gamma\delta$ T cell conference, Kiel (Germany), May 19-21, 2010 (Oral presentation)

Lança T., Correia D. V., Moita C. F., Raquel H., Neves- Costa A., Ferreira C., Ramalho J. S., Barata J. T., Moita L. F., Gomes A. Q. and Silva-Santos B. The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. 4th International $\gamma\delta$ T cell conference, Kiel (Germany), May 19-21, 2010 (Poster Presentation).

deBarros A., Chaves-Ferreira M., d'Orey F., Correia D. V. and Silva-Santos B. CD27-CD70 signals promote human V γ 9V δ 2 T cell proliferation and cytokine secretion. 4th International $\gamma\delta$ T cell conference, Kiel (Germany), May 19-21, 2010 (Poster presentation).

Ribot J. C., Chaves-Ferreira M., d'Orey F., Gonçalves-Sousa N., Decalf J., Simas J. P. and Silva-Santos B. CD27 and Toll-like receptors provide activation signals crucial for the expansion of distinct pro-inflammatory $\gamma\delta$ T cell subsets. 14th International Congress of Immunology, Kobe, Japan, August 22-27, 2010 (Oral presentation).

Lança T., Correia D. V., Moita C. F., Raquel H., Neves- Costa A., Ferreira C., Ramalho J. S., Barata J. T., Moita L. F., Gomes A. Q. and Silva-Santos B. The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. 14th International of Congress of Immunology, Kobe (Japan), August 22-27, 2010 (Poster Presentation).

Communications in National Conferences

Lança T., Correia D. V., Moita C. F., Raquel H., Neves- Costa A., Ferreira C., Ramalho J. S., Barata J. T., Moita L. F., Gomes A. Q. and Silva-Santos B. The MHC class Ib protein ULBP1 is a non-redundant determinant of leukemia/ lymphoma susceptibility to $\gamma\delta$ T-cell cytotoxicity. XXXVI Annual Meeting of the Portuguese Society for Immunology (Braga), September 20-22, 2010 (Oral Presentation).

deBarros A., Chaves-Ferreira M., d'Orey F., Ribot J. and Silva-Santos B. CD70-CD27 interactions promote the survival and proliferation of Th1-biased human $\gamma\delta$ T cells. XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga (Portugal), September 20-22, 2010 (Poster presentation).

Ribot J.C., Chaves-Ferreira M., d'Orey F., Wencker M., Gonçalves-Sousa N., Decalf J., Simas P., Hayday A.C. and Silva-Santos B. Adaptive versus innate receptor signals selectively control the pool sizes of murine IFN- γ - or IL-17-producing $\gamma\delta$ T cells upon infection. XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga (Portugal), September 20-22, 2010 (Poster presentation)

Correia D.V., Mavilio D. and Silva-Santos B. Phytohaemagglutinin induces the expression of Natural Cytotoxicity Receptors in human $\gamma\delta$ T cells and enhances their cytotoxicity against tumor cells. XXXVI Annual Meeting of the Portuguese Society for Immunology, Braga (Portugal), September 20-22, 2010 (Poster Presentation).

Prizes, honours and awards

2nd Prize in “Prémio Internacional de Investigação CESPUP 5^a Edição” (2010) to Julie Ribot, Ana de Barros e Bruno Silva-Santos for the work “A critical role for CD27 in $\gamma\delta$ T lymphocyte activation and expansion during immune responses to infection”.

Best Poster Award at the XXXVI Annual Meeting of the Portuguese Society for Immunology (2010) to Ana de Barros et al., “CD70-CD27 interactions promote the survival and proliferation of Th1-biased human $\gamma\delta$ T cells”.

Advanced teaching

Silva-Santos B. lectured at the IMM “Biology of Cancer” nanocourse, IMM, 20 April 2010.

Silva-Santos B. lectured at the GABBA PhD course, Instituto de Biologia Molecular e Celular, Universidade do Porto, Portugal, 14 June 2010.

Silva-Santos B. lectured at the EMBO Young Scientists Forum, Prague, Czech Republic, 8-10 June 2010.

Silva-Santos B. co-organized and lectured the EMBO YIP PhD course “Spotlights on current biology”, EMBL, Heidelberg, Germany, 20-25 September 2010.

Science and Society

deBarros A. and Silva-Santos B (2010). “Visualização e Representação do Real em Imunologia”. Book chapter in “As Imagens com que a Ciência se faz”, published by Centro de Filosofia das Ciências da Universidade de Lisboa and Editora Fim de Século, Lisboa, Portugal.

Silva-Santos B. “A carreira de investigação em Biomedicina”. IX Seminário de Saídas Profissionais. Faculdade de Medicina, Universidade de Lisboa, 30 April 2010.

Silva-Santos B. “Activação linfocitária e reconhecimento molecular de células malignas”. Conferência Oncologia R&D. Pfizer, Porto Salvo, 29 May 2010.

Silva-Santos B. “Oportunidades profissionais para bioquímicos: a carreira de investigação”. Mesa Redonda: “Bioquímicos da FCUL, que carreira?”. Faculdade de Ciências, Universidade de Lisboa, 25 November 2010.

Silva-Santos B. appeared made the following media appearances:

Master thesis completed

Natacha Gonçalves Sousa (2010), “Controlo da actividade dos linfócitos T $\gamma\delta$ por células reguladoras CD4⁺ CD25⁺ Foxp3⁺”, Master of Science. Universidade Lusófona. 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, FML

Principal Investigators

José Melo Cristino, MD, PhD – Full Professor, FML

Thomas Hänseid, MD, PhD - Assistant Professor, FML

João Carriço, PhD - Assistant Investigator, FML

Research Team

Pedro Tiago Monteiro, PhD	Post Doc Fellowship, IMM
Sandra Aguiar	PhD Fellowship, FCT
Maria João Frias	PhD Fellowship, 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

Development of an MLST typing scheme for *S. disgalactiae* and description of frequent recombination with *S. pyogenes*.

Implementation of a streptococcal biofilm model and identification of the impact of prophage carriage in biofilm formation.

Description of the changes in the pneumococcal population in the post-vaccine era – identification of emerging serotypes and characterization of diverse lineages in serotype 19A

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.

Recent Most Relevant Publications

Aguiar SI, Serrano I, Pinto FR, Melo-Cristino J and Ramirez M (2008) The presence of the pilus locus is a clonal property among pneumococcal invasive isolates. *BMC Microbiol* **8**, 41 (IF: 2.890, Citations: 16)

Hänscheid T, Egan TJ, Grobusch MP (2007) Haemozoin: from melatonin pigment to drug target, diagnostic tool, and immune modulator. *Lancet Infect. Dis* **7**, 675-685. (IF: 15.583, Citations: 23)

Martins ER, Pessanha MA, Ramirez M, Melo-Cristino J and The Portuguese Group for the Study of Streptococcal Infections (2007) Analysis of group B streptococcal isolates from infants and pregnant women in Portugal revealing two lineages with enhanced invasiveness. *J Clin Microbiol* **45**, 3224-9. (IF: 4.162, Citations: 14)

Carriço JA, Silva-Costa C, Melo-Cristino J, Pinto FR, de Lencastre H, Almeida JS, Ramirez M (2006) Illustration of a common framework for relating multiple typing methods by application to macrolide-resistant *Streptococcus pyogenes*. *J Clin Microbiol* **44**, 2524-2532. (IF: 4.162, Citations: 36)

Pinho MD, Melo-Cristino J, Ramirez M and the Portuguese group for the study of streptococcal infections (2006) Clonal relationships between invasive and noninvasive Lancefield group C and G streptococci and *emm*-specific differences in invasiveness. *J Clin Microbiol* **44**, 841-846. (IF: 4.162, Citations: 15)

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)

2009/2011 Does malaria increase susceptibility to tuberculosis? The role of malaria-pigment induced immune-suppression, FCT Coordinator T. Hänscheid. PIC/IC/83214/2007. €150 000

2008/2011 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

2007/2011 Caracterização microbiológica e molecular de *Streptococcus spp.* patogénicos e sua importância na profilaxia e terapêutica das infeções humanas em Portugal. Fundação Calouste Gulbenkian. Coordinator J. Melo Cristino, €125 045

2010/2011 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

Carrolo M, Frias MJ, Pinto FR, Melo-Cristino J and Ramirez M (2010) Prophage spontaneous activation promotes DNA release enhancing biofilm formation in *Streptococcus pneumoniae*. *PLoS ONE* **5**, e15678. (Journal IF: 4.351, Citations: 0)

Campuzano-Zuluaga G, Hanscheid T and Grobusch MP (2010) Automated haematology analysis to diagnose malaria. *Malar J* **9**, 346. (Journal IF: 2.995, Citations: 0)

Ramirez M and Melo-Cristino J (2010) Expanding the diagnosis of pediatric bacteremic pneumococcal pneumonia from blood cultures to molecular methods: advantages and caveats. *Clin. Infect. Dis* **51**, 1050-1052. (Journal IF: 8.195, Citations: 0)

Hänscheid T and Grobusch MP (2010) Biosafety and tuberculosis laboratories in Africa. *Lancet Infect Dis* **10**, 582-583. (Journal IF: 15.583, Citations: 0)

McMillan DJ, Bessen DE, Pinho M, Ford C, Hall GS, Melo-Cristino J and Ramirez M (2010) Population genetics of *Streptococcus dysgalactiae* subspecies *equisimilis* reveals widely dispersed clones and extensive recombination. *PLoS ONE* **5**, e11741. (Journal IF: 4.351, Citations: 0)

Melo-Cristino J, Santos L, Silva-Costa C, Friães A, Pinho MD and Ramirez M (2010) The Viriato Study: Update on antimicrobial resistance of microbial pathogens responsible for

community-acquired respiratory tract infections in Portugal. *Paediatr. Drugs* **12**, 11-17. (Journal IF: NA, Citations: 0)

Aguiar SI, Brito MJ, Gonçalo-Marques J, Melo-Cristino J and Ramirez M (2010) Serotypes 1, 7F and 19A became the leading causes of pediatric invasive pneumococcal infections in Portugal after 7 years of heptavalent conjugate vaccine use. *Vaccine* **28**, 5167-73 (Journal IF: 3.616, Citations: 1)

Pinho MD, Melo-Cristino J and Ramirez M (2010) Fluoroquinolone resistance in *Streptococcus dysgalactiae* subsp. *equisimilis* and evidence for a shared global gene pool with *Streptococcus pyogenes*. *Antimicrob. Agents Chemother.* **54**, 1769-1777. (Journal IF: 4.802, Citations: 0)

Martins ER, Melo-Cristino J and Ramirez M (2010). Evidence for rare capsular switching in *Streptococcus agalactiae*. *J Bacteriol* **192**, 1361-1369 (Journal IF: 3.940, Citations: 0)

Brilha S, Proença H, Cristino JM and Hänscheid T (2010) Use of flow cytometry (Sysmex) UF-100) to screen for positive urine cultures: in search for the ideal cut-off. *Clin. Chem. Lab. Med* **48**, 289-292. (Journal IF: 1.886, Citations: 1)

Simões AS, Sá-Leão R, Eleveld MJ, Tavares DA, Carriço JA, Bootsma HJ and Hermans PWM (2010) Highly penicillin-resistant multidrug-resistant pneumococcus-like strains colonizing children in Oeiras, Portugal: genomic characteristics and implications for surveillance. *J Clin Microbiol* **48**, 238-46 (Journal IF: 4.162, Citations: 1)

Aguiar SI, Pinto FR, Nunes S, Serrano I, Melo-Cristino J, Sá-Leão R, Ramirez M and de Lencastre H (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. (Journal IF: 4.162, Citations: 4)

Other publications National

Ramirez M. 2010. Resistência em bactérias de Gram positivo. *Cadernos de Saúde* 3:87-92.

Vieira, A.M., Machado, M.V., Lito, L., Melo Cristino, J., Fernandes, A., Maldonado, R., Valente, A., Palma, R., Alexandrino, P., Velosa, J. 2010. Diarreia associada a *Clostridium difficile* num hospital central. *Jornal Português de Gastrenterologia* **17**: 10-17.

Invited Lectures and Seminars

J. Melo-Cristino. O Laboratório de Microbiologia e a Pediatria. 5º Curso de Infecçologia Pediátrica. Coimbra, Portugal. January 28-29, 2010

J. Melo-Cristino. Evolução da resistência microbiana aos antibióticos. IV Reunião do Departamento de Pediatria do Hospital Fernando da Fonseca, E.P.E. Lisboa, Portugal. April 23, 2010

M. Ramirez. Distribution of the competence pheromone may be a major driving force in pneumococcal evolution. 7th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD) Tel Aviv, Israel, March 14-18, 2010.

M. Ramirez. Infecções por Gram-positivo. Jornadas Ibero-Americanas de Infecçologia. Hospital da Prelada, Porto, Portugal. May 17-18, 2010.

J. Melo-Cristino. Doença Pneumocócica Invasiva- repercussão na política vacinal. VIII Congresso Nacional da Sida e X Congresso Nacional de Doenças Infecciosas, Coimbra, Portugal, 6-9 October 2010.

M. Ramirez. Pneumococcal antibiotic resistance in Europe. Pneumococcal conjugate vaccines III – Bridging to the future. Barcelona, Spain, November 18-19, 2010.

Communications in International Conferences

Almeida J., Tiple J., Mário Ramirez, Melo-Cristino J., Vaz C., Francisco A.P. and Carriço, J.A. 2010. An Ontology and REST API for Sequence-based Microbial Typing Data. X Jornadas de Bioinformática, Malaga, Spain, 27-19 October. (Oral presentation).

Silva-Costa, C., A. Friães, M.D. Pinho, M. Ramirez, J. Melo-Cristino. 2010. In vitro susceptibility to Tigecycline and to an extended panel of antimicrobials of Gram-positive and Gram-negative isolates in Portugal (E-1585). 50th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Boston, MA, 12-15 September. (Poster presentation)

Francisco A, C Vaz ,J Melo-Cristino ,M Ramirez and JA Carriço. 2010. Phyloviz: a open-source platform for epidemiological data integration, analysis and visualization (WSII.2). 9th International Meeting on Microbial Epidemiological Markers, Wernigerode, Germany, Sep 1-4. (Oral presentation)

Severiano A , Carriço JA, F Pinto and M Ramirez. 2010. New developments in methods for typing and strain characterization (WSII.3). 9th International Meeting on Microbial Epidemiological Markers, Wernigerode, Germany, Sep 1-4. (Oral presentation)

Santos, MD, Paiva, JAP, Gomes A, Fonseca PGS, Carriço JA, AT Freitas. 2010. GEDI - GENomic Data Information System. 14th International Conference on Research in Computational Molecular Biology. Lisbon, Portugal, Aug 12-15. (Poster presentation)

Francisco A, C.Vaz, J. Melo-Cristino, M. Ramirez and João A.Carriço.2010. Phyloviz: Visualizing epidemiological information on phylogenetic relationships inferred by goeBURST algorithm. 14th International Conference on Research in Computational Molecular Biology. Lisbon, Portugal, Aug 12-15. (Oral presentation)

Gouveia C., C. Neves, M. Ramirez. 2010. Community-acquired Staphylococcus aureus musculoskeletal infections in children: role of panton-valentine leukocidin and methicillin resistance (A-229-0004-01186). 28th European Society for Paediatric Infectious Diseases (ESPID) Annual Meetings. Nice, France. 4-8 May. (Poster presentation)

Aguiar, S.I., J. Melo-Cristino, M. Ramirez. 2010. Pili distribution among invasive pneumococci in Portugal after 7-valent conjugate vaccine (O156). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Oral presentation)

P. Machado, A. Silva, L. Lito, J. Melo Cristino, A. Duarte. Emergence of *Klebsiella pneumoniae* ST-11 producing KPC-3 carbapenemase at a Lisbon hospital. (O129). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Oral presentation)

S. Costa, C. Falcão, M. Viveiros, J. Melo Cristino, L. Amaral, I. Couto. Importance of efflux systems on the resistance to fluoroquinolones in *Staphylococcus aureus*. (P955). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

S. Serqueira, P. Machado, J. Marto, A. Silva, L. Lito, J. Melo Cristino, A. Duarte. Virulence factors and antibiotic resistance in uropathogenic *Klebsiella pneumoniae* isolates from paediatric units at a Portuguese hospital. (P1484). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

C. Caneiras, A. Narcisa, MJ Salgado, L. Lito, J. Melo Cristino, A. Duarte. Virulence factors and pathogenicity islands in extended-spectrum beta-lactamase producing *Escherichia coli* bloodstream isolates. (P1939). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

Friães, A., M. Ramirez, J. Melo-Cristino. 2010. Antimicrobial resistance among invasive *Streptococcus pyogenes* isolates in Portugal (O481). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Oral presentation)

Friães, A., C. Silva-Costa, J. Melo-Cristino, M. Ramirez. 2010. Infrequent deletion of the chromosomal genes *speB* and *speF* in GAS clinical isolates (O83). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Oral presentation)

Silva-Costa, C., M. Ramirez, J. Melo-Cristino. 2010. Phenotypic and molecular characterization of *Streptococcus pyogenes* isolated scarlet fever patients (P2670). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

Pinho, M.D., M. Ramirez, J. Melo-Cristino. 2010. Molecular characterization of levofloxacin resistance in *Streptococcus dysgalactiae* subsp. *equisimilis* isolates from Portugal (P1002). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

Martins, E.R., J. Melo-Cristino and M. Ramirez. 2010. Evidence for capsular switching in *Streptococcus agalactiae* (P 1978). 20th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria, 10-13 April. (Poster presentation)

Aguiar, S.I., F. Pinto, S. Nunes, R. Sá-Leão, I. Serrano, J. Melo-Cristino, M. Ramirez, H. de Lencastre. 2010. Serotype 19A lineages in pneumococci recovered from carriage and infection in Portugal (P121). 7th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD) Tel Aviv, Israel, March 14-18. (Poster presentation)

Aguiar, S.I., J. Melo-Cristino, M. Ramirez. 2010. Characterization of pneumococcal strains of serogroup 6 in Portugal (P003). 7th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD) Tel Aviv, Israel, March 14-18. (Poster presentation)

Rebello MS, Frita R, Pamplona A, Häscheid T. 2010. A novel drug sensitivity assay based on flow cytometric detection of hemozoína (P 302). Malaria: New Approaches to Understanding Host-Parasite Interactions Copper Mountain, Colorado, USA, 11-16 April. (Poster presentation)

Communications in National Conferences

Frita R, Pamplona A, Vigário AM, Saraiva M, Castro AG, Mota MM, Häscheid T. Malária e tuberculose: o papel do pigmento malárico (P 026). VIII Congresso Nacional da Sida e X Congresso Nacional de Doenças Infecciosas, Coimbra, Portugal, 6-9 October 2010.

Rebello MS, Frita R, Pamplona A, Häscheid T. Um novo teste de sensibilidade para *Plasmodium* spp. baseado na detecção de hemozoína (P 027). VIII Congresso Nacional da Sida e X Congresso Nacional de Doenças Infecciosas, Coimbra, Portugal, 6-9 October 2010.

Organisation of Conferences

J.A.Carriço. Member of the organizing committee of Fourteenth International Conference on Research in Computational Molecular Biology (RECOMB). Lisboa, Portugal, August 12-15, 2010.

J.A.Carriço. Member of the scientific committee of the X Jornadas de Bioinformática (JBI) Malaga, Spain, 27-29 October, 2010

Ramirez, M. Member of the scientific committee of the 7th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD) Tel Aviv, Israel, March 14-18, 2010.

Internationalization

- We have completed a publication in collaboration with Australian and American colleagues (McMillan et al. 2010. Population genetics of *Streptococcus dysgalactiae* subspecies *equisimilis* reveals widely dispersed clones and extensive recombination. PLoS ONE 5:e11741)
- 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* (paper published in the Lancet Infectious Diseases, 2010).
- 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

Prizes, honours and awards

Poster prize (best poster) 2010 to Maria Rebelo at the VIII Congresso Nacional da Sida e X Congresso Nacional de Doenças Infecciosas, Coimbra, Portugal.

Advanced teaching

J. A. Carriço . Bioinformatics: What? When? How? – Nano Course for the IMM PhD program - <http://im.fm.ul.pt/dokuwiki/doku.php?id=courses:bioinformatics>. Responsible for the organization of the nanocourse.

J. Melo Cristino, T. Häscheid and M. Ramirez. Master Course in Emerging Infectious Diseases 2007-2008 and 2008-09, Faculty of Medicine of Lisbon. Responsible for the organization of a module in Microbiology and teaching of multiple courses.

J. Melo-Cristino. Infecção Sistémica e do Sistema Nervoso Central – Perspectiva do Microbiologista. Curso Pós-Graduado de Atualização: Microbiologia na Pediatria Clínica. April 16 – May 21, 2010.

Master thesis completed

Maria Sousa Rebelo (2010) “Malarial pigment (hemozoin): flow cytometric detection of hemozoin in infected erythrocytes to monitor drug-effects” Master in Applied Microbiology, Faculdade de Ciências da Universidade de Lisboa. Supervisors: Thomas Häscheid e Ana Reis.

André Filipe Magalhães Gomes (2010) ,“A System for Automated Genome Annotation”, Master in Biomedical Engineering, Instituto Superior Tecnico, Universidade Tecnica de Lisboa, Supervisors: Ana Teresa Freitas e João André Carriço

Ricardo Rubén dos Santos Aires (2010) ,“Visual Analysis of Regulatory Networks”, Master in Biomedical Engineering, Instituto Superior Tecnico, Universidade Tecnica de Lisboa, Supervisors: Sara Madeira, Alexandre Francisco e João André Carriço

André Valério Raposo Carreiro (2010),”Classification of clinical expression time series: A case study in patients with multiple sclerosis”, Master in Biomedical Engineering, Instituto Superior Técnico, Universidade Técnica de Lisboa, Supervisors: Sara Madeira e João André Carriço

Molecular Parasitology Unit

Major interests / Objectives

The *Plasmodium* parasite alternates between mosquito vector and vertebrate host, with transmission relying on highly specialized parasite stages. Once inside the new host, developmental progression gives 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 on a transcriptional and post-transcriptional level the gene expression control mechanisms during the transmission of the rodent malaria parasite from and to the mammalian host.

Head of Unit

Gunnar Mair, Assistant Professor – PhD, Queen’s University of Belfast, N. Ireland, U.K.

Principal Investigators

Celine Carret – PhD, Montpellier, France

Research Team

Natalia Kozlova, PhD	Post Doctoral Fellowship, FCT
Jorge Santos, MSc	PhD Fellowship, FCT
Ana Guerreiro, MSc	Technician, FCT
Ana Gomes	Technician, FCT; MSc December 2010 (left October 2010)
Marcelo Pereira	Master’s Student

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 [1*]. Through RNA-immunoprecipitation [2*], and global expression

profiling of KO mutants we highlighted crucial repressors of maternally supplied mRNAs. Our data define P bodies as critical for post-fertilisation development during the initial stages of *Plasmodium* mosquito infection. During the transmission from the mosquito to the mammalian host we have identified the RNA binding protein Pumilio as a regulator of development [3*]; in its absence sporozoites develop prematurely into liver stage forms with accompanying changes in gene expression profiles that are typical of liver development.

Recent Most Relevant Publications

Mair GR, Lasonder E, Garver LS, Franke-Fayard B, Carret CK, Wiegant J, Dirks R, Dimopoulos G, Janse CJ, Waters AP (2010) An evolutionarily ancient P body controls sexual development in the protozoan Plasmodium. *PLoS Pathog* **6** (2), e1000767 (Journal IF: 8.978, Citations: 1)

Baum J, Papenfuss AT, Mair GR, Janse CJ, Waters AP, Cowman AF, Crabb BS, de Konig-Ward T (2009) Molecular genetics and comparative genomics suggests RNAi is not functional in malaria parasites. *Nucleic Acid Res* **37** (11), 3788-98 (Journal IF: 7.479, Citations: 10)

Yuda M, Iwanaga S, Shigenobu S, Mair GR, Janse CJ, Waters AP, Kato T, Kaneko I (2009) Identification of a transcription factor in the mosquito-invasive stage of malaria parasites. *Mol Microbiol* **71** (6), 1402-14 (Journal IF: 5.361, Citations: 23)

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*, **7** (4), e84. (Journal IF: 12.916, Citations: 19)

Lasonder E, Janse CJ, van Gemert GJ, Mair GR, Vermunt AM, Douradinha BG, van Noort V, Huynen MA, Luty AJ, Kroeze H, Khan SM, Sauerwein RW, Waters AP, Mann M, Stunnenberg HG (2008) Proteomic profiling of Plasmodium sporozoite maturation identifies new proteins essential for parasite development and infectivity. *PLoS Pathogens*; **4** (10), e1000195. (Journal IF: 8.978, Citations: 26)

Ongoing Research Projects

2010/2012 Transcriptional regulation of Plasmodium during host-vector transmission, FCT. Coordinator: GR Mair PTDC/BIA-BCM/105610/2008; € 191710

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; € 19943; CK Carret Bolseiro 10%

2009/2010 GAPIC reward to Ana Rita Gomes; € 2500

Publications in peer reviewed Journals

1* Mair GR, Lasonder E, Garver LS, Franke-Fayard B, Carret CK, Wiegant J, Dirks R, Dimopoulos G, Janse CJ, Waters AP (2010) An evolutionarily ancient P body controls sexual development in the protozoan Plasmodium. *PLoS Pathog.* **6** (2), e1000767 (Journal IF: 8.978, Citations: 1)

Diogo, ELF; Santos, JM; Phillips, AJL (2010) Phylogeny, morphology and pathogenicity of *Diaporthe* and *Phomopsis* species on almond in Portugal. *Fungal Diversity* **44** (1), 107-115 (Journal IF: 3.803, Citations: 0)

Santos, JM; Correia, VG; Phillips, AJL (2010) Primers for mating-type diagnosis in *Diaporthe* and *Phomopsis*: their use in teleomorph induction in vitro and biological species definition. *Fungal Biology (formerly Mycological Research)* **114** (2-3), 255-270 (Journal IF: 2.921, Citations: 1)

Other publications International

Mwai L, Diriye A, Masseno V, Muriithi S, Feltwell T, Musyoki J, Feller A, Lemieux J, Marsh K, Newbold C, Nzila A, Carret C (2010) Transporter genes other than *pmdr1* and *pfcr1* may alter the response of *Plasmodium falciparum* to lumefantrine. ASTMH 59th Annual Meeting, Atlanta, GA, USA. *Am J Trop Med Hyg* (Journal IF: 2.795, Citations: 0)

Gomes-Santos CSS, Braks JAM, Prudêncio M, Carret CK, Gomes AR, Pain A, Feltwell T, Khan SM, Waters AP, Janse CJ, Mair GR, Mota MM (2010) Developmental transition of *Plasmodium* sporozoites into liver-stage forms is regulated by the RNA binding protein Pumilio 2. From Parasite to Prevention: Advances in the understanding of malaria, Edinburgh, UK. October 2010 *Malaria Journal* **9** (Suppl 2):P13

McVeigh P, Mair GR, Novozhilova E, Day A, Zamanian M, Marks NJ, Kimber MJ, Day TA, Maule AG. Probing the function of schistosome *Sm-npp-1* exposes a new family of helminth neuropeptides. 18th International Symposium on Regulatory Peptides, Belfast, N. Ireland, UK; *Reg Peptides* **164** (1):P27 (Journal IF: 2.160, Citations: 0)

Invited Lectures and Seminars

Carret CK. First Translational Bioinformatics Meeting, IGC, Oeiras, Portugal, June 2010.

Mair GR. Invited Seminar: Graduate program of Microbiology, Yale University School of Medicine, New Haven, CT., USA, September 2010.

Mair GR. Invited Lecture: Course "Regulação e Diferenciação" within the Genetics and Molecular Biology Master, Faculty of Sciences, University of Lisbon, Portugal, May 2010.

Communications in International Conferences

2* Carret CK, Pain A, Guerreiro A, Mair GR. *Plasmodium berghei* P granule-members associate with distinct mRNA subsets in gametocytes. Molecular Parasitology Meeting, Woods Hole, Mass. USA, September 2010 (Poster)

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3* Gomes-Santos CSS, Braks JAM, Prudencio 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. Molecular Parasitology Meeting, Woods Hole, Mass. USA, September 2010 (Poster)

Mwai L, Diriye A, Masseno V, Muriithi S, Feltwell T, Musyoki J, Feller A, Lemieux J, Marsh K, Newbold C, Nzila A, Carret C. Transporter genes other than pmdr1 and pfcr1 may alter the response of Plasmodium falciparum to lumefantrine. American Society for Tropical Medicine and Hygiene 59th Annual Meeting, Atlanta, GA, USA, November 2010 (Poster)

McVeigh P, Mair GR, Novozhilova E, Day A, Zamanian M, Marks NJ, Kimber MJ, Day TA, Maule AG. Probing the function of schistosome Sm-npp-1 exposes a new family of helminth neuropeptides. Regulatory Peptides 18th International Symposium, Belfast, N. Ireland, U.K. November 2010 (Talk)

Santos, J.M., Correia V.G., Phillips, A.J.L. (2010) Towards meaningful species definitions in *Diaporthe* and *Phomopsis*, 13th MPU Congress, Rome, Italy (Talk)

Sánchez, C., Ferreira-Pinto, M.M., Santos, J.M., Ramos, A.P., Barreiro, M. da G. (2010). Characterization of *Aureobasidium pullulans*, a promising biocontrol agent for postharvest diseases, 28th International Horticultural Congress, Lisbon, Portugal (Talk)

Berraf, A., Bouznad, Z., Santos, J.M., Coelho, M.A., Phillips, A.J.L. (2010). *Phaeoacremonium* species associated with grapevine decline in Algeria, 13th MPU Congress, Rome, Italy (Poster)

Diogo, E.L.F., Santos, J.M., Phillips, A.J.L. (2010). Morphologic and molecular characterization of *Diaporthe/Phomopsis* species on almond in Portugal, 9th EFPP – 6th SPF Congress, Évora, Portugal (Poster)

Communications in National Conferences

Santos JM, Carret CK, Mair GR. Role of Plasmodium surface proteins in sexual development and malaria transmission. IMM PhD Student Meeting 2010, IMM, Lisbon (Poster)

Carret CK. First Translational Bioinformatics Meeting 2010, IGC, Oeiras, Lisbon (Talk)

Internationalization

Mair GR. September 2010 Invited Seminar: Graduate program of Microbiology, Yale University School of Medicine, New Haven, CT., USA

Prizes, honours and awards

Gomes ARB, GAPIC Award 2010

Gomes ARB, GAPIC Best Talk Award 2010.

Carret CK, Referee for the ANR/MIE (“Agence Nationale de la Recherche/Maladies Infectieuses, Immunité et Environnement”, French funding agency) grant calls 2010.

Carret CK and Mair GR; Ad hoc Referees for PLoS Pathogens, International Journal for Parasitology, Journal for Morphology, BMC Genomics

Advanced teaching

Mair GR. Invited Lecture at the Graduate program of Microbiology, Yale University School of Medicine, New Haven, CT., USA, September 2010

Mair GR. Invited Lecture: Course "Regulação e Diferenciação" within the Genetics and Molecular Biology Master, Faculty of Sciences, University of Lisbon, Portugal, May 2010

Master thesis completed

Ana Rita B. Gomes (2010), Master Thesis: The role of a newly discovered family of transcription factors, ApiAP2, during the development of the rodent malaria parasite *Plasmodium berghei*. IMM, 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, 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

Principal Investigators

Helena Cortez-Pinto, MD, PhD - Consultant of Gastroenterology HSM, Associate Professor with “agregação” FMUL.

Isabel Monteiro-Grillo, MD, PhD - Director of the Radiotherapy and Oncology Departments HSM, Associate Professor FMUL.

Paula Ravasco, PhD, Auxiliary Professor FMUL.

Research Team

Mariana Verdelho Machado	MD, Specialist in Gastroenterology, HSM
Catarina Sousa Guerreiro	MsC in Nutrition, PhD Student, assistant FMUL
Carolina Bóleo-Tomé	Nutrition degree, Research Fellowship
Mariana Chaves	Nutrition degree, Research Fellowship (left 15 December 2010)

Keywords/Research Areas

Hepatology, steatohepatitis, obesity, insulin resistance;
Oncology, radiotherapy;
Nutrition and Outcomes;
Nutrition and Cancer.

Major scientific achievements

Still the only Research Nutrition and Metabolism Unit in Portugal, its high quality of advanced Education and research are widely recognized. Both achievements are shown in Publications in Journals with the highest impact factors in their areas, e.g. *Hepatology*/*Journal of Hepatology/Oncologist*/*Journal of Clinical Oncology*, in the internationalization shown by major roles in international bodies, lectures in key 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.

Nutrition is increasingly chosen by medical students for the integrated Master degree in Medicine.

Recent Most Relevant Publications

Cortez-Pinto H, de Moura MC, Day CP (2006) Non-alcoholic steatohepatitis: From cell biology to clinical practice. *Journal of Hepatology* **44**, 197-208 (Journal IF: 7.818, citations: 61).

Machado M, Marques-Vidal P, Cortez-Pinto H (2006) Hepatic histology in obese patients undergoing bariatric surgery. *Journal of Hepatology* **45**, 600-606 (Journal IF: 7.818, Citations: 49)

Ravasco P, Monteiro-Grillo I, Marques-Vidal P, Camilo ME (2005) Dietary counseling improves patient' outcomes: a prospective randomized controlled trial in colorectal cancer patients undergoing radiotherapy. *Journal of Clinical Oncology* **23**, 1431-1438 (Journal IF: 17.793, Citations: 79)

Ravasco P, Monteiro-Grillo I, Marques-Vidal P, Camilo ME (2005) Impact of nutrition on outcome: A prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head & Neck* **27**, 659-668 (Journal IF: 2.283, Citations: 60)

Ribeiro P, Cortez-Pinto H, Solá S, Castro R, Ramalho R, Baptista A, Moura M, Camilo ME, Rodrigues C (2004). Hepatocyte Apoptosis, Expression of Death Receptors and Activation of NF- κ B in the Liver of Non-alcoholic and Alcoholic Steatohepatitis Patients. *American Journal of Gastroenterology* **99**, 1708-17 (Journal IF: 6.012, Citations: 107)

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.

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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.

ONCOLOGY, RADIOTHERAPY

PI: Isabel Monteiro Grilo

2008/2010 Quality of Life in the prostate cancer patient undergoing radiotherapy. PI: Filipe Barbosa, Coordinator: Isabel Monteiro Grillo.

2010 I Monteiro-Grillo. Participant in Research Projects with Prof. Ducla Soares from the Faculty of Sciences.

2010 Combined HDR BT and 3D-CRT in intermediate and high risk prostate cancer patients: a dose escalation method. Participants: Olalla Santa Cruz, Carlos Jesus, João Melich-Cerveira, Gisela Marcelino, Isabel Monteiro-Grillo.

2010 Salvage External Beam Radiotherapy after Biochemical Recurrence or following prostatectomy (differs) in prostatectomized patients. Participants: João Melich-Cerveira, Gisela Marcelino, Pedro Marques-Vidal, Isabel Monteiro Grillo.

NUTRITION AND CANCER

PI: Paula Ravasco

2009/2011 Nutrition in Cancer: relevance and guidelines for clinical practice, FCT Pluriannual Funding. Coordinator: Paula Ravasco.

2008/2012 Body composition, metabolic pattern and cancer histological aggressiveness, FCT Pluriannual Funding. Coordinator: Paula Ravasco.

2006/2010 Colorectal Cancer and cytokines, FCT Pluriannual Funding. Coordinator: Paula Ravasco.

2003/2011 Cancer: metabolic dysfunction, nutrition intervention, Quality of Life and prognosis, FCT Pluriannual Funding. Coordinator: Paula Ravasco.

Publications in peer review Journals

Machado MV, Cortez-Pinto H (2010) Osteopontin: A Missing Link between Hedgehog Signaling and Fibrosis in Nonalcoholic Steatohepatitis. Editorial. *Hepatology* **53**, online Dec 21 (Journal IF: 10.840)

Chaves MR, Boléo-Tomé C, Monteiro-Grillo I, Camilo M, Ravasco P (2010) The Diversity of Nutritional Status in Cancer: New Insights. *The Oncologist* **15**, 523-530 (Journal IF: 6.701)

Mehdad A, McBride E, Monteiro Grillo I, Camilo M, Ravasco P (2010) Nutritional status and eating pattern in prostate cancer patients. *Nutricion Hospitalaria* **25**, 422-7 (Journal IF: 1.065)

Amaral P, Miguel R, Mehdad A, Cruz C, Monteiro Grillo I, Camilo M, Ravasco P (2010) Body fat and poor diet in breast cancer women. *Nutricion Hospitalaria* **25**, 456-61 (Journal IF: 1.065)

Ravasco P, Aranha MM, Borralho PM, da Silva IBM, Correia L, Fernandes A, Rodrigues CMP, Camilo M (2010) Colorectal cancer: Can nutrients modulate NF-kappa B and apoptosis? *Clinical Nutrition* **29**, 42-46 (Journal IF: 3.274)

Ferencova J, Krajnak S, Chaves M, Cruz C, Grillo IM, Camilo ME, Ravasco P (2010) International exchange program between medical schools: the relevance of a clinical research training in nutrition. *Nutricion Hospitalaria* **25**, 869-870 (Journal IF: 1.065)

Ravasco P, Anderson H, Mardones F (2010). Métodos de valoración del estado nutricional. *Nutrición Hospitalaria (Supl. 3)* **25**, 57-66 (Journal IF: 1.065)

Castro R, Barroso M, Rocha M, Esse R, Ramos R, Ravasco P, Rivera I, de Almeida IT (2010) The TCN2 776C> G polymorphism correlates with vitamin B-12 cellular delivery in healthy adult populations. *Clinical Biochemistry* **43**, 645-649 (Journal IF: 2.019)

Jorge Z, Carvalho MR, Guerra AS, Alves N, de Almeida JM, Fagundes MJ, Cortez-Pinto H, do Carmo I (2010) Malnutrition in morbid nutrition. *Acta Médica Portuguesa* **23**, 273-76 (no IF, cited on medline)

Machado MV, Oliveira AG, Cortez-Pinto H (2010) Hepatic steatosis in patients coinfectd with human immunodeficiency virus/hepatitis C virus: A meta-analysis of the risk factors. *Hepatology* **52**, 71-78 (Journal IF: 10.840)

Ratziu 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: 7.818)

Cortez-Pinto H, Gouveia M, Pinheiro LD, Costa J, Borges M, Carneiro AV (2010) The burden of disease and the cost of illness attributable to alcohol drinking – results of a national study. *Alcoholism – Clinical and Experimental Research* **34**, 1442-1449 (Journal IF: 3.392)

Cravo M, Sousa Guerreiro C, Moura dos Santos P, Brito M, Paula P, Fidalgo C, Tavares L, Dias Pereira A (2010) Risk factors for metabolic bone disease in Crohn's disease patients. *Inflammatory Bowel Disease* **16**, 2217-24 (Journal IF: 4.643)

Ferreira P, Cravo M, Guerreiro CS, Tavares L, Santos PM, Brito M (2010) Fat intake interacts with polymorphisms of Caspase9, FasLigand and PPARgamma apoptotic genes in modulating Crohn's disease activity. *Clinical Nutrition*. **29**, 819-23. (Journal IF: 3.274)

Marcelino G, Oliveira JM, Ravasco P, Marques-Vidal P (2010) Body image, weight concerns and related practices by Portuguese adolescents. *Nutritional Therapy and Metabolism* **27**, 189-192 (no IF yet, cited on medline)

Wanden-berghe C, Camilo ME, Culebras J (2010) Conceptos y definiciones de la desnutrición iberoamericana. *Nutrición Hospitalaria (Supl. 3)* **25**, 1-9 (Journal IF: 1.065)

Feldman-Stewart D, Caprici C, Brennenstuhl S, Tong C, Abacioglu U, Gawkowska-Suwinska M, Van Gils F, Heyda A, Igdem S, Macias V, Monteiro Grillo I, Moynihan C, Pijls-Johannesma M, Parker C, Pimentel N, Wordehoff H (2010) Information needs of early-stage prostate cancer patients: A comparison of nine countries. *Radiotherapy and Oncology* **94**, 328-333 (Journal IF: 4.343)

Vala IS, Martins LR, Imaizumi N, Nunes RJ, Rino J, Kuonen F, Carvalho LM, Rugg C, Monteiro Grillo I, Barata JT, Mareel M, Constantino S (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *Plos one* **5**, 1-13 (Journal IF: 4.351)

Mendonça V, Jorge M, Monteiro Grillo I, Palhano MJ, Feijó S (2010) Tracheal chondrosarcoma. *Clinical and Translational Oncology* **12**, 576-580 (Journal IF: 1.146)

Antunes MI, Bujor L, Monteiro Grillo I (2010) Anal canal plasmacytoma - An uncommon presentation site. *Reports of Practical Oncology & Radiotherapy*, Online Publication, December 2010 (Journal IF: N/A)

Other publications International

Ravasco P. Ética en la investigación en nutrición clínica (2010) In: Alemany M, Bernabeu-Mestre J (Eds). *Bioética y Nutrición*. Alicante: Colección Amalgama, Universidad de Alicante – Aguacleara Editorial, 2010: 283-294 (ISBN: 978-84-8018-333-8)

Ravasco P, Monteiro Grillo I, Camilo M. Nutritional wasting in cancer & quality of life: the value of early individualised nutritional counselling (2010) In: Preedy VR and Watson RR (Eds). *Handbook of Disease Burdens and Quality of Life Measures*. New York: Springer Science+Business Media LLC 2010: 3190-3201 (ISBN-13: 978-0-387-78664-3)

Other publications National

Sousa Guerreiro C, Cravo M (2010) Alimentação & Doença Inflamatória do Intestino. A importância de uma alimentação adequada. Merck-Sharp. Pág:16-19. Lisboa

Ravasco P, Chaves M (2010) O impacto de uma alimentação desequilibrada na génese do cancro. *APNews* March 2010. *NewLetter* Comunidade da Associação Portuguesa de Nutricionistas.

Invited Lectures and Seminars

Ravasco P. A relevância da Nutrição no Doente Respiratório, Jornadas de Reabilitação Respiratória / Reunião da Comissão de Reabilitação Respiratória da Sociedade Portuguesa de Pneumologia, Porto, Portugal, February 6, 2010.

Ravasco P. Nutrição em Doentes Oncológicos, Jornadas de Nutrição ISCS-N/CESPU- Nutrição dos 0 aos 100, Porto, Portugal, April 29, 2010.

Ravasco P. Patients and nutrition: the impact of compliance in Quality of Life, in: Satellite Symposium promoted by NESTLE: New perspectives in oncology nutrition therapy: from compliance to effectiveness, XXV Annual Congress SENPE (Sociedad Española de Nutrición Parenteral y Enteral), Girona, Spain, May 13, 2010.

Ravasco P. Nutrição na Qualidade de Vida e Prognóstico no doente oncológico, I Simpósio de Ciências da Saúde da Universidade de Lisboa - Nutrição em Oncologia, Lisbon, Portugal, June 1, 2010.

Ravasco P. Nutrição: faz diferença no tratamento do câncer? Multidisciplinary Symposium at the IV Congresso Brasileiro de Nutrição e Câncer (CBNC), II International Congress of Nutritional Oncology (ICNO 2010), Congresso Anual GANEPÃO 2010, XII Fórum Paulista de Pesquisa em Nutrição Clínica, promoted by GANEP Nutrição Humana (Grupo de Apoio de Nutrição Enteral e Parenteral), São Paulo, Brazil, June 15-19, 2010

Ravasco P. Qualidade de Vida, Nutrição e Câncer: é possível? Scientific Symposium and Interactive Case Study IV Congresso Brasileiro de Nutrição e Câncer (CBNC), II International Congress of Nutritional Oncology (ICNO 2010), Congresso Anual GANEPÃO 2010, XII Fórum Paulista de Pesquisa em Nutrição Clínica, promoted by GANEP Nutrição Humana (Grupo de Apoio de Nutrição Enteral e Parenteral), São Paulo, Brazil, June 15-19, 2010

Ravasco P. A eficácia do controle de peso. Scientific symposium on Recomendações Finais para a Prevenção do Câncer. IV Congresso Brasileiro de Nutrição e Câncer (CBNC), II International Congress of Nutritional Oncology (ICNO 2010), Congresso Anual GANEPÃO 2010, XII Fórum Paulista de Pesquisa em Nutrição Clínica, promoted by GANEP Nutrição Humana (Grupo de Apoio de Nutrição Enteral e Parenteral), São Paulo, Brazil, June 15-19, 2010

Ravasco P. Intervenção nutricional em oncologia e Qualidade de Vida, Round table - Alimentação e cancro: mitos e realidades, XII Congresso Anual da APNEP (Associação Portuguesa de Nutrição Entérica e Parentérica), Lisbon, Portugal July 2-3, Revista da APNEP vol. IV, Nº1: 45.

Ravasco P. Mechanisms of wasting in cancer cachexia, Curso de Formação Avançada para Creditação de Formação Médica em Nutrição (CME): Educational Long Life Learning on Nutritional support in cancer, 32º Annual Congress ESPEN (European Society for Clinical Nutrition and Metabolism), Nice, France, September 5-8, 2010.

Ravasco P. Nutrition, Quality of Life and clinical outcomes after Radiotherapy: long term follow-up of a prospective randomised controlled trial in colorectal cancer, Symposium under the theme Management of Rectal Cancer, IX Annual Congress ESTRO (European Society of Therapeutical and Radiology and Oncology), Barcelona, Spain, September 12-16, 2010.

Ravasco P. Eficácia do Controle na Prevenção do Câncer, IX Congresso Norte-Nordeste de Nutrição Parental e Enteral and I Simpósio Norte-Nordeste de Nutrição Oncológica, SBC (Sociedade Brasileira de Câncer) and SBNPE (Sociedade Brasileira de Nutrição Parenteral e Enteral), Salvador da Baía, Brazil, October 14-16, 2010.

Ravasco P. Nutrição, inflamação e NFKappa-B, IX Congresso Norte-Nordeste de Nutrição Parental e Enteral and I Simpósio Norte-Nordeste de Nutrição Oncológica, SBC (Sociedade Brasileira de Câncer) and SBNPE (Sociedade Brasileira de Nutrição Parenteral e Enteral), Salvador da Baía, Brazil, October 14-16, 2010.

Chaves M. A alimentação na prevenção do cancro. I Simpósio de Ciências da Saúde – Faculdade de Medicina da Universidade de Lisboa, Portugal, June 1, 2010

Boléo-Tomé C. Problemas nutricionais em Oncologia. I Simpósio de Ciências da Saúde – Faculdade de Medicina da Universidade de Lisboa, Portugal, June 1, 2010.

Cortez-Pinto H. DHGNA e risco cardiovascular. V Simpósio Sul-Americano do Aparelho Digestivo, Gramado, Brazil, 20-22 May 2010.

Cortez-Pinto H. Increasing burden of alcoholic liver disease in Europe: need for action. Symposium: New trends in alcoholic liver disease. 45th Annual Meeting of the European Association for the Study of the Liver (EASL), Vienna, Austria, April 14-18, 2010.

Cortez-Pinto H. Fígado e Doença Cardiovascular, XXI Congresso Português de Cardiologia, Lisbon, Portugal, April 2010.

Cortez-Pinto H. The Best of UEGW/WCOG GASTRO2009 in DDW: Liver, Annual Meeting of the American Gastroenterological Association (AGA), New Orleans, USA, May 3-5, 2010.

Cortez-Pinto H. Esteato-hepatite não-alcóolica: tratamento. Estado da arte. V Simpósio Sul-Americano do Aparelho Digestivo, Gramado, Brazil, May 20-22, 2010.

Cortez-Pinto H. HCV e esteatose hepática. V Simpósio Sul-Americano do Aparelho Digestivo, Gramado, Brazil, May 20-22, 2010.

Cortez-Pinto H. DHGNA - motivos para crermos que é uma doença séria. V Simpósio Sul-Americano do Aparelho Digestivo, Gramado, Brazil, May 20-22, 2010.

Cortez-Pinto H. Increased burden of alcoholic organ damage in Europe: need for action. ESBRA Nordmann & ISBRA Satellite Meeting Alcohol and cancer, Heidelberg, Germany, September 17-18, 2010

Cortez-Pinto H. Guidelines for treating ALD. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Cortez-Pinto H. Public burden and costs of alcohol related diseases. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Cortez-Pinto H. Lunch Session: How to manage NAFLD/NASH. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Cortez-Pinto H. Increasing Burden of Alcoholic Liver Disease in Europe: Need for Action. Alcoholic Liver disease, Monothematic Conference of the European Association for the Study of the Liver (EASL), Athens, Greece, December 10-11, 2010

Monteiro Grillo, I. Terapêutica Complementar: Quando, Como e Porquê? 9^a Reunião Internacional de Cirurgia, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, January 28-30, 2010.

Monteiro Grillo, I. Reunião de utilizadores Nucletron: European Oncentra Brachy Best Practice Workshop, Valencia, Spain, June 10-15 2010.

Communications in International Conferences

Ferreira DM, Castro RE, Machado M, Silvestre AP, Evangelista T, Carepa F, Coutinho J, Cortez-Pinto H, Rodrigues CMP. Association between progression of non-alcoholic fatty liver disease and muscle insulin resistance in overweight patients. 45th Annual Meeting of European Association for the Study of Liver, Vienna, Austria, April 2010. *Journal of Hepatology*: 52 (Poster presentation).

Machado MV, Coutinho J, Carepa F, Costa A, Cortez-Pinto H. NAFLD fibrosis is not accurate to identify advanced fibrosis in morbid obesity. 45th Annual Meeting of European Association for the Study of Liver, Vienna, Austria, April 2010. *Journal of Hepatology*, 52: S148 (Poster presentation).

Machado MV, Silvestre AR, Evangelista, T, Coutinho J, Carepa F, Costa A, Cortez-Pinto H. In morbid obesity, nonalcoholic fatty liver disease associates to fat overload in the muscle but not muscle mitochondrial Dysfunction. 45th Annual Meeting of European Association for the Study of Liver, Vienna, Austria, April 2010. *Journal of Hepatology*, 52: S149 (Poster presentation).

Machado MV, Gonçalves S, Costa A, Carepa F, Coutinho J, Cortez-Pinto H. Non alcoholic steatohepatitis is associated with early changes on glomerular filtration rate in morbid obesity. 61st Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2010, Boston, USA, 30 October - 2 November 2010. *Hepatology*, 52: S650 (Poster presentation).

Ferreira D, Castro R, Machado MV, Evangelista T, Silvestre A, Costa A, Coutinho J, Carepa, Cortez-Pinto H, Rodrigues CM. Progression of non-alcoholic fatty liver disease and insulin resistance in liver, muscle and adipose tissues of morbid obese patients, 61st Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2010, Boston, USA, 30 October - 2 November 2010. *Hepatology*: 52, S654 (Poster presentation).

Machado MV, Oliveira AG, Cortez-Pinto H. Hepatic steatosis in hepatitis B virus infected patients – a meta-analysis of risk factors and comparison with hepatitis C infected patients. 61st Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2010, Boston, USA, 30 October - 2 November 2010. *Hepatology*: 52, S679 (Poster presentation).

Ferreira C, Rodrigues T, Cortez-Pinto H, Serejo F, Ramalho F, Velosa F. Persistent alcohol consumption is the only factor associated with two or more hospital readmissions after first decompensation of liver cirrhosis. EASL Monothematic Conference: Alcoholic Liver Disease, Athens, Greece, December 2010 (Poster presentation).

Ravasco P, Chaves M, Boléo-Tomé C, Monteiro Grillo I, Camilo M. Insights on body composition in cancer patients. 32nd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Nice, France, September 2010. *Clinical Nutrition*: 5 (suppl 2): 19 (Oral presentation).

Ravasco P, Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo M. MUST in Oncology: Nutrition integration works! 32nd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Nice, France, September 2010. *Clinical Nutrition*: 5 (suppl 2): 134 (Poster presentation).

Ravasco P, Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo M. MUST is validated in cancer! 32nd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Nice, France, September 2010. *Clinical Nutrition*: 5 (suppl 2): 150-151 (Poster presentation).

Correia J, Chaves M, Camilo M, Ravasco P. Depression and nutrition: a complex association. 32nd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Nice, France, September 2010. *Clinical Nutrition*: 5 (suppl 2): 143-144 (Poster presentation).

Vasconcelos, A., Jorge, M., Mendonça, V., Antunes, I., Monteiro Grillo, I., Jesus. C. Breast Ductal Carcinoma in Situ – Conservative Treatment Assessment, 29 ° Congresso da ESTRO, Barcelona, Spain, September 12-16 2010. (Poster presentation).

Communications in National Conferences

Cortez-Pinto H, Gouveia M, Pinheiro LS, Costa JM, Carneiro AV. A Carga e o custo de doença atribuível ao álcool – resultados de um estudo nacional. XXX Congresso Nacional de Gastreterologia e Endoscopia Digestiva, Vilamoura, Portugal, June 2010 (Oral presentation).

Vieira Lima C, Ferreira A, Machado M, Jorge Z, Nobre E, Carvalho R, Cortez-Pinto H, Velosa J. Resultados a médio/longo prazo da colocação de balões intra-gástricos para tratamento da obesidade mórbida em 94 doentes. XXX Congresso Nacional de Gastreterologia e Endoscopia Digestiva, Vilamoura, Portugal, June 2010 (Poster presentation).

Machado MV, Silvestre AR, Evangelista T, Coutinho J, Carepa F, Costa A, Cortez-Pinto H. Na obesidade mórbida, o fígado gordo não alcoólico associa-se a sobrecarga de lípidos no músculo, mas não a disfunção mitocondrial. XXX Congresso Nacional de Gastreterologia e Endoscopia Digestiva, Vilamoura, Portugal, June 2010 (Oral presentation).

Machado MV, Oliveira AG, Cortez-Pinto H. Esteatose hepática em doentes co-infectados com VIH e vírus da Hepatite C – Meta-análise dos factores de risco. XXX Congresso Nacional de Gastreterologia e Endoscopia Digestiva, Vilamoura, Portugal, June 2010 (Oral presentation).

Ferreira DM, Castro RE, Machado MV, Evangelista T, Silvestre AR, Costa A, Coutinho J, Carepa F, Rodrigues CMP, Cortez-Pinto H. Progressão do fígado gordo não alcoólico e resistência à insulina, a nível hepático e muscular, em doentes com obesidade mórbida. XXX Congresso Nacional de Gastreterologia e Endoscopia Digestiva, Vilamoura, Portugal, June 2010 (Oral presentation).

Correia J, Chaves M, Camilo M, Ravasco P. Qual a associação entre nutrição e depressão? XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 124 (Poster presentation).

Rolão A, Chaves M, Monteiro Gillo I, Camilo M, Ravasco P. Qual o perfil nutricional e de estilos de vida do doente oncológico? Um estudo piloto. XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 125 (Poster presentation).

Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo M, Ravasco P. Ensino da integração da nutrição: o MUST em oncologia. XII Congresso Anual da Associação Portuguesa de Nutrição

Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 126 (Poster presentation).

Boléo-Tomé C, Chaves M, Monteiro Grillo I, Camilo M, Ravasco P. O MUST validado em oncologia! XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 127 (Poster presentation).

Fernandes J, Boléo-Tomé C, Camilo M, Ravasco P. Qual o perfil nutricional e de estilos de vida em meio empresarial? Um estudo transversal. XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 128 (Poster presentation).

Chaves MR, Boléo-Tomé C, Monteiro Grillo I, Camilo M, Ravasco P. Composição corporal no doente oncológico: novas perspectivas. XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica (APNEP), Lisbon, July 2010. *Revista da APNEP* vol. IV, Nº1: 129 (Poster presentation).

Antunes, M.I., Bujor, L. Amado, A., Monteiro Grillo, I. PUB3 – Sequelas Neuro-Cognitivas da RTE Crânio-Encefálica (RTE CE) em Doente Jovem Imunocompetente com Linfoma primário do SNC (LPSNC). Reunião Anual da Sociedade Portuguesa de Hematologia, Troia, Portugal, November 11-13, 2010 (Poster presentation).

Ribeiro, T., Jesus, C., Peralta, L., Rêgo, F., Monteiro Grillo, I. In vivo dosimetry implementation tests in HDR ¹⁹²Ir Brachytherapy. Portuguese Physics for Health Summer School. Covilhã, Portugal, July 26-28, 2010. (Oral presentation).

Mareco, V., Bujor, L., Monteiro Grillo, I. Tractografia em Radioterapia - Progressos na Delimitação de Tumores do Cérebro com nova Técnica de Imagem, 3º Congresso Nacional da Associação Portuguesa de Neuro- Oncologia (APNO), Sesimbra, Portugal, October 22-23, 2010. (Oral presentation).

Antunes, M.I., Bujor, L., Amado, A., Vasconcelos, A., Monteiro Grillo, I. Radioterapia Hemostática a Metástase do Cólon, 6º Simpósio Nacional de Cancro Digestivo, Albufeira, Portugal, October 28-31, 2010. (Oral presentation).

Organisation of Conferences

Guerreiro, CS. Organizing Committee of XII Congresso Anual da Associação Portuguesa de Nutrição Entérica e Parentérica, Lisbon, Portugal, July 2-3, 2010.

Ravasco, P. Organizing Committee of the I Simpósio de Ciências da Saúde da Universidade de Lisboa, Nutrição em Oncologia, Lisbon, Portugal, June 2010.

Cortez-Pinto, H. Co-organizer of the 18th United European Gastroenterology Week (UEGW) as the representative of the European Association for the Study of Liver Disease (EASL), Barcelona, Spain, October 23-27, 2010.

Cortez-Pinto, H. Co-organizer of the 19th United European Gastroenterology Week (UEGW), to be held in Stockholm 2011, as the representative of the European Association for the Study of Liver Disease (EASL).

Monteiro-Grillo I. Member of the Scientific Committee 29th Estro Meeting, Barcelona, Spain, September 12-16, 2010.

Monteiro-Grillo I. Co-organizer of “Evidence – based Radiation Oncology: A clinical Refresher Course with a methodological basis”, ESTRO, Estoril, Portugal, October 2010.

Internationalization

Cortez-Pinto H. Collaborative multicenter study to assess non-invasive tests to detect liver disease in NAFLD. Coordinator: Musso G, University of Turin/Italy; Representative of the European Association for the Study of Liver Disease in the organization of the Annual United European Gastroenterology Week

Guerreiro CS. E-learning for Health Agents Program in Europe a Life Learning Programme European Commission financed; *Key-Member* representing Portugal at the European Society for Clinical Nutrition and Metabolism

Ravasco P, Guerreiro CS. Erasmus EU financed network DIETS= Dieticians Improving Education Training Standards across Europe

Ravasco P. EU funded consortium of Palliative Cancer Care investigators – European, Canadian and US experts, DELPHI panel of cachexia specialists to set evidence based practice guidelines, criteria for clinical trials’ inclusion

Ravasco P. Invited member of the Nature reader panel; Editorial Board of World Journal of Clinical Oncology; Member of the Research Group of Digestive Cancer, Coordinator of nutrition in gastric/intestinal/esophageal cancer

Ravasco P. Member of the Judging Committee of XII Fórum Paulista de Pesquisa em Nutrição Clínica e Experimental. IV Congresso Brasileiro de Nutrição e Câncer

Ravasco P. Supervisor of research training in Clinical Nutrition of medical students: Emelina Stambolliu, Athens University/Greece and Jan Bogataj from Slovenia Medical School, in the Faculty of Medicine of Lisbon/foreign Medical schools cooperation project “Standing Committee on Research” of the International Federation of Medical Students’ Associations

Monteiro-Grillo I. Editorial Board of Radiotherapy and Oncology, Journal of the European Society for Therapeutic Radiology and Oncology; Editorial Board of Journal of Contemporary Brachytherapy of the Polish Brachytherapy Society, and of Reports of Practical Oncology and Radiotherapy/Poland

Camilo ME. TOOLTIPS Partner = Erasmus EU financed Intensive Programme

Prizes, honours and awards

Prize for the 2nd best poster presentation, at Congresso da Associação Portuguesa de Nutrição Entérica e Parentérica, to Carolina Boléo-Tomé, Mariana Ramos Chaves, Isabel Monteiro Grillo, Maria Ermelinda Camilo and Paula Ravasco. “Ensino da integração da nutrição: o MUST em oncologia”. XII Congresso da APNEP, Lisbon, Portugal, June 2010.

Travel Award to young investigators (one per country) for their best first presented abstract at the ESPEN 32nd Congress of European Society for Clinical Nutrition and Metabolism to Mariana Chaves, Nice, France, 2010. Ravasco P, Chaves M, Boléo-Tomé C, Monteiro Grillo I, Camilo M. Insights on body composition in cancer patients. 32nd Congress of the European Society for Clinical Nutrition and Metabolism (ESPEN), Nice, France, 5-8 September 2010.

Finalists Nutrition Awards 2010 (among the 6 best projects) in Categoria de Investigação em Ciências da Nutrição. Project entitled “Nutrição e Cancro – da ciência à integração!”. Authors: Boléo-Tomé C, Chaves M, Raimundo MC, Diegues I, Monteiro-Grillo I, Camilo ME, Ravasco P. Diploma and oral presentation.

Bolsa Universidade de Lisboa/ Fundação Amadeu Dias 2010/2011 to Carla Joana dos Santos Samuel de Sousa, a 2nd year Health Sciences undergraduate student for the project entitled: “Nutrição e Oncologia: a investigação e seu impacto na clínica e ensino”. Coordinator: Ravasco P. Tutor: Boléo-Tomé C.

Advanced teaching

Camilo ME. Partner of TOOLTIPS = Erasmus EU financed Intensive Programme “Tools targeted on obesity intervention and prevention strategies for efficient and sustained implementation”, 2 weeks advanced intensive Course, held once a year in Austria (2010-2012).

Cortez-Pinto H. Lecturer at the Postgraduate course of the American Gastroenterology Association. New Orleans-USA, May 2010.

Cortez-Pinto H. Genética e Doença Hepática Alcoólica. Lecture Armando Porto, 23^o Course of Hepatobiliary Diseases, Coimbra, Portugal, November 19-20, 2010.

Cortez-Pinto H. Moderation of a Basic Science Session. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Cortez-Pinto H. Moderation of a Clinical Case Session. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Cortez-Pinto H. Moderation of a Poster Session. 18th United European Gastroenterology Unit (UEGW), Barcelona, Spain, October 23-27, 2010

Monteiro Grillo, I. Moderator of the Round Table: Diagnóstico e Impactos Clínicos. 9^a Reunião Internacional de Cirurgia, Faculdade de Medicina da universidade de Lisboa, Lisbon, Portugal, January 28-30, 2010.

Monteiro-Grillo, I. Terapia com Radiações I. Master Course Radiações Aplicadas às Tecnologias da Saúde, Escola Superior de Tecnologia da Saúde de Lisboa.

Ravasco, P. Lecturer “Patologias e Terapêutica Nutricional”, module “Nutrição” at the Master Program in Nutrition of the Faculty of Medicine of Lisboa.

Ravasco P. Moderator in Scientific Session Exploring the quality of breast cancer radiation therapy, IX Annual Congress ESTRO (European Society of Therapeutic and Radiology and Oncology), Barcelona, Spain, September 12-16, 2010.

Ravasco, P. Lecturer “Mechanisms of wasting in cancer cachexia” at the Advanced Course of Educational Long Life Learning on Nutritional support in cancer for accreditation of Medical Formation in Nutrition (CME) from the European Society for Clinical Nutrition and Metabolism, 32nd Annual ESPEN Congress, September 2010, Nice, France.

Ravasco P. Moderator of a Scientific Session: Nutrição e cancro digestivo, I Jornada de Nutrição e Oncologia, Serviço de Nutrição e Alimentação do Instituto Português de Oncologia do Porto e Escola Portuguesa de Oncologia do Porto, Porto, Portugal, October 22, 2010.

Ravasco, P. President of the Master Program Board in Dietetics and Nutrition 2008-2010. Other board members: Camilo M E. and Cortez-Pinto H.

Ravasco, P. President of the Master Program Board in Nutrition 2010-2012. Other board members: Camilo M E. and Cortez-Pinto H.

Ravasco, P. Supervisor of Boléo-Tomé C. and Chaves M. research projects.

Gustavo de Carvalho (2010) Qual a importância da nutrição no doente oncológico, integrated Master degree in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paula Ravasco.

Ana Lúcia Coronha (2010) Qual a relevância da composição corporal no doente oncológico? integrated Master degree in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paula Ravasco.

Jerónima Isabel Carvalho Correia Raposo (2010) Factores associados à variação de peso em doentes com depressão, Master in Dietetics and Nutrition, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paula Ravasco.

Andreia Filipa Nisa Rolão (2010) Qual o perfil nutricional e de estilos de vida do doente oncológico? Um estudo transversal, integrated Master degree in Medicine, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Paula Ravasco.

Dina Raquel Fernandes João (2010) Protocolo de intervenção nutricional em oncologia: evidência internacional adaptada à realidade Portuguesa. Master in Clinical Nutrition, Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto. Supervisor: Paula Ravasco. Presidente of the examination Board: I. Monteiro-Grillo.

Manuel João Costa de Cutileiro Ferreira (2010) Análise da referenciação médica de doentes para uma Unidade de Cuidados Paliativos”. Faculdade de Medicina Universidade de Lisboa. Presidente of the examination Board: I. Monteiro-Grillo.

Mayra Armani Delalibera (2010) Adaptação e Validação Portuguesa do Instrumento de Avaliação do Luto Prolongado – Prolonged Grief Disorder (PG-13)”. Faculdade de Medicina Universidade de Lisboa. Presidente of the examination Board: I. Monteiro-Grillo.

Maria Elsa Azeredo Soares (2010) Impacto do meio Sócio-económico-demográfico, na qualidade de vida e reacções emocionais (ansiedade e depressão), da mulher mastectomizada”. Faculdade de Medicina Universidade de Lisboa. President of the examination Board: I. Monteiro-Grillo.

Science and Society

Ravasco P. Participation in the debate “Distúrbios Alimentares” in Semana de Prevenção de Jovens para Jovens, organized by Escola Técnica Psicossocial de Lisboa, Auditório Natália Correia, Lisbon, Portugal, February 2010.

Ravasco P. Training session in the debate “Substâncias Psicoactivas: qual o sentido e que implicações na nutrição?” in Feira da Saúde under the theme “Prevenção do consumo de substâncias psico-activas”, organized by Escola Secundária Dona Luísa de Gusmão, Lisbon, Portugal, April 27.

Ravasco P., Boléo-Tomé C. and Chaves M. Training session “Mitos e crenças da Alimentação: que Alimentos? Que realidade? Que dietas?” in the programme Estilos de Vida e Promoção da Saúde na Adolescência, Escola Secundária Vitorino de Nemésio, Lisbon, Portugal.

Ravasco P., Boléo-Tomé C. and Chaves M. Training session “Perigos e consequências para a saúde das Dietas Impulsivas” in the programme Estilos de Vida e Promoção da Saúde na Adolescência, Escola Secundária Vitorino de Nemésio, Lisbon, Portugal.

Ravasco P., Boléo-Tomé C. and Chaves M. Training session “Como modular períodos de *stress* na escola através da alimentação?” in the programme Estilos de Vida e Promoção da Saúde na Adolescência, Escola Secundária Vitorino de Nemésio, Lisbon, Portugal.

Monteiro-Grillo I. President of a Round Table and Speaker at the ONCOFORUM-APEGSAUDE, Fundação C. Gulbenkian, Lisbon, Portugal, October 7, 2010.

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	Training Fellowship
Francisco Aresta Branco	Training Fellowship
Ana Martins Ribeiro	Masters student
Isabella Marcomini	Masters student (left in November 2010)

Keywords/Research Areas

antigenic variation
chromatin
epigenetic
gene expression
parasitology

Major scientific achievements

I spent 2010 establishing my laboratory, which involved learning a lot of administrative procedures, writing grants, hiring collaborators, buying equipment and reagents, setting up tissue culture and beginning the first experiments. So far, we managed to successfully establish the golden gate cloning system in our laboratory, to obtain transgenic parasites and to perform the first phenotypic assays.

The Group Leader was an invited speaker at the annual meeting of the American Society of Tropical Medicine and Hygiene. She has also been awarded two FCT grants, the Crioestaminal prize and an EMBO Installation grant.

In October 2010, the Group Leader initiated the Chromatin Club in the Lisbon area, which gathers 11 groups of four different institutions. The club is sponsored by ActiveMotif and it meets every four weeks for scientific discussions.

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: 3,806, Citations: 5)

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: 31,152, Citations: 15)

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: 12,075, Citations: 34)

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: 17,644, Citations: 21)

Figueiredo LM, Janzen CJ, Cross GAM (2008) A histone methyltransferase modulates antigenic variation in African trypanosomes. *PLoS Biol* **6**, e161 (Journal IF: 12,916, Citations: 27)

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 €)

2009/2014 Startup provided by Instituto de Medicina Molecular (30 000 €)

Publications in peer review Journals

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: 3,806, Citations: 5)

Invited Lectures and Seminars

Figueiredo LM. The role of chromatin in antigenic variation of African trypanosomes. Seminar at Instituto Gulbenkian Ciência. Oeiras, July 16, 2010.

Figueiredo LM. Epigenetic regulation in African trypanosomes. Seminar at Instituto de Higiene e Medicina Tropical. Lisboa, April 29, 2010.

Communications in International Conferences

Figueiredo LM. Epigenetics of antigenic variation: defining new drug targets to make African trypanosomes more susceptible to the host immune response. 59th Annual meeting of the American Society of Tropical Medicine and Hygiene, Atlanta (GA, USA), November 3-7 2010. (Invited oral presentation)

Organisation of Conferences

Figueiredo LM. Organizer and fundraiser of the Lisbon Chromatin Club. Monthly meetings from Oct 2010 to June 2011. Lisboa.

Internationalization

Collaborators:

Prof. Brian Chait, The Rockefeller University, New York, USA

Dr. Christian Janzen, University of Munich, Munich, Germany

Prizes, honours and awards

Prémio Crioestaminal (2010) for the project “Chromatin and antigenic variation: The role of histone H1 in gene regulation in African trypanosomes”.

Rheumatology Research Unit

Major interests / Objectives

The Rheumatology Research Unit (RRU) is a partnership between the Instituto de Medicina Molecular/Faculdade de Medicina da Universidade de Lisboa and the Rheumatology Department of the Santa Maria Hospital. Multidiscipline scientists and clinicians work closely 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 (such as osteoporosis) in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies.

Ongoing research projects are devoted to; the study of the cellular and cytokine environment in very early arthritis; the analysis of the effects of inflammation on atherogenesis in RA and SLE and to the relevance of genetic polymorphisms in the prognosis and pharmacogenetics of RA and SpA. Additionally we are involved in bone quality research in cooperation with Instituto Superior Técnico and the Orthopedic Department of Santa Maria Hospital. Our experimental methodologies are based on a dual approach, which includes human samples and animal models of rheumatic diseases. Finally, we are also involved in several other areas such as ~~in~~ clinical trials; development and coordination of national registries (in collaboration with the Portuguese Society of Rheumatology) and epidemiological studies; ~~in~~ providing services to the community such as offering advisory expertise to governmental institutions and postgraduate teaching.

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 (FML); Rheumatologist, Rheumatology Department, Santa Maria Hospital (HSM); Lisbon, Portugal

Principal Investigators

Helena Canhão, MD, PhD – Assistant Professor, Faculdade de Medicina da Universidade de Lisboa (FML); Rheumatologist, Rheumatology Department, Santa Maria Hospital (HSM); Lisbon, Portugal

Research Team

Joaquim Pereira, MD	Assistant, FML and Training Fellowship
Ana Rodrigues, MD	Assistant, FML and Training Fellowship
Susana Capela, MD	Assistant, FML, Rheumatologist
Filipa Ramos, MD	Assistant, FML, Rheumatologist
Elsa Sousa, MD	Assistant, FML, Rheumatologist
João Dias, MD	Training Fellowship

Cristina Ponte, MD	Training Fellowship
Raquel Marques, MD	Training Fellowship
Pamela Weinmann, PhD	Post Doc Fellowship, FCT (left in July 2010)
Saba Abdulghani, PhD	Post Doc Fellowship, ECTS/Servier grant
Márcio Navalho, MD	PhD student
Rita Moura	PhD Fellowship, FCT
Joana Caetano-Lopes	PhD Fellowship, FCT
Rita Cascão	PhD Fellowship, FCT
Luis Santos	PhD Fellowship, FCT
Ana Catarina Vale	PhD Fellowship, FCT
Maria José Santos, MD	PhD student, Rheumatologist
Ana Filipa Mourão, MD	PhD Fellowship, FCT, assistant, FCML, Rheumatologist
Marketa Fojtíková, MD	PhD student (EULAR fellowship) (left in May 2010)
Inês Perpétuo	Assistant Researcher, IMM
Inês Aleixo	Research Grant, FCT (left in May 2010)
Ana Farinho	Master Student (left in November 2010)
Ana Lopes	Lab Manager, IMM
Bruno Vidal	Research grant, FCT
Diana Fernandes	Assistant Researcher, IMM

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 2010 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- Describing the differences in cardiovascular risk between RA and SLE patients.
- 6- Contribution for the elaboration of international guidelines for diagnosis and monitoring of undifferentiated arthritis (3e Initiative).
- 7- Coordinating the elaboration and establishment of the national databases and registries of rheumatic diseases treated with biotechnology drugs.
- 8- Coordination of the Portuguese Rheumatology Biobank, a part of the IMM biobank.
- 9- Participation in multinational clinical trials as national coordinators allowing refractory patients to have access to the state of art in biotechnological therapies.

10- 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.

11- 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.

Recent Most Relevant Publications

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: 6.368, Citations: 18)

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, 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: 8.111, Citations: 41)

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: 8.111, Citations: 28)

Fonseca JE, Cortez-Dias N, Francisco A, Sobral M, Canhão H, Resende C, Castelão W, Macieira C, Sequeira G, Saraiva F, Pereira da Silva JA, Carmo-Fonseca M, Viana Queiroz M (2005) Inflammatory cell infiltrate and RANKL/OPG expression in rheumatoid synovium– comparison with other inflammatory arthropaties and correlation with outcome. *Clin Exp Rheumatol* **23**, 185-192. (Journal IF: 2,396, Citations: 16)

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: 7.332, Citations: 24)

Ongoing Research Projects

15-07-2007 / 14-07-2010. Effects of inflammation on bone and cartilage: collagen pattern and biomechanical properties, FCT. Coordinator: JE Fonseca (ref. PTDC/SAU-BEB/65992/2006)

The main objectives were:

- 1- To characterize bone and cartilage collagen matrix and to evaluate their organization in areas of pannus (inflammatory infiltrate) and erosions by multiphoton microscopy and to correlate them with the serum levels of joint inflammation and destruction mediators (TNF, IL1, IL6, RANKL and OPG);
- 2- To assess bone mechanical properties in chronic inflammation and to correlate them with the serum levels of joint inflammation and destruction mediators (TNF, IL1, IL6, RANKL and OPG);

3- To verify the correlation between bone collagen matrix structure, bone mineral density in patients with rheumatoid arthritis evaluated by dual X-ray absorptiometry, bone chemical elements quantification in mice with arthritis by spectroscopy (EDS) associated with scanning electron microscopy and bone mechanical properties evaluated by mechanical tests;

4- To identify the serological pattern associated to the most disturbed bone matrix structure and to severe degradation of the biomechanical properties, with consequent greater joint destruction.

We had previously shown the presence of a low RANKL/OPG ratio in the synovial tissue of RA patients. This work is focused on the translational consequences of this observation. In the first 18 months of the project, we have concentrated our efforts in the SKG mouse, which develops a chronic autoimmune polyarthritis, resembling human RA. Our data demonstrated that chronic inflammation induces a reduction in bone density, also affecting the trabecular organization of the bone, leading to the degradation of bone biomechanical properties, namely stiffness, ductility and bone strength. Furthermore, we have shown for the first time that chronic arthritis by itself impairs bone matrix architecture, probably due to disturbed bone remodeling and increased collagen turnover. Other complementary observations were performed in RA patients through the use of MRI and ultrasound. We have also started to gather human material and more than 300 femoral heads have been already frozen. Our interim analysis showed a correlation between the probability of fracture given by the fracture risk assessment tool FRAX and the bone biomechanical properties, suggesting that this score may reflect the current mechanical bone behaviour of an individual patient (paper submitted). We have published 12 papers that are related to this project.

01-01-2009 / 31-12-2011. Cardiovascular risk and inflammation- contribution to the etiopathogenesis of atherosclerosis and cardiovascular disease, FCT. Coordinator: JE Fonseca (ref. PIC/IC/82920/2007)

Our unit have been involved in the understanding of the assessment of short and long term damage in Systemic Lupus Erythematosus patients and we have applied that to the evaluation of new treatment strategies and to cardiovascular risk assessment. In this project we aimed to evaluate the mechanisms and the repercussion of inflammation on the development and severity of atherosclerosis in patients with inflammatory conditions (rheumatoid arthritis and systemic lupus erythematosus) through the following procedures:

- 1- Evaluate the relevance of inflammatory mediators and bone remodeling cytokines on the development of subclinical atherosclerosis and arterial calcifications.
- 2- Evaluate the influence of the TNF gene promoter region and LTA gene polymorphisms on the development and severity of atherosclerosis.
- 3- Identify early prognostic markers of atherogenesis.

The main interim results were: 1) IL-6 promoter -174G/C polymorphism is not a major susceptibility factor to SLE, but predisposes to distinct clinical features (nephritis); 2) The LTA 252 A/G polymorphisms might be a marker for RA susceptibility; 3) The prevalence of subclinical atherosclerosis is not increased in patients with mild lupus; 4) SLE and RA patients present some alterations in hemorheological parameters, which are more pronounced in lupus patients. These results are being integrated in several papers that are in the process of being written or submitted.

So far our Unit have published 7 papers that are related with this project.

01-07-2009 / 30-06-2011. Evaluation of bone quality and its relation to osteoporotic fracture risk, Associação Portuguesa de Osteoporose, Merk Research Grant, Servier Research Grant. Coordinator: H Canhao

The aim of this study is to evaluate the impact of bone quality parameters on the fracture risk calculated by the WHO FRAX tool. In order to fulfill this main goal, a cross-sectional study among patients submitted to hip replacement surgery will be conducted. Femoral epiphysis will

be collected and several bone quality parameters will be studied, namely mechanical properties, microarchitecture, collagen matrix organization and bone structure and mineralization. The magnitude of the association between each bone quality measure and fracture risk calculated by FRAX will be estimated.

Until now, one paper was published related to this project.

01-07-2009 / 30-06-2012. The role of B cells in early Rheumatoid Arthritis, Portuguese Society of Rheumatology. Coordinator: JE Fonseca

The very early inflammatory reaction that occurs in the rheumatoid synovium is mainly constituted by neutrophils. However, this first inflammatory infiltrate quickly leads to increased expression of inflammatory cytokines, chemokines and adhesion molecules, inducing the recruitment of B, T cells and macrophages. In fact, it is this secondary cell infiltrate that supports the persistence of the inflammatory response and mediates cartilage and bone destruction. Although RA has long been considered as a T cell centred disorder, recent evidence suggests that B cells do play an important role in the onset and perpetuation of this disease. B cells function both as interleukin producing cells and antigen presenting cells that activate T cells and are also responsible for the production of autoantibodies, such as rheumatoid factor (RF). RF can interact with Fc γ RIIIa (CD16) receptors on monocytes and macrophages inducing the production of tumour necrosis factor (TNF). Moreover, B cell depletion therapy with Rituximab, a monoclonal antibody directed to CD20, have confirmed the importance of these cells in established RA. Several studies have shown that following B cell depletion in patients with RA, there is clinical and serological improvement which parallels a decrease in RF levels. Despite the evidence for a critical role of B cells in established RA, the knowledge on the participation of these cells in the early phase of the disease is still very scarce. In addition, the effect of commonly used Disease Modifying Anti-Rheumatic Drugs (DMARDs), such as MTX, on B cells is also largely unknown. Moreover the need for rituximab retreatment and biological markers that could lead this decision is still unexplored.

The major goals of this study are:

- 1) Characterize B cell subpopulations in the peripheral blood in the initial phase of RA.
- 2) Differentiate the behaviour of B cells in early and established RA as compared to other forms of arthritis.
- 3) Characterize the influence of immunosuppressive therapies on B cells functional activity and apoptosis in early and established RA patients.
- 4) Characterize the biological markers predictive of response to B cell depleting therapy

Three papers were published.

01-01-2010 / 31-12-2012. 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

This project was approved for funding and will be started in the beginning of 2010. It will focus on the pre-clinical development of carbon monoxide releasing molecules (CORMs) for the treatment of rheumatoid arthritis (RA). Carbon monoxide (CO) has been shown to have a number of anti-inflammatory properties which turn it into an exceptionally promising compound against chronic inflammatory diseases such as RA. In its gaseous form, however, CO will hardly be applicable as a drug in most clinical settings. One proponent SME, Alfama, has conceived and produced a large number of molecules which will release or donate CO, inside the organism, in specific physiological or pathological conditions. These molecules, called CORMs, hold the promise of delivering CO in controlled amounts, at specific rates and in a targeted manner to inflamed tissues such as arthritic joints. We will be responsible, in an animal model of arthritis, to test the effect on the synovial tissue, synovial fluid, cartilage and bone of some of these

compounds. In addition we will assess also the impact of the selected CORMs on the synovial fluid of RA patients (Neutrophils activation state, functional aspects, apoptosis and cytokine production).

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

Osteoporosis (OP) is as a systemic bone disease, characterised by low bone mass and microarchitectural deterioration of the bone tissue, leading to enhanced bone fragility and increased fracture risk. OP is believed to be linked to an imbalance in the remodeling process where more bone is being removed than is being rebuilt through cellular activities. Such imbalance is believed to induce changes in the bone's components (mineral and organic phases), which are responsible for its strength and stiffness, and consequently lead to degraded mechanical properties. Therefore the aim of this study is to characterise the bone's mineral and organic phases during different stages of OP in a mouse model and show that such changes are responsible for the degraded mechanical properties of the osteoporotic bone which consequently lead to its higher fragility and increased fracture risk.

2010-2014. Response-to-anti-TNF treatment biomarkers in Rheumatoid Arthritis Coordinator: Canhão H (ref. HMPS-ICS/SAU-ICT/002/2010)

The main aim of this project is to identify clinical and genetic factors predicting response to TNF antagonist therapy. This will be pursued through an analysis of clinical factors collected from the national database for biological therapies in RA (BioRePortAR) and by performing a genetic wide association study (collaboration with Broad Institute, MIT, USA).

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.

The aim of this study is to identify the role of the NALP3 inflammasome in the initiation, amplification and progression of RA.

The specific objectives are:

- a. To quantify inflammasome activation on blood and synovial fluid samples of patients with early non RA arthritis, early and established RA.
- b. To characterize and measure the inflammasome activation on synovial tissue samples of patients with early non RA arthritis, early and established RA.
- c. To test new molecules that inhibit IL1 production in an animal model of arthritis.

2009-2011 International recommendation for the use of methotrexate. Abbott Research Grant. Local Coordinator: H Canhão. General Coordinator: Bombardier.

Collaborative international effort for the use of methotrexate in rheumatic diseases. Already published and in phase of divulgation.

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. (2010) Dissemination and evaluation of the 3E initiative recommendations for use of methotrexate in rheumatic disorders: results of a study among 2,233 rheumatologists. *Ann Rheum Dis* (Journal IF: 8.111)

2006-2012 Research Projects involving National and International Databases and Registries. Cooperation with Institutional Health Organizations. Coordinator: JE Fonseca

The RRU in association with the Portuguese Society of Rheumatology have been developing National Databases and Registries for rheumatoid arthritis, ankylosing spondylitis, juvenile

idiopathic arthritis and psoriatic arthritis. These databases are being used by all the Portuguese rheumatology departments and are also web-linked to Direcção Geral de Saúde and INFARMED (health governmental institutions). In addition, rheumatoid arthritis databases were connected to an international database network (METEOR) allowing international changes of information and experience. Integrated in this effort the Instituto de Medicina Molecular hosts the Portuguese Society of Rheumatology National Biobank, storing and managing human samples from all the Portuguese Rheumatology departments. JE Fonseca is the Portuguese representative in the European League Against Rheumatism (EULAR) Committee on Investigative Rheumatology, since 2003.

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.

The RRU clinical researchers are leading partners in the development of clinical monitoring protocols, guidelines and recommendations promoted by the Portuguese Society of Rheumatology.

National Recommendations for Clinical Practice:

Fonseca JE, Canhão H, Reis P, Santos MJ, Branco J, Quintal A, Malcata A, Araújo D, Ventura F, Figueiredo G, da Silva JC, Pato JV, de Queiroz MV, Santos RA, Neto AJ, de Matos A, Rodrigues A, Mourão AF, Ribeiro AS, Cravo AR, Barcelos A, Cardoso A, Vilar A, Braña A, Faustino A, Silva C, Godinho F, Cunha I, Costa JA, Gomes JA, Pinto JA, da Silva JA, Miranda LC, Inês L, Santos LM, Cruz M, Salvador MJ, Ferreira MJ, Rial M, Bernardes M, Bogas M, Araújo P, Machado P, Pinto P, de Melo RG, Cortes S, Alcino S, Capela S; Grupo de Estudos de Artrite Reumatóide da Sociedade Portuguesa de Reumatologia. (2010) Portuguese guidelines for the use of biological agents in rheumatoid arthritis - March 2010 update. *Acta Reumatol Port.* Jan-Mar;35(1):95-8. (Journal IF: 0.726, Citations:1)

Publications in peer review Journals

Caetano-Lopes J, Nery AM, Canhão H, Duarte J, Cascão R, Rodrigues A, Perpétuo I, Abdulghani S, Amaral PM, Sakaguchi S, Kontinen YT, Graça L, Vaz MF, Fonseca JE (2010) Chronic arthritis leads to disturbances in the bone collagen network. *Arthritis Res Ther* **12**, R9 (Journal IF: 4.271, Citations: 1) (Editor's Choice)

Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE (2010) Neutrophils in Rheumatoid Arthritis: more than simple final effectors. *Autoimmun Rev* **9** (8), 531-5 (Journal IF: 6.368, Citations: 2)

Mourão AF, Rustin MHA, Isenberg D (2010) Exacerbation of psoriatic skin lesions in 3 patients with psoriatic arthritis receiving anti-tumour necrosis factor-alpha therapy. *Clin Exp Rheumatol* **28** (3), 408-10 (Journal IF: 2,396, Citations: 0)

Moura RA, Weinmann P, Pereira PA, Caetano-Lopes J, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Graça L, Fonseca JE (2010) Alterations on peripheral blood B cell subpopulations in very early arthritis patients. *Rheumatology (Oxford)* **49** (6), 1082-92 (Journal IF: 4.236, Citations: 2)

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 (2010) Dissemination and evaluation of the 3E

initiative recommendations for use of methotrexate in rheumatic disorders: results of a study among 2,233 rheumatologists. *Ann Rheum Dis* Epub ahead of print (Journal IF: 8.111, Citations: 0)

Bogas M, Machado P, Mourão AF, Costa L, Santos MJ, Fonseca JE, Silva JA, Canhão H (2010) Methotrexate treatment in rheumatoid arthritis: management in clinical remission, common infection and tuberculosis. Results from a systematic literature review. *Clin Rheumatol* **29** (6), 629-35 (Journal IF: 1.668, Citations: 0)

Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, Combe B, Cutolo M, de Wit M, Dougados M, Emery P, Gibofsky A, Gomez-Reino JJ, Haraoui B, Kalden J, Keystone EC, Kvien TK, McInnes I, Martin-Mola E, Montecucco C, Schoels M, van der Heijde D, T2T Expert Committee (2010) Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis* **69** (4), 631-7. (Journal IF: 8.111, Citations: 17)

Duarte J, Agua-Doce A, Oliveira VG, Fonseca JE, Graca L (2010) Modulation of IL-17 and Foxp3 Expression in the Prevention of Autoimmune Arthritis in Mice. *PLoS One* **10**, 5 (5) :e10558. (Journal IF: 4.351, Citations: 2)

Jónsdóttir T, Gunnarsson I, Mourão AF, Lu TY, van Vollenhoven RF, Isenberg D. (2010) Clinical improvements in proliferative vs membranous lupus nephritis following B-cell depletion: pooled data from two cohorts. *Rheumatology (Oxford)* **49** (8), 1502-4 (Journal IF: 4.236, Citations:0)

Fonseca JE, Brandi ML. (2010) Mechanism of action of strontium ranelate: what are the facts? *Clin Cases Miner Bone Metab* **7**, 17–18 (Journal IF: N/A)

de la Torre I, Moura RA, Leandro MJ, Edwards J, Cambridge G (2010) B-cell-activating factor receptor expression on naive and memory B cells: relationship with relapse in patients with rheumatoid arthritis following B-cell depletion therapy. *Ann Rheum Dis* **69** (12), 2181-8 (Journal IF: 8.111, Citations: 0)

Santos L, Romeu JC, Canhão H, Fonseca JE, Fernandes PR.(2010) A quantitative comparison of a bone remodeling model with dual-energy X-ray absorptiometry and analysis of the inter-individual biological variability of femoral neck T-score. *J Biomech* **43** (16), 3150-5 (Journal IF: 2.567, Citations: 0)

Cascão R*, Moura RA*, Perpétuo I, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2010) Identification of cytokine network sustaining neutrophils and Th17 activation in early Rheumatoid Arthritis. *Arthritis Res Ther* **12**, R196 *Both authors contributed equally to this work. (Journal IF: 4.271, Citations: 0)

Moura RA*, Cascão R*, Canhão H, Sousa E, Mourão AF, Polido-Pereira J, Rodrigues AM, Queiroz MV, Souto-Carneiro MM, Rosário HS, Graça L, Fonseca JE (2010) Cytokine pattern in early Rheumatoid arthritis favours B cell activation and survival. *Rheumatology (Oxford)* Epub ahead of print. *Both authors contributed equally to this work. (Journal IF: 4.236, Citations: 0)

Machado P, Castrejon I, Katchamart W, Koevoets R, Kuriya B, Schoels M, Silva-Fernández L, Thevissen K, Vercoutere 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, Ostergaard M, Sheane B, Xavier RM, Zochling J, Bombardier C (2010) 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*. Epub ahead of print. (Journal IF: 8.111, Citations: 0)

Santos MJ, Fernandes D, Capela S, da Silva JC, Fonseca JE (2010) Interleukin-6 promoter polymorphism -174 G/C is associated with nephritis in Portuguese Caucasian systemic lupus erythematosus patients. *Clin Rheumatol* [Epub ahead of print] (Journal IF: 1.668, Citations:0)

Fonseca JE, Canhão H, Reis P, Santos MJ, Branco J, Quintal A, Malcata A, Araújo D, Ventura F, Figueiredo G, da Silva JC, Patto JV, de Queiroz MV, Santos RA, Neto AJ, de Matos A, Rodrigues A, Mourão AF, Ribeiro AS, Cravo AR, Barcelos A, Cardoso A, Vilar A, Braña A, Faustino A, Silva C, Godinho F, Cunha I, Costa JA, Gomes JA, Pinto JA, da Silva JA, Miranda LC, Inês L, Santos LM, Cruz M, Salvador MJ, Ferreira MJ, Rial M, Bernardes M, Bogas M, Araújo P, Machado P, Pinto P, de Melo RG, Cortes S, Alcino S, Capela S, Grupo de Estudos de Artrite Reumatóide da Sociedade Portuguesa de Reumatologia (2010) Portuguese guidelines for the use of biological agents in rheumatoid arthritis - March 2010 update. *Acta Reumatol Port* **35** (1), 95-8. (Journal IF: 0.726, Citations:1)

Mourão AF, Canhão H, Sousa E, Cascão R, Costa JB, Almeida LS, Oliveira ME, Gomes MM, Queiroz MV, Fonseca JE (2010) From a neutrophilic synovial tissue infiltrate to a challenging case of rheumatoid arthritis. *Acta Reumatol Port* **35** (2), 228-231. (Journal IF: 0.726, Citations:1)

Campanilho-Marques R, Polido-Pereira J, Rodrigues A, Ramos F, Saavedra MJ, Costa M, Martins F, Pereira da Silva JA, Canhão H, Fonseca JE (2010) BioRePortAP, an electronic clinical record coupled with a database: an example of its use in a single centre. *Acta Reumatol Port* **35**(2), 176-83 (Journal IF: 0.726, Citations:0)

Fonseca JE, Santos MJ, da Silva JA, Coelho P, Tavares V, Marques A, Branco J, da Silva JR, Queiroz MV, Figueirinhas J, Martins R, Canhão H (2010) Acta Reumatologica Portuguesa: impact factor attributed in June 2010 *Acta Reumatol Port* **35** (2), 129-30 (Journal IF: 0.726, Citations:0)

Santos MJ, Vinagre F, Canas da Silva J, Gil V, Fonseca JE. (2010) Cardiovascular risk profile in systemic lupus erythematosus and rheumatoid arthritis: a comparative study of female patients. *Acta Reumatol Port* **35**, 325-332 (Journal IF: 0.726, Citations: 0)

Ramiro S, Canhão H, Branco JC. (2010) EpiReumaPt Protocol- Portuguese epidemiologic Study of the Rheumatic diseases. *Acta Reumatol Port* **35**, 384-390 (Journal IF: 0.726, Citations: 0)

Canhão H (2010) Mudar e Evoluir. *Acta Reumatol Port*. **35**, 293 (Journal IF: 0.726, Citations: 0)

Ribeiro A, Machado P, Ramiro S, Duarte C, Mourão AF, Bogas M, Costa L, Bernardes M, Santos MJ, Fonseca JE, Canhão H (2010) Portuguese Recommendations «How to diagnose, monitor and treat undifferentiated peripheral inflammatory arthritis»: systematic literature review and expert opinion. *Acta Reumatol Port* **35**, 475-496 (Journal IF: 0.726, Citations:0)

Ferreira AR, Santos MJ, Canas da Silva J, Fonseca JE, Gil V (2010) Avaliação não invasiva da função endotelial em doentes com Lúpus Eritematoso Sistémico. *Rev Port Cardiol*; **29** (Supl 1):69

Other publications International

Sousa E, Fonseca JE, McInnes I, Treatment of Rheumatoid Arthritis in EULAR Compendium on Rheumatic Diseases (online course and book in press)

Other publications National

Fonseca JE, Canhão H, Santos MJ, Mourão AF, Sousa E, Caetano Lopes J, Moura R, Weinmann P, Pereira da Silva JA, Branco J, Queiroz MV Uma nova visão das doenças reumáticas inflamatórias: um exemplo de interacção da biologia celular e molecular com a clínica. Edições Bial. Lisboa 2010. ISBN 978-989-95520-8-1

Invited Lectures and Seminars

Fonseca JE. The relevance of IL6 in the physiopathology of Rheumatoid Arthritis. XXXVIII Congresso Mexicano de Reumatologia, Morelia, Mexico, February 20, 2010.

Canhão H. Challenges - Relationship Specialist & Primary Care, 1st European Interdisciplinary Rheumatology Conference, Dubrovnik, Croatia, March 19-21,2010

Fonseca JE. The Rheumatology Research Unit IMM and the Day Care Unit HSM. Sessão do Serviço de Reumatologia do Hospital Gregório Marañón, Madrid, Espanha, April 15, 2010

Moura R. B cells in early arthritis. Sessão do Serviço de Reumatologia do Hospital Gregório Marañón, Madrid, Espanha, April 15, 2010

Fonseca JE. From acute to chronic unremitting arthritis towards an hematooncological strategy for the treatment of chronic arthritis. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010

Fonseca JE. JCW Edwards Retirement-The global impact, University College London, London, UK, July 8, 2010

Fonseca JE. Disease Course and Management of rheumatoid arthritis. 2nd European Clinical Medicine Conference for Family Doctors, General Practitioners and Internists, Bucharest, Romania , October 1-3, 2010.

Fonseca JE. Novas alternativas terapêuticas para osteoartrose. XIV Jornadas Nacionais Patient Care, Lisbon, Portugal, February 25-26, 2010

Fonseca JE. Artrite Psoriática ou Psoríase Artropática: duas orientações para o mesmo doente, III Fórum das Espondiloartropatias, Óbidos, Portugal, February 27, 2010

Fonseca JE. Cytokines, Bone and Biomechanics. IMM Seminar, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, March 8, 2010

Canhão H. Osteoporose, quem tratar e como tratar. Jornadas do Hospital Garcia de Orta, Almada, Portugal, March 26, 2010

Canhão H. Revisão do Ano. Ciência Básica. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Canhão H. Simpósio da Abbot. Novos conceitos nas espondilartropatias. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Canhão H, Caetano-Lopes J, Perpétuo IP, Rodrigues A, Fonseca JE. O papel das citocinas na remodelação óssea. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE, Treat to target in rheumatoid arthritis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Mourão AF, S. Falcão. Encontro com Especialista: Reumatismos peri-articulares mais frequentes na prática clínica. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Canhão H, Caetano-Lopes J, Perpétuo IP, Rodrigues A, Fonseca JE. O papel das citocinas na remodelação óssea. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE. Rituximab no tratamento da artrite reumatóide: otimizar os resultados na prática clínica. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Santos MJ. Aterosclerose prematura nas doenças reumáticas sistémicas. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Canhão H. Avanços terapêuticos nas Doenças Reumáticas Sistémicas. Hospital da Luz, Lisbon, Portugal, April 21, 2010

Canhão H. Vivência na Clínica, Docência e Investigação. Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal April 21, 2010

Polido-Pereira J. Patologia Frequente no Idoso – Fibromialgia. III Jornadas da Família, Lisbon, Portugal, May 6- 8, 2010

Fonseca JE. É a aterosclerose uma doença inflamatória? Inflamação e aterosclerose. Aula Magna da Faculdade de Medicina de Lisboa, Lisbon, May, 11, 2010

Santos MJ. Tendo em conta a realidade nacional quais as estratégias futuras para alcançar a remissão num maior numero de doentes? Estratégia hemato-oncológica. Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May 14, 2010

Canhão H. Hospital de dia de Reumatologia: uma unidade polivalente: HD como centro de

investigação clínica. Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May 14, 2010

Mourão AF, Rodrigues A, Polido-Pereira J, Machado P. Difficult Case Reports. Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May 14, 2010

Fonseca JE. B cell Research Forum Discussion panel. Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May 14, 2010

Moura R. New data from UCL and IMM. Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May 14, 2010

Santos L. Qualitative Analysis of the Osteoporotic Bone Implementing synergies in Biomedical Engineering- IEEE Engineering in Medicine & Biology Lisbon, Portugal, June 11, 2010

Rodrigues A. Fracture Risk and Bone Biomechanics. Implementing synergies in Biomedical Engineering - IEEE Engineering in Medicine & Biology Lisbon, Portugal, June 11, 2010

Polido-Pereira J. Tocilizumab, análise interina do ActSure. Meeting of the rheumatology department, Hospital de Santa Maria, Lisbon, Portugal, June 22, 2010

Fonseca JE. Does the FRAX fracture risk score have a biomedical meaning? Encontro com a ciência e tecnologia em Portugal - Ciência 2010, July 4-7, 2010

Canhão H. Clinical and genetic predictors of response to anti-tnf treatment in patients with Rheumatoid Arthritis. Harvard Medical School, Boston, EUA, July 28, 2010

Canhão H. O que aprendemos sobre segurança com os dados dos registos de doentes em terapêutica biológica? III Summit Reumatologia, Évora, Portugal, September 18, 2010

Fonseca JE. Psoriatic Arthritis: the role of the Dermatologist and why should we have joint clinics Lisbon, Golimumab National Launch, Portugal, November 20, 2010

Rodrigues A, Miguel C, Ramiro S. What are the risk/predictive factors for chronic pain in patients with inflammatory arthritis? 3e Initiative 2010. Cascais, Portugal, October 2010.

Rodrigues A. “Avaliação da qualidade do osso de epífises femorais e correlação com os factores de risco de fractura em doentes com fractura de fragilidade da anca”.5ª Bolsa de Investigação Fundação Astrazeneca/FML.13ª Workshop Educação pela Ciência. Lisbon, Portugal. December 14, 2010

RodriguesA. Osteoporose “back to the basis”. Meeting of the rheumatology department, Hospital de Santa Maria, Lisbon, Portugal, March 9 2010.

Polido-Pereira J. Fibromialgia. Meeting of the rheumatology department,Hospital de Santa Maria, Lisbon, Portugal, June 29, 2010

Polido-Pereira J. Poliartrite: Diagnóstico Diferencial. Meeting of the rheumatology department,, Hospital de Santa Maria, Lisbon, Portugal, October 19, 2010

Perpétuo I. Differences in osteoclastic activity between Rheumatoid Arthritis and Ankylosing spondylitis. Meeting of the rheumatology department, Hospital de Santa Maria, Lisbon, Portugal, October 26, 2010

Fonseca JE. "Treating Rheumatoid Arthritis with Biologics" e "Treating Lupus with Biologics". Segunda Reunião do Núcleo de Doenças Autoimunes do Hospital de Santa Maria, Lisbon, Portugal, November 19, 2010

Cascão R. Caspase-1 is active since the early phase of Rheumatoid Arthritis. Meeting of the rheumatology department, Hospital de Santa Maria, Lisbon, Portugal, November 23, 2010

Cascão R. Caspase-1 is active since the early phase of Rheumatoid Arthritis. IV IMM PhD Students Meeting, Lisbon, Portugal, November 22-23, 2010

Moura R. B-Cell-Activating Factor Receptor expression on naïve and memory B cells: relationship with relapse in patients with Rheumatoid Arthritis following B cell depletion therapy. IV IMM PhD Students Meeting, Lisbon, Portugal, November 22-23, 2010

Communications in International Conferences

Perpétuo I, Fernandes D, Cascão R, Moura R, Caetano-Lopes J, Rodrigues A, Polido-Pereira J, Viana Queiroz M, Fonseca JE, Canhão H. TNF Antagonists and tocilizumab have a higher impact on rheumatoid arthritis osteoclastogenic stimuli than methotrexate.

30th European Workshop of Rheumatology Research, Bamberg, Germany, March 4- 7, 2010 (Poster presentation)

XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Oral presentation)

Moura R, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues A, Polido-Pereira J, Viana Queiroz M, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine profile in serum and synovial fluid of established rheumatoid arthritis patients.

30th European Workshop of Rheumatology Research, Bamberg, Germany, March 4- 7, 2010 (Poster presentation)

7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Oral presentation)

11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Cascão R, Moura R, Canhão H, Sousa E, Mourão AF, Rodrigues A, Polido-Pereira J, Viana Queiroz M, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine network in the first 6 weeks of rheumatoid arthritis onset.

30th European Workshop of Rheumatology Research, Bamberg, Germany, March 4- 7, 2010 (Poster presentation)

7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Oral presentation)

11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Rodrigues A, Caetano-Lopes J, Perpétuo I, Aleixo I, Pena A, Faustino A, Polido-Pereira J, Sousa E, Romeu JC, Amaral PM, Monteiro J, Queiroz MV, Vaz MF, Fonseca JE, Canhão H. Absolute risk of fracture calculated by FRAX reflects bone mechanical properties.

IOF World Congress on Osteoporosis & 10th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, Florence, Italy, May 5-8, 2010 (Poster presentation)

11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Oral presentation)

37th European Symposium on Calcified Tissues, Glasgow, Scotland, June 26-30, 2010 (Poster presentation)

Rodrigues A, Caetano-Lopes J, Perpétuo I, Aleixo I, Pena A, Faustino A, Polido-Pereira J, Sousa E, Romeu JC, Amaral PM, Monteiro J, Queiroz MV, Vaz MF, Fonseca JE, Canhão H. Apolipoprotein E is correlated with bone biomechanical properties and fracture risk calculated by FRAX.

IOF World Congress on Osteoporosis & 10th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, Florence, Italy, May 5-8, 2010 (Poster presentation)

11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Caetano-Lopes J, Rodrigues A, Aleixo I, Perpétuo IP, Fernandes D, Lopes A, Faustino A, Pena A, Polido-Pereira J, Sousa E, Romeu JC, Amaral PM, Monteiro J, Queiroz MV, Vaz MF, Fonseca JE, Canhão H. Fracture risk assessed by FRAX translates bone cell activity.

IOF World Congress on Osteoporosis & 10th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, Florence, Italy, May 5-8, 2010 (Poster presentation)

11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

37th European Symposium on Calcified Tissues, Glasgow, Scotland, June 26-30, 2010 (Poster presentation)

Perpétuo I, Caetano-Lopes J, Rodrigues A, Polido-Pereira J, Viana Queiroz M, Fonseca JE, Canhão H. Influence of anti-TNF drugs, tocilizumab and methotrexate on osteoclast differentiation. 30th European Workshop of Rheumatology Research, Bamberg, Germany, March 4- 7, 2010 (Poster presentation)

Caetano-Lopes J, Aleixo I, Rodrigues A, Perpétuo IP, Fernandes D, Lopes A, Pena AS, Faustino A, Vale M, Amaral PM, Monteiro J, Vaz MF, Canhão H, Fonseca JE. Bone cell activity influence bone fragility and fracture risk. 30th European Workshop of Rheumatology Research, Bamberg, Germany, March 4- 7, 2010 (Poster presentation)

Santos MJ, Fernandes D, Vinagre F, Perpétuo I, Cascão R, Capela S, Canas da Silva J, Fonseca JE. Higher Leptin levels in lupus patients are associated with irreversible damage. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Poster presentation)

Santos MJ, Fernandes D, Vinagre F, Perpétuo I, Cascão R, Capela S, Canas da Silva J, Fonseca JE. Does adiponectin have a protective effect in women with rheumatoid arthritis? 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Poster presentation)

Polido-Pereira J, Ferreira, AI, Rodrigues AM, Carvalho AM, Saavedra MJ, Barros R, Catita C, Marques A, Canhão H, Queiroz MV, Canas da Silva J, Fonseca JE. Tuberculosis safety monitoring of rheumatoid arthritis patients treated with TNF inhibitors based on an electronic

registry – (BioReportar) - Single centre experience. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Poster presentation)

Figueiredo R, Caetano-Lopes J, Perpetuo I, Vidal B, Sousa, E, Canhão H, Parente M, Pereira J, Borges R, Queiroz MV, Fonseca JE. Ankylosing spondylitis patients carrying the tumor necrosis factor gene promotor -308GA/AA genotypes have better symptomatic and functional response to TNF antagonists. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Poster presentation)

Bogas M, Santos MJ, Fonseca JE, Dias C, EASI Group. Antinuclear antibodies in clinical practice: questionnaire applied to portuguese rheumatologists. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010 (Poster presentation)

Moura RA, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Established Rheumatoid Arthritis synovial fluid cytokine pattern favours B cell stimulation and Th17 differentiation. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Pimentel-Santos FM, Mourão AF, Ribeiro C, Costa J, Santos J, Barcelos A, Sousa E, Pinto P, Godinho F, Cruz M, Rabiais S, Félix J, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC, CORPOREA Study Group. Spectrum of Ankylosing Spondylitis in Portugal. BASDAI, BASFI, BASMI and MSASSS reference centile charts in this population. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Pimentel-Santos FM, Thomas G, Matos M, Mourão AF, Costa J, Santos H, Sousa E, Pinto P, Godinho F, Barcelos A, Cruz M, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC, CORPOREA Study Group. Peripheral blood gene expression profiles in ankylosing spondylitis: new insights in immunopathogenesis? 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Falcão S, De Miguel E, Mourão A, Papoila A, Matos A, Araújo P, Castelão W, Branco J. Sensibility to change of ultrasound guided intra-articular injection of triamcinolone hexacetonide in patients with aseptic arthritis: interim analysis. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Pimentel-Santos FM, Ribeiro C, Pinto L, Ribeiro A, Sousa M, Sousa E, Pinto P, Barcelos A, Godinho F, Cruz M, Rabiais S, Fonseca JE, Félix J, Branco JC, CORPOREA Study Group. Explaining generic health related quality of life with disease specific measures in ankylosing spondylitis. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Santos MJ, Fernandes D, Caetano-Lopes J, Perpétuo I, Vidal B, Vinagre F, Canhão H, Canas da Silva J, Fonseca JE. Lymphotoxin 252 A>G polymorphism in portuguese rheumatoid arthritis patients. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Moura RA, De La Torre I, Leandro MJ, Edwards J, Cambridge G. BAFF-R expression on naive and memory B cells: relationship with relapse in patients with rheumatoid arthritis (RA) following B cell depletion therapy. 11th Annual European Congress of Rheumatology, Italy, Rome, June 16-19, 2010 (Poster presentation)

Pimentel-Santos FM, Matos M, Ligeiro D, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Pinto P, Sousa E, Godinho F, Cruz M, Fonseca JE, Trindade H, Guedes-Pinto H, Branco JC, CORPOREA Study Group. HLA class I and II associations of ankylosing spondylitis. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

De La Torre I, Moura R, Leandro M, Edwards JC, Cambridge G. Expression of the idiotope 9G4 on autoantibodies and B cells from patients with Rheumatoid Arthritis (RA): description of a new B cell phenotype. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Madruza Dias J, Costa M, Schaller Dias J, Almeida A, Fernandes A, Pereira da Silva J, Viana de Queiroz M. Case report of osteomesopyknosis: a rare cause of back pain. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Madruza Dias J, Costa M, Pereira da Silva J, Viana de Queiroz M. Sexuality, fertility and pregnancy in Rheumatic Diseases. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Madruza Dias J, Costa M, Pereira da Silva J, Viana de Queiroz M. Review of 5 years of peripheral and axial septic arthritis in a portuguese rheumatology department. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Gonzalez A, Suarez-Gestal M, Calaza M, Witte T, Papasteriades C, Marchini M, Migliaresi M, Kovacs A, Ordi-Ros J, Bijl M, Santos MJ, Ruzickova S, Pullmann R, Carreira P, Skopouli FN, D'Alfonso S, Sebastiani GD, Suarez A, Blanco FJ, Gomez-Reino JJ, European Consortium of SLE DNA Collections. Differences of systemic Lupus Erythematosus clinical features between two large European population subgroups. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)

Laires P, Fonseca JE, Garcia EB. Association between rheumatoid arthritis and diabetes mellitus type 2. 11th Annual European Congress of Rheumatology, Rome, Italy, June 16-19, 2010 (Poster presentation)
International Society for Pharmacoeconomics and Outcomes Research, 13th Annual European Congress, Prague, Czech Republic, November 6-9, 2010 (Poster presentation)

Perpétuo I, Caetano-Lopes J, Rodrigues A, Polido-Pereira J, Viana Queiroz M, Fonseca JE, Canhão H. Influence of TNF blockers, tocilizumab and methotrexate on osteoclast differentiation in Rheumatoid Arthritis patients. 37th European Symposium on Calcified Tissues, Glasgow, Scotland, June 26-30, 2010 (Poster presentation)

Rodrigues A, Perpétuo I, Caetano-Lopes J, Aleixo I, Pena A, Faustino A, Polido-Pereira J, Sousa E, Romeu JC, Amaral PM, Monteiro J, Queiroz MV, Vaz MF, Fonseca JE, Canhão H. Negative correlation between osteocalcin serum levels and bone mechanical properties. 37th European Symposium on Calcified Tissues, Glasgow, Scotland, June 26-30, 2010 (Poster presentation)

Santos L, Fernandes PR, Fonseca JE. Simulation of BMU activity and mineralization in trabecular bone for the measurement of BMDD. 17th Congress of the European Society of Biomechanics University of Edinburgh, UK, July 5 – 8, 2010 (Oral presentation)

Marques R, Ponte C, Fonseca JE, Pereira J, Rodrigues A, Macieira C, Stone R, Simão C, Almeida M, Canhão H, Ramos F, Pereira da Silva JA. Mycophenolate mofetil use in refractory juvenile systemic lupus erythematosus. 17th Pediatric Rheumatology European Society Congress, Valencia, Spain, September 9-12, 2010 (Poster presentation)

Laires PA, Fonseca JE, Benito EG. The Epidemiologic Relationship Between Rheumatoid Arthritis and Diabetes Mellitus Type 2. EuroEPI - Congresso Europeu de Epidemiologia, Florência, Itália, November 6-9, 2010 (Poster presentation)

Laires PA, Fonseca JE, Benito EG. The underlying Factors for the increased risk of Diabetes Mellitus Type 2 in Rheumatoid Arthritis Patients. 18th annual EUPHA (The European Public Health Association) meeting, Amesterdão, Holanda, November 10-13, 2010 (Poster presentation)

Haraoui B, Smolen JS, Aletaha D, Breedveld FC, de Wit M, Dougados M, Emery P, Gibofsky A, Van Der Heijde DM, Burmeste GR, Cardiel-Rios M, Codreanu C, Durez P, Fonseca JE, Graninger WB, Hamuryudan V, Jannaut-Pena MJ, Kalden J, Kvien TK, Laurindo I, Montecucco C, Pereira DaSilva JA, Poor G, Santos Moren PI, Stanislawska-Biernat E, Takeuchi T and Treat to Target Taskforce. Treating Rheumatoid Arthritis to Target: Multinational Recommendations Assessment Questionnaire. 74th Annual Scientific Meeting of the American College of Rheumatology, November 6 -11, 2010 Atlanta, Georgia (Poster presentation)

De La Torre I, Valon L, Moura RA, Leandro MJ, Edwards J, Cambridge G. BAFF Binding Receptors (BBR) Related To Relapse after Rituximab in Patients with Rheumatoid Arthritis (RA). 74th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, November 6 -11, 2010 (Poster presentation)

Pimentel-Santos FM, Ligeiro D, Matos M, Mourão AF, Costa J, Santos H, Sousa E Barcelos A, Godinho F, Fonseca JE, Guedes-Pinto H, Branco JC, Brown MA, Gethin T (2010) Whole Blood Transcriptional Profiling in Ankylosing Spondylitis Identifies Novel Putative Candidate Genes for Both the Inflammatory and Tissue-Destructive Aspects of the Disease. 74th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, November 6 -11, 2010 (Poster presentation)

Rygg M, Pistorio A, Ravelli A, Maghnie M, Di Iorgi N, Demirkaya E, Pasic S, Ozdogan H, Bader-Meunier B, Da Silva CM, Harel L, Molina MR, Canhão H, Roth J, Wouters C, Barash J, Ammar R, Dracou C, Gandon-Laloum S, Martini A and Ruperto N. Longitudinal Study on Growth Failure and Height Deflection in Juvenile Systemic Lupus Erythematosus (JSLE): The Result of a Prospective Multicentre PRINTO Study. 74th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, November 6-11, 2010 (Poster presentation)

De La Torre I, Moura RA, Leandro MJ, Jonathan C., Edwards J, Cambridge G. Expression of the Idiotope G4 on Autoantibodies and B Cells from Patients with Rheumatoid Arthritis (RA): Description of a New B Cell Phenotype. 74th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, November 6 -11, 2010 (Poster presentation)

Caetano-Lopes J, Lopes A, Rodrigues A, Fernandes D, Perpétuo IP, Monjardino T, Lucas R, Monteiro J, Kontinen YT, Canhão H, Fonseca JE. Upregulation of inflammatory genes and downregulation of sclerostin are key elements for fracture healing. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Cascão R, Moura R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early Rheumatoid Arthritis. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Moura R, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Cytokine pattern in very early Rheumatoid arthritis favours B cell activation and survival. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Moura R, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graça L, Fonseca JE. Spondyloarthritis and Rheumatoid arthritis: Two different diseases, a similar cytokine network. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (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. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Campanilho-Marques R, Polido-Pereira J, Rodrigues A, Ramos F, Saavedra MJ, Costa M, Martins F, Pereira da Silva JA, Canhão H, Fonseca JE. BioRePortAP, an electronic clinical record coupled with a database: an example of its use in a single centre. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Mourão AF, Canhão H, Moura R, Cascão R, Weinmann P, Pereira J, Resende C, Capela S, Pereira da Silva J, Fonseca JE. Predictors of chronicity and the discriminative value of the new ACR/EULAR rheumatoid arthritis classification criteria in an untreated polyarthritis cohort with less than 6 weeks of disease duration. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Mourão AF, Rodrigues A, Vinagre F, Sousa E, Polido-Pereira J, Macieira C, Ramos F, Costa J, Gomes P, Pereira da Silva J, Fonseca JE, Santos MJ, Canhão H. Eight years of experience with biological treatment in juvenile idiopathic arthritis. Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, December 1-3, 2010 (Poster presentation)

Marques R, Ponte C, Fonseca JE, Pereira J, Rodrigues A, Macieira C, Stone R, Simão C, Almeida M, Canhão H, Ramos F, Pereira da Silva JA. Mycophenolate mofetil use in refractory juvenile systemic lúpus erythematosus. Fifth European Workshop on Immune-Mediated Inflammatory Diseases Sitges, Barcelona, Spain, December 1-3, 2010 (Poster presentation)

Communications in National Conferences

Falcão S, Eugénio de Miguel, Mourão AF, Papoila A, Matos AA, Araújo P, Castelão W, Branco JC. Sensibility to change of ultrasound guided intra-articular injection of triamcinolone

hexacetonide in patients with aseptic arthritis: interim analysis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Polido-Pereira J, Rodrigues A, Castro S, Canhão H, Fonseca JE, Queiroz MV Lúpus-like induzido por etanercept manifestando-se como polisserosite. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Ramiro S, Roque R, Godinho F, Gonçalves P, Garcês S, Vinagre F, Cordeiro A, Tavares V, Canas da Silva J, Santos MJ. Avaliação da resposta a terapêuticas biológicas em doentes com Artrite Reumatóide. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Leitão A, Rodrigues A, Polido-Pereira J, Ramos F, Macieira C, Neto A, Fonseca JE, Queiroz MV, Canhão H. Cinco Casos de Dermatômiosite Juvenil. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Navalho M, Resende C, Gaspar A, Pereira da Silva J. Ressonância magnética dinâmica das mãos e punhos em 3,0 tesla no estudo de poliartropatias inflamatórias: experiência inicial e correlação clínica. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Perpétuo I, Caetano-Lopes J, Rodrigues A, Polido-Pereira J, Queiroz MV, Fonseca JE, Canhão H. Influence of anti-TNF drugs, tocilizumab and methotrexate on osteoclast differentiation. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Roque R, Ramiro S, Cordeiro A, Godino F, Gonçalves P, Santos MJ, Canas da Silva J. Experiência do Hospital Garcia de Orta com Rituximab na Artrite Reumatóide. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Polido-Pereira J, Rodrigues A, Vieira M, Carvalho AM, Saavedra MJ, Marques A, Catita C, Castro S, Canhão H, Queiroz MV, Fonseca JE. Aplicação da BioRePortAR na avaliação de eficácia dos agentes anti-TNF no Hospital de Santa Maria. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Melo Gomes JA, Mourão AF, Caetano-Lopes J. Terapêutica biológica em doentes com Artrite Idiopática Juvenil. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Roque R, Vinagre F, Ramiro S, Godinho F, Gonçalves P, Santos MJ, Canas da Silva J. Espondilite Anquilosante e Neoplasias em doentes medicados com anti-TNF α coincidência ou causalidade? XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Pimentel-Santos FM, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Sousa E, Pinto P, Godinho F, Cruz M, Rabiais S, Félix J, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC, CORPOREA Study Group. Spectrum of ankylosing spondylitis in Portugal. BASDAI, BASFI, BASMI and MSASSS reference centile charts in this population. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Pimentel-Santos FM, Matos M, Ligeiro D, Mourão AF, Ribeiro C, Costa J, Santos H, Barcelos A, Barcelos A, , Pinto P, Sousa E, Godinho F, Cruz M, Fonseca JE, Trindade H, Guedes-Pinto H, Branco JC, CORPOREA Study Group. HLA class I and II associations of ankylosing spondylitis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Rodrigues A, Resende C, Polido-Pereira J, Sousa E, Guerra J, Queiroz MV, Canhão H, Fonseca JE. Safe use of etanercept in an ankylosing spondylitis patient with a kidney transplant treated with tacrolimus and micophenolate mophetil. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Pimentel-Santos FM, Mourão AF, Ribeiro C, Santos H, Sousa E, Barcelos A, Ribeiro A, Godinho F, Pinto P, Cruz M, Fonseca JE, Rabiais S, Félix J, Guedes-Pinto H, Branco JC, CORPOREA Study Group. Explaining generic health related quality of life with disease specific measures in ankylosing spondylitis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Ribeiro C, Silva I, Mourão AF, Araújo P, Pimentel F, Mateus M, Patricia N, Falcão S, Castelão W, Matos AA, Branco JC. Doença de Mikulicz - Caso clínico. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Ribeiro C, Silva I, Pinto L, Mourão AF, Araújo P, Pimentel F, Mateus M, Patricia N, Falcão S, Castelão W, Pimentão JB, Matos AA, Branco JC. Miosites inflamatórias e rastreio oncológico - A propósito da nossa casuística. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Rodrigues A, Canhão H, Sousa E, Marques A, Romeu JC, Costa M, Canhão P, Morgado C, Fonseca JE, Pereira da Silva JA, Queiroz MV. Reversible posterior leucoencephalopathy syndrome in Systemic Lupus Erythematosus. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Roque R, Ramiro S, Vinagre F, Cordeiro A, Godinho F, Gonçalves P, Tavres V, Santos MJ, Canas da Silva J. Amiloidose secundária a doenças reumáticas sistémicas. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Falcão S, Mourão AF, Silva I, Nero P, Mateus M, Martins MJ, Branco JC. Efeitos adversos da vacina Pandermix em doentes com doenças reumáticas inflamatórias. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Weinmann P, Cascão R, Ferreira AC, Mourão AF, Canhão H, Queiroz MV, Fonseca JE. Diminuição da apoptose e da capacidade de activação dos neutrófilos em doentes com poliartrite em fase inicial. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Mourão AF, Falcão S, Ribeiro C, Silva I, Nero P, Pimentel F, Branco JC. “Bate bate coração”...Granulomatose de Wegener com envolvimento cardíaco. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Rodrigues A, Caetano-Lopes J, Perpétuo I, Aleixo I, Pena AS, Faustino A, Polido-Pereira J, Sousa E, Romeu C, Amaral P, Monteiro J, Viana Queiroz M, Vaz F, Fonseca JE, Canhão H.

Absolute risk of fracture calculated by FRAX reflects bone mechanical properties. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Ribeiro C, Silva I, Pinto L, Mourão AF, Araújo P, Pimentel F, Mateus M, Nero M, Falcão S, Castelão W, Pimentão JB, Matos AA, Branco JC. Manifestações reumatológicas de doença renal - Caso clínico. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Marques R, Capela S, Canhão H, Ramos F, Romeu JC, Pereira da Silva JA, Queiroz MV. "Sacrolite" na Insuficiência Renal Crónica - Um caso de Osteodistrofia Renal associada a Hiperparatiroidismo Secundário. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Caetano-Lopes J, Rodrigues A, Perpétuo I, Aleixo I, Fernandes D, Lopes A, Faustino A, Pena A, Polido-Pereira J, Sousa E, Romeu JC, Amaral P, Monteiro J, Viana Queiroz M, Vaz F, Fonseca JE, Canhão H. Fracture risk assessed by FRAX translates bone cell activity. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Gomes JA, Mourão AF. Relação quantidade/qualidade óssea: uma análise utilizando os dados disponíveis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Moura R, Cascão R, Perpétuo I, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto- Carneiro MM, Graça L, Fonseca JE. O padrão de citocinas no líquido articular da artrite reumatóide estabelecida favorece a diferenciação de células B e TH17. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Castelão W, Nero P, Mateus M, Pimentel F, Araújo P, Fonseca JE, Branco JC. Caracterização da população de doentes com Artrite Reumatóide que suspenderam medicação anti-tnf alfa de forma definitiva no Serviço de Reumatologia do Hospital de Egas Moniz – Uma experiência de 10 anos. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Polido-Pereira J, Ramiro S, Ferreira AI, Roque R, Rodrigues AM, Carvalho AM, Saavedra MJ, Barros R, Catita C, Marques A, Canhão H, Queiroz MV. Canas da Silva J, Santos MJ, Fonseca JE, Tuberculosis safety monitoring and the use of TNF inhibitors in Portuguese rheumatoid arthritis patients. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Polido-Pereira J, Rodrigues A, Canhão H, Fonseca JE, Queiroz MV. Cirrose biliar primária e Artrite Reumatóide - desafio terapêutico. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Poster presentation)

Polido-Pereira J, Vieira M, Rodrigues A, Carvalho AM, Saavedra MJ, Catita C, Marques A, Canhão H, Queiroz MV, Canas da Silva J, Santos MJ, Fonseca JE. Avaliação da segurança das terapêuticas biotecnológicas em doentes com artrite reumatóide com base na BioRePorTAR no Hospital de Santa Maria. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Cascão R, Moura R, Canhão H, Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto- Carneiro MM, Graça L, Fonseca JE, Caracterização do padrão de citocinas nas primeiras 6 semanas de evolução da artrite reumatóide. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Ramiro S, Roque R, Godinho F, Gonçalves P, Garcês S, Vinagre F, Cordeiro A, Tavres V, Canas da Silva J, Santos MJ, Biológicos e switch na Artrite Reumatóide – estamos a ser mais agressivos? XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Barbosa L, Ramiro S, Roque R, Feliz J, Godinho F, Gonçalves P, Santos MJ, Canas da Silva J. Satisfação dos doentes em relação ao hospital dia de reumatologia. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Rodrigues A, Caetano-Lopes J, Perpétuo I, Aleixo I, Pena AS, Faustino A, Polido-Pereira J, Sousa E, Romeu C, Amaral P, Monteiro J, Viana Queiroz M, Vaz F, Fonseca JE, Canhão H. Apolipoprotein E is correlated with bone biomechanical properties and fracture risk calculated by FRAX. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Pimentel-Santos FM, Thomas G, Matos M, Mourão AF, Costa J, Santos H, Sousa E, Pinto P, Godinho F, Barcelos A, Cruz M, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC, CORPOREA Study Group. Peripheral blood gene expression profiles in ankylosing spondylitis: new insights in immunopathogenesis? XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Marques R, Polido Pereira J, Ramos F, Rodrigues A, Canhão H, Queiroz MV, Fonseca JE. BioRePortAP - first analysis from a single centre. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Mourão AF, Rodrigues A, Vinagre F, Sousa E, Polido-Pereira J, Macieira C, Ramos F, Costa J, Gomes P, Queiroz MV, Fonseca JE, Santos MJ, Canhão H. Seven years of experience with biological treatment in Juvenile Idiopathic Arthritis. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Rodrigues A, Capela S, Polido-Pereira J, Canhão H, Rodrigues R, Marques M, Graça L, Queiroz MV. Consulta pré-concepcional de doenças reumáticas- um ano de experiência. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Fernandes D, Perpétuo I, Vinagre F, Canhão H, Santos MJ, Fonseca JE. sRANKL/OPG ratio is Increased in Systemic Lupus Erythematosus Patients. XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010 (Oral presentation)

Ferreira AR, Santos MJ, Canas da Silva J, Fonseca JE, Gil VM. Avaliação não invasiva da função endotelial em doentes com lúpus eritematoso sistémico. XXXI Congresso Português de Cardiologia, Vilamoura, Portugal, Abril 7- 10, 2010 (Oral presentation)

Mourão AF. Artrites Idiopáticas Juvenis. XII Jornadas Internacionais de Reumatologia Pediátrica, Lisbon, Portugal, May 13-14, 2010 (Oral presentation)

Fonseca JE. Fisiopatologia das Manifestações extra intestinais das doenças inflamatórias intestinais. Manifestações extra intestinais das doenças inflamatórias intestinais, Óbidos, Portugal, Outubro 9, 2010 (Oral presentation)

Polido-Pereira J, Sousa E, Fonseca JE. Rheumatoid Arthritis. What is refractory disease and how to manage it ? 1st Porto's Autoimmunity Meeting, Porto, Portugal, Outubro 8-9, 2010 (Oral presentation)

Organisation of Conferences

Canhão H. Chairman in lecture Patient treatment profile. Optimising Treatment of Rheumatoid Arthritis, Barcelona, Spain, January 29-30, 2010.

Fonseca JE. Chairman in lecture Arthritis, infection and autoimmunity: are we ready to change the pace of arthritis treatments. 7th International Congress on Autoimmunity, Ljubljana, Slovenia, May 5-9, 2010

Fonseca JE. Chairman in lecture Inflammation and systemic disease in Making Connections in Chronic Kidney Failure Prague, Czech Republic, October 29-30, 2010

Fonseca JE. Member of the Organizing Steering Committee, Fifth European Workshop on Immune-Mediated Inflammatory Diseases, Barcelona, Spain, December 1-3, 2010

Fonseca JE. Chairman in lecture Autoimmune diseases diagnosis. Can we facilitate a more rational ordering process and use of autoantibodies? Isabel Abreu (Lisbon, Portugal). Systemic Autoimmune Diseases, 8th Medinterna International Meeting, Porto, Portugal, January 20-23, 2010

Fonseca JE and Canhão H. Organizers "Sessão Científica de Homenagem ao Professor Viana Queiroz. Ordem dos Médicos", Lisbon, Portugal, February 23, 2010

Canhão H. Chairman in lecture. Dermatomiosite juvenil . Curso de Reumatologia da Sociedade Portuguesa de Pediatria. Óbidos, Portugal, March 12- 14, 2010

Fonseca JE and Canhão H. Organizers and members of the Scientific Committee. XV Portuguese Congress of Rheumatology. Funchal, Portugal, April 7-10, 2010

Fonseca JE. Chaired the session "Artrite Reumatoide". XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE. Chaired the session "RNA Therapy: The Next big thing after monoclonal antibodies." Maria Carmo-Fonseca (Lisbon, Portugal). XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE. Chaired the session "Simpósio da Roche". XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE. Organizer and chairman of "Curso Pré Congresso: Imunologia Clínica". A Imunologia das doenças reumatológicas. Marta Monteiro, Luís Graça (Lisbon, Portugal), XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010

Fonseca JE. Chaired a session “Para além da articulação”. Reunião da Associação Nacional de Doentes com Artrite Reumatóide. Portugal. April, 14, 2010.

Fonseca JE Chairman in lecture Childhood Connective Tissue Diseases in the XII Jornadas Internacionais de Reumatologia Pediátrica, Lisbon, May 13- 14, 2010
JE Fonseca. Chaired a session in XII Jornadas Internacionais de Reumatologia Pediátrica, Lisbon, Portugal, May 13-14, 2010

Canhão H. Chaired a session in XII Jornadas Internacionais de Reumatologia Pediátrica, Lisbon, Portugal, May 13-14, 2010

Fonseca JE. Co-chair in Rheumatoid arthritis: from practical issues to cutting edge translational research, Lisbon, Portugal, May, 14, 2010

Fonseca JE. Organized and chaired the meeting “Rheumatoid Arthritis: From Practical issues to cutting edge translational research”. Lisbon, Portugal, May 14, 2010

Internationalization

RRU has set a number of collaborative international research projects:

- 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 Kontinen Mari and Ainola))
- Bone biology, structure and biomechanics (in collaboration with University of Helsinki (YT Kontinen and Mari Ainola))
- Epidemiology of Rheumatic Diseases, Cohorts, Registries and Databases. Recommendations and Guidelines (in collaboration with Brigham Women Hospital, Harvard Medical School (Daniel Solomon and Michael Weinblatt))

Prizes, honours and awards

Associação Portuguesa de Osteoporose/ Merck Sharp Dohme Award 2009 was awarded in January 2010 to Rodrigues AM, Caetano Lopes J, Aleixo I, Vidal B, Perpétuo I, Sousa E, Pereira J, Pereira MF, Romeu JC, Vaz MF, Viana Queiroz M, Monteiro J, Fonseca JE, Canhão H for the project "Avaliação da qualidade do osso de epífises femorais e correlação com os factores de risco clínicos de fractura em doentes submetidos a artroplastia da anca".

Senior Clinical Award, Harvard Medical School- Portugal Program was awarded in February 2010 to Canhão H.

ECTS/Servier award 2010 was awarded in March 2010 to Abdulghani S.

Best oral communication Award. Pimentel-Santos FM, Thomas G, Matos M, Mourão AF, Costa J, Santos H, Sousa E, Pinto P, Godinho F, Barcelos A, Cruz M, Fonseca JE, Guedes-Pinto H, Brown MA, Branco JC Peripheral blood gene expression profiles in ankylosing spondylitis: new

insights in immunopathogenesis? XV Congresso Português de Reumatologia, Funchal, Madeira, Portugal, April 7-10, 2010.

FML/ASTRA award 2010 was awarded in December 2010 to Marques R, Perpétuo I, Pereira da Silva JA, Fonseca JE for the project “Differences in osteoclastic activity between rheumatoid arthritis and ankylosing spondylitis”.

Industry contract research

Pfizer Research Grant: 2009-2011. The role of inflammasome in the initiation and perpetuation of Rheumatoid Arthritis: Contribution for new targeted therapies. Coordinator: JE Fonseca.

Merk Research Grant and Servier Research Grant: 01-07-2009 / 30-06-2011. Evaluation of bone quality and its relation to osteoporotic fracture risk, Associação Portuguesa de Osteoporose,. Coordinator: H Canhão

Government/Organization contract research

The RRU in association with the Portuguese Society of Rheumatology have been developing National Databases and Registries for rheumatoid arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and psoriatic arthritis. These databases are being used by all the Portuguese rheumatology departments and are also web-linked to Direcção Geral de Saúde and INFARMED (health governmental institutions). In addition, rheumatoid arthritis databases were connected to an international database network (METEOR) allowing international changes of information and experience. Integrated in this effort the Instituto de Medicina Molecular hosts the Portuguese Society of Rheumatology National Biobank, storing and managing human samples from all the Portuguese Rheumatology departments.

Advanced teaching

Fonseca JE and Baeten D. Inflammatory Immune Mediated Diseases: Rheumatoid Arthritis as a paradigm, Program For Advanced Medical Education, Gulbenkian Foundation, Lisbon, Portugal, January 27, 2010

Fonseca JE, Rodrigues A and Capela S. Dor e Doenças Reumáticas, Mestrado de Dor, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, February 19, 2010.

Canhão H. Apresentação de casos clínicos de dermatomiosite juvenil (workshop interactivo de casos clínicos). Curso de Reumatologia da Sociedade Portuguesa de Pediatria. Óbidos, Portugal, March 12- 14, 2010

Canhão H. Fisiopatologia da Osteoporose. 1º Simpósio da Coluna Vertebral – Patologia da Coluna Vertebral Osteoporótica, Lisbon, Portugal April 16-17, 2010

Canhão H. Terapêutica da Osteoporose. I Curso Teórico-Prático de Técnicas Ginecológicas de Ambulatório, Évora, Portugal, April 17- 18, 2010

Fonseca JE. Importância da referência precoce na artrite. XXXI Curso de Reumatologia, Hospitais da Universidade de Coimbra, Coimbra, Portugal, October 21-23, 2010

Fonseca JE and Caetano-Lopes J. "Osteoimmunology", in Shoenfeld, Y. (ed.), Autoimmunity: Etiology, pathogenesis, clinical manifestation and diagnostic methodologies, The Biomedical & Life Sciences Collection, Henry Stewart Talks Ltd, London, 2010, Learning audio and video session. (online at <http://hstalks.com/?t=BL0162715-Fonseca>)

Canhão H and Fonseca JE, members of 3e Steering Committee Members participated in interactive web site designed to disseminate the UPIA recommendations, 2010

Science and Society

Ana Rodrigues and Helena Canhão participated, in January 2010, in 1 TV program (Porto Canal) to discuss the osteoporosis prevention and research in bone diseases (after being awarded by a Grant from Associação Portuguesa de Osteoporose/MSD).

João Eurico Fonseca participated, in April 2010, in TV program, Bom Dia Portugal - RTP1 to discuss what is Rheumatoid Arthritis and what are its consequences.

Helena Canhão participated, in April 2010 in a press conference for discussing the project "Response-to-anti-TNF treatment biomarkers in Rheumatoid Arthritis".

João Eurico Fonseca participated, in May 2010 in the public release of the book "Bioquímica" Eds. Professor Martins e Silva and Professora Carlota Saldanha

João Eurico Fonseca participated, in May 2010 in TV program Falar Global - Sic Notícias to discuss what is Rheumatoid Arthritis and what have the research in this field produced so far with implications for the daily living of patients. RRU participated in a report, May 2010 TV program Falar Global - Sic Notícias.

Master thesis completed

Alexandra Faustino (2010) "Caracterização de doentes com fractura do colo do fémur". Medicine Master Thesis. Supervisors: João Eurico Fonseca and Helena Canhão

Ana Lopes (2010) "Procedimentos e técnicas utilizadas num laboratório de investigação em inflamação e osso" Biomedical Master Thesis. Supervisor: Helena Canhão

André Leitão (2010) "Cinco casos de dermatomiosite juvenil" Medicine Master Thesis Supervisor: Helena Canhão

Pedro Castelhanito (2010) "Qualidade óssea: efeito do génes e do envelhecimento" Medicine Master Thesis Supervisor: Helena Canhão

Joana Moreira (2010) "Evolução clínica e laboratorial dos doentes com artrite idiopática juvenil tratados com agentes biológicos" Medicine Master Thesis Supervisor: Helena Canhão

Miguel Mendonça Pinto (2010) "Late-onset febrile neutropenic in a rhus patient treated with rituximab" Medicine Master Thesis Supervisor: Joaquim Polido Pereira

Fabio Viana (2010) “Safe use etanercept in association with tacrolimus and microphenolate mofetil in an ankylosing spondylitis patient that realized renal transplant” Medicine Master Thesis: Joaquim Polido Pereira

Ana Sofia Pena (2010) “Caracterização da população de doentes com coxartrose submetidos a artroplastia da anca no Hospital de Santa Maria” Medicine Master Thesis Supervisor: Helena Canhão

Sara Guerreiro de Castro (2010) “ Anti-TNF induced lupus-like syndrome in a patient with rheumatoid arthritis” Medicine Master Thesis Supervisor: Joaquim Polido Pereira

Margarida Vieira (2010) “Avaliação da segurança dos antagonistas do TNF em doentes com artrite reumatoide seguidos no HSM com base na BioReportar” Medicine Master Thesis Supervisor: Helena Canhão

Ana Isabel Ferreira (2010) ”Tuberculosis safety monitoring of the use of TNF inhibitors in Portuguese rheumatoid arthritis patients based on an electronic medical chart and registry – BioReportar – Experience of a single centre” Medicine Master Thesis Supervisor: Joaquim Polido Pereira

Ricardo da Silva Borges (2010) “BioReportar: The first analysis” Medicine Master Thesis. Supervisor: Joaquim Polido Pereira

Liliana Dias Gomes (2010) “ Contágio sexual de *Brucella spp.* A propósito de uma caso clínico” Medicine Master Thesis. Supervisor: Susana Capela

Ana Rita Farinho (2010) “Caracterização funcional, histológica e celular da longa porção do bicipite em doentes com tendinopatia” Biologic Master Thesis. Supervisor: Helena Canhão

Other Thesis

João Eurico Fonseca (2010) Habilitation in Medicine, Speciality Rheumatology. Faculdade de Medicina da Universidade de Lisboa.

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, FML

Research Team

Marta Miranda, PhD	Post Doc Fellowship, FCT
Sofia Marques, PhD	Post Doc Fellowship, FCT
Teresa Carlos, PhD	Post Doc Fellowship, FCT
Lénia Rodrigues, PhD	Post Doc Fellowship, FCT
Jérémie Decalf, PhD	Post Doc Fellowship, IMM
Marta Alenquer, PhD	Post Doc Fellowship, IMM
Filipa Lopes	PhD Fellowship, FCT
Cristina Silva	PhD Fellowship, FCT
Alexandre Costa	Technician

Keywords/Research Areas

Viral Pathogenesis
Prion diseases

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

Gammaherpesvirus latent infection: immunological synapse modulation (PTDC/SAU-MII/099314/2008)

Patogénese de gamma-herpesvírus: modulação dos factores de transcrição celulares NF-kB e MYC (PTDC/SAU-MIC/110887/2009)

Publications in peer review Journals

Ribot JC, Chaves-Ferreira M*, d'Orey F *, Wencker M, Gonçalves-Sousa N, Decalf J, Simas JP, Hayday AC and Silva-Santos B (2010) Cutting Edge: Adaptive versus innate receptor signals selectively control the pool sizes of murine IFN-gamma- or IL-17-producing gamma-delta T cells upon infection. *Journal of Immunology* **185** (11), 6421-5. (Journal IF: 5.646)

Orge L, Oliveira A, Machado C, Lima C, Ochoa C, Silva J, Carvalho R, Tavares P, Almeida P, Ramos M, Pinto MJ, Simas JP (2010) Putative emergence of classical scrapie in a background of enzootic atypical scrapie. *Journal of General Virology* **91** (Pt 6), 1646-50. (Journal IF: 3.241)

Invited Lectures and Seminars

Simas P., *Translating viral functions into pathogenesis*, Berlin Life Science Colloquium, Max Planck Institute for Infection Biology, Paul Ehrlich Lecture Hall - Campus Charité, September 30, 2010

Communications in National Conferences

Simas P., Invited Speaker at 4th National Meeting on Signal Transduction, SINAL 2010, IBB/CBME - Centre for Molecular and Structural Biomedicine, Faro, Universidade do Algarve, May 21-22, 2010

Internationalization

Collaboration with Philip Stevenson, University of Cambridge , UK.

Mycobacteria-Host Interactions Unit

Major interests / Objectives

The ability of Koch's bacilli (Mtb) to create tuberculosis or a latent infection rely, 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
Marta Barroso	Training Fellowship, FCT (left Nov 2010)
Leonor Freire Santos	Training Fellowship, FCT

Keywords/Research Areas

Innate immunity
Intracellular trafficking
Host-pathogen interactions
Tuberculosis

Major scientific achievements

- 1) We found that ESAT-6 is the major Mtb PAMP activating the NLRP3/ASC inflammasome and that other's inflammasomes are activated in the context of Mtb infection (Mishra et al, 2010).
- 2) We set up two methods: a fluorimetric and alternative method to the Colony forming Unit assay, to assess Mtb intracellular survival within macrophages and; applications of Confocal Microscopy for Quantification of Intracellular Mycobacteria in Macrophages (Bettencourt et al., 2010).
- 3) We found that Mtb activates the over-expression and down-regulation of a set of miRNAs during macrophage phagocytosis. Some of the miRNAs are involved in controlling actin dynamics during infection (Bettencourt et al. in prep).
- 4) Exosomes released from mycobacteria-infected cells have recently been shown to be pro-

inflammatory. Infected macrophages release more exosomes and the exosomes they released had more Hsp70 on their surface leading to NF-KB activation and TNFalpha release in uninfected macrophages (Anand et al. 2010).

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:4)

Kuehnel M, Rybin V, Anand P, Anes E and Griffiths G (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 8)

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 10)

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 15)

Anes E, Kuhnel MP, Bos E, Moniz-Pereira J, Habermann A and 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

2009/2011. 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.

2010/2012. 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.

2010/2012. 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

2010/2012. 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)

2010/2012. 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

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:4)

Prakash H, Lüth A, Grinkina N, Holzer D, Wadgaonkar R, Gonzalez AP, Anes E, Kleuser B (2010) Sphingosine kinase-1 (SphK-1) regulates *Mycobacterium smegmatis* infection in macrophages. *PLoS One* **5** (5), e10657. (Journal IF 4,5, Citations:0)

Anand PK, Anand E, Bleck CK, Anes E, Griffiths G (2010) Exosomal Hsp70 induces a pro-inflammatory response to foreign particles including mycobacteria. *PLoS One* **5** (4), e10136. (Journal IF 4,5, Citations:1)

Other publications International

Bettencourt P, Pires D, Carmo N and Anes E (2010) Application of Confocal Microscopy for Quantification of Intracellular Mycobacteria in Macrophages. *Microscopy: Science, Technology, Applications and Education A*. Méndez-Vilas and J. Díaz (Eds.), *Microscopy Book series 2010*.

Xuan L, David P, Ainsa JA, Mulhovo S, Anes E, Ferreira MJU (2010) Antimycobacterial activity of traditional medicinal plants used in Mozambique *PLANTA MEDICA* Volume: 76 Issue: 12 Pages: 1294-1294

Pires D, Bettencourt P, Carmo N, Bergant T, Jordao L and Anes E (2010) Interference of *Mycobacterium tuberculosis* with the endocytic pathways on macrophages and dendritic cells from healthy donors: role of Cathepsins. *Drug Discovery Today* Volume 15 issue 23-24 pg 1112

Pires P, Bettencourt P, Carmo N, Niederweis M and Anes E (2010) Role of *Mycobacterium tuberculosis* outer-membrane porins in bacterial survival within macrophages. *Drug Discovery Today* Volume 15 issue 23-24 pg 1112-1113

Invited Lectures and Seminars

Anes, E. Identificação e manipulação das vias de sinalização que activem os mecanismos bactericidas de macrófagos infectados com micobactérias". "Centro de Malária e Doenças Tropicais, CMDT", Ciclo de palestras 2009/2010, Instituto de Higiene e Medicina Tropical, Lisboa, July 26, 2010.

Anes, E. 2010. Why phagocytosis need not be a degrading experience for mycobacteria? IMM seminar, July 19

Communications in International Conferences

Pires, D., Bettencourt, P., Carmo, N., Bergant, T., Jordao, L and Anes, E. Interference of *Mycobacterium tuberculosis* with the endocytic pathways on macrophages and dendritic cells from healthy donors: role of Cathepsins. 3Th Cellular Delivery of Therapeutic Macromolecules International Symposium, CDTM 2010, Cardiff, Wales, June 26-29, 2010 (Poster presentation)

Pires, P., Bettencourt, P., Carmo, N., Niederweis, M., and Anes, E. Role of *Mycobacterium tuberculosis* outer-membrane porins in bacterial survival within macrophages 3rd Cellular Delivery of Therapeutic Macromolecules International Symposium, CDTM 2010, Cardiff, Wales, June 26-29, 2010 (Poster presentation)

Pires, D., Bettencourt, P., and Anes, E. Cathepsins B and S Content in *Mycobacterium* Containing Compartments in Human Macrophages and Dendritic cells. Current Opinion Conferences: Cellular Host-Pathogen Interactions, Amsterdam, Netherlands, September 5-7, 2010 (Poster presentation)

Mishra, B.B., Moura-Alves P., Sonawane A., Hacohe N., Griffiths G., Moita LF., and Anes, E. *Mycobacterium tuberculosis* Protein ESAT-6 is a Potent Activator of the NLRP3/ASC Inflammasome. Current Opinion Conferences: Cellular Host-Pathogen Interactions, Amsterdam, Netherlands, September 5-7, 2010 (Poster presentation)

Anes, E. The human macrophage and the killing mechanisms for mycobacteria. European Science Foundation EMRC Exploratory Workshop EW09-007 Multi-disciplinary consortium for the development of effective, but non-toxic drugs against MDR-TB and XDR-TB, Lisboa, Portugal, December 1-3, 2010 (Invited Oral presentation).

Xuan L., David P., Ainsa J.A., Mulhovo S., Anes E., Ferreira M.J.U. 2010 Antimycobacterial activity of traditional medicinal plants used in Mozambique 7th Tannin Conference/58th International Congress and Annual Meeting of the Society-for-Medical-Plant-and-Natural-Product-Research, Berlin, Germany, August 29 - September 02, 2010 (Poster presentation)

Communications in National Conferences

Anes, E. *Mycobacterium tuberculosis* protein ESAT-6 is a potent activator of the NLRP3/ASC inflammasome. XXXVI Annual Meeting of the Portuguese Society for Immunology Fighting Intracellular Pathogens: from bench to bedside, Braga, September 20-22, 2010. (Invited Oral presentation).

Organisation of Conferences

Anes, E. Organized the URJA/IMM seminar *Mycobacterium tuberculosis* interactions with host cells. Olivier Neyrolles, Institute of Pharmacology & Structural Biology (IPBS) CNRS, University of Toulouse France, April 9, 2010

Anes, E. Organized the URJA/IMM seminar The Wiskott-Aldrich Syndrome: How can impaired phagocytosis lead to increased autoimmunity? Ted Strom Blood Bank and Hematology Section, Pathology and Laboratory Medicine Service Memphis VA Medical Center, April 30, 2010

Internationalization

All our publications are in collaboration with foreign groups.

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)

Advanced teaching

Elsa Anes. 2010. Endocytic Pathways: new avenues for drug delivery and targeting. Lessons from pathogens. Master in “Farmacotecnia Avançada: Farmacotecnia avançada III”. April 18

Elsa Anes. 2010. Innate immunity mechanisms for bacterial infections. Module Microbiologia e Saúde of the Master of “Microbiologia Aplicada UL.” February 25

Elsa Anes 2010. Why phagocytosis need not be a degrading experience for tuberculosis bacilli? Master in “Biologia Molecular em Saude ICSS”, June 26

Elsa Anes 2010. Cellular Biology. Co-ordinator. Integrated master in Pharmaceutical Sciences FFUL

Elsa Anes. 2010. Immunity to tuberculosis. Immunology (2nd year). Integrated master in Pharmaceutical Sciences FFUL

Master thesis completed

David Alexandre Pires (2010) Role of mycobacteria porins and efflux pumps on the intracellular survival within macrophages. Master in Applied Microbiology. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes.

Marta Maria Seixas Barroso (2010) “Desenvolvimento de um método para avaliar a sobrevivência/morte de *Mycobacterium tuberculosis* em macrófagos humanos por fluorimetria” . Master in Applied Microbiology. Faculdade de Ciências da Universidade de Lisboa. Supervisor: Elsa Anes.

Retroviruses Research Unit

Major interests / Objectives

We were interested in identifying cellular proteins and pathways involved in the multistep process of HIV-1 infection that may result in the discovery of more adapted and effective therapeutic targets. Using shRNA libraries, we have focused in the discovery of kinases and phosphatases that are essential for HIV-1 replication but dispensable for cell viability, aiming to find new anti-HIV drug targets. Moreover, we selectively manipulate the transcription of genes controlling the HIV-1 life-cycle, specifically using zinc-finger library screening and answering questions related to the mechanism of APOBEC3G expression/regulation. We are also developing strategies to inhibit HIV-1 infectivity. These strategies are based on the platform of small antibody scaffolds that use a unique variable region. We are targeting both the receptor and co-receptors of HIV-1 together in identifying novel targeting epitopes in HIV-1 gp160.

Head of Unit

João Gonçalves, PhD – Associate Professor, Faculdade de Farmácia da Universidade de Lisboa.

Principal Investigators

Inês Soeiro, PhD – Kings College

Research Team

Inês Soeiro, PhD	Post Doc Fellowship, FCT
Mariana Santa-Marta, PhD	Ciência 2009
Paula Brito, PhD	Post Doc Fellowship, FCT
Cátia Cantante	PhD Fellowship, FCT
Sylvie Rato	PhD Fellowship, FCT
Soraia Oliveira	PhD Fellowship, FCT
Lidia Fonseca	PhD Fellowship, FCT
Luis Ferreira	PhD Fellowship, FCT
Andreia Couto	PhD Fellowship, FCT
André Ferreira	Training Fellowship
Ana Catarina Santos	Training Fellowship

Keywords/Research Areas

HIV-1
functional screenings
recombinant antibodies
lentiviral vectors

Major scientific achievements

- A) We identified new 14 proteins essential 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 (Rato et al. PlosOne, 2010).
- B) We designed new synthetic small domain antibodies that are able to target gp41 and inhibit HIV-1 and HIV-2 infection (Santos et al. J. Virology, 2010). 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 (Cadima-Couto et al. JNP, 2010). Moreover, we showed that modelling the intracellular half-life of A3G can induce its Vif-independent targeting to the ubiquitin-proteasome system (Cadima-Couto et al, Virology, 2010).

Recent Most Relevant Publications

Cadima-Couto I, Freitas-Vieira A, Nowarski R, Britan-Rosich E, Kotler M, Goncalves (2009) Ubiquitin-fusion as a strategy to modulate protein half-life: A3G antiviral activity revisited. *Virology* **393**, 286-94. (Journal IF: 4.5, Citations 5).

Rato S, Maia S, Brito PM, Resende L, Pereira CF, Moita C, Freitas RP, Moniz-Pereira J, Hacoen N, Moita LF, Goncalves J. (2010) Novel HIV-1 knockdown targets identified by an enriched kinases/phosphatases shRNA library using a long-term iterative screen in Jurkat T-cells. *PLoS One* **5** (2), e9276. (Journal IF: 6.5, Citations 6).

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. *J Virology* (In press). (Journal IF: 5.9).

Cadima-Couto I, Saraiva N, Santos ACC, Goncalves J. Vif Interaction with APOBEC3 and its Characterization by a New Sensitive Assay. *Journal of Neuroimmune Pharmacology* (In press). (Journal IF: 3.6).

Esteves AIS, Nicolai M, Humanes M and Goncalves J. 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).

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.

Publications in peer review Journals

Rato S, Maia S, Brito PM, Resende L, Pereira CF, Moita C, Freitas RP, Moniz-Pereira J, Hacoheh N, Moita LF, Goncalves J. (2010) Novel HIV-1 knockdown targets identified by an enriched kinases/phosphatases shRNA library using a long-term iterative screen in Jurkat T-cells. PLoS One. 5(2):e9276. (Journal IF: 6.5, Citations 6).

Other publications International

Rato S, Maia S, Brito PM, Resende L, Pereira CF, Moita C, Freitas RP, Moniz-Pereira J, Hacoheh N, Moita LF, Goncalves J. (2010) Novel HIV-1 knockdown targets identified by an enriched kinases/phosphatases shRNA library using a long-term iterative screen in Jurkat T-cells. Centennial Retroviruses Meeting. Prague, 2010.

Other publications National

José Azevedo-Pereira, João Gonçalves. “Replicação Viral”. Microbiologia, Lidel, 2010

Invited Lectures and Seminars

Joao Goncalves, Qualidade dos medicamentos biológicos. Hospital de Évora. December 2, 2010.

Joao Goncalves, Research and Development of Biologics. Merck, Sesimbra. April 18, 2010.

Joao Goncalves, Course of Biologic Medicines, APFH, Coimbra, May 13-14, 2010.

Joao Goncalves, Molecular Biology of HIV, Ordem Farmacêuticos, FFUL. November 18, 2010.

Communications in International Conferences

Goncalves, J. Intracellular immunity to HIV-1 by APOBEC3G. Closing the Gap between basic research and clinical practice, IMM-Lisboa. January 22-23. (Oral Presentation).

Rato S., Resende L., Brito P.M., Pereira C.F., Moita C., Freitas R.P., Hacoheh N., Moita L.F., Goncalves J. Functional shRNA screen reveals kinases and phosphatases essential for HIV-1 replication. 2010 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 2010. 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, Milan. October 23. (Poster presentation).

Oliveira, S, Aires da Silva, F, Goncalves J. The potential use of combinatorial strategies to multimerize single-domain antibodies. Antibody Engineering 2010, San Diego, USA. December 4-9. (Oral presentation).

Organisation of Conferences

Goncalves, J. co-organized the meeting “Closing the Gap between basic research and clinical practice” IMM-Lisboa. January 22-23.

Goncalves, J. co-organized the meeting “Closing the Gap between basic research and clinical practice” IMM-Lisboa. January 22-23.

Patents/prototypes

Albumin-binding Domain-fusions and use thereof to improve protein pharmacokinetics. USPTO 61104594

Advanced teaching

Goncalves, J. Lectured a seminar at the PhD course at the Faculty of Medicine of Coimbra “ApoBec3G and HIV-1 restriction.” Coimbra, November 14, 2010.

Goncalves, J. Lectured a seminar at the Master course at the Faculty of Pharmacy of Coimbra “Recombinant antibodies.” Coimbra, November 2, 2010.

Goncalves, J. Lectured a seminar at the Protein Nanocourse at IMM. “Recombinant antibodies against HIV-1” . May 2, 2010.

Master and Ph.D. thesis completed

PhD Thesis

Claudia Ferreira (2010) “Measles vírus: Early infection and progression” PhD thesis, Faculdade de Farmácia da Universidad de de Lisboa. Supervisors: João Gonçalves and Roberto Cattaneo.

Sylvie Rato (2010) “Cell-host interaction: Assessing the role of helper factors during HIV-1 replication”. PhD thesis, Faculdade de Farmácia da Universidad de de Lisboa. Supervisors: João Gonçalves.

Master Thesis

Ana Catarina Santos (2010) “Functional aspects of new helper factors for HIV replication”. Mestrado em Microbiologia Aplicada, Faculdade de Ciências da Universidade de Lisboa e faculdade de Farmácia da Universidade de Lisboa. Supervisor: João Gonçalves.

Neurosciences

Programme Coordinator: Ana Sebastião and Mamede de Carvalho

Heads of Unit:

Isabel Rocha, PharmD, PhD

Tiago Fleming Outeiro, PhD

José Ferro, MD, PhD

Mamede de Carvalho, MD, PhD

Joaquim Alexandre Ribeiro, MD, PhD

Principal Investigators:

Isabel Rocha, José Ducla-Soares, Pedro Freire Costa, Diana Cunha-Reis, Edgar Almeida

Tiago Fleming Outeiro, Teresa Pais

José Ferro, Alexandre Casto Caldas, Alexandre de Mendonça, Isabel Pavão Martins, José Pimentel, Cristina Sampaio, Teresa Paiva, Sofia A. Oliveira, Patrícia Canhão, Joaquim Ferreira

Mamede de Carvalho

Joaquim Alexandre Ribeiro, Ana Sebastião, Alexandre Mendonça, Luísa Lopes, Maria José Diógenes, Cláudia Valente

Autonomic Nervous System Unit

Major interests / Objectives

The Unit of Autonomic Nervous System is devoted to the study of the autonomic nervous system in areas related to cardiovascular control. It assembles researchers with medical and non-medical degrees. The research protocols embrace both ex-vivo and in-vivo animal lab studies which are complemented by the clinical evaluation of patients with dysautonomy performed at our human autonomic lab. Our staff also contributes to the teaching of Physiology in Medical and non-Medical curricula involving around 900 students per school year. The Unit also give support to students under mobility schemes being strongly involved in the spreading of knowledge on autonomic function and dysfunction through international post-graduated courses and advisory actions at both national and international levels.

Head of Unit

Isabel Rocha, PharmD, PhD – Associate Professor with “Agregação” in Physiology, Faculty of Medicine of Lisbon

Principal Investigators

Isabel Rocha, PharmD, PhD, Associate Professor with “Agregação”, Faculty of Medicine University of Lisbon

José Ducla Soares, MD, PhD, Full Professor of Medicine, Faculty of Medicine, University of Lisbon (left during 2010)

Pedro Freire Costa, MD, PhD, Full Professor of Physiology, Faculty of Medical Sciences, New University of Lisbon

Diana Cunha-Reis, PhD, Instituto de Medicina Molecular & Faculty of Sciences, University of Lisbon

Edgar Almeida, MD, PhD, Faculty of Medicine of Lisbon, University of Lisbon

Research Team

Ana Moura Santos; PhD	Assistant Professor Physiology , FMC
Carlos Marques Neves, MD, PhD	Assistant Professor Physiology, FML
Cristiano Tavares dos Santos, MSc	Junior researcher
Fernanda Vargas Amaral MSc (Jan 2010-Nov 2010)	Junior researcher
Gabriela Postolache, PhD	Assistant Professor Physiology UATLA
Mariana Santos, MD (left during 2010)	Neurologist
Mário Oliveira, MD, PhD	Cardiologist
Nataniel Rosa, DMV	Junior researcher
Sérgio Laranjo, MD	Resident Cardiology
Vera Geraldes, MSc	PhD Student

Keywords/Research Areas

Autonomic nervous system
cardiovascular regulation
signal processing,
disautonomy,
autonomic evaluation, autonomic remodelling, heart,
Hilbert-Huang, wavelets

Major scientific achievements

- Contribution to the clarification of the inner mechanisms that regulate ocular circulation, in particular, the choroidal circulation. We were able to show that intrinsic vasomotion is revealed in the ophthalmic artery in the absence of central nervous control and we established a controlled ex vivo model that can be used to study the effects of putative therapeutic drugs on ocular circular circulation, which is of major importance in ocular pathologies which have a vascular component.
- Development of methodologies of data analysis on the time-scale domain applied to biological variables (e.g., heart rate, blood pressure, intraocular pressure, urinary bladder pressure) that are currently used to access autonomic function and disautonomy in a diagnostic perspective as well as to be used in the patients follow-up (.
- Combination of the analysis of human pathology with rabbit and rat models that are contributing to clarify and elucidate the interference of autonomic nervous system in the genesis and maintenance of atrial fibrillation (PAF). Experimental tools have been used to demonstrate the effects of vagal stimulation on atrial electrical conduction and refractoriness properties and on the vulnerability for the initiation and maintenance of AF. In particular, the anesthetized rabbit model with preserved autonomic innervation has been useful to demonstrate the effects of vagal stimulation on atrial electrical conduction and refractoriness properties and on the vulnerability for the initiation and maintenance of AF and human studies on patients with PAF associated an increased dispersion of atrial refractoriness upon PAF induction. Using a rat model of auricular pacing combined with sympathetic and parasympathetic stimulation, changes on molecular expression of ion channels and conexins were observed and correlated with the initiation and termination of atrial fibrillation
- Modulatory effects of insulin on voltage-activated potassium currents in a neuronal cell line with origin in the sympathetic system - whole-cell voltage-clamp recordings in differentiated N1E-115 neuroblastoma cells – and CA1 neurones.

Recent Most Relevant Publications

Oliveira M, Nogueira Silva M, Geraldés V, Xavier R, Laranjo S, Silva V, Postolache G, Ferreira R, Rocha I (2010) Acute vagal modulation of electrophysiology of the atrial and pulmonary veins increases vulnerability to atrial fibrillation. *Exp Physiol*, Epub 2010 Oct 15 (Journal IF: 3,2, Citations:)

Oliveira M, Nogueira da Silva M, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R. Effects of acute autonomic modulation on atrial conduction delay and

local electrograms duration in paroxysmal atrial fibrillation. *Int J Cardiol*, [Epub ahead of print] (Journal IF: IF 3,5 Citations:)

Ducla-Soares JL, Santos-Bento M, Laranjo S, Andrade A, Ducla-Soares E, Boto JP, Silva-Carvalho L, Rocha I (2007) Wavelet analysis of autonomic outflow of normal subjects on head-up tilt, cold pressure test, Valsalva manoeuvre and deep breathing tests. *Exp Physiol* **92**, 677-686. (Journal IF: 3,2, Citations: 6)

Lima PA, Vicente MI, Alves FM, Dionísio JC, Costa PF (2008) Insulin increases excitability via a dose-dependent dual inhibition of voltage-activated K⁺ currents in differentiated N1E-115 neuroblastoma cells. *Eur. J. Neurosc* **27** (8), 2019–2032 (Journal IF 3,4, Citations: 2)

Ongoing Research Projects

2009/2011 – Autonomic nervous system influences on renal stone disease FCT / PIC/IC/83243/2007 , Coordinator Isabel Rocha (€50 000)

2010/2012 – Genetic modification of paraventricular hypothalamic nucleus and rostroventrolateral medulla to control chronically hypertension FCT / PTDC/SAU-OSM/109081/2008 , Coordinator Isabel Rocha (€126 034)

2010/2012 – Mechanical control of respiration in a rat model of respiratory failure- development of a rat diaphragmatic pacemaker FCT / PTDC/EEA-ELC/109083/2008 , Coordinator Isabel Rocha (€147 256)

2009/2011 – Correlation of molecular misfolding and autonomic influences on heart rate and blood pressure of an animal model of parkinson disease” FCT / PIC/IC/82760/2007),_Coordinator Tiago Outeiro

2006/2010- Anatomical-functional identification of putative nervous cardiac fibers and its role on the genesis of atrial fibrillation FCT / POCTI/SAU-ESP/2004, Coordinator. J Queiroz e Melo

2010/2012. A influência dos ácidos biliares na infecção do fígado por malária. The influence of bile acids on malaria liver infection. Coordinator: Miguel Prudêncio. PTDC/SAU-MII/099118/2008 (total € 179.182,00)

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. Coordinator : Dina Cunha Reis PTDC/SAU-NEU/103639/2008 (total €120.000)

Publications in peer review Journals

Oliveira M, da Silva MN, Geraldés V, Xavier R, Laranjo S, Silva V, Postolache G, Ferreira R, Rocha I (2010) Acute vagal modulation of electrophysiology of the atrial and pulmonary veins increases vulnerability to atrial fibrillation. *Exp Physiol* Epub 2010 Oct 15 (Journal IF: 3.168)

Oliveira M, da Silva N, Gerales V, Postolache G, Xavier R, Laranjo S, Rocha I, Ferreira R, Silva Carvalho (2010) Effect of vagal stimulation on the initiation and termination of atrial fibrillation in the anaesthetized rabbit. *Rev.Port Cardiol.* **29** (3), 375-89. (Journal IF: N/A)

Oliveira M, da Silva N, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R (2010) Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation. *Int J Cardiol*, [Epub ahead of print]

Vicente MI, Costa PF, Lima PA (2010) Galantamine inhibits slowly inactivating K⁺ currents with a dual dose-response relationship in differentiated N1E-115 cells and in CA1 neurones. *Eur J Pharmacol* **634** (1-3), 16-25 (Journal IF: 2.585)

Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L. (2010). Amlodipine effects on vasomotion in rabbit external ophthalmic artery. *Graefes Arch Clin Exp Ophthalmol* **248** (2), 213-21. (Journal IF: 2.102)

Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L (2010) Endothelin-1 effects on spontaneous oscillations in choroidal arterioles. *Acta Ophthalmol* **88** (7), 742-7. (Journal IF: 2.441)

Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L. (2010) L-arginine and L-nitroarginine methylester effects on vasomotion in isolated rabbit eyes. *Ophthalmic Res* **43** (3), 113-21 (Journal IF: 2.441)

Invited Lectures and Seminars

Oliveira M. “Estamos preparados para expandir as indicações de ablação de FA.” Lisbon Arrhythmia Meeting, Feb 2010.

Oliveira M. How to optimize settings for discharge in CRT. New horizons in Heart Failure, Paris, Mar 2010.

Oliveira M. Atrial fibrillation management: which outcomes are important, XXXI Portuguese Cardiology Meeting, April 2010.

Oliveira M. Angina Crónica Estável - novas opções terapêuticas significam novas direcções? Ranolazina - o ponto de vista do electrofisiologista. Congresso Português de Cardiologia, April 2010.

Rocha I, Neurogenic orthostatic hypotension, hypertension and other cardiovascular diseases, EFAS Taormina, Italy, May 2010.

Oliveira M. Novos antiarrítmicos na Fibrilhação auricular. Reunião Nacional de Pacing, Elvas, June 2010.

Rocha I, Autonomic dysfunction in Parkinson disease, From Molecules to Cure. Workshop under the Harvard-Portugal Educational Schemes, Sesimbra, July 2010.

Rocha I, Autonomic nervous system physiology. EFASchool2010, Lisbon, July 2010.

Rocha I. Mathematical methodologies and ANS evaluation. A hands-on session with Fisiosinal, EFASchool2010, Lisbon, July 2010.

Oliveira M. Autonomic influences in cardiac dysrhythmias: Pathophysiological significance in atrial fibrillation. International Autonomic School EFAS, July 2010.

Ducla-Soares JL. Autonomic evaluation in clinical practice, EFASchool2010, Lisbon, July 2010.

Laranjo S. Mathematical methodologies and ANS. EFASchool2010, Lisbon, July 2010.

Oliveira M. How to improve the success rate of ventricular ablation? ESC Stockholm Sweden Sep 2010.

Rocha I. Arterial stiffness and hypertension. ESC Stockholm Sweden Sep 2010.

Rocha I. The Heart-Brain Axis, AECVP, Lisbon, Portugal, Oct 2010.

Oliveira M. Autonomic influences on cardiac electrophysiology: insights into the pathophysiology of atrial fibrillation. 12nd International Coimbra Meeting on Cardiovascular Diseases, Oct 2010.

Oliveira M. Quando o cérebro tem razões que a fibrilhação auricular conhece. O coração e outros órgãos. Amigos? Ou partes de uma ligação perigosa. XVI Jornadas de Cardiologia de Santarém, Out 2010.

Oliveira M. Arrhythmias in adults with congenital heart disease: from ECG to ICD. Pediatric cardiology : 40 years after - unsolved questions, Estoril, Oct 2010.

Oliveira M. Miocardiopatia Arritmogénica do Ventriculo Direito. Sociedade Portuguesa de Cardiologia Nov 2010.

Oliveira M. Ablação de FA “permanente”: antiarrítmicos em altas doses pré-ablação? A importância do ciclo de base. Reunião Anual de Electrofisiologia, Lousa, Nov 2010.

Oliveira M. Certification in electrophysiology. BioIntelligence Cancun Nov 2010.

Oliveira M. Non-invasive risk stratification of sudden death: is it obsolete? T-WAVE ALTERNANS. XIV International Symposium on Progress in Clinical Pacing Rome Dec 2010.

Communications in International Conferences

Oliveira M, Postolache G, Geraldés V, Gomes JP, Nunes A, Silva V, Laranjo S, Ferreira R, Rocha I. Time Course of ionic and gap junctional remodeling induced by short-term rapid atrial pacing, Lisbon Arrhythmia Meeting, Feb 2010. (Oral Communication)

Laranjo S, Oliveira M, Tavares C, Geraldés V, Silva V, Raposo S, Santos S, Oliveira E, Rocha I, Ferreira R. Tilt training increases vasoconstrictor reserve in patients with neurocardiogenic syncope, XXXI Portuguese Cardiology Meeting, April 2010. (oral communication)

Oliveira M, Cunha P, Nogueira da Silva M, Feliciano J, Lousinha A, Santos N, Galrinho A, Santos S, Marques F, Ferreira R. Guided isolation of culprit pulmonary veins. Is it enough for ablation of paroxysmal atrial fibrillation? ECAS 2010, Munich, April 2010. (oral communication)

Laranjo S, Oliveira M, Tavares C, Raposo S, Vaz-da-Silva V, Geraldes V, Ferreira R, Rocha I Tilt Training increases vasoconstrictor reserve in patients with refractory neurocardiogenic syncope, XII Congress of EFAS, Taormina, Italy, May 2010. (oral communication)

Oliveira M, Laranjo S, Tavares C, Vaz-Silva V, Geraldes V, Silva S, Ferreira R, Rocha I. Baroreflex sensitivity during orthostatic stress in patients with lone paroxysmal atrial fibrillation. XII Congress of EFAS, Taormina, Italy, May 2010. (oral communication)

G. Postolache; V. Geraldes; M. Oliveira; I. Rocha. Acute ethanol administration potentiates inducibility of atrial fibrillation related with enhanced autonomic tonus: na in vivo rabbit study, Research Society on Alcoholism, St Antonio, USA, June 2010. (oral communication)

Abegão-Pinto L, Raposo S, Rocha I, Marques-Neves C. Hemodynamic response of the ophthalmic artery to cold pressor test in young subjects, 9th Congress of European Society of Glaucoma, Madrid, Spain, Sept 2010. (oral communication)

Oliveira M, Postolache G, Geraldes V, Silva V, Laranjo S, Tavares C, Raposo S, Silva N, Ferreira R, Rocha I. Acute electrophysiological modulation of the atria and pulmonary veins: effects of sympathetic and parasympathetic interaction on atrial fibrillation inducibility, ESC Congress 2010, Stockholm, Sweden, Sept 2010. (oral communication)

Oliveira M, Postolache G, Geraldes V, Gomes J, Nunes A, Tavares C, Laranjo S, Silva N, Rocha I. Alterations in atrial ion channel and connexin gene expression induced by autonomic stimulation: a potential substrate for neurogenic atrial fibrillation, ESC Congress 2010, Stockholm, Sweden, Sept 2010. (poster communication)

Osório-Oliveira A, Geraldes V, Rocha I, Outeiro TF A model for Parkinsonism and Autonomic dysfunction, SFN, San Diego, Oct 2010. (poster communication)

Oliveira M, Postolache G, Geraldes V, Tavares C, Laranjo S, Silva V, Gomes J, Ferreira R, Rocha I. Alterations in connexin and ion channel gene expression induced by autonomic stimulation: a potential modulation factor of atrial remodeling? Heart Rhythm, May, Denver, USA, Nov 2010. (poster communication)

Laranjo S, Oliveira M, Tavares C, Geraldes V, Silva V, Santos S, Oliveira E, Ferreira R, Rocha I. Unravelling the mechanisms behind the hemodynamic and autonomic remodelling induced by orthostatic training. Heart Rhythm, May, Denver, USA, Nov 2010. (poster communication)

Laranjo S, Oliveira M, Tavares C, Geraldes V, Silva V, Santos S, Oliveira E, Rocha I Beneficial effects of tilt training in preventing neurocardiogenic syncope: What are the possible mechanisms? XIV International Symposium On Progress in Clinical Pacing 2010, Rome, Dec 2010. (oral communication)

Communications in National Conferences

Oliveira M, Postolache G, Geraldês V, Gomes JP, Nunes A, Silva V, Laranjo S, Ferreira R, Rocha I. Time course of ionic and gap junctional remodeling induced by short term atrial pacing”, 31st Congresso Português de Cardiologia, Lisbon, April 2010.

Laranjo S, Oliveira M, Tavares C, Geraldês V, Silva V, Raposo S, Santos S, Oliveira E, Rocha I, Ferreira R. Tilt training increases the vasoconstrictor reserve in patients with neurocardiogenic syncope, 31st Congresso Português de Cardiologia, Lisbon, April 2010.

Oliveira M, Nogueira da Silva M, Cunha P, Feliciano J, Lousinha A, Santos N, Abreu J, Pimenta R, Santos S, Ferreira R. Ablação percutânea de fibrilhação auricular persistente e de longa duração: a execução de linhas é sempre necessária? 31st Congresso Português de Cardiologia, Lisbon, April 2010.

Oliveira M, Postolache G, Geraldês V, Silva V, Laranjo S, Tavares C, Nogueira da Silva M, Ferreira R, Rocha I. Modulação electrofisiológica das aurículas e veias pulmonares: interacção da estimulação simpática e parassimpática na inducibilidade de fibrilhação auricular num modelo experimental in vivo. 31st Congresso Português de Cardiologia, Lisbon, April 2010.

Organisation of Conferences

EFAS2010- European school on clinical autonomic function, European Federation of Autonomic Societies, Medical Board Association and Faculty of Medicine of Lisbon, July 2010.

M. Oliveira, member of the organizing committee of the XXXI Congresso Português de Cardiologia, 2010.

Internationalization

Isabel Rocha is advisor for the MSCurriculum of the Department of the Department of Health, UK and coordinator of the Education Committee of the European Federation of autonomic Societies which purpose is to build an European network on clinical autonomic research.

Mario Oliveira, member of the Adverse Effects Board for the BITAC and OPTION trials, the steering committee SynarFlash Study and the European Board of Consultants for Medtronic. Also coordinates the PORTLINK – Portuguese Registry on Remote Monitoring CARELINK. Mário Oliveira is founding-member of Associação Bate-Bate Coração, September 2010.

Prizes, honours and awards

Best oral communication prize at Lisbon Arrhythmia Meeting to “Time course of ionic and gap junctional remodeling induced by short term atrial pacing” by Mário Oliveira, Gabriela Postolache, Vera Geraldês, João Paulo Gomes, Alexandra Nunes, Vitor Silva, Sérgio Laranjo, Rui Ferreira, Isabel Rocha, Lisbon, February 2010.

Best oral communication prize at XXXI Portuguese Cardiology Meeting Congresso Português de Cardiologia, Abril, 2010 to “Tilt training increases the vasoconstrictor reserve in patients with neurocardiogenic syncope” by Sérgio Laranjo, Mário Oliveira, Cristiano Tavares,

Vera Geraldês, Vitor Silva, Susana Raposo, Sofia Santos, Eunice Oliveira, Isabel Rocha, Rui Ferreira, Lisbon, April 2010.

Prize Jorge Quininha 2010(a): Oliveira M, da Silva MN, Geraldês V, Xavier R, Laranjo S, Silva V, Postolache G, Ferreira R, Rocha I. Acute vagal modulation of electrophysiology of the atrial and pulmonary veins increases vulnerability to atrial fibrillation. *Exp Physiol*, Epub Oct 15, 2010.

Prize Jorge Quininha 2010(b): Oliveira M, da Silva N, Geraldês V, Postolache G, Xavier R, Laranjo S, Rocha I, Ferreira R, Silva Carvalho (2010). Effect of vagal stimulation on the initiation and termination of atrial fibrillation in the anaesthetized rabbit. *Rev.Port Cardiol.* 2010 **29** (3), 375-89.

Prize Jorge Quininha 2010 (c): Oliveira M, da Silva N, Cunha P, Ramos R, Marques F, Santos S, Rocha I, Silva-Carvalho L, Ferreira R (2010). Effects of acute autonomic modulation on atrial conduction delay and local electrograms duration in paroxysmal atrial fibrillation. *Int J Cardiol*, [Epub ahead of print]

Patents/prototypes

Fisiosinal: autonomic data analysis software for autonomic evaluation in the time, frequency and time-scale domains

Advanced teaching

Rocha I. Functional organization of the autonomic nervous system. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010.

Rocha I. Receptors and autonomic neurotransmission. Sympathetic preganglionic neurons and determinants of sympathetic nerve discharge. Vagal preganglionic neurons. Central autonomic pathways. Sensory innervation of the viscera. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010.

Rocha I. Regulation of body homeostasis. Cardiorespiratory control. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010.

Neves C. Autonomic control of the eye. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010

Santos M. Functions of sympathetic innervation of the skin. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010

Oliveira M. Maintenance of a steady-state Autonomic influence on the initiation, maintenance and termination of atrial fibrillation. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010

Laranjo S. Studying the autonomic nervous system. Animal studies and human evaluation: Invasive vs non invasive methodologies. Biological signal processing and the search for an

autonomic signature. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010

Rocha I. Experimental approach. Interpretation and treatment of biological signals. PhD program in neurosciences, Faculty of Medicine of Lisbon, January 2010

Rocha I. Autonomic function and dysfunction. Rocha I. Autonomic function and dysfunction. PhD program in neurosciences, Faculty of Medicine of Coimbra, March 2010.

Neves C. Autonomic control of the eye. PhD program in neurosciences, Faculty of Medicine of Coimbra, March 2010.

S Laranjo. Mathematical methodologies and ANS. European Federation of Autonomic Societies (EFAS) School on Autonomic Nervous System 2010, Lisbon, July 2010.

Rocha, I. Central control of autonomic functions. European Federation of Autonomic Societies (EFAS) School on Autonomic Nervous System 2010, Lisbon, July 2010.

Oliveira, M. ANS and cardiac dysrhythmias. European Federation of Autonomic Societies (EFAS) School on Autonomic Nervous System 2010, Lisbon, July 2010.

Santos, M. Practical evaluation of autonomic function. European Federation of Autonomic Societies (EFAS) School on Autonomic Nervous System 2010, Lisbon, July 2010.

Oliveira M. Studies overview on CRT – mechanisms, impact on heart failure progression and clinical outcome. Management of cardiac resynchronization therapy, Lisbon, September and December 2010.

Oliveira M. Device programming anti-bradycardia pacing in ICD recipients. Advanced Management of the ICD Patient, Paris, November 2010.

Science and Society

Oliveira M. International Meeting on Arrhythmias CREATE Forum. Paris Dec 2010

Oliveira M, coordinates the PORTLINK – Portuguese Registry on Remote Monitoring CARELINK

Oliveira M, membro fundador da Associação BATE BATE CORAÇÃO, September 2010

Autonomic laboratory evaluation open to the community providing a specialized service in terms of autonomic evaluation by an autonomic research reference centre.

Media appearances

Oliveira M. Ablação *versus* farmacoterapia no tratamento da FA. Tempo de Medicina, April 2010

Oliveira M. Mudança de abordagem no tratamento da fibrilação auricular. Patient Care, April 2010

Oliveira M. Fibrilhação auricular: mudança na abordagem do tratamento. Mundo Médico, April, 2010

Oliveira M. Como se regula a pressão arterial. Bom Dia Portugal, RTP, July 19th, 2010

Rocha I. As doenças do sistema nervoso autónomo, Fórum Hospital do Futuro, July 2010

Rocha I. Escola para médicos em autónomo, Destak, July 2010

Rocha I. EFAS 2010: Portugal recebe a primeira escola europeia em sistema nervoso autónomo, JasFarma comunicação, July 2010

Rocha I. O sistema autónomo que regula o organismo, Revista Prevenir, Sept 2010

Rocha I. O que é o sistema nervoso autónomo? Tempo Medicina, Setp 2010

Oliveira M. Hipertensão Arterial. Programa Bom Dia Portugal, Oct 2010

Oliveira M. Gravidez e Pacemaker. Relação possível. Mãe Ideal, Nov 2010

Oliveira M. Influência do sistema nervoso autónomo no substrato funcional da fibrilhação auricular. Mundo Médico, Nov 2010

Master and Ph.D. thesis completed

PhD Thesis

Mario Martins Oliveira, 2010, The role of autonomic nervous system on the initiation, maintenance and termination of paroxysmal atrial fibrillation, Faculty of Medicine University of Lisbon, supervision Isabel Rocha

Master Thesis

Tiago Barra, 2010. Crosstalk between A5 region of the brainstem and sublobule IXb of the cerebellum to control blood pressure, Faculty of Medicine University of Lisbon, supervision Isabel Rocha

Cristiano Tavares, 2010. Computacional tools for cardiac variability analysis” Instituto Superior Técnico, supervision Isabel Rocha in collaboration with R.C. Martins

Filipe Linda, 2010. Crosstalk between brainstem A1 and A2a receptors during the defence reaction in the rat. Faculty of Medicine University of Lisbon, supervision Isabel Rocha

Raluka Ivanov 2010. Autonomic dysfunction in a population with changes in glucose metabolism Faculty of Medicine University of Lisbon, supervision Isabel Rocha

Marta Faria 2010. Development of an intradermic CO₂/O₂ sensor, Instituto Superior Técnico Lisbon (supervision R.C. Martins in collaboration with Isabel Rocha)

Joana Alves, 2010, Closing of atrial appendage and cardio-embolic prophylaxis in atrial fibrillation, Faculty of Medicine University of Lisbon, co-supervision Eduardo Infante de Oliveira and Isabel Rocha

Ana Paninho, 2010, Análise da concentração de chumbo em sangue de ratos Wistar sujeitos a uma exposição continuada. Faculty of Sciences and Technology, co-supervision Jose Paulo Santos and Isabel Rocha

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, FML

Principal Investigators

Teresa Pais, Ph.D., Staff Scientist

Research Team

Sandra Tenreiro	Postdoc
Rita Oliveira	Postdoc
Joana Matos	Postdoc (left in September 2010)
Mónica Cunha	Postdoc
Federico Herrera	Postdoc
Hugo Miranda	Postdoc
Zrinka Marjjanovic	Postdoc
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	Master's student
Andreia Peixoto	Technician
Ana Oliveira	Technician/Ph.D. Student
Dina Hernandez	Technician

Keywords/Research Areas

- Protein misfolding, oligomerization and aggregation
- Yeast models for Parkinson's and Huntington's disease
- Epigenetics and Alzheimer's disease
- Modulators of protein aggregation and toxicity
- Microscopy-based methods for investigating the molecular nature of the toxic proteinaceous species in Parkinson's disease
- **In vivo** imaging using multi-photon microscopy

Major scientific achievements

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

Tauber E, Miller-Fleming L, Mason RP, Kwan W, Clapp J, Butler NJ, Outeiro TF, Muchowski PJ, Giorgini F (2010) Functional gene expression profiling in yeast implicates translational dysfunction in mutant huntingtin toxicity. *J Biol Chem* (Journal IF:5,328, Citations:0)

Gonçalves SA, Matos JE, Outeiro TF (2010) Zooming into protein oligomerization in neurodegeneration using BiFC. *Trends Biochem Sci.* **35** (11), 643-51 (Journal IF:12,374, Citations: 0)

Outeiro TF, Putcha P, Tetzlaff JE, Spoelgen R, Koker M, Carvalho F, Hyman BT, McLean PJ (2008) Formation of toxic oligomeric alpha-synuclein species in living cells. *PLoS One* **3** (4), e1867. Erratum in: *PLoS One.* 2008; **3** (5) (Journal IF:4,351, Citations: 31)

Outeiro TF, Kontopoulos E, Altmann SM, Kufareva I, Strathearn KE, Amore AM, Volk CB, Maxwell MM, Rochet JC, McLean PJ, Young AB, Abagyan R, Feany MB, Hyman BT, Kazantsev AG (2007) Sirtuin 2 inhibitors rescue alpha-synuclein-mediated toxicity in models of Parkinson's disease. *Science.* 2007 Jul 27;**317** (5837), 516-9 (Journal IF:30,631, Citations: 142)

Outeiro TF, Lindquist S. (2003) Yeast cells provide insight into alpha-synuclein biology and pathobiology. *Science.* **302** (5651), 1772-5 (Journal IF:30,631, Citations: 179)

Ongoing Research Projects

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 International Journals 2010

Teixeira MC, Cabrito TR, Hanif ZM, Vargas RC, Tenreiro S, Sá-Correia I Yeast response and tolerance to polyamine toxicity involving the drug: H⁺ antiporter Qdr3 and the transcription factors Yap1 and Gcn4, *SGM Microbiology*, Epub ahead of print. (Journal IF: N/A)

da Costa G, Guerreiro A, Correia CF, Gomes RJ, Freire A, Monteiro E, Barroso E, Coelho AV, Outeiro TF, Freire AP, Cordeiro C (2010) A non-invasive method based on saliva to characterize transthyretin in familial amyloidotic polyneuropathy patients using FT-ICR high-resolution MS. *Proteomics Clin Appl* **4** (6-7), 674-8 (Journal IF: 1.875)

Büttner S, Delay C, Franssens V, Bammens T, Ruli D, Zaunschirm S, de Oliveira RM, Outeiro TF, Madeo F, Buée L, Galas MC, Winderickx J (2010) Synphilin-1 enhances α -synuclein aggregation in yeast and contributes to cellular stress and cell death in a Sir2-dependent manner. *PLoS One*. **5** (10), e13700. (Journal IF: 4.351)

Tauber E, Miller-Fleming L, Mason RP, Kwan W, Clapp J, Butler NJ, Outeiro TF, Muchowski PJ, Giorgini F. Functional gene expression profiling in yeast implicates translational dysfunction in mutant huntingtin toxicity (2010) *J Biol Chem* [Epub ahead of print] (Journal IF: 5,328)

Diógenes MJ, Outeiro TF (2010) Neurotrophic factors as a protective strategy in Parkinson's disease. *CNS Neurol Disord Drug Targets*. **9** (6), 754-63 (Journal IF: 3.571)

Kazantsev AG, Outeiro TF (2010) Drug discovery for CNS disorders: from bench to bedside. *CNS Neurol Disord Drug Targets* **9** (6), 668 (Journal IF: 3.571)

de Oliveira RM, Pais TF, Outeiro TF (2010) Sirtuins: common targets in aging and in neurodegeneration. *Curr Drug Targets* **11**(10), 1270-80 (Journal IF: 3.932)

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Marques SC, Oliveira CR, Pereira CM, Outeiro TF (2010) Epigenetics in neurodegeneration: A new layer of complexity. *Prog Neuropsychopharmacol Biol Psychiatry* [Epub ahead of print] (Journal IF: 2.823)

de Oliveira RM, Pais TF, Outeiro TF (2010) Sirtuins: Common Targets in Aging and in Neurodegeneration. *Curr Drug Targets*. Epub ahead of print (Journal IF: 3.932)

Tenreiro S, Outeiro TF (2010) Simple is good: yeast models of neurodegeneration. *FEMS Yeast Res* **10** (8), 970-9 (Journal IF: 1.785)

Gonçalves SA, Matos JE, Outeiro TF. Zooming into protein oligomerization in neurodegeneration using BiFC. *Trends Biochem Sci.* **35** (11), 643-51. (Journal IF:12,374)

Marques SC, Oliveira CR, Outeiro TF, Pereira CM (2010) Alzheimer's disease: the quest to understand complexity. *J Alzheimers Di* **21** (2), 373-83.. (Journal IF: 3.832)

Nakhjavani M, Morteza A, Khajeali L, Esteghamati A, Khalilzadeh O, Asgarani F, Outeiro TF (2010) Increased serum HSP70 levels are associated with the duration of diabetes. *Cell Stress Chaperones* **15** (6), 959-64. (Journal IF: 2.167)

Vicente Miranda H, Outeiro TF (2010) The sour side of neurodegenerative disorders: the effects of protein glycation. *J Pathol* **221** (1), 13-25. (Journal IF: 6.466)

Su LJ, Auluck PK, Outeiro TF, Yeger-Lotem E, Kritzer JA, Tardiff DF, Strathearn KE, Liu F, Cao S, Hamamichi S, Hill KJ, Caldwell KA, Bell GW, Fraenkel E, Cooper AA, Caldwell GA, McCaffery JM, Rochet JC, Lindquist S (2010) Compounds from an unbiased chemical screen reverse both ER-to-Golgi trafficking defects and mitochondrial dysfunction in Parkinson's disease models. *Dis Model Mech* **3** (3-4), 194-208 (Journal IF: 3.304)

Other publications International

Herrera, F., Tenreiro, S., Outeiro, TF. Visualization of mutant huntingtin oligomerization in living cells. *J Neurology Neurosurgery and Psychiatry*. Vol 81, supp 1,page A1. DOI: 10.1136/jnnp.2010.222570.2. 2010

Lopes, LV and Outeiro, TF. Synaptic dysfunction in Parkinson's disease: from protein misfolding to functional alterations, 2010, Springer.

Marques, S and Outeiro, TF. Epigenetics and Neurodegeneration: A Connection Overlooked, Novascience.

Other publications National

Outeiro, TF. (2010) A biomedicina na prevenção, diagnóstico e terapia de doenças, *Cadernos de Saúde*. Vol. 2, No. 2. 7-10.

Invited Lectures and Seminars

Herrera, F. Retinoic acid receptor alpha links major astroglial pathways. Lisbon Area of Neuroscience Meetings, Instituto de Medicina Molecular, Lisbon, Portugal, January 20, 2010.

Outeiro, TF. Unravelling the molecular basis of neurodegeneration: from cells to drugs, Göttingen, Germany, Feb 2010

Outeiro, TF. The UPS and downs of α -synuclein in Parkinson's disease. EMBO Workshop on Proteolysis. Madrid, CSIC, June 2010

Outeiro, TF., Unravelling the molecular basis of neurodegeneration: from cells to drugs Istanbul, Turkey, September 2010

Outeiro, TF. Neurotic yeasts as a model for Parkinson's disease. Rome, Italy, September 2010

Outeiro, TF., Unravelling the molecular basis of neurodegeneration: from cells to drugs. Aarhus, Denmark, September 2010

Outeiro, TF. From cells to drugs: unraveling the molecular basis of neurodegeneration. University of Granada, Granada, Spain, October 2010.

Herrera, F. Retinoic acid receptor alpha links major astroglial pathways. Lisbon Area Neuroscience Meetings, Instituto de Medicina Molecular, Lisbon, Portugal, January 20, 2010.

Miranda, H.V., Oliveira, R.M., Costa, G., Tenreiro, S., Oliveira, L.M.A., Quintas, A., Cordeiro, C., Outeiro, T.F. Protein Glycation in Yeast: Novel Insights into the molecular basis of Parkinson's Disease. Lisbon Area Neuroscience Meeting, 3rd Season, Instituto Gulbenkian Ciência, Oeiras, Portugal

Maiolino, F. Functional effects of α -synuclein on hippocampal synaptic activity: involvement of NMDA receptors. Lisbon Area Neuroscience Meeting, 4th Season, Instituto de Medicina Molecular, Lisbon, Portugal, December 15, 2010.

Miller-Fleming, L. Using yeast as a model to decipher the role of DJ-1 in the etiology of Parkinson's Disease, Pizza seminar, Instituto de Medicina Molecular, Lisboa, September 21, 2010

Gonçalves, S.A. Genetic modifiers of α -synuclein oligomerization, University of Göttingen, Germany, December 10, 2010

Marques, O. Investigating the role of extracellular α -synuclein in Parkinson's disease. Pizza seminar, Lisboa, Portugal, December 7, 2010.

Communications in International Conferences

Badiola, N., De Oliveira, R.M., Herrera, F., Guardia-Laguarta, C., Pera, M., Suarez-Calvet, M., Outeiro, T.F., Lleó, A. Tau enhances α -synuclein aggregation in a cellular model of synucleinopathy. Society for Neuroscience Meeting, San Diego, USA, November 13-17, 2010 (Poster presentation)

Herrera, F., Tenreiro, S., Outeiro, T.F. Live imaging of mutant huntingtin oligomerization in cell cultures. Society for Neuroscience Meeting, San Diego, USA, November 13-17, 2010 (Oral presentation)

Herrera, F., Tenreiro, S., Outeiro, T.F. Visualization of mutant huntingtin oligomerization in living cells. European Huntington's Disease Network Meeting, Prague, Czech Republic, September 3-5, 2010 (Poster presentation).

Osório-Oliveira, A., Geraldes, V., Rocha, I., Outeiro, T.F., A model for Parkinsonism and autonomic dysfunction, International Society for Neurosciences 2010, San Diego – CA, USA , 13-17 November 2010. (Poster presentation)

Herrera, F., Tenreiro, S., Outeiro, T.F. Visualization of mutant huntingtin oligomerization in living cells. European Huntington's Disease Network Meeting, Prague, Czech Republic, September 3-5, 2010. (Poster presentation)

Faria, C., Borges, N., Tenreiro, S., Outeiro, T.F., Santos, H. What is the role of mannosylglycerate in vivo? Hints from fluorescence microscopy using a yeast model for Parkinson's disease. EXTREMOPHILES 2010, Azores, Portugal. September 12-16, 2010. (Poster presentation)

Marques, S.C.F., Pereira, C.M.F., Outeiro, T.F. Neurodegeneration: an epigenetic perspective. 7th Forum of European Neuroscience (FENS). Amsterdam, July 3-7, 2010. Poster presentation.

Maiolino, F., Diógenes, M.J., Guerreiro, P., Miranda, H.V., Rombo, D., Dias, R.A., Oliveira, L.M., Quintas, A., Lopes, L.V., Outeiro, T.F. Functional effects of alpha-synuclein on hippocampal synaptic activity: involvement of NMDA receptors. Society for Neuroscience. San Diego (USA) 13-17 November 2010.(Poster Presentation)

Gonçalves, S.A., Genetic modifiers of alpha-synuclein oligomerization in living cells, EMBO Workshop "Proteolysis and Neurodegeneration", Fundación Ramón Areces, Madrid, Spain, May 2010. (Poster presentation)

Miller-Fleming, L., Giorgini, F., Outeiro, T.F. Deciphering the role of DJ-1 in Parkinson's disease using yeast as a model, Parkinson's UK meeting, York UK, November 1-2, 2010. (Poster presentation)

Communications in National Conferences

Herrera, F., Tenreiro, S., Outeiro, T.F. Visualization of mutant huntingtin oligomerization in living cells. Congresso de Neurologia 2010 «Plasticidade, Reorganização e Recuperação Funcional», Sociedade Portuguesa de Neurologia, Espinho, Portugal, November 5-7, 2010. (Poster presentation)

Tenreiro, S., Carreto, L., Basso, E., Cunha, E.M., Outeiro, T.F. Dissecting the role of alpha-synuclein phosphorylation in Parkinson's disease: insights from a yeast model. XVIII Jornadas de Biologia de Leveduras "Nicolau van Uden", Lisbon, Portugal, June 18-19, 2010.

Miranda, H.V., Tenreiro, S., Oliveira, L.M.A., Freire, A.P., Quintas, A., Cordeiro, C., Outeiro, T.F.. 2010. The effects of glycation on alpha-synuclein misfolding and toxicity in a yeast model

of Parkinson's disease. XVIII Jornadas de Biologia de Leveduras "Nicolau van Uden", Lisbon, Portugal. June 18-19, 2010. (Oral presentation)

Dos Santos, S.C., Palma, M., Tenreiro, S., Moreira, A.M., Sá-Correia, I. Transcriptomic profiling of the yeast response to quinine evidenced a glucose limitation response related glucose uptake inhibition. XVIII Jornadas de Biologia de Leveduras "Nicolau van Uden", Lisbon, Portugal. June 18-19, 2010. (Oral presentation)

Teixeira, M.C., Cabrito, T.R., Hanif, Z.M., Vargas, R.C., Tenreiro, S., Sá-Correia, I. The multidrug resistance transporter QDR3 plays a role in polyamine homeostasis. XVIII Jornadas de Biologia de Leveduras "Nicolau van Uden", Lisbon, Portugal. June 18-19, 2010. (Oral presentation)

Marques, S.C. An epigenetic perspective into Alzheimer's disease. VIII Encontro Anual Do Centro de Neurociências e Biologia Celular e Reunião Anual do Programa Doutoral em Biologia Experimental e Biomedicina, Coimbra, 20 and 21 December 2010. (Oral Presentation)

Guerreiro, P.S. The role of LRRK2 in Parkinson's disease: from function to dysfunction. IMM PhD Meeting, Instituto de Medicina Molecular, Lisbon, November 22-23, 2010. (Poster presentation)

Guerreiro, P.S. The role of LRRK2 in Parkinson's disease: from function to dysfunction. Neuroscience Seminar, Instituto de Medicina Molecular, Lisbon, February 12, 2010. Oral presentation.

Pais, T. When and how do microglial cells start to be deleterious?. Workshop : Molecular Mechanisms in Neurodegeneration: From Molecule to Cures. Harvard Medical School- Portugal. July 2010.

Gonçalves, S.A., Monitoring alpha synuclein intracellular dynamics using photoactivation, IV IMM PhD Student Meeting, Instituto de Medicina Molecular, Lisbon, Portugal, November 2010. (Poster presentation)

Miller-Fleming, L., Giorgini, F., Outeiro, T.F. Deciphering the role of DJ-1 in Parkinson's disease using yeast as a model, XVIII Jornadas de Biologia de Leveduras "Professor Nicolau van Uden" / III Conferência da Tapada, Lisboa, June 18 – 19 2010

Marques, O. The role of alpha-synuclein secretion in microglia activation and neurodegeneration in Parkinson's disease. IV IMM PhD Students Meeting, Instituto de Medicina Molecular, Lisboa, November 22, 2010

Outeiro, TF, Proteostasis imbalance: from cell stress to neurodegeneration and back. Portuguese Society of Biochemistry, Porto, December 2010. (Oral Presentation)

Organisation of National and International Conferences

Outeiro, TF. Organized the EMBO NeuroYIP sectoral meeting at the IMM, June 2010.

Internationalization

Joint Publications

Büttner S, Delay C, Franssens V, Bammens T, Ruli D, Zaunschirm S, de Oliveira RM, Outeiro TF, Madeo F, Buée L, Galas MC, Winderickx J (2010) Synphilin-1 enhances α -synuclein aggregation in yeast and contributes to cellular stress and cell death in a Sir2-dependent manner. *PLoS One* **5** (10), e13700.

Tauber E, Miller-Fleming L, Mason RP, Kwan W, Clapp J, Butler NJ, Outeiro TF, Muchowski PJ, Giorgini F (2010) Functional gene expression profiling in yeast implicates translational dysfunction in mutant huntingtin toxicity. *J Biol Chem*, Epub ahead of print.

Kazantsev AG, Outeiro TF (2010) Drug discovery for CNS disorders: from bench to bedside. *CNS Neurol Disord Drug Targets*. 2010 Dec;9(6):668.

Nakhjavani M, Morteza A, Khajeali L, Esteghamati A, Khalilzadeh O, Asgarani F, Outeiro TF (2010) Increased serum HSP70 levels are associated with the duration of diabetes. *Cell Stress Chaperones*. 2010 Nov;15(6):959-64. Epub 2010 May 23.

Joint Projects

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)

CRUP – Portugal-Germany.

CRUP/British Council – Portugal-UK.

Prizes, honours and awards

Outeiro, TF. Rapid Response Innovation Award, MJ Fox Foundation, October 2010

Advanced teaching

Outeiro, TF. "Neurodegenerative disorders", PGFMA and IMM PhD Program, IMM, Lisbon, February 2010.

Outeiro, TF. "Protein Folding and Misfolding", GABBA PhD Program, IBMC, Porto, March 2010.

Outeiro, TF. "Protein Misfolding in Biology and Disease", CNC PhD Program, University of Coimbra, June, 2010.

Outeiro, TF. "Protein misfolding in biology and disease", Harvard Medical School-Portugal Program Workshop, Sesimbra, July 2010

Outeiro, TF, Protein Misfolding in Biology and Disease, Master's Program in Neurosciences, Faculty of Medicine, Lisbon, Portugal. December, 2010.

Tenreiro, S. Drug discovery and preclinical development, lecture to the MSc in Neurosciences. Instituto de Medicina Molecular/Faculdade de Medicina de Lisboa. May 27, 2010

Pais, T. Why imaging the nervous system in vivo by two-photon excitation microscopy? Curso de Mestrado/doutoramento em Ciências Biofarmacêuticas. Faculdade de Farmácia. Universidade de Lisboa. October 2010.

Pais, T. Neuron-microglia interactions" Mestrado de Genética Molecular e Biomedicina. Universidade Nova de Lisboa. November 2010.

Public Perception of Science

Outeiro, TF "Neurodegenerative disorders", Brain Awareness Week, Lisbon, March 2010.

Outeiro, TF "Novos avanços na investigação na doença de Parkinson", Associação Portuguesa de Doentes de Parkinson, Faro, November 2010.

Outeiro, TF "A investigação do cérebro em Portugal", Scool, Odivelas, December 2010.

Tenreiro, S. Leveduras parkinsonicas: pequenos detectives nos meandros do cérebro, Brain Awareness Week, Lecturer at secondary school from Lumiar, Lisboa.

Tenreiro, S. Organizer of "yeast station" during the IMM open day where about tree hundred students from secondary schools were received and get insights about the neurosciences research that takes place on our institute.

Guerreiro, P., Miller-Fleming, L., Participation in several activities from the project "Semana Internacional do Cérebro". IMM, Lisbon, March 14-20, 2010.

Osório-Oliveira, A., Marques, O., Participated in Brain Awareness Week – 2010, in sessions with secondary-schools students, Instituto de Medicina Molecular, IMM auditorium 57, 19th March 2010

Marques, O. Participated in Café de Ciência, Pavilhão do Conhecimento – Ciência Viva, Portugal, August 28, 2010.

Marques, O., Gonçalves, S.A. Organization of 3rd Season Lisbon Area Neuroscience Meetings (LANM), Instituto de Medicina Molecular/ Instituto Gulbenkian Ciência, Lisbon, Portugal, October 2009 - 2010

Herrera, F., Basso, E., Organization of 4th Season Lisbon Area Neuroscience Meetings (LANM), Instituto de Medicina Molecular, Lisbon, Portugal, October 2010 - present.

Osório-Oliveira, A. Participation in the workshop CIÊNCIA, POLÍTICA e os MEDIA Fundação Calouste de Gulbenkian, Lisbon, April 15, 2010

Master Thesis completed

Patrícia Rosa, July 2010. Microfluidic devices: Gradient generation for biomedical applications. INESC – IST, Co-supervisor: Tiago F. Outeiro.

Tomás Fonseca, December 2010, Zebrafish as a model for Parkinson's disease. Supervisor: Tiago F. Outeiro.

Diana Macedo, December 2010. Polyphenols as antioxidants for Parkinson's disease: studies in cell models. Co-supervisor: Tiago F. Outeiro and Sandra Tenreiro.

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, FML/HSM

Principal Investigators

Alexandre Castro Caldas, MD, PhD	Full Professor, Catholic University of Portugal
Alexandre de Mendonça, MD, PhD	Principal Investigator, FML and IMM
Cristina Sampaio MD, PhD,	Associated Professor, FML
Isabel Pavão Martins, MD, PhD	Associated Professor of Neurology
Joaquim Ferreira, MD, PhD	Auxiliary Professor, FML:
José M. Ferro, MD, PhD	Full Professor, FML/HSM
José Pimentel, MD, PhD	Professor Associado com Agregação, FML
Patrícia Canhão, MD, PhD	Auxiliary Professor, FML / HSM
Sofia A. Oliveira, PhD	Invited Auxiliary Professor, FML
Teresa Paiva, MD, PhD	Associated Professor

Research Team

<i>full time researchers</i>	
Alexandre de Mendonça, MD, PhD	Principal Investigator, FML/IMM
Antonina Pereira, PsyD, PhD	Post-doc fellowship, IMM
Madalena Martins, PhD	Post-doc Fellowship, FCT
Manuela Guerreiro, PsyD, PhD	Investigator, FML
<i>part time researchers</i>	
Alexandre Castro Caldas, MD, PhD	Full Professor, UCP

Ana Marta Teixeira Anes	Pharmacist
Ana Mineiro, PhD	Auxiliary Professor, ICS-UCP
Ana Rita Peralta, MD, MSc	Assistant, HSM
Carolina Maruta, MSc	Psychologist, research fellow
Cristina Sampaio, MD, PhD	Professor Clinical Pharmacology and Therapeutics, FML
Isabel Pavão Martins, MD, PhD	Associated Professor of Neurology, FML
João Costa, MD, PhD	Neurologist, HSM, Auxiliary Professor, FML
Joaquim Ferreira, MD, PhD	Neurologist, HSM, Auxiliary Professor, FML
José Fonseca	Speech Therapist, FML
José M. Ferro, MD, PhD	Full Professor, FML/HSM
José Pimentel, MD, PhD	Associate Professor, FML/HSM
Leonor Correia Guedes, MD	Auxiliary Professor, FML
Maria Vânia Nunes, PhD	Auxiliary Professor, ICS-UCP
Mário Miguel Rosa, MD	Neurologist, HSM, Auxiliary Professor, FML
Martin Lauterbach, MD, PhD	Post-doc Fellowship, FCT
Miguel Coelho, MD	Neurologist, HSM, Auxiliary Professor, FML
Patrícia Canhão, MD, PhD	Neurologist, Auxiliary Professor, FML / HSM
Sofia A. Oliveira, PhD	Invited Auxiliary Professor, FML
Teresa Paiva, MD, PhD,	Full Professor, FML
Tiago Mestre, MD	Training Fellowship, HSM

occasional collaboration	
Anabela Valadas, MD	Resident, HSM
Carla Bentes, MD	Auxiliary Professor, FML / HSM
Dulce Neutel, MD	Training Fellowship
Filipa Ribeiro, PhD	Psychologist, PhD degree, FML, volunteer
Helena Pedrosa, PsyD	Psychologist, Master degree, FML, volunteer
Luísa Albuquerque, MD	Neurologist, HSM
Maria Carolona Pires, MD	Training Fellowship
Patrícia Lobo, MD	Training Fellowship
Sandra Ginó, PsyD	Psychologist, Master Degree, ULHT, volunteer
Teresa Pinho e Melo, MD	Neurologist, Assistant, FML / HSM
Tiago Mendes, MSc	Psychologist, HSM
Vítor Oliveira, MD, PhD	Neurologist, Auxiliary Professor, FML / HSM

<i>PhD students</i>	
Ana Catarina Fonseca, MD	HSM, PhD student, FML
Ana Verdelho, MD	Neurologist, HSM, PhD student
Bruno Miranda, MD	PhD student, FML
Catarina Santos, PsyD	PhD student, FML
Dina Silva, PsyD	Psychologist, PhD student, FML
Frederico Simões do Couto, MD	Psychiatrist, PhD student, FML
Graça Melo	Nurse, PhD student, UL
Joana Xavier, MSc	hD student, FML
Lara Caeiro, PsyD	PhD student, FML
Manuela Lopes	Artist, PhD student, FML
Patrícia Abrantes	PhD student
Raquel Gil-Gouveia, MD	Neurologist, PhD student, FML

Sara Fernandes	PhD student
Sofia Madureira, PsyD	PhD student, FML
Tiago Krug, MSc	PhD student, FML

<i>Master students</i>	
Catarina Chester	Master in Neurosciences, FML
Helena Bárrios	Master in Palliative Care, FML
Liliana Gouveia	Master student
Sandra Cardoso	Master in Cognitive Sciences, FML
Sara Câmara	Master student
Vanda Freitas	Master in Neurosciences, FML

<i>technicians</i>	
Ana Noronha, Biology Degree	Technician
Ana Rita Silvestre, MSc	Technician, HSM
Andreza Viegas, Biochemical degree	Technician
Carla Firmo, MSc	Technician, HSM
Clara Loureiro, MSc	Psychologist, FML
Ema Roque, Management Degree	Technician
Fátima Soares	Technician
Gabriela Leal	Speech Therapist, HSM
Joana Pires, MSc	Technician, HSM
João Sobral	Research technician, FCT
Lígia Ferreira	Technician, HSM
Luisa Farrajota	Speech Therapist, HSM
Maria Finisterra	Technician, HSM
Nádia Rei, MSc	Research technician, FCT
Paulo Batista	Technician, HSM
Rosa Santos	Technician, HSM

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 reviews
 - Guidelines
 - 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 2010 significant scientific contributions expressed in as much as 70 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

De Rouen TA, Martin MD, Leroux BG, Townes BD, Woods JS, Leitao J, Castro-Caldas A, Luis H, Bernardo M, Rosenbaum G, Martins IP (2006) Neurobehavioral effects of dental amalgam in children: a randomized clinical trial. *JAMA* **295**, 1784-1789 (Journal IF: 31.718, Citations: 75)

Inzitari D, Simoni M, Pracucci G, Poggesi A, Basile AM, Chabriat H, Erkinjuntti T, Fazekas F, Ferro JM, Hennerici M, Langhorne P, O'Brien J, Barkhof F, Visser MC, Wahlund LO, Waldemar G, Wallin A, Pantoni L, LADIS Study Group (2007) Risk of rapid global functional decline in

elderly patients with severe cerebral age-related white matter changes: the LADIS study. *Arch Intern Med* **167**, 81-88. (Journal IF: 9.813, Citations: 37)

Vellas B, Andrieu S, Sampaio C, Coley N, Wilcock G; European Task Force Group (2008) Endpoints for trials in Alzheimer's disease: a European task force consensus *Lancet Neurol* **7**, 436-450 (Journal IF: 18.126, Citations: 19)

Zerr I, Kallenberg K, Summers DM, Romero C, Taratuto A, Heinemann U, Breithaupt M, Varges D, Meissner B, Ladogana A, Schuur M, Haik S, Collins SJ, Jansen GH, Stokin GB, Pimentel J, Hewer E, Collie D, Smith P, Roberts H, Brandel JP, van Duijn C, Pocchiari M, Begue C, Cras P, Will RG, Sanchez-Juan P (2009) Updated clinical diagnostic criteria for sporadic Creutzfeldt Jakob disease. *Brain* **132**, 2659-2668 (Journal IF: 9.603, Citations: 13)

Ferro JM, Massaro AR and Mas JL (2010) Aetiological diagnosis of ischaemic stroke in young adults. *Lancet Neurol* **9**, 1085-1096 (Journal IF: 18.126, Citations: 0)

Ongoing Research Projects

1996- Editorial Base of the Cochrane Movement Disorders Group: several financing sources negotiable annually (Fundação MDS, Fundação Grunenthal). In the context of the Cochrane Collaboration, we coordinate all of the activities of the Movement Disorders Group and produce top priority systematic revisions.

1998/2010 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

2000- European Multiple System Atrophy Study Group (EMSA-SG [Proposal N°: QLRT – 2000 - -00661]. Participation of Department of Neurology in the sub-studies of natural history, DNA study and dysautonomia. This was a project financed by the European Commission. The financed period ended in 2005 but the activities are being maintained and new financing support is being sought.

2001- Movement Disorders Clinical Trial Unit: Presently, this unit is part of the Clinical Neurology Research Unit. It exist since 1986 under the designation "Neuropharmacology Group" when it functioned under the context of the Centro de Neurociências de Lisboa. It is financed by clinical trial contracts.

2002- Characterization of the incidence, typology and determining factors of adverse drug reactions in hospitals. Financed by the Pharmacovigilance Unit.

2003- Advanced stage Parkinson's Disease: transversal study on a hospital-based population of patients with Parkinson's disease in an advanced stage in collaboration with the Movement Disorders Unit of Hospital Clinic Barcelona, Spain.

2003- Development of measurement instruments usable in clinical trials focused on Movement Disorders (part of a task force of the International Society for Movement Disorders).

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2004- “Caracterização de Perfis de Envelhecimento na População Portuguesa Normal” - Fundação Calouste Gulbenkian

2004/2010 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

2005- “Avaliação do impacto na saúde das doenças neurológicas crónicas. Uma contribuição para a definição de resultados relevantes na perspectiva do doente e para a metodologia de avaliação dos serviços de saúde” - financed by FEDER and FCT.

2005-2008, extended to 2010 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 Coordinator: José M. Ferro

2007/2010 - Brain plasticity for language: evidence from aphasia in childhood, FCT. Coordinator: I.P. Martin. PTDC/PSI/74294/2006

2007/2010 microRnomics and proteomics of Parkinson’s disease, FCT. PI: Oliveira SA. PTDC/SAU-GMG/64428/2006

2007/2011 Genetic epidemiology of stroke in the post-genomic era, FCT. PI: Oliveira SA. PTDC/SAU-GMG/64426/2006

2008 – 2010 “Turma Piloto em Língua Gestual Portuguesa” - Fundação Calouste Gulbenkian

2009/2010 Genetics of Primary Spontaneous Pneumothorax (PSP). SPP/UCB Pharma Grant. PI: Feijó, Co-PI: Oliveira SA

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 - Lisling in 3D images. Project inserted in Mestrado integrado de Engenharia Electrotécnica e de Computadores. Coordinator: Yves Ryherczyk (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 Geraldês - PIC/IC/82991/2007.

2009/2015 An international, Prospective, TIA-clinic based, Web-based registry with long-term follow-up. Principal Investigator: Patrícia Canhão.

2009-2010 Pesquisa de Novas Mutações em Genes Responsáveis por Demência Familiar A. de Mendonça, principal investigator; collaboration with Gabriel Miltenberger, GenoMed; Grunenthal.

2009-2011 Neuropsychological predictors of the outcome in non-demented subjects with cognitive complaints, A de Mendonça, principal investigator; FCT.

2010 “Dicionários Terminológicos de LGP” - Fundação PT

2010/2012 - Frontal lobe dysfunction during migraine attacks. Raquel Gil-Gouveia, Isabel Pavão Martins, P. Vilela (Tecnifar Grant for Headache Research of Sociedade Portuguesa de Cefaleias)

2010/2012 - RAPS. Reading Analysis with neuroPhysiological Signs, FCT. Coordinator: N. Guimarães. PTDC/EIA-EIA/113660/2009

2010/2012 - VITHEA. Virtual Therapist for Aphasia treatment, FCT. Coordinator: Alberto Abad Garetá. RIPD/ADA/109646/2009

2010/2012 BEDGET: deciphering BEhçet’s Disease GEnETics, FCT. PI: Oliveira SA. PTDC/SAU-GMG/098937/2008

2010/2013 - Mindful ageing. Avoiding age related cognitive decline, Bial Fundation and Nunes Vicente Grant (SPN). Coordinator: I.P Martins

2010-2011 Estudo Genético de Famílias com Demência sem Mutações Reconhecidas. A. de Mendonça, principal investigator; collaboration with Gabriel Miltenberger, GenoMed; Grunenthal.

2010-2012 - Detection of brain microstates in Fibromyalgia, FCT. Coordinator: J Sanches. (IST).

2010-2012 – Reading analysis with neurophysiological signals, FCT. Coordinator: Nuno Guimarães. Participant: Carla Bentes. PTDC/EIA-EIA/113666/2009

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 – Estudo do Padrão Circadiário das Crises em Doentes com Epilepsia Temporal Mesial Refractária, em Ambulatório – 13º Programa “Educação pela Ciência” – 2009-2010 – GAPIC Coordinator: Carla Bentes. Student: Ruben Ferreira.

EHDN is an European network with the goal to develop and test therapeutic interventions and improve the quality of life of people with Huntington's disease. Our centre is actively involved in the cohort Registry and ongoing clinical trials. Prof. Joaquim Ferreira is the Science Director of the EHDN and Dr. Leonor Correia-Guedes is the Language coordinator for Portugal.

Late-Stage Huntingtons`s disease: study on the later stages of Huntington disease. A project approved by and as part of the collaboration within the European network for Huntington`s disease (EURO-HD).

MODEP (Modeling Epidemiological Data to study Parkinson disease progression) in collaboration with Department of Neurodegeneration, German Center for Neurodegenerative Diseases, Hertie Institute of Clinical Brain Research and University of Tübingen, Tübingen, Germany.

SLEEPMSA: Multicenter European study of the EMSA-SG (European MSA Study Group) to assess the prevalence of excessive daytime sleepiness in patients with MSA; correlation of excessive daytime sleepiness with other clinical features in this group of patients, compared to excessive daytime sleepiness between patients with MSA, Parkinson's disease and healthy subjects, matched to gender, age and severity of the disease. 15 individuals were included in our center.

Slow and Rapid Progression Parkinson's Disease: Molecular Determinants and Biomarkers in collaboration with The Cellular and Molecular Neuroscience Unit, Instituto de Medicina Molecular, directed by Tiago Outeiro (FCT grant)

Study of determinants of prescription patterns in Special population Movement Disorders and Very Old.

Study of genetic determinants in parkinson disease cohorts in collaboration with University of Rotherdam.

Publications in peer review Journals

Aartsma-Rus A, Atkinson L, Brasseur D, Braun S, Buccella F, Bushby, K, Campion G, Catlin N, Connor E, Cwick V, Eagle M, Ellis JA, Florence J, Furlong P, Goemans N, Griggs R, Heslop E, Hoffman E, Hofmeister S, Kayadjanian N, Kirshner J, Levin A, Lynn S, McCormack P, McNeil E, Muntoni F, Narayanan G, Popat D, Porter J, Rose M, Saint-Raymond A, Sampaio C, Shrewsbury S, Straub V, Vamvakas S, Voit T, Vroom E, Wells D, Westermarck K, Wilks M, Woods S (2010) The development of antisense oligonucleotide therapies for Duchenne muscular dystrophy: report on a TREAT-NMD workshop hosted by the European Medicines Agency (EMA). *Neuromuscul Disord* **20**, 355-362. (Journal IF 2.807)

Afonso P, Figueira L, Paiva T (2010) Schizophrenia patients with predominant positive symptoms have more disturbed sleep-wake cycles measured by actigraphy, *Psychiatry Res*, Epub ahead of print (Journal IF: 2.373)

Afonso P, Brissos S, Figueira ML, Paiva T (2010) Discrepant nocturnal melatonin levels in monozygotic twins discordant for schizophrenia and its impact on sleep. *Schizophr Res* **120** (1-3), 227-8 (Journal IF: 4.458)

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. Epub ahead of print *Neurology* (Journal IF: 8.172)

Ardila A, Bertolucci P, Braga LW, Castro-Caldas A, Judd T, Kosmidis M, Matute E, Nitrini R, Ostrosky F, Rosselli M (2010) Illiteracy: The Neuropsychology of Cognition Without Reading, *Arch Clin Neuropsychol* **25**, 689–712 (Journal IF: 2.497)

Baptista MV, Ferreira S, Pinho-E-Melo T, Carvalho M, Cruz VT, Carmona C, Silva FA, Tuna A, Rodrigues M, Ferreira C, Pinto AA, Leitão A, Gabriel JP, Calado S, Oliveira JP, Ferro JM and PORTuguese Young STROKE Investigators (2010) Mutations of the GLA gene in young patients

with stroke: the PORTYSTROKE study--screening genetic conditions in Portuguese young stroke patients. *Stroke* **41**, 431-436. (Journal IF: 7.041)

Bentes C, Costa J, Pires J, et al (2010) AM recall and seizures in patients with temporal lobe epilepsy, *Epilepsia* **51**, 100- (Journal IF: 4.052)

Branco JC, Zachrisson O, Perrot S, Mainguy Y (2010) Multinational Coordinator Study Group. A European multicenter randomized double-blind placebo-controlled monotherapy clinical trial of milnacipran in treatment of fibromyalgia. *J Rheumatol* **37** (4), 851-9. (Journal IF: 2.225)

Bronzova J, Sampaio C, Hauser RA, Lang AE, Rascol O, Theeuwes A, van de Witte SV, van Scharrenburg G; Bruegel Study Group (2010) Double-Blind Study of Pardoprunox, a New Partial Dopamine Agonist, in Early Parkinson's Disease, *Mov Disord* **25**, 638-746 (Journal IF: 4.014)

Caldeira D, David C, Sampaio C (2010) Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis *J Hosp Infect.* Epub ahead of print.(Journal IF:3.016)

Candid M, Vicario CM, Abreu AM and Aglioti SM, (2010) Competing Mechanisms for Mapping Action-Related Categorical Knowledge and Observed Actions, *Cerebral Cortex Advance* **20** (12), 2832-41 (Journal IF: 6.979)

Cardim N, Toste J, carvalho V, Nunes I, Ferreira D, Carmelo V, Oliveira ASN, Ferro JM, Mariana S, Almeida A, Machado FP, Roquette J (2010) Playing games with a thrombus: a dangerous match. Paradoxical embolism from a huge central venous catheter thrombus: a case report. *Cardiovasc Ultrasound* **8**, 6- (Journal IF: 1.22)

Cavaco S, Anderson SW, Correia M., Magalhães M, Pereira C, Tuna A, Taipa R, Pinto P, Pinto C, Cruz R, Lima AB, Castro-Caldas A, da Silva AM and Damásio H (2010) Task-specific contribution of the human striatum to perceptual-motor skill learning, *J Clin Exp Neuropsychol* **5**, 1-12. (Journal IF: 1.885)

Coelho M, Marti MJ, Tolosa E, Ferreira JJ, Valldeoriola F, Rosa M, Sampaio C (2010) Late-stage Parkinson's disease: the Barcelona and Lisbon cohort, *J Neurol* **257**, 1524-1532 (Journal IF: 2.903)

Colaço D, Mineiro A, Leal G and Castro-Caldas A (2010) Revisiting "The influence of literacy in paraphasias of aphasic speakers". *Clin Linguistics & Phonetics* **24**, 890-905. (Journal IF: 3.020)

Colosimo C, Martinez-Martin P, Fabbri G, Hauser RA, Merello M, Miyasaki J, Poewe W, Sampaio C, Rascol O, Stebbins GT, Schrag A, Goetz CG (2010) Task Force Report on Scales to Assess Dyskinesia in Parkinson's Disease: Critique and Recommendations, *Mov Disord* **25**, 1131-1142. (Journal IF: 4.014)

Conceição I, Evangelista T, Castro J, Pereira P, Silvestre A, Coutinho CA, Carvalho M (2010) Acquired amyloid neuropathy in a portuguese patient after domino liver transplantation. *Muscle Nerve* **42**, 836-839 (Journal IF: 2.287)

Correia Guedes L, Ferreira JJ, Rosa MM, Coelho M, Bonifati V, Sampaio C (2010) Worldwide frequency of G2019S LRRK2 mutation in Parkinson's disease: A systematic review, *Parkinson & Related Disord* **16**, 237-242. (Journal IF: 2.406)

Costa J, Gomes C, de Carvalho M (2010) Diagnosis, Pathogenesis and Therapeutic Targets in Amyotrophic Lateral Sclerosis, *CNS & NEUROLOGICAL DISORDERS-DRUG TARGETS* **9**, 764-778 (Journal IF: 3.571)

Costa J, Gonzalez HA, Valdeoriola F, Gaig C, Tolosa E, Valle Sole J (2010) Nonlinear Dynamic Analysis of Oscillatory Repetitive Movements in Parkinson's Disease and Essential Tremor, *Mov Disord* **25**, 2577-2586 (Journal IF: 4.014)

Coutinho JM, Ferro JM, Canhão P, Barinagarrementeria F, Bousser MG, Stam J and ISCVT Investigators (2010) Unfractionated or low-molecular weight heparin for the treatment of cerebral venous thrombosis. *Stroke* **41**, 2575-2580 (Journal IF: 7.041)

De Carvalho M, Pinto S, Costa J, Evangelista T, Ohana B, Pinto A (2010) A randomized, placebo-controlled trial of memantine for functional disability in amyotrophic lateral sclerosis, *Amyotroph Lateral Scler* **11**, 456-460 (Journal IF: 2.963)

de Mendonça A, Cunha RA (2010) Therapeutic opportunities for caffeine in Alzheimer's disease and other neurodegenerative disorders. *J Alzheim Dis* **20** (suppl 1), S1-S2, S249-S252. (Journal IF: 5.101)

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 and 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**, 528-537 (Journal IF: 3.538)

Einhäupl K, Stam J, Bousser MG, De Bruijn SF, Ferro JM, Martinelli I and Masuhr F (2010) EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. *Eur J Neurol* **17**, 1229-1235. (Journal IF: 2.510)

Ferreira JJ, Lew MF (2010) Immunogenicity analysis from an extension of a randomised, double-blind trial comparing botulinum neurotoxin type B vs. type A in previously toxin-naïve patients with cervical dystonia: study 402CD-EU, *J Neur Transm* **117**, 1234-1234. (Journal IF: 2.259)

Ferreira JJ, Neutel D, Mestre T, Coelho M, Rosa MM, Rascol O, Sampaio C (2010), Skin Cancer and Parkinson's Disease, *Mov Disord* **25**, 139-148 (Journal IF: 4.014)

Ferreira JJ, Rascol O, Poewe W, Sampaio C, Rocha JF, Nunes T, Almeida L, Soares da Silva P (2010) A Double-Blind, Randomized, Placebo and Active-Controlled Study of Nebicapone for the Treatment of Motor Fluctuations in Parkinson's Disease, *CNS NEUROSCIENCE & THERAPEUTICS* **16**, 337-347. (Journal IF 2.690)

Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F, Stolz E; ISCVT Investigators (2010) Cerebral venous thrombosis with nonhemorrhagic lesions: clinical correlates and prognosis. *Cerebrovasc Dis* **29**, 440-445 (Journal IF: 3.535)

Ferro JM, Massaro AR and Mas JL (2010) Aetiological diagnosis of ischaemic stroke in young adults. *Lancet Neurol* **9**, 1085-1096. (Journal IF: 18.126)

Fonseca AC, Geraldés R, Reimão S, Pinho e Melo T and Ferro JM (2010) Neck hematoma after intravenous thrombolysis for stroke treatment. *Cerebrovasc Dis* **30**, 101-102. (Journal IF: 3.535)

Foreid H, Barroso C, Evangelista T, Campos A, Pimentel J (2010) Intracerebral amyloidoma: case report and review of the literature. *Clin Neuropathol* **29**, 217-222. (Journal IF: 1.037)

Foreid H, Bentes C, Pimentel J (2010) The use of placebo as a provocative test in the diagnosis of psychogenic non epileptic seizures. *Neuroethics* **3**, 95-98. (Journal IF: 12.79)

Friedman JH, Alves G, Hagell P, Marinus J, Marsh L, Martinez-Martin P, Goetz CG, Poewe W, Rascol O, Sampaio C, Stebbins G, Schrag A (2010) Fatigue Rating Scales Critique and Recommendations by the Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, *Mov Disord* **25**, 805-822 (Journal IF 4.014)

Gil-Gouveia R, Martins IP (2010) Validation of the Portuguese Version of ID-Migraine. *Headache* **50**, 396-402 (Journal IF: 2.896)

Ginó S, Mendes T, Maroco J, Ribeiro F, Schmand BA, de Mendonça A, Guerreiro M, (2010) Memory complaints are frequent but qualitatively different in young and old healthy people. *Gerontology* **56**, 272-277. (Journal IF: 1.69)

Gouveia LO and Canhão P (2010) MTHFR and the risk for cerebral venous thrombosis- a meta-analysis. *Thromb Res* **125**, e153-158. (Journal IF: 2.449)

HÃagl B, Arnulf I, Comella C, Ferreira J, Iranzo A, Tilley B, Trenkwalder C, Poewe W, Rascol O, Sampaio C, Stebbins GT, Schrag A, Goetz CG (2010) Scales to assess sleep impairment in Parkinson's disease: critique and recommendations, *Mov Disord* **25**, 2704-2716. (Journal IF 4.014)

Hampel H, Wilcock G, Andrieu S, Aisen P, Blennow K, Broich K, Carrillo M, Fox NC, Frisoni GB, Isaac M, Lovestone S, Nordberg A, Prvulovic D, Sampaio C, Scheltens P, Weiner M, Winblad B, Coley N, Vellas B; for the Oxford Task Force Group. (2010) Biomarkers for Alzheimer's disease therapeutic trials, 2010 Dec 2. *Prog Neurobiol* Epub ahead of print. (Journal IF:11.554)

Kollensperger M, Geser F, Ndayisaba JP, Boesch S, Seppi K, Ostergaard K, Dupont E, Cardozo A, Tolosa E, Abele M, Klockgether T, Yekhlef F, Tison F, Daniels C, Deuschl G, Coelho M, Sampaio C, Bozi M, Quinn N, Schrag A, Mathias CJ, Fowler C, Nilsson CF, Widner H, Schimke N, Oertel W, del Sorbo F, Albanese A, Pellecchia MT, Barone P, Djaldetti R Colosimo C, Meco G, Gonzalez-Mandly A, Berciano J, Gurevich T, Giladi N, Galitzky M, Rascol O, Kamm C, Gasser T, Siebert U, Poewe W, Wenning G K (2010) Presentation, Diagnosis, and Management of Multiple System Atrophy in Europe: Final Analysis of the European Multiple System Atrophy Registry. *Mov Disord* **25**, 2604-2612 (Journal IF: 4.014)

Krug T, Manso H, Gouveia L, Sobral J, Xavier JM, Albergaria I, Gaspar G, Correia M, Viana-Baptista M, Simões RM, Pinto AN, Taipa R, Ferreira C, Fontes JR, Silva MR, Gabriel JP, Matos I, Lopes G, Ferro JM, Vicente AM, Oliveira SA. (2010) Kalirin: A novel genetic risk factor for ischemic stroke. *Human Genetics* **127**, 513-23. (Journal IF: 4.042)

Louis ED, Ferreira JJ (2010) How Common Is the Most Common Adult Movement Disorder? Update on the Worldwide Prevalence, Essential Tremor. *Mov Disord* **25**, 534-541. (Journal IF: 4.014)

Madureira S, Verdelho A, Moleiro C, Ferro JM, Erkinjuntti T, Jokinen H, Pantoni L, Fazekas F, Van der Flier W, Visser M, Waldemar G, Wallin A, Hennerici M and Inzitari D (2010) Neuropsychological predictors of dementia in a three-year follow-up period: data from the LADIS study. *Dement Geriatr Cogn Disord* **29**, 325-334. (Journal IF: 2.578)

Manso H, Krug T, Sobral J, Albergaria I, Gaspar G, Ferro JM, Oliveira SA, Vicente AM. (2010) Variants of the Matrix Metalloproteinase-2 but not the Matrix Metalloproteinase-9 genes significantly influence functional outcome after stroke. *BMC Medical Genetics* **11**, 40-. (Journal IF: 2.76)

Martins IP, Loureiro C, Rodrigues S, Dias B, Slade P (2010) Factors Affecting The Retrieval of Famous Names. *Neurol Sci* **31**, 269–276. (Journal IF: 1.236)

Martins M, Martins IP (2010) Memory Malingerer: Evaluating WMT criteria. *Applied Neuropsychol* **17**, 177-182. (Journal IF: 1.027)

Maruta C, Guerreiro M, de Mendonça A, Hort J, Scheltens P (2010) The Use of Neuropsychological Tests across Europe: The Need for a Consensus in the Use of Assessment Tools for Dementia. *Eur J Neurol* [Epub ahead of print]. (Journal IF: 2.732)

Mestre T, Ferreira JJ (2010) Pharmacotherapy in Parkinson's disease: case studies. *Adv Neurol Disord* **3**, 117-26. (Journal IF: N/A)

Mestre T, Lang AE (2010) The Grasp Reflex: A Symptom in Need of Treatment, *Mov Disord* **25**, 2479-2485. (Journal IF: 4.014)

Miranda B, Ferro JM, Canhão P, Stam J, Boussier MG, Barinagarrementeria F, Scoditti U and ISCVT Investigators (2010) Venous thromboembolic events after cerebral vein thrombosis. *Stroke* **41**, 1901-1906. (Journal IF: 7.041)

Morgado J, Rocha CS, Maruta C, Guerreiro M, Martins IP (2010) Cut-off scores in MMSE: a moving target? *Eur J Neurol*. **17** (5), 692-695. (Journal IF: 3.020)

Nielsen TR, Vogel A, Riepe MW, de Mendonça A, Rodriguez G, Nobili F, Gade A, Waldemar G (2010) Assessment of dementia in ethnic minority patients in Europe – A European Alzheimer's Disease Consortium survey. *Int Psychogeriatr*. [Epub ahead of print]. (Journal IF: 2.21)

Nunes T, Fragata I, Ribeiro F, Palma T, Maroco J, Cannas J, Secca M, Menezes C, Carmo I, Cunha G, Castelo Branco M, Guerreiro M, de Mendonça A (2010) The outcome of elderly patients with cognitive complaints but normal neuropsychological tests. *J Alzheimers Dis* **19**, 137-145. (Journal IF: 5.101)

Pedrosa H, de Sá A, Guerreiro M, Maroco J, Simões MR, Galasko D, de Mendonça A (2010) Functional Evaluation distinguishes MCI patients from healthy elderly people - the ADCS/MCI/ADL scale. *J Nutr Health Aging* **14**, 703-709. (Journal IF: 2.321)

Pimentel J, Bentes C, Campos A, Gonçalves Ferreira A, and the Epilepsy Surgery Group (2010) Long-term and late seizure outcome after surgery for temporal lobe epilepsy. *Epileptic Disord* **12**(1), 54-58. (Journal IF: 1.198)

Rosa MM, Ferreira JJ, Coelho M, Freire R, Sampaio C (2010) Prescribing Patterns of Antiparkinsonian Agents in Europe. *Mov Disord* **8**, 1053-1060. (Journal IF: 4.014)

Sampaio C, Ferreira JJ (2010) PARKINSON DISEASE ADAGIO trial hints that rasagiline slows disease progression. *Nat Rev Neurol* **6**, 126-128. (Journal IF: N/A)

Sampaio C, Ferreira JJ (2010) PARKINSON DISEASE Adjunctive entacapone therapy increases risk of dyskinesia. *Nat Rev Neurol* **6**, 590-591 (Journal IF: ND)

Santos C, Lunet N, Azevedo A, de Mendonça A, Ritchie K, Barros H (2010) Caffeine intake is associated with a lower risk of cognitive decline: a cohort study from Portugal. *J Alzheimer Dis* **20** (suppl 1), S175-S185. (Journal IF: 5.101)

Schmidt R, Ropele S, Ferro J, Madureira S, Verdelho A, Petrovic K, Gouw A, van der Flier WM, Enzinger C, Pantoni L, Inzitari D, Erkinjuntti T, Scheltens P, Wahlund LO, Waldemar G, Rostrup E, Wallin A, Barkhof F, Fazekas F and LADIS study group (2010) Diffusion-weighted imaging and cognition in the leukoaraiosis and disability in the elderly study. *Stroke* **41**, e402-408. (Journal IF: 7.041)

Teodorczuk A, Firbank MJ, Pantoni L, Poggesi A, Erkinjuntti T, Wallin A, Wahlund LO, Scheltens P, Waldemar G, Schrotter G, Ferro JM, Chabriat H, Bazner H, Visser M, Inzitari D, O'Brien JT and LADIS Group (2010) Relationship between baseline white-matter changes and development of late-life depressive symptoms: 3-year results from the LADIS study. *Psychol Med* **40**, 603-610. (Journal IF: 5.012)

Truelle JL, Koskinen S, Hawthorne G, Sarajuuri J, Formisano R, Von Wild K, Neugebauer E, Wilson L, Gibbons H, Powell J, Bullinger M, Höfer S, Maas A, Zitnay G, Von Steinbuechel N; Qolibri Task Force, (2010) Quality of life after traumatic brain injury: the clinical use of the QOLIBRI, a novel disease-specific instrument, *Brain Inj* **24**, 1272-91. (Journal IF: 1.533)

Verdelho A, Madureira S, Moleiro C, Ferro JM, Santos CO, Erkinjuntti T, Pantoni L, Fazekas F, Visser M, Waldemar G, Wallin A, Hennerici M, Inzitari D and LADIS Study (2010) White matter changes and diabetes predict cognitive decline in the elderly: the LADIS study. *Neurology* **75**, 160-167. (Journal IF: 8.172)

von Campenhausen S, Winter Y, Silva AR, Sampaio C, Ruzicka E, Barone P, Poewe W, Guekht A, Mateus C, Pfeiffer KP, Berger K, Skoupa J, Bätzel K, Geiger-Gritsch S, Siebert U, Balzer-Geldsetzer M, Oertel WH, Dodel R, Reese JP (2010) Costs of illness and care in Parkinson's Disease: An evaluation in six countries. *Eur Neuropsychopharmacol* Epub ahead of print.. (Journal IF:3.68)

Other publications International

Adamec O, Domingues A, Paiva T, Sanches JM (2010) Statistical characterization of actigraphy data during sleep and wakefulness states, *Conf Proc IEEE Eng Med Biol Soc* **1**, 2342-5 .

Domingues A, Adamec O, Paiva T, Sanches J (2010) Automatic annotation of actigraphy data for Sleep disorders diagnosis purposes. *Conf Proc IEEE Eng Med Biol Soc.* 2010; **1**, 5081-4.

Sanches J, Pereira B, Paiva T (2010) Headset Bluetooth and cell phone based continuous central body temperature measurement system. *Conf Proc IEEE Eng Med Biol Soc.* 2010 **1**, 2975-8.

Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T (2010) Dream recall frequency and content in patients with temporal lobe epilepsy. *JSR* **19** (Suppl. 2) 24.

Bentes C, Costa J, Pires J, Pereira P, Paiva T (2010) Dream recall and Seizures in patients with Temporal Lobe Epilepsy, *Epilepsia* **51** (Suppl. 4), 100.

de Mendonça A, Perry G. (2010) Obituary – Edgar da Cruz e Silva 1958-2010. *J Alzheim Dis* **21**, 1037.

Ferreira L, Santos R, Pires J, Paiva T (2010) Cyclic alternating pattern in congenital deaf quantitative and topographic analysis. *JSR* **19** (Suppl. 2) 278.

Ferro J, Martins IP, Caeiro L. (2010) Behavioral neurology of stroke. In: Brainin M, Heiss WD, eds. Textbook of Stroke Medicine. Cambridge, Cambridge University Press, 178-193.

Ferro JM, Canhão P (2010) Venous infarcts in young adults. In: Pezzini A, Padovani A, eds. Cerebral ischemia in young adults: Pathogenic and clinical perspectives. Nova Publishers, 509-524.

Foreid H, Bentes C, Pimentel J (2010) The use of placebo as a provocative test in the diagnosis of psychogenic non epileptic seizures. *Neuroethics* **3**, 95-98.

Leitão A, Peralta R, Gerales R, Bentes C (2010) Symptomatic narcolepsy after transverse myelitis: a clinical case. *JSR* **19** (Suppl. 2) 148.

Mameniskiene R, Wolf P, and the European Study Group on Epilepsia partialis continua (2010) Non-Rasmussen, Non-stroke epilepsia partialis continua. *Epilepsia* **51** (Suppl. 4), 50-51.

Mineiro A, Lagarto JR, Nunes MV and Castro Caldas A (2010) Enseñanza y aprendizaje a distancia para sordos: bases metodológicas del desarrollo curricular de la licenciatura en Lengua de Señas Portuguesa, In: Memorias del Séptimo Simposium Iberoamericano de Educación, Cibernética y Informática: SIECI 2010 - Novena Conferencia Iberoamericana en Sistemas, Cibernética y Informática, Orlando, Florida.

Neutel D, Pita Lobo P, Mestre T, Peralta R, Bentes C (2010) Hypersomnia and coeliac disease. *JSR* **19** (Suppl. 2) 278.

Paiva T, Peralta R, Pires J, Sousa P (2010) Sensory dysfunction impact upon dream content. *JSR* **19** (Suppl. 2) 175.

Peralta R (2010) Working visual memory in OSAS patients: a fMRI study. *JSR* **19** (Suppl. 2) 74.

Peralta R, Bentes C, Henriques I (2010) Inter-ictal epileptic activity topographies detected in morning and afternoon post-sleep deprivation EEGs. *Epilepsia*, **51** (Suppl. 4), 101.

Peralta R, Bentes C, Moreira S, Staats R, Valença J (2010) Residual somnolence on CPAP – residual respiratory disturbances or concomitant sleep diseases. *JSR* **19** (Suppl. 2) 375.

Pereira J, Morais I, Duarte L and Mineiro A (2010) Diachronic Variation in Portuguese Sign Language In: (Ed) Maria Mertzani, Sign Language Teaching and Learning, Applied Sign Linguistics (Vol.I), Peer-reviewed selected papers presented at the Applied Sign Linguistics Symposium 2009. University of Bristol, Centre for Deaf Studies, University of Bristol: Bristol, p.93-101.)

Pimentel J, Bentes C, Campos A, Ferreira AG and Epilepsy Surgery Group (2010) Long-term and late seizure outcome after surgery for temporal lobe epilepsy. *Epileptic Disord* **12** (1), 54-8.

Pimentel J, Peralta R, Campos A, Bentes C (2010) Antiepileptic drugs management and long-term seizure outcome in post surgical mesial temporal lobe epilepsy. *Epilepsia*, 51 (Suppl. 4), 132.

Pires J, Peralta R, Paiva T (2010) EEG mapping of deaf subject's dreams. *JSR* **19** (Suppl. 2), 174.

Pita Lobo P, Neutel D, Peralta R, Bentes C, Pimentel J (2010) Nocturnal choking: sleep apnoea or seizures? *JSR* **19** (Suppl. 2) 369.

Rebello Pinto H, Rebello Pinto T, Peralta R, Paiva T (2010) Group and individual approach of insomnia treatment in a cognitive behavioural perspective. *JSR* **19** (Suppl. 2) 290.

Other publications National

Baeta, E. and Pimentel, J. (2010) Epilepsia in Manual de Terapêutica Médica. Lidel (eds).

Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T (2010) Recordação onírica em Doentes com Epilepsia do Lobo Temporal. *Sinapse* **10**, Nº 2 151.

Bentes C, Peralta R (2010) Perturbações Neurológicas do Sono – Manual de Terapêutica Médica (Ed: Lidel).

Canhão P, Melo TP, Martins IP. (2010) Acidentes Vasculares Cerebrais. Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Coordenação: Prof. Roberto Palma dos Reis, ed, Verlag Dashöfer, 131-137. (Book Chapter)

Canhão P. (2010) Breves notas históricas sobre a trombose venosa cerebral. *Sinapse*, 24-27.

Canhão, P, Martins, I.P., Melo, T.P. (2010) Acidentes Vasculares Cerebrais in Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Roberto Palma dos Reis, ed, Verlag Dashöfer, 131-137.

Canhão, P., Martins, I.P., Melo, T.P. (2010) Epilepsia in Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Roberto Palma dos Reis, ed, Verlag Dashöfer, 138-142.

Castro-Caldas A., (2010) The social Brain in: Comunicação, Cognição e Media, Vol 1, Publicações da Faculdade de Filosofia da Universidade Católica Portuguesa, Braga

Costa, S., Marques, J., Firmo, C., Pimentel, J. (2010) Ganglioglioma desmoplásico pigmentado não infantil. *Sinapse* 10(2), 114 (Abstract).

de Mendonça A. A doença de Alzheimer, hoje. *Rev Port Clin Geral* 2010 26 34-36.

de Mendonça A. Caféina Para a Memória. Notícias Magazine. *Diário de Notícias e Jornal de Notícias*, 4th July 2010.

de Mendonça A. O Tratamento do Futuro. Dossier Saúde - Dia Mundial da Doença de Alzheimer. *Diário de Notícias e Jornal de Notícias*, 21th September 2010.

Dores, A.R., Carvalho, I. & Castro-Caldas, A. (2010) As novas tecnologias ao serviço da reabilitação cognitiva de pacientes com Lesão Cerebral adquirida. Actas das Jornadas sobre Tecnologia e Saúde, Instituto Politécnico da Guarda, Guarda.

Dores, A.R., Carvalho, I. & Castro-Caldas, A., (2010) O desenvolvimento de um programa de reabilitação cognitiva com recurso a tecnologias informáticas. Actas do VII Simpósio Nacional de Investigação em Psicologia, Braga, Portugal.

Dores, A.R., Carvalho, I.P., Guerreiro, S., Almeida, I., Romero, L., Nunes, J. & Castro-Caldas, A. (2010) A reabilitação das funções executivas: Teste de um protótipo. Proceedings of International Neuropsychological Society Mild-year Meeting, Krakow, Poland

Fernandes, S., Novais Dos Santos, S & Castro-Caldas, Alexandre, (2010) Potenciação Neurológica: um desafio à ética e à identidade pessoal», Para uma Bioética Global? Porto, Universidade Católica Portuguesa

Fernandes, S. & Castro-Caldas, A., (2010) A Pessoa é o seu Cérebro?, in AAVV, Gravitações Bioéticas, Lisboa, Centro de Bioética da Faculdade Medicina de Lisboa

Fernandes, S., (2010) Notas de Bioética sobre Youth Without Youth de Mercia Eliade. Uma abordagem Literária do problema da Potenciação Humana, in AAVV, Pena & Bisturi. Reflexão Ética a partir da criação literária, Porto, Instituto de Bioética da Universidade Católica Portuguesa

Ferro JM, Melo TP, Canhão P, Farias JP. (2010) Acidentes vasculares cerebrais in Manual de terapêutica médica. Ponce P (ed). Lidel, 395-409. (Book Chapter)

Ferro JM. Triflusal na prevenção de fenómenos vasculares. Tecnifar, 2010

Ferro, J., Martins, I.P., Caeiro, L. (2010) Behavioral neurology of stroke in Textbook of Stroke Medicine, Brainin, M., and Heiss, W., D. (eds.) Cambridge University Press.

Fonseca CA, Peralta R, Henriques I, Bentes C (2010) Electroencefalograma na primeira crise epiléptica. *Sinapse* 10, Nº 2 147.

Foreid H, Miranda B, Peralta R, Bentes C, Biscoito L, Albuquerque L, Valle S. Leucoencefalopatia posterior reversível manifestada por estado de mal epiléptico após início de quimioterapia para tratamento de Linfoma Não – Hodgkin. *Sinapse* 10, Nº 2 117.

Guerreiro M. Testes de rastreio de defeito cognitivo e demência: uma perspectiva prática. *Rev Port Clin Geral* 2010 26 46-53.

Lauterbach, M., Leal, G., Martins, I.P., Willmes, K. (2010) Teste de afasia de Aachen (PAAT). Avaliação Psicológica, Revista de Psicologia, Educação e Cultura, XV: 227-248.

Madureira S. A educação dos cuidadores. *Rev Port Clin Geral* 2010 26 62-67.

Marques, J., Costa, S., Firmo, C, Campos, A., Pimentel, J. (2010) Sarcoma com Metaplasia Epitelial Secundário a Glioblastoma Multiforme Irradiado. *Sinapse* 10(2), 115-1116 (Abstract).

Marques, J., Costa, S., Firmo, C., Albuquerque, L., Aronica, E., Pimentel, J. (2010) Tumor Teratóide/Rabdóide Atípico no Adulto. *Sinapse* 10(2), 116 (Abstract).

Martins IP, Melo TP, Canhão P. (2010) Síndrome Vertiginosa aguda. Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Coordenação: Prof. Roberto Palma dos Reis, ed, Verlag Dashöfer, 129-130. (Book Chapter)

Martins N, Ferreira A, Pimentel J (2010) Caracterização quantitativa do núcleo basolateral da amígdala na esclerose mesial. *Sinapse* 10(1), 151-152 (Abstract).

Martins, IP (2010) Cefaleias in Manual de Terapêutica Médica, ed. Pedro Ponce, Manual Lidel, 2ª Edição.

Martins, IP, Melo, TP, Canhão, P (2010) Cefaleias na Urgência in Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Roberto Palma dos Reis, ed, Verlag Dashöfer, 126-128.

Martins, IP, Melo, TP, Canhão, P (2010) Neurologia: Coma e outras perturbações da vigília in Guia Prático de Medicina de Urgência. Do Diagnóstico à Terapêutica. Roberto Palma dos Reis, ed, Verlag Dashöfer, 121-125.

Martins, IP, Pavão, L (2010) Imagens para o cérebro. *Sinapse* 10 (1): 5-8.

Miranda B, Rodrigues D, Coelho M, Peralta R, Albuquerque L. Epilepsia parcial contínua no adulto. *Sinapse* 10, Nº 1 84

Moreira E, Branquinho A, Pimentel J (2010) Caracterização quantitativa do Hilo do Gyrus Dentatus na esclerose mesial. *Sinapse* 10(1), 146-147 (Abstract).

Neutel D, Peralta R, Biscoito L, Pinho e Melo T, Albuquerque L (2010) Acidente Vascular Cerebral em Doente com Arterite de Células Gigantes. *Sinapse* 10, Nº 1 133.

Neutel D, Peralta R, Ferreira J (2010) Movimentos involuntários de tipo mioclónico multifocais: caso clínico de etiologia não conclusiva. *Sinapse* 10, Nº 1 86.

Nunes M.V e Castro-Caldas A., (2010) Introdução às Neurociências, Vol. 5. UCP Editora: Lisboa, ISBN 978-972-54-0265-8

Oswald W (coordinator), Caramona M, Esteves, A P, Gonçalves J, Macedo T, Mendonça J, Pinheiro R L, Rodrigues A, Sampaio C, Sepodes, B, Teixeira AA, *Prontuário Terapêutico* 9, Infarmed, March 2010.

Paiva T and Penzel T (2010) “O Centro de Medicina do Sono. Manual Prático.” (The Sleep Medicine Center- Practical Manual). Eds Lidel ISBN 978-972-757-719-4

Paiva T and Rebelo Pinto H (2010) Dormir é bom, dormir faz bem. (Sleep is good, Sleep makes good). Eds Bertrand ISBN 978-972-25-2160-4

Paiva T and Rebelo Pinto H (2010) O meu amigo, o Sono. (My friend Sleep) Eds Bertrand ISBN 978-972-25-2206-9

Paiva T and Rebelo Pinto H (2010) Os Mistérios do Sono. (The Mysteries of Sleep) Eds Bertrand ISBN 978-972-25-2111-6, 2nd Edition

Paiva, T (2010) Sleep and Headaches; in the volume of Sleep Disorders of the Handbook of Clinical Neurology, eds Schokroverty and P Montagna Handb Clin Neurol. 2010; 99:1073-86. PubMed PMID: 21056243.

Peralta R, Bentes C, Henriques I (2010) EEGs com sono pós privação – importância da hora do dia no tipo e topografia da actividade epiléptica detectada. *Sinapse* **10**, Nº 2 151.

Pereira Alves R, Caetano AI. O papel do Médico de Família no diagnóstico e seguimento dos doentes com defeito cognitivo e demência. *Rev Port Clin Geral* 2010 26 69-74.

Pimentel J, Peralta R, Campos A, Bentes C (2010) Estratégia da terapêutica antiepiléptica e recorrência das crises epiléticas após cirurgia da epilepsia mesial temporal. *Sinapse* 10(1), 146 (Abstract).

Pimentel J, Peralta R, Campos A, Bentes C (2010) Estratégia da terapêutica antipirética e recorrência das crises epiléticas após cirurgia da epilepsia mesial temporal. *Sinapse* **10**, Nº 2 146.

Pires, A, Ferro J, Pimentel J (2010) Avaliação da amusia em doentes epiléticos submetidos a amigdalohipocampectomia. *Sinapse* 10(1), 149 (Abstract).

Rato, J.R. & Castro-Caldas, A., (2010) Competências matemáticas emergentes: Avaliação neuropsicológica de crianças em idade pré-escolar. In C. Nogueira, I. Silva, L. Lima, A. T. Almeida, R. Cabecinhas, R. Gomes, C. Machado, A. Maia, A. Sampaio & M. C. Taveira (Eds.), Actas do VII Simpósio Nacional de Investigação em Psicologia (pp. 607-625).

Rato, J.R. & Castro-Caldas, A., (2010) Neurociências e educação: Realidade ou ficção? In C. Nogueira, I. Silva, L. Lima, A. T. Almeida, R. Cabecinhas, R. Gomes, C. Machado, A. Maia, A. Sampaio & M. C. Taveira (Eds.), Actas do VII Simpósio Nacional de Investigação em Psicologia (pp. 626- 644).

Simões do Couto F, de Mendonça A. Sintomas psiquiátricos e Comportamentais da Demência. *Rev Port Clin Geral* 2010 55-60.

Simões do Couto F, Verdelho A, Mendonça A. (2010) Demência in Manual de terapêutica médica. Ponce P (ed). Lidel, 418-425. (Book Chapter)

Verdelho A. Prevenção do defeito cognitivo e demência – os factores de risco vascular. *Rev Port Clin Geral* 2010 26 38-44.

Oertel WH, Berardelli A, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Ferreira JJ, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Sch ü pbach M, Tolosa E, Trenkwalder C, CHAPTER 15, Late (complicated) Parkinson' s disease, in Major Neurological Diseases, 2010

Oertel WH, Berardelli A, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Ferreira JJ, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Sch ü pbach M, Tolosa E, Trenkwalder C, CHAPTER 14, Early (uncomplicated) Parkinson' s disease, in Major Neurological Diseases, 2010

Invited Lectures and Seminars

Bentes C. (commentor) “Pernas Inquietas”, Geraldo Rizzo, 1º Simpósio Luso – Brasileiro de Medicina do Sono, Centro de Congressos de Lisboa, Lisboa, September 14, 2010.

Bentes C. (commentator) VI Reunião Luso-Espanhola – Epilepsia e Malformações do Desenvolvimento Cortical, Hotel VIP Executive Art's, Parque das Nações, Lisboa, October 30, 2010.

Bentes C. 3ª Reunião dos Centros de Cirurgia da Epilepsia, Anfiteatro do Hospital Santo António Porto, March 18, 2010.

Bentes C. Advisory Board UCB – Locosumida e politerapia racional, Batalha, November 2010.

Bentes C. Cluster Analysis and Data Mining - XXXV Reunião anual da Associação Portuguesa de EEG e Neurofisiologia Clínica – Hotel da Rocha, Portimão, May 28-29 2010. (moderator)

Bentes C. Participation on “An introduction to Medtronic DBC Therapy for Epilepsy, A virtual peer-to-peer seminar” hosted by: Robert Fischer, MD, PhD – SANTE Lead Principal Investigator and Michael Kaplitt, MD, PhD, November 22, 2010.

Bentes C. Sessão de revisões temáticas sobre manifestações funcionais – Fórum de Neurologia 2010 – Sintomas funcionais em Neurologia – Grande Hotel do Luso, May 14-15, 2010. (moderator)

Canhão P. Cerebral Vein and Sinus Thrombosis. EuroNeuro. Porto, Fevereiro 2010.

Canhão P. Cerebral venous thrombosis: clinical investigation of a rare disease. Neuroscience Seminar. IMM. Lisboa, April 19, 2010.

Canhão P. Organização de Consultas de AVC e AIT. 1ª Reunião de Unidades de AVC, Lisboa, January, 2010. 4º Congresso Português do AVC, Porto, February 4-6, 2010.

Canhão P. Risco vascular, risco cognitivo, risco coronário. 1ªs Jornadas de Imagiologia. Tomar, October 22, 2010

Canhão P. Trombose Venosa Cerebral. 4º Curso de Actualização em Doença Vascular Cerebral do Hospital de São João. Porto, April 2010.

Castro-Caldas A, Ciclo de Conferências Saber mais sobre, “As Cefaleias”, Lisbon, November 24, 2010

Castro-Caldas A., “Debate “Saber Estudar- Saberão os alunos aprender?” Universidade Católica Portuguesa, Lisboa, October 20, 2010

Castro-Caldas A. – 1^{as} Jornadas de Cuidados Continuados Integrados L’Nostrum – “Avaliação Neuropsicológica”, Mafra, November 26, 2010

Castro-Caldas A. – 31^o Congresso Português de Geriatria – “A Doença de Alzheimer”, Lisboa, October 12, 2010

Castro-Caldas A. – 4^a Conferência Internacional do Plano Nacional de Leitura – “O Cérebro com que se aprende a ler depois dos 50”, FCG, October 15, 2010

Castro-Caldas A. - 8^o Simpósio Fundação Bial “Aquém e Além do Cérebro” (organizing committee), Porto, April 07-10, 2010

Castro-Caldas A. – Colóquio «Visões do Eu» – “O Cérebro e Eu”, Faculdade de Letras de Lisboa, October 28, 2010

Castro-Caldas A. – Conferência Internacional sobre envelhecimento, Fundação D. Pedro IV – “A Geriatria e envelhecimento Saudável” Universidade Nova de Lisboa, October 15, 2010

Castro-Caldas A. – Conferência Leitura: Aspectos Psicolinguísticos e Neurocognitivos – “O Cérebro e a Leitura” (moderator), Faculdade de Letras de Lisboa, October 18, 2010

Castro-Caldas A. – Congresso de Neurologia 2010 – “Neuroplasticity and functional recovery after brain lesions” (moderator), Espinho, November 5, 2010

Castro-Caldas A. – Debate “Os Equipamentos, os Serviços e as Pessoas com Demência” (moderator), FCG, December 10, 2010

Castro-Caldas A. – Fórum de Neurologia 2010 – “Conferência Psychogenic Movement Disorders (Mark Edwards)” (moderator), Luso, May 15, 2010

Castro-Caldas A. – II Conferência Satélite "A Mente dos Jovens - uma preocupação emergente". – “Smart Pills”, Faculdade de Farmácia de Lisboa, November 2, 2010

Castro-Caldas A. – Sociedade Portuguesa de Andrologia – XII Congresso Nacional de Andrologia Outras Fronteiras, “Falar do Cérebro”, Lisbon, May 21, 2010

Castro-Caldas A., “A Doença de Parkinson”, Conferência ICS-UCP, Lisbon, March 17th, 2010

Castro-Caldas A., “A Fisiopatologia da Dislexia de Desenvolvimento”, DISLEXIA: o UNIVERSO e o controverso, Porto, May 14, 2010

Castro-Caldas A., “A Viagem ao Cérebro e a algumas das suas competências”, Escola Secundária Emílio Navarro, Viseu, March 5, 2010

Castro-Caldas A., “O Cérebro e o Canto”, Curso Saúde e Canto, Universidade Católica Portuguesa, Lisbon, April 27, 2010

Castro-Caldas A., “O que é uma demência. Aspectos do diagnóstico e do tratamento”, “As Demências na RNCCI – Qual o papel dos Cuidadores?”, Porto, November 18, 2010

Castro-Caldas A., “O que é uma demência. Aspectos do diagnóstico e do tratamento”, “As Demências na RNCCI – Qual o papel dos Cuidadores?”, Coimbra, November 11, 2010

Castro-Caldas A., “O que é uma demência. Aspectos do diagnóstico e do tratamento”, “As Demências na RNCCI – Qual o papel dos Cuidadores?”, Faro, November 4, 2010

Castro-Caldas A., “O que é uma demência. Aspectos do diagnóstico e do tratamento”, “As Demências na RNCCI – Qual o papel dos Cuidadores?”, Évora, October 28, 2010

Castro-Caldas A., “O que é uma demência. Aspectos do diagnóstico e do tratamento”, “As Demências na RNCCI – Qual o papel dos Cuidadores?”, Lisbon, October 22, 2010

Castro-Caldas A., 2º Curso Médico-Cirúrgico em Neurociências (chairperson), Porto, January 22, 2010

Ferreira JJ, Basic strategies for therapy in the advanced stage: What is evidence-based? 14th International Congress of Parkinson’s Disease and Movement Disorders’s, Buenos Aires, Argentina, 13-17 June, 2010

Ferreira JJ, Bench to Bedside: Novel anti-dyskinetic treatments being tested in the clinic, 2nd World Parkinson, Glasgow, UK Congress September 28 – October 1, 2010

Ferreira JJ, Calidad de vida en la distonia, VI Jornada de Distonía en Cataluña, Barcelone, Spain, November 15, 2010

Ferreira JJ, Chorea 3rd MDS European Summer School for Young Neurologistse Netherlands, 9-11 July, 2010

Ferreira JJ, Clinical Treatment of Motor Complications: Gait Disorders and Falls , Treatment of Parkinson’s disease, São Paulo , Brasil, October 16, 2010

Ferreira JJ, Clinical Trials Design: Focus on Dyskinesias, 2nd World Parkinson Congress, Glasgow, UK, September 28 – October 1, 2010,

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, Treatment on Non-motor features, sleep disorders, dysautonomia and pain, Treatment of Parkinson’s disease, São Paulo , Brasil, October 16, 2010

Ferreira JJ, What is the impact of Cervical Dystonia on the Daily Lives of Patients?, First International Congress on Treatment of Dystonia, Hannover, May 6-8, 2010,

Ferro JM. Agitation and delirium. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010

Ferro JM. Cerebral vein thrombosis. 21st International Thrombosis Congress, Milan, Italy, July 6-9, 2010.

Ferro JM. Effective protection of stroke in atrial fibrillation. XXXI Congresso Português de Cardiologia, Lisboa, April 9-12, 2010.

Ferro JM. How to structure a medical research paper. Congresso de Neurologia 2010, Espinho, November 5-7, 2010.

Ferro JM. O estado da arte da investigação clínica com neuroprotectores. 4º Congresso Português do AVC, Porto, February 4-6, 2010.

Ferro JM. Secondary prevention of cardioembolic stroke: old and new drug. 21st International Thrombosis Congress, Milan, Italy, July 6-9, 2010.

Ferro JM. Small vessel diseases: an increasing health problem. 20th Meeting of the European Neurological Society, Berlin, Germany, June 19-23, 2010.

Ferro JM. Stroke prevention. Symposium for the official Inauguration of the Neurocenter of Southern Switzerland, Lugano, Switzerland, May 6, 2010.

Ferro JM. The clinical spectrum of cerebral venous thrombosis. 14th Congress of the European Federation of Neurological Societies, Geneva, Switzerland, September 25-28, 2010.

Ferro JM. The Neurologist's point of view - Management of sources of embolism: the role of echocardiography. European Society of Cardiology Congress 2010, Stockholm, Sweden, August 28- September 1, 2010.

Ferro JM. Tia should be treated in TIA clinics, not admitted to stroke. 19th European Stroke Conference, Barcelona, Spain, May 25-28, 2010.

Ferro JM. Venous thrombosis syndromes. 7th World Stroke Congress, Seoul, Korea, October 13-16, 2010.

Fonseca, J. Linguagem e hemisfério direito. Jornadas Internacionais. Centro de Medicina de Reabilitação de Alcoitão. November 25, 2010.

Martins, I.P. Plasticidade das lesões do hemisfério direito na neuroreabilitação. Jornadas Internacionais. Centro de Medicina de Reabilitação de Alcoitão. November 25, 2010.

Melo TP. Decisões específicas no tratamento da fase aguda. 4º Congresso Português do AVC, Porto, February 4-6, 2010.

Melo TP. Tratamento trombolítico. Actualidades no tratamento agudo. 3º Congresso Português do AVC, Porto, February 5-7, 2010.

Melo TP. Trombólise em Portugal: evolução no último ano. 4º Congresso Português do AVC, Porto, February 4-6, 2010.

Melo TP. Trombólise no AVC agudo. XXXI Congresso Português de Geriatria, Lisboa, October 12-15, 2010

Melo TP. Trombólise para além das 4,5h – contra. 11º Simpósio de Doença Vasculiar Cerebral da Sociedade Portuguesa de Medicina Interna, Porto, November 12-12, 2010

Paiva T. 3rd National Meeting of Pediatrics, Child Insomnia, April 2010.

Paiva T. Congresso Brasileiro de Neurologia, Rio Janeiro - August 2010.

Paiva T. Congresso Brasileiro de Neurologia, Rio Janeiro, Course on Sleep - Complex nocturnal behaviours, August 2010.

Paiva T. Congresso Brasileiro de Neurologia, Rio Janeiro, Round table – RBD and synucleopathies, August 2010.

Paiva T. ESRS Marie Curie Symposium – Career development – How to write/review a scientific paper – Seon, July 2010.

Paiva T. Sleep disorders, Encontro Transmontano do Clínico Geral, Alijó 2010.

Paiva T. Supervision of small projects on Sleep and Conferences in Schools for students, title: To sleep, why? On High School of Leiria, High School Miguel Torga – Queluz, Schools of Vila Boim, Pedro Hispano Institute, School of S Roque do Pico and High School of Caneças 2010.

Paiva T. The Sleepless Child, Encontro Neuropsiquiatria Infantil, Beja 2010.

Peralta R. “Perturbação do ritmo de Sono no AVC” 4º Curso de Actualização em Doença Vasculiar Cerebral, Porto 2010.

Pinho e Melo T, Bentes C. Sessão de revisões temáticas sobre manifestações funcionais, Fórum de Neurologia 2010, Sintomas funcionais em Neurologia, Grande Hotel do Luso, May 14-15 2010. (moderators)

Sampaio C, A regulator’s perspective on the Disease modifying Challenge, 5th annual Huntington’s Disease Therapeutics Conference: A Forum for Drug Discovery & Development, Palm Springs, USA, February 7-9, 2010 (Oral presentation)

Sampaio C, Challenges in Design and Conduct for Clinical Trials for PD, 2nd World Parkinson Congress. September 28 – October 1, 2010, Glasgow, UK

Sampaio C, Clinical Trials: Methodological issues, 14th International Congress of Parkinson’s Disease and Movement Disorders’s, Buenos Aires, Argentina, 13-17 June, 2010

Sampaio C, Discussant.Recommendations for Improving Assay Sensitivity in Chronic Pain Clinical Trials, IMMPACT-XIII, USA, June 24 – 25, 2010

Sampaio C, Ensaios de desenho flexível, I Jornadas da Comissão de Ética para a Investigação Clínica 2010, Lisboa, January 21, 2010. (Oral presentation)

Sampaio C, New evaluation methods: the MDS-UPDRS; how to use it?, Société Française de Neurologie, Maladie de Parkinson : Miscellanées 2010, Journées Internationales, Paris, France, 7 – 8 Octobre 2010

Sampaio C, Outcomes in Parkinson Disease , Movement Disorders Meeting Kiel, Germany, September 10, 2010

Sampaio C, Parkinson's disease treatment: what is new?., 6º Congresso Brasileiro do Cérebro, Comportamento e Emoções, Belo Horizonte, Brasil, June 8-10, 2010

Sampaio C, Preventive trials in Alzheimer's Disease, Clinical Trials on Alzheimer's Disease, Toulouse, France, November 3-5, 2010.

Sampaio C, Safety of antipsychotics: pharmacovigilance and regulatory commitments, Benefit/risks ratio of antipsychotics: how to improve the effectiveness of our therapeutic armamentarium, 16th World Congress on Basic and Clinical Pharmacology, Copenhagen, Denmark, July 19-23, 2010

Sampaio C, Treatment of Parkinson's Disease and depression, 10 th International Forum on Mood and Anxiety Disorders, Vienna, Austria, November 17-19, 2010

Sampaio C, What do you need to know about rating scales?, 14th International Congress of Parkinson's Disease and Movement Disorders's, Buenos Aires, Argentina, June 13-17, 2010

Sampaio C, Why so few drugs for AD: A regulatory view point, 11th International Geneva/Springfield Symposium on Advances in Alzheimer Therapy, Geneva, Switzerland, March 24-28, 2010 (Oral presentation)

Sampaio C. Chairperson and Discussant Proposals of Guidelines in Drug Treatment of Minor Depression in Elderly People, Rome, Italy, July 2-3, 2010

Sofia A. Oliveira. Stroke and genetics. 6th Congress EURONEURO, Porto, Feb 4-6, 2010.

Verdelho A. Epidemiologia. 4º Congresso Português do AVC, Porto, February 4-6, 2010.

Verdelho A. Impact of lacunar infarcts on cognition and disability in elderly subjects: the LADIS experience. Ferro JM. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010.

Communications in International Conferences

Almeida V, Batista P, Soares F, Oliveira V. Mobile carotid thrombus identified by ultrasound. 15th meeting of the European Society of Neurosonology and Cerebral Hemodynamics, Madrid, Spain, May 22-24, 2010 (poster presentation).

Barone, P; Fernandez, H; Ferreira, JJ, et al., MOTION (satinamide add-On To dopamine agonist in early Idiopathic Parkinson's disease) study design: A 24-week, double-blind, placebo-controlled study of the efficacy and safety of safinamide, 14th International Congress of Parkinson's Disease and Movement Disorders, *Mov Disord* 25: 7: Pages: S289-S289, June 13-17, 2010.

Batista P, Almeida V, Soares F, Oliveira V. Ultrasound evaluation of carotid atherosclerosis progression. 15th meeting of the European Society of Neurosonology and Cerebral Hemodynamics, Madrid, Spain, May 22-24, 2010 (poster presentation).

Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T. Dream recall frequency and content in patients with temporal lobe epilepsy. 20th Congress of the European Sleep Research Society, Lisboa, September 14– 18, 2010. (Oral presentation)

Bentes C, Costa J, Pires J, Pereira P, Paiva T. Dream recall and Seizures in patients with Temporal Lobe Epilepsy. 9th European Congress on Epileptology, Rhodes, Greece, 27 June – July 1 2010. (Poster presentation)

Bronzova JB, Sampaio C, Hauser RA, et al., Pardoprinox adjunctive to L-dopa for treating motor symptoms in advanced PD: Results from a randomized, double-blind, placebo-controlled study, : *Mov Disord* 25 Issue: 7, Pages: S291-S291 Supplement: Suppl. S (June 13-17, 2010)

Canhão P, Campos ST, Fonseca MG, Abreu LF, Mourato MB. Stroke after TIA in a weekly TIA clinic. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (poster presentation)

Coutinho J, Ferro JM, Bousser M-G, Canhão P, Barinagarrementeria F, Stam J. Unfractionated or low-molecular weight heparin for the treatment of cerebral venous thrombosis: analysis of the iscvt data. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (oral presentation)

Crassard I, Bousser M-G, Canhão P, Coutinho J, Stam J, Ferro JM. Decompressive surgery in cerebrovenous thrombosis (CVT). A systematic review of individual patient data. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (poster presentation)

de Mendonça A. Methodological Limitations and Type of Questions that Can Be Addressed in Human Studies. Workshop on Coffee and Cognition in the Elderly, Paris, September 2010.

Ferreira JJ, Bhidayasiri R, Colosimo C, et al., Secondary non response (SNR) to botulinum toxins type A (BoNT-A) in cervical dystonia (CD) patients: Definition and therapeutic strategies results from an international survey, *Mov Disord* 25 Issue: 7, : S234-S235 Supplement: Suppl. S Meeting Abstract: 146, Jun 13-17, 2010

Ferreira L, Santos R, Pires J, Paiva T. Cyclic alternating pattern in congenital deaf quantitative and topographic analysis. 20th Congress of the European Sleep Research Society, Lisboa, 14 – 18 September 2010. (Poster presentation)

Ferro JM, Bousser M-G, Canhão P, Barinagarrementeria F, Cucchiara B, Massaro A, Stolz E, Viana-Baptista M, ISCVT investigators. A case-control study of decompressive surgery in cerebrovenous thrombosis. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (oral presentation)

Ferro JM, Bousser M-G, Stam J, Canhão P, Crassard I, Derex L, Lichy C, Dutra AP, Masjuan J, Matamala G, Poli S, Saadatnia M. Decompressive surgery in cerebrovenous thrombosis (CVT). A retrospective multicentre registry (ISCVT2). 19th European Stroke Conference. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (oral presentation)

Ferro JM, Crassard I, Coutinho J, Canhão P, Barinagarrementeria F, Cucchiara B, Derex L, Lichy C, Masjuan J, Massaro AR, Matamala G, Poli S, Saadatnia M, Stolz E, Viana –Baptista M, Stam J, Bousser M-G. Decompressive surgery in cerebrovenous thrombosis (CVT). A systematic review of individual patient data. 7th World Stroke Congress, Seoul, Korea, October 13-16, 2010 (oral presentation)

Fonseca AC, Geraldes R, Pinho e Melo T, Ferro JM. Neck hematoma following intravenous thrombolysis for stroke treatment. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (poster presentation)

Fonseca AC, Peralta R, Bentes C. Electroencephalography after a first seizure. 20th Meeting of the European Neurological Society, Berlin, Germany. June 19-23, 2010 (poster presentation)

Fonseca AC, Peralta R, Bentes C. Electroencephalography after a first seizure. 20th Meeting of the European Neurological Society, Berlin, Germany. June 19-23, 2010 (Poster presentation)

Geraldes R, Fonseca AC, Canhão P, Pinho e Melo T, Ferro JM. Plasma complement and C reactive protein in patients with acute ischemic stroke and short term clinical outcome. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (poster presentation)

Geraldes, R., Lopes da Silva, R., Alonso, I., Pinto-Basto, J., Martins, I.P. A case of progressive spastic paraparesis, cerebellar ataxia, sensorymotor neuropathy and cognitive decline with thin corpus callosum. 14th Congress of the European Federation of Neurological Societies. Geneve, Switzerland. September 25-28, 2010 (Poster presentation)

Gouveia, R., Martins IP. Development and validation of a cognitive impairment scale for migraine attacks - the MIG-COG. 2ND European Headache and Migraine Trust International Congress. Nice, France. October 28-31, 2010 (Poster presentation)

Guedes, LC; Ferreira, JJ, Hyposmia and dopaminergic therapy in Parkinson's disease: Case report, 14th International Congress of Parkinsons Disease and Movement Disorders, Mov Disord 25, Issue: 7: S399-S400, June 13-17, 2010

Kovitz-Lensch J, Poppe AY, Swartz R, Demchuk A, Putaala J, Ferro JM Crassard I, de Windt A, Odier C, Michel P, Lanthier S. International Study of primary angiitis of the Central nervous system (I-SPACE): a proposal. 1st Canadian Stroke Congress, Quebec City, Canada, June 7-8, 2010. (poster presentation)

Lauterbach, M., Fonseca, J., Leal G., Martins. I. From fluent to non-fluent, from right to left – atypical evolution of speech fluency in a case of aphasia. 20th Meeting of the European Neurological Society, Berlin, Germany. June 19–23, 2010 (Oral presentation)

Lauterbach, M., Fonseca, J., Leal G., Martins. I. From fluent to non-fluent, from right to left – atypical evolution of speech fluency in a case of aphasia. Second Meeting of the Federation of the European Societies of Neuropsychology. Amsterdam, The Netherlands. September 22-24, 2010 (Poster presentation)

Lauterbach, M., Gil da Costa, R., Leal, G., Willmes, K., Martins, I.P. Recovering from acquired childhood aphasia (ACA) – 20 years later, learning about the neuroplasticity of language. Second Meeting of the Federation of the European Societies of Neuropsychology. Amsterdam, The Netherlands. September 22-24, 2010 (Oral presentation)

Lauterbach, M., Gil da Costa, R., Leal, G., Willmes, K., Martins, I.P. Recovering from acquired childhood aphasia (ACA) – 20 years later, learning about the neuroplasticity of language. 14th Congress of the European Federation of Neurological Societies. Geneve, Switzerland. September 25-28, 2010 (Poster presentation)

Lauterbach, M., Gil da Costa, R., Leal, G., Willmes, K., Martins, I.P. Investigating the neuroplasticity of language processing: recovering from acquired childhood aphasia (ACA). 40th Annual Meeting of Neuroscience Meeting, San Diego, USA. November 13-17, 2010 (Poster presentation)

Lauterbach, M., Leal G., Martins. I. Bilateral perisylvian polymicrogyria (BPP) with normal cognitive functions in a profound modified brain – a clinical and imaging case-study. 20th Meeting of the European Neurological Society, Berlin, Germany, June 19–23, 2010 (Poster presentation)

Leitão A, Peralta R, Geraldes R, Bentes C. Symptomatic narcolepsy after transverse myelitis: a clinical case. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Poster presentation)

Mameniskiene R, Wolf P, and the European Study Group on Epilepsia partialis continua. Non-Rasmussen, Non-stroke epilepsia partialis continua. 9th European Congress on Epileptology, Rhodes, Greece, June 27 – July 1, 2010. (Poster presentation)

Manso H, Krug T, Sobral J, Albergaria I, Gaspar G, Correia M, Taipa R, Silva MR, Gabriel JP, Lopes G, Matos I, Ferro JM, Oliveira SA, Vicente AM. Evidence for an association of the NOS1 and NOS3 gene with stroke susceptibility, Washington, USA, November 2-6, 2010 (Poster presentation)

Martins M, Rosa A, Fonseca BV, Violante S, Guedes LC, Mestre T, Coelho M, Rosa MM, Vance JM, Ferreira J, Oliveira SA. Integrative microRNA and proteomic approaches in Parkinson's Disease (PD). European Human Genetics Conference, Gothenburg, Sweden, 12-15 June 2010. (Poster presentation)

Martins, I.P., Gil-Gouveia, R., Silva, C., Maruta, C., Gouveia, A. Migraine, headaches and cognition. 14th Congress of the European Federation of Neurological Societies. Geneva, Switzerland. September 25-28, 2010 (Poster presentation)

Marto S, Silva C, Coelho M, et al., Family dysfunction after deep brain stimulation of the subthalamic nucleus for advanced Parkinson's disease, *Mov Disord* 25 Issue: 7: S441-S441 Supplement: Suppl. S Meeting Abstract: 772, June 13-17, 2010.

Mestre TA, Coelho M, Ferreira JJ, Therapeutic indications and prescription habits in Huntington's disease: Results from the REGISTRY observational study, *Mov Disord* 25 Issue: 7, S274-S274, Supplement, June 13-17, 2010

Mestre TA, Coelho M, Ferreira JJ, Therapeutic indications and prescription habits in Huntington's disease: Results from the REGISTRY observational study Conference Information: 14th International Congress of Parkinson's Disease and Movement Disorders *Mov Disord* 25, Issue: 7: S274-S274, Supplement: Suppl. S, June 13-17, 2010

Miranda B, Ferro JM, Canhão P, Stam J, Bousser M-G, Barinagarrementeria F, Scoditti U, ISCVT Investigators. Venous thromboembolic events after cerebral vein thrombosis. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010 (oral presentation)

Miranda B, Madureira S, Verdelho A, Ferro JM. Location of white-matter changes and risk of dementia. 20th Meeting of the European Neurological Society, Berlin, Germany, June 19-23,

2010. (oral presentation)

Neutel D, Geraldés R, Pimentel J, Melo TP. Cerebral vascular disease in cystinotic patient. 20th Meeting of the European Neurological Society, Berlin, Germany, June 19-23, 2010. (poster presentation)

Neutel D, Peralta R, Biscoito L, Pinho e Melo T, Albuquerque L. Giant Cell Arteritis with Intracranial Stenosis. 14th Congress of the European Federation of Neurological, European Federation of Neurological, , Geneva, Suíça, September 25-28, 2010. (Poster presentation)

Neutel D, Pita Lobo P, Mestre T, Peralta R, Bentes C. Hypersomnia and coeliac disease. 20th Congress of the European Sleep Research Society, Lisboa, 14 – 18 September 2010. (Poster presentation)

Neutel, D., Peralta, R., Biscoito, L., Pinho e Melo, T., Albuquerque, L. Giant cell arteries with intracranial stenosis. 14th Congress of the European Federation of Neurological Societies. Geneva, Switzerland. September 25-28, 2010 (Poster presentation)

Oliveira SA, Shafiee NM, Xavier JM, Ghaderi F, Abdollahi BS, Shahram F, Davatchi F. Replication of a GWAS for Behçet's disease confirms the association of the KIAA1529 gene. 2-6 November 2010, Washington, USA. (Poster presentation)

Oliveira TF, Ferreira L, Paiva T, Sanches JM. Dissociated States in Fibromyalgia. 40th Annual Meeting of Neuroscience 2010, Society of Neuroscience, San Diego, November 13–17, 2010. (Poster presentation)

Orth M; European Huntington's Disease Network, Handley OJ, Schwenke C, Dunnett SB, Craufurd D, Ho A, Wild EJ, Tabrizi SJ. Observing Huntington's Disease: the European Huntington's Disease Network's REGISTRY. PLoS Curr. September, 2010

Paiva T, Peralta R, Pires J, Sousa P. Sensory dysfunction impact upon dream content. 20th Congress of the European Sleep Research Society, Lisboa, 14 August – 8 September, 2010. (Poster presentation)

Peralta R, Bentes C, Henriques I. Inter-ictal epileptic activity topographies detected in morning and afternoon post-sleep deprivation EEGs, 9th European Congress on Epileptology, Rhodes, Greece, June 27 – July 1, 2010. (Poster presentation)

Peralta R, Bentes C, Moreira S, Staats R, Valença J. Residual somnolence on CPAP – residual respiratory disturbances or concomitant sleep diseases?. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Poster presentation)

Peralta R. Working visual memory in OSAS patients: a fMRI study. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Oral presentation)

Pimentel J, Peralta R, A. Campos, Bentes C. Antiepileptic drugs management and long-term seizure outcome in post surgical mesial temporal lobe epilepsy, 9th European Congress on Epileptology, Rhodes, Greece, June 27 – July 1, 2010. (Poster presentation)

Pires J, Peralta R, Paiva T. EEG mapping of deaf subject's dreams. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Poster presentation)

Pita Lobo P, Neutel D, Peralta R, Bentes C, Pimentel J. Nocturnal choking: sleep apnoea or seizures?. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Poster presentation)

Rebello Pinto H, Rebello Pinto T, Peralta R, Paiva T, Group and individual approach of insomnia treatment in a cognitive behavioural perspective. 20th Congress of the European Sleep Research Society, Lisboa, September 14–18, 2010. (Poster presentation)

Sampaio C, Bronzova JB, Hauser RA, et al, Pardoprinox in early stage Parkinson's disease: Results from two large studies. *Mov Disord* 25 Issue: 7, S308-S308, Supplement, June 13-17, 2010.

Shafiee NM, Xavier JM, Ghaderi F, Abdollahi BS, Shahram S, Davatchi F, Oliveira SA. Replication of association in *KIAA1529* gene with Behçet's disease. 14th International Conference on Behçet's disease, London, UK, 8-10 July 2010. (Poster presentation)

Winter Y, von Campenhausen S, Reese JP, et al., Health-economic burden of Parkinson's disease in six European countries: multicentre study of the EuroPa study group, *J Neurol* 257, S13-S13 Supplement: Suppl. 1 Meeting Abstract: O53, June 19-23, 2010.

Xavier JM, Krug T, Shafiee M, Sadeghi B, Fonseca BV, Jesus G, Barcelos F, Vedes J, Salgado M, Patto JV, Davatchi F, Crespo J, Oliveira SA. Expression and association analyses implicates the ErbB signalling pathway in Behçet's disease (BD). 14th International Conference on Behçet's disease, London, UK, July 8-10, 2010. (Poster presentation)

Xavier JM, Krug T, Shafiee M, Sadeghi B, Fonseca BV, Jesus G, Barcelos F, Vedes J, Salgado M, Patto JV, Davatchi F, Crespo J, Oliveira SA. Expression and association analyses implicate genes of the epidermal growth factor family in Behçet's disease (BD) susceptibility, Washington, USA, November 2-6, 2010. (Poster presentation)

Xavier JM, Shafiee NM, Ghaderi F, Abdollahi BS, Shahram F, Rosa A, Davatchi F, Oliveira SA. Mitochondrial genome association with Behçet's disease (BD). 14th International Conference on Behçet's disease, July 8-10, 2010, London, UK. (Poster presentation)

Communications in National Conferences

Almeida V, Soares F, Batista P, Oliveira V. Diagnóstico por ultrassonografia de trombo carotídeo livre. 4^o Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Alves, I., Cruz, V.T., Brandão, E., Ferreira, A., Tuna, A., Tuna, A., Barros, J., Santorelli, F., Stevanin, G., Martins, I.P., Loureiro, J.L., Coutinho, P. (2010) Duas famílias portuguesa com paraparésia espástica autossômica recessiva de Charlevoix-Saguenay. Congresso de Neurologia. Espinho, November 5-7 (Poster presentation)

Antunes AP, Melo TP. Densidades hemáticas de novo após uma hemorragia subaracnoideia: re-hemorragia ou redistribuição? 8^a Reunião da Sociedade Portuguesa do Acidente Vascular Cerebral, Fátima, October 23, 2010. (oral presentation)

Antunes AP, Valadas A, Lobo P, Melo TP. Caso clínico: parésia crural aguda. Fórum de Neurologia, Luso, May 14-15, 2010. (oral presentation)

Antunes P, Grupo da Cirurgia da Epilepsia do HSM. Epilepsia refractária com Ressonância Magnética negativa - Caso Clínico pelo Grupo da Cirurgia da epilepsia do HSM. Fórum Bial de Neurologia 2010, November 20, 2010.

Batista P, Soares F, Almeida V, Oliveira M, Santos I, Oliveira V. Progressão da aterosclerose carotídea avaliada por ultrassonografia. 4º Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T. Recordação onírica em Doentes com Epilepsia do Lobo Temporal. 22º Encontro Nacional de Epileptologia, Porto, March 19-20, 2010. (Poster presentation)

Bentes C, Grupo da Cirurgia da Epilepsia do HSM. Insular Seizures? – 4ª Reunião dos Centros de Cirurgia da Epilepsia, Figueira da Foz, October 1, 2010. (Oral presentation)

Bentes C. Perturbações do Sono – Temas de Neurologia IV em Medicina Geral e Familiar, Hotel Villa Rica, Lisboa - February 20, 2010. (Oral presentation)

Campos S, Fonseca M, Mourato B, Abreu L, Fonseca AC, Canhão P. Recorrência de eventos vasculares após Acidente Isquémico Transitório. 4º Congresso Português do AVC, Porto, February 4-6, 2010. (oral presentation)

Canhão P, Faria de Abreu L, Ferro JM, Investigadores do International Study on Cerebral Veins and Dural Sinus Thrombosis. Punção lombar em doentes com trombose venosa cerebral – resultados de um estudo multicêntrico internacional. Congresso de Neurologia 2010, Espinho, November 5-7, 2010. (oral presentation)

Canhão P, Fonseca AC, Campos S, Correia M. Prognóstico de acidentes neurológicos transitórios numa consulta de Acidentes Isquémicos Transitórios. Fórum de Neurologia, Luso, May 14-15, 2010. (oral presentation)

Chester, C., Freitas, V., Maruta C, Ginó, S., Guerreiro, M., de Mendonça, A. Quando o que parece não é... Fórum de Neurologia 2010, Luso, May 14-16 (Oral presentation)

Coelho M, Mestre T, Ferreira JJ, Estádio avançado da doença de Huntington . um coorte da rede europeia de Huntington, Congresso de Neurologia, Plasticidade, reorganização e recuperação funcional nas doenças do sistema nervoso, Espinho, Portugal, Nov 5-7, 2010

Costa J, González H, Vallderiola F, Gaig Carles, Toloa E, Valls-Solé J, Análise da dinâmica não-linear de movimentos oscilatórios repetitivos em doentes de Parkinson e tremor essencial, Fórum de Neurologia, Luso, May 14-15, 2010 (Oral presentation)

Costa J, Santos C, Santos J, Vaz-Carneiro A, Lunet N, A cafeína reduz o risco de doença de Parkinson: revisão sistemática e meta-análise de estudos observacionais, Fórum de Neurologia, Luso, May 14-15, 2010 (Oral presentation)

Costa P, Neto L, Almeida V, Geraldês R, Pinho e Melo T. Acidente vascular isquémico após consumo de cocaína e anfetamina. 8ª Reunião da Sociedade Portuguesa do Acidente Vascular Cerebral, Fátima, October 23, 2010. (oral presentation)

Costa, S., Marques, J., Firmo, C., Pimentel, J. Ganglioglioma desmoplásico pigmentado não infantil. Congresso de Neurologia 2010, Espinho, November 5-7, 2010 (Poster presentation).

Ferreira L. Factores condicionantes do sono, III Mesa redonda: Sono, II Jornadas de Neurofisiologia, Porto, May 21-22, 2010. (Oral presentation)

Ferreira R. Estudo padrão circadiário das crises em doentes com epilepsia temporal mesial refractária, em ambulatório. 13º Workshop Educação pela Ciência, Projectos de Investigação Científica de Alunos da FMUL, Edifício Egas Moniz, Lisboa, December 14, 2010. (Poster presentation)

Fonseca AC, Geraldès R, Melo TP. Hematoma cervical após trombólise intravenosa. 4º Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Fonseca CA, Peralta R, Henriques I, Bentes C. Electroencefalograma na primeira crise epiléptica. 22º Encontro Nacional de Epileptologia, Porto, March 19-20, 2010. (Oral presentation)

Fonseca, J. Terapia da Fala e AVC. Que relação? Que formação? 4º Congresso Português do AVC da Sociedade Portuguesa do Acidente Vascular Cerebral, Porto, February 4-6, 2010 (Oral presentation)

Foreid H, Miranda B, Peralta R, Bentes C, Biscoito L, Albuquerque L, Valle S. Leucoencefalopatia posterior reversível manifestada por estado de mal epiléptico após início de quimioterapia para tratamento de Linfoma Não – Hodgkin. Congresso de Neurologia 2010, Plasticidade, Reorganização e Recuperação Funcional nas Doenças do Sistema Nervoso, Espinho, November 5-7, 2010. (Poster presentation)

Foreid, H., Miranda, B., Peralta, R., Bentes, C., Biscoito, L., Albuquerque, L., Valle, S. (2010) Leucoencefalopatia posterior reversível manifestada por estado de mal epiléptico após início de quimioterapia para tratamento de Linfoma Não-Hodgkin. Congresso de Neurologia. Espinho, November 5-7 (Poster presentation)

Geraldès R, Fonseca AC, Melo TP. Será a determinação da proteína C reactiva e de factores de comportamento útil no AVC isquémico? 4º Congresso Português do AVC, Porto, February 4-6, 2010. (oral presentation)

Geraldès, R., Lopes da Silva, R., Pereira, C., Alonso, I., Pinto-Basto, J., Martins, I.P. (2010) Um caso de paraparésia espástica hereditária associada a corpo caloso fino, defeito cognitivo e neuropatia. Fórum de Neurologia 2010, Luso, May 14-16 (Oral presentation)

Gil Gouveia R, Miranda B, Albuquerque L, Rosa MM, Costa J, Carvalho M, Ferro J, As Minhas pernas ficam presas! , Fórum de Neurologia, Luso, Portugal May 14-15, 2010 (Oral presentation)

Guerreiro, M. Qual o papel da BLAD hoje? Caminhos para o futuro. Forum Futuro Grunenthal. Cascais, March 5-6, 2010 (Oral presentation)

Guerreiro, M. Testes neuropsicológicos – a sua utilidade prática. 4º Congresso Português do AVC da Sociedade Portuguesa do Acidente Vascular Cerebral, Porto, February 4-6, 2010 (Oral presentation)

Lauterbach, M., Gil da Costa, R., Leal G., Willmes, K., Martins, I.P. Recuperar de afasia adquirida na infância – 20 anos depois, aprender sobre a neuroplasticidade para a linguagem. Congresso de Neurologia. Espinho, November 5-7 (Oral presentation)

Leal, G., Fonseca, J., Martins, I.P. Defeitos de discurso recorrentes numa mulher com doença de Behçet, Fórum de Neurologia 2010, 14-16 (Oral presentation)

Lobo PP, Coelho M, Mestre T, Rosa MM, Ferreira JJ, Hemiparkinsonismo pós-traumático com flutuações motoras, Congresso de Neurologia, Plasticidade, reorganização e recuperação funcional nas doenças do sistema nervoso, Espinho, Portugal, Nov 5-7, 2010

Marques, J., Costa, S., Firmo, C, Campos, A., Pimentel, J. Sarcoma com Metaplasia Epitelial Secundário a Glioblastoma Multiforme Irradiado. Congresso de Neurologia 2010, Espinho, November 5-7, 2010 (Poster presentation).

Marques, J., Costa, S., Firmo, C., Albuquerque, L., Aronica, E., Pimentel, J. Tumor Teratóide/Rabdóide Atípico no Adulto. Congresso de Neurologia 2010, Espinho, November 5-7, 2010 (Poster presentation).

Martins, N., Ferreira, A., Pimentel, J. Caracterização quantitativa do núcleo basolateral da amígdala na esclerose mesial. 22º Encontro Nacional de Epileptologia, Porto, March 19-20, 2010 (Poster presentation).

Miranda B, Rodrigues D, Coelho M, Peralta R, Albuquerque L. Epilepsia parcial contínua no adulto. Fórum de Neurologia 2010 – Sintomas funcionais em Neurologia – Grande Hotel do Luso, May 14-15 2010. (Poster presentation)

Miranda B, Rodrigues D, Coelho M, Peralta R, Albuquerque L. Epilepsia parcial contínua no adulto. Congresso de Neurologia 2010, Plasticidade, Reorganização e Recuperação Funcional nas Doenças do Sistema Nervoso, Espinho, November 5-7, 2010. (Oral presentation)

Miranda, B., Rodrigues, D., Coelho, M., Peralta, R., Albuquerque, L. Eventos epilépticos ou não epilépticos? Fórum de Neurologia 2010, Luso, May 14-16 (Oral presentation)

Moreira, E., Branquinho, A., Pimentel, J. Caracterização quantitativa do Hilo do Gyrus Dentatus na esclerose mesial. 22º Encontro Nacional de Epileptologia, Porto, March 19-20, 2010 (Oral presentation).

Neutel D, Peralta R, Biscoito L, Melo TP, Albuquerque L. Acidente vascular cerebral em doente com arterite de células gigantes. 4º Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Neutel D, Peralta R, Biscoito L, Pinho e Melo T, Albuquerque L. Acidente Vascular Cerebral em Doente com Arterite de Células Gigantes, 4º Congresso Português do AVC, Centro de Congressos do Porto, Palácio Hotel, Porto, February 4-6, 2010. (Poster presentation)

Neutel D, Peralta R, Ferreira JJ, Movimentos involuntários do tipo mioclónico multifocais: caso clínico de etiologia não conclusiva, Fórum de Neurologia, Luso, May 14-15, 2010 (Oral presentation)

Oliveira TF, Ferreira L, Paiva T, Sanches JM. Estados dissociados na Fibromialgia. 16th edição da conferência Portuguesa em Pattern Recognition, Universidade UTAD, Vila Real, October 29, 2010. (Poster presentation)

Oliveira V, Baptista P, Soares F, Almeida V, Quintas S. Dissecção carotídea neo-natal diagnosticada por ultrassonografia. 4^o Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Peralta R, Bentes C, Henriques I. EEGs com sono pós privação – importância da hora do dia no tipo e topografia da actividade epiléptica detectada. 22^o Encontro Nacional de Epileptologia, Porto, March 19-20, 2010. (Poster presentation)

Peralta R, Grupo da Cirurgia da Epilepsia do HSM. Discussão de casos clínicos - Um caso de displasia cortical. 3^a Reunião dos Centros de Cirurgia de Epilepsia, Anfiteatro do Hospital de Santo António, Porto, March 18, 2010. (Oral presentation)

Peralta R. Crises Epilépticas. Aspectos Práticos - Temas de Neurologia IV em Medicina Geral e Familiar, Hotel Villa Rica, Lisboa, February 20, 2010. (Oral presentation)

Pimentel, J. Anatomia das vias vestibulares. II Reunião de Inverno da Associação Portuguesa de Otoneurologia, II Reunião da Associação Portuguesa de Otoneurologia, Ericeira, March 27, 2010 (Oral presentation).

Pimentel, J., Peralta, R., Campos, A., Bentes, C. Estratégia da terapêutica antiepiléptica e recorrência das crises epilépticas após cirurgia da epilepsia mesial temporal. 22^o Encontro Nacional de Epileptologia, Porto, March 19-20, 2010 (Oral presentation).

Pires C, Nunes L, Geraldes R, de Carvalho M, Canhão P. Caso clínico: Hemiparésia esquerda de instalação súbita. Fórum de Neurologia, Luso, May 14-15, 2010. (oral presentation)

Pires C, Soares F, Geraldes R, Melo TP. Acidente isquémico transitório em puérpera com múltiplas dissecções cervicais espontâneas. 8^a Reunião da Sociedade Portuguesa do Acidente Vascular Cerebral, Fátima, October 23, 2010. (oral presentation)

Pires, A., Ferro, J., Pimentel, J. Avaliação da amusia em doentes epilépticos submetidos a amigdalohipocampectomia. 22^o Encontro Nacional de Epileptologia, Porto, March 19-20, 2010 (Oral presentation).

Pires, C., Miranda, B., Geraldo, A., Geraldes, R., Coelho, M., Albuquerque, L. (2010) Biparésia facial isolada como variante de Síndrome Guillain-Barré. Congresso de Neurologia. Espinho, November 5-7 (Poster presentation)

Pita Lobo P, Campos J, Neto L, Canhão P. Padrão perimesencefálico de hemorragia subaracnoideia causado por aneurisma da artéria cerebral posterior. 4^o Congresso Português do AVC, Porto, February 4-6, 2010. (oral presentation)

Pita Lobo P, Pires C, Canhão P, Ferreira J. Cefaleia em salvas associada a dissecção da artéria carótida interna. Congresso de Neurologia 2010, Espinho, November 5-7, 2010. (poster presentation)

Quintas S, Grupo da Cirurgia da Epilepsia do HSM. Discussão de casos clínicos - Um caso de Calsotonia. 3ª Reunião dos Centros de Cirurgia de Epilepsia, Anfiteatro do Hospital de Santo António, Porto, March 18, 2010. (Oral presentation)

Rocha, L., Fonseca, J., Leal, G. (2010) Um defeito articulatorio para três terapeutas da fala. Fórum de Neurologia 2010, Luso, May 14-16 (Oral presentation)

Rocha, S., Loureiro, C., de Carvalho, M. (2010) Defeitos de escrita num doente com Esclerose Lateral Amiotrófica. Fórum de Neurologia 2010, Luso, May 14-16 (Poster presentation)

Sampaio C, Ensaio de desenho flexível, I Jornadas da Comissão de Ética para a Investigação Clínica 2010, Lisboa, January 21, 2010. (Oral presentation)

Silvestre, A., Sousa, A., Costa, J., Barroso, C., Evangelista, T. Predictors of pain after muscle biopsy. 4º Congresso Nacional SPEDNM, Vale do Lobo, April 23-25, 2010 (Poster presentation).

Silvestre, A.R., Machado, M., Vilarinho, L., Cortez-Pinto, H., Evangelista, T. Efeitos da obesidade mórbida e da resistência à insulina no músculo esquelético. 4º Congresso Nacional SPEDNM, Vale do Lobo, April 23-25, 2010 (Oral presentation).

Soares F, Batista P, Almeida V, Oliveira V. Fístula arteriovenosa pulmonar – utilidade do Doppler transcraniano no seu diagnóstico. 4º Congresso Português do AVC, Porto, February 4-6, 2010. (poster presentation)

Organisation of Conferences

Canhão P, Member of the Cientific Committee of "Congresso da Sociedade Portuguesa do AVC", Porto 2010

Castro Caldas A. 8th Symposium of BIAL Foundation "Aquém e Além do Cérebro" , Porto, April 7–10, 2010

Castro Caldas A. International Conferences on Neuropsychology, Professor Cornelius Weiller, "Towards a neurobiological basis of recovery from aphasia", UCP, May 26, 2010

Castro Caldas A. International Conferences on Neuropsychology, Professor Edward de Haan, "The prognostic value of neuropsychological testing in the subacute phase", UCP, February 24, 2010

Castro Caldas A. International Conferences on Neuropsychology, Professor Antonio Benitez Burraco, "Los genes del lenguaje y la language de los genes", UCP, April 21, 2010

Castro Caldas A. International Conferences on Neuropsychology, Professor Salvatorie Aglioti, "Catching on it early: predictive action coding in naive and expert brains", UCP, March 24, 2010

Ferreira JJ organized the course: "First Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 20, 2010.

Ferreira JJ, Martins Isabel Pavão, organized the course” How do I succeed in publishing a paper in a scientific journal?” , Sociedade Portuguesa de Neurologia, Congresso de Neurologia , Espinho, Portugal, November 7, 2010

Ferro JM. Organized Educational Symposium 2. Stroke and poverty. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010

Martins, I.P. (2010) Organized Curso de Estatística da Sociedade Portuguesa de Neurologia para internos de Neurologia. Organizatizon Sociedade Portuguesa de Neurologia / Unidade de Neurologia de Investigação Clínica. Lisboa, Portugal, 28 June-3 July.

Martins, I.P. Ferreira JJ (organizers) (2010). How do I succeed in publishing a paper in a scientific Journal? Congress of Sociedade Portuguesa de Neurologia, Espinho, Portugal, November 5-7, 2010.

Martins, I.P. Organizer of Congress of Sociedade Portuguesa de Neurologia. November 5-7, 2010, Espinho, Portugal.

Martins, I.P. Organizer of Fórum of Sociedade Portuguesa de Neurologia, Luso, Portugal. May 14-15, 2010.

Paiva T. Chairman of the European Sleep Research Congress, Lisbon, September 2010.

Paiva T. Organizing Committee of the 1 Portuguese Brazilian Symposium in Sleep Medicine, Lisbon, September 2010.

Peralta R. Organizing Committee of the European Sleep Research Society Congress, Lisbon, September 2010.

Sampaio C co-organized at the European medicines agency chaired by Bruno Flamion, Cristina Sampaio, Kerstin Westermark, Developing medicinal products for pre-symptomatic carriers: Autosomal Dominant Alzheimer’s Disease (ADAD) and Huntington’s Disease (HD) as models, ,Focus in Alzheimer's and Huntington's Diseases: **Design Regulatory Issues**, London, November 8, 2010

Silvestre, A. Co-organized the XI Congresso Técnico de Anatomia Patológica. Évora, Portugal, May 7-9, 2010.

Internationalization

Cochrane collaboration- the group host one of the review groups

EADC – European Alzheimer’s Disease Consortium. A de Mendonça is coordinator of the centre in Lisbon

EFNS – European Federation of Neurological Societies. A de Mendonça is the national representative in the Dementia Panel

Epilepsia partialis continua-European Study Group: Mameniskiene R, Bast T, Bentes C, Canevini M P, Dimova P, Granata T, Hogenhaven H, Jakubi BJ, Marusic P, Melikyan G, Michelucci R, Mukhin KY, Oehl, B, Ragona F, Rossetti AO, Rubboli G, Schubert S, Stephani U, Stroble J, Vignoli A, Zarubova J, Wolf P, Clinical course and variability of non-Rasmussen, non-stroke motor and sensory epilepsia partialis continua. A European survey and analysis of 65 cases.

European Huntington Group in Lead by Joaquim Ferreira

International Carotid Stenting Study investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, Lo TH, Gaines P, Dorman PJ, Macdonald S, Lyrer PA, Hendriks JM, McCollum C, Nederkoorn PJ and Brown MM (2010) Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* **375**,985-997.

Movement Disorders Society – members of the group (C Sampaio, Ferreira JJ) hold leading positions in the Society and are Heads of lines of work with the society at a worldwide level.

VITATOPS Trial Study Group (2010) B vitamins in patients with recent transient ischaemic attack or stroke in the VITAMins TO Prevent Stroke (VITATOPS) trial: a randomised, double-blind, parallel, placebo-controlled trial. *Lancet Neurol* **9**,855-865.

Prizes, honours and awards

Award “Bolsa anual de investigação D. Manuel de Mello to Catarina Fonseca – “N-terminal do Peptídeo Natriurético Cerebral na classificação do tipo AVC isquémico”, 2010.

Award “Egas Moniz da Sociedade Portuguesa de Neurologia” to Patrícia Canhão e Ana Catarina Fonseca for the presentation “Preditores clínicos de acidentes neurológicos transitórios”, 2010.

Award of the Liga Portuguesa Contra a Epilepsia. Dream Recall Frequency and Content in Patients with Temporal Lobe Epilepsy to Carla Bentes, João Costa, Rita Peralta, Joana Pires, Paula Sousa, Teresa Paiva.

Award of the World Association of Sleep Medicine for the program The Mysteries of Sleep, considered the best organization of the World Sleep Day, 2010 to Teresa Paiva.

Second Tecnifar Award (Portuguese Headache Society) – 2010 to Isabel Pavão Martins, Raquel Gil-Gouveia, C. Silva and Carolina Maruta (Migraine and Cognition)

The prize “Investigação em Epilepsia da Liga Portuguesa Contra a Epilepsia” Dias, A.M., Pimentel, J., Ferro, J. “Avaliação da amúsia em doentes epilépticos com esclerose mesial submetidos a amígdalohipocampectomia” (2010)

Young Investigator Award to Joana Xavier from the International Society for Behçet’s Disease (2010).

Patents/prototypes

Sistema de Monitorização de Temperatura Central para Diagnósticos de Distúrbios de Sono. João Sanches, Teresa Paiva, Bruno Pereira e Rui Neves.

Patente de Invenção Nacional Nº 104115 (Concedido)

Metodologia de Registo de Eventos em Diário Electrónico, Implementado em Telemóvel, para auxílio no diagnóstico de Distúrbios do Sono. Pedro Pires, João Sanches e Teresa Paiva . Patente de Invenção Nacional Nº 104157 (Concedido)

Industry contract research

Clinical trials

2007/2010 - PERFORM- Principal Investigator - Patrícia Canhão, Servier

2008/ - ICTUS Principal Investigator - Teresa Pinho e Melo, Ferrer International

2009/2013 - TIMI - Principal Investigator - Patrícia Canhão, Icon

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 Apolipoproteína E ε4. 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 Apolipoproteína E ε4. 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 ε4 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 ε4 Noncarriers and Participated in Study 3133K1-3001-WW, (3133K1-3003-WW) National Coordinator A. Mendonça

2010/ Clinical trial in AD with the histamine H₃ receptor antagonist, SAR110894D, Sanofi. National Coordinator A. Mendonça

2004/2010 - 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

2009/2010 - Efficacy and safety of Eslicarbazepine Acetate as preventive therapy for patients with migraine: a double-blind, double-dummy, randomised, placebo controlled, parallel-group, multicentre clinical trial, BIAL Foundation. Coordinator: I.P. Martins (BIA-2093-209)

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 pachebo and temozolomida in patients with recent diagnosis of glioblastoma. Coordinator: L. Albuquerque (clinical trial AVAGLIO –BO21990)

Government/Organization contract research

Einhäupl K, Stam J, Bousser MG, De Bruijn SF, Ferro JM, Martinelli I and Masuhr F (2010) EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. *Eur J Neurol* **17**,1229-1235.

The group is deeply involved in the Regulation of Medicines Evaluation, at the Level of Portuguese authority (INFARMED) and The European Medicines Agency (EMA). There several official reports published those that are in the public domain are accessible at <http://www.ema.europa.eu> and members of our group are credited.

Advanced teaching

Electronic publications Sleep elearning 2010 published in English and, Portuguese, by the Medical Faculty of Lisbon, Eds Paiva T and Penzel T. It is a 15-module interactive online course with three optional modules hosted on a self e-learning system, with the purpose of giving specific and quality education on Sleep Medicine. The target audience of the course includes general practitioners, pharmaceutical company staff, CPAP technicians, shift-work managers, sleep technicians, nurses, psychologists and dentists and prosthetics. It provides 6 ECTS, but it can be splitted in smaller units according to the user needs.

Albuquerque, L. “Tratamento Médico dos Gliomas”. XIV Curso da Sociedade Portuguesa de Neurocirurgia, Aveiro, October 8, 2010

Bentes C, Paiva T. Pharmacologic treatment of Sleep disorders – E-learning – Lesson 16 for the basic course concerning sleep and sleep disorders, FML, 2010.

Bentes C, Peralta R. Lectured in the clinical neurophysiology curricular unit of the Neurosciences Master/PhD, FML, 2010.

Bentes C. Chairman of the session “Automatic Processing” in the meeting Sleep Laboratory of the Mestrado em Ciências do Sono (2009/2010), Lisbon, January 8, 2010.

Bentes C. Chairman of the session “Parasomnia” in the meeting Sleep Disorders of the Mestrado em Ciências do Sono (2009/2010), Lisbon, April 16, 2010.

Bentes C. Chairman of the session “Sleep in Childhood and Adolescence” in the meeting Sleep in Children and Adolescents of the Mestrado em Ciências do Sono (2009/2010), Lisbon, September 10, 2010.

Bentes C. Chairman of the session “Sleep Regulation” in the meeting Sleep Disorders and Sleep Regulation of the Mestrado em Ciências do Sono (2009/2010), Lisbon, February 27, 2010.

Bentes C. Chairman of the session “Vídeos” in the meeting Sleep Disorders of the Mestrado em Ciências do Sono (2009/2010), Lisbon, April 16, 2010.

Bentes C. Co-organized and lectured in the Ciclo de Estudos Especiais de Neurofisiologia Clínica – HSM, Lisboa, 2010.

Bentes C. Lecture the session “Other Parasomnias” in the meeting Sleep Disorders of the Mestrado em Ciências do Sono (2009/2010), Lisbon, April 16, 2010.

Bentes C. Lecture the session “Quality of life in Epilepsy” in the meeting Sleep medicine and quality of life of the Mestrado em Ciências do Sono (2009/2010), Lisbon, November 12, 2010.

Caeiro L. Metodologia de um caso neuropsicológico. XI Master in Neurosciences, University of Lisbon, Lisbon, May 5, 2010

Canhão P, coordinator of Research in Clinical Neurosciences module in Master and PhD programmes in Neurosciences. Faculdade de Medicina de Lisboa, Lisboa, Portugal, May 2010

Canhão P, participation in the PhD Programme in Voice, Language and Communication, University of Lisbon, May 2010

Canhão P. Current treatments in Neurology: TIA and its differential diagnosis. 20th Meeting of the European Neurological Society, Berlin, Germany, June 19-23, 2010.

Canhão P. Estudos de coorte. Factores de risco e factores de prognóstico. XI Master in Neurosciences, University of Lisbon, Lisbon, May 20, 2010

Canhão P. Investigação clínica em neurociências- Tipos de estudos. XI Master in Neurosciences, University of Lisbon, Lisbon, May 4, 2010

Coelho M, Diagnosis and management of tremor, “II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular”, Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Coelho M, Treatment of dystonia and hemifacial spasm, First Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 20, 2010

Coelho M. Diagnosis and management of dystonia, “II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular”, Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Costa J, Systematic reviews and meta-analysis, MASTERS/PhD IN NEUROSCIENCES, Faculty of Medicine, University of Lisbon, June 14, 2010

Cristina Sampaio and Joaquim Ferreira, were discussants at the Workshop in Familial Neurodegenerative disorders: Developing medicinal products for pre-symptomatic carriers: Autosomal Dominant Alzheimer’s Disease (ADAD) and Huntington’s Disease (HD) as models, ,Focus in Alzheimer's and Huntington's Diseases: **Design Regulatory Issues**, London, November 8, 2010

de Mendonça A. Afinal Sempre É Doença de Alzheimer... Meeting of Hospital de Santa Maria, Lisbon, March 2010.

de Mendonça A. Clinical Aspects of Protein Misfolding and Aggregation. Short Course, Sociedade Portuguesa de Biofísica, Santarém, October 2010.

de Mendonça A. Clinical Trials in Alzheimer’s Disease. Workshop Harvard Medical School – Portugal, Molecular Mechanisms in Neurodegeneration: From Molecules to Cures, Sesimbra, July 2010.

de Mendonça A. Defeito Cognitivo no Idoso, Colóquio O Mundo do Idoso e O Idoso no Mundo, Hospital de Santa Maria, March 2010.

de Mendonça A. Studies on Coffee /Caffeine in Alzheimer's Disease and Other Neurodegenerative disorders. 23th International Conference in Coffee Science, Bali, October 2010.

de Mendonça A. Um Princípio de Alzheimer. Ciência 2010, Lisbon, July 2010.

de Mendonça A. Uso do Placebo, I Jornadas CEIC, Lisbon, January 2010.

Ferreira JJ , Guedes L C, Mestre T, Valadas A, Lobo P, Neutel D, organized the course "II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular", Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Ferreira JJ organized the course "Curso Revisões Sistemáticas Como Projecto de Investigação Clínica", Lisbon, June 2-9, 2010

Ferreira JJ, "Molecular Mechanisms in Neurodegeneration: From Molecule to Cures": Parkinson's disease and dystonias, Convento da Arrábida, Portugal , July 2010

Ferreira JJ, Diagnosis and management of chorea , "II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular", Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Ferreira JJ, Ferreira, Jacinto J, Coelho M, Other indications, Video session with treatment demonstration, Carlo Colosimo, First Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 20, 2010

Ferreira JJ, How to manage a botulinum toxin clinic, First Instituto de Medicina Molecular Botulinum Toxin Training Course", Lisbon, Portugal, November 20, 2010

Ferreira JJ, Martins Isabel Pavão, organized the course" How do I succeed in publishing a paper in a scientific journal?" , Sociedade Portuguesa de Neurologia, Congresso de Neurologia , Espinho, Portugal , November 7, 2010

Ferreira JJ, Master Investigação Clínica, Exposição oral, Casos de estudo, Lisbon, Portugal, March 13, 2010

Ferreira L. Teaching lesson "Os factores Condicionantes do Sono" to students of Engenharia Biomédica, IST/FML, Lisbon, November 3, 2010.

Ferro JM. Cardioembolic stroke. 14th ESO Stroke Summer School, Warsaw, Poland, 25 June-3 July, 2010.

Ferro JM. Cerebral Venous thrombosis. 14th ESO Stroke Summer School, Warsaw, Poland, 25 June-3 July, 2010.

Ferro JM. Consciência e conceito de pessoa: problemas éticos do estado vegetativo persistente. 2º Curso Pós-Graduado de actualização de decisões éticas em fim de vida. Master programme Bioética 2009-2011. University of Lisbon, Lisbon, March 18, 2010

Ferro JM. Estado vegetativo. XI Master in Neurosciences, University of Lisbon, Lisbon, January 5, 2010.

Ferro JM. Estudos casos-controlo. XI Master in Neurosciences, University of Lisbon, Lisbon, May 18, 2010

Ferro JM. Ischemic stroke: diagnosis and treatment. Postgraduate Educational Programme, European Congress of Radiology, Vienna, Austria, March 4-8, 2010.

Fonseca, J. “Avaliação invasiva da linguagem”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, April 23, 2010.

Guedes LC, Genetic studies: which and when to ask? “II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular”, Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Guerreiro, M. “Afasia Progressiva e Demência”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, December 16, 2010.

Guerreiro, M. “Afasia progressiva nas doenças degenerativas”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, February 5, 2010.

Guerreiro, M. “Cognitive rehabilitation” Master in Neurosciences. FM da UL, Lisboa, March 16, 2010

Guerreiro, M. “Episodic memory.” Master in Neurosciences. FM da UL, Lisboa, March 11, 2010.

Lauterbach, M “Plasticidade cerebral para a linguagem”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, April 23, 2010.

Lauterbach, M. “Avaliação de Linguagem”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, January 22, 2010.

Lauterbach, M. “Avaliação de Linguagem”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, December 10, 2010.

Lauterbach, M. “Functional image for the study of language organization”. Master in Neurosciences. FM da UL, Lisboa, March 23, 2010.

Madureira, S. Avaliação Neuropsicológica, módulo Mestrado Integrado, ISCTE-IUL
Marti MJ, Ferreira JJ, Rosa MM, Coelho M, Clinical observation of patients in small working groups, “II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular”, Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010.

Martins, I.P. “Semantic memory – proper names”. Master in Neurosciences. FM da UL, Lisboa, March 25, 2010.

Martins, I.P. (2010) Preparação de Casos Clínicos para Publicação. Curso de Curta Duração. Comunicar Ciência em Medicina. Gabinete de Apoio à Investigação Científica, Tecnológica e Inovação. Faculdade de Medicina da Universidade de Lisboa. Lisboa, Portugal, 24 June. Organizer and Lecturer

Martins, I.P. “Linguagem e afasia”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, January 22, 2010.

Martins, I.P. “Written language” Master in Neurosciences. FM da UL, Lisboa, March 18, 2010

Martins, I.P. and Gil Gouveia R (2010) Cefaleias. Curso de Ciências da Dor. Faculdade de Medicina de Lisboa. Lisbon, Portugal, 11 February.

Martins, I.P. is one of the coordinators of Doctoral Programme Voice, Language and Communication and of the Master and Doctoral In Neurosciences Lisbon faculty of Medicine, UL.

Martins, M. “Linguagem e recursividade”. Doctoral Programme Voice, Language and Communication. FM da UL, Lisboa, December 10, 2010.

Maruta, C. "Temas de Fronteira entre Engenharia e Medicina – Mecanismos da Memória", Master in Biomedic Engeneering, Instituto Superior Técnico/Faculty of Medicine of Lisbon, November 24, 2010.

Oliveira SA. Lecturer in the Mestrado de Neurociências, FML, May 2010.

Oliveira SA. Lecturer in the Mestrado em Doenças Metabólicas, January 2010.

Paiva T. Organized and lectured in the Master degree and elearning courses, 2010.

Peralta R, Bentes C, Santos R, Ferreira L, Pires J. Practical teaching on unit “Fisiologia de Sistemas”, 2010.

Peralta R. Chairman of the session “Hypersomnias” in the meeting Sleep Disorders of the Mestrado em Ciências do Sono (2009/2010), Lisbon, April 16, 2010.

Peralta R. Lecture on the Biomedical Engeneering Course curricular unit “Fisiologia de Sistemas”, 2010.

Peralta R. Lecture the session “Sleep and Gender” in the meeting Sleep Gender and elderly of the Mestrado em Ciências do Sono (2009/2010), Lisbon, September 11, 2010.

Peralta R. Lecture the session “Sleep and other functions – Cognitive Function” in the meeting Sleep Disorders and Sleep Regulation of the Mestrado em Ciências do Sono (2009/2010), Lisbon, February 27, 2010.

Pimentel, J. “ Human prion diseases” Licenciatura em Nutrição, Faculdade de Medicina de Lisboa, Lisboa, January, 2010

Pimentel, J. “Epilepsia do lobo temporal” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, Lisboa. February 9-18, 2010.

Pimentel, J. “Tumores cerebrais - gliomas” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, Lisboa. February 9-18, 2010.

Pimentel, J. “Tumores gliais e mixtos” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, Lisboa. February 9-18, 2010.

Rosa MM, Diagnosis and management of myoclonus, “II Teaching Course in Movement Disorders of the Neurological Clinical Research Unit Instituto de Medicina Molecular”, Instituto de Medicina Molecular, Lisbon Faculty of Medicine, Lisbon, Portugal, 2010

Rosa MM, Safety of medicinal products and medical devices, MASTERS/PhD IN NEUROSCIENCES, Faculty of Medicine, University of Lisbon, June 7, 2010

Sampaio C, Clinical outcomes and biomarkers in neurological diseases, MASTERS/PhD IN NEUROSCIENCES, Faculty of Medicine, University of Lisbon, June 2, 2010

Sampaio C, History, development and basic pharmacology of Botulinum Toxin, First Instituto de Medicina Molecular Botulinum Toxin Training Course”, Lisbon, Portugal, November 20, 2010

Silvestre, A.R. “Alterações musculares na obesidade mórbida” Mestrado em Neurociências, Faculdade de Medicina de Lisboa, February 9-18, 2010.

Verdelho A. Headache in stroke. 19th European Stroke Conference, Barcelona, Spain. May 25-28, 2010.

Science and Society

Bentes C. Participation on the “Jornal da Manhã”, TVI, Lisbon, 2010.

Catarina Santos- A ira no acidente vascular cerebral. Determinantes e impacto na adesão ao tratamento e no bem-estar dos cuidadores for 12^o students from Escola Secundária do Pombal, Lisboa, November 23, 2010.

Chester, C. and Martins, I.P. (2010). Inteligência. Lecture to students of 12^o ano of Escola secundária do Pombal. Anfiteatro Almeida Lima, Serviço de Neurologia, Hospital Santa Maria, Lisboa, November, 2010.

Freitas, V. and Martins, I.P. (2010). Funções executivas, pesquisa de símbolos e teste de Stroop. Lecture to students of 12^o ano of Escola secundária do Pombal. Anfiteatro Almeida Lima, Serviço de Neurologia, Hospital Santa Maria, Lisboa, November, 2010.

Mares, I. and Martins, I.P. (2010). Contacto ocular e evocação de nomes. Lecture to students of 12^o ano of da Escola secundária do Pombal. Anfiteatro Almeida Lima, Serviço de Neurologia, Hospital Santa Maria, Lisboa, November, 2010.

Martins, I.P. “Art and the Brain”(2010). Co-Organizer of a Round table at Pavilhão do Conhecimento on Brain Awareness week. European Brain Council, a joint initiative of the Portuguese Societies of Neuroscience and Neurology. Lisbon, 2010

Martins, I.P., Chairperson: Raposo, A., R., Ferreira M., B. (2010) Bater o pé sem bater as botas: como o cérebro entende o significado das palavras. Museu de Ciência da Universidade de Lisboa, Portugal.

Peralta R. Participation on the “Bom dia Portugal”, RTP1, Lisbon, 2010.

Peralta R. Participation on the “Consultório” TVI, Lisbon, 2010.

Peralta R. Participation on the “Jornal da Manhã”, TVI, Lisbon, 2010.

Sofia Madureia- Alterações da Substância Branca: da experiência europeia à vivência lusitana, uma década de viagem for 12º students from Escola Secundária do Pombal, Lisboa, November 23, 2010.

Visit to the Doppler Laboratory of the 12º students from Escola Secundária do Pombal, Lisboa, November 23, 2010.

Visit to the Sleep EEG Laboratory of the students from Escola Secundária do Pombal, November 23, 2010.

Visit to the Sleep EEG Laboratory on the Biomedical Engineer Day, 2010.

Master and Ph.D. thesis completed

PhD thesis

Joana Coelho (2010) Presynaptic mechanisms in the hypoxia-induced suppression of synaptic transmission in the rat hippocampus. Tese de Doutoramento. Supervisor. A. Mendonça

Master thesis

Ana Coito (2010) “Topographic EEG analysis in OSAS” co-supervision: IST .Profs João Sanches e Teresa Paiva. Finished 2010. Grade: 18

Ana Rita Castro Brito (2010) “Análise espectral do EEG nos Movimentos periódico do sono e nas pernas Inquietas (Spectral analysis of Restless legs and Periodic Limb Movements)”. Finished 2010. Very Good. (Grade: 19 out of 20)

Ana Rita Dias (2010) “Oxido nítrico e Apneia do Sono (Exhaled Nitric oxide in OSAS)”. Finished 2010. Very Good. (Grade: 19 out of 20)

Andreia Catarina Costa Duarte (57296) “Biomedical Signal Processing, Storing and Transmitting by Mobile Phone”, 2009/2010, co-supervision with João Sanches.

Andreia Duarte (2010) “Mobile Acquisition platform for Sleep Assessment” IST. co-supervision: Profs João Sanches. Finished 2010. Grade: 18

Carla Alexandra dos Santos Costa (2010) “Efeito da terapia de orientação para a realidade em doentes com o diagnóstico de demência”. Mestrado em Gerontologia. Faculdade de Medicina da Universidade de Lisboa. Supervisor: Manuela Guerreiro.

Erica Marcelino (2010). Excitatory and inhibitory effects of caffeine in the neocortex – a transcranial magnetic stimulation study. Tese de Mestrado. Supervisor. A. Mendonça.

Isabel Luzeiro (2010) “Percepção do doente com enxaqueca em relação à sua doença”. Mestrado em Ciências da Dor da Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão Martins.

José Loureiro, “Empatia na Relação Médico-Doente: Análise da evolução e relação com as motivações para Medicina em estudantes do 1º ano da Faculdade”, Master Thesis, Universidade Católica Portuguesa, October 13.

Josefa Domingos, “Effects of an intensive Multitask Gait Training program on spatiotemporal gait parameters in Parkinson disease: a case study”, Master Thesis, Universidade Católica Portuguesa, November 19.

Luís Pedro Abreu (2010) Punção Lombar em doentes com Trombose Venosa Cerebral. Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: Patrícia Canhão.

Mafalda Ferreira (2010) “Percepção do Sono na Apneia (Sleep perception in OSAS patients)”. Finished 2010. Very Good. (Grade: 18 out of 20)

Magda Lopes dos Santos (2010) “A influência da idade na recuperação da afasia adquirida - Um estudo sobre plasticidade cerebral”. Mestrado em Psicobiologia do Instituto Superior de Psicologia Aplicada. Supervisor: Martin Lauterbach.

Maria Inês Aparício, “Terapia pelo Espelho – uma nova técnica para a reabilitação da função motora da mão parética em indivíduos com Acidente Vascular Cerebral”, Master Thesis, Universidade Católica Portuguesa, June 25.

Maria Moura (2010) “O papel da polissonografia na insónia crónica”, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Teresa Paiva Argente: Carla Bentes.

Maria Rosália Ferreira, “Treino Bilateral dos Membros Superiores de Indivíduos após Acidente Vascular Encefálico – Implicações na Recuperação da Função Motora,” Master Thesis, Universidade Católica Portuguesa, October 11.

Maria Teresa Mota, “Campanha Educacional para Redução da Tensão Arterial”, Master Thesis, Universidade Católica Portuguesa, May 26.

Mariana Correia (2010) Prognóstico de acidentes neurológicos transitórios de diagnóstico indeterminado. Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: Patrícia Canhão

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Mário Canastro (2010) “Os efeitos da privação parcial de sono no humor e atenção de militares no contexto de uma missão operacional”, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Teresa Paiva, Arguente: Carla Bentes.

Pedro Custódio (2010) “Use of EEG as Neurocognitive approach to Advertising Research” IST. co-supervision: Prof Lucas de Freitas. Finished 2010. Grade: 19

Pedro Rodrigues (2010) “Cirurgia na epilepsia refractária – Discussão de um caso clínico”, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Carla Bentes.

Pedro Schiappa de Azevedo (2010) “Perception of commercial brands: the emotional and social value - A spatiotemporal EEG analysis.” IST. co-supervision: Prof Lucas de Freitas. Finished 2010. Grade: 19.

Raquel Rosa (2010) “Evocação de nomes próprios”. Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade de Lisboa. Supervisor: Isabel Pavão Martins

Rosa Milheiro Pires (2010) “Avaliação da amusia em doentes epilépticos com esclerose mesial submetidos a amigdalohipocampectomia”. Mestrado Neurociências, Faculdade de Medicina de Lisboa. Supervisor: José Ferro

Rosa Milheiro Pires (2010) Avaliação da amusia em doentes epilépticos com esclerose mesial submetidos a amigdalohipocampectomia. Master thesis. Faculdade de Medicina de Lisboa. Co-supervisor: José Pimentel

Sara Campos (2010) Recorrência de eventos vasculares em doentes com Acidentes Isquémicos Transitórios. Mestrado Integrado de Medicina, Faculdade de Medicina de Lisboa. Supervisor: Patrícia Canhão

Sofia Bento Rebocho (2010) “Hiperonirismo e microestrutura do Sono (Excessive dreaming an sleep microstructure”. Finished 2010. Very Good. (Grade: 19 out of 20)

Neuromuscular Unit

Description and Objectives

The main role of the Neuromuscular Unit is the investigation of Neuromuscular Disorders. This encompasses clinical phenotypes, clinical neurophysiology, neuropathology, rehabilitation, trials and studies on molecular biomarkers. Although, we favor clinical research, we collaborate with other institutions and with other groups of IMM involved in basic investigation. We are much interested in searching biomarkers of respiratory insufficiency in motor neuron disease-amyotrophic lateral sclerosis, as well as early markers of nerve dysfunction in familial amyloid polyneuropathy. Moreover, we search motor cortex and axonal excitability, and motor unit recruitment. We are particularly interested in exploring neurophysiology as a tool to increase our knowledge on the pathophysiology of several disorders, encompassing nervous system plasticity. We are internationally very competitive in two main areas. In motor neuron disease-amyotrophic lateral sclerosis, specifically on respiratory care and neurophysiology; in familial amyloid polyneuropathy, in particular on markers of early involvement and in the longitudinal evaluation of patients submitted to liver transplantation.

Head of the Unit

Mamede de Carvalho, MD, PhD – Associated Professor, FML

Research Team

Michael Swash, MD, PhD	Invited Full Professor, FML
Anabela Pinto, MD, PhD	Assistant Professor, FML
Conceição Azevedo Coutinho, MD, PhD	Assistant Professor, FML
Teresinha Evangelista, MD	Assistant, FML
Isabel Conceição, MD	Investigator
Cândida Barroso, MD	Investigator
Susana Pinto, MD	PhD student
Benjamim Ohana, MD	Investigator
José Pedro Almeida, MD	PhD student
Vânia Almeida, MD	Investigator
Luz Rocha, Speech Therapist	Investigator
Pedro Pereira, Technician	PhD student
José Castro, Technician	Master Student

Research areas

Neuromuscular Diseases
 Amyotrophic Lateral Sclerosis
 Familial Amyloid Polyneuropathy
 Clinical Neurophysiology
 Skin biopsy

Major scientific achievements

A - In motor neuron disease-amyotrophic lateral sclerosis we described that a wireless ventilatory care control system, as supported by internet transmission of a number of clinical data and online change of the respiratory-device setup, is not only feasible but reduces costs and number of medical complications. We developed a new model for testing the corticomotoneuronal hypothesis for the origin of this disease, which did not confirm that concept. We demonstrated that phrenic nerve responses are useful to evaluate the number of motor units of the diaphragm and that is a valid non-volitional test for respiratory function. We showed that cortical silent period is a sensitive measurement to quantify upper motor neuron degeneration in ALS. Finally, our neurophysiological studies indicate that spinal cord motor columns have a specific vulnerability for disease spreading.

B - In familial amyloid polyneuropathy we observed that neuralgic pain and organ involvement are more frequent in old-onset patients, as opposed to young-onset ones who present with autonomic dysfunction. We showed that skin sympathetic skin response is an early marker of small fiber dysfunction in FAP patients; in addition, we reported that sympathetic dysfunction is an early marker of autonomic lesion of the heart. We described that skin biopsy is sensitive in this group of patients and we emphasized the problem of acquired amyloid neuropathy in receivers of FAP livers in domino liver-transplantation.

Recent Most Relevant Publications

Pinto A, Almeida JP, Pinto S, Pereira J, Oliveira AG, de Carvalho M (2010) Home telemonitoring of non invasive ventilation decreases healthcare utilization in a prospective controlled trial of ALS patients. *J Neurol Neurosurg Psychiatry* **81**, 1238-1242. (Journal IF: 4.869, Citations: 1)

Turner M, Swash M, Ebers G (2010) Lockhart Clarke's contribution to the description of amyotrophic lateral sclerosis.. *Brain* **133**, 3470-3479 (Journal IF: 9.490, Citations:0)

Pinto S, Turkman A, Pinto A, Swash M, de Carvalho M (2009) Predictive value of respiratory tests for respiratory insufficiency in amyotrophic lateral sclerosis. *Clin Neurophysiol* **120**, 941-946. (Journal IF: 3.122, Citations 7)

Conceição I, Castro JF, Scotto M, de Carvalho M (2008) Neurophysiological markers in familial amyloid polyneuropathy: early changes. *Clin Neurophysiol* **119**, 1082-1087. (JIF: 3.122, Citations: 2)

de Carvalho M, Dengler R, Eisen A, England JD, Kaji R, Kimura R, Mills K, Mitsumoto H, Nodera H, Shefner J, Swash M (2008) Electrodiagnostic criteria for diagnosis of ALS: consensus of an International Symposium sponsored by IFCN. *Clin Neurophysiol* **119**, 497-503. (Journal IF: 3.122, Citations 40)

Ongoing Research Projects

1994/present – *ESTEEM* - *European Project for Investigation in Electromyography*. (no current funding).

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 (FoldRx Pharmaceuticals, Inc.).*

2008/2010 - *An Open-Label Extension of Study Fx-005. Evaluating Long-Term Safety and Clinical Outcomes of Fx-1006A in Patients with Transthyretin Amyloid Polyneuropathy (Clinical Protocol Number Fx-006 - FoldRx Pharmaceuticals, Inc.)*

2010-2011 - *Open-Label Safety Evaluation of Fx-1006A in Patients with Transthyretin Amyloidosis. (FoldRx Pharmaceuticals, Inc.)*

2008/2010 - *Early Markers in FAP. To determine early disease markers in asymptomatic and early symptomatic Val30Met carriers (FoldRx Pharmaceuticals, Inc.)*

2009/2011 - *Complement polymorphism analyses in FAP type I populations. To test for correlation between polymorphisms in CIQA , with age of onset in Portuguese, Greek and further Cypriot patients with FAP type I. (Instituto de Biologia Molecular e Celular do Porto e Center for Neurology and Genetics – Chipre)*

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).*

2009/2011 - *Caracterização Clínica e Diagnóstica de Doentes com Patologia Neuromuscular – Estudo Epidemiológico em Portugal (ENDOMUS). Coordinator: Teresinha Evangelista (Sociedade Portuguesa de Estudos de Doenças Neuromusculares (SPEDNM).*

2009/2011- *MUNIX – Multicentric International study to evaluate a new method for motor unit number estimation. (no current funding).*

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).*

2009-2011 – *Respiratory Rehabilitation in Amyotrophic Lateral Sclerosis: Clinical and Biochemical Impact. FCT. Coordinator: M de Carvalho. (PICIC/82765/2007).*

2010 - *Estudo do Gene da “Vitamin D-Binding Protein” (DBP) no DNA de Doentes com Esclerose Lateral Amiotrófica. Coordinator: M de Carvalho. (GAPIC/2009012).*

Publications in International Journals

Almeida V, Mestre T, de Carvalho M (2010) Pseudobulbar syndrome in two patients with Human Immunodeficiency virus infection. *Amyotr Lat Scler* **11**, 220-222. (Journal IF: 2.963).

Almeida V; de Carvalho M (2010) Lesion of the Deep Palmar Branch of the Ulnar Nerve: causes and clinical outcome. *Neurophysiol Clin* **36**, 219-226. (Journal IF: 1.169).

Conceição I, Evangelista P, Castro J, Pereira P, Silvestre A, Coutinho CA, de Carvalho M (2010) Acquired amyloid neuropathy in a Portuguese patient after domino liver transplantation. *Muscle Nerve* **42**, 836-838. (Journal IF: 2.287)

Costa J, Gomes G, de Carvalho M (2010) Diagnosis, pathogenesis and therapeutic targets in amyotrophic lateral sclerosis. *Cur Drug Targets* **9**, 764-778. (Journal IF: 3.932, Citations: 0)

Cudkowicz ME, Swash M (2010) CSF markers in amyotrophic lateral sclerosis. Has the time come? (Editorial). *Neurology* **24**, 949-950. (Journal IF: 8.172)

de Almeida JPL, Pinto AC, Pereira J, Pinto S, de Carvalho M (2010) Implementation of a wireless device for real-time telemedical assistance of home-ventilated ALS patients - A feasibility study. *Telemed J E Health* **16**, 883-888. (Journal IF: 0.967)

de Almeida JPL, Saldanha C (2010) Dithiothreitol revisited in red cells: a new head for an old hat. *Clin Hemorheol Microcirc* **46**, 51-56. (Journal IF: 1.780)

de Almeida JPL, Saldanha C (2010). Non-neuronal cholinergic system in human erythrocytes: biological role and clinical relevance. *J Membrane Biol* **234**, 227-234. (Journal IF: 2.190)

Saldanha C, de Almeida JPL, Freitas T, Oliveira S, Silva-Herdade AS (2010). Erythrocyte deformability responses to shear stress under external and internal stimuli influences. *Series on Biomechanics* **25**, 54-60. (Journal IF: N/A)

de Carvalho M (2010). Olfactory ensheathing cells for human spinal cord injury (letter). *Neurorehabil Neural Repair* **24**, 772. (Journal IF: 5.398)

de Carvalho M, Marcelino E, de Mendonça A (2010). Electrophysiological studies in healthy subjects involving caffeine. *J Alzh Dis* **20** (suppl 1): S63-S69 (Journal IF: 3.832).

de Carvalho M, Pinto S, Costa J, Evangelista T, Ohana B, Pinto A (2010). A randomised, placebo-controlled trial of Memantine for Functional Disability in Amyotrophic Lateral Sclerosis. *Amyotr Lat Scler* **11**, 456-460 (Journal IF: 2.963, citations:1).

de Carvalho M, Pinto S, Swash M (2010) Association between paraspinal muscles and diaphragm denervation in ALS *Amyotr Lat Scler* **11**, 63-66 (Journal IF: 2.963).

de Carvalho M, Swash M (2010). Sensitivity of electrophysiological tests for upper and lower motor neuron dysfunction in ALS: A six-month longitudinal study. *Muscle Nerve* **40**, 318 (Journal IF: 2.287).

de Carvalho M, Swash M (2010). The Onset of ALS? *Clin Neurophysiol* (Editorial) **121**, 1709-1710 (Journal IF: 3.122).

de Carvalho M, Swash M (in press) Fasciculation-cramp syndrome preceding anterior horn cell disease: an intermediate syndrome? *J Neurol Neurosurg Psychiatry* Epub ahead of print (Journal IF: 4.869).

Geraldes R, de Carvalho M (2010) Transcranial magnetic stimulation is a useful diagnostic test in psychogenic paralysis (e-letter). *J Neurol Neurosurg Psychiatry* (Journal IF: 4.869). <http://jnnp.bmj.com/cgi/eletters/jnnp;79/12/1412#6589>

Faria C, Miguéns J, Antunes JL, Salgado D, Nunes S, Barroso C, Martins Mdo C, Nunes VM, Roque L (2010) Pediatric brain tumors: genetics and clinical outcome. *J Neurosurg Pediatr* 5, 263-70. (Journal IF: 0.171)

Foreid H, Barroso C, Evangelista T, Campos A, Pimentel J (2010). Intracerebral amyloidoma: case report and review of the literature. *Clin Neuropathol* 29, 217-22 (Journal IF: 1.037).

Pato MP, Santos NJG, Areias P, Pires EB, de Carvalho M, Pinto S, Lopes DS (2010). Finite element studies of the mechanical behavior of the diaphragm in normal and pathological cases. *Comput Methods Biomech Biomed Engin* Epub ahead of print (Journal IF: 1.454).

Petros P, Swash M (2010) Sacrocolpopexy may cause difficult defecation by inhibiting the external opening out mechanism. *Int Urogynecol J Pelvic Floor Dysfunct* Epub ahead of print.

Pinto A, Almeida JP, Pinto S, Pereira J, Oliveira AG, de Carvalho, M (2010). Home telemonitoring of non invasive ventilation decreases healthcare utilization in a prospective controlled trial of ALS patients. *J Neurol Neurosurg Psychiatry* 81, 1238-1242 (Journal IF: 4.869).

Pinto S, de Carvalho M (2010) Is a 4-hour use of non-invasive ventilation enough to define compliance? *Amyotr Lat Scler* 11, 250-252 (Journal IF: 2.963).

Pinto, S; de Carvalho, M (2010). Symmetry of phrenic nerve motor response in amyotrophic lateral sclerosis. *Muscle Nerve* 42, 882-884 (Journal IF: 2.287)

Pugdahl K, Fuglsang-Frederiksen A, Johnsen B, Tankisi H, de Carvalho; Fawcett P, Labarre-Vila A, Liguori R, Nix W, Schofield I (2010). Variation in the neurophysiological examination of Amyotrophic Lateral Sclerosis in Europe. *Amyotr Lat Scler* 11, 443-448 (Journal IF: 2.963).

Santos R, Oliveira J, Vieira E, Coelho T, Carneiro AL, Evangelista T, Dias C, Fortuna A, Geraldo A, Negrão L, Guimarães A, Bronze-da-Rocha E (2010). Private dysferlin exon skipping mutation (c.5492G>A) with a founder effect reveals further alternative splicing involving exons 49-51. *J Hum Genet* 55, 546-9 (Journal IF: 2.431).

Swash M (2010) Apraxia contributes to the motor deficit in Parkinson's disease and multiple system atrophy (Editorial). *Eur J Neurol* 17, 346-347 (Journal IF: 2.510).

Swash M (2010) Coping with motor neuron disease: how do people adapt to the devastating news? Swash M. *J Neurol Neurosurg Psychiatry* 81, 826 (Journal IF: 4.869).

Swash M (2010) Internet facilitated management improves home ventilation in amyotrophic lateral sclerosis (Editorial). *J Neurol Neurosurg Psychiatry* 81, 1180 (Journal IF: 4.869).

Swash M (2010) Lithium time-to-event trial in amyotrophic lateral sclerosis stops early for futility (Editorial). *Lancet Neurol* 9, 449-451 (Journal IF: 18.126).

Turner M, Swash M, Ebers G (2010). Lockhart Clarke's contribution to the description of amyotrophic lateral sclerosis. *Brain* 133, 3470-3479 (Journal IF: 9.490)

Publications in Peer Review National Journals

Hasmucrai,D., Mendes, AC., Correia, I., Evangelista, T., Bugalho de Almeida A (2010). Pulmonary disease in polymyositis. Rev Port Pneumol16:671-7.

Other publications International

de Carvalho, M (2010). **Esclerose Lateral Amiotrófica**. In DOENÇAS RARAS de A a Z. Federação das Doenças Raras de Portugal, pp 22-23.

de Carvalho, M (2010). **S de Guillain- Barré**. In DOENÇAS RARAS de A a Z. Federação das Doenças Raras de Portugal, pp 40-41.

Evangelista, T (2010). **Distrofia Muscular de Duchenne/Becker**. In: Manual sobre Doenças Neuromusculares. Técnicos e Profissionais de Saúde. Associação Portuguesa de Doentes Neuromusculares. Almedina, pp 93-95

Pato PMP, Santos NJG, Pires EB, Areias P, de Carvalho M, Pinto S, Lopes DS (2010). **Finite Element Studies of the Mechanical Behavior of the Diaphragm in Normal and Pathological Cases**. In Proceedings of the 9th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering.

Swash M (2010). **The pelvic floor: functional concepts and neurocontrol**. In: GA Santoro, P Wiczerek, C Bartram (Eds) Pelvic Floor Disorders: imaging and a multidisciplinary approach to management. London, Springer-Verlag,33-42.

Pereira A, Silva M, Martins J, de Carvalho M. Development of a Hill-Type Muscle Model with Fatigue for the Calculation of the Redundant Muscle Forces using Multibody Dynamics. www.ondrcies.webd.pl/imsd/papers/imsd2010_181_paper.pdf.

Communications in International Conferences

Pato MPM, Santos NGS, Areias P, Pires EB, de Carvalho M; Pinto S, Lopes DS. **Finite Element Stimulation of the Deformation of the Diaphragmatic Floor in Healthy and Pathological Conditions**. Computer Methods In Biomechanics and Biomedical Engineering 2010. Valência, February 2010 (oral communication).

Coelho T, Maia L, Martins da Silva A, Waddington-Cruz M, Planté-Bordeneuve, Lozeron P, Suhr O, Campistol J, Conceicao I, Schmidt H, Trigo P, Packman J, Grogan RD. **Tafamidis (Fx-1006A): A First-in-Class Disease-Modifying Therapy for Transthyretin Amyloid Polyneuropathy**. American Academy of Neurology (AAN) 2010. Toronto, April 2010 (oral communication).

Pinto S, de Carvalho M. **Lower motor Neurons Loss in Cervical Myotomes in Amyotrophic Lateral Sclerosis**. 17th European Congress of the European Society of Physical and Rehabilitation Medicine. Venice, May 2010 (oral communication).

Pereira A, Silva M, Martins J, de Carvalho M. **Development of a Hill-Type Muscle Model with Fatigue for the Calculation of the Redundant Muscle Forces using Multibody Dynamics.** Joint International Conference on Multibody System Dynamics. Lappeenranta. May 2010 (oral communication).

Almeida V, Pinto S, Pinto S, Ohana B, de Carvalho M. **Prognostic factors in primary lateral sclerosis.** 20th Meeting of the European Neurological Society. Berlin. June 2010 (oral communication).

Lobo AP, Pinto S, Rocha L, Reimão S, de Carvalho M. **Asymmetric oro-facial apraxia in primary lateral sclerosis – a perplexing clinical manifestation.** 20th Meeting of the European Neurological Society. Berlin. June 2010 (oral communication).

Conceição I, Evangelista T, Pereira P, Vieira E, Oliveira J., Santos R. **Report of a family with two different hereditary diseases leading to early cardiac involvement.** XII International Congress on Neuromuscular Diseases. Naples, July 2010 (poster).

Conceição I, Evangelista T, Castro J, Silvestre A, de Carvalho M. **Acquired Amyloid Neuropathy in a Portuguese Patient after Domino Liver Transplantation.** XII International Congress on Neuromuscular Diseases. Naples, July 2010 (poster).

Carilho R, de Carvalho M, Kuehl U, Pinto S, Kromminga A, Costa J. **Levels of plasma erythropoietin and cerebrospinal fluid β -trace protein from Portuguese patients with Amyotrophic Lateral Sclerosis** ESF Workshop on Glycomarkers for Disease. Mikolajki. September 2010 (poster).

Pires MC, Nunes L, Castro J, Geraldés R, Canhão P, de Carvalho M. **Conversion Disorder versus Stroke: a difficult differential diagnosis.** 14th Congress of the European Federation of Neurology. Geneva. September 2010. (poster).

Almeida V, Andersen P, de Carvalho M. **Progressive Muscular Atrophy associated with TDP-43 Mutation.** 14th Congress of the European Federation of Neurology. Geneva. September 2010 (poster).

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. **Sustainability of response to tafamidis, a disease-modifying therapy for transthyretin type familial amyloid polyneuropathy.** 14th Congress of the European Federation of Neurology. Geneva. September 2010 (oral communication).

D. Neutel, M. Coelho, C. Barroso, T. Evangelista. **One or two diseases? The phenotypical. The phenotypical expression of G13513A mutation in mitochondrial DNA.** 14th Congress of the European Federation of Neurology. Geneva. September 2010 (poster).

de Almeida JPL. **Non-neuronal Cholinergic System in Human Erythrocytes.** 9th Congress for Microcirculation, Paris, September 2010 (oral communication).

de Almeida JPL, Saldanha C. Fibrinogen-dependent signaling in microvascular erythrocyte function – Implications on nitric oxide efflux. 9th Congress for Microcirculation, Paris, September 2010 (poster).

Conceição I, Castro JF, Costa JP, de Carvalho M. **Early-detection of Small-Fiber Neuropathy in Familial Amyloid Polyneuropathy Patients.** 29th International Congress of Clinical Neurophysiology. Kobe. November 2010 (poster).

Castro J, Sousa M, Costa J, de Carvalho M. **The Radial to Median Sensory Potential Differential Diagnosis of Carpal Tunnel Syndrome.** 29th International Congress of Clinical Neurophysiology. Kobe. November 2010. (poster).

Pinto S, Scotto M, Pinto A, Swash M, de Carvalho M. **The Predictive Value of the Phrenic Nerve Motor Response for Non-invasive Ventilation.** 21st International Symposium on ALS/MND. Orlando. December 2010 (poster).

de Carvalho M, Pinto S, Swash M. **Sternocleidomastoid and Scalenus Anterior Muscles Investigation in Amyotrophic Lateral Sclerosis: an electromyographic study.** 21st International Symposium on ALS/MND. Orlando. December 2010 (poster).

Communications in National Conferences

Almeida V, Moreno T, Fonseca MJ, Evangelista T. **Miopatia sem diagnóstico em dois irmãos.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Almeida V, Moreno T, Fonseca MJ, Evangelista T. **Ganglioneuropatia idiopática com sinais piramidais?** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Almeida V, Moreno T, Fonseca MJ, Evangelista T. **Doença mitocondrial de transmissão mendeliana com apresentação clínica distinta em duas gerações.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Antunes AN, Vilarinho L, Dores L, Evangelista T. **Implante Coclear no Síndrome MELAS.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (poster).

Conceição I, Lobo P, Evangelista T. **Uma mulher com antecedentes pessoais de Doença de Hanssen com disestesias de predomínio noturno nos pés e mãos.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Evangelista T. **Limb-girdle weakness and ptosis. What to do?.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Marques J, Costa S, Oliveira J, Santos R, Silvestre AR, Evangelista T. **Leucodistrofia: um achado importante no diagnóstico de Defeito Parcial de Laminina – alfa2.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Santos M, Ferreira C, Fineza I, Evangelista T, Lima JLM, Dias AI, Vieira JP, Coelho T, Lochmuller H. **Apresentação dos casos Portugueses de Miastenia Congénita.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Silvestre AR, Machado M, Vilarinho L, Cortez-Pinto H, Evangelista T. **Efeitos da obesidade mórbida e da resistência à insulina no músculo esquelético.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (oral communication).

Silvestre AR, Sousa A, Costa J, Barroso C, Evangelista T. **Predictors of pain after muscle biopsy.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010 (poster).

Pereira P, Evangelista T. **Contagem de fibras nervosas intraepidérmicas em indivíduos saudáveis – contributo para o esclarecimento e dados normativos.** Forum de Neurologia. Luso. May, 2010 (oral communication).

Pinto S, Swash M, de Carvalho M. **Avaliação Neurofisiológica da Hipótese Corticomotoneuronal na Esclerose Lateral Amiotrófica.** Forum de Neurologia. Luso. May, 2010 (oral communication).

Almeida V, Andersen P, de Carvalho M. **Atrofia muscular progressiva associada a mutação do gene TDP-43.** Forum de Neurologia. Luso. May, 2010 (poster communication).

Rocha L, Loureiro C, de Carvalho M. **Defeitos de escrita num doente com esclerose lateral amiotrófica.** Forum de Neurologia. Luso. May, 2010 (poster communication).

Castro J, Costa J, de Carvalho M. **MUNIX.** XXXV Reunião Anual da Associação Portuguesa de EEG e Neurofisiologia Clínica. Portimão, May 2010 (oral communication).

Miltényi G, Neutel D, Silva I, Coelho H, de Carvalho M. **Resultados genéticos de um paciente com coreo-acantocitose – descrição de 3 novas variantes do gene VPS13A.** Congresso de Neurologia de 2010. Espinho, November 2010 (oral communication).

Neutel D, Miltenberger-Miltényi G, Silva I, Coelho H, de Carvalho M. **Um caso atípico de coreia-acantocitose com manifestação motora.** Congresso de Neurologia de 2010. Espinho, November 2010 (poster communication).

Antunes AP, Nogueira C, Rocha H, Vilarinho L, Evangelista T. **Deficiência da Acil-CoA Desidrogenase dos Ácidos Gordos de Cadeia Muito Longa – Miopatia Metabólica com Início na Idade Adulta.** Congresso de Neurologia de 2010. Espinho, November 2010 (oral communication).

Neutel D, Coelho M, Barroso C, Evangelista T. **Síndrome de sobreposição MELAS\Neuropatia Óptica Hereditária de Leber numa mulher com a mutação G13513A.** Congresso de Neurologia de 2010. Espinho, November 2010 (poster communication).

Coelho T, Maia L, Silva AM, Waddington-Cruz M, Planté-Bordeneuve V, Lorezon P, Suhr O, Conceição I, Schmidt H, Trigo P, Packman J, Grogan R, **Apresentação dos resultados positivos**

do ensaio piloto com Tafamidis em doentes com polineuropatia amiloidótica familiar. Congresso de Neurologia de 2010. Espinho, November 2010 (oral communication).

C. Mariano, P. Pereira, F. Cardoso, I. Palmela, A. R. Vaz, A. Fernandes, S. L. Silva, A S. Falcão, E. Torrado, A. R. Campos, A. Gonçalves Ferreira, K. S. Kim, D. Brites, M. A. **Scrutinizing the brain for tricellulin, a new tight junction protein.** XVII Congresso Nacional de Bioquímica, December 2010 (poster)

Invited Lectures and Seminars

Castro JF. **Laser Evoked Potentials** – II Jornadas de Neurofisiologia da ESTSP-IPP. Porto. May 2010

de Carvalho, M. **Electromyography in Amyotrophic Lateral Sclerosis.** Department of Neurosciences, Katholieke Universiteit Leuven. Leuven, February 2010.

de Carvalho, M. **EMG in Motor Neuron Disease.** Medizinische Hochschule Hannover, University of Hannover. Hannover, March 2010.

de Carvalho, M. **Les Uns et les Autres.** *Neuroscience Seminar.* IMM-Faculty of Lisbon. Lisbon, March 2010.

de Carvalho, M. **Dor, Defeito de Força e de Sensibilidade.** Temas de Neurologia em Medicina Geral e Familiar IV. Lisbon, March 2009.

de Carvalho, M. **Stratégie exploratoire ENMG devant une suspicion de SLA.** 17^{ème} Journées Francophones d'Electroneuromyographie. Lyon, June 2010.

de Carvalho, M. **Testing transsynaptic degeneration in ALS.** Lisbon Area Neuroscience Meeting. IMM-Faculty of Lisbon. Lisbon, June 2010

de Carvalho, M. **Neurophysiological Markers of Disease Progression in ALS.** Encontro com a Ciência e Tecnologia em Portugal. Lisbon, July 2010

de Carvalho, M. **Diagnóstico precoce da Esclerose Lateral Amiotrófica.** XXIV Congresso Brasileiro de Neurologia. Rio de Janeiro, August 2010

de Carvalho, M. **Tratamento actual da ELA: evidências científicas.** XXIV Congresso Brasileiro de Neurologia. Rio de Janeiro, August 2010

de Carvalho, M. **Familial Amyloid Polyneuropathy.** 29th International Congress of Clinical Neurophysiology. Kobe, November 2010.

de Carvalho, M. **Physiology of ALS.** 29th International Congress of Clinical Neurophysiology. Kobe, November 2010.

Conceicao I. **Contribuição de Lisboa na história da Paramiloidose.** Dia Nacional da Paramiloidose. Porto, Junho 2010.

Evangelista T. **Clinica das miopatia mitocondriais com mutações nos genes nucleares.** Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares. Vale do Lobo, April 2010.

Pinto A. **Telemedicine: International experiences and Insights into the Future.** 14th - Symposium satélite do Grupo Linde. Porto, Novembro 2010.

Pinto A. **Uma clínica de ELA Dia Nacional da ELA no dia de Charcot.** Lisboa, November 2010

Pinto A. **Atribuição de Tecnologias de Apoio para Pessoas com Necessidades Complexas de Comunicação.** Comunicar 2010 IST. Lisboa, November 2010.

Pinto A. **Hospital@Home: a que distância estamos no controlo da VNI?.** AO 2ND I-MED 2010. Lisboa, November 2010.

Swash M. **An introduction to Neurodegenerative Diseases.** Queen Mary. University of London. London, January 2010.

Swash M. **Motor Neuron Disease.** Association of British Neurology. London, May 2010.

Swash M. **The life and work of Lord Brain.** London, June, 2010

Swash M. **The neuron theory.** Oxford Neuroscience Course Oxford, June, 2010

Swash M. **Neurological practice.** Lecture to Life Insurance Underwriters (UK and Ireland). London, November, 2010

Organisation of National and International Conferences

Conceição I. Co-organizer and chairman of the **Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares.** Vale do Lobo, Abril 2010.

Conceição I. Co-organizer and chairman of the **XXXV Reunião Anual da Associação Portuguesa de EEG e Neurofisiologia Clínica.** Portimão, May 2010.

De Carvalho M. Co-organizer and chairman of the **XXXV Reunião Anual da Associação Portuguesa de EEG e Neurofisiologia Clínica.** Portimão, May 2010.

De Carvalho, M. Co-chairman of the session **Physiology of Polyneuropathies.** 29th International Congress of Clinical Neurophysiology. Kobe, November 2010.

De Carvalho, M. Co-chairman of the session **Surrogate Markers.** 21th International Symposium on ALS/MND. Orlando, December 2010

Evangelista T. Co-organizer and chairman of the **Congresso da Sociedade Portuguesa de Estudos de Doenças Neuromusculares.** Vale do Lobo, April 2010.

Evangelista T. Chairman of the session **Terapêutica em várias Patologias Neurológicas.** Congresso de Neurologia de 2010. Espinho, November 2010

Prizes

1º Prize Corino de Andrade-Novartis – “Sociedade Portuguesa de Neurologia” - *Is phrenic nerve motor response predictive of survival in Amyotrophic Lateral Sclerosis?*; de Pinto S, de Carvalho M. 2010.

M Swash. **Association of British Neurologist – silver medal** for professional commitments. London, May 2010.

A Pinto. **Prémio da Federação Europeia das Doenças Raras (FEDRA) 2010 - Medalha de Mérito**

Advanced Teaching

Carvalho, M. lectured “Basic Principals of Clinical Neurophysiology and Electromyography”, in Master Degree and Doctoral Program on Neurosciences, IMM, April 13, 2010.

Carvalho, M. Laryngeal EMG in Master Degree and Doctoral Program on Voice, Language and Communication IMM, Lisbon, April 2010

Carvalho, M. lectured “Sleep and Neuromuscular disorders” in Master Degree and Doctoral Program on Sleep, IMM, Lisbon, May 2010

Carvalho, M. lecture “EMG de superfície”, in Biomechanics - Biomedical Engineering integrated master degree, IMM Lisbon, October 16, 2010

Conceição, I. lectured “Potenciais Evocados”, in Master Degree and Doctoral Program on Neurosciences, IMM, Lisbon, April 15, 2010

Conceição, I. lectured “Polineuropatia Amiloidotica Familiar Tipo I”, in Master Degree and Doctoral Program on Neurpathology, IMM, Lisbon, February 18, 2010

Conceição, I. lectured “Técnicas de Neurofisiologia” in Biomechanics - Biomedical Engineering integrated master degree, IMM Lisbon, October 16, 2010

Evangelista, T. “Neuropathology in Neuromuscular Disorders” in Advanced Course for Neuropediatrics, Hospital Santo Antonio, Porto, 2010

Ohana, B. lectured “Alteração da Marcha”, lessons in Biomechanics - Biomedical Engineering integrated master degree, IMM, Lisboa, October 2010

Anabela Pinto

Pinto, A. lectured “Doença crónica e a reabilitação; in Master degree on Physical Medicine and Rehabilitation, IMM, Lisbon, 2010

Pinto, A. lectured “Reabilitação nos grandes quadros neurológicos” in Master degree on Physical Medicine and Rehabilitation, IMM, Lisbon, 2010

Pinto, A. lectured “Intervenção reabilitadora na doença cardio-respiratóriae o papel do exercício” in Master degree on Physical Medicine and Rehabilitation, IMM, Lisbon, 2010

Pinto, A. lectured “Research with non-pharmacologic therapeutic interventions” in Master Degree and Doctoral Program on Neurosciences, IMM, June, 2010

Pinto, S. lectured “A Marcha Humana em Análise”, lessons in Biomechanics - Biomedical Engineering integrated master degree, IMM, Lisboa, October, 2010

Master and PhD Thesis

PhD Thesis

Matilde Pós-De-Mina Pato (2010) “**Deformação Activa de Músculos Esqueléticos-Modelos, Simulação pelo Método dos Elementos Finitos e Aplicações**”. Instituto Superior de Engenharia de Lisboa-Instituto Superior Técnico (Engenharia Biomédica). Co-supervisor: M de Carvalho

Master Thesis

Erica Marcelino (2010) “**Excitatory and inhibitory effects of caffeine in the neocortex – a transcranial magnetic stimulation study**”. Faculty of Medicine – Lisbon. Co-supervisor: M de Carvalho.

Anna Caroline (2010) “**Necessidades dos Doentes Portadores de Esclerose Lateral Amiotrófica e seu Cuidador Principal: sua influência na qualidade de vida**”. Faculty of Medicine – Lisbon. Supervisor: A. Pinto.

Cristina Soares (2010) “**A Vibração Muscular como Facilitadora da Activação Cortical. Pode a estimulação vibratória ser usada como ferramenta na fisioterapia?**” Catholic University, Lisbon. Supervisor: M de Carvalho

Sergio Gonçalves (2010) “**Advanced Computer Methods for Pathological and Non-Pathological Human Movement Analysis**”. Instituto Superior Técnico,UTL and Faculdade de Medicina da Universidade de Lisboa. Co-supervisor: M de Carvalho.

Neurosciences Unit

Major interests / Objectives

The unit aims the elucidation of cellular and molecular mechanisms involved in tuning and fine-tuning of neuronal communication, in particular 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:

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: 9.140, Citations: 182). A project aiming to identify a role for adenosine in animal models of amyotrophic lateral sclerosis (ALS) has been initiated.

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., *Prog Neurobiol*, 48, 167-189 - Journal IF: 9.140, Citations: 187), which besides acting itself as an endogenous neuroprotective agent, interacts with other substances 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.

Receptor Biology and Cognition group - To understand how brain structures involved in memory are affected in situations of cognitive decline. We are particularly interested in changes occurring with ageing and whether these changes are hastened or exacerbated by several pathological conditions, namely depression and anxiety, epilepsy, neurodegenerative diseases. 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), 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 - A better understanding of neuronal cell death mechanisms induced by noxious conditions. We are particularly interested in the loss of endogenous neuronal trophic support observed in Alzheimer's disease patients and the potential direct involvement of A β aggregates in this loss. The age-related changes of neurotrophins-mediated control of synaptic transmission (for a recent publication by the group leader see Diógenes et al., *Hippocampus*, 17: 577-585 - Times cited: 17, Journal IF: 3.913) and plasticity are also a focus of the group.

Inhibitory Synapses Group - Understanding of the molecular mechanisms of inhibitory synapses, focusing upon glycinergic ones, and their modulation in the brain. It 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 occurs in epilepsy (MS on the topic, submitted by the group leader as senior author in the press at *J Neurochem*).

Head of Unit

Joaquim Alexandre Ribeiro, MD, PhD – Full Professor, FMUL

Principal Investigators

Joaquim Alexandre Ribeiro, MD, PhD	Full Professor, FMUL
Ana Maria Ferreira de Sousa Sebastião, PhD	Associate Professor, FMUL
Alexandre Valério de Mendonça, MD, PhD	Principal Investigator, FMUL
Luisa V. Lopes PhD	Staff Scientist, IMM
Maria José Diógenes, PhD	Auxiliar Professor, FMUL
Claudia Alexandra Valente de Castro, PhD	Research Fellow, FMUL

Research Team

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)
Alexandra Marçal, PhD	Investigator, MNHN/UL
Diana Cunha Reis, PhD	Post-Doc Fellowship, FCT (ended June 2010)
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	PhD. Fellowship, FCT
Frederico Simões do Couto, MD	Assistant, FMUL
Nuno Canas, MD, MSc	Assistant, FMUL
António F. Francisco, MD	Assistant, FMUL
Nádia Rodrigues, MSc	BI fellowship (ended September, 2010)
Armando Cruz, Degree Biochemistry	MSc Student (ended November 2010)
Mariana Rocha	MSc Student (started September 2010)
Joao Baião	Technician, FMUL

Neuroprotection Group**Principal Investigator:** Ana Maria Sebastião, PhD, Associate Professor (c/agregação), FMUL

Natália Assaife-Lopes, MSc	Ph.D Fellowship, FCT (finished October 2010)
Vasco Sousa, Basic Degree Biology	Ph.D Fellowship, FCT (PhD thesis submitted September 2010)
Catarina Fernandes, Basic Degree in Biology	Ph.D. Fellowship, FCT
Raquel Dias, Basic Degree in Biology	Ph.D. Fellowship, FCT
Sandra Vaz, Basic Degree in Biochemistry	Ph.D. Fellowship, FCT
Sofia Cristóvão-Ferreira, Basic Degree in Biochemistry	Ph.D Fellowship, FCT
Diogo Rombo, Degree in Biology	Ph.D Fellowship, FCT
Rita Aroeira, Degree in Biochemistry	Ph.D Fellowship, FCT (co-supervised by Claudia Valente)
Ana Filipa Ribeiro, MSc	MSc Student in 2010, presently Ph.D Fellowship, FCT
Joaquim Jacob, Degree in Biology	MSc Student (Neurosciences); start September 2010
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); start September 2010
Afonso Felix de Oliveira, Medical Student	GAPIC fellow (start September 2010)
Elvira Duarte	Technician, FMUL (retired in November 2010)
João Baião	Technician, FMUL

Receptor Biology and Cognition group**Principal Investigator:** Luisa Vaqueiro Lopes, PhD, IMM Staff Scientist

Vânia Batalha, MSc	PhD Fellowship, FCT
Joana Vital, Degree in Biology	MSc Student (Neurosciences) (ended June 2010)
Jorge Valadas, Degree in Biochemistry	MSc student (ended November 2010); presently BI fellowship
João Baião	Technician, FMUL

Regulation of Neuronal Death group**Principal Investigator:** Maria José Diógenes, PhD, Auxiliary Professor, FMUL

André Jerónimo Santos, MSc in Biochemistry	PhD Fellowship, FCT
Daniela Calçada, Degree in Biochemistry	MSc Neuroscience Student
Júlia Pinho, degree in Biology	MSc Neuroscience Student (started September 2010)
Rúben Duque do Vale, pregraduation Medical	GAPIC Fellow

Student	
António Caetano	GAPIC Fellow (co-supervised by LV Lopes)
Sofia Lérias	GAPIC Fellow (co-supervised by S Vaz)
Sara Parreira	GAPIC Fellow (co-supervised by S Vaz)
Carla Leão	GAPIC Fellow (co-supervised by S Vaz)
Carla Nunes	GAPIC Fellow (co-supervised by S Vaz)
Joana Tavares	GAPIC Fellow (co-supervised by S Vaz)

Inhibitory Synapses Group

Principal Investigator: Cláudia Valente, PhD Research Fellow, FMUL

Research Team

Rita Aroeira, MSc in Biochemistry	PhD fellowship, FCT
Catarina Luís	MSc Neuroscience Student
Renato Nogueira, pregraduation Medical Student	GAPIC fellow
David Correia, pregraduation Medical Student	GAPIC fellow
Inês Figueiredo, pregraduation Medical Student	GAPIC fellow

Keywords/Research Areas

Metamodulation,
Tripartite synapse mechanisms
Neuronal Excitation/Inhibition balance
Chronic stress
Ageing
Neurodegenerative mechanisms

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 2010 include the following findings:

- 1) By the first time it was observed the influence of adenosine A2A receptors on receptor mobility, namely upon TrkB translocation to lipid rafts (signaling specialized membrane domains). Doing this we identified a key step in the understanding of the molecular mechanisms through which adenosine A2A receptors trigger synaptic actions of neurotrophins.
- 2) Also, we found that A2A receptors influence AMPA receptor mobility. Thus, A2A receptors are responsible for setting part of the endogenous phosphorylation tonus of glutamate GluR1 subunits and hence, the availability of the GluR1-containing AMPA receptor extrasynaptic pool for synaptic insertion and reinforcement of synaptic strength.

- 3) While carefully looking at the influences of adenosine A_{2A} receptors on synaptic transmission in very young (peri-weaning) animals, we could identify for the first time that, at least at the neuromuscular junction, tonic activation of A_{2A} receptors predominates over A₁ receptor activation, challenging an old paradigm that inhibition by adenosine predominates over excitation.
- 4) Members of the Unit in collaboration with Darwin Berg at the University of California, San Diego, clearly found that lateral mobility of nicotinic acetylcholine receptors (nAChRs) is determined by mechanisms that are domain specific, receptor subtype dependent, and cell-type constrained. They also identified a key role for alpha7-nAChRs in adult neurogenesis allowing predicting that loss of these receptors cause progressive impairment in hippocampal circuitry and functioning over time.
- 5) In a study aiming to evaluate reciprocal influences between adenosine A₁ and cannabinoid CB₁ receptors (the two main targets of the most widely used psychoactive and recreational drugs, caffeine and tetrahydrocannabinol) we clearly found that A₁ receptors exert a negative modulatory effect on CB₁-mediated inhibition of GABA release, and in collaboration with the University of Strathclyde, Glasgow, provided first evidence that chronic caffeine consumption induces alterations in the cannabinoid system with functional implications in spatial memory. That caffeine in concentrations selective for adenosine receptors affects synaptic plasticity has been identified in another study by the Unit.
- 6) While investigating the mechanisms behind the neuroprotective actions of pro-inflammatory interleukin-6 (IL-6)-type cytokines, in a collaboration with Knut Biber (Univ Groningen) we found that IL-6 and oncostatin (OSM), but not the leukemia inhibitory factor (LIF), are neuroprotective because they induce an upregulation of A₁ receptors in neuronal cells, strongly suggesting that IL-6 type cytokines, despite known structural and functional similarities, use different mechanisms to achieve neuromodulation and neuroprotection.
- 7) The pathophysiology and long-term outcome of reversible tumor-like lesions induced by status epilepticus as well as of transient periictal MRI abnormalities was matter of research, being clear the urge for fast control of status epilepticus to avoid brain damage.

In conclusion, the major scientific achievements along the year reinforce concepts that have been developed and highlighted by the Unit members over the last years, that adenosine A_{2A} and A₁ receptors, via regulating mobility and action of other agents that protect and/or reinforce synapses, have a major role in the balance between neuronal inhibition and excitation, therefore 'synchronizing' or 'desynchronizing' directly or indirectly neuronal synaptic activity.

Recent Most Relevant Publications

Fernandes CC, Pinto-Duarte A, Ribeiro JA, Sebastião AM (2008) Postsynaptic action of brain-derived neurotrophic factor attenuates alpha7 nicotinic acetylcholine receptor-mediated responses in hippocampal interneurons. *Journal of Neuroscience* **28**, 5611-5618 (Journal IF: 7.178, Citations: 6)

Diógenes, MJ, Fernandes CC, Sebastião AM, Ribeiro JA (2004) Activation of adenosine A_{2A} receptor facilitates BDNF modulation of synaptic transmission in hippocampal slices. *Journal of Neuroscience* **24**, 2905-2913. (Journal IF: 7.178, Citations: 45)

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. (Journal IF: 3.292, Citations: 44)

Sebastião AM, Ribeiro JA (2000) Fine tuning neuromodulation by adenosine. *Trends in Pharmacological Sciences (TIPS)* **21**, 341-346. (Journal IF: 9.064, Citations: 136)

Ribeiro JA & Sebastião AM (1987). On the role, inactivation and origin of endogenous adenosine at the frog neuromuscular junction. *J.Physiol.Lond* **384**, 571-585. (Journal IF: 4.764, Citations: 108) (due to *J.Physiol Lond* policy at the time, authors are by alphabetical order).

Ongoing Research Projects

Neuromodulation and Plasticity Group

National:

2010/2013 – Cross talk between neurotrophic factor receptors (TrkB) and adenosine A2A receptors: implications for amyotrophic lateral sclerosis (ALS). (PTDC/SAU-NEU/101752/2008). Coordinator: J.A. Ribeiro

2008/2011 – Membrane receptors and mediators involved in plastic changes induced by neuronal insults: implications for neuroprotection. (PTDC SAU-FCF 68607 2006). Coordinator: J.A. Ribeiro

2005/2010 - Interaction between endocannabinoids and adenosine in the hippocampus (FCT - POCTI/SAU-FCF/57973/2004). Coordinator: J.A. Ribeiro.

2005/2010 - Role of TrkB receptors in ageing (Gulbenkian Foundation JG/ N°. 0494). Coordinator: J.A. Ribeiro.

International:

2007/2010 – COST B30 European Science Foundation Action on Neural Regeneration and Plasticity (NEREPLAS).

2008/2010. 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 Camen Lluís (Univ Barcelona). A manuscript with data already obtained has been recently submitted to an international Journal, with shared 1st authorship and shared senior authorship (Lisbon and Bethesda):

The main objective of the research of the above projects is to understand how adenosine, released through specific bi-directional transporters from most cells, including neurones and glia, once in the extracellular space affects neuronal and glial functioning. The type of G-protein-adenosine coupled receptors (GPCR) that can inhibit (A(1)) or enhance (A(2A)) neuronal communication and/or neuron-astrocyte interactions are matter of on going investigation. How interactions between these high affinity adenosine receptors and other G-protein-coupled receptors can occur, and how they might contribute to a fine-tuning for neuronal functioning is presently under investigation in hippocampal slices and in models of nerve terminals (synaptosomes). By understanding the role of adenosine as a ‘fine tuner’ of the brain, one could predict how manipulations of adenosine receptors, with agonists or antagonists, can influence sleep and

arousal, cognition and memory, neuronal damage and degeneration. These actions might have therapeutic implications for neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, as well as for other neurological situations such as epilepsy, idiopathic pain or even drug addiction. As we consider adenosine as a fine-tuner, we hope then the study of their subtle effects, which promote the harmonization of the neurotransmitter actions, will contribute to understand some of the mechanisms involved in brain dysfunctions. So, our studies imply that whenever adenosine homeostasis is disrupted, pathology may be installed and selective adenosine receptor antagonism or agonism required.

Neuroprotection Group

National:

2011/2014 - Modulation of GABAergic transmission in the hippocampus by adenosine. (FCT, PTDC/SAU-NMC/110838/2009). Coordinator: Ana M Sebastião

2007/2010 – Trophic actions of neurotrophic factors: dependency of co-activation of A2A adenosine receptors. PTDC/SAU-NEU/64126/2006. Project coordinator: A.M. Sebastião. Other partner Institutions: Centro Neurociências de Coimbra (IP: Emília Duarte), Faculdade de Farmácia, Univ Lisboa (IP: Rui Silva)

International:

2009/2011 –Control of GABA transport in astrocytes. Collaborations with Rafael Franco, University of Pamplona, Carmen Dias, University of Barcelona, Spain, for detection of A1/A2A heteromerization, and with Ulrik Gether, University of Copenhagen, for evaluation of GAT-1 trafficking, and with F Conti, Univ Ancona, Italy) for visualization of GAT-1 in astrocytes. The project leader is the group in Lisbon, which performs all functional and most biochemical experiments. Interactions with other groups implied short stays of PhD students from Lisbon in Barcelona (S Cristovão-Ferreira), Copenhagen (S Vaz) and Ancona (S Cristovão-Ferreira) to use techniques available in those labs and need to solve specific questions in the project. Two manuscripts are being prepared with the data already obtained, the first and last authors being from the Lisbon group.

2009/2011 - Role of neuronal NF- κ B in synaptic transmission in the adult murine hippocampus. Collaborative project with Lesley Probert, Hellenic Pasteur Institute, Athens. This project is leadered by Athens, the role of Lisbon group being the synaptic transmission and plasticity experiments. It involved a short stay of a PhD student from Athens to Lisbon, to perform electrophysiological experiments.

2008/2011 – Modulation by adenosine of the BDNF synaptic influences, in collaboration with Detlev Boisson (Oregon) who developed mice strains over or under-expressing adenosine kinase, in collaboration with Bruno Franguelli (Warwick University, UK) for quantification of extracellular adenosine levels, in collaboration with Moses Chao (New York Univ, USA) to evaluate Translocation of TrkB receptors into lipid rafts by adenosine A2A receptors, and in Collaboration with Regeneron Pharmaceuticals (USA) that supplies BDNF. This project is leadered by the Lisbon group. A collaborative paper was published in 2010 (Assaife Lopes et al, see list of publications), and another MS to submit to an international Journal is in preparation, the first and last authors being from the Lisbon group.

2008/2010 – Mechanisms of neuroprotection by cytokines: interplay with adenosine. Collaborative project with Knut Biber (Groningen, presently in Freiburg, Germany), involving research done in parallel at Groningen University and at IMM in complementary techniques. This project is leadered by the group in Freiburg, the role of the Lisbon group being to do electrophysiological experiments. A collaborative work was published in 2010 (Moidunny, Dias et al, see list of publications)

2007/2010 - Regulation of Nicotinic alpha-7 receptor clusters on hippocampal neurons, in collaboration with Darwin Berg (Univ California, San Diego) involving 2 years stay of Catarina Fernandes (PhD student) in S. Diego. This project is leadered by the S Diego group, being in line with the goals of the PhD project of Catarina Fernandes. Two papers have been published in 2010 (see Fernandes et al and Campbell, Fernandes et al, in the list of publications)

2007/2010 COST B30 Action (EU): Neural Regeneration and Plasticity (NEREPLAS). This is a Concerted European Union Action, therefore mostly devoted to increase mobility within Europe, and involves several European countries, the chair being Delgado-Garcia, JM (Sevilla, Spain). A.M. Sebastião is the Chair of Neurobiology Group.

2007/2010 – Interplay between A1 receptors and CB1 receptors at the behavioural level, in collaboration with Judith Pratt and Rose Brett (Glasgow). Also in collaboration with the Neuromodulation and Plasticity Group and the Receptor Biology and Cognition Group. This project is leadered by the Lisbon group and it involved stays of a PhD student in Glasgow since the group in Glasgow has expertise in cannabinoid research *in vivo*. A collaborative paper has been published in 2010 (Sousa et al, see list of publications, the first and last authors being from the Lisbon group).

2008/2011 - Dopaminergic Plasticity in the Retina and its functional implications. Programa CAPES (Brasil)-GRICES (Portugal). Coordenador: Fernando Garcia de Mello, Rio de Janeiro. IP at IMM: A.M. Sebastião; IP at CNC, Coimbra: João Malva. Research will be done in parallel in the several institutions involved, using complementary techniques and sharing animal and cell models.

A main objective of most of the ongoing research projects listed above is to further investigate the molecular mechanisms involved in the interaction between BDNF and adenosine in the hippocampus, and its relevance for neuroprotection, neuronal proliferation and neurite outgrowth. Cross-talk between second messengers, direct protein-protein interactions and reorganization of receptor molecules in membrane microdomains is under evaluation. Another objective is to identify if the observed interaction between adenosine A_{2A} receptors and TrkB receptors is also extended to other actions of BDNF in neurones and glia. Attention is being paid to the actions of BDNF on synaptic plasticity and on glutamate and GABA turnover at nerve terminals as well as astrocytes and neurones. A project in collaboration with the University of Freiburg, Germany, aims to understand the upregulation of A1 adenosine responses caused by some, but not all, cytokines (released by glial cells). A project in collaboration with Universidade Federal do Rio de Janeiro e Centro de Neurociências de Coimbra aims to test the hypothesis that mice Muller cells in retina, if induced to a dopaminergic neuronal phenotype, can reinsert in damaged mice retinas, contributing to restore functional retinal circuits; our role at IMM is to monitor cell functionality, through electrophysiological techniques. More recently we focused upon the control of the inhibition/excitation balance, focusing upon the control of synaptic and extrasynaptic AMPA and GABA_A receptor function.

Receptor Biology and Cognition group

(2010-2013) Principal Investigator: Luísa Lopes - Role of the adenosine A2A receptors in chronic stress - implications for learning and memory (PTDC/SAU-NEU/099853/2008) 130 000EUR

(2010-2012) Co-Principal Investigator: Luísa Lopes – “Psychological indicators of stress reactivity and disease adaptation” – BIAL Foundation Fellowship 38 000 EUR

(2008-2011) Principal Investigator – Luísa Lopes - “Brain-gut interaction” – Project financed by Nestlé Research Center (Nestec/IMM/474/2008) 190 000 EUR

National and international collaborations

Nuno Sousa (ECVS, Universidade do Minho, Braga, Portugal)

Rodrigo A. Cunha (CNC, Coimbra, Portugal)

Jian-Fan Chen (Boston Univ, USA)

Christa Muller (Bonn Univ., Germany)

David Blum (INSERM, Lille, France) – INSERM/IMM cooperation programme

Michael Bader (Charitéand Max Delbrück Center for Molecular Medicine, Berlin, Germany)

Magalie Faure (Nestlé Research Center, Switzerland)

Regulation of Neuronal Death group

2008/present- Deciphering the role of A β toxicity in the loss of endogenous neuroprotection.
Coordinator: Maria José Diógenes

2008/present – Dysfunctional or compensatory enhanced plasticity upon ageing?

Inhibitory Synapses Group

2009/2013 - Characterization of glicineric neurotransmission in the hippocampus

Publications in peer review Journals

The publications, communications and other 2010 output initiatives by researchers from the groups of the Neurosciences Unit are listed together

Sousa, VC, Assaife-Lopes N, Brett RR, Ribeiro JA, Pratt JA, Sebastião AM. (2010) Regulation of hippocampal cannabinoid CB1 receptor actions by adenosine A1 receptors and chronic caffeine administration: implications for the effects of tetrahydrocannabinol on spatial memory. *Neuropsychopharmacology* Epub ahead of print (Journal IF: 6.993).

Sebastião AM, Assaife-Lopes N, Diógenes MJ, Vaz S, Ribeiro JA (2010) Modulation of brain-derived neurotrophic factor (BDNF) actions in the nervous system by adenosine A(2A) receptors and the role of lipid rafts.. *BBA Biomembranes*, Epub ahead of print (Journal IF: 4.180).

Dias R, Ribeiro JA and Sebastião A M. (2010) Enhancement of AMPA currents and GluR1 membrane expression through PKA-coupled adenosine A2A receptors. *Hippocampus*, Epub ahead of print (Journal IF: 3.913)

Fernandes CC, Berg DK, Gómez-Varela D (2010) Lateral mobility of nicotinic acetylcholine receptors on neurons is determined by receptor composition, local domain, and cell type. *J Neurosci.*, **30**, 8841-8851. (Journal IF: 7.178).

Assaife-Lopes N, Sousa VC, Pereira DB, Ribeiro JA, Chao MV, Sebastião AM (2010) Activation of adenosine A2A receptors induces TrkB translocation and increases BDNF-mediated phospho-TrkB localization in lipid rafts: implications for neuromodulation. *J Neurosci* **30**: 8468–8480. (Journal IF: 7.178, citations: 1)

Canas N, Breiac P, Soares P, Saraiva P, Calado S, Jordão C and Vale J (2010). The electroclinical-imagiological spectrum and long-term outcome of transient perictal MRI abnormalities. *Epilepsy Res* **91**, 240-252. (Journal IF: 2.479)

Moidunny S, Dias RA, Wesseling E, Sekino Y, Boddeke HWGM, Sebastiao AM, Biber K (2010). Interleukin (IL)-6-type cytokines in Neuroprotection and Neuromodulation: OSM, but not LIF, requires neuronal Adenosine A₁ Receptor function. *J Neurochem* **114**, 1667-1677. (Journal IF: 3.999)

Campbell NR, Fernandes CC, Halff AW, Berg DK (2010) Endogenous signaling through alpha7-containing nicotinic receptors promotes maturation and integration of adult-born neurons in the hippocampus. *J Neurosci* **30**, 8734-8744. (Journal IF: 7.178)

Diogenes MJ, Outeiro TF (2010) Neurotrophic Factors as a Protective Strategy in Parkinson's Disease. *CNS Neurol Disord DR* : **9**, 754-763. (Journal IF: 3.571)

Sebastião AM (2010) Adenosine and epilepsy-thinking beyond A(1) receptors. *Purinergic Signal* **6**, 1-2. (Journal IF: 2.870)

Costenla AR, Cunha RA, de Mendonça A (2010) Caffeine, adenosine receptors and synaptic plasticity. *J Alzheimer dis* **20**, 25-34. (Journal IF: 3.832)

Ribeiro JA and Sebastião AM (2010) Modulation and MetaModulation of Synapses by Adenosine. *Acta Physiol* **199**, 161-169. (Journal IF: 2.455)

Ribeiro JA and Sebastiao AM (2010) Caffeine and Adenosine. *J Alzheimer dis* **20**, 3-13. (Journal IF: 3.832).

Canas N, Soares P, Calado S, Calado S, Pestana R, Ribeiro C, Vale J (2010) Pathophysiology and Long-Term Outcome of Reversible Tumor-Like Lesions Induced by Presenting Status Epilepticus. *J Neuroimaging* **20**, 169-174. (Journal IF: 1.719)

de Carvalho M, Marcelino E, de Mendonça A (2010) Electrophysiological Studies in Healthy Subjects Involving Caffeine. *J Alzheimer Dis* **20**, 63-69. (Journal IF: 3.832)

Pousinha PA, Correia AM, Sebastião AM and Ribeiro JA (2010) Predominance of adenosine excitatory over inhibitory effects on transmission at the neuromuscular junction of infant rats. *J Pharmacol Exp Ther* **332**, 153-163. (Journal IF: 4.093, citations: 1).

Other publications International

Pedata F, Pugliese AM, Sebastião AM and Ribeiro JA (2010) Adenosine A₃ receptor signaling in the central nervous system. *A3 Adenosine Receptors from Cell Biology to Pharmacology and Therapeutics*, P.A. Borea (ed) . Springer Science+Business Media B.V.

Outeiro TF and Lopes LV (2010) Synaptic dysfunction in Parkinson's disease: from protein misfolding to functional alterations. In: *Protein folding for the synapse*, Ed by Wyttenbach and V. O'Connor, Springer, Chapter 13, 257 -267.

Other Publications National

Ribeiro J.A. (2010). Neuroética, a emergência de uma nova disciplina em neurociências. *Sinapse*, 40, 32-33

Invited Lectures and Seminars

Ribeiro JA, Triggering neurotrophic factor actions through adenosine receptors, Purines 2010 meeting, Tarragona, May, 2010

Sebastião AM, Revisiting A2A receptors and hippocampal excitability: implications for brain dysfunction, Purines 2010 meeting, Tarragona, May, 2010

Ribeiro JA, Triggering neurotrophic factor actions through adenosine receptors. EU COST B30 NEREPLAS, Carmona, June 2010.

Sebastião AM, Adenosine A2A receptors at the tripartite synapse: consequences for plasticity. EU COST B30 NEREPLAS, Carmona, June 2010.

Sebastião AM, Research possibilities for pre-graduate students at the Faculty of Medicine, University of Lisbon: over 10 years of experience with the GAPIC programme. Federation of European Biochemical Society Meeting, Gotenburh, July 2010.

Lopes LV, "Adenosine A2A receptors: implications in ageing and stress" – Lecture Program of the Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil, December 8, 2010.

Lopes LV, "Adenosine A2A receptors: implications in ageing and stress", II Neurosciences Symposium, Universidade Federal Fluminense, Niterói, Brasil, December 6, 2010.

Sebastião AM, Recording and modulating synaptic and action potentials at hippocampal neurons. VIII Encontro de Engenharia Biomédica, Lisboa, Novembro 2010.

Batalha V, Congresso Nacional de Psiquiatria, "Chronic stress models: Maternal Separation", Estoril, December 2010.

Sebastião AM, Caffeine and adenosine antagonism in the brain. Coffee, Caffeine and Sports Meeting. Faculdade de Motricidade Humana, Lisboa 2010

Ribeiro, Implementing Synergies in Biomedical Engineering: 'The Medical Perspective', IST, June 2010

Communications in International Conferences

Sebastiao A, Cristovao-Ferreira S, Dias RA, et al. (2010), Revisiting A2A receptors and hippocampal excitability: implications for brain dysfunction. *Purinergic Signalling* Volume: 6 Pages: 20-20 Supplement: Suppl. 1 Published: JUN

Moidunny S, Boddeke E, Dias R, et al. (2010), Interleukin-6-type cytokines in neuroprotection and neuromodulation: OSM, but not LIF, requires neuronal adenosine A1 receptor function. *Purinergic Signalling* Volume: 6 Pages: 111-111 Supplement: Suppl. 1 Published: JUN

Moidunny S, Dias R, van Calker D, et al. (2010), Interleukin-6-type cytokines in neuroprotection and neuromodulation: Oncostatin M, but not leukemia inhibitory factor, requires neuronal Adenosine A1 receptor function. Conference Information: 27th CINP Congress Meeting 2010, JUN 06-10, 2010 Hong Kong, PEOPLES R CHINA, *Int J. Neuropsychopharmacol* Volume: 13 Pages: 190-191

Sebastiao A, Barroso A . (2010), Research possibilities for pre-graduate students at the Faculty of Medicine, University of Lisbon: over 10 years of experience with the GAPIC programme. Conference Information: 35th Congress of the Federation-of-European-Biochemical-Societies, JUN 26-JUL Gothenburg, SWEDEN. *FEBS J.* Volume: 277 Pages: 29-29 Published: JUN 2010

Ribeiro JA, Triggering neurotrophic factor actions through adenosine receptors. *Purinergic Signalling*, Volume: 6 Pages: 29-29 Supplement: Suppl. 1 Published: JUN 2010.

Pousinha P, Correia AM, Sebastiao AM, Ribeiro JA Modulation of the rat neuromuscular transmission by adenosine upon ageing *Purinergic Signalling* Volume: 6 Pages: 102-102 Supplement: Suppl. 1 Published: JUN 2010

Pousinha P, Correia AM, Sebastiao AM, Ribeiro JA (2010) Neuromuscular transmission and ageing: the role of adenosine. Society for Neuroscience Meeting, San Diego, USA, November 2010.

Ribeiro FF, Neves-Tome R, Assaife-Lopes N, Ribeiro JA, Sebastiao AM . Adenosine A2A and BDNF TrkB receptors have independent roles upon neuronal maturation. *Purinergic Signalling* Volume: 6 Pages: 40-40 Supplement: Suppl. 1 Published: JUN 2010 **1st prize (best poster)**.

Rombo DM, Dias RA, Ribeiro JA, Sebastiao AM. Activation of adenosine A1 receptors inhibits extrasynaptic GABAergic currents in hippocampus. *Purinergic Signalling* Volume: 6 Pages: 104-104 Supplement: Suppl. 1 Published: JUN 2010

Batalha VL, Sebastião AM, Ribeiro JA, Lopes L.V. (2010) Modification of the levels of adenosine receptors in the rat hippocampus induced by maternal separation. *Purinergic Signalling* Volume: 6 Pages: 104-105 Supplement: Suppl. 1 Published: JUN 2010

Cunha-Reis D, Rodrigues NC, Ribeiro JA On the cellular and molecular pathways involved in the inhibition of LTP in the CA1 area of the hippocampus: *Journal of Molecular Neuroscience*: 42: 278. (Journal IF: 2.720)

Costenla, A. J. Vital, A. M. Sebastião, L. V. Lopes (2010) Maternal separation compromises LTP and spatial reference memory in aged rats, Society for Neuroscience Meeting, San Diego, USA, November 2010 - selected as hot topic in Neuroscience 2010 for the official SFN Press release

Vaz SH, Ferré S, Franco R, Ribeiro JA, Sebastião AM. Functional interactions between galanin and dopamine receptors: effects on acetylcholine release and synaptic transmission. Society for Neuroscience Meeting, San Diego, USA, November 2010.

Batalha VL, Valadas JS, Hockemeyer J, Müller CE, Sebastião AM and Lopes LV. The oral administration of an adenosine A2A receptor antagonist, to adult rats, reduces the learning deficits and anxious behaviour induced by maternal separation. FENS meeting, Amsterdam, The Netherlands, July 2010.

Rombo DM, Dias RA, Ribeiro JA, Sebastião AM. Extrasynaptic GABAergic currents in hippocampus are inhibited by adenosine A1 receptors. GABA Signalling and Brain Networks, Amsterdam, The Netherlands, 30 June – 2 July, 2010.

Rombo DM, Dias RA, Ribeiro JA, Sebastião AM. Inhibition of GABAergic extrasynaptic currents by adenosine A1 receptor activation in rat hippocampal neurons. FENS 2010, Amsterdam, The Netherlands July, 2010.

Aroeira RI, Ribeiro JA, Sebastião AM and Valente CA. Glycine receptor in rat hippocampus: changes in expression and subcellular localization over development. FENS 2010, Amsterdam, , July 2010.

Jerónimo-Santos A, Diógenes MJ, Ribeiro JA and Sebastião AM. Amyloid-beta induces changes in TrkB receptors expression: consequences for loss of neuroprotection by BDNF? FENS 2010, Amsterdam, The Netherlands, July 2010.

Sebastião AM, Neves-Tomé R, Diógenes MJ, Boison D, Ribeiro JA. Adenosine kinase activity determines tonic activation of adenosine receptors to trigger BDNF modulation of synaptic transmission. FENS 2010, Amsterdam, The Netherlands, July 2010.

Communications in National Conferences

Valadas, J. S., VL Batalha; Diógenes MJ, Sebastião AM and Lopes LV. Role of Adenosine A2A receptors in the neuroprotective effect of corticotrophin releasing factor (CRF). XVII Portuguese Biochemical Society Meeting, Porto, December 2010.

Duque do Vale, R, Lopes LV, Ribeiro JA, Sebastião AM, de Mendonça AV, Diógenes MJ. Detailing the age-related effects of memantine on long-term potentiation. Yes Meeting, September 2010.

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., YES meeting, Porto, Portugal, September 24-26, 2010 (Poster presentation). **1st Prize.**

Duque do Vale, R., Lopes, L.V., Ribeiro, J.A., Sebastião, A.M., de Mendonça, A., Diógenes, M.J. Efeito da memantina na Potenciação de Longa Duração do hipocampo, durante o envelhecimento, Enjoy med, Lisboa, Portugal, December 11-12, 2010 (Oral presentation). **Honours.**

Nogueira RM, Sebastião AM, Valente CA. Characterization of glycinergic transmission in primary hippocampal cultures - Potential role in epilepsy. Workshop GAPIC 2010, FMUL, December 2010.

Duque do Vale R, Diogenes MJ. Effect of memantine on rat hippocampal long-term potentiation upon ageing. Workshop GAPIC 2010, FMUL, December 2010.

Caetano A, Lopes LV and Vale MJ Impact of neonatal administration of a neurotrophic-factor enriched diet on rat development. . Effect of memantine on rat hippocampal long-term potentiation upon ageing. Workshop GAPIC 2010, FMUL, December 2010. (oral) **1st prize**

Organization of Conferences

Luísa Lopes - Since 2009 – Co-organizer of the IMM Neuroscience Seminar Series (NeuroSeS). The goal of these seminars is to invited world experts in the field of neuroscience in order to promote connections with the IMM groups and the students

Ribeiro, J A, member of Scientific Committee of PURINES 2010 meeting (Terragona).

Sebastião AM, member of Scientific Committee of PURINES 2010 meeting (Terragona).

Sebastião A.M, Head of the Working group on Neurobiology and organizer of a session in COST B30 on Neuronal Plasticity, Bilbao.

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, follows:

With joint papers published in 2010

Moses Chao (Univ New York, USA). 1st and senior authorship from Lisbon

Knut Biber (Univ Groningen, presently in Freiburg). 1st and senior authorship from Groningen

Darwin Berg (Univ California, San Diego). 2 papers; senior authorship from San Diego; one paper with 1st authorship from Lisbon.

Judith Pratt and Rose Brett (Strathclyde Univ, Glasgow). 1st and senior authorship from Lisbon

With joint manuscripts submitted to International refereed Journals

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

Eero Castrén (Helsinki Univ) and H. Tanila (Univ Kuopio) – 1st and senior authorship from Kuopio.

With joint manuscripts under preparation to be submitted soon

Rafael Franco (Univ Pamplona), Carmen Lluís (Univ Barcelona) and Francis Conti (Univ Ancona, Italy). 1st and senior authorship from Lisbon

Ulrik Gether (Univ. Copenhagen). 1st and senior authorship from Lisbon

Detlev Boison (Oregon, USA), Bruno Franguelli (Warwick University, UK). 1st and senior authorship from Lisbon

Other international collaborations running (see project descriptions for details)

L Probert, Hellenic Pasteur Institute, Athens

Jian-Fan Chen (Boston Univ, USA)

Christa Muller (Bonn Univ., Germany)

David Blum (INSERM, Lille, France) – INSERM/IMM cooperation programme

Michael Bader (Charité and Max Delbrück Center for Molecular Medicine, Berlin, Germany)

Magalie Faure (Nestlé Research Center, Switzerland)

Lori Wetmore (Univ Wisconsin)

2. The Unit often **invites foreign speakers** to give seminars/discuss projects/scientific achievements. A list of those invited in 2010 follows:

David Blum (INSERM, Lille)

Roberto Paes de Carvalho (Univ Niteroi, Brasil)

Juan Carlos Arévalo (Univ Salamanca)

Michael A. Schwarzschild (Harvard, USA)

Sergi Ferré (Bethesda, USA)

3. PIs of the Unit quite often go abroad to **give seminars/discuss projects/scientific achievements**, namely:

A.M. Sebastião to Univ Pamplona

AM Sebastião to Univ Leipzig

LV Lopes to Nestlé Research Center

LV Lopes to Center for Molecular Medicine, Berlin

LV Lopes to Univ Rio de Janeiro

LV Lopes to Univ Niteroi

MJ Diogenes to Nestlé Research Center

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 2010 follows:

Sofia Cristovão-Ferreira to Univ. Ancona, Italy

Daniela Calçada to Univ Wisconsin, USA

Vasco Sousa to Strathclyde Univ, Glasgow

Raquel A Dias to attend an intensive two weeks practical international workshop on the Microelectrode Techniques, Plymouth, UK.

5. The Master and PhD project in Neurosciences, co-coordinated by Unit members, belongs to the **European Network of Neuroscience Schools**.

6. 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*

Ribeiro, J.A. – Member of the Scientific Programme Committee of the Purines 2010

Ribeiro, J.A. – IP selection for CNC, Univ Coimbra.

Ribeiro, J.A. President Jury of Mastercourse Neuroscience Thesis at FMUL

Ribeiro, J A. – External evaluator of scientific proposals for the European Science Foundation (ESF) and Wellcome Trust, U.K.

Ribeiro, J A. – Rapporteur for the EMRC (ESF)

Sebastião, A.M.- Member of the Editorial Board and Handling Editor of the *Journal of Neurochemistry*; Total number of manuscripts handled (since 2001): 391; number of manuscripts handled in 2010: 32.

Sebastião, AM – Member of the Editorial Board of *European Journal of Pharmacology*

Sebastião, A.M. – Member of the Editorial Board of *Purinergic Signalling*.

Sebastião, A.M. – Coordinator Committee of the PhD/Master course in Neurosciences, Faculdade de Medicina, Universidade de Lisboa.

Sebastião, A.M. – Coordinator Committee of the PhD/Master course in Cognitive Sciences, Universidade de Lisboa.

Sebastião, A.M. – Coordination at Faculdade de Medicina (FMUL) of the Biomedical Engineering (Basic and Master course), a degree running jointly at FMUL and Instituto Superior Técnico (IST)

Luisa V. Lopes - Member of the Board of SPN (Sociedade Portuguesa de Neurociências) since May 2007.

Members of the Group acted as reviewers of papers submitted to:

J Neuroscience (*J.A. Ribeiro*)

European Journal of Pharmacology (*J.A. Ribeiro*)

Neuroscience (*J.A. Ribeiro*)

Eur J Neurosci (*J A Ribeiro*)

BBA (*J.A. Ribeiro*)

Sebastião AM acted as reviewer of projects submitted to Neurological Foundation New Zealand

Luísa Lopes acted as referee for the journals:

- Journal of Alzheimer's Disease
- European Journal of Neuroscience
- Brain research
- Journal of Neurochemistry
- Cerebral cortex
- Pharmacology & Toxicology

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: 'Celular 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 Sciences, UL; organizer of the block: Neurosciences, October-December 2010.

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

Cunha-Reis D. Co-coordinator of the Neurochemistry course at the Medical Biochemistry Master, FCUL

Lopes LV - Adenosine A2A receptors as therapeutic targets in brain disorders - Harvard Medical School-Portugal Workshop: Molecular Mechanisms in Neurodegeneration: From Molecule to Cures, Sesimbra, July 2010.

Lopes LV. Molecular Mechanisms of Memory - Harvard Medical School-Portugal Workshop: Molecular Mechanisms in Neurodegeneration: From Molecule to Cures, Sesimbra, July 2010

Sebastião AM. Neuromodulation and neurotrophins - Harvard Medical School-Portugal Workshop: Molecular Mechanisms in Neurodegeneration: From Molecule to Cures, Sesimbra, July 2010.

Valente CC. Modulation of glycinergic transmission in hippocampus - function in epilepsy. Neuroscience Seminars, January 2010.

Pousinha P. Net Modulation of adenosine A1/A2A receptors of the neuromuscular transmission upon ageing. Neuroscience Seminars, February 2010.

do Couto FS. Depression as a risk factor for dementia. Neuroscience Seminars, February 2010

Ribeiro JA. Writing and reading Scientific papers. Neuroscience Seminars, March 2010.

Dias RA. AMPA receptors and adenosine: together in sickness and in health. Neuroscience Seminars, April 2010.

Assaife-Lopes N. The role of lipid rafts in the cross-talk between adenosine A2A and TrkB receptors. Neuroscience Seminars, April 2010.

Diógenes, MJ. Increased LTP: Friend or enemy? Neuroscience Seminars, May 2010.

Cristovão-Ferreira S. Striatal circuits and movement control. Neuroscience Seminars, May 2010.

Jerónimo-Santos A. Amyloid-beta induces changes on TrkB receptors levels: a contribution for neuronal death? Neuroscience Seminars, May 2010.

Rombo DM. Adenosine as a modulator of inhibitory transmission in the hippocampus: from neurons to interneurons. Neuroscience Seminars, June 2010.

Batalha V. Involvement of adenosine A2A receptors in the stress induced impairments of rat hippocampal function. Neuroscience Seminars, September 2010.

Rocha M. The synaptic transmission and its modulation by adenosine in the SOD1G93A transgenic mice model of amyotrophic lateral sclerosis. Neuroscience Seminars, September 2010

Lopes LV. Adenosine A2A receptors in the hippocampus: implications in ageing and stress. Neuroscience Seminars, September 2010

Dias RA. Course report: Microelectrode techniques for Cell Physiology. Neuroscience Seminars, October 2010.

Luís C. Characterization of glycinergic transmission in primary cultures of hippocampus: potential role in epilepsy. Neuroscience Seminars, November 2010.

Silva A. Calcium signalling modulation in astrocytes by adenosine receptors. Neuroscience Seminars, November 2010.

Calçada D. The role of lithium on apoptotic cell death induced by amyloid-beta peptide. Neuroscience Seminars, November 2010.

Valadas, J. Role of adenosine A2A receptors in the neuroprotective effect of corticotrophin release hormone (CRH). Neuroscience Seminars, November 2010.

Ribeiro JA. Neurosciences of ethics and ethics of Neurosciences. Master and PhD Programmes in Neurosciences, January 2010.

Sebastião AM. Neuronal organization and neuronal excitability, Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October 2010.

Sebastião AM. Main molecules involved in neuronal excitability, Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October 2010.

Sebastião AM. Inhibitory and excitatory synaptic transmission. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October 2010.

Diogenes MJ. Synaptic plasticity and neurotrophic factors. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, October 2010.

Sebastião AM. Research facilities on Basic Neurosciences at CAML. Master and PhD Programmes in Neurosciences, October 2010.

Rombo D. Evaluation of synaptic activity through electrophysiological recording techniques; modulation of GABAergic currents. Master and PhD Programmes in Neurosciences, October 2010

Dias RA. Modulation of AMPA receptors by a G-protein coupled receptor. Master and PhD Programmes in Neurosciences, October 2010.

Cristovão-Ferreira S. Modulation of GABA transport in nerve terminals and astrocytes. . Master and PhD Programmes in Neurosciences, October 2010.

Ribeiro JA. Cell and molecular mechanisms of drug dependence. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, November 2010.

Lopes LV. Corticoids, stress axis, alterations in synaptic plasticity and in behavior. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, November 2010.

Batalha V. Corticoids, stress and neuromodulation by adenosine. Master and PhD Programmes in Neurosciences, Master and PhD Programmes in Cognitive Sciences, November 2010.

Ribeiro JA. Models and main circuits affected in neurodegenerative diseases. Master and PhD Programmes in Neurosciences, November 2010.

Vaz S. Calcium signalling in astrocytes; implications for neuronal communication. Master and PhD Programmes in Neurosciences, November 2010.

Valente C. Imaging of single molecules by immunofluorescence. Master and PhD Programmes in Neurosciences, November 2010.

Jerónimo-Santos A. Beta-Amyloid peptide, neurotrophins and neuronal death. Master and PhD Programmes in Neurosciences, November 2010.

Aroeira R. Glycine receptors and glycinergic synapses during synapse maturation Master and PhD Programmes in Neurosciences, November 2010.

Sebastião AM. Neuron and glial cells. Master in Medical Biochemistry, FCUL, February 2010.

Sebastião AM. Basic rules for the interaction between ligands and receptors Master in Medical Biochemistry, FCUL, February 2010.

Sebastião AM. Principles of neuronal excitability. Master in Medical Biochemistry, FCUL, March 2010.

Cunha-Reis D. Synaptic Transmission. Master in Medical Biochemistry, FCUL, March 2010.

Valente C. Fluorescence microscopy techniques for nervous system research. Master in Medical Biochemistry, FCUL, March 2010.

Dias RA. Microelectrophysiological Techniques. Master in Medical Biochemistry, FCUL, March 2010.

Lopes LV. Main neurotransmitters and their receptors. Master in Medical Biochemistry, FCUL, April 2010.

Lopes LV. Signalling pathways, Master in Medical Biochemistry, FCUL, April 2010.

Cunha-Reis D. Synaptic Plasticity Plasticidade sináptica. Master in Medical Biochemistry, FCUL, April 2010.

Sebastião A. Neuromodulation and co-transmission. Master in Medical Biochemistry, FCUL, April 2010.

Ribeiro. JA. Mechanisms of Drug Addiction. Master in Medical Biochemistry, FCUL, April 2010.

Vaz S. Modulation of neurotransmitter transporters by neurotrophins. Master in Medical Biochemistry, FCUL, April 2010.

Diogenes MJ. Neurotrophic Factors Factores neurotróficos. Master in Medical Biochemistry, FCUL, April 2010.

Cristovão-Ferreira S. Modulation of neurotransmitter transporters by adenosine. Master in Medical Biochemistry, FCUL, April 2010.

Cunha-Reis D. Mechanisms of Neuronal Degeneration and Death. Master in Medical Biochemistry, FCUL, May 2010.

Mendonça A. Neurodegenerative Diseases. Master in Medical Biochemistry, FCUL, May 2010.
Cunha-Reis D. Plastic changes in neurodegenerative diseases. Master in Medical Biochemistry, FCUL, May 2010.

Lopes LV. Stem cells, neurogenesis and neuronal repair. Master in Medical Biochemistry, FCUL, May 2010.

Ribeiro JA. Neuroethics. Master in Medical Biochemistry, FCUL, June 2010.

Lopes LV. Animal models in brain research. Master Programme in Bioethics, FMUL

Sebastião AM. Electrophysiological Techniques. Master in Physics, Instituto Superior Técnico, March 2010.

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 2010.

Sebastião AM. Pharmacodynamics. Master in Cardiovascular Techniques, Escola Superior de Tecnologias da Saúde, January 2010.

Diogenes MJ. Pharmacokinetics. Master in Cardiovascular Techniques, Escola Superior de Tecnologias da Saúde, January 2010.

Ribeiro, J.A. Lecture on The Toxic effects of Psychopharmacological Agents in the Mastercourse in Legal Medicine and Forensic Sciences

Cristovão-Ferreira S. A1R-A2AR heteromers modulate GABA uptake by astrocytes IV IMM PhD Student meeting, November 22, 2010

Dias RA Endogenous AMPA receptor modulation by A2A adenosine receptors impacts synaptic plasticity. 4th IMM PhD Student Meeting, IMM, Lisbon, Portugal, November 22-24, 2010.

Rombo DM. Extrasynaptic GABAergic currents are inhibited by adenosine A1 receptors in rat hippocampus. IMM PhD Students Meeting, Lisbon, Portugal, November 22-24, 2010.

Dias RA. Postsynaptic modulation of AMPA receptors by Gs-coupled adenosine A2A receptors: implications for synaptic plasticity. Lisbon Area Neuroscience Meeting, IMM, Lisbon, Portugal, November 22-24, 2010.

Sousa, V. Regulation of Cannabinoid effects by A1 receptors and caffeine: implications for spatial memory. Clinical Neurology Meeting, July 2010.

Science and Society

Luísa Lopes with Paula Pousinha - March 2010 – Co-coordinators of the actions of the Brain Awareness Week in Lisbon (FMUL). Organizer of the IMM Brain Awareness Week Open day to High School students.

- Institute of Molecular Medicine open day – The Institute was open on March 20th to visits from high schools. The students participated on «hands on activities» coordinated by investigators from the Neurosciences Unit.
- Seminars and round-tables related to brain issues, held in schools and other institutions, by neuroscience researchers. Lectures, workshops and interaction between scientist and high school students were promoted.

Lectures and sessions to a broad audience:

Diógenes, MJ – “O envelhecimento neuronal” - Palestra no Club Setubalense, April 2010.

Visits to Basic and Secondary Schools during Brain Awareness Week

Members of the Neurosciences Unit went to the following Basic and High Schools, who applied to have a session on the Brain to their students. Total Number of participants: 1690 people. Activity coordination: Luísa V. Lopes and Paula A. Pousinha

Grade	School	Localization	Investigator
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EB	Jacques Magalhães	Alverca	Vânia Batalha e Diogo Rombo
EB	Colégio José Álvaro Vidal	Alverca	Vânia Batalha e Diogo Rombo
ES	M. ^a Amália Vaz de Carvalho	Lisboa	Paula Pousinha
ES	Rainha D. Leonor	Lisboa	Luísa Lopes
ES	Colégio Manuel Bernardes	Lisboa	Cláudia Valente
ES	Colégio S. Miguel	Fátima	Frederico Couto
ES	Sebastião e Silva	Oeiras	Ana Sebastião
EBS	Isidoro de Sousa	Viana do Alentejo	Maria José Diogenes

Participation of the Unit at the IMM open day “hands on activities”: «O que é que te passa pela cabeça?». Activity coordination: Luísa V. Lopes and Paula A. Pousinha

The Institute of Molecular Medicine was open on 20th march to visits from high schools. This activity, coordinated by investigators from the Unit of Neurosciences, also involved researchers from the following IMM units: UNCM, UBD, BIU, CTU.

Investigators of the Unit Involved	Participating Schools
Luísa V. Lopes Paula Pousinha Cláudia Valente M. ^a José Diógenes Diogo Rombo Rita Aroeira Vânia Batalha André Santos Sofia Ferreira Sandra Vaz Ana Filipa Ribeiro Raquel Dias	ES Dr. Azevedo Neves – Amadora ES Maria Amália – Lisboa Colégio N Senhora Fátima ES Domingos Sequeira – Leiria ES Sebastião e Silva- Oeiras EP Gustave Eiffel – Lumiar ES Henriques Nogueira - Torres Vedras

The activity was sponsored by ZEISS (Eng.^a Laura Machado). Total number of people involved: 33 researchers, 235 students and 17 teachers.

Thesis completed

PhD Thesis

Natália Assaife-Lopes, (2010). Molecular Interactions Between Neurotrophins and Adenosine Receptors at Neuronal Plasma Membranes, Faculdade de Medicina da Universidade de Lisboa. – Supervisor: A. M. Sebastião

Gomes C.A. (2010) Neurotrophic Factors Modulation by Adenosine Receptors and Dopamine Release in the Rat Striatum. Faculty of Medicine, University of Lisbon, Supervisor: J. A. Ribeiro January 2010.

Vasco C Sousa (2010). Cross-talk mechanisms between adenosine and cannabinoid receptors: implications for the effects of Δ^9 -tetrahydrocannabinol on spatial memory. Faculdade de Medicina da Universidade de Lisboa. –Supervisors: A. M. Sebastião and Rose Brett.

Master Thesis

Ribeiro A.F. (Medical Biochemistry MSc) – Modulation of Neuronal Maturation: Influence of Neurotrophic Factors and Neuromodulators. November 2010, Faculty of Sciences Lisbon, Supervisor: A. M. Sebastião

Cruz, A. (Medical Biochemistry MSc) - The influence of epilepsy in synaptic plasticity in the hippocampus: neuroprotective role of VIP and its receptors, November 2010, Faculty of Sciences Lisbon, Supervisor: D. Cunha-Reis.

Figueiredo J V (Neurosciences MSc) – Efeito da Separação Maternal na Memória Dependente do Hipocampo de Rato, April 2010, Faculty of Medicine Lisbon, Supervisor: L.V. Lopes.

Valadas J. (Medical Biochemistry MSc) - Role of Adenosine A2A Receptors In the Neuroprotective Effect of Corticotrophin Releasing Hormone (CRH), October 2010, Faculty of Sciences Lisbon, Supervisor: L.V. Lopes.

Facilities and Support

Alongside with 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 and a Histology Service. All Resource Units have dedicated staff that provides support to IMM community and to develop initiatives that promote research.

Management	Margarida Pinto Gago, Manager
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

Management Unit

Major Objectives

The Management Unit is responsible for the overall IMM legal, human resources, administrative, and financial issues. It covers, mainly:

- Accounts and budget management – all activities to assure the preparation of IMM statutory accounts and tax returns; cost accounting per project/activity and overall budget control – for Research Projects, Facilities, Support Units and Management;
- Project management and reporting - contractual, administrative and financial aspects of research projects, from the moment of funding approval to the date of project termination;
- Human resources - all tasks associated to new appointments, individual files updating and contracts termination (advertising, selection, contracts preparation, all legally and internal registrations).
- Legal support – to researchers, namely intellectual property issues and consortium agreements; all types of contracts (funding, HR, suppliers, scientific collaborations, MTA, etc)
- Scientific protocols management – current support and updating
- Quality Management System
- 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
Sandra Duarte	Accounts and Projects Manager
Ana Marcelino	Accounts
Inês Bernardes	Accounts (left in June 2010)
Ricardo Pereira	Accounts (joined in August 2010)
Vera Rego	Accounts
Isabel Roque	Special projects
Maria José Antunes	Projects management
Andreia Vaz	Projects management
Filipa Aperta	Projects management (11-1 to 30-6-2010)
Mónica Vieira	Projects management (joined in July 2010)
Cláudia Soeiro	Front desk(left in September 2010)
Cristina Costa	Front Desk (joined in August 2010)
Patrícia Cúcio	Board of Directors Secretary

Keywords/Areas

Human Resources;
Accounts and budget control;
Project Management;
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 mostly, by Dr. André Fialho, as legal support for IMM.

Improvements were made to the finance and management software and internal databases to enable greater interaction between different areas and give better access to information by different support areas. Also the new module to facilitate the preparation of periodic project reporting was improved.

Revision of internal cost accounting model for FCT projects reporting

Quality Management System was re-launched, with the support of the Lab Management Unit, aiming effective completion in 2011

Organization and participation in periodic meetings with IMM Board and the other support units for a better common and coordinated response to researcher's issues.

Launch of Management Unit intranet area

Laboratory Management Unit

Major interests / Objectives

The Lab Management mission is the maintenance and safety of the institute's infrastructures and equipments, in order to ensure high standards of usability and quality to all research units.

It is responsible for the Purchasing Office, Washing Room and for the supply of carbon dioxide, dry ice, liquid nitrogen; the management of chemical products; the design of new laboratory infrastructures, the development of standard operating procedures and the implementation of good health and safety practices in work, according to the National Legislation.

The PO, which includes the Supply Center and Internal Storehouse, is responsible for all institute acquisitions (products, services and equipments), including import / export services and provides information on prices, ongoing promotions, new products and delivery conditions.

The WR provides researchers with clean and sterilized material and it is equipped for the preparation and sterilization of all types of materials and solutions.

Head of Unit

Alexandra Maralhas – Degree in Biotechnology Engineering

Luís Moita, MD – University of Lisbon –Scientific Adviser

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, FML
Edna Gomes	Washing Room technician, FML
Aida Barros	Washing Room technician (started July 2010)
Carlos Curado	Washing Room technician (started July 2010)

Keywords/Research Areas

Infrastructure and equipments maintenance

Health and Safety

Laboratory Design

Purchases

Major scientific achievements

The Intranet System developed to become the default supplier of information, with procedures of equipment and safety in the lab, updates on prices and new products in the PO. This, coupled with the effort to increase the support and interaction with all research and support units, led to a

Helpdesk system that contributed to a faster response to situations and allowed the tracking of all communications between the unit and the researchers in IMM.

We have followed a preventive maintenance policy, with maintenance contracts and several inspections for the equipment's and better rules and procedures for the people. This policy, coupled with rounds of the building for the assessment of conditions, allowed for a better overview of all material. We helped with the repair of all equipments, contacting the technicians and following up with ways to minimize the downtime for the researchers. We are now further implementing the Quality Management System in IMM, according to ISO 9001. Meetings were carried out with the Faculty, allowing for the assessment of technical feasibility and level of safety of the units in the building.

Advanced teaching

Maralhas, A. lectured a theoretical session for the BLS3 course “Biosafety training for use of the IMM BSL3 Facility”, Instituto de Medicina Molecular, Lisboa, October 27-28, 2010.

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 2011, the projects will mainly focus on IMM Infra-Structure and Information Workflow.

Head of Unit

Maria do Carmo Fonseca, PhD – Full Professor, FML

Team

Daniel Silva	PhD Fellowship, IMM
Pedro Eleutério	Training Fellowship, IMM
Ruben Alves	Technician, IMM (left August 2010)
Daniel Guerreiro	Technician, IMM
Emanuela Simões	Technician, IMM (started December 2010)

Research/Service Areas

Information Systems
Databases
Computer Network maintenance
Helpdesk

Ongoing Projects

1. IMM Information System. Objectives: integration of IMM databases whenever useful for data coherence and productivity; simplifying routine tasks and processes.
2. Implementation of an Enterprise Content Management System
3. Implementation of a Backup System for IMM data

4. Increasing Data Storage Capacity for IMM
5. Implementation of an automatic Self-Testing System for accessing Infra-Structure performance

Major achievements

1. IMM Website was substantially improved, in terms of speed and navigation;
2. An electronic registering system was developed and is now in use, reducing register time for new IMM members and creating automatic Human Resources input for IMM Information System;
3. Data Storage System was delivered to IMM and is now in use.

Communication and Training Unit

Major interests / Objectives

Institutional Communication

- Promote IMM corporate image, nationally and internationally
- Public relations support
- Build on internal communication
- Dissemination of information
- Place IMM and Portuguese Science in the media agenda

Science Communication

- Promote two-way dialogue between researchers and audiences
- Establish partnerships with key players

Advanced Training

- CAML PhD Programme Executive Coordination
- Support to IMM PhD Students and their activities
- Promote advanced training initiatives at IMM

Science funding

- Foster an environment for additional science funding
- Provide information on funding opportunities
- Support grant application and negotiation

Transversal activities

- Promote an integrated approach to science communication, training and funding
- Support to IMM Direction and IMM events
- Foster networking with partner institutions

Head of Unit

Marta Agostinho, PhD, University of Lisbon, Staff Scientist Ciência 2008

Principal Investigators

Margarida Trindade, PhD, University College London, Staff Scientist Ciência 2007

Inês Crisóstomo, PhD, Univ. Nova de Lisboa/The Rockefeller Univ., Staff Scientist Ciência 2008

Research Team

Joana Costa, PhD	BGCT Fellowship, FCT
Cheila Almeida, MsC	Communication Assistant, IMM Fellowship (left June 2010)
Ana Catarina Rebelo, MsC	Communication Assistant, IMM Fellowship
Sandra Moreira, MsC	Communication Assistant, IMM Fellowship (since July 2010)

Keywords/Research Areas

Institutional communication
Science communication
Advanced training
Grant management and funding

Major scientific achievements

Communication

Production of materials (IMM reports, folders, bookmarks); website development (expansion of intranet, training for editors)
Consolidation of dissemination (51 editions of IMM newsletter; mailing lists development)
Increased IMM presence in media (total:758 ;17 press releases)
Launching of IMM in social networks (Facebook, LinkedIn, Twitter)

Funding

Expansion of information on opportunities (436 updated entries online; weekly releases; 8 briefing sessions)
Survey on funding service (positive outcome)
Individual support (270 email requests, 72% increase from 2009)
Recorded 44 national and 48 international proposals; 8 contract negotiations concluded

Training

CAML PhD programme implementation
Strengthening activities for PhD Students (new nanocourses, successful evolution of onboard talks to Pizza Seminar, open day for candidates)

Transversal

Networking/internationalization (e.g. FincaPé meetings launch)
Organization of events (e.g., SAC Immunology, Award Ceremonies, PI Retreat, Feedback Facilities)

Ongoing Projects

2009/2010 LiveAlife, QREN, Coordinator: Pedro Pinto, Take the Wind. PI: Margarida Trindade and Marta Agostinho, €5000 (IMM)

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. Participants: Marta Agostinho and Margarida Trindade. FP7-PEOPLE-2009-IRSES, €73800 (total €181800)

Other publications International

Almeida, C., Xavier, J., Domingues, I. and Agostinho, M. “Workshop *Science, Politics and the media*: an initiative to trigger science in the public agenda”, Proceedings of the 11th International Conference on Public Communication of Science and Technology (PCST-2010), 728-733.

Invited Lectures and Seminars

Agostinho, M. “Communicating science as a professional career”, Symposium Careers in Science, Porto, Portugal, June 17, 2010 (invited speaker).

Agostinho, M. “Disseminating science in Portugal”, Encontro com a Ciência e a Tecnologia em Portugal, Lisbon, Portugal, July 4-7, 2010 (invited speaker).

Agostinho, M. Chaired the session “Dialogical Approaches in science communication”, 11th International Conference on Public Communication of Science and Technology, New Delhi, India, December 4-10, 2010.

Crisóstomo, I. “Round table: I've got a PhD. Now what?”, 1st ITQB PhD Students Meeting. Oeiras, Portugal, October 22

Trindade, M. Science is fun...ding. 15th Anniversary of the Curia Meetings, Curia, Portugal December 27 and 28, 2010 (invited speaker).

Communications in International Conferences

Agostinho, M. “Workshop *Science, Politics and the media*: an initiative to trigger science in the public agenda”, 11th International Conference on Public Communication of Science and Technology, New Delhi, India, December, 4-10, 2010 (oral presentation)

Communications in National Conferences

Trindade, M. Science Funding and Philantropy services at Rush University Medical centre in Chicago, FincaPé Meetings, Lisbon FincaPé Meetings, IMM, Lisbon Portugal, April 20, 2010 (oral communication)

Crisóstomo, I. Meeting report “ORPHEUS 5th Conference: The Advancement of European Biomedical and Health Science PhD Education by Cooperative Networking”, Associação Viver a Ciência, Lisbon, Portugal, June 16, 2010 (oral communication)

Trindade, M. Applying for Grants. Workshop on Molecular Mechanisms in Neurodegeneration: from molecules to cures, Portugal-Harvard Medical School Program, Sesimbra, Portugal, July 15-21, 2010 (oral communication)

Agostinho, M. Inquiry –based learning e o papel dos instutos investigação, FincaPé Meetings, ITQB, Oeiras, Portugal, September 8, 2010 (oral communication)

Costa , M. Serviços de procura de financiamentos - uma boa opção em Portugal?, FincaPé Meetings, Inst. Superior Técnico, Lisbon, Portugal, November 10, 2010 (oral communication)

Organisation of Conferences

Agostinho, M. coordinator of “FincaPé Meetings”, series of science communication and science management meetings for professionals of the Lisbon metropolitan area, held every two month since April 2010.

Agostinho, M. and Almeida, C. co-organized the Workshop “Science, Politics and the Media” for researchers, journalists and policy makers. Fundação Calouste Gulbenkian, Lisbon, Portugal, April 25, 2010.

Agostinho, M. co-organized the meeting “HIV/AIDS: closing the gap between basic research and clinical practice”, IMM, Lisbon, January 22-23, 2010.

Crisóstomo, I. organized “Open Day for PhD Candidates”, IMM, Lisbon, May 14, 2010

Crisóstomo, I. co-organized the meeting “IV IMM PhD Students Meeting”, IMM, Lisbon, November 22-23, 2010.

Internationalization

UCOM has a high degree of internationalization ranging all areas of activity. We have participated in an international internship programme for research managers, co-organized by the European Association of Research Managers and Administrators and the National Council of University Research Administrators. Under this programme, M. Trindade carried out a two week internship at Rush University Medical Centre, Chicago, Illinois (21 March to 4 April, 2010), and hosted Beth Seaton at IMM. Beth Seaton is the Director of Sponsored Projects at Western Illinois University, US. Furthermore, M. Trindade attended the 16th EARMA Conference “*Grand Challenges in Research Management and Administration in Europe*” at the University of Ljubljana (20 - 23 June, 2010) and is currently a member of this association.

We are involved in outreach initiatives from FEBS (the Federation of the Societies of Biochemistry and Molecular Biology), where M. Agostinho is an elected member of the Science and Society Committee and from the European Commission, where M. Trindade has acted as expert evaluator under the programmes People (Researcher’s Night) and Capacities (Science in Society).

We have participated at the International Public Communication of Science & Technology Conference in New Delhi, India. M. Agostinho presented an UCOM science communication project and chaired a session at this meeting. UCOM’s participation on the project “MEMPEPACROSS - Membrane-active peptides across disciplines and continents” (Marie Curie Action) entangles activities of science communication and management. In 2010, we co-organized with Mauricio Luz from Fiocruz in Brazil a science communication activity for secondary students called “Bioquímica de Portas Abertas” at the National biochemistry meeting, held in Porto (14-18 December, 2010. in addition, Inês Crisóstomo participated in ORPHEUS 5th Conference on the Advancement of European Biomedical and Health Science PhD Education by Cooperative Networking in Vienna, Austria (April 8-10, 2010).

Prizes, honours and awards

Agostinho, M. Elected member of the 2010/2012 FEBS Science and Society Committee.

Advanced teaching

Trindade, M. Co-organizer and Lecturer of the course “Preparing for Research”, Doctoral Programme for Physicians of Fundação Calouste Gulbenkian, Portugal, March 1-4, 2010

Agostinho, M. Organizer and lecturer of the Course “Interacting with different publics”, IMM PhD Programme, Portugal, September 28-29, 2010

Trindade, M. Lecturer of “Getting Funded” at course “Managing your research & Getting funded”, PhD Programme of the Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Portugal, October 21-26, 2010

Trindade, M. Lecturer of “Grant Writing” at course “Presenting your research: from bench to peers”, IMM PhD Programme, Portugal, October 28-29, 2010

Agostinho, M. Lecturer of “Communicating to your peers: Dissemination and impact” at course “Presenting your research: from bench to peers”, IMM PhD Programme, IMM, Lisbon, Portugal, October 28-29, 2010.

Crisóstomo, I. Lecturer of “Managing your research” at course “Managing your research & Getting funded”, PhD Programme of the Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisbon. October 21-26, 2010

Crisóstomo, I. Organizer and Lecturer of course “Presenting your research: from bench to peers”, IMM PhD Programme, IMM, Lisbon. October 28-29, 2010

Science and Society

2010 Artistic Residency of Herwig Turk at IMM - Ciencia Viva programme of artistic residencies. Scientific Tutor: Marta Agostinho

Programme of school visits to IMM/IMM to schools: a total of 385 students from all levels of schooling, most particularly secondary school, engaged in school visits to IMM or IMM researchers to school, co-organized by UCOM.

IMM at Science and Technology Week – organization of “Cientistas Online”, an initiative where IMM researchers and non scientists interacted online in real time through Facebook, November 22-26, 2010.

Agostinho, M. and Almeida, C. participated in the organization of the IMM neuroscientists open day during the Brain Awareness week, IMM, March, 2010

Agostinho, M. Jury of the national science communication competition “FameLab Portugal” organized by, Sintra, Portugal, April 17, 2010.

Agostinho, M. and Almeida, C. organized IMM participation in “Estudar Medicina na FMUL - Dia do Candidato”, FMUL, April 21, 2010.

Agostinho, M. Jury of the national science communication competition “Faz Portugal Melhor”, May 2010.

Agostinho, M. Lecturer at secondary school meeting “Espaços de Ciência”, E.S. M.A. Vaz de Carvalho, Lisbon, May 21, 2010.

Agostinho, M. Jury of the national science communication EUPA’s competition “Proteomics Photography and Graphic Arts”, September, 2010.

Agostinho, M. Jury of the international science communication competition “Ciencia en Acción”, Santiago de Compostella, Spain, May and October, 2010.

Agostinho, M. coordinated group work on “Medicina personalizada - deve o diagnóstico precoce ser obrigatório para todos?” under the European Project “2 ways”, Pavilhão do Conhecimento, Lisbon, October 23, 2010.

Agostinho, M. Co-organized “Bioquímica de portas abertas”, a series of seminars for secondary school students, 2010 Congresso nacional de Bioquímica, Porto, December 15-17, 2010.

FMUL Newsletter - 4 articles published

Nº 13 April 2010

Bolsa Terry Fox atribuída ao Investigador do IMM João Barata

Nº 14 May 2010

Investigadora do IMM ganha bolsa do Programa Harvard Medical School Portugal

Nº 15 June / July 2010

Prémio Gulbenkian “Investigação na Fronteira das Ciências da Vida” distingue investigação do Instituto de Medicina Molecular sobre Dengue

Nº 16 August / September 2010

Investigadores do IMM identificam nova população de células do sistema imunitário com potencial terapêutico

Media

Support to over 50 media visits to IMM

Increased regular presence of IMM and IMM researchers in reference general and specialized media.

17 Press Releases:

4-Jan-10 | Estudo Português mostra que queixas cognitivas dos pacientes são aviso para possível doença neurodegenerativa

17-Fev-10 | Prémio Ciência Pulido Valente 2009 distingue investigação em oncologia desenvolvida no Instituto de Medicina Molecular

11-Mar-10 | O que é que te passa pela cabeça?” - Dia aberto no IMM na Semana Internacional do Cérebro

12-Mar-10 | Profilaxia contra a malária - Patente de grupo português concedida e publicada nos EUA

- 22-Mar-10 | Antivirais contra infecção por HIV-1 - Portugueses mostram como aumentar eficácia dos fármacos que impedem entrada do vírus em células humanas
- 7-Apr-10 | Instituto de Medicina Molecular comemora Dia Internacional da Doença de Parkinson com curso para cuidadores
- 12-Apr-10 | A Ciência é Notícia para um Político? - Cientistas, políticos e jornalistas reúnem-se para perceber como melhor traduzir descobertas científicas em conhecimento acessível a todos
- 10-May-10 | Investigadores Portugueses publicam estudo sobre uma nova forma de tratamento da artrite reumatóide - Estudo feito em modelo animal semelhante a artrite humana
- 24-Jun-10 | Estudo Português permite otimizar a radioterapia - Olhar à volta do tumor para melhorar o tratamento
- 17-Jul-10 | O maior financiamento de sempre para investigadores Portugueses das Ciências da Vida - A última candidatura das prestigiadas bolsas do Conselho Europeu de Investigação rendeu cinco Starting Grants
- 10-Aug-10 | Estudo Português identifica nova população de células do sistema imunitário com potencial terapêutico - Investigadores criam spin-off para desenvolver terapia
- 6-Oct-10 | Colocar o fígado e o pâncreas no sítio certo: Investigadores Portugueses identificam mecanismo de controlo do “GPS embrionário” de vertebrados
- 25-Oct-10 | Acellera Therapeutics vence prémio em Concurso Nacional de Inovação BES - Investigação premiada na categoria das Tecnologias da Saúde foi desenvolvida no Instituto de Medicina Molecular
- 4-Nov-10 | Fundação Michael J. Fox financia investigador português para estudar a doença de Parkinson
- 10-Nov-10 | Fundação Bill & Melinda Gates financia cientistas em Portugal a investigar malária
- 23-Nov-10 | Investigadores do Instituto de Medicina Molecular somam e seguem em Novembro: Bruno Silva-Santos vence bolsa da Organização Europeia de Biologia Molecular (EMBO)
- 6-Dec-10 | Luísa Figueiredo vence bolsa da Organização Europeia de Biologia Molecular (EMBO) - Depois do Prémio Crioestaminal, investigadora do IMM vence prestigiante Installation Grant da EMBO

Animal Facility

Major interests / Objectives

The IMM has one small, conventional animal facility and a new, larger barrier facility. The **conventional facility** hosts 1200 mice. The new **barrier facility** has the capacity to host 15000 mice and rats, and includes one Production area, one Experimental area, one Quarantine, one Transitional Animal Room, one Surgical Suite, and two Procedure Rooms. 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

Alina Costa	Facility Manager, IMM
Dolores Bonaparte	Veterinarian
Joel Filipe	Technician, IMM
Yuri Leite	Technician, IMM
Olena Pinho	Animal Caretaker, IMM
Nuno Inácio	Animal Caretaker, IMM
José Vila Chã	Animal Caretaker, IMM

Keywords/Research Areas

Animal Facility
Mice
Rats
SPF

Major scientific achievements

The new facility opened in August 2010. Rules of access and use were implemented, and Standard Operating Procedures designed according to the rules and recommendations for good practices and animal welfare. Both internal and external services were made available for academia, pharma, biotech and other fields of research. These services run from animal hosting to procedure performance such as:

-Experimental procedures

-Surgical Procedures

-*In vivo* imaging

-Assisted Reproduction Techniques such as timed pregnancies, *in vitro* fertilization, embryo & cesarean derivation, and cryopreservation.

Licensing of projects (that involve the use of animals) by the Direcção Geral de Veterinária is done following approval by the Ethical Committee of the facility.

A 40h Course in Laboratory Animal Science (FELASA cat. B), is organized at least once a year to train researchers and grant them accreditation to work with animals.

A database for animal facility management is at the final stage of development and will be implemented during the first semester of 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 co-organized with Tom Kirchhausen (Harvard Medical School) the Harvard Medical School – Portugal Program Workshop on “Quantitative Light Microscopy in Living Cells”, which took place at IMM in April 2010. The five-day event included both lectures and practical sessions and was attended by 35 students from all of Portugal, one student from Denmark and another two from Poland.

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 assess cellular internalization and degradation of IL-7Ralpha in T cells (*Henriques et al, Blood, 2010*), nuclear internalization of pyrazolyl-diamine ligands with potential therapeutic applications (*Esteves T et al, Org Biomol Chem, 2010*) and embryonic angiogenic sprouting in zebrafish following low doses of ionizing radiation (*Vala et al, PLoS One, 2010*).

In 2010 the BioImaging Unit services were used by 172 users from 34 different research units (7 of them from outside the IMM), which corresponds to an increase of 29 % in the total number of users relative to 2009. We trained 73 new users in different microscopy systems during the year.

Recent Most Relevant Publications

Henriques CM, Rino J, Nibbs RJ, Graham GJ, Barata JT (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7Ralpha in T cells. *Blood*, **115** (16), 3269-77 (Journal IF: 10.555, Citations: 0)

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

Publications in peer review Journals

Esteves T, Xavier C, Gama S, Mendes F, Raposinho PD, Marques F, Paulo A, Pessoa JC, Rino J, Viola G, Santos I. (2010) Tricarbonyl M(I) (M = Re, (99m)Tc) complexes bearing acridine fluorophores: synthesis, characterization, DNA interaction studies and nuclear targeting. *Org Biomol Chem* **8** (18), 4104-16 (Journal IF: 3.762)

Sofia Vala I, Martins LR, Imaizumi N, Nunes RJ, Rino J, Kuonen F, Carvalho LM, Rüegg C, Grillo IM, Barata JT, Mareel M, Santos SC (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *PLoS One*. **5** (6), e11222 (Journal IF: 4.351)

Henriques CM, Rino J, Nibbs RJ, Graham GJ, Barata JT (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7Ralpha in T cells. *Blood*, **115**(16):3269-77 (Journal IF: 10.555)

Internationalization

José Rino co-organized with Tom Kirchhausen (HMS - Harvard Medical School) the Harvard Medical School – Portugal Program Workshop on “Quantitative Light Microscopy in Living Cells”, which took place at IMM in April 2010. The five-day event included Faculty from HMS, IMM, IGC and FCUL and was attended by 35 students from all of Portugal, one student from Denmark and another two from Poland.

Advanced teaching

Rino, J. lectured on “Quantitative Imaging” at the PIBS Tech Week Workshop for the IGC PhD Programme in Integrative Biomedical Sciences, Oeiras, Portugal, November 16, 2010

Rino, J. lectured on “Fluorescent Probes” at the ‘EMBO Practical Course on 3D Developmental Imaging’, Instituto Gulbenkian de Ciência, Oeiras, Portugal, October 5, 2010

Temudo, A. lectured the practical teaching for the ‘EMBO Practical Course on 3D Developmental Imaging’, Instituto Gulbenkian de Ciência, Oeiras, Portugal, October 5, 2010

Rino J. co-organized the Zeiss on Your Campus 2010 Workshop on “Live Cell Imaging”, IMM, Lisboa, Portugal, July 13-15, 2010

Rino, J. co-organized and lectured at the Harvard Medical School – Portugal Program Workshop on “Quantitative Light Microscopy in Living Cells”, April 14-18, 2010, IMM, Lisboa, Portugal

Temudo, A. lectured the practical teaching for the Harvard Medical School – Portugal Program Workshop on “Quantitative Light Microscopy in Living Cells”, April 14-18, 2010, IMM, Lisboa, Portugal

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 involving *Mycobacterium tuberculosis*, HIV and other 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. Accordingly, the Facility provides education, training, and guidance for researchers and will be constantly monitored by fully dedicated staff. Applications to use the IMM's BSL3 laboratories are reviewed and must be approved by the Facility's Director and Scientific Commission before access is granted.

Head of Unit

Miguel Prudêncio, PhD - Staff Scientist, IMM

Research Team

Inês Matos	Technician, IMM
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Keywords/Research Areas

Biosafety Level 3
Containment
BSL3
ABSL3

Major scientific achievements

The IMM P3 Facility underwent a thorough process of upgrade and verification. Standard Operation Procedures were designed and implemented to meet the highest safety standards. A 2-day course on level 3 biosafety practices and specific aspects of operations in the IMM P3 Facility was held, free of charge, to all potential users in the IMM. This process culminated in the Facility opening in November 2010, for use with non-airborne pathogens.

Advanced teaching

Prudêncio, M. organised the course "Biosafety training for use of the IMM BSL3 Facility", 27-28 October 2010, Instituto de Medicina Molecular, Lisboa, Portugal

Flow Cytometry Unit

Objectives

The Flow Cytometry Unit at the IMM is a core facility that provides support and training to IMM and external researchers who require this technology in their research projects. The cell analysers are operated by researchers after training provided by our staff, whereas cell sorting is a service that requires prior booking and is provided by our staff only. Training is provided at an individual basis whenever required and through workshops. We aim to train researchers in the adequate use of the instruments and also on flow cytometry principles, experiment design, as well data analysis and interpretation. UCF staff are also involved in research projects in collaboration with other IMM Units.

Head of Unit

Maria Soares, PhD, University College London, London, UK

Team

Ana Luisa Caetano	Technician, FML
Alexandre Varela	Technician (From July 2009 to February 2010)
Ana Isabel Pinto	Technician (since February 2010)

Keywords

Flow Cytometry
High Speed Cell Sorting

Major achievements

In 2010, the usage of UCF instruments has continued to grow, with a particularly high demand for cell sorting and data acquisition on the FACSCanto. A total of 24 IMM Units used our facility, in addition to two external units and one company, representing a total of 123 users. Sorting times were increased by 46% as compared to 2009 and the FACSCanto had a 66% increase in usage. This overwhelming increase in demand for sortings and greater than 4 colour analysis, led to the recognition that more instruments were required to provide a quality service for IMM researchers. To overcome the problems in sorter availability, a new high speed cell sorter (BD FACSAria III) was installed in December 2010. The negotiations for the acquisition of new 8 colour analysers was concluded and the installation of two new BD LSR Fortessa will be completed in early 2011, creating a significant upgrade to the Flow Cytometry services available at the IMM. UCF will therefore be equipped with two High Speed Cell Sorters (FACSAria I and FACSAria III), one FACSCalibur and two LSR Fortessa.

Ongoing Research Projects

2008/2011 Immune Reconstitution after Unrelated and Haplotype-Mismatched Stem Cell Transplantation, FCT. Coordinator: Maria Soares (PTDC/SAU-MII/67662/2006). This project is ongoing at the Clinical Immunology Unit at the IMM, please see UIC report for details.

Participation in projects from other Units:

2007/2010, Maria Soares: participant in the project "Molecular and Functional Effects of TAL1 and LMO2 Overexpression in Normal Human Hematopoietic Stem Cells: Impact on T-cell leukemogenesis, FCT. Coordinator: João T. Barata (PTDC/SAU-OB/69974/2006)

2007/2011, Maria Soares: participant in the project "HIV-2 infection and thymus", FCT. Coordinator: Ana E. Sousa (PTDC/SAU-MII/66248/2006)

2009/2012, Maria Soares: participant in the project "Long-term impact of thymectomy performed in early infancy", FCT. Coordinator: Ana E. Sousa (PIC/IC/83068/2007)

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)

Advanced teaching

The Flow Cytometry Unit organized one PhD Programme nanocourse, 29th - 31st of March 2010

This course was attended by 12 participants with lectures by:

Rui Gardner, Head of the Flow Cytometry Core Facility, IGC on "Fundamentals of Flow Cytometry".

Mario Roederer, Vaccine Research Center, NIH, Bethesda, USA, who gave an IMM seminar ("Single Cell Analysis: Past, Present, and Future") and also lectures on flow cytometry compensation, calibration and quality control.

UCF Staff lectured on Flow Cytometry Applications (Maria Soares) and Basic notions on Fluorescence-Activated Cell Sorting (Ana Luísa Caetano). The practical modules were focused on three-color calibration/acquisition- FACSCalibur (Maria Soares), introduction to Diva. Six-color calibration/acquisition - FACSCanto (Ana L. Caetano).

The Flow Cytometry hosted a visit from a group of 30 Bioengineering Students Escola Superior de Tecnologia e Gestão – Portalegre. Maria Soares and Ana L Caetano gave tutorials on flow cytometry basic principles and a demonstration on our instruments work. 17th of November 2010, UCF, IMM

Histology Service

Major interests / Objectives

Starting on September 09, the Histology Service was implemented in IMM, resulting from collaboration with the Histology Institute of FML. The Histology Service has a permanent technician, and is located in the Histology facilities of the Histology Institute of FML.

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); 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 several research Units have used the available services in a regular basis. Researcher's formation in standard procedures had also a high demand and training and tutorship maintained as one of our main goals in 2010. In 2010 the HS increased the number of Units using the facility and the number of self-service users. It is also our purpose to implement new services according to the needs of the IMM Research Units. Several Units demonstrated a strong interest in performing Transmission Electron Microscopy (TEM), not available in our Service or Institute. We successfully establish a collaboration with the Instituto Gulbenkian de Ciência, and now have available a new service of processing and visualization of samples for TEM.

Zebrafish Facility

Major Objectives

To implement 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.

Head of Unit

Leonor Saúde, PhD Invited Auxiliary Professor, FML

Research Team

Lara Carvalho	Unit manager
Fábio Valerio	Technician

Major achievements

Renovation construction works were carried out to expand the Zebrafish Facility and to build a Quarantine Room.

We have now a completed WTU system operating 6 racks. We have also a new stand alone allocated exclusively to the Quarantine and another stand alone for Wild-type fish.

We acquired a water reservoir that allows us to feed the system with no water breakdowns.

Publications

The work done using the zebrafish of the IMM facility generated the following publications:

Vala I, Martins L, Imaizumi N, Nunes R, Rino J, Kuonen F, Carvalho L, Rüegg C, Grillo I, Barata J, Mareel M and Constantino Rosa Santos S (2010) Low doses of ionizing radiation promote tumor growth and metastasis by enhancing angiogenesis. *PlosONE* **5** (6), e11222.

Lourenço R, Lopes SS and Saúde L (2010) Left-right function of *dmrt2* genes is not conserved between zebrafish and mouse. *PlosONE* **5** (12); e14438.

Lopes SS, 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.

Invited Lectures and Seminars

Carvalho, L. Working with Zebrafish. Lab Animal Science @the IMM, Lisbon, Portugal, February 3-13, 2010.

Advanced teaching

March 2010 - Lara Carvalho and Fábio Valério provided training on zebrafish husbandry to Instituto Gulbenkian de Ciência and Universidade do Algarve facility managers.

Science and Society

February 2010 - Lara Carvalho and Fábio Valério hosted a guided tour of the IMM zebrafish facility to student from Amália Vaz de Carvalho High School.

Companies

GenoMed – Diagnósticos de Medicina Molecular, SA

Major interests / Objectives

GenoMed is a spin-off company of IMM created in 2004. The mission of GenoMed is to provide cutting-edge technology transfer services relevant for medical applications. Currently, GenoMed offers over 250 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)

Principal Investigators

Rute Marcelino, MSc, University of Lisbon

Gabriel Miltenberger-Miltenyi, MD, PhD (Genetics Coordinator, IMM staff scientist, CIÊNCIA 2007)

Research Team

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
Diana Colom, Lic. Biology	Technician
Rosário Sanches	Technician, (left July 2010)
Sónia Santos, PhD	Citogenetics Unit Coordinator
Paula Costa, Lic. Biochemistry	Technician
Ana Carla Sousa, Lic. Applied Chemistry/Biotechnology	Technician
Renata Casimiro, Lic. Marine Biology/Biotechnology	Technician
Susana Ramos, Lic. Pathology and Cytology	Technician
Rosana Rocha, Msc	Technician (left May 2010)
Sónia Matos, MSc	Hemato-Oncology-Molecular Biology Unit Coordinator
Sara Malveiro, Lic. Cellular and Molecular Biology	Technician

Sílvia Kakoo, Lic. Pathology and Cytology	Technician
Rute Marcelino, MSc	Virology Unit Coordinator
Paula Mimoso, Lic. Applied Chemistry/Biotechnology	Technician
Fabíola Rosa	Direction Assistant
Ana Flores	Management Assistant
João Pedro Rebelo	Financial Manager (left March 2010)
Júlia Plínio	Management Assistant (left June 2010)

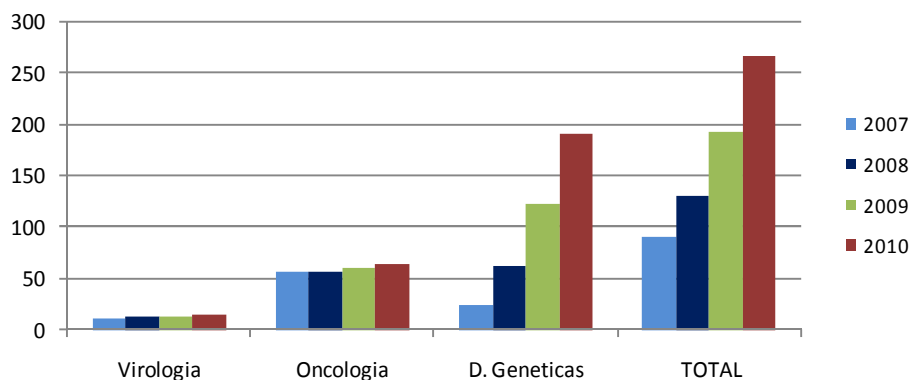
Keywords/Research Areas

Molecular Diagnosis

Major scientific achievements

New molecular tests were made available.

Total Number of tests available



Ongoing Research Projects

2009/present: Multicenter comparison of assays for cerebrospinal fluid markers for Alzheimer's Disease, University Medical Center Funding Amsterdam, Netherland. Coordinators: Niek Verwey.

2009/present: Multicentre study of comparison of different testing strategies of K-ras mutations in tumorous tissue of colorectal cancer, Roche Funding. Coordinators: Prof.Dr. J. Han J.M. van Krieken University Nijmegen Medical Centre, Netherland and Gabriel Miltenberger-Miltenyi.

2009/present: 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), Roche/APEF Funding. Coordinator: Rute Marcelino

2008/present: Genetics of obesity - a study of polymorphisms, FCT Funding. Coordinators: Helena Cortez Pinto and Gabriel Miltenberger-Miltenyi. (PTDC/SAU-OSM/100878/2008)

2008/present: Genetics of alcohol - a study of polymorphisms, APEF/Schering-Plough Farma Funding. Coordinators: Helena Cortez Pinto and Gabriel Miltenberger-Miltenyi.

Publications in peer review Journals

Antunes J, Filipe P, André M, Fraga A, Miltenberger-Miltenyi G and Marques Gomes M (2010) Livedoid Vasculopathy Associated with Plasminogen Activator Inhibitor-1 Promoter Homozygosity (4G/4G) and Prothrombin G20210A Heterozygosity: Response to t-PA Therapy. *Acta Derm Venereol* **90** (1), 91-2. (IF: 3.007, cited: 0)

Cardoso, BM, Castanhinha S, Dupont J, Albuquerque M, Pereira SV, Miltenberger-Miltenyi G and Oliveira G (2010) Cleidocranial Dysplasia with Severe Parietal Bone Dysplasia: a new (p.Val124Serfs) RUNX2 mutation. *Clinical Dysmorphology* **19** (3), 150-2 (IF: 0.468, cited: 0)

Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS and Santos NC (2010) Atomic Force Microscopy-Based Molecular Recognition of a Fibrinogen Receptor on Human Erythrocytes. *ACS Nano* **4** (8), 4609-20. (IF: 7.493, cited: 0)

Invited Lectures and Seminars

Matos, S. e Costa, P. Testes de Citogenética/Biologia Molecular em Hemato-oncologia, Serviços de Patologia Clínica e Hematologia do CHLO, Hospital de S. Francisco Xavier, Lisbon, Portugal. November 25, 2010.

Matos, S. LMC: Monitorização da Resposta e Mecanismos de Resistência. Annual Meeting of Portuguese Hematology Society 2010, Tróia, Portugal. November 12, 2010.

Carmo-Fonseca, M. Changing Paradigms in the Diagnosis of Lung Cancer, EGFR gene mutation testing. Workshop Astrazeneca, Lisbon, Portugal. May 29, 2010

Porta Nova, T. Diagnóstico Genético e sua aplicação na Personalização de Medicamentos. VIII Simpósio do Núcleo de Estudantes de Ciências Farmacêuticas do ISCS. Monte da Caparica, Portugal. May 26 2010.

Porta Nova, T. O uso da Genética no mundo jurídico. Conferência O direito médico e a Advocacia. JPAB Sociedade de Advogados e Espírito Santo Saúde, Lisboa, Portugal. May 21, 2010.

Marcelino, R. Hepatite B e Infecção Oculta: Conceitos, Problemas e Diagnóstico; Quantificação do DNA viral. 3º Congresso Português de Hepatologia, Évora, Portugal. May 14, 2010.

Santos S. e Matos S. Discussão de dois casos clínicos com apresentação dos resultados obtidos na GenoMed, Reunião dos Serviços de Anatomia Patológica e Hematologia e Transplantação de Medula do CHLN, Hospital de Santa Maria, Lisbon, Portugal. April 22, 2010.

Marcelino, R. Diagnóstico Serológico de Hepatites Virais, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal. March 25, 2010

Carmo-Fonseca, M. Da célula ao feto – estado de arte da tecnologia. II Simpósio Gravidez após os 40 anos. Hospital da Luz. Lisboa, Portugal. February, 24-25, 2010.

Santos-Sousa, P., Gomez, B., Guerra, L., Matos S., Santos, S. Leucemia Mielóide Crónica no século XXI: uma revolução terapêutica. Experiência do Serviço de Hematologia e Transplantação de Medula do CHLN-HSM. Sessões Clínicas da Faculdade de Medicina de Lisboa/Hospital de Santa Maria, Lisboa, Portugal. January 21, 2010.

Communications in International Conferences

Matos, S., Santos, S., Guerra, L., Raposo, J., Porta Nova, T. and Alves do Carmo, J. Monitoring Cytogenetic and Molecular Responses in CML: an experience of 5 Years. ELN Frontiers Meeting – Continuing the CML revolution: Expanding options in targeted therapy. Vienna, Áustria. October 22–24, 2010 (Poster presentation)

Miltenberger-Miltenyi, G. Presentation of GenoMed and IMM at the EUNEFRON Yearly Meeting 2010 and Symposium, Paris, France. October 22–23, 2010 (Oral presentation)

Miltenberger-Miltenyi, G., Neutel, D., Silva, I., Coelho, H., Mamede de Carvalho Chorea-acanthocytosis. Congress of the Austrian Society of Human Genetics, Vienna, Austria. September 24, 2010 (Oral presentation)

Miltenberger-Miltenyi, G., Real Mendes, L., Simão, C., Pereira, S.V. and Almeida, M. Análise Genética da Síndrome Nefrótica Congénita – primeiros resultados e descrição de quatro novas mutações. V Congresso Hispânico-Português de Nefrologia Pediátrica, Guimarães, Portugal. June 24–26, 2010 (Oral presentation)

Miltenberger-Miltenyi, G., Sandes, A.R., Mendes, P., Silva, J.E., Pereira, S.V. and Stone R. Pesquisa do Gene NPHS2 em Crianças com Glomerulosclerose Focal e Segmentar – Descrição de Duas Novas Mutações. V Congresso Hispânico-Português de Nefrologia Pediátrica, Guimarães, Portugal. June 24–26, 2010 (Oral presentation)

Coutinho, A.M., Nolasco, R., Silva, I., HSM Genetic Counselling Unit, Miltenberger-Miltenyi, G and Carmo-Fonseca, M BRCA genetic variation in a Portuguese breast/ovarian cancer population. EMBO | EMBL Symposia 2010 “Human Variation: Cause and Consequence”, Heidelberg, Germany. June 20–23, 2010 (Poster presentation)

Miltenberger-Miltenyi, G., Calado, J., Carvalho, F., Pereira, S.I., Teixeira, C., Jorge, S., Viana, H., Gomes da Costa, A. and Almeida, E. Medullary cystic kidney disease: analysis of a large Portuguese family. Congress of the European Society of Human Genetics, Gotenborg, Sweden. June 12–15, 2010 (Poster presentation)

Santos-Sousa, P., Guerra, L., Gomez, B., Valle, S., Lopes, C., Raposo, J., Martins, C., Costa, M. J., Esteves, G., Fajardo, J., Forjaz Lacerda, J., Santos, S., Sousa, C., and Alves do Carmo, J. Chronic Myeloid Leukemia in the Imatinib Era: The predictive value of optimal response at 12 months of therapy on achieving molecular response and disease progression. 15th Congress of the European Association, Barcelona, Spain. June 10–13, 2010 (Abstract publication)

Miltenberger-Miltenyi, G., Calado, J., Carvalho, F., Pereira, S.I., Teixeira, C., Jorge, S., Viana, H., Gomes da Costa, A. and Almeida, E. Further evidence on genetic heterogeneity of medullary

cystic kidney disease: report on a large Portuguese family. Congress of the German Society of Human Genetics, Hamburg, Germany. March 2-4, 2010 (Poster presentation)

Communications in National Conferences

Viveiros, C., Martins, H., Neves, M., Alves, I., Ferreira, C., Matos, S., Santos, S., Morais, A., Raposo, J. Linfoma de Células T Hepato-esplénico – Um Caso Raro. Annual Meeting of Portuguese Hematology Society 2010, Tróia, Portugal. November 11-13, 2010 (Poster presentation)

Miltenberger-Miltenyi, G., Neutel, D., Silva, I., Coelho, H. e Mamede de Carvalho Resultados genéticos dum paciente com coreia-acantocitose – descrição de três novas variantes no gene VPS13A. Congresso da Sociedade Portuguesa de Neurologia, Espinho, Portugal. November 5-7 2010 (Poster presentation)

Pereira, S.V., Silva, M. e Miltenberger Miltenyi, G. Genetic testig of dementia – results on a Portuguese patient cohort. XXIV Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demências, Tomar, Portugal. June 25-26, 2010 (Oral presentation)

Luís, I.V., Ribeiro, J., Matias, M., Fernandes, I., Casa-Nova, M., Cortes, P., Pereira, S.V., Miltenberger- Miltenyi, G., Costa, L. Impacto do estado mutacional do KRAS nos tempos de sobrevivência global na neoplasia do cólon metastizada: Avaliação retrospectiva. "Oncologia 2010 - Encontros da Primavera", Sociedade Portuguesa de Oncologia, Évora, Portugal. April 8-11, 2010 (Poster presentation)

Organisation of Conferences

Santos, S. co-organized and lecture of Citogenetics/IPSS in SMD. 1º Curso teórico-prático Síndrome Mielodisplásica, Faculty of Medicine, University of Coimbra, Coimbra, Portugal. October 16, 2010.

Internationalization

2009/present: Multicenter comparison of assays for cerebrospinal fluid markers for Alzheimer's Disease, University Medical Center Funding. Coordinators: Niek Verwey.

2009/present: Multicentre study of comparison of different testing strategies of K-ras mutations in tumorous tissue of colorectal cancer, Roche Funding. Coordinators: Prof. Dr. J. Han J.M. van Krieken and Gabriel Miltenberger-Miltenyi.

Prizes, honours and awards

3ª Menção Honrosa Portuguesa 2010 to Gabriel Miltenberger-Miltenyi, for oral presentation "Análise Genética da Síndrome Nefrótica Congénita – primeiros resultados e descrição de quatro novas mutações". V Congresso Hispânico-Português de Nefrologia Pediátrica. Guimarães, Portugal.

Prémio de Melhor Trabalho Português 2010 to Gabriel Miltenberger-Miltenyi for oral presentation “Pesquisa do Gene NPHS2 em Crianças com Glomerulosclerose Focal e Segmentar – Descrição de Duas Novas Mutações”. V Congresso Hispânico-Português de Nefrologia Pediátrica. Guimarães, Portugal.

Advanced teaching

Santos, S. co-organized and lecture of Citogenetics/IPSS in SMD. 1º Curso teórico-prático Síndrome Mielodisplásica, Faculty of Medicine, University of Coimbra, Coimbra, Portugal. October 16, 2010.

Marcelino, R. “Módulo de biologia molecular” Curso de Mestrado em Doenças Infecciosas Emergentes. FMUL, Lisboa, Portugal. January 7 and 14, 2010.

Technophage

TechnoPhage, SA is a Biotechnology company focused on the discovery and development of biopharmaceuticals, using different proprietary technologies. TechnoPhage is engaged in three main R&D programs:

- R&D of novel bacteriophage-based products for the treatment and diagnosis of bacterial infections caused by antibiotic-resistant bacteria. Ongoing projects aim the specific elimination of topical infections, using bacteriophages or phage lytic enzymes.
- R&D of recombinant single domain antibody fragments (sdAbs), for therapeutic and diagnostic applications. Ongoing projects in the areas of inflammation, oncology and thrombosis.
- Drug discovery using the zebrafish as an in vivo screening system on skeletal formation and regeneration. Ongoing projects in the area of bone disorders.

The company laboratories are located at the Institute of Molecular Medicine (IMM), under a scientific collaboration protocol.