MM Lisboa

Instituto
de Medicina
Molecular

Report 2015

Instituto de Medicina Molecular — iMM Lisboa
Faculdade De Medicina Da Universidade De Lisboa
Avenida Professor Egas Moniz
Edifício Egas Moniz · 1649-028 Lisbon · Portugal

imm.medicina.ulisboa.pt
Phone +351 217 999 411 **Fax** +351 217 999 412
imm@medicina.ulisboa.pt
facebook.com/immolecular
twitter.com/IMMolecular
Linkedin.com/companiesinstituto-
-de-medicina-molecular

Project Concept and Management
iMM Communication
imm-communication@medicina.ulisboa.pt

Design
GBNT — Shaping Communication
www.gbnt.pt

Edition
200 copies

June, 2016

chasing questions :

contents

1st iMM Scientific Retreat

Director's message

Highlights 2015

This was a record-breaking year for grants from the ERC and recognition of our scientific excellence from the European community.

Wow... this is quite impressive! After a truly memorable 2014, also 2015 revealed itself to be full of events and achievements. The facts speak louder than I ever could.

To begin, several of our established group leaders - João Barata (Cancer), Henrique Veiga-Fernandes, and Bruno Silva-Santos (Immunity and Infection), were awarded the highly coveted European Research Council (ERC) Consolidator Grants. Then, newcomers to the iMM, Vanessa Morais (who also received an EMBO Installation Grant) and Cláudio Franco, were both awarded the ERC Starting Grants for their projects in neurosciences and vascular biology, respectively. Finally, Edgar Gomes, was awarded an ERC Proof-of-Concept Grant to explore the opportunity to commercialize a novel 3D in vitro system for screening and validating drug candidates to treat muscle disorders. This was a record-breaking year for grants from the ERC and recognition of our scientific excellence from the European community.

Naturally, the impressive success of our research institute, which was achieved in such a short time, is dependent, not only on its extraordinary group leaders, but also on the incessantly inquisitive minds of all our scientists, together with the enthusiasm, hard work and commitment of our entire community. Building on this, we, in the Direction, felt it was time for a whirlwind change: A re-branding of the iMM that gives a new face for our institute. This change of image represents a newly refreshed attitude towards excellence and represents ideals that clearly capture the vibrant scientific environment which, we have created together. With this in mind, we at the iMM are committed to continue do what we do best.

Here, at iMM Lisboa "we chase questions" – the most fundamental and conceptually innovative ones.

We wanted not only to extend to the local community, but also contribute to increase our commitment to improve our international research collaboration and outreach. Accordingly, our participation within Horizon 2020, and its Programme "Spreading Excellence and Widening Participation", saw three projects approved under the Twinning action, an effort coordinated by Edgar Gomes in Cancer, Ana Sebastião in Neurosciences and myself in Immunity and Infection. These projects intend to enhance the collaboration between the iMM Lisboa and other renowned European partner institutions and international leaders in their respective areas of research. The partnerships include the Institut Pasteur, The Francis Crick Institute, University of Eastern Finland, Università Di Roma, Lancaster University, Institut Curie and DKFZ. Still in 2015, iMM Lisboa received 2,5M€ funding from the Horizon 2020 ERA Chairs call. This project will allow iMM Lisboa to foster excellence on a sustainable basis through the recruitment of an ERA Chair in Immunity and Infection. Additionally, iMM is strengthening its advanced training with the coordination or participation in several Horizon 2020 International Training Networks by several of our group leaders, namely Gonçalo Bernardes, Ana E. Sousa and Luís Graça. Altogether, we are paving the way for a true internationalization of our research community.

While we believe that projecting our name outside our community is already proving its worth, we have been working hard to build a stronger bridge and strengthen the interactions with the Faculty of Medicine as well as with the Hospital Santa Maria, our key partners in the Lisbon Academic Medical Center.

While our scientific community has been very successful in terms of grants and institutional funds, we now need to expand our horizons and take bold steps to create new bonds with third-party funders.

Finally, 2015 also witnessed the 1st annual scientific retreat open to the entire iMM research community with the presence of our Scientific Advisory Board. I want to thank Carlos Caldas, Gustave Moonen and Phillipe Sansonetti for their open and passionate suggestions.

Still, we know we can still do better...much better! So I challenge you. In what and how can we excel?

To support the brightest minds is one of the most noble, clever and far-sighted ways to do charity!

Since day one, iMM has always aimed to attract the most forward-thinking and creative minds. Our recruitment policy has been based solely on excellence, encouraging researchers with an integrative and systems biology perspective to join us. We now want to establish a strict independent evaluation by international standards. Recruitment, evaluation and promotion are critical steps to establish a dynamic structure that fosters outstanding research.

But, in addition to creative and enthusiastic scientists, we also need critical resources and the funding to get us there. While our scientific community has been very successful in terms of grants and institutional funds, we now need to expand our horizons and take bold steps to create new bonds with third-party funders. In 2012, we took our first baby steps with the creation of "Centro de Investigação de Tumores Cerebrais". Most recently we took yet another step with the "Fundo Laço-iMM" in 2015. This was possible through the generous help and initiative of Cláudia Faria (neurosurgeon at Hospital Santa Maria and iMM researcher) and Lynne Archibald (Laço President) and visionary investment of various private funders, who believed in the potential of our research and its great impact in patients' life in a near future.

However, this is only the beginning and as with any successful scientific project, we need a creative and sustained design, as well strong leaders willing to move it forward. We need to, not only think strategically but also think outside the box: appeal to the private domain; appeal to those who may benefit from our contributions; appeal to our citizens; appeal to industry, invite them to be strategic in fostering innovation and take a share in the education of young scientists and technical personnel.

So, how do we achieve such a herculean task? First, we need to continue to do the best science, as illustrated in the following pages of this report. Second, we need to reach out to society and communicate our science. We need to send out the message to the population that an investment in research and our researchers, is an investment in themselves, in their society, in their community, in their future. To support the brightest minds is one of the most noble, clever and far-sighted ways to do charity!

We are a young institute, not only in the number of years since the founding of the iMM, but also in what makes-up the iMM everyday: its people. And like any young being we have the thirst to explore, to go further and to enjoy every step along the way, and to grow.

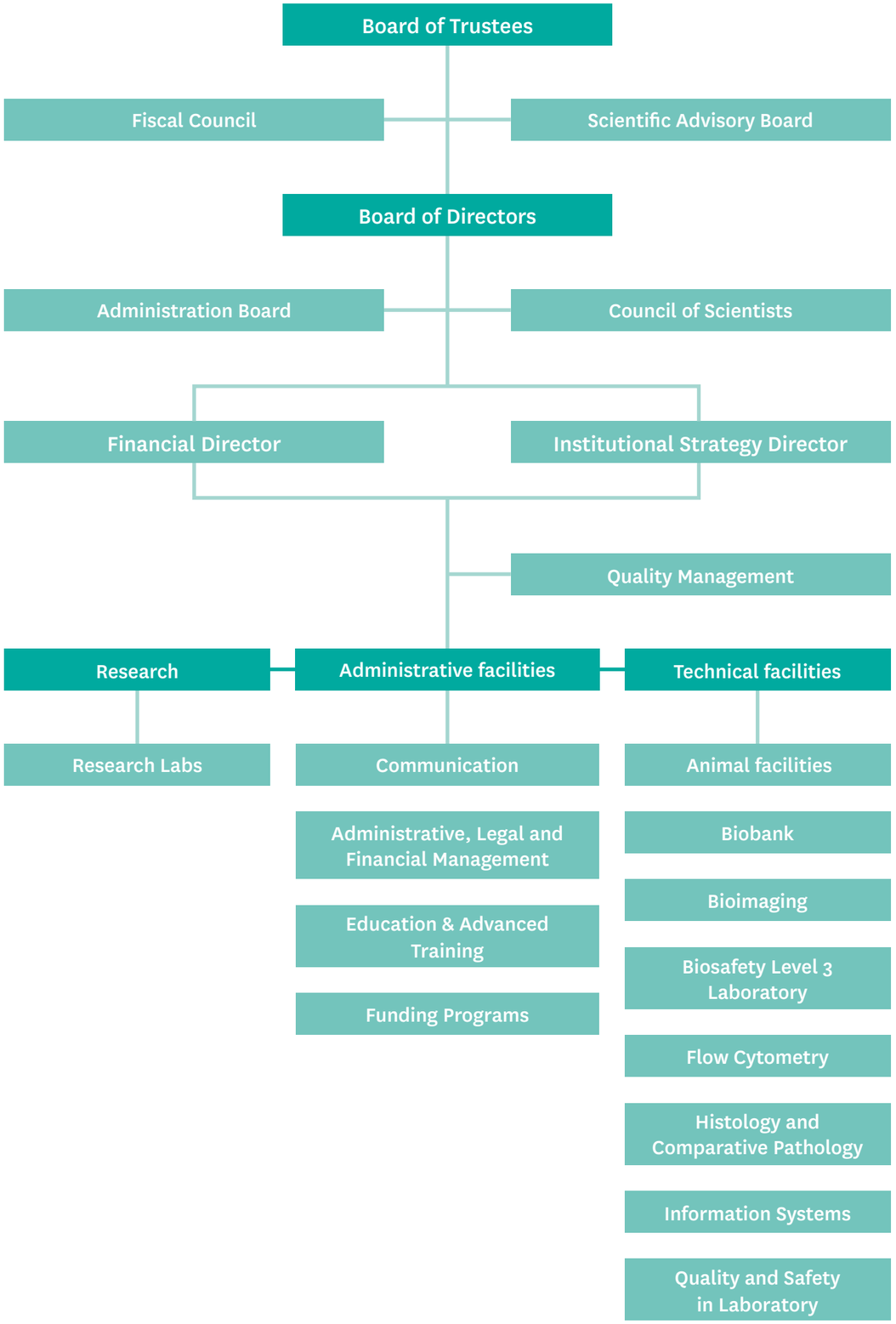
Thank you all for your dedication, hard work and enthusiastic spirit. Never forget: aim for excellence and keep chasing questions.

Maria M. Mota
Executive Director

Thank you all for your dedication, hard work and enthusiastic spirit.
Never forget: aim for excellence and keep chasing questions.

Structure and Organisation

Board of Directors
(left to right) Margarida Pinto Gago, Henrique veiga-Fernandes, M. Carmo-Fonseca, Maria M. Mota and Bruno Silva-Santos



Board of Directors

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

M. Carmo-Fonseca
MD, PhD – President

Maria M. Mota
PhD - Executive Director

Bruno Silva-Santos
PhD - Vice-President

João Lobo Antunes
MD, PhD – President Emeritus

Scientific Advisory Board

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

Carlos Caldas
MD, PhD - Cambridge Cancer Centre, UK

Philippe Sansonetti
MD, PhD - Pasteur Institute, France

Gustave Moonen
MD, PhD - Université de Liége, Belgium

Caetano Reis e Sousa
PhD - Francis Crick Institute, London, UK

Paul Peter Tak
MD, PhD - University of Amsterdam, Netherlands

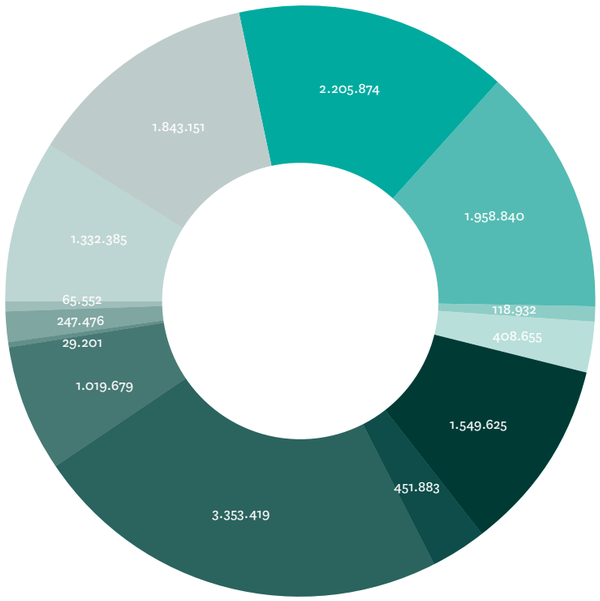
Maria da Graça Carvalho
European Parliament

iMM Lisboa Highlights 2015

Expenditure in 2015 by Funding Source

Total Expenditure

14.584.673 €



Institutional
4.692.301 €

- Core
- Competitive
- Donations
- Services

Research Labs
9.892.372 €

- FCT Grants
- Other National Grants
- EU Grants
- Other International Grants
- Awards
- Donations
- Services
- Work contracts FCT
- Fellowship FCT

Patents

New patent applications or provisional patent application in 2015

PT108132 "ADIPOSE TISSUE IS A MAJOR TARGET OF T. BRUCEI PARASITES" GL Luisa Figueiredo
Provisional Patent Application

PT108181 "DESIGN OF PEPTIDES FOR BRAIN DELIVERY" GL Miguel Castanho
Provisional Patent Application

US62/191126 "COMPOSITIONS FOR THE TREATMENT OF MALARIA" GL Maria M. Mota
Provisional Patent Application

US62/192004 "COMPOSITIONS FOR THE TREATMENT OF MALARIA" GL Maria M. Mota
Provisional Patent Application

PT108829 "Celastrol decreases CD68 synovial macrophages in arthritic rats preventing synovial inflammation and bone damage" GL João Eurico-Fonseca
Provisional Patent Application

PT108856 "Means and methods for *in vitro* production of highly differentiated mature myofibers" GL Edgar Gomes
Provisional Patent Application

Ongoing patent application at 31/12/2015

PT105724;PCT/BR2012/000162 "Denv-Derived peptides for the inhibition of the flavivírus replication" GL Nuno Santos
Patent Application – PCT

PCT/PT2012/000034 "The anthracycline for the treatment of sepsis" GL Luis Ferreira Moita
Patent Application — PCT

PCT/IB2012/052545 "Generation of peripheral blood gamma-delta t-cells expressing natural cytotoxicity receptors for cancer immunotherapy" GL Bruno Silva-Santos
Patent Application – PCT

PT106189; PCT/BR2012/000162 "Means and methods for the inhibition of the flavivirus replication" GL Nuno Santos
Patent Application – PCT

PCT/IB2013/053050 "Genetically modified rodent plasmodium parasites as platforms for a whole-organism malaria vaccine" GL Maria M. Mota – GL Miguel Prudêncio
Patent Application – PCT

PCT/IB2013/055261 "The use of ret agonist molecules for haematopoietic stem cell expansion protocols and transplantation therapy and a ret agonist kit" GL Henrique Veiga- Fernandes
Patent Application – PCT

iMM Lisboa at a glance

232
Publications International Journals

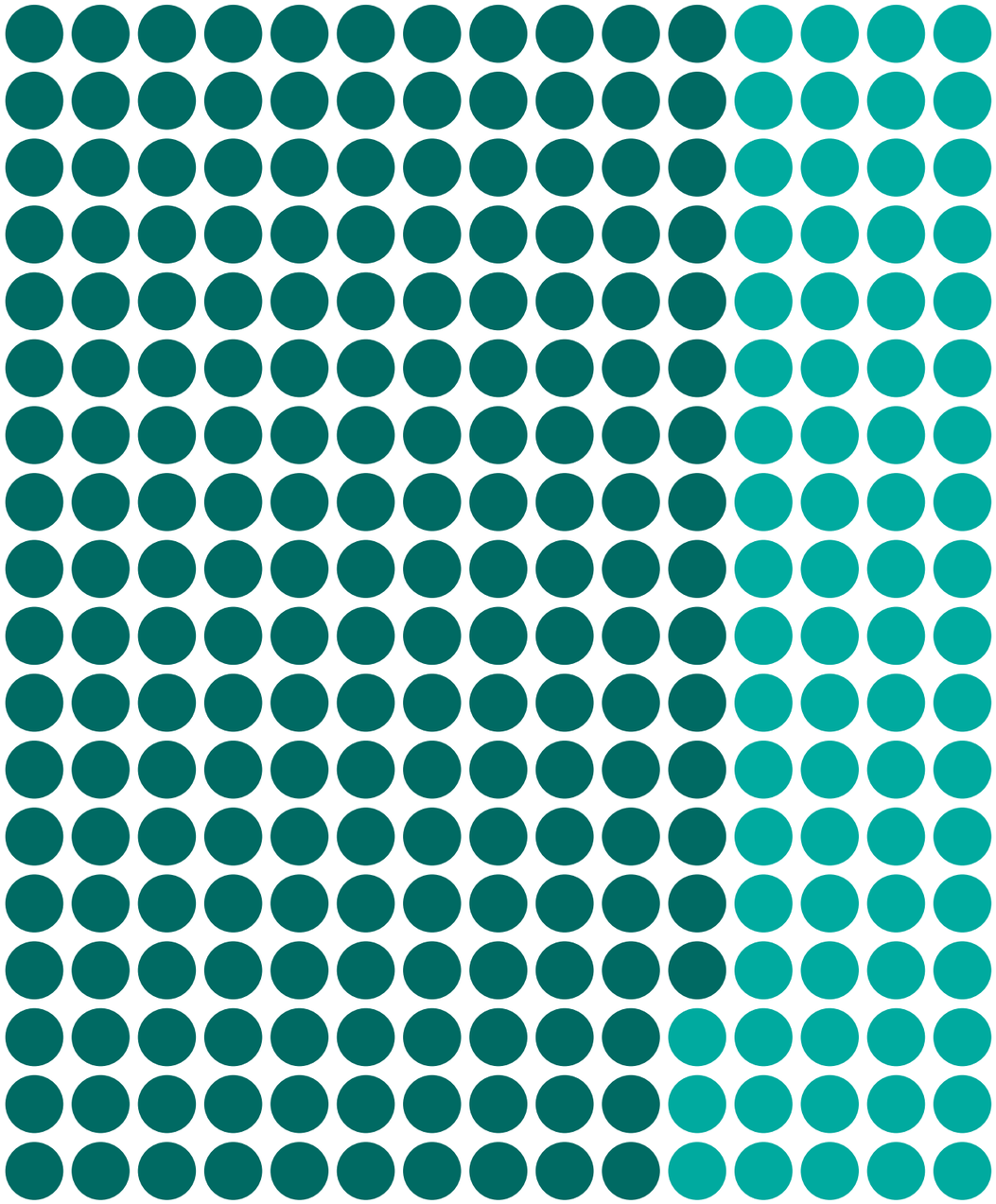
56
...in journals with an impact factor between 5-10

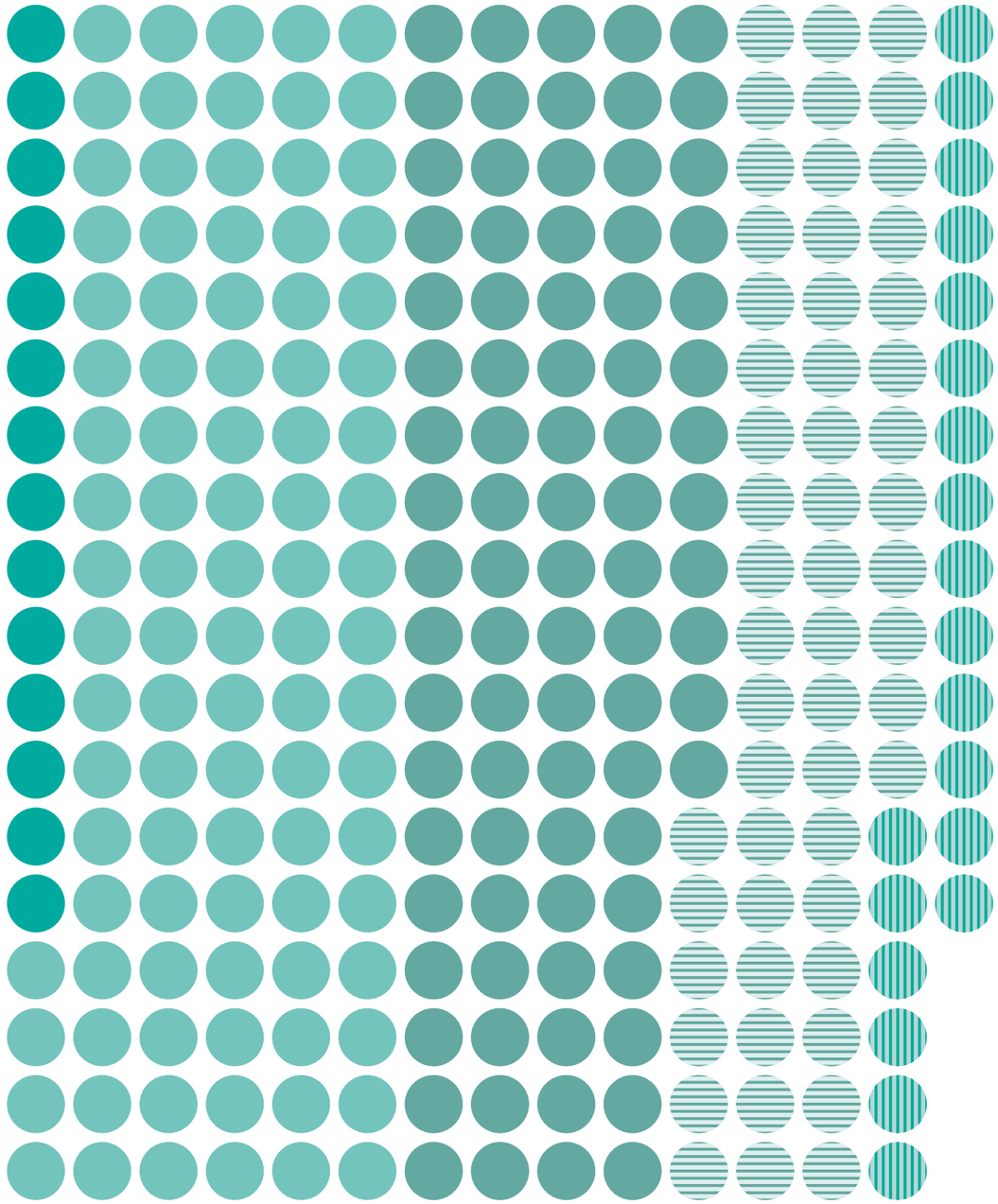
11
...in journals with an impact factor higher than 10

Research Highlights

Sum of the Times Cited

27059

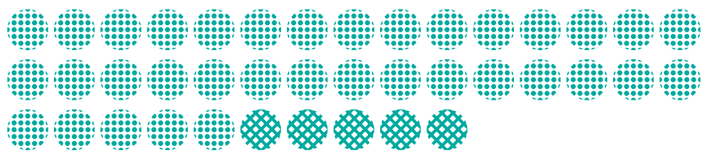




536 Researchers

of wich 70 are International Researcher Fellows

- 195 PhD Researchers
- 89 PhD Students
- 94 M.Sc Researchers
- 84 M.Sc Students
- 54 Graduate
- 20 Others



- 35 Research Laboratories
- 5 Start-ups

1 year in the life of iMM Lisboa

Egas Moniz Building – FMUL

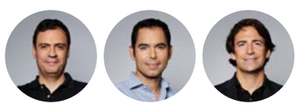
January

2nd Edition of the International PhD Program — LisbonBioMed

February

Ana Rita Fragoso received the LPCC - NRS - Terry Fox 2015/2016 Grant

João Barata, Henrique Veiga-Fernandes and Bruno Silva-Santos were each awarded an European Research Council (ERC) Consolidator Grant



iMM Lisboa was awarded an Horizon 2020-ERA Chair Project

March

IX IMM/CAML PhD Meeting

International Brain Awareness Week

SEMANA INTERNACIONAL DO CÉREBRO
14 A 21 DE MARÇO DE 2015

April

1st iMM Scientific Retreat

iMM Lisboa — Open Day

May

Launch of new institutional image
iMM Lisboa : Chasing questions

Instituto de Medicina Molecular Lisboa

Gonçalo Bernardes (coordinator) Ana E. Sousa and Luis Graça (participants) received an Horizon 2020 ITN — Innovative Training Network Grant

June

Laço and Instituto de Medicina Molecular (iMMLisboa) teamed up to investigate breast cancer

FUNDO iMM - LAÇO
A CAMINHO DA CURA

July

Workshop iMM Lisboa with the support of Associação Laço and participation of the researcher and Group Leader Sérgio Dias and the PhD students Marie Bordone (Nuno Morais Lab) and Pedro Barbacena (Cláudio Franco Lab)

August

Fundraising Activities

Luso de Fruta Power on: support for Fundo Laço e iMM (50% of the total value of registrations goes to the Fund)

September

Ana Sebastião, Edgar Gomes and Maria M. Mota were awarded an Horizon 2020 – Twinning Grant

iMM PostDoc Day

Lisboa Instituto de Medicina Molecular

3rd iMM Postdoc Day :

October

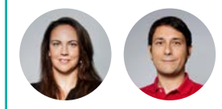
Fundraising Activities

Corrida Saúde + Solidária: support for Centro de Investigação de Tumores Cerebrais (50% of the total value of registrations goes to the Center)

João Carriço (participant) was awarded an European Food Safety Authority (EFSA) Grant

November

Vanessa Morais and Cláudio Franco were each awarded a European Research Council (ERC) Starting Grant



Helena Cabaço was awarded a Gilead GÉNESE Program 2015 Edition

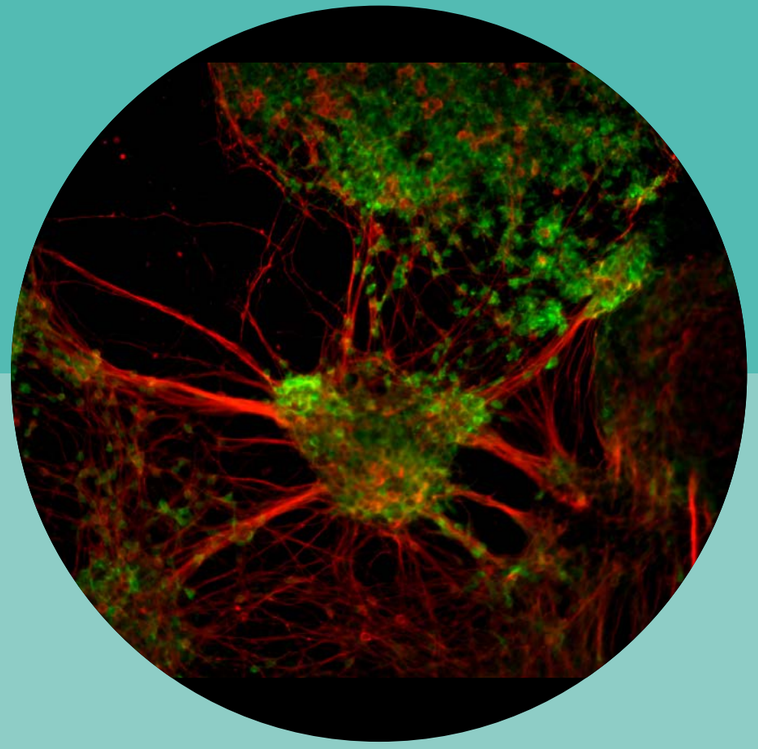
INFARMED
Fundo para a investigação em saúde
- Scientific Area Oncobiology — Julie Ribot
- Scientific Area Scientific Area Cerebrovascular Diseases — Ana Catarina Fonseca

December

Vanessa Morais received an EMBO Installation Grant

1 2 3 4 5 6 7 8 9 10 11 12

Laboratories



Neurons differentiating in culture, organized in clusters and with multiple extensions to toher clusters.

Barata, João T.

Signaling in Cancer

João Taborda Barata :
Group Leader at iMM Lisboa since 2006

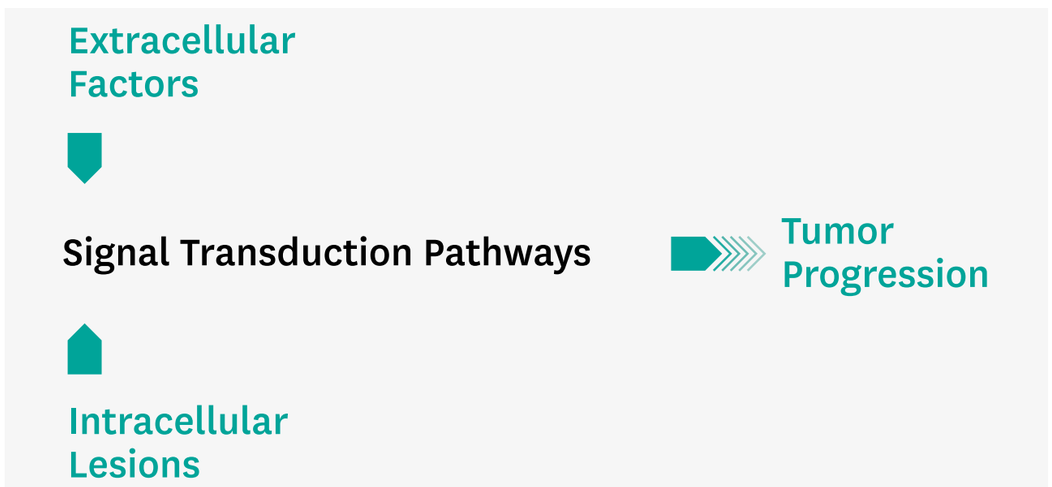
joao_barata@medicina.ulisboa.pt

- PhD (2003) in Biomedical Sciences at Harvard Medical School, USA, and Universidade do Porto
- Post-doctoral researcher at iMM Lisboa, Institut Pasteur, France, and Utrecht University, The Netherlands

Keywords

Cancer Biology • Leukemia • Signal transduction • Cellular and molecular biology • Rational targeted therapies

Our research focuses on the role that both cell-intrinsic aberrations (at the gene and protein levels) and micro-environmental factors (particularly cytokines) might play during tumor development.



Major Interests — Objectives

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

Selected Publications

— Sarmento L.M, Póvoa V, Nascimento R, Real G, Antunes I, Martins L.R, Moita C, Alves P.M, Abecasis M, Moita L.F, Parkhouse R.M.E, Meijerink J.P.P, Barata J.T (2015). CHK1 overexpression in T-cell acute lymphoblastic leukemia is essential for proliferation and survival by preventing excessive replication stress. **Oncogene** 34(23): 2978-2990. (Citations: 3)

— Mendes RD*, Sarmento LM*, Canté-Barrett K, Zuurbier L, Buijs-Gladdines J, Póvoa V, Smits WK, Abecassis M, Yunes JA, Sonneveld E, Horstmann MA, Pieters R, Barata JT **, Meijerink JPP ** (2014). PTEN microdeletions in T-cell acute lymphoblastic leukemia are caused by illegitimate RAG-mediated recombination events. **Blood** 124 (4): 567--578. *co-first authors; ** co-senior authors (Citations: 7)

— Lonetti A*, Antunes IL*, Chiarini F, Orsini E, Buontempo F, Ricci F, Tazzari PL, Pagliaro P, Melchionda F, Pession A, Bertaina A, Locatelli F, McCubrey JA, Barata JT**, Martelli AM** (2014). Activity of the pan-class I phosphoinositide 3-kinase inhibitor NVP-BKM120 in T-cell acute lymphoblastic leukemia. **Leukemia** 28, 6, 1196–1206. *co-first authors; ** co-senior authors (Citations: 15)

— Zenatti P.P, Ribeiro D, W. Li, Zuurbier L, Silva M.C, Paganin M, Tritapoe J, Hixon J.A, Silveira A.B, Cardoso B.A, Sarmento L.M, Correia N, Toribio M.L, Kobarg J, Horstmann M, Pieters R, Brandalise S.R, Ferrando A.A, Meijerink J.P, Durum S.K, Yunes J.A, Barata J.T (2011) Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia. **Nature Genetics** 43, 932. Citations: 95)

— Henriques C.M, Rino J, Nibbs R.J, Graham G.G, Barata J.T (2010) IL-7 induces rapid clathrin-mediated internalization and JAK3-dependent degradation of IL-7R? in T cells. **Blood** 115, 3269. (Citations: 38)

Bernardes, Gonçalo J.L

Chemical Biology & Pharmaceutical Biotechnology

Gonçalo Bernardes :
Group Leader at iMM Lisboa since 2013

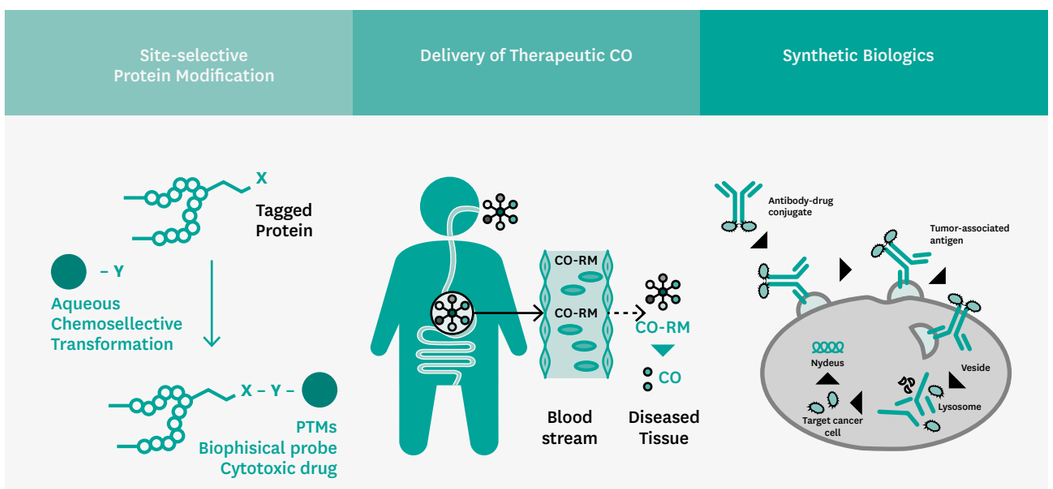
gbernardes@medicina.ulisboa.pt

- DPhil (2008) in Chemical Biology at the University of Oxford, UK
- Post-doctoral studies at the Max-Planck Institute (Berlin, Germany) and ETH Zürich (Switzerland)
- Group Leader – Royal Society University Research Fellow at the Department of Chemistry, University of Cambridge, UK since 2013

Keywords

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

We work at the interface of Chemistry and Biology with a focus on new methods for protein modification and their use to provide new biological insight and towards the development of protein-based therapeutics



Major Interests — Objectives

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

Selected Publications

— Ferreira MC, Albuquerque IS, Matak-Vinkovic D, Coelho AC, Carvalho SM, Saraiva LM, Romão CC, Bernardes GJL* (2015) Spontaneous CO Release from RuII(CO)2-Protein Complexes in Aqueous Solution, Cells and Mice. **Angew Chem**, 54, 1172. (Citations: 13)

— Amgarten B, Rajan R, Martínez-Sáez N, Oliveira BL, Albuquerque IS, Reid DG, Brooks RA, Duer MJ, Bernardes GJL*(2015) Collagen labelling with an azide-proline chemical reporter in live cells. **Chem Commun** 51, 5250-5252. 96. (Citations: 1)

— Seixas JD, Chaves-Ferreira M, Montes-Grajales D, Gonçalves AM, Marques AR, Saraiva LM, Olivero-Verbel J, Romão CC, Bernardes GJL (2015) A N-acetyl cysteine ruthenium tricarbonyl conjugate enables simultaneous release of CO and ablation of ROS species. **Chem Eur**, 21, 14708. (Citations: 0)

— Albuquerque IS, Jeremias HF, Chaves-Ferreira M, Matak-Vinkovic D, Boutureira O, Romão CC, Bernardes GJL* (2015) Histidine-selective metallation in Interleukin-8 with a ruthenium dicarbonyl fragment. **Chem Commun**, 51, 3993-3996. (Citations: 0)

— Crockett MP, Evans AM, Worthington MJH, Albuquerque IS, Slattery AD, Gibson CT, Bernardes GJL, Chalker JM (2015) Sulfur-Limonene Polysulfide: A Material Synthesized Entirely from Industrial Waste and Its Use in Removing Toxic Metals from Water and Soil. **Angew Chem**, 54, 1-6. (Citations: 0)

— Martínez-Sáez N, Castro-López J, Valero-González J, Madariaga D, Compañón I, Somovilla VJ, Salvadó M, Asensio JL, Jiménez-Barbero J, Avenoza A, Busto JH, Bernardes GJL, Peregrina JM, Hurtado-Guerrero R, Corzana F (2015) X-ray Structures decipher the Non-equivalence of Serine and Threonine O-glycosylation points: Implications for the Molecular Recognition of the Tn Antigen by an anti-MUC1 Antibody. **Angew Chem**, 54, 9830. (Citations: 1)

Carmo - Fonseca, Maria

RNA & Gene Regulation

Maria Carmo-Fonseca :
President of the iMM Lisboa since 2014

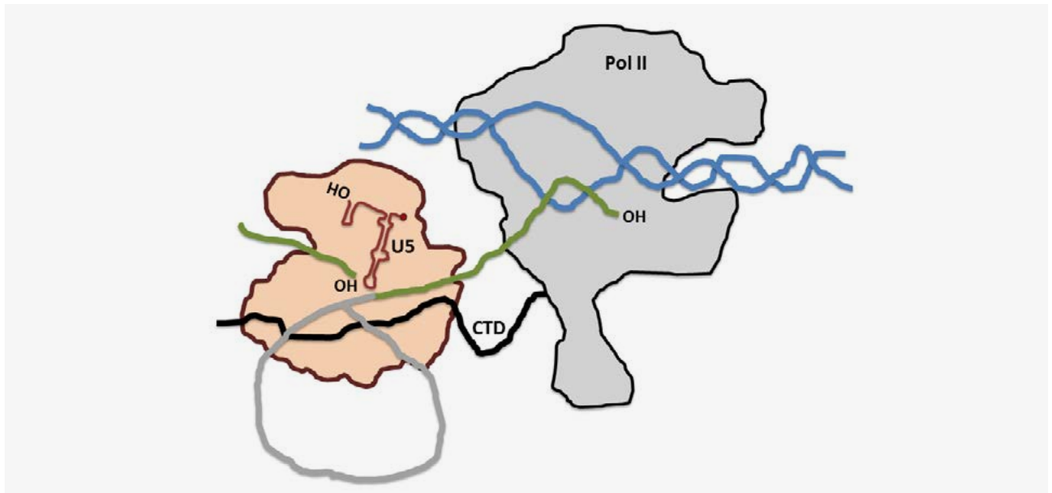
carmo.fonseca@medicina.ulisboa.pt

- MD (1983) and PhD (1988) in Cell Biology at Faculdade de Medicina da Universidade de Lisboa (FMUL)
- Post-doctoral researcher at EMBL in Heidelberg, Germany
- Full Professor at Faculdade de Medicina da Universidade de Lisboa
- Executive Director of iMM Lisboa between 2002-2014

Keywords

Cell and Molecular Biology • RNA biology • RNA in disease

Transcription and splicing are fundamental steps in gene expression. Using a new methodology for genome-wide analysis of nascent RNA profiles we found that splicing is coupled to a specific phosphorylation pattern of Pol II carboxyl-terminal domain (CTD).



Major Interests — Objectives

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

Selected Publications

— Nojima T, Gomes T, Grosso AR, Kimura H, Dye MJ, Dhir S, Carmo-Fonseca M, and Proudfoot N. (2015) Mammalian NET-seq reveals genome-wide nascent transcription coupled to RNA processing. **Cell** 161, 526. (Citations: 8)

— Martin RM, Rino, J, Carvalho, C, Kirchhausen, T, Carmo-Fonseca, M. (2013) Live-cell visualization of pre-mRNA splicing with single-molecule sensitivity. **Cell Reports** 4, 1144. (Citations: 15)

— de Almeida, SF, Grosso, AR, Koch, F, Fenouil, R, Carvalho, S, Andrade, J, Levezinho, H, Gut, M, Eick, D, Gut, I, Andrau, JC, Ferrier P, Carmo-Fonseca, M (2011) Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 Lys36. **Nature Struct. Mol. Biol.** 18, 977. (Citations: 92)

— Martins, SB, Rino, J., Carvalho, T., Carvalho, C., Yoshida, M., Klose JM, de Almeida, SF, Carmo-Fonseca, M. (2011) Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3' end of human genes. **Nature Struct. Mol. Biol.** 18, 1115. (Citations: 40)

— Grosso, A.R., Gomes, A.Q., Barbosa-Morais, N.L., Caldeira, S., Thorne, N.P., Grech, G., von Lindern, M., and Carmo-Fonseca, M (2009) Tissue-specific splicing factor gene expression signatures. **Nucleic Acids Research** 36, 4823. (Citations: 68)

Castanho, Miguel

Physical Biochemistry of Drugs & Targets

Miguel Castanho :
Group Leader at iMM Lisboa since 2008

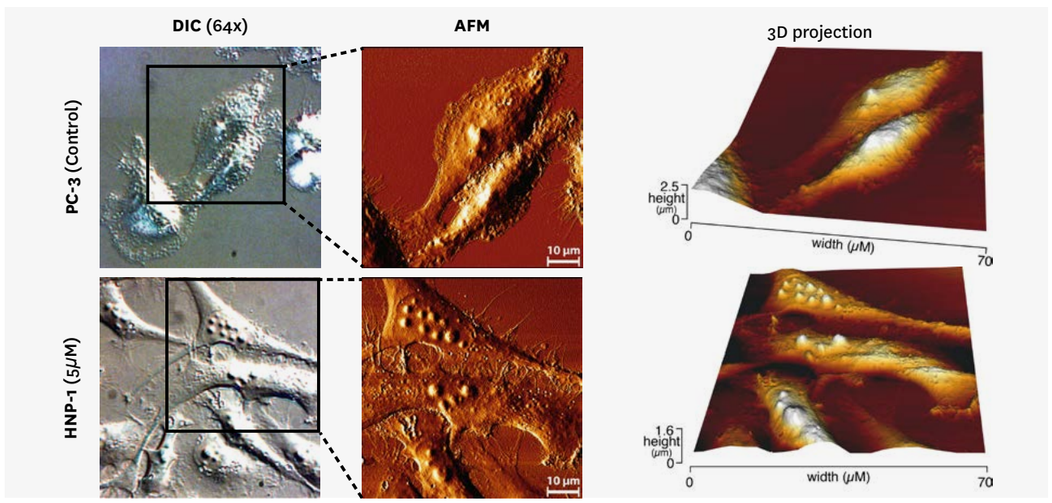
macastanho@medicina.ulisboa.pt

- PhD (1993) in Molecular Biophysics at Universidade Técnica de Lisboa
- Post-doctoral research at University of Hawaii, USA, and at Rocasolano Institute, Madrid, Spain
- Full Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Drug discovery • Peptide • Antimicrobials/anticancer Drugs • HIV • • Dengue • Blood-brain barrier

Morphological examination of tumor cells using atomic force microscopy (AFM). Differential interference contrast (DIC) images, AFM error images, and three-dimensional (3D) projections of human prostate adenocarcinoma (PC-3) cells reveal tumor cells' morphology in the absence and presence of the human neutrophil peptide-1 (HNP-1). Incubation of the tumor cells with HNP-1 compromises the epithelial morphology observed for control cells and promotes cells' collapse and nuclear fragmentation.



Major Interests — Objectives

There are many biological processes that depend on the interaction between peptides/proteins and membrane lipids, such as viral fusion, translocation across epithelia or innate immune defence. Some of these may be inspiring to develop innovative therapeutical tools. The goal of the MCastanho Lab is to unravel the physical principles that govern lipid-peptide interactions, with implications in viral fusion (HIV and Dengue virus are of particular interest), analgesia and translocation of the blood-brain barrier, and development of antimicrobial and anticancer drugs. We are interested not only in drug targets and drug discovery itself, but also in the molecular-level mechanism of action of efficient and safe drugs.

Selected Publications

— Freire JM, Almeida Dias S, Flores L, Veiga AS and Castanho MARB. (2015) Mining viral proteins for antimicrobial and cell-penetrating drug delivery peptides. **Bioinformatics** 31, 2252–2256. (Citations: 2)

— Gaspar D, Freire JM, Pacheco TR, Barata JT, Castanho MARB (2015) Apoptotic human neutrophil peptide-1 anti-tumor activity revealed by cellular biomechanics. **Biochim Biophys Acta – Mol Cell Res**, 1853, 308-316. (Citations: 3)

— Freire JM, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, Da Poian AT, Castanho MA. (2014) Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein: design and mechanism of action. **FEBS J.**, 281, 191-215. (Citations: 7)

— Santos SM, Garcia-Nimo L, Sá Santos S, Tavares I, Cocho JA, Castanho MA (2013) Neuropeptide kyotorphin (tyrosyl-arginine) has decreased levels in the cerebro-spinal fluid of Alzheimer's disease patients: potential diagnostic and pharmacological implications. **Front Aging Neurosci.**, 5, 1. (Citations: 2)

— Veiga AS, Sinthuvanich C, Gaspar D, Franquelim HG, Castanho MA, Schneider JPB (2012) Arginine-rich self-assembling peptides as potent antibacterial gels. **Biomaterials**, 33, 8907–8916. (Citations: 44)

— Franquelim HG, Chiantia S, Veiga AS, Santos NC, Schwille P, Castanho MA (2011) Anti-HIV-1 antibodies 2F5 and 4E10 interact differently with lipids to bind their epitopes. **AIDS**, 25, 419-28. (Citations: 1)

Costa, Luis

Translational Oncobiology

Luís Costa :
Group Leader at iMM Lisboa since 2007

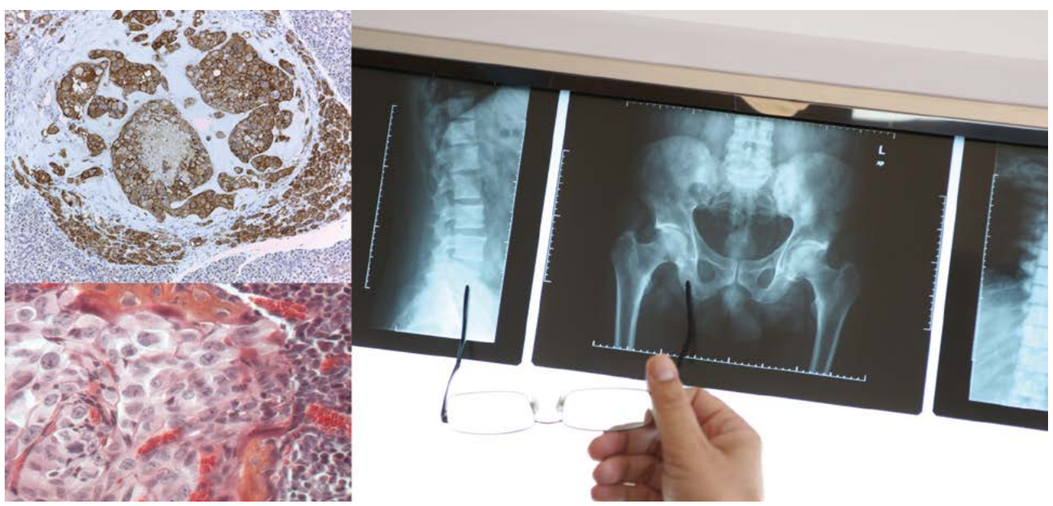
lcosta@medicina.ulisboa.pt

- MD (1985) and PhD (2002) in Bone metastases at Faculdade de Medicina da Universidade de Lisboa (FMUL)
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa
- Director of Oncology Division at Hospital de Santa Maria- -CHLN-Lisboa

Keywords

Metastasis • Metastatic organotropism • • Tumor Microenvironment • Leader Genes Signatures • • Tumor Heterogeneity

Translational research relies on a strict interplay between clinicians and researchers. A multidisciplinary approach is fundamental to successfully translate important clinical questions into relevant research projects with impact in the course of diseases. In our projects, whereas clinical co-investigators at HSM collaborate in the collection and analysis of clinical samples and data, researchers at our laboratory use techniques that integrate basic science (using in vitro approaches, animal models and human samples) into clinical outcomes.



Major Interests — Objectives

In cancer, metastases are the hallmark of lethality. This unique and complex phenomenon is related not only to the genomic alterations in the cancer cell but also to the heterotypic signaling between cancer cells and host tissues, which could explain metastatic organotropism and how tumours reinvent themselves as new tissues in the target organ. We aim to contribute to the understanding of molecular mechanisms involved in tumour progression at the metastatic site (using bone metastases as paradigm) and to unravel molecular signatures of organotropism by identifying “leader genes signatures” common to primary tumour and the corresponding site of metastases (using Colorectal Cancer (CRC) as model) and, also, to study the relevance of Phospholipase C family of enzymes in CRC progression.

Selected Publications

— Mendes D, Alves C, Afonso N, Cardoso F, Passos Coelho JL, Costa L, Andrade S, Marques FB (2015) The benefit of HER2 targeted therapies on overall survival of patients with metastatic HER2+ breast cancer - a systematic review. **Breast Cancer Res.** 17: 140. (Citations: 0)

— Tato Costa J, Casimiro S, Pacheco T, Pires R, Fernandes A, Alho I, Pereira P, Costa P, Castelo HB, Ferreira J, Costa L (2015) Therapy-induced cellular senescence induces epithelial-to-mesenchymal transition and increases invasiveness in rectal cancer. **Clinical Colorectal Cancer** published online. (Citations: 0)

— Casimiro S, Mohammad Khalid S., Pires R, Tato-Costa J, Alho I , Teixeira R, Carvalho A, Ribeiro S, Lipton A, Guise TA, Costa L (2014) RANKL/RANK/MMP-1 Molecular Triad Contributes to the Metastatic Phenotype of Breast and Prostate Cancer Cells In Vitro. **Plos One** 8(5), e63153. (Citations: 17)

— Casimiro S, Fernandes A, Oliveira AG, Franco M, Pires R, Peres M, Matias M, Tato-Costa J, Guerra N, Ramos M, Cruz J, Costa L (2014) Metadherin expression and lung relapse in patients with colorectal carcinoma. **Clin Exp Metastasis** 31, 689. (Citations: 4)

— Pakala SB, Rayala SK, Wang RA, Ohshiro K, Mudvari P, Reddy SD, Zheng Y, Pires R, Casimiro S, Pillai MR, Costa L, Kumar R. (2013) MTA1 promotes STAT3 transcription and pulmonary metastasis in breast cancer. **Cancer Res** 73, 3761. (Citations: 14)

— David H, Luis L, Goldwasser F, Hirsh V, Hungria V, Prausova J, Scagliotti GV, Sleeboom H, Spencer A, Vadhan-Raj S, Moos Roger von, Willenbacher W, Woll P J, Wang J, Jiang Qi, Jun Susie, Dansey R, Yeh H (2011) A Randomized, Double-blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma. **JCO** 29(9), 1125-1132. (Citations: 117)

De Almeida, Sérgio

Chromatin & Epigenetics

Sérgio de Almeida :
Group Leader at iMM Lisboa since 2013

sergioalmeida@medicina.ulisboa.pt

- PhD (2007) in Biomedical Sciences at Universidade do Porto
- Post-doctoral research (2007-2013) at iMM Lisboa

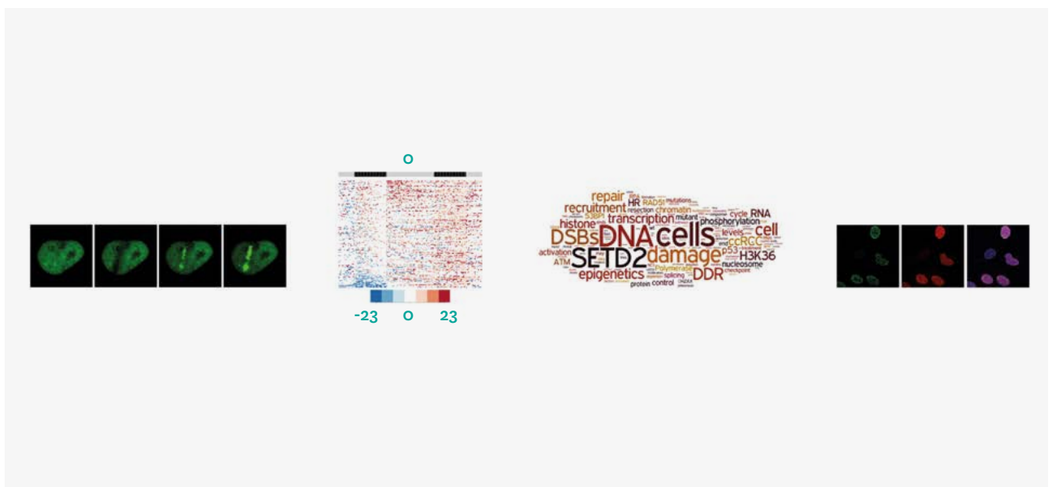
Keywords

Epigenetics • Chromatin Biology • Cancer Biology • • Gene Expression • DNA repair

Major Interests — Objectives

Our research focuses on the mechanisms that regulate chromatin dynamics during transcription and DNA damage response and how they coordinate with the processes that safeguard the genome integrity. Our general aims are twofold: first, we aim at investigating the epigenetic regulation of transcription; in addition, we study the molecular mechanisms that sense, signal and repair DNA damage. A major focus of our research is to understand how changes in transcription, chromatin modification and DNA repair are linked to the development of human diseases such as cancer.

Schematic representation of our main research interests.



Selected Publications

— Grosso AR, Leite AP, Carvalho S, Matos MR, Martins FB, Vítor AC, Desterro JM, Carmo-Fonseca M, de Almeida SF (2015) Pervasive transcription read-through promotes aberrant expression of oncogenes and RNA chimeras in renal carcinoma. **eLife** 4. (Citations: 0)

— Carvalho S, Vitor A, Sridhara SC, Martins FB, Raposo AC, Desterro JM, Ferreira J, de Almeida SF (2014) SETD2 is required for DNA double-strand break repair and activation of the p53-mediated checkpoint. **eLife** 3. (Citations: 14)

— Carvalho S, Raposo AC, Martins FB, Grosso AR, Sridhara SC, Rino J, Carmo-Fonseca M, de Almeida SF (2013) Histone methyltransferase SETD2 coordinates FACT recruitment with nucleosome dynamics during transcription. **Nucleic Acids Research**, 41, 2881. (Citations: 28)

— de Almeida SF, Grosso AR, Koch F, Fenouil R, Carvalho S, Levezinho H, Eick D, Gut I, Andrau JC, Ferrier P, Carmo-Fonseca M. (2011) Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 lysine 36. **Nature Structural and Molecular Biology**, 18, 977. (Citations: 92)

— de Almeida SF, Garcia-Sacristan S, Custodio N and Carmo-Fonseca M (2010) A link between nuclear RNA surveillance, the human exosome and RNA polymerase II transcriptional termination. **Nucleic Acids Research**, 38, 8015. (Citations: 33)

De Carvalho, Mamede

Translational Clinical Physiology

Mamede de Carvalho :
Group Leader at iMM Lisboa since 2005

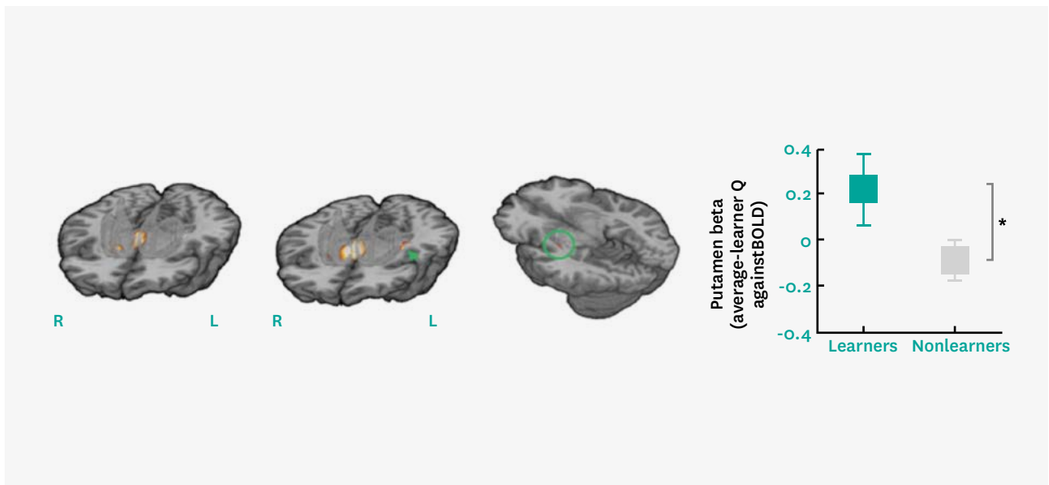
mamedealves@medicina.ulisboa.pt

- 1985 MD at Faculdade de Ciências Médicas, Universidade Nova de Lisboa
- 2000 PhD at Faculdade de Medicina da Universidade de Lisboa
- Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Amyotrophic Lateral Sclerosis • Neurophysiology and Respiratory Involvement • Atrial Fibrillation and Autonomic Nervous System • Neurocomputational Modelling of Brain Disorders • Familial Amyloid Polyneuropathy and Early Markers of Disease • Attention Deficit Hyperactivity Disorder • Biological Signal Processing

Activation of the striatum during reinforcement learning in humans (left).
Activation of the putamen distinguishes subjects who learn from those who do not (right).
From Horga*, Maia*, et al. in Human Brain Mapping, Vol. 36, No. 2, pp.793-803. *Authors contributed equally.



Major Interests — Objectives

Our laboratory investigates the motor neuron function and its degeneration, peripheral nerve function and small fibre neuropathy, modulation of central nervous system function, behaviour and imaging-neurocomputational models of brain dysfunction. We are contributing to a more complete comprehension of the electrophysiological signs in motor neuron degeneration, reliable evaluation of the small fibres, electrical current influence on nervous system activity and on the understanding of brain structures in behaviour disturbances. In the future, we aim to approach new techniques to measure small fibre and anterior horn cells function, plasticity of the spinal cord motor activity, and the interaction between brain imaging, behaviour, motor movement disorders and electrophysiology.

Selected Publications

— Horga*, G., Maia*, T. V., Marsh, R., Hao, X., Xu, D., Duan, Y., Tau, G. Z., Graniello, B., Wang, Z., Kangarlu, A., Martinez, D., Packard, M. G., Peterson, B. S. (2015) Changes in corticostriatal connectivity during reinforcement learning in humans. **Human Brain Mapping**, 36, 793-803. (Citations: 1)

— Neuwirth C, Barkhaus PE, Burkhardt B, Castro J, Czell D, de Carvalho M, Nandedkar S, Stålberg E, Weber M (2015). Tracking motor neuron loss in a set of 6 muscles in amyotrophic lateral sclerosis using the Motor Unit Number Index (MUNIX) – a 15 months longitudinal multicentre trial. J **Neurol Neurosurg Psychiatry,** 2015;86:1172-1179. (Citations: 0)

— Lefaucheur, J. P., André-Obadia, N., Antal, A., Ayache, S. S., Baeken, C., Benninger, D. H., & Devanne, H. (2014). Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). **Clinical Neurophysiology**, 125(11), 2150-2206. (Citations: 166)

— Turner, M. R., Hardiman, O., Benatar, M., Brooks, B. R., Chio, A., de Carvalho, M. & Kiernan, M. C. (2013) Controversies and priorities in amyotrophic lateral sclerosis. **Lancet Neurology** 322, 310. (Citations: 174)

— de Carvalho, M. and Swash, M., (2013). Fasciculation potentials and earliest changes in motor unit physiology in ALS. J **Neurol Neurosurg Psychiatry**, 84:963-968. (Citations: 21)

— Maia, T. V., & Frank, M. J (2011) From reinforcement learning models to psychiatric and neurological disorders. **Nature Neuroscience** 162, 154. (Citations: 241)

Dias, Sérgio

Vascular Biology & Cancer Microenvironment

Sérgio Dias :
Group Leader at iMM Lisboa since 2012

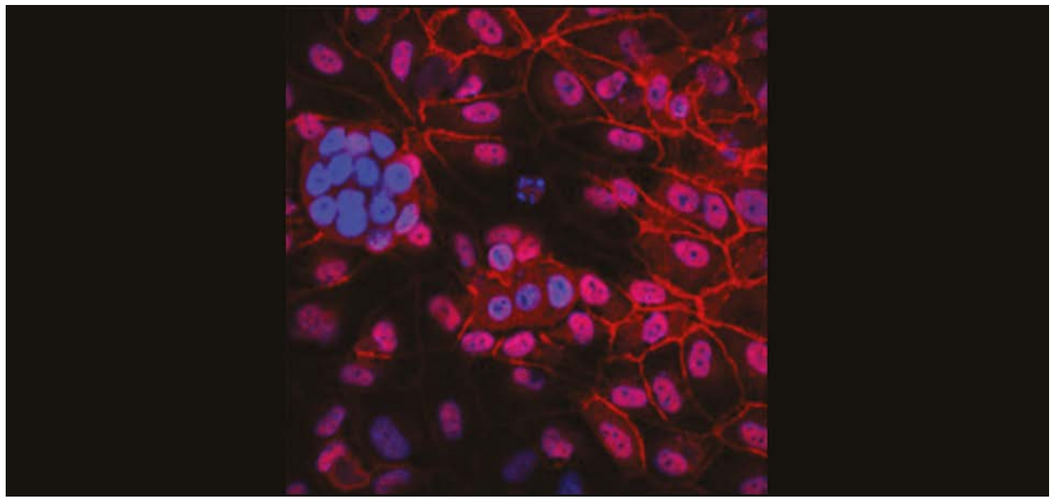
sergiodias@medicina.ulisboa.pt

- PhD (1998) in Tumor Immunology, University College London, UK
- Post-doctoral (1999-2001) at the Department of Hematology, Cornell University, New York
- Principal Investigator (2002-2012) and coordinator (2003-2012) of the Molecular Pathobiology Department at Instituto Português de Oncologia Francisco Gentil (IPO Lisboa)
- Associate Professor (2012) at Faculdade de Medicina da Universidade de Lisboa

Keywords

Angiogenesis • Tumor spread • Metabolism

Tumor cell: blood vessel interactions. Confocal image of an In vitro co-culture of breast tumor cells (arrows) and blood vessel endothelial cells. Endothelial VE-cadherin molecules are stained in red to show cell to cell contacts. Nucleus are depicted in blue. This system is used to study transmigration of cancer cells through endothelial monolayers during metastasis.



Major Interests — Objectives

We study the role of blood vessels, and of endothelial cells, in regulating normal organ function and in disease. In detail, we study cancers (solid and hematologic) as a systemic disease that involves (and requires) blood vessels for its onset and progression. In addition to the role of blood vessels, we also study the involvement of bone marrow-derived cells and of metabolic systemic signals in cancer onset and progression.

Selected Publications

— Silva LS, Goncalves LG, Silva F, Domingues G, Maximo V, Ferreira J, Lam EW, Dias S, Felix A, Serpa J (2015) STAT3:FOXM1 and MCT1 drive uterine cervix carcinoma fitness to a lactate-rich microenvironment. **Tumour Biol**. 2015 pp 1-11. (Citations: 0)

— Costa A, Afonso J, Osório C, Gomes AL, Caiado F, Valente J, Aguiar SI, Pinto F, Ramirez M, Dias S. (2013) miR-363-5p regulates endothelial cell properties and their communication with hematopoietic precursor cells. **Journal of Hematology and Oncology** 6(1), 87. (Citations: 10)

— Caiado F, Carvalho T, Rosa I, Remedio L, Costa A, Matos J, Heissig B, Yagita H, Hattori K, da Silva JP, Fidalgo P, Dias Pereira A and Dias S (2013) Bone marrow-derived CD11b+Jagged2+ cells promote epitelial to mesenchymal transition and metastization in colorectal cancer. **Cancer Research** 73(14), 4233-46. (Citations: 13)

— Caiado F, Carvalho T, Silva F, Castro C, Clode N, Dye JF and Dias S. (2011) The role of fibrin E on the modulation of endothelial progenitors adhesion, differentiation and angiogenic growth factor production and the promotion of wound healing. **Biomaterials** 32(29), 7096-105. (Citations: 32)

— Gomes AL, Carvalho T, Torre C, Serpa J and Dias S. (2010) Hypercholesterolemia promotes bone marrow cell mobilization by perturbing the SDF1:CXCR4 axis. **Blood** 115(19), 3886-94. (Citations: 58)

— Serpa J, Caiado F, Carvalho T, Torre C, Goncalves LG, Casalou C, Lamosa P, Rodrigues M, Zhu Z, Lam EW, Dias S (2010) Butyrate rich colonic microenvironment is a relevant selection factor for metabolically adapted tumour cells. **Journal of Biological Chemistry** 285(50), 39211-23. (Citations: 18)

Ferreira, Joaquim J.

Clinical Pharmacology

Joaquim Ferreira :
Group Leader at iMM Lisboa since 2013

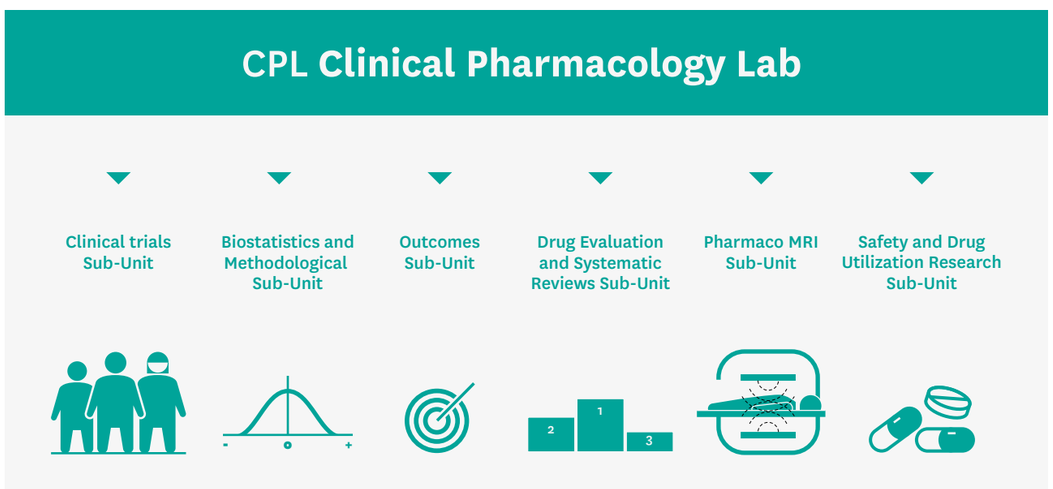
jferreira@medicina.ulisboa.pt

- MD (1992) and PhD (2009) in Neurology at Faculdade de Medicina da Universidade de Lisboa
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa since 2012
- Director of Laboratory of Clinical Pharmacology and Therapeutics, FMUL (2011)

Keywords

Parkinson's disease • Huntington Disease • Movement Disorders • • Neuropharmacology • Clinical trials • Systematic reviews

Coelho M, Marti MJ, Sampaio C, Ferreira JJ, Valldeoriola F. (2015) Dementia and severity of parkinsonism determines the handicap of patient´s in late-stage Parkinson´s disease: the Barcelona-Lisbon cohort. **European Journal of Neurology**, 22(2):305-312. (Citations: 2)



Major Interests — Objectives

The main mission of our lab is to contribute to the development of effective and safe therapeutic interventions through the establishment of optimized methodologies for the design, conduction, analysis and report of clinical trials. The main clinical pharmacology domains of interest are clinical trials methodology, outcomes, systematic reviews, safety, pharmaco MRI and drug utilization. The emphasis is mainly on novel, early phase proof-of-principle clinical studies and new methodological and trial designs but the scope extends throughout the clinical development spectrum. We also envision collaborations with the pharmaceutical industry, facilitating the conduction of clinical trials to a shared role in the early stages of drug and planning of clinical development.

Selected Publications

— Coelho M, Marti MJ, Sampaio C, Ferreira JJ, Valldeoriola F. (2015) Dementia and severity of parkinsonism determines the handicap of patient´s in late-stage Parkinson´s disease: the Barcelona-Lisbon cohort. **European Journal of Neurology**, 22(2):305-312. (Citations: 2)

— Ferreira JJ, Lees A, Rocha JF, Poewe W, Rascol O, Soares-da-Silva P; Bi-Park 1 investigators. (2015) Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: a randomised, double-blind, controlled trial. **Lancet Neurol**. (Citations: 1)

— Fernandes RM, Plint AC, Terwee CB, Sampaio C, Klassen TP, Offringa M, van der Lee JH. (2015) Validity of bronchiolitis outcome measures. **Pediatrics**, 135, 1399-408. (Citations: 3)

— Reimão S, Pita Lobo P, Neutel D, Correia Guedes L, Coelho M, Rosa MM, Azevedo P, Ferreira J, Abreu D, Gonçalves N, Nunes RG, Campos J, Ferreira JJ (2015) Substantia nigra neuromelanin-MR imaging differentiates Essential tremor from Parkinson's disease. **Movement Disorders**, 30(7), 953-959. (Citations: 5)

— Ferreira JJ, Rosser A,Craufurd D, Squitieri F, Mallard N, Landwehrmeyer B. (2015) Eicosapentaenoic Acid Treatment in Huntington's Disease: A Placebo-Controlled Clinical Trial. **Movement Disorders**, 30(10), 1426-1429. (Citations: 1)

— Caldeira D, Rodrigues FB, Barra M, Santos AT, de Abreu D, Gonçalves N, Pinto FJ, Ferreira JJ, Costa J. (2015) Non-vitamin K antagonist oral anticoagulants and major bleeding-related fatality in patients with atrial fibrillation and venous thromboembolism: a systematic review and meta-analysis. **Heart**, 101(15), 1204-11. (Citations: 6)

Ferro, José

Clinical Research in Non-communicable Neurological Diseases

José Ferro :
Group Leader at iMM Lisboa since 2003

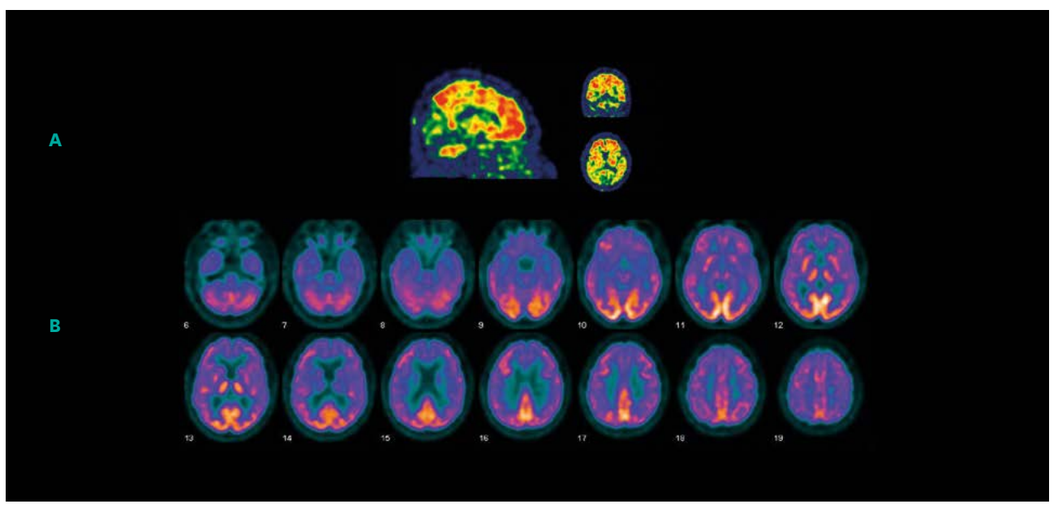
jmferro@medicina.ulisboa.pt

- MD (1975) and PhD (1987) at Faculdade de Medicina da Universidade de Lisboa (FMUL)
- Full Professor and Chairman at FMUL and Hospital de Santa Maria

Keywords

Stroke • Aphasia • Cognitive decline • Complex Diseases • • Genetics • Clinical Trials

A• PET-PIB in Alzheimer disease patient **B**• PET-FDG in Alzheimer disease



Major Interests — Objectives

The general objective of UNIC is to increase the knowledge and foster the prevention and treatment of major prevalent and disabling disorders involving the brain, such as stroke and Alzheimer's disease. The main advantage of the lab is the strong collaboration among the experienced PIs, based on common clinical investigation methodologies and particular features of research expertise, expanded by multiple national and international collaborations in the areas of basic neurosciences, clinical genetics, advanced statistical methods, biological engineering, and neuroimaging. The researchers of UNIC conducted clinical trials and assessed the clinical impact of different interventions in multinational efforts to get new treatments for these prevalent and disabling brain disorders.

Selected Publications

— Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, Mali WP, Beard JD, Cleveland T, Engelter ST, Lyrer PA, Ford GA, Dorman PJ, Brown MM; International Carotid Stenting Study investigators. (2015) Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. **Lancet** 385:529-538. (Citations: 18)

— Fonseca AC, Brito D, Pinho e Melo T, Geraldes R, Canhão P, Caplan LR, Ferro JM. (2014) N-terminal pro-brain natriuretic peptide shows diagnostic accuracy for detecting atrial fibrillation in cryptogenic stroke patients. **Int J Stroke** 9, 419-425. (Citations: 6)

— Crespo ÂC, Silva B, Marques L, Marcelino E, Maruta C, Costa S, Timóteo A, Vilares A, Couto FS, Faustino P, Correia AP, Verdelho A, Porto G, Guerreiro M, Herrero A, Costa C, de Mendonça A, Costa L, Martins M. (2014) Genetic and biochemical markers in patients with Alzheimer's disease support a concerted systemic iron homeostasis dysregulation. **Neurobiol Aging** 35, 777-785. (Citations: 17)

— Canhão P, Abreu LF, Ferro JM, Stam J, Bousser MG, Barinagarrementeria F, Fukujima MM; for the ISCVT Investigators. (2013) Safety of lumbar puncture in patients with cerebral venous thrombosis. **Eur J Neurol** 20:1075-1080. (Citations: 5)

— Verdelho A, Madureira S, Moleiro C, Ferro JM, O'Brien JT, Poggesi A, Pantoni L, Fazekas F, Scheltens P, Waldemar G, Wallin A, Erkinjuntti T, Inzitari D (2013) Depressive symptoms predict cognitive decline and dementia in older people independently of cerebral white matter changes: the LADIS study. **J Neurol Neurosurg Psychiatry**. 84, (11), 1250-4 (Citations: 11)

— Dávalos A, Alvarez-Sabín J, Castillo J, Díez-Tejedor E, Ferro J, Martínez-Vila E, Serena J, Segura T, Cruz VT, Masjuan J, Cobo E, Secades JJ; International Citicoline Trial on acUte Stroke (ICTUS) trial investigators. (2012) Citicoline in the treatment of acute ischaemic stroke: an international, randomised, multicentre, placebo-controlled study (ICTUS trial). **Lancet** 380:349-57. (Citations: 66)

Figueiredo, Luisa

Biology of Parasitism

Luísa M Figueiredo :
Group Leader at iMM Lisboa since 2009

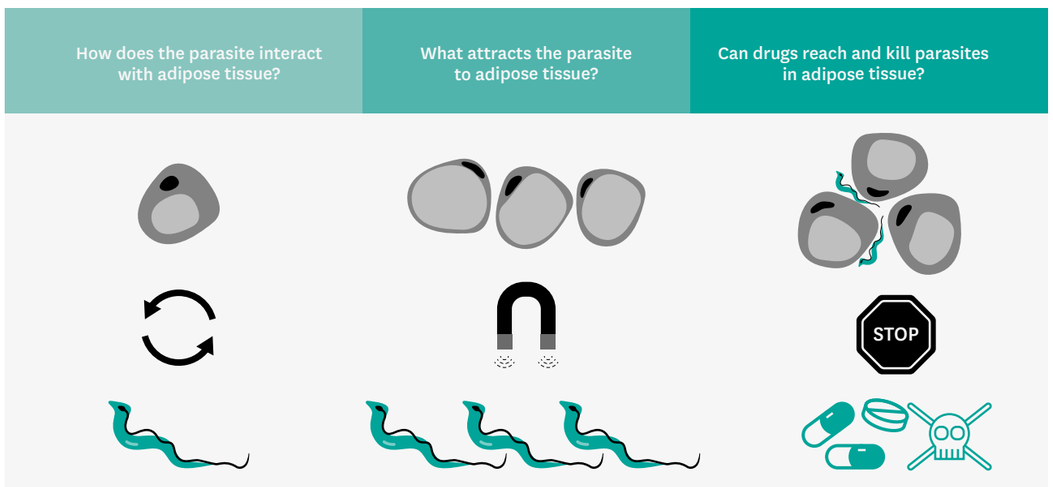
lmf@medicina.ulisboa.pt

- PhD (2002) from Universidade do Porto and Institut Pasteur, France
- Post-doctoral research at The Rockefeller University, New York, USA
- Research Associate at The Rockefeller University, New York, USA (2008-2009)

Keywords

Antigenic variation • Chromatin • Gene Expression • Parasitology • • Host-parasite Interaction • Glycobiology

In the bloodstream, Trypanosoma brucei parasites are covered by an electronic dense coat of Variant Surface Glycoproteins, which is shed periodically to avoid elimination by the cells of the immune system.



Major Interests — Objectives

Sleeping sickness is a fatal neglected disease caused by Trypanosoma brucei a unicellular parasite. Parasites exploit their host to increase their reproductive success and to enhance their transmission efficiency. Efficient parasitism depends on the cross-talk between parasite, host and environment. In T. brucei, such mechanisms include antigenic variation, cell differentiation and interference with sleep pattern and circadian rhythm of the host. In our group, we use genetic, biochemical and molecular approaches to study these interactions with the prospect to uncover fundamental exploitable differences that can lead to new diagnostic and therapeutic tools.

Selected Publications

— Aresta-Branco F, Pimenta S, Figueiredo LM (2015) A transcription-independent epigenetic mechanism is associated with antigenic switching in Trypanosoma brucei. **Nucl Acids Res**, doi:10.1093/nar/gkv1459. (Citations: 0)

— Rodrigues JA, Acosta-Serrano A, Aebi M, Ferguson MAJ, Routier FH, Schiller I, Soares S, Spencer D, Titz A, Wilson IBH and Izquierdo L (2015) Parasite glycobiology: A bittersweet symphony. **PLoS Pathogens**, 11(11):e1005169. (Citations: 0)

— Pena AC, Pimentel MR, Manso H, Vaz-Drago R, Pinto-Neves D, Aresta-Branco F, Rijo-Ferreira F, Guegan F, Pedro Coelho L, Carmo-Fonseca M, Barbosa-Morais NL, Figueiredo LM (2014) Trypanosoma brucei histone H1 inhibits RNA polymerase I transcription and is important for parasite fitness in vivo. **Molecular Microbiology**, 93(4), 645-63. (Citations: 4)

— 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. (Citations: 30)

— Boothroyd, C. E., Dreesen, O., Leonova, T., Ly, K. I., Figueiredo, L. M., Cross, G. A. M., and Papavasiliou, F. N. (2009). A yeast-endonuclease-generated DNA break induces antigenic switching in Trypanosoma brucei. **Nature** 459, 278-281. (Citations: 77)

Filipe, Paulo

Dermatology Research

Paulo Filipe :
Group Leader at iMM Lisboa since 2014

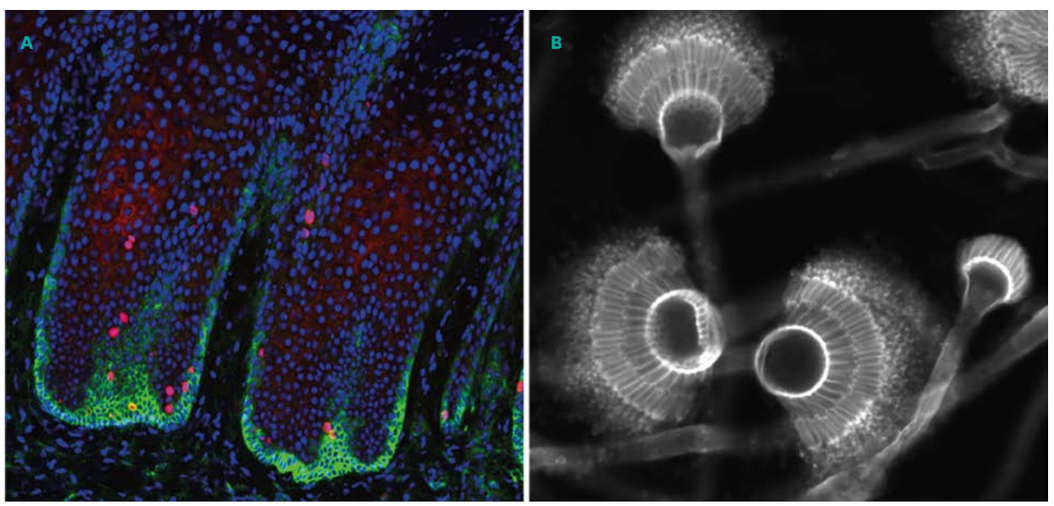
pfilipe@medicina.ulisboa.pt

- PhD in Medicine (2005) at Faculdade de Medicina da Universidade de Lisboa
- MD (1988) at Faculdade de Medicina de Lisboa da Universidade de Lisboa

Keywords

Psoriasis • Th9 and Tc9 cells; Th17 and Tc17 cells • Phototoxicity

A. Psoriasis - Skin lesion from a psoriatic patient is shown. Proliferating epidermal cells (red signal), basal epidermal cells (green signal), nuclei (blue signal).
B. Aspergillus terreus - cultivated from a skin ulcer on the leg.



Major Interests — Objectives

We devote our efforts to the search of clinically useful markers and drug targets in common skin diseases afflicting humans such as psoriasis. After healing, psoriasis tends to recur within previously affected skin areas invoking some sort of tissue immunological memory. Knowledge-based manipulation of this memory compartment may contribute to a better long-term management of human psoriasis. We aim at characterizing the cellular components of this memory compartment in clinical samples from patients treated with phototherapy and/or anti-IL17/ IL-23 antibodies, and the mechanisms involved in its activation and maintenance, namely the role of the IL-9/Th9 axis, in the pre-clinical model.
We are also using proteomics analyses of serum proteins to identify early markers of disease recurrence.

Selected Publications

— Morlière P, Boscá F, Silva AM, Teixeira A, Galmiche A, Mazière JC, Nourry V, Ferreira J, Santus R, Filipe P. (2015) A molecular insight into the phototoxic reactions observed with vemurafenib, a first-line drug against metastatic melanoma. **Photochem. Photobiol.** Sci.,14, 2119-2127. (Citations: 0)

— Pinheiro T, Silva R, Fleming R, Gonçalves A, Barreiros MA, Silva JN, Morlière P, Santus R, Filipe P. (2014) Distribution and quantitation of skin iron in primary haemochromatosis: Correlation with total body iron stores in patients undergoing phlebotomy. **Acta Derm Venereol.** 94 (1). (Citations: 0)

— Morlière P, Hug GL, Patterson LK, Mazière JC, Ausseil J, Dupas JL, Ducroix JP, Santus R, Filipe P.(2014) Chemistry of free radicals produced by oxidation of endogenous α-aminoketones. A study of 5 aminolevulinic acid and α-aminoacetone by fast kinetics spectroscopy. **Biochim Biophys Acta** 1840 (10): 3190-7. (Citations: 0)

— Paul C, Puig L, Kragballe K, Luger T, Lambert J, Chimenti S, Girolomoni G, Nicolas JF, Rizova E, Lavie F, Mistry S, Bergmans P, Barker J, Reich K; (2014) Transition to ustekinumab in patients with moderate-to-severe psoriasis and inadequate response to methotrexate: a randomized clinical trial (TRANSIT). **Br J Dermatol.**; 170 (2): 425-34. (Citations: 5)

— Filipe P, Morlière P, Silva JN, Mazière JC, Patterson LK, Freitas JP, Santus R. (2013) Plasma lipoproteins as mediators of the oxidative stress induced by UV light in human skin: a review of biochemical and biophysical studies on mechanisms of apolipoprotein alteration, lipid peroxidation, and associated skin cell responses. **Oxid Med Cell Longev.** (Citations: 0)

Fonseca, João Eurico

Rheumatology Research

João Eurico-Fonseca :
Group Leader at iMM Lisboa since 2004

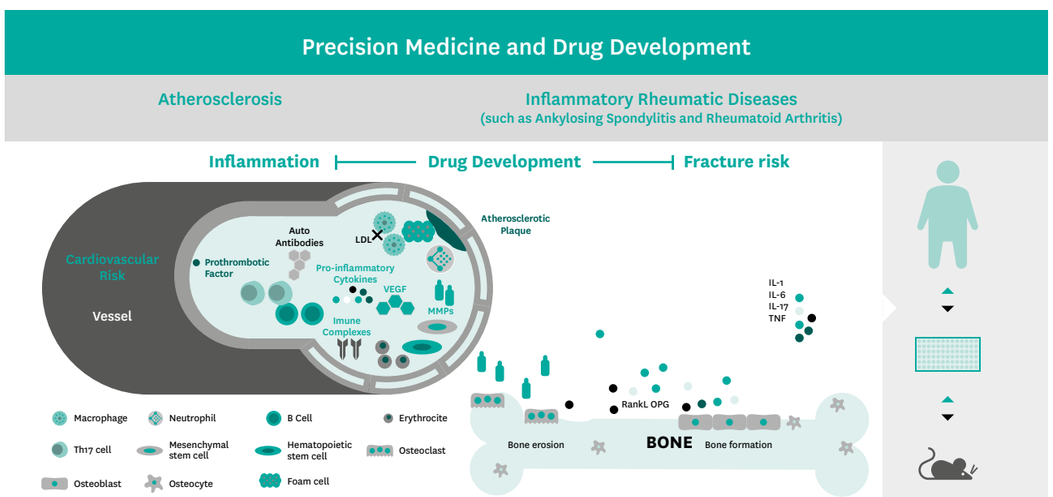
jcfonseca@medicina.ulisboa.pt

- MD (1992) and PhD (2004) in Rheumatology at Faculdade de Medicina da Universidade de Lisboa
- Associate Professor with Habilitation, Faculdade de Medicina da Universidade de Lisboa
- Rheumatologist, Rheumatology Department at Hospital de Santa Maria

Keywords

Joint Inflammatory Diseases • Rheumatoid Arthritis • Psoriatic Arthrits • Ankylosing Spondylitis and Juvenile Idiopathic Arthritis • Systemic Effects of Inflammation and Effects of Inflammation on Bone — Osteoporosis • Osteoarthritis and Rheumatoid Arthritis • Bone Biology • Chronic Inflammation and Cardiovascular Risk — Atherosclerosis and Bone • Epidemiology of Rheumatic Diseases

Our Lab is devoted to the translational study of the early burden of inflammatory rheumatic diseases on bone and vessel, seeking prognostic markers, predictors of treatment response and new treatment targets



Major Interests — Objectives

Our lab results from a partnership between the iMM/FMUL and the Rheumatology Department of the Santa Maria Hospital. Basic scientists and clinicians closely work together to promote translational research and clinical excellence in the field of Rheumatology. Our specific research objectives are the study of the impact of inflammatory joint diseases (such as Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Spondyloarthritis (SpA) and Systemic Lupus Erythematosus (SLE)) on bone and vessel in order to characterize potential tools for early diagnosis and prognosis and potential targets for novel therapies. The long-term objective is to achieve recognition as an European League Against Rheumatism Centre of Excellence in Rheumatology.

Selected Publications

— Cascão R, Vidal B, Raquel H, Neves-Costa A, Figueiredo N, Gupta V, Fonseca JE, Moita LF. (2012)Effective treatment of rat adjuvant-induced arthritis by celastrol. **Autoimmun Rev** 11:856-62 (Citations: 24)

— Cascão R, Moura RA, Perpétuo I, Canhão H, Vieira-Sousa E, Mourão AF, Rodrigues AM, Polido-Pereira J, Queiroz MV, Rosário HS, Souto-Carneiro MM, Graca L, Fonseca JE. (2010) Identification of a cytokine network sustaining neutrophil and Th17 activation in untreated early rheumatoid arthritis. **Arthritis Res Ther**, 12(5), R196. (Citations: 24)

— 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. (Citations: 22)

— Cascão R, Rosário HS, Souto-Carneiro MM, Fonseca JE. (2010) Neutrophils in rheumatoid arthritis: More than simple final effectors. **Autoimmun Rev**, 9, 531-535. (Citations: 47)

— Fonseca JE, Santos MJ, Canhão H, Choy E. (2009) Interleukin-6 as a key player in systemic inflammation and joint destruction. **Autoimmun Rev**, 538-542, 8. (Citations: 122)

— Caetano-Lopes J, Canhão H, Fonseca JE. (2009) Osteoimmunology-the hidden immune regulation of bone. **Autoimmun Rev**, 8(3), 250-5. (Citations: 36)

Franco, Cláudio A.

Vascular Morphogenesis

Cláudio Franco :
Group Leader at iMM Lisboa since 2013

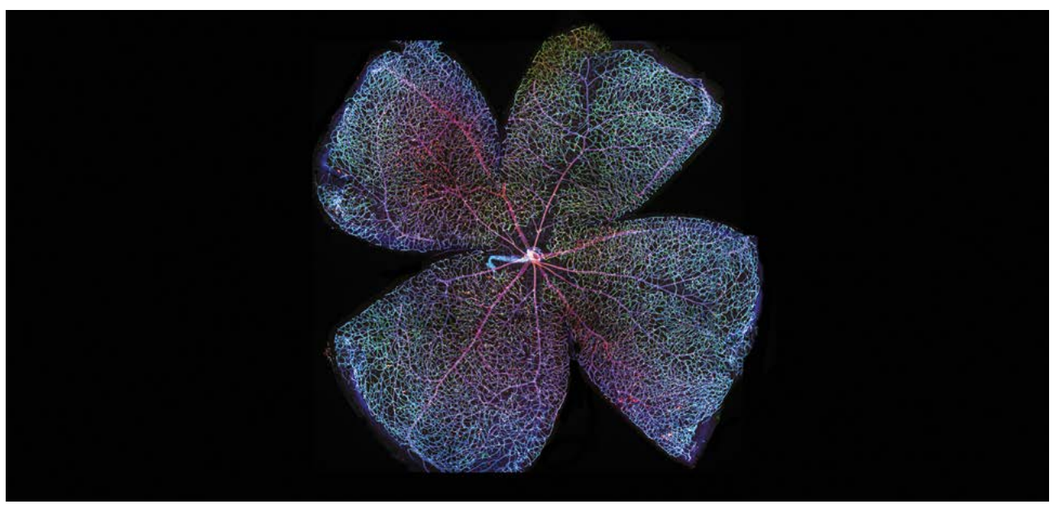
cfranco@medicina.ulisboa.pt

- PhD (2004-2008) at Pierre and Marie Curie University, France
- Post-Doctoral (2009-2013) research at London Research Institute – CRUK, UK

Keywords

Angiogenesis • Cell Migration • Tumour Angiogenesis • Endothelial Cells • Vascular Patterning

Blood vessels in a mouse retina: Overview of the complexity and hierarchical structure of the vascular network using IsolectinB4 (blue), Icam2 (green) and collagenIV (red).



Major Interests — Objectives

The Vascular Morphogenesis Lab has the aim to understand the molecular mechanisms regulating coordinated endothelial cell behaviour during sprouting and remodelling phases of the angiogenic process. Improving the knowledge on the molecular regulation of vascular morphogenesis will certainly create new possibilities for medical prevention and treatment of various human conditions.

We want to:

— Finding novel regulators of endothelial cell migration in sprouting angiogenesis
— Molecular regulation of endothelial cell axial polarity
— Effects of haemodynamic forces in vascular patterning
— Novel anti-angiogenic therapies blocking tumour angiogenesis

Selected Publications

— Franco CA, Jones ML, Bernabeu MO, Geudens I, Mathivet T, Rosa A, Lopes FM, Lima AP, Ragab A, Collins RT, Phng LK, Coveney PV, Gerhardt H. (2015) Dynamic endothelial cell rearrangements drive developmental vessel regression. **PLoS Biology** 13(5) e1002163. doi: 10.1371/journal.pbio.1002163. (Citations: 10)

— Aspalter IM, Gordon E, Dubrac A, Ragab A, Narloch J, Vizán P, Geudens I, Collins RT, Franco CA, Abrahams CL, Thurston G, Fruttiger M, Rosewell I, Eichmann A, Gerhardt H. (2015) Alk1 and Alk5 inhibition by Nrp1 controls vascular sprouting downstream of Notch. **Nature Communications** 17; 6: 7264 (Citations: 8)

— Bentley K, Franco CA, Philippides A, Blanco R, Dierkes M, Gebala V, Stanchi F, Jones J, Cagna G, Kutschera S, Claesson-Welsh L, Vestweber D, Gerhardt H. (2014) The role of differential VE-cadherin dynamics in cell rearrangement during angiogenesis. **Nature Cell Biology** 16, 309-21. (Citations: 54)

— Bernabeu MO, Jones M, Nielsen JH, Kruger T, Nash RW, Groen D, Hetherington J, Gerhardt H, Franco CA, Coveney PV (2014) Computer simulations reveal complex distribution of haemodynamic forces in a mouse retina model of angiogenesis. **J R Soc Interface** 11, http://rsif.royalsocietypublishing.org/content/11/99/20140543.long. (Citations: 5)

Gomes, Edgar

Cell Architecture

Edgar Gomes :
Group Leader at iMM Lisboa since 2013

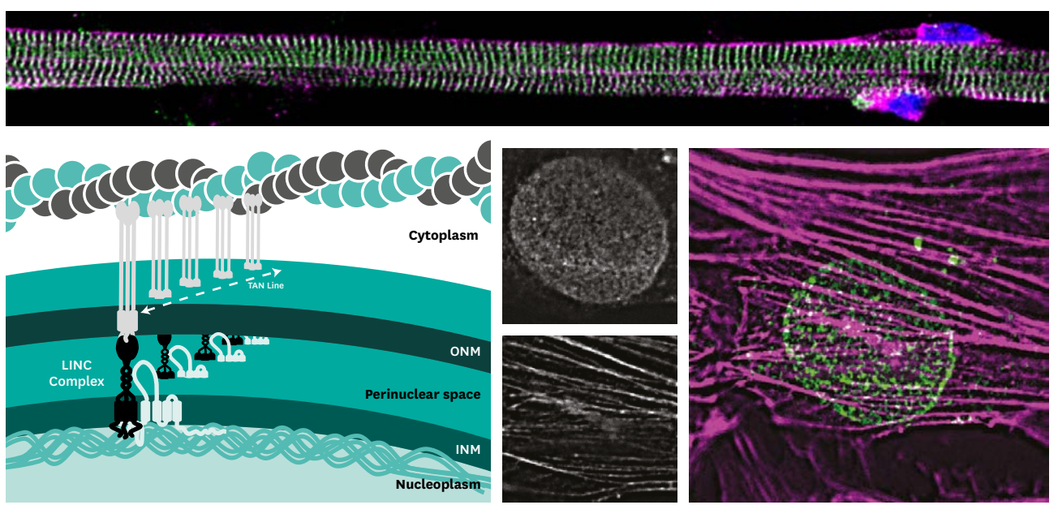
edgarfomes@medicina.ulisboa.pt

- PhD in Cell Biology (2002) at Center for Neuroscience, Universidade de Coimbra, Portugal
- Pos-Doctoral research (2002--2007), Department of Anatomy and Cell Biology, Columbia University, New York, USA
- Team leader (since 2007) UMR S 787-Group Myologie, Paris France

Keywords

Skeletal Muscle • Cell Biology • Cytoskeleton • Cell Migration

Connecting the nucleus to the cytoskeleton.
Top - skeletal muscle fiber differentiated in vitro with highly differentiated transversal triads and nuclei at the periphery.
Bottom left - how the nuclear envelope connects to the actin cytoskeleton using the linc complex.
Bottom right - the actin cytoskeleton surrounds the nucleus of migrating cells.



Major Interests — Objectives

Connecting the nucleus to the cytoskeleton is relevant for multiple cellular processes and disruption of these connections result in multiple pathologies. Nuclear positioning within cell cytoplasm requires the connection between the nucleus and the cytoskeleton. We are interested in understanding the processes involved in these connections and the role for nuclear positioning in cell function.

We study cell migration and skeletal myofiber formation which involves the connection between the nucleus and the cytoskeleton and precise nuclear positioning. We use different molecular and cellular approaches in combination with time-lapse imaging analysis to address these questions.

Selected Publications

— D'Alessandro, M., Hnia, K., Gache, V., Koch, C., Gavriilidis, C., Rodriguez, D., Nicot, A.-S., Romero, N.B., Schwab, Y., Gomes, E.R., Labouesse, M., Laporte, J. (2015) Amphiphysin 2 Orchestrates Nucleus Positioning and Shape by Linking the Nuclear Envelope to the Actin and Microtubule Cytoskeleton. **Developmental Cell** 35, 186. (Citations: 2)

— Falcone S., Roman W., Hnia K., Gache V., Didier N., Lainé J., Aurade F., Marty I., Nishino I, Charlet-Berguerand N., Romero N., Marazzi G., Sassoon D., Laporte J., Gomes E.R. 6, 1455–1475 (2014) N-WASP is required for Amphiphysin-2/BIN1 dependent nuclear positioning and triad organization in skeletal muscle and is involved in the pathophysiology of centronuclear myopathy. **EMBO Mol Med** 6, 1455. (Citations: 1)

— Cadot, B., Gache, V., and Gomes, E.R. (2014) Fast, Multi-Dimensional and Simultaneous Kymograph-Like Particle Dynamics (SkyPad) Analysis. **PLoS One** 19, 9 (2). (Citations: 0)

— Metzger, T., Gache, V., Xu, M., Cadot, B., Folker, E., Richardson, B., Gomes, E.R.*, Baylies, M.K.*. (2012) MAP and Kinesin dependent nuclear positioning is required for skeletal muscle function. **Nature** 484, 120. *co-corresponding authors.(Citations: 52)

— Luxton GW*, Gomes ER*, Folker ES, Vintinner E, Gundersen GG. (2010) Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement. **Science** 329, 5994. (Citations: 140)

Graça, Luis

Lymphocyte Regulation

Luís Graça :
Group Leader at iMM Lisboa since 2005

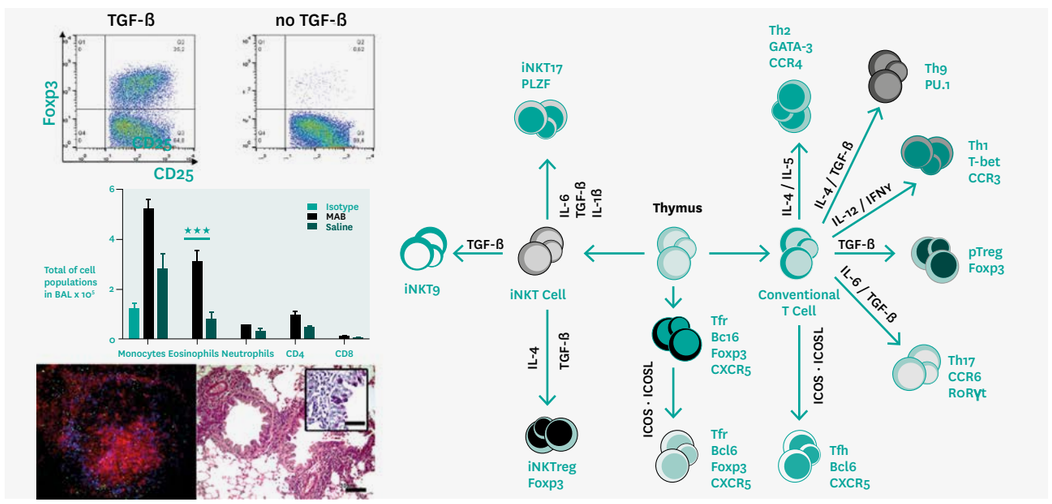
lgraca@medicina.ulisboa.pt

- MD (1995) at Faculdade de Medicina da Universidade de Lisboa (FMUL)
- PhD (2002) in Immunology at the University of Oxford, UK
- Post-doctoral research at University of Oxford, UK, and at University of Western Australia, Perth
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Immune tolerance • Regulatory T cell subsets • T follicular helper (Tfh) cells • Allergy • Autoimmunity • Transplantation

Our research interests are focused on the acquisition of specialized functional characteristics by T cell subsets, and the functional impact of those T cells in immune pathology. We are particularly interested in studying different Foxp3+ lymphocyte subsets, and their role in the regulation of germinal centre responses (micrograph in the bottom) and allergic diseases (images on top).



Major Interests — Objectives

Our Lab studies mechanisms underlying induction and maintenance of immune tolerance. In other words, we research methods to reprogramme the immune response in situations where the immune system is causing a disease, such as allergy, autoimmunity and transplant rejection. In addition, we are interested in defining the functional properties of lymphocytes that can promote immune tolerance by suppressing pathogenic immune responses. We have been studying how different types of lymphocytes with regulatory function can be induced in the periphery. We believe that in the foreseeable future antibody therapy, as well as other strategies to modulate the immune system, will have an important repercussion in the quality of life of people suffering from immune mediated diseases.

Selected Publications

— Monteiro M, Agua-Doce A, Almeida CF, Fonseca-Pereira D, Veiga-Fernandes H, Graca L (2015) IL-9 expression by invariante NKT cells is not imprinted during thymic development. **J Immunol**. 195(7):3463-3471. (Citations: 0)

— Oliveira VG, Agua-Doce A, Curotto de Lafaille MA, Lafaille JJ, Graca L. (2013) Adjuvant facilitates tolerance induction to factor VIII in hemophilic mice through a Foxp3-independent mechanism that relies on IL-10. **Blood** 121, 3936. (Citations: 9)

— Monteiro M, Almeida CF, Agua-Doce A, Graca L. (2013) Induced IL-17-producing invariant NKT cells require activation in presence of TGF-b and IL-1b. **J Immunol**. 190, 805. (Citations: 29)

— Oliveira VG, Caridade M, Paiva RS, Demengeot J, Graca L. (2011) Sub-optimal CD4+ T-cell activation triggers autonomous TGF-b-dependent conversion to Foxp3+ regulatory T cells. **Eur J Immunol**. 41, 1249. (Citations: 34)

— Wollenberg I, Agua-Doce A, Hernández A, Almeida C, Oliveira VG, Faro J, Graca L. (2011) Regulation of the germinal center reaction by Foxp3+ follicular regulatory T cells. **J Immunol**. 187, 4553. (Citations: 145)

— 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-?. **J Immunol**. 185, 2157. (Citations: Citations: 76)

Henrique, Domingos

Stem Cells & Neurogenesis

Domingos Henrique :
Group Leader at iMM Lisboa since 2005

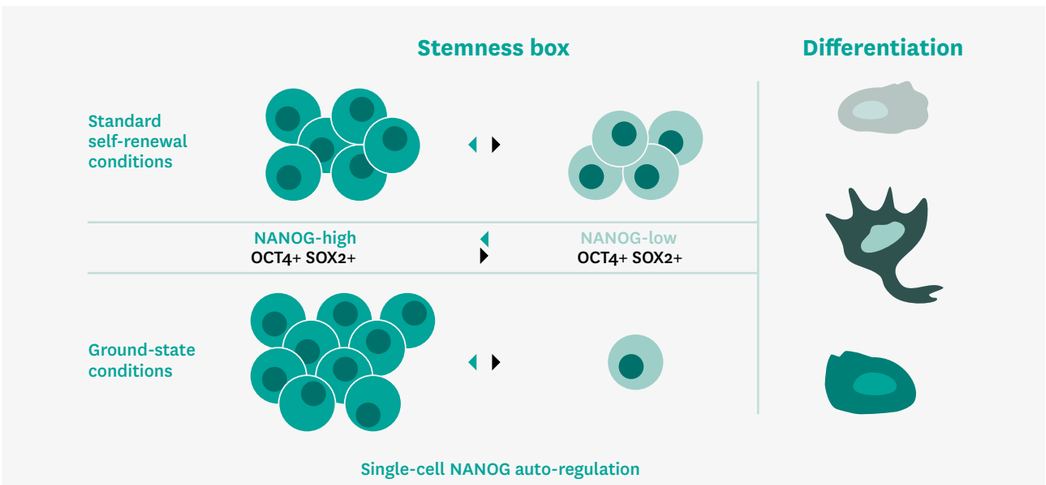
henrique@medicina.ulisboa.pt

- PhD (1991) at Universidade de Lisboa
- Pos-Doctoral research at NIMR and ICRF, UK and Institut d' Embryologie Cellulaire et Moleculaire, France
- Investigator at Faculdade de Medicina da Universidade de Lisboa

Keywords

Stem cells • Notch signalling • Pluripotency • Neurogenesis • Gene regulatory Networks • Systems Biology

Embryonic stem cells fluctuate between different states of competence to differentiation, in a process controlled by the Nanog gene. Understanding how pluripotency is maintained, and how exit to differentiation is controlled, is fundamental to progress into clinical applications of stem cells.



Major Interests — Objectives

Research in our laboratory has been focused on understanding how cells decide which differentiation paths they follow during embryonic development to generate tissues and organs. Our aim is to elucidate the gene regulatory networks that control cell-fate decision processes in the embryo, using 2 experimental models: i) embryonic stem cells to study the mechanisms underlying their pluripotent state, and ii) neural retina to investigate how neural progenitors generate the variety of neurons that compose the adult eye. The main goal is to understand the molecular mechanisms governing decision processes that stem/progenitor cells employ to differentiate along various fates, thereby generating correctly patterned tissues and organs.

Selected Publications

— Costa A, Sanchez-Guardado L, Juniat S, Gale JE, Daudet N, Henrique D. (2015) Generation of sensory hair cells by genetic programming with a combination of transcription factors. **Development**. 142(11):1948-59. (Citations: 0)

— Abranches E, Guedes AMV, Moravec M, Maamar H, Svoboda P, Raj A, Henrique D. (2014), Stochastic NANOG fluctuations allow mouse embryonic stem cells to explore pluripotency. **Development**, 141, 2770-9. (Citations: 15)

— Abranches, E., Bekman, E., Henrique, D. (2013) Generation and characterization of a novel mouse embryonic stem cell line with a dynamic reporter of Nanog expression. **Plos One**, 8, e59928. (Citations: 9)

— Vilas-Boas, F., Fior, R., Swedlow, J.D., Storey, K.G., Henrique, D. (2011) A novel Reporter of Notch Signalling indicates regulated and random Notch Activation during Vertebrate Neurogenesis. **BMC Biology** 9, 58.
(Citations: 14)

— Abranches, E., Silva, M., Pradier, L., Schulz, H., Hummel, O., Henrique, D., Bekman, E. (2009) Neural Differentiation of Embryonic Stem Cells in vitro: a Road Map to Neurogenesis in the Embryo. **PlosOne**, 4(7): e6286. (Citations: 35)

— Rocha, S.F, Lopes, S.S., Gossler, A. and Henrique, D. (2009) Dll1 and Dll4 function sequentially in the retina and pV2 domain of the spinal cord to regulate neurogenesis and create cell diversity. **Developmental Biology**, 328, 54. (Citations: 22)

Lacerda, João F.

Hematology and Transplantation Immunology

João Forjaz de Lacerda :
Group Leader at iMM Lisboa since 2013

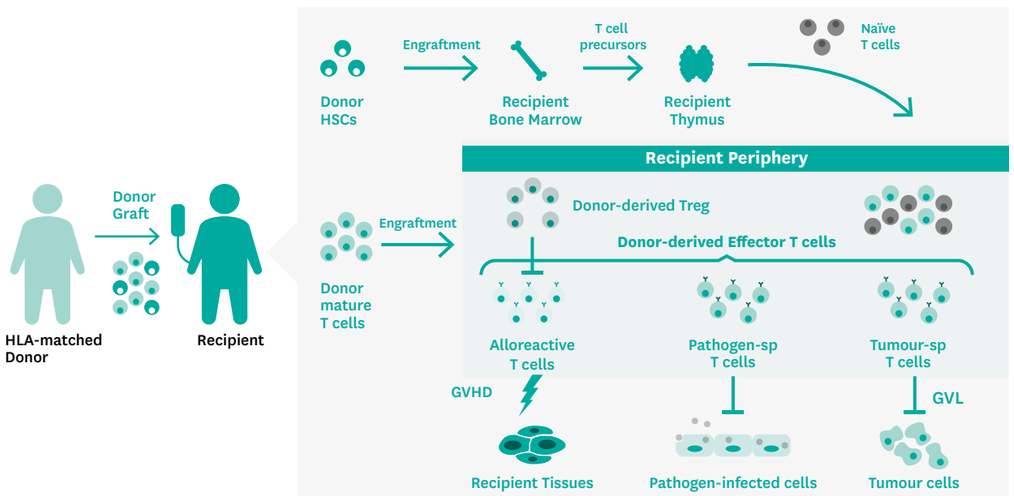
jlacerda@medicina.ulisboa.pt

- MD (1988), PhD (1998), Universidade de Lisboa
- Hematology and Bone Marrow Transplant Fellowship, Hospital de Santa Maria, Lisboa, and Memorial Sloan-Kettering Cancer Center, New York (1991-1995)
- Senior Attending Physician at the Hematology and Marrow Transplantation Service, Hospital de Santa Maria, Lisboa (since 2005)
- Associate Professor with Habilitation, Faculdade de Medicina da Universidade de Lisboa (since 2010)
- Senior Staff Scientist (2008-2013) at iMM Lisboa

Keywords

Immune reconstitution after hematopoietic stem cell transplantation (HSCT) • Homeostasis of regulatory T cells in patients submitted to HSCT • Adoptive immunotherapy after HSCT • Pathogen-specific immunity after HSCT • Genetic susceptibility for fungal and viral infections

Our work at JLacerda's Lab has been mainly focused on the prospective monitoring of immune reconstitution in patients undergoing allogeneic Hematopoietic Stem Cell Transplantation (HSCT) (upper panel). As a translational research unit, we further aim to develop adoptive T cell therapy strategies to treat severe complications post-HSCT, such as infusing donor regulatory T cells (Treg) to treat graft-versus-host disease (GVHD) or donor pathogen-specific T cells to treat viral infections post-transplant (lower panel).



Major Interests — Objectives

Donor-derived immune cells play a pivotal role in the protection against pathogens, such as Aspergillus, CMV and EBV, and in the emergence of graft-versus-host disease (GVHD) and graft-versus-leukemia effect arising after hematopoietic stem cell transplantation (HSCT). Our lab is interested in the study of immune reconstitution and in the development of strategies that modulate immune responses after HSCT. We are currently conducting a Phase I/II clinical trial with CliniMACS-selected donor regulatory T cells in patients with steroid-resistant chronic GVHD. We are also studying the genetic susceptibility for infections arising after HSCT and involved in the development of pathogen-specific T cell therapies with the ultimate goal of improving patient survival and quality of life.

Selected Publications

— Alho Ana C., Kim Haesook T., Chammas Marie J., Reynolds Carol G., Matos Tiago R., Forcade Edouard, Whangbo Jennifer, Nikiforow Sarah, Cutler Corey S., Koreth John, Ho Vincent T., Armand Philippe, Antin Joseph H., Alyea Edwin P., Lacerda Joao F., Soiffer Robert J., Ritz Jerome (2015) Unbalanced recovery of regulatory and effector T cells after allogeneic stem cell transplantation contributes to chronic GVHD. **Blood** ,127, 5 , 646-57.

— Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Löffler J, Maertens JA, Bell AS, Inforzato A, Barbati E, Almeida B, Santos e Sousa P, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano L, Luppi M, Mantovani A, Velardi A, Romani L, Carvalho A. (2014) Genetic PTX3 deficiency and aspergillosis in stem-cell transplantation. **N Engl J Med**. 30; 370(5):421-32. (Citations: 37)

— Azevedo RI, Soares MV, Albuquerque AS, Tendeiro R, Soares RS, Martins M, Ligeiro D, Victorino RM, Lacerda JF, Sousa AE (2013) Long-Term Immune Reconstitution of Naive and Memory T Cell Pools after Haploidentical Hematopoietic Stem Cell Transplantation. **Biology of Blood and Marrow Transplantation** 19, 703. (Citations: 3)

— Gomes AQ, Correia DV, Grosso AR, Lança T, Ferreira C, Lacerda JF, Barata JT, Silva MG, Silva-Santos B. (2010) Identification of a panel of ten cell surface protein antigens associated with immunotargeting of leukemias and lymphomas by peripheral blood gammadelta T cells. **Haematologica** 95, 1397. (Citations: 24)

— Azevedo RI, Soares MV, Barata JT, Tendeiro R, Serra-Caetano A, Victorino RM, Sousa AE (2009) IL-7 sustains CD31 expression in human naive CD4+ T cells and preferentially expands the CD31+ subset in a PI3K-dependent manner. **Blood** 113, 2999. (Citations: 35)

Lopes, Luisa V.

Neurobiology of Ageing & Disease

Luísa V. Lopes :
Group Leader at iMM Lisboa since 2013

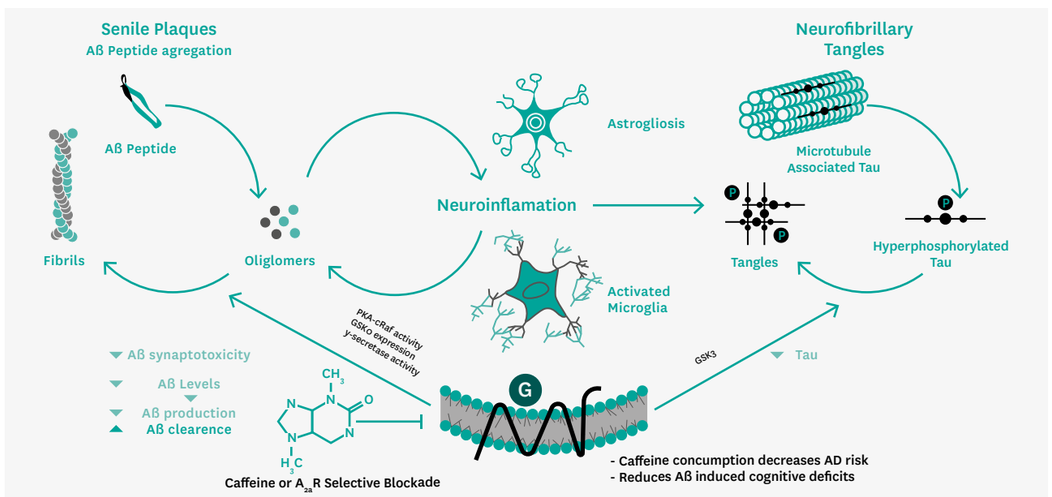
lvlopes@medicina.ulisboa.pt

- 2003 - PhD in Neurosciences, FMUL, University Lisbon — Dept Pharmacology, University of Cambridge and Karolinska Institute, Sweden
- 2003-2006 - Postdoctoral research fellow at Nestlé Research Center, Lausanne, Switzerland
- Staff Scientist (Ciência 2007--2008-2012) and Postdoctoral research fellow (2006-2008) at iMM Lisboa-FMUL

Keywords

Aging • Neurosciences • Cognition • Hippocampus

Potential pathways involved in protective effects provided by caffeine and adenosine A2A receptor blockade in Alzheimer's disease, characterized by accumulation of senile plaques (composed of aggregated Aß peptide) and neurofibrillary tangles (composed by hyperphosphorylated Tau) in the brain.
Source: Laurent C, Burnouf S, Ferry B, Batalha VL, Coelho JE, Baqi Y, Malik E, Marciniak E, Parrot S, Van der Jeugd A, Faivre E, Flaten V, Ledent C, d'Hooge R, Sergeant N, Hamdane M, Humez S, Müller CE, Lopes LV, Buée L, Blum D. A2A adenosine receptor deletion is protective in a mouse model of Tauopathy. Molecular Psychiatry (in press, 2015).



Major Interests — Objectives

Ageing, stress and neurodegenerative diseases are among the conditions that contribute to the accelerated loss of cognitive function. Our group's work is focused on understanding the mechanisms inducing this "early-ageing", which render the hippocampus - the brain area related to learning and memory – particularly susceptible. We focus on characterizing the molecular mechanisms associated to hippocampal loss of function and its outcome in behavior performance and synaptic function, using rodent models. We ensure the translation to the human brain, by testing these molecular imprints in healthy and diseased human brain tissue. We are currently focused into exploring the role of adenosine A2A receptors as potential cognitive modulators both in vitro and in vivo

Selected Publications

— Ferreira DG, Batalha VL, Vicente Miranda H, Coelho JE, Gomes R, Gonçalves FQ, Real JI, Rino J, Albino-Teixeira A, Cunha RA, Outeiro TF, Lopes LV (2015) Adenosine A2A Receptors Modulate a-Synuclein Aggregation and Toxicity. **Cerebral Cortex**. (Citations: n/a)

— Sousa VC, Vital J, Costenla AR, Batalha VL, Sebastião AM, Ribeiro JA, Lopes LV (2014) Maternal separation impairs long term-potentiation in CA1-CA3 synapses and hippocampal-dependent memory in old rats. **Neurobiol Aging**, 35, 1680. (Citations: 13)

— Laurent C, Burnouf S, Ferry B, Batalha VL, Coelho JE, Baqi Y, Malik E, Mariciniak E, Parrot S, Van der Jeugd A, Faivre E, Flaten V, Ledent C, D'Hooge R, Sergeant N, Hamdane M, Humez S, Müller CE, Lopes LV, Buée L, Blum D. (2014) A2A adenosine receptor deletion is protective in a mouse model of Tauopathy. **Molecular Psychiatry**, 21, 97-107. (Citations: n/a)

— Batalha VL, Pego JM, Fontinha BM, Costenla AR, Valadas JS, Baqi Y, Radjainia H, Müller CE, Sebastião AM, Lopes LV. (2013) Adenosine A(2A) receptor blockade reverts hippocampal stress-induced deficits and restores corticosterone circadian oscillation. **Molecular Psychiatry**, 18, 320. (Citations: 30)

— Diógenes MJ, Dias RB, Rombo DM, Vicente Miranda H, Maiolino F, Guerreiro P, Nässtrom T, Franquelim HG, Oliveira LM, Castanho MA, Lannfelt L, Bergström J, Ingelsson M, Quintas A, Sebastião AM, Lopes LV, Outeiro TF. (2012) Extracellular alpha-synuclein oligomers modulate synaptic transmission and impair LTP via NMDA-receptor activation. **Journal of Neuroscience**, 32, 11750. (Citations: 45)

Morais, Nuno

Computational Biology

Nuno Morais :
Group Leader at iMM Lisboa since 2015

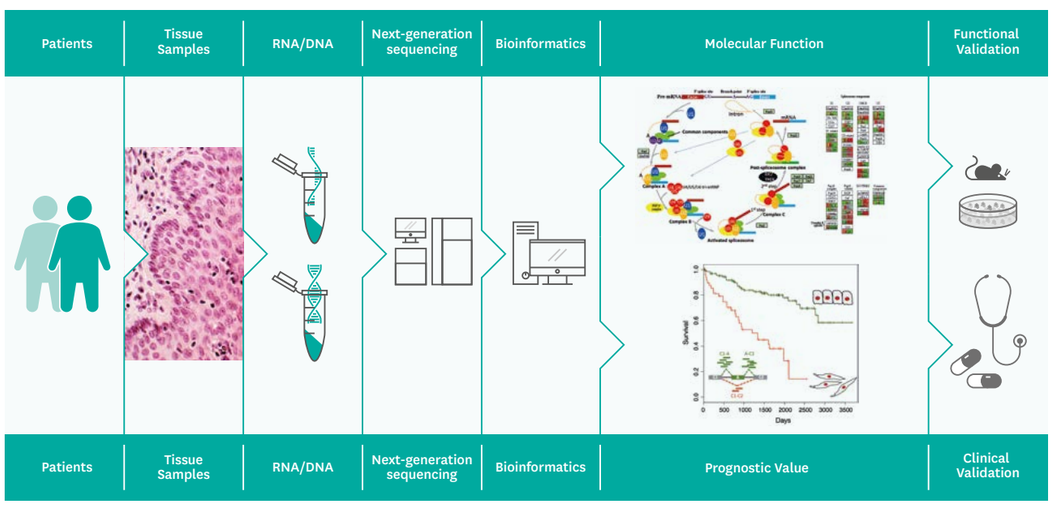
nmorais@medicina.ulisboa.pt

- Senior Postdoctoral Fellow (2010-2013) at University of Toronto, Canada
- Research Associate (2006-2010) at University of Cambridge, UK
- PhD in Biomedical Sciences (2007) at University of Lisbon Medical School, Portugal

Keywords

Computational Biology • Transcriptomics • Alternative Splicing • • Cancer • Parkinson ’s disease

The NMorais Lab employs computational biology analyses of next-generation sequencing data from clinical samples to find disease-specific molecular signatures, aiming to understand how the regulation of gene expression is affected in different pathologies and thereby to identify molecular targets for functional exploration *in vitro* and *in vivo*. The NMorais Lab also combines molecular and clinical information for the unveiling of novel candidate prognostic factors and therapeutic targets.



Major Interests — Objectives

We have a long-term interest in the systems-level transcriptional regulation underlying mammalian cell specification, often perturbed in disease. In particular, we are studying the mechanisms responsible for the association between aberrant splicing and pathologies like cancer and neurodegenerative disorders. We employ computational biology approaches for the analysis of next-generation sequencing data to find disease-specific transcriptomic signatures, aiming to understand how the regulation of alternative splicing is affected in different pathologies and thereby to identify molecular targets for functional exploration in vitro and in vivo. We also combine molecular and clinical information for the unveiling of novel candidate prognostic factors and therapeutic targets.

Selected Publications

— Braunschweig U, Barbosa-Morais NL, Pan Q, Nachman EN, Alipahani B, Gonatopoulos-Pournatzis T, Frey B, Irimia M, Blencowe BJ (2014) Widespread intron retention in mammals functionally tunes transcriptomes. **Genome Research**, 24, 1774. (Citations: 31)

— Pena AC, Pimentel MR, Manso H, Vaz-Drago R, Neves D, Aresta-Branco F, Ferreira FR, Guegan F, Coelho LP, Carmo-Fonseca M, Barbosa-Morais NL, Figueiredo LM (2014) Trypanosoma brucei histone H1 inhibits RNA polymerase I transcription and is important for parasite fitness in vivo. **Molecular Microbiology**, 93, 645. (Citations: 3)

— Ward MC, Wilson MD, Barbosa-Morais NL, Schmidt D, Stark R, Pan Q, Schwalie PC, Menon S, Lukk M, Watt S, Thybert D, Kutter C, Kirschner K, Flicek P, Blencowe BJ, Odom DT (2013) Latent Regulatory Potential of Human-Specific Repetitive Elements. **Molecular Cell**, 49, 262. (Citations: 19)

— Barbosa-Morais NL, Irimia M, Pan Q, Xiong HY, Gueroussov S, Lee LJ, Slobodeniuc V, Kutter C, Watt S, Colak R, Kim T, Misquitta-Ali CM, Wilson MD, Kim PM, Odom DT, Frey BJ, Blencowe BJ (2012) The evolutionary landscape of alternative splicing in vertebrate species. **Science**, 338, 1587. (Citations: 158)

— Barbosa-Morais NL, Dunning MJ, Samarajiwa SA, Darot JF, Ritchie ME, Lynch AG, Tavaré S (2010) A re-annotation pipeline for Illumina BeadArrays: improving the interpretation of gene expression data. **Nucleic Acids Research**, 38, e17. (Citations: 92)

Morais, Vanessa

Mitochondria Biology & Neurodegeneration

Vanessa Morais :
Group Leader at iMM since 2015

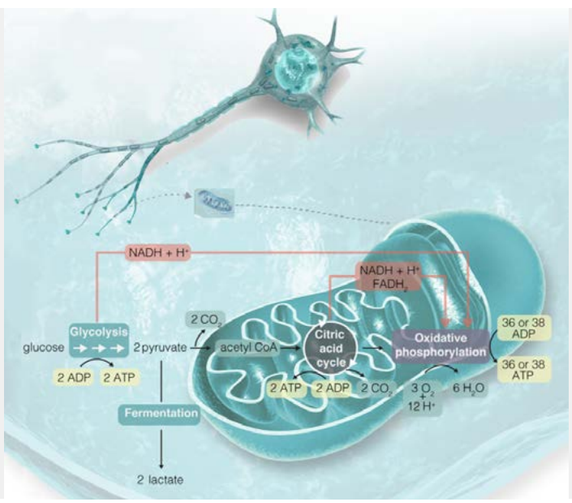
vmorais@medicina.ulisboa.pt

- Invited Professor (since 2013) at K.U.Leuven (Belgium)
- Staff Scientist (2009 to 2015) at VIB-Leuven (Belgium)
- Post-Doctoral Researcher (2006 to 2009) at K.U.Leuven and VIB (Belgium)
- PhD (2006) in Biochemistry from UNL (Portugal); within the PhD program a Visiting scholar (2002 to 2004) at the CNDR at University of Pennsylvania (U.S.A.)

Keywords

Mitochondria • Neurodegeneration • Mitophagy • Quality control • • Parkinson's Disease

Mitochondria are involved in multiple functions that are crucial for cellular homeostasis, namely the production of the high energy compound ATP. Neuronal mitochondria compared to mitochondria in other cells, need to cope with increased calcium load, more oxidative stress, and high demands of energy generation during synaptic activity. Synaptic mitochondria have a pivotal role in neurotransmitter release, but almost nothing is known about synaptic mitochondria composition or specific functions. Our research is focused on unraveling the specific mechanisms that synaptic mitochondria have acquired to manage local stress and maintain quality control. Our overarching goal is to define fundamental mechanisms relevant for maintenance of synaptic activity and establishment of new synapses, and how the disruption of these mechanisms contribute to neurodegeneration.



Major Interests — Objectives

Mitochondria homeostasis is a process involving an intimate crosstalk between energy production, quality control and mitophagy. Perturbances of this intricate system are widely speculated to contribute to neurodegeneration, highlighting the importance of these mechanisms for the functional maintenance of neurons. My research focuses on understanding synaptic mitochondria and how they go astray in neurodegeneration, to decipher the mechanisms involved in mitochondrial quality control processes and bioenergetics compensation pathways. I will use several mitochondrial proteins, namely PINK1 and Complex I subunits, as the working models to address this challenging, albeit intriguing and novel aspects of mitochondrial function to further scrutinize their relevance for the diseased brain.

Selected Publications

— Aerts L, Craessaerts K, De Strooper B*, Morais VA* (2015). PINK1 Kinase Catalytic Activity Is Regulated by Phosphorylation on Serines 228 and 402. **J Biol Chem**. 290: 2798-811*shared corresponding authors (Citations: 8)

— Morais VA*, Haddad D, Craessaerts K, De Bock P, Swerts J, Vilain S, Aerts L, Overbergh L, Grünewald A, Seibler P, Klein C, Gevaert K, Verstreken P, De Strooper B* (2014). PINK1 Loss of Function Mutations Affect Mitochondrial Complex I Activity via NdufA10 Ubiquinone Uncoupling. **Science**. 344 (6180), 203-207. *shared corresponding authors (Citations: 45)

— Haddad D, Vilain S, Vos M, Esposito G, Matta S, Kalscheuer V, Craessaerts K, Leyssen M, Nascimento R, Vianna-Morgante A, De Strooper B, Van Esch H, Morais VA*, Verstreken P* (2013). Mutations in the Intellectual Disability Gene Ube2a Cause Neuronal Dysfunction and Impair Parkin-Dependent Mitophagy. **Molecular Cell**. 50 (6), 831-43. *shared corresponding authors (Citations: 23)

— Vos M, Esposito G, Edirisinghe J, Vilain S, Haddad D, Slabbaert J, Van Meensel S, Schaap O, De Strooper B, Meganathan R, Morais VA, Verstreken P (2012). Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency. **Science**. 336 (6086), 1306-10. (Citations: 90)

— Vilain S, Esposito G, Haddad D, Schaap O, Dobreva M, Vos M, Van Meensel S, Morais VA, De Strooper, B, Verstreken P (2012). The yeast complex I equivalent NADH dehydrogenase rescues pink1 mutants. **PLoS Genetics**. 8 (1). (Citations: 36)

— Morais VA, Verstreken P, Roethig A, Smet J, Snellinx A, Vanbrabant M, Haddad D, Frezza C, Mandemakers W, Vogt-Weisenhorn D, Van Coster R, Wurst W, Scorrano L, De Strooper B (2009) Parkinson's disease mutations in PINK1 result in decreased Complex I activity and deficient synaptic function. **EMBO Molecular Medicine**. 1 (2), 99-111. (Citations: 139)

Mota, Maria M.

Biology & Physiology of Malaria

Maria Manuel Mota :
Executive Director of the iMM Lisboa since 2014

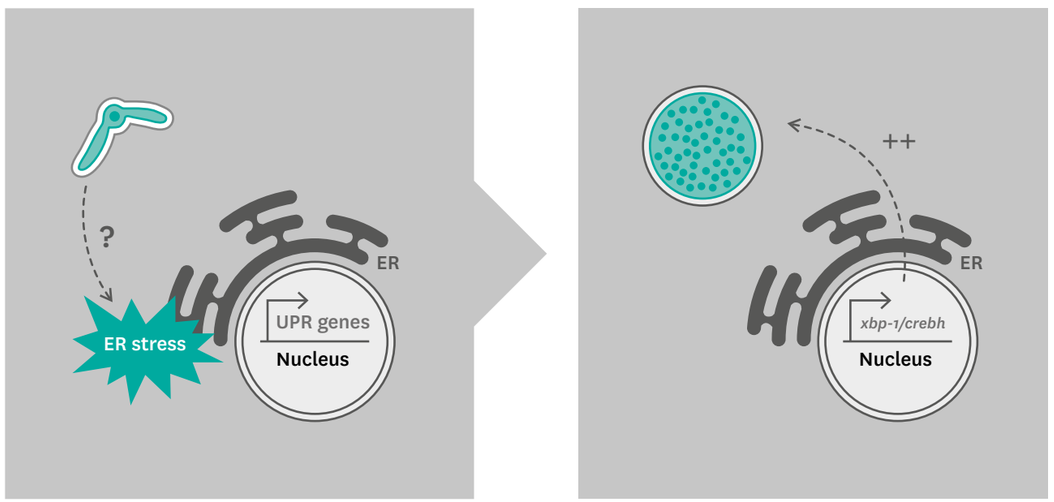
mmota@medicina.ulisboa.pt

- PhD (1998) in Molecular Parasitology at University College London, UK
- Post-doctoral research at New York University Medical Center, USA (1999-2001)
- Principal Investigator at Instituto Gulbenkian de Ciência, Oeiras (2002-2005)
- Professor at the Faculdade de Medicina da Universidade de Lisboa (since 2005)
- Executive Director of the iMM Lisboa since 2014
- Group Leader at iMM Lisboa since 2004

Keywords

Host-*Plasmodium* interactions • Nutrient acquisition • Innate immune response against *Plasmodium* infection • Iron metabolism during *Plasmodium* infection • Using transgenic parasites as malaria vaccines

In this study we show for the first time the activation of ER stress and the unfolded protein response (UPR) in hepatocytes upon *Plasmodium* infection. The consequence of UPR induction *in vivo* is an increased parasite liver burden, in an example of modulation of host pathways to favour infection.



Major Interests — Objectives

Malaria is one of the most serious parasitic infectious diseases, with a toll of up to 600,000 deaths every year. It is now consensual that malaria control or elimination will never be feasible until we gain a better understanding of the complex interactions occurring between its main players: Plasmodium, the causative agent of disease, and its hosts. Yet, important gaps subsist in our knowledge of the processes that occur at the parasite-host interface. Thus, the overall goal of our laboratory is to identify key host factors and host-Plasmodium interactions that contribute to: (i) the establishment of a malaria infection during the initial steps of Plasmodium replication inside liver hepatocytes and (ii) the onset of malaria pathology while Plasmodium infects red blood cells.

Selected Publications

— Hanson KK, March S, Ng S, Bhatia SN, Mota MM. (2015) In vitro alterations do not reflect a requirement for host cell cycle progression during Plasmodium liver stage infection. **Eukaryot Cell**. 14(1):96-103. (Citations: 0)

— Liehl P, Zuzarte-Luís V, Chan J, Zillinger T, Baptista F, Carapau D, Konert M, Hanson KK, Carret C, Lassnig C, Müller M, Kalinke U, Saeed M, Chora AF, Golenbock DT, Strobl B, Prudêncio M, Coelho LP, Kappe SH, Superti-Furga G, Pichlmair A, Vigário AM, Rice CM, Fitzgerald KA, Barchet W, Mota MM. (2014) Host-cell sensors for Plasmodium activate innate immunity against liver-stage infection. **Nature Medicine** 20 (1), 47-53. (Citations: 33)

— Itoe MA, Sampaio JL, Cabal GG, Real E, Zuzarte-Luis V, March S, Bhatia SN, Frischknecht F, Thiele C, Shevchenko A, Mota MM. (2014) Host Cell Phosphatidylcholine Is a Key Mediator of Malaria Parasite Survival during Liver Stage Infection. **Cell Host Microbe** 16(6), 778-86. (Citations: 7)

— Hanson KK, Ressurreição AS, Buchholz K, Prudêncio M, Herman-Ornelas JD, Rebelo M, Beatty WL, Wirth DF, Hänscheid T, Moreira R, Marti M, Mota MM. (2013) Torins are potent antimalarials that block replenishment of Plasmodium liver stage parasitophorous vacuole membrane proteins. **Proc Natl Acad Sci U S A** 110(30), E2838-E2847. (Citations: 15)

— Portugal S, Carret C, Recker M, Armitage AE, Gonçalves LA, Epiphanio S, Sullivan D, Roy C, Newbold CI, Drakesmith H, Mota MM. (2011) Host-mediated regulation of superinfection in malaria. **Nature Medicine** 17(6), 732-7. (Citations: 94)

Oliveira, Sofia A.

Genomics of Complex Diseases

Sofia A. Oliveira :
Group Leader at iMM Lisboa since 2013

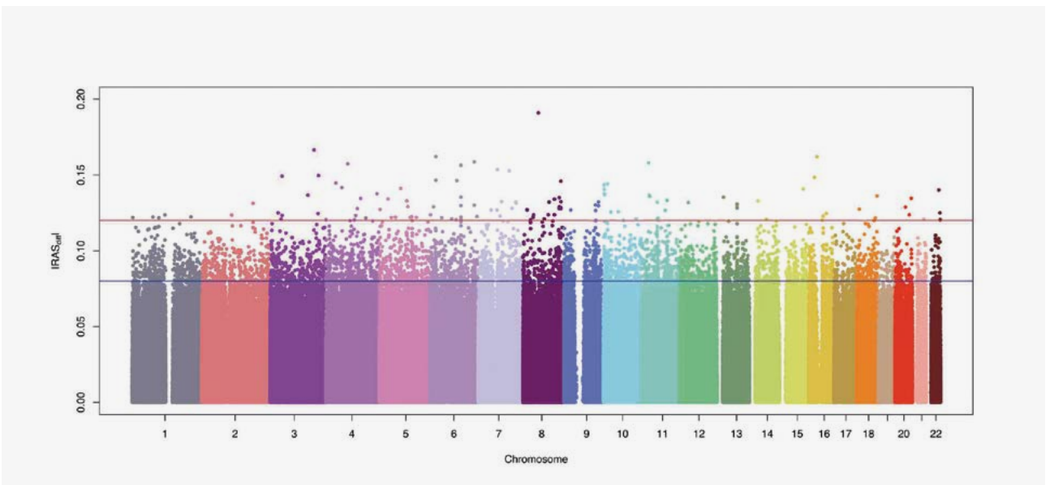
aaoliveira@medicina.ulisboa.pt

- PhD (2002) Faculdade de Medicina da Universidade de Lisboa (FMUL), Portugal
- Post-doctoral fellow (2001-2004), Center for Human Genetics, Duke University Medical Center, USA
- Group Leader (2004-2008), Instituto Gulbenkian Ciência, Oeiras, Portugal
- Senior Staff Scientist (2008-2013) at iMM Lisboa
- Invited Assistant Professor (since 2008), FMUL, Portugal

Keywords

Genetics • Genomics • Complex traits

Modified Manhattan plot for the primary spontaneous pneumothorax genome-wide association study. The absolute value of the relative allele score difference between cases and controls (|RASdiff|) is shown for 868,260 autosomal SNPs, ordered by chromosomal position. The red and blue lines represent the 12% and 8% |RASdiff| thresholds, respectively.



Major Interests — Objectives

Our research focuses on understanding the genetic architecture of complex diseases such as Stroke, Behçet's Disease, Primary Spontaneous Pneumothorax, and Intracranial Aneurysms. Common diseases result from the interaction of environmental and genetic factors, and an in-depth evaluation of their genetic underpinnings will not only unravel complex inheritance patterns but will also enable a better understanding of the environmental risks.

We use both traditional and new approaches to identify novel susceptibility genes. We believe that studies with a multifaceted and multidisciplinary framework will have the greatest success in dissecting the complex etiology of common disorders and that they will ultimately lead to the development of novel prevention strategies and targeted therapies.

Selected Publications

— Xavier JM, Shahram F, Sousa I, Davatchi F, Matos M, Abdollahi BS, Sobral J, Nadji A, Oliveira M, Ghaderibarim F, Shafiee NM, Oliveira SA. (2015) FUT2: filling the gap between genes and environment in Behçet's disease? **Annals of the Rheumatic Diseases**, 74, 618-624. (Citations:0)

— Xavier JM, Davatchi F, Abade O, Shahram F, Francisco V, Sadeghi Abdollahi B, Trindade H, Nadji A, Mojarad Shafiee N, Ghaderibarmi F, Ligeiro D and Oliveira SA (2015) Characterization of the major histocompatibility complex locus association with Behçet's disease in Iran. **Arthritis Research & Therapy** 17, 81. (Citations: 0)

— Traylor M, Farrall M, Holliday EG, et al. (2012) Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE Collaboration): a meta-analysis of genome-wide association studies. **Lancet Neurology**, 11, 951-962. (Citations: 63)

— Xavier JM, Shahram F, Davatchi F, Rosa A, Crespo J, Abdollahi BS, Nadji A, Jesus G, Barcelos F, Patto JV, Shafiee NM, Ghaderibarim F, Oliveira SA. (2012) Association study of IL10 and IL23R-IL12RB2 in Iranian Behçet's disease patients. **Arthritis & Rheumatism**, 64, 2761-2772. (Citations: 20)

— Krug T, Gabriel JP, Taipa R, Fonseca BV, Domingues-Montanari S, Fernandez-Cadenas I, Manso H, Gouveia L, Sobral J, Albergaria I, Gaspar G, Jiménez-Conde J, Rabionet R, Ferro JM, Montaner J, Vicente AM, Silva MR, Matos I, Lopes G, Oliveira SA. (2012) Tetratricopeptide repeat domain 7B emerges as a novel risk factor for ischemic stroke through the convergence of several genome-wide approaches. **Journal of Cerebral Blood Flow and Metabolism,** 32, 1061-1072. (Citations: 5)

— Xavier JM, Shafiee NM, Ghaderi F, Rosa A, Abdollahi BS, Nadji A, Shahram F, Davatchi F, Oliveira SA. (2011) Association of mitochondrial polymorphism m.709G>A with Behçet's disease (BD). **Annals of the Rheumatic Diseases,** 70, 1514-16. (Citations: 1)

Prata, Diana

Human Neurobiology and Cognitive Neuroscience

Diana Prata :
Group Leader at iMM Lisboa since 2015

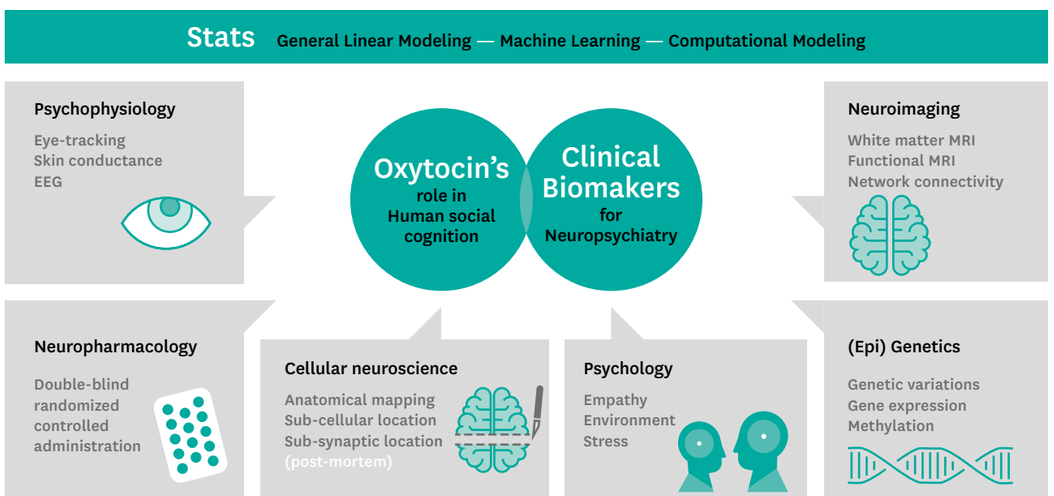
diana.prata@medicina.ulisboa.pt

- PhD (2018) in Neuroimaging Genetics, Section of Genetics & Section of Neuroimaging of the Division of Psychological Medicine and Psychiatry of the Institute of Psychiatry, King's College of London, UK
- Post-Doctoral (2008-2010) researcher for Optimal Medicine, Ltd & Institute of Psychiatry, King's College of London, UK
- Lecturer and National Institute for Health Research Post--Doctoral fellow (2010-2013)
- Department of Psychosis Studies of the Institute of Psychiatry, King's College of London, UK
- Present: Visiting Assistant Professor, Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College of London, UK

Keywords

Neuroimaging • Genetics • Psychiatry • Social Cognition • Machine Learning Classification • Neuropharmacology

Highly interdisciplinary research takes place in DPrataLab, within its two mais research streams: a basic stream (on the mechanisms of the oxytocin's role in social cognition) and a translational stream (on the development of neuroimaging-based biomarkers for neuropsychiatric illnesses).



Major Interests — Objectives

Our interest is the molecular biology of human behaviour, which we aim to translate into improving etiological and therapeutic models of neuropsychiatric disorders. We have reported on the influence of genetic variations on: mental illness risk, brain function/structure and drug treatment response. We are now majorly interested in: 1) the role of oxytocin in social cognition, and its relevance to psychosis, autism and anorexia; and 2) building clinically useful multimodal biomarkers for aiding clinical diagnostic and prognostic predictions. For this, we combine psychological and neuropharmacological experimentation with (epi)genetics, neuroimaging and psychophysiological tools - which is made possible by a diverse team of biophysics engineers, psychologists, biologists and medical doctors.

Selected Publications

— Prata DP, Mechelli A, Kapur S. (2014) Clinically meaningful biomarkers for psychosis: a systematic and quantitative review. **Neuroscience and Biobehavioural Reviews** 45, 134. (Citations:11)

— Prata DP, Kanaan KA, Barker GJ, Shergill S, Woolley J, Georgieva L, Picchioni MM, Kravariti E, Walshe M, Allin M, Toulopoulou T, Bramon E, McDonald C, Giampietro V, Murray RM, Brammer M, O'Donovan M, McGuire PK.(2013) Risk variant of oligodendrocyte lineage transcription factor 2 is associated with reduced white matter integrity. **Human Brain Mapping**. 34 (9):2015-31. (Citations: 4)

— Prata DP, Mechelli A, Fu C, Picchioni M, Kane F, Kalidindi S, McDonald C, Kravariti E, Toulopoulou T, Bramon E, Walshe M, Murray R, Collier DA, McGuire PK. (2012) Effect of D-amino acid oxidase activator (DAOA; G72) on brain function during verbal fluency. **Human Brain Mapping**. 33, 143. (Citations: 8)

— Prata DP, Mechelli A, Fu C, Picchioni M, Toulopoulou T, Bramon E, Walshe M, Murray R, Collier DA, McGuire P. (2009) Epistasis between the DAT 3'UTR VNTR and COMT Val158Met SNP on cortical function in healthy subjects and patients with schizophrenia. **Proceedings of the National Academy of Sciences of the United States of America (PNAS)**. 106, 13600. (Citations: 49)

— Prata DP, Mechelli A, Picchioni M, Fu C, Toulopoulou T, Bramon E, Walshe M, Murray R, Collier DA, McGuire. (2009) Altered effect of dopamine transporter 3'UTR VNTR genotype on prefrontal and striatal function in schizophrenia. **Archives of General Psychiatry** (now JAMA Psychiatry) 66, 1162. (Citations: 19)

— Prata DP, Mechelli A, Fu C, Picchioni M, Kane F, Kalidindi S, McDonald C, Howes O, Kravariti E, Demjaha A, Toulopoulou T, Diforti M, Murray R, Collier DA, McGuire. (2009) Opposite effects of COMT Val158Met on cortical function in healthy subjects and patients with Schizophrenia. **Biological Psychiatry** 6, 473. (Citations: 57)

Prudêncio, Miguel

Plasmodium Infection & Anti-malarial Interventions

Miguel Prudêncio :
Group Leader at iMM Lisboa since 2013

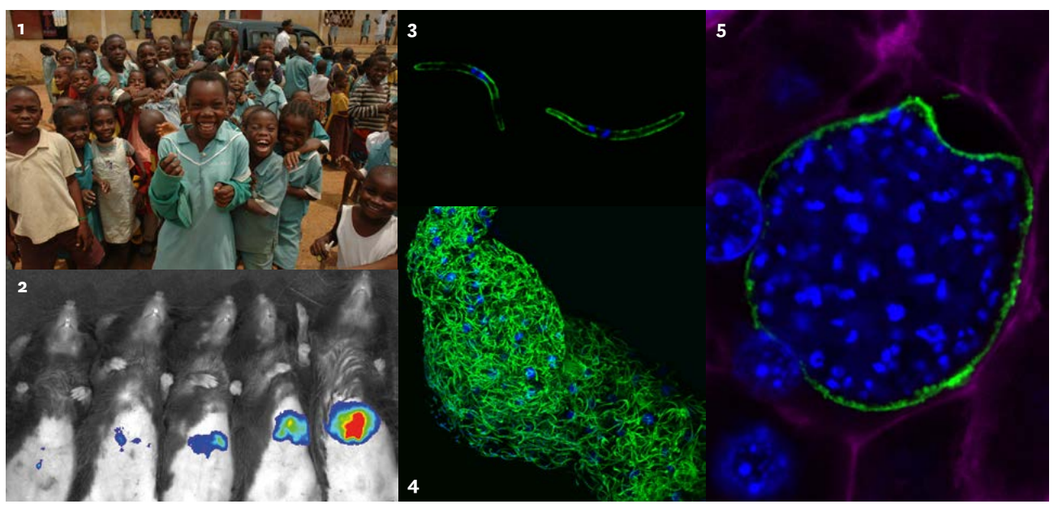
mprudencio@medicina.ulisboa.pt

- PhD (2000) in Biochemistry at University of East Anglia, Norwich, UK
- Post-doctoral researcher (2000--2004) at University of Leiden, Leiden, The Netherlands
- Post-doctoral researcher (2004) at Instituto Gulbenkian de Ciência, Oeiras, Portugal
- Post-doctoral researcher (2005-2008) at iMM Lisboa
- Senior Staff Scientist at iMM Lisboa (2008-2013)

Keywords

Malaria • Parasitology • Vaccines • Host-pathogen interactions • Liver-stage infection • Plasmodium

The Prudêncio lab focuses its reasearch on the liver stage of infection by the Plasmodium parasite, the causative agente of malaria, and on the development of anti-malarial intervention strategies. Clockwise from the top left image: **(1)** a group of schoolchildren in the malaria-endemic country of Cameroon (photo: António Mendes); **(2)** *Plasmodium* sporozoites, the mosquito salivary gland-resident, liver-infective form of the malaria parasite; **(3)** a *Plasmodium* parasite developing inside a liver cell; **(4)** a salivary gland of an infected *Anopheles* mosquito containing thousands of GFP-expressing *Plasmodium* sporozoites; **(5)** rodent models of malaria displaying different loads of liver infection by luciferase-expressing Plasmodium parasites.



Major Interests — Objectives

Our interests span a wide range of topics within the malaria field, with particular emphasis on the hepatic stage of infection. We are interested in elucidating novel aspects of the biology of Plasmodium infection, unveiling novel host-parasite interactions, understanding co-infections between Plasmodium and other parasites, and developing new drug- and vaccine-based anti-malarial strategies.

Research Areas

— Nutrient acquisition and metabolism during *Plasmodium* development inside hepatic cells
— Novel host-*Plasmodium* molecular interactions
— Identification of compounds active against *Plasmodium* liver stages
— Malaria vaccines
— The reciprocal influence of *Plasmodium* and *Trypanosoma* co-infections

Selected Publications

— Liehl P, Meireles P, Albuquerque I.S, Pinkevych M, Baptista F , Mota M.M, Davenport M.P , Prudêncio M (2015) Innate immunity induced by Plasmodium liver infection inhibits malaria reinfections. **Infection and Immunity**, 83, 1172-1180. (Citations: 2)

— Pereira N.A.L. , Monteiro Â.,Machado M, Gut J, Molins E, Perry M.J, Dourado J, Moreira R, Rosenthal PJ, Prudêncio M,* and Santos M.M.M* (2015), "Enantiopure Indolizinoindolones with in vitro Activity against Blood- and Liver-Stage Malaria Parasites". **ChemMedChem**. 10(12):2080-9. (Citations: 0)

— Liehl P., Zuzarte-Luís V, Chan J, Zillinger T, Baptista F, Carapau D.I, Konert M, Hanson H, Carret C, Lassnig C, Müller M, Kalinke U, Saeed M, Chora A.F, Golenbock D.T, Strobl B., Prudêncio M., Coelho L.P., Kappe S.H., Superti-Furga G., Pichlmair A., Vigário A.M., Rice C.M., Fitzgerald K.A., Barchet W., Mota M.M. (2014) Host cell sensors for Plasmodium activate innate immunity against liver stage infection. **Nature Medicine**, 20, 47-53. (Citations: 30)

— Oliveira R, Guedes RC, Meireles P, Albuquerque IS, Gonçalves LM, Pires E, Bronze MR, Gut J, Rosenthal PJ, Prudêncio M, Moreira R, O'Neill P.M, Lopes F. (2014) Tetraoxane-Pyrimidine Nitrile Hybrids as Dual Stage Antimalarials. **J. Med. Chem.**, 57, 4916-4923. (Citations: 7)

— da Cruz F.P., Martin C., Buchholz K K., Lafuente-Monasterio M.J., Rodrigues T., Sönnichsen B., Moreira R, Gamo FJ, Marti M, Mota M.M, Hannus M, Prudêncio M. (2012) Drug Screen Targeted at Plasmodium Liver Stages Identifies a Potent Multi-Stage Anti-Malarial Drug. **J. Inf. Dis.**, 205, 1278-1286. (Citations: 26)

— Prudêncio M, Mota M.M, Mendes A.M (2011) A toolbox to study liver stage malaria. **Trends Parasitol**, 27, 565-574. (Citations: 25)

Ramirez, Mário

Molecular Microbiology & Infection

Mário Ramirez :
Group Leader at iMM Lisboa since 2004

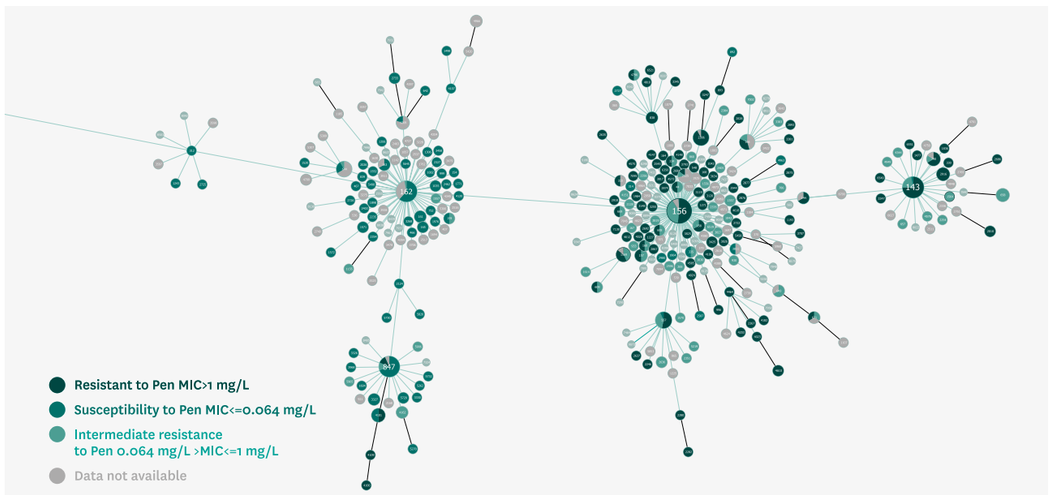
ramirez@medicina.ulisboa.pt

- PhD (1998) in Molecular Biology at Universidade Nova de Lisboa and at The Rockefeller University, USA
- Post-doctoral research at Instituto de Tecnologia Quimica e Biologica, Oeiras
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Population biology and genomics • Bioinformatics • Detection of antimalarial drug resistance • Molecular epidemiology • • Diagnostic tools • Antibiotic resistance

Integrating metadata with MLST using PHYLOViZ: the example of the ST156 and ST162 subgroups on the largest CC in Streptococcus pneumoniae. The colors represent penicillin susceptibility: Susceptible (Green) MIC ≤ 0.064 mg/L; Intermediate (Orange) 0.09mg/L ≤ MIC ≤ 1 mg/L; Resistant (Red) MIC > 1 mg/L.



Major Interests — Objectives

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations .We 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 genomics, microbial typing data sharing, data analysis and visualization tools is ongoing. The development of novel laboratory methodologies for the diagnosis of infectious diseases is also an active area of research.

Selected Publications

— Friães A, Pato C, Melo-Cristino J, Ramirez M. (2015). Consequences of the variability of the CovRS and RopB regulators among Streptococcus pyogenes causing human infections. **Sci Rep** 5:12057. (Citations: 0)

— Aguiar, S.I., M. Brito, Horácio, A. N., J. Lopes, M. Ramirez, J. Melo-Cristino, and Portuguese Group for the Study of Streptococcal Infections and the Portuguese Study Group of Invasive Pneumococcal Disease of the Paediatric Infectious Disease Society. (2014) Decreasing incidence and changes in serotype distribution of invasive pneumococcal disease in persons aged under 18 years since introduction of 10-valent and 13-valent conjugate vaccines in Portugal, July 2008 to June 2012. **Euro Surveill**, 19. (Citations: 8)

— Silva-Costa, C., J. A. Carriço, M. Ramirez, and J. Melo-Cristino. (2014) Scarlet fever is caused by a limited number of Streptococcus pyogenes lineages and is associated with the exotoxin genes ssA, speA and speC. **Pediatr Infect Dis J**, 33, 306-10. (Citations: 6)

— Melo-Cristino J., C. Resina, V. Manuel, L. Lito, M. Ramirez (2013) First case of infection with vancomycin-resistant Staphylococcus aureus in Europe. **The Lancet**, 382, 205. (Citations: 21)

— Rebelo, M., C. Sousa, H. M. Shapiro, M. M. Mota, M. P. Grobusch, and T. Hänscheid (2013) A novel flow cytometric hemozoin detection assay for real-time sensitivity testing of Plasmodium falciparum. **PLoS ONE** 8:e61606. (Citations: 7)

— Francisco, A. P., C. Vaz, P. T. Monteiro, J. Melo-Cristino, M. Ramirez, and J. A. Carriço (2012) Phylogenetic inference and data visualization for sequence based typing methods. **BMC bioinformatics**, 13, 87. (Citations: 76)

Remondes, Miguel

Neural Mechanisms of Perception, Memory & Decision

Miguel Remondes :
Group Leader at iMM Lisboa since 2014

mremondes@medicina.ulisboa.pt

- PhD (1998) Candidate in the VI Gulbenkian Ph.D. Program in Biology and Medicine
- PhD(1999) in Biomedical Sciences – Neuroscience, California Institute of Technology and University of Coimbra (Medical School)
- Postdoctoral Scholar(2004) at the Picower Institute – Massachusetts Institute of Technology
- Research Scientist (2009) at the Picower Institute – Massachusetts Institute of Technology

Keywords

Cortex-hippocampus • Optogenetics-pharmacogenetics • • Behavior • Spatial maps • Decison • Sensory stimulus

We recorded brain activity in rats during periods of quiet alertness between behavioral trials and found that neurons in the cingulate cortex respond to hippocampal SWR during these stages, and that these responses correlate with increased slow-γ coordination between the cingulate cortex and hippocampus.

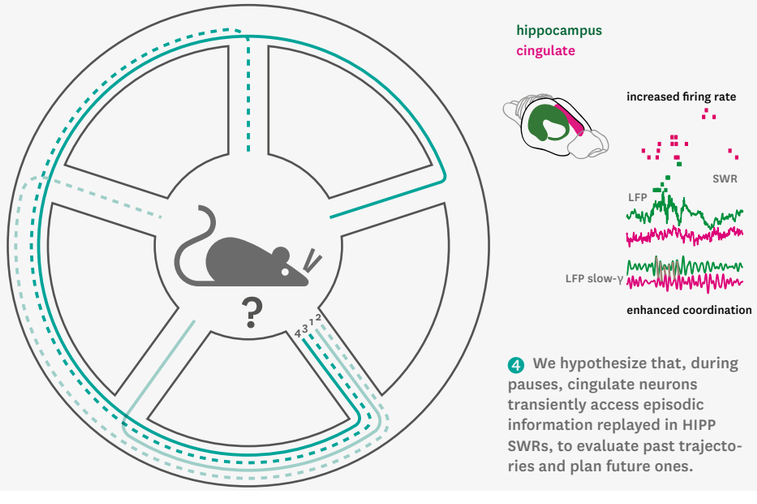
GRAPHICAL ABSTRACT

Cingulate cortical neurons respond to hippocampal memory replay during wakefulness

1 In a behavioral task, rats plan trajectories based on the outcome of previous choices (e.g. presence of Reward)

2 Between trials on a maze, the hippocampus replays the memory of previous events during SWR oscillations.

3 Neurons in cingulate cortex change their firing rate in response to hippocampal SWRs, while synchronized to the hippocampal slow-γ rhythm.



4 We hypothesize that, during pauses, cingulate neurons transiently access episodic information replayed in HIPP SWRs, to evaluate past trajectories and plan future ones.

Major Interests — Objectives

Independent life relies on mentally mapping, in place and time, the distribution of resources and threats, to inform adaptive behavior. How does the brain store, update, retrieve, and use, such information? The hippocampal formation forms a complex circuit with regions of sub- and neocortex, to store neural maps of context, which are subsequently "read" to inform decisions. To dissect the mechanisms underlying this process we use techniques from multiple disciplines: a) Anatomy, and *in vitro* electrophysiology, to identify neural circuits connecting HIPP with cortex. b) In vivo electrophysiology, to investigate neural activity in these circuits during behavior. c) Fine genetically-encoded neural manipulations. d) Behavioral tasks involving spatial memory and decision-making.

Selected Publications

— Remondes M * and Wilson M (2015) Slow-gamma rhythms coordinate cingulate cortical responses to hippocampal sharp-wave ripples during choice behavior. **Cell Reports**. 17; 13(7):1327-35. doi: 10.1016/j.celrep.2015.10.005. (Citations: 0)

— Wilson M *, Varela C and Remondes M (2015) Phase organization of network computations. **Curr Opin Neurobiol**. 31:250-3. doi: 10.1016/j.conb.2014.12.011. Epub 2015 Feb 11. Review. (Citations: 4)

— Remondes M * and Wilson M (2013) Cingulate-hippocampus Coherence and Trajectory Coding in a Sequential Choice Task. **Neuron**. 80(5):1277-89. doi: 10.1016/j.neuron.2013.08.037. (Citations: 13)

Saldanha, Carlota

Blood Cells Recruitment & Inflammation

Carlota Saldanha :
Group leader at iMM Lisboa since 2008

carlotasaldanha@medicina.ulisboa.pt

- PhD (1986) in Biochemistry (Cellular Physiology) at Universidade Nova de Lisboa
- Master(2000) in Medical Education joint degree at University of Wales and University of Lisbon Associate
- Professor with Habilitation at FMUL

Keywords

Inflammation • Microcirculation • Neutrophil • Erythrocyte • • Leukocyte recruitment • Inflammation • Hemorheology • Microcirculation

A close look into the action of blood cells in inflammation

Major Interests — Objectives

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

Selected Publications

— P Teixeira, N Duro, P Napoleão,C Saldanha. (2015) Acetylcholinesterase Conformational States Influence Nitric Oxide Mobilization in the Erythrocyte. **J Membrane Biol**, 248, 349-354. (Citations: 0)

— Silva-Herdade AS, Freitas T, Almeida JP, Saldanha C (2015) Erythrocyte deformability and nitric oxide mobilization under pannexin-1 and PKC dependence. **Clinical Hemorheology and Microcirculation** 59, 155-162. (Citations: 1)

— Napoleão P, Ramos C, Cabral LBP, Selas M, Monteiro MC, Criado MB, Viegas-Crespo AM, Saldanha C, Mota Carmo M, Ferreira RC, Pinheiro T. (2015) Changes of sCD40L in the progression of acute myocardial infraction associate to eNOS polymorphisms and VEGF but not to platelet CD62P expression. **Translational Research**, 166, 650-659. (Citations: 0)

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

— de Oliveira, S., Reyes-Aldasoro, C.C., Candel, S., Renshaw, S.A., Mulero, V., Calado, A. (2013). Cxcl8 (Interleukin-8) mediates neutrophil recruitment and behavior in the zebrafish inflammatory response. **J.Immunol**, 190, 4349-4359. (Citations: 3)

— de Oliveira S, Vitorino de Almeida V, Calado A, Rosário HS, Saldanha C. (2012) Integrin-associated protein (CD47) is a putative mediator for soluble fibrinogen interaction with human red blood cells membrane. **Biochim Biophys Acta**, 1818, 481-490. (Citations: 2)

Santos, Nuno C.

Biomembranes & Nanomedicine

Nuno C. Santos :
Group Leader at iMM Lisboa since 2008

nsantos@medicina.ulisboa.pt

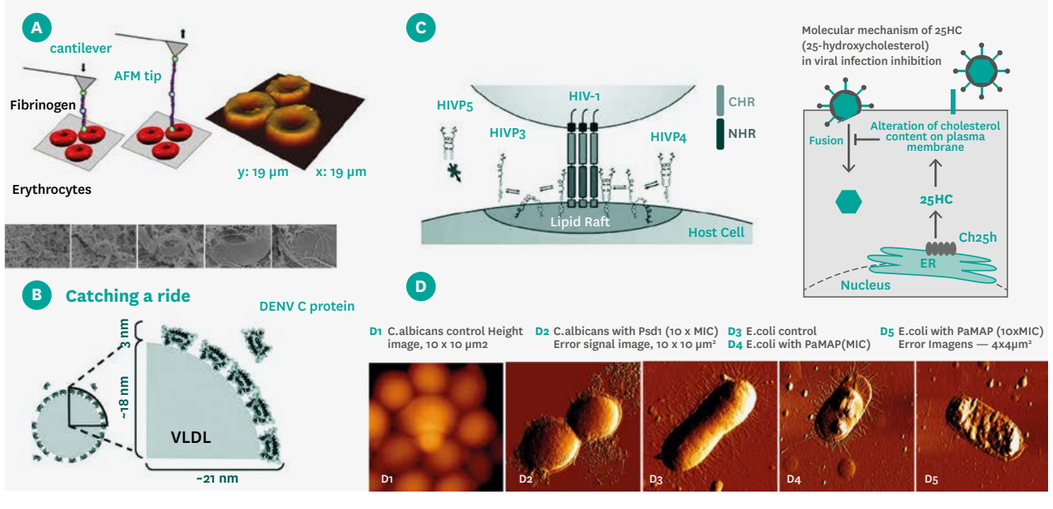
- PhD (1999) at Universidade de Lisboa
- Research at the Universidade Técnica de Lisboa and at the University of California, Santa Barbara (USA)
- Associate Professor with Habilitation at the Faculdade de Medicina da Universidade de Lisboa

Keywords

Membranes • HIV • Dengue • West Nile virus and respiratory viruses • Peptide-based therapies (CPPs • AMPs • pep14-23) • • Atomic Force Microscopy (AFM) • Fibrinogen • Nanomedicine

Major research projects ongoing at Nsantos Lab:

A Studying fibrinogen — erythrocyte interactions in cardiovascular diseases;
B Dengue virus capsid protein: towards a novel drug target;
C Understanding the mechanism of action of HIV — fusion inhibitors;
D The potential therapeutic use of new antimicrobial agents.



Major Interests — Objectives

Biochemical and biophysical processes occurring in membranes of human cells, as well as of their viral and bacterial pathogens. Study of the two steps of the enveloped viruses life cycle (HIV-1, dengue virus, West Nile virus and pediatric respiratory viruses) that involve biomembranes – the entrance of the virus or its content into the target cell (including its inhibition) and the assembly of new virions. Study of the binding of fibrinogen to the erythrocyte membrane in cardiovascular diseases. Pre-clinical evaluation of the membrane activity and mechanism of action of antimicrobial peptides (AMP). On the Nanomedicine area, work on the development of innovative protein-ligand interactions biosensor systems (nanoparticles and amyloid-based biosensors).

Selected Publications

— Faustino AF, Martins IC, Carvalho FA, Castanho MA, Maurer-Stroh S, Santos NC. (2015) Understanding dengue virus capsid protein interaction with key biological targets, **Sci. Rep.**, 5, 10592 (Citations: 1)

— Vigant F, Santos NC, Lee B. (2015) Broad-spectrum antivirals against viral fusion, **Nature Rev. Microbiol.**, 13, 426-437 (Citations: 7)

— Hollmann A, Gonçalves S, Augusto MT, Castanho MA, Lee B, Santos NC. (2015) Effects of singlet oxygen generated by a broad-spectrum viral fusion inhibitor on membrane nanoarchitecture. **Nanomedicine** (NBM), 11, 1163-1167 (Citations: 1)

— Hauser CA, Maurer-Stroh S, Martins IC (2014) Amyloid-Based Nanosensors and Nanodevices. **Chem. Soc. Rev.**, 43, 5326-5345, (Citations: 22)

— Faustino AF, Carvalho FA, Martins IC, Castanho MARB, Mohana-Borges R, Almeida FC, Da Poian AT, Santos NC (2014) Dengue virus capsid protein interacts specifically with very lowdensity lipoproteins. **Nanomedicine**: NBM, 10, 247-255, (Citations: 11)

— Carvalho FA, Connell S, Miltenberger-Miltenyi G, Pereira SV, Tavares A, Ariëns RAS, Santos NC (2010) Atomic force microscopy-based molecular recognition of a fibrinogen receptor on human erythrocytes. **ACS Nano**, 4, 4609-4620, (Citations: 63)

Saúde, Leonor

Embryonic Development & Regeneration

Leonor Saúde :
Group Leader at iMM Lisboa since 2007

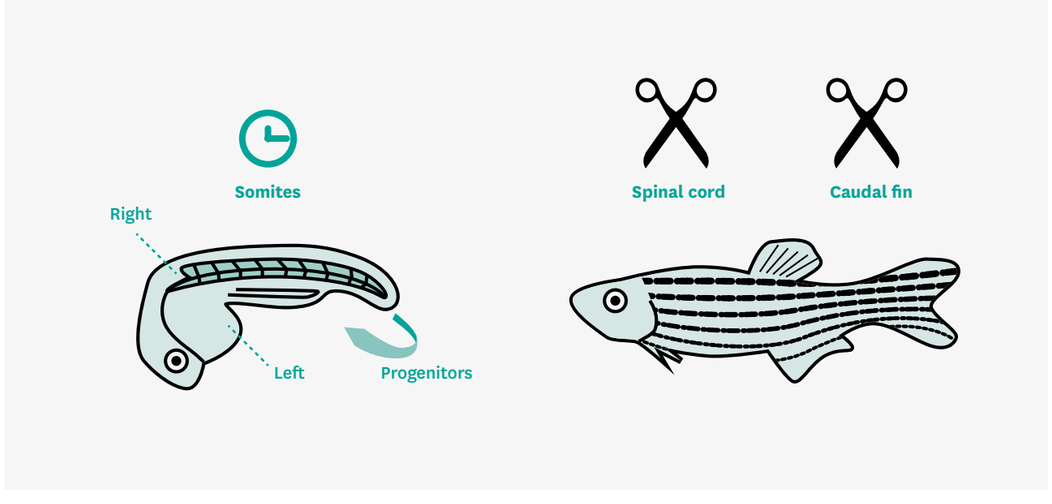
msaude@medicina.ulisboa.pt

- PhD (2001) in Developmental Biology at University College London, UK
- Post-doctoral research at Instituto Gulbenkian de Ciência (IGC)
- Group Leader at IGC (2005-07)
- Invited Auxiliary Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Left-right asymmetry • Somite formation • Tissue/organ regeneration

The zebrafish is an important vertebrate model to dissect mechanisms of development and regeneration.



Major Interests — Objectives

A fascinating question in biomedicine is how a single cell, the fertilized egg, differentiates into a variety of cell types in their correct positions allowing the formation of impeccably allocated organs, that constitute a perfect body.

Our research aims to understand the cellular and molecular mechanisms controlling the left-right asymmetric placement of internal organs and the bilateral symmetric formation of musculoskeletal elements in vertebrates. In addition we are interested in making the bridge between the fundamental developmental processes that we have been studying with the mechanisms that have to be activated during regeneration upon severe injury.

We expect our research to help uncover the etiology of human disorders such as congenital heart and vertebrae malformation as well as contribute to new therapeutic strategies for human neuronal diseases based on the ability to generate long-term persisting neurons and glial cells after lesion.

Selected Publications

— Mendes R.V., Martins G.G., Martins A.M. and Saúde L. (2014) N-cadherin locks left-right asymmetry by ending the leftward movement of Hensen's node cells. **Developmental Cell**, 30(3), 353-60. (Citations: 1)

— Fior R., Maxwell A.A., Ma T.P., Vezzaro A., Moens C.B., Amacher S.L., Lewis J. and Saúde L. (2012) Differentiation and movement of presomitic mesoderm progenitor cells are both controlled by Mesogenin1. **Development**, 139(24), 4656-65. (Citations: 13)

— Azevedo A.S., Sousa S., Jacinto A. and Saúde L. (2012) An amputation resets positional information to a proximal identity in the regenerating zebrafish caudal fin. **BMC Developmental Biology**, 12(1), 24. (Citations: 7)

— Azevedo A.S., Grotek B., Jacinto A., Weidinger G. and Saúde L. (2011) the regenerative capacity of the zebrafish caudal fin is not affected by repeated amputations. **PloS ONE**, Vol. 6(7), e22820. (Citations: 17)

— Lopes S.S., Lourenço R., Pacheco L., Moreno N., Kreiling J. and Saúde L. (2010) Notch signalling regulates left-right asymmetry through ciliary length control. **Development**, Vol.137 (21), 3625-32. (Citations: 43)

Sebastião, Ana

Neuronal Communication & Synaptopathies

Ana Sebastião :
Group Leader at iMM Lisboa since 2003

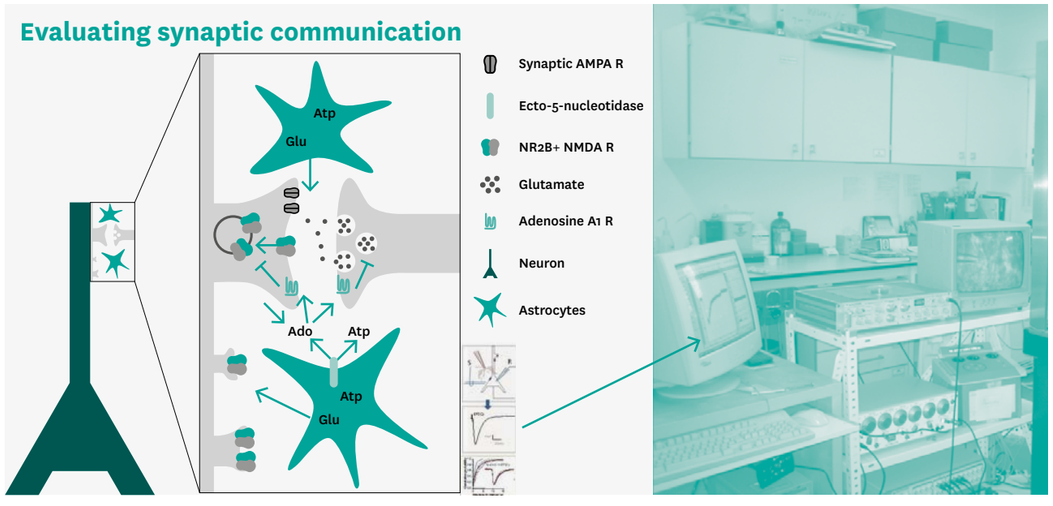
anaseb@medicina.ulisboa.pt

- PhD (1987) in Cell Physiology, Universidade Nova de Lisboa
- Pos-Doctoral research at Instituto Gulbenkian de Ciências, Oeiras
- Full Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

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

Glutamatergic (figure), GABAergic and Cholinergic transmission are major focus. Besides electrophysiological approaches (Figure Insets) molecular, cellular and integrated approaches are used. Programme lines aim to cover questions from molecules to behaviour.



Major Interests — Objectives

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

Selected Publications

— Rombo DM, Dias RB, Duarte ST, Ribeiro JA, Lamsa KP, Sebastião AM (2015). Adenosine A1 receptor suppresses Tonic GABAA receptor currents in hippocampal pyramidal cells and in a defined subpopulation of interneurons. **Cereb Cortex**, Volume 26, 3, 1081-1095. (Citations: 0)

— Diógenes MJ, Neves-Tomé R, Fucile S, Martinello K, Scianni M, Theofilas P, Lopatár J, Ribeiro JA, Maggi L, Frenguelli BG, Limatola C, Boison D, Sebastião AM (2014). Homeostatic Control of Synaptic Activity by Endogenous Adenosine is Mediated by Adenosine Kinase. **Cereb Cortex**. 24:67-80. (Citations: 11)

— Dias RB, Rombo DM, Ribeiro JA, Sebastião AM (2013) Ischemia-induced synaptic plasticity drives sustained expression of calcium-permeable AMPA receptors in the hippocampus. **Neuropharmacology**, 65:114-122. (Citations: 24)

— Rocha, MC, Pousinha PA, Correia AM, Sebastião AM, Ribeiro JA (2013) Early changes of neuromuscular transmission in the SOD1(G93A) mice model of ALS start long before motor symptoms onset. **PLOS ONE**, 8(9):e73846. doi: 10.1371/journal.pone.0073846. (Citations: 19)

— Dias RB, Rombo DM, Ribeiro JA, Henley JM, Sebastião AM (2012) Adenosine: setting the stage for plasticity. **Trends in Neurosciences** (TINS). 36, 248-257. (Citations: 31)

— Diogenes MJ, Costenla AR, Lopes LV, Jerónimo-Santos A, Sousa VC, Fontinha BM, Ribeiro JA, Sebastião AM (2011) Enhancement of LTP in aged rats is dependent on endogenous BDNF. **Neuropsychopharmacology** 36:1823-1836. (Citations: 41)

Silva - Santos, Bruno

T cell Differentiation & Tumor Targeting

Bruno Silva-Santos :
Vice - President of the iMM Lisboa since 2014

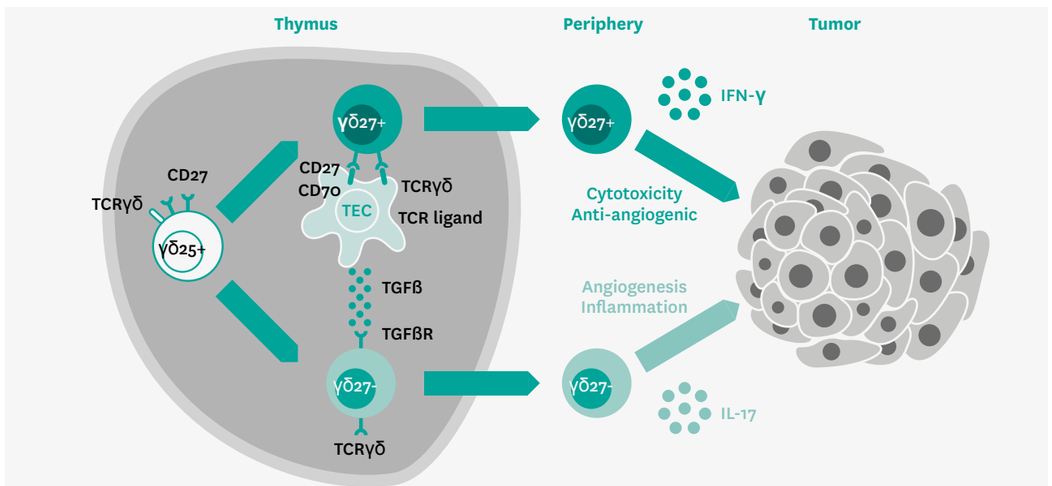
bssantos@medicina.ulisboa.pt

- PhD (2002) in Immunology at University College London, UK
- Post-Doctoral (2002-2005) research at King's College London, UK
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa
- Vice -President of the iMM Lisboa since 2014
- Group-Leader at iMM Lisboa since 2006

Keywords

T cell differentiation • T cell activation • Tumour immunology • • Leukaemia clonal evolution • Neuroimmunology • • Immunopathogenesis of Severe Malaria

Our work has shown that gamma-delta T cells differentiate into two distinct subsets in the murine thymus, which segregate with CD27 expression and produce either interferon-gamma or interleukin-17. These subsets can play strikingly opposing roles in tumor progression: whereas CD27+ gamma-delta T cells promote tumor eradication, their CD27- IL-17+ counterparts promote inflammation, angiogenesis and ultimately tumor growth.



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 and autoimmune diseases. We also study human peripheral blood T cells and, in particular, their recognition and targeting of lymphomas and leukaemias. 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.

Selected Publications

— Silva-Santos B, Serre K, Norell H. (2015) γδ T cells in cancer. **Nature Reviews Immunology** 15(11):683-91. (Citations: n/a)

— Rei M, Gonçalves-Sousa N, Lança T, Thompson RG, Mensurado S, Balkwill FR, Kulbe H, Pennington DJ and Silva-Santos B (2014). Murine CD27(-) Vγ6(+) γδ T cells producing IL-17A promote ovarian cancer growth via mobilization of protumor small peritoneal macrophages. **Proc Natl Acad Sci U S A** 111(34): E3562-70. (Citations: 19)

— Schmolka N, Serre K, Grosso AR, Rei M, Pennington DJ and Silva-Santos B (2013) Epigenetic and transcriptional signatures of stable versus plastic differentiation of proinflammatory γδ T cell subsets. **Nature Immunology**, 14 (10), 1093. (Citations: 21)

— Coquet J*, Ribot JC*, Babala N, Middendorp S, Xiao Y, Neves JF, Fonseca-Pereira D, Jacobs H, Pennington DJ, Silva-Santos B** and Borst J** (*Co-first Authors; **Co-senior Authors) (2013) Epithelial and dendritic cells in the thymic medulla promote CD4+ Foxp3+ regulatory T cell development via the CD27-CD70 pathway. **Journal of Experimental Medicine**, 210(4), 715. (Citations: 32)

— Correia DV, Fogli M, Hudspeth K, da Silva MG, Mavilio D and Silva-Santos B. (2011) Differentiation of human peripheral blood Vdelta1+ T cells expressing the natural cytotoxicity receptor NKp30 for recognition of lymphoid leukemia cells. **Blood**, 118, 992-1001. (Citations: 42)

— 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 interferon-γ- and interleukin 17–producing γδ T cell subsets. **Nature Immunology**, 10, 427-36. (Citations: 203)

Simas, Pedro

Herpesvirus Pathogenesis

Pedro Simas :
Group Leader at iMM Lisboa since 2004

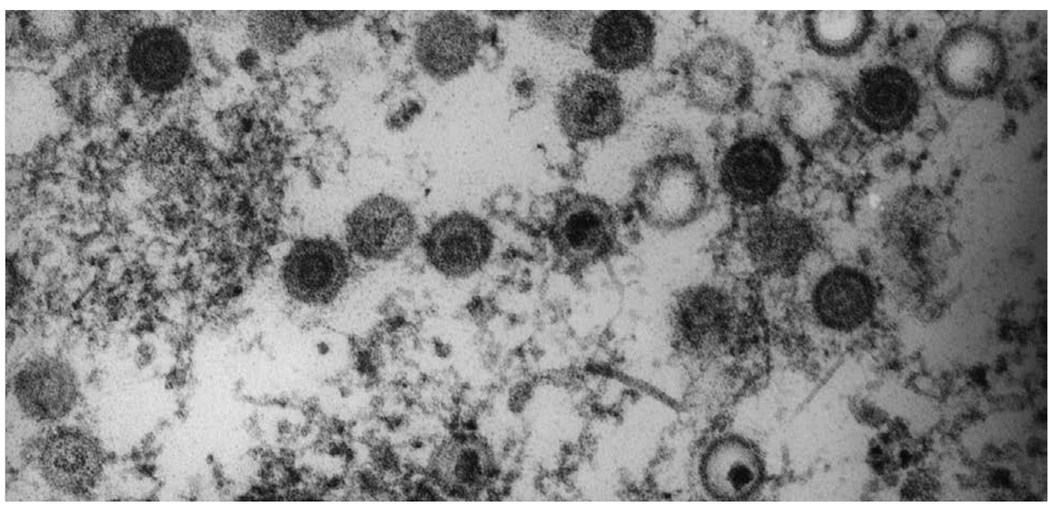
psimas@fm.ul.pt

- PhD (1994) in Viral Pathogenesis at the University of Cambridge, UK
- Post-doctoral research at the University of Cambridge, UK
- Principal Investigator at Instituto Gulbenkian de Ciência (until 1999)
- Associate Professor at Faculdade de Medicina da Universidade de Lisboa

Keywords

Herpes virus • B lymphocytes • Chronic infection • • Kaposi sarcoma herpesvirus (KSHV) • B cell and Lymphomas • • MuHV-4 and animal model of infection

Herpes Virus (MuHV-4) in infected cells visualized by electron microscopy.



Major Interests — Objectives

We utilize murid herpesvirus 4, which causes persistent infection in B lymphocytes in laboratory mice, as a model to study human gammaherpesvirus pathogenesis, namely Kaposi's sarcoma associated herpesvirus (KSHV). KSHV is the etiologic agent of KS and primary effusion lymphoma. KSHV infection of tumor cells is primarily latent and KSHV drives cells to proliferate. KSHV persists in latently infected tumor cells as an extrachromosomal, multi-copy episome (plasmid). KSHV latency-associated nuclear antigen (kLANA) mediates KSHV episome persistence, thus tumor cell viability. Since there is no tractable animal model for KSHV, the MuHV-4 model provides a unique opportunity to study gammaherpesviruses in vivo.

Selected Publications

— Fontinha D, Lopes FB, Marques S, Simas JP. (2015) Murid Gammaherpesvirus Latency-Associated Protein M2 Promotes the Formation of Conjugates between Transformed B Lymphoma Cells and T Helper Cells. **PLoS ONE**. 10(11): e0142540. doi:10.1371/journal.pone.0142540. (Citations: 0)

— Decalf Jérémie, Godinho-Silva Cristina, Fontinha Diana, Marques Sofia, Simas J. Pedro (2014) Establishment of Murine Gammaherpesvirus Latency in B Cells Is Not a Stochastic Event. **PLoS Pathogens** 10(7), e1004269. (Citations: 0)

— Godinho-Silva, C., Marques, S., Fontinho, D., Stevenson, P.G., Simas, J.P (2014) Defining Immune Engagement Thresholds for in vivo Control of virus-driven Lymphoproliferation. **PLoS Pathogens** 10(6):, e1004220. (Citations: 1)

— Pires de Miranda M, Lopes FB, McVey CE, Bustelo XR, Simas JP. (2013) Role of Src-homology domain binding in signaling complexes assembled by the murid gammaherpesvirus M2 protein. **Journal of Biological Chemistry** 288, 3858. (Citations: Citations: 5)

— Correia, B., Cerqueira, S.A., Beauchemin, C., Pires de Miranda, M., Li S., Ponnusamy, R., Rodrigues, L., Schneider, T.R., Carrondo, M.A., Kaye, K.M., Simas, J.P., McVey C.E. (2013) Crystal structure of the gamma-2 herpesvirus LANA DNA binding domain identifies charged surface residues which impact viral latency. **PLoS Pathogens** 9(10), e1003673. (Citations: 2)

— Rodrigues L, Popov N, Kenneth MK, and Simas JP (2013) Stabilization of Myc Through Heterotypic Poly-Ubiquitination by mLANA is Critical for γ-Herpesvirus Lymphoproliferation. **PLoS Pathogens** 9(8), e1003554. (Citations: 2)

Sousa, Ana E.

Human Immunodeficiency & Immune Reconstitution

Ana E. Sousa :
Group Leader at iMM Lisboa since 2003

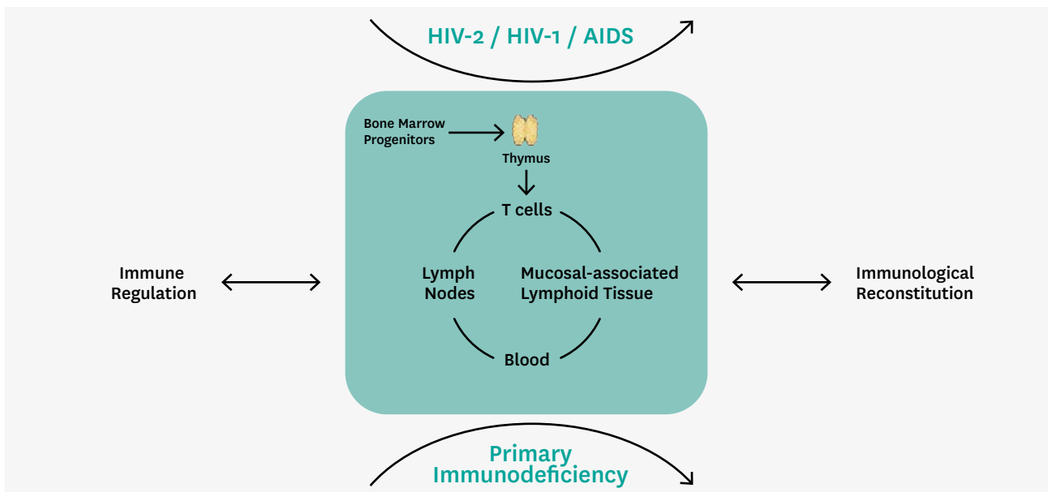
anasousa@medicina.ulisboa.pt

- MD (1986) and PhD (2000) in Clinical Immunology at Faculdade de Medicina da Universidade de Lisboa (FMUL)
- Investigator and Associate Professor at FMUL

Keywords

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

T cell homeostasis, human immunodeficiency, and immune reconstitution



Major Interests — Objectives

Human Immunodeficiency & Immune Reconstitution Lab research focuses on human T cell homeostasis and immune regulation with the ultimate goal of identifying new strategies for immunological reconstitution and targets for immune-based therapies. An important part of Human Immunodeficiency & Immune Reconstitution Lab research effort is centered on HIV/AIDS immunopathogenesis, mainly through the study of HIV-2 infection, a naturally attenuated form of HIV disease. Human Immunodeficiency & Immune Reconstitution Lab prioritizes the "bedside to the bench" approach and, given the transversal nature of Clinical Immunology, brings together physician/clinical researchers, from different medical areas, and basic researchers.

Selected Publications

— Caramalho I, Nunes-Silva V, Pires AR, Mota C, Pinto AI, Nunes-Cabaço H, Foxall RB, Sousa AE. (2015) Human regulatory T-cell development is dictated by Interleukin-2 and -15 expressed in a non-overlapping pattern in the thymus. **J Autoimmun**. 56, 98-110. (Citations: 0)

— Nunes-Cabaço H, Matoso P, Foxall RB, Tendeiro R, Pires AR, Carvalho T, Pinheiro AI, Soares RS, Sousa AE. (2015) Thymic HIV-2 infection uncovers posttranscriptional control of viral replication in human thymocytes. **J Virol**. 89, 2201-8. (Citations: 5)

— Fernandes SM, Pires AR, Ferreira C, Foxall RB, Rino J, Santos C, Correia L, Poças J, Veiga-Fernandes H, Sousa AE. (2014) Enteric mucosa integrity in the presence of a preserved innate IL-22 compartment in HIV-1 treated individuals. **J Infect Dis**, 210, 630-40. (Citations: 7)

— Tendeiro R, Foxall RB, Baptista AP, Pinto F, Soares RS, Cavaleiro R, Valadas E, Gomes P, Victorino RM, Sousa AE. (2012) PD-1 and its ligand PD-L1 are progressively up-regulated on CD4 and CD8 T-cells in HIV-2 infection irrespective of the presence of viremia. **AIDS**, 26, 1065-1071. (Citations: 20)

— Markert ML, Marques JG, Neven B, Devlin BH, McCarthy EA, Chinn IK, Albuquerque AS, Silva SL, Pignata C, de Saint Basile G, Victorino RM, Picard C, Debre M, Mahlaoui N, Fischer A, Sousa AE (2011) First use of thymus transplantation therapy for FOXN1 deficiency (nude/SCID): a report of 2 cases. **Blood**, 117, 688. (Citations: 18)

— 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. (Citations: 35)

Veiga-Fernandes, Henrique

Lymphocyte Function & Development

Henrique Veiga-Fernandes :
Group Leader at iMM Lisboa since 2008

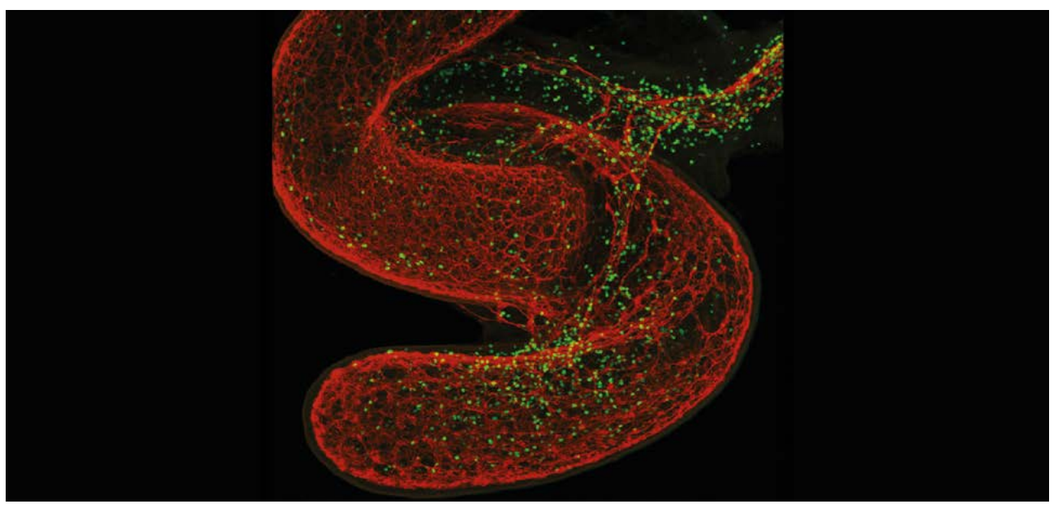
jhfernandes@medicina.ulisboa.pt

- PhD (2002) in Molecular and Cell Biology at Université Rene Descartes Paris V, France
- Post-doctoral research at Institut Necker, France and NIMR, UK
- Senior investigator scientist at NIMR, UK (2006-08)

Keywords

Lymphoid organogenesis • Haematopoiesis • Innate Lymphoid Cells • Lymphocyte function

Fetal intestine. Red: neurons; Green: innate lymphoid cells



Major Interests — Objectives

The immune system is a key player in the resolution and prevention of severe pathologies, such as infectious and inflammatory diseases. To accomplish their function throughout life, immune cells interact with each other and with their external environment. Thus, all immune cell processes, ranging from haematopoiesis to immune cell response to pathogens, require the establishment of effective cellular and molecular interactions. However, the mechanisms that underpin immune cell function and communication with their environment remain largely elusive. Our research is cantered on novel communication pathways that determine immune cell fate and disease progression in the context of lymphoid organogenesis and lymphoid cell development and function.

Selected Publications

— Veldhoen, M and Veiga-Fernandes, H (2015). Feeding immunity: skepticism, delicacies and delights. **Nature Immunol**. 16:215-219. (Citations: 1)

— Xu, W., Domingues, R.G., Fonseca-Pereira, D., Ferreira, M., Ribeiro, H., Lopez-Lastra, S., Motomura, Y., Moreira-Santos, L., Bihl, F., Braud, V., Kee, B., Brady, H., Coles, M.C., Vosshenrich, C., Kubo, M., Di Santo, J.P. and Veiga-Fernandes, H. (2015). NFIL3 orchestrates the emergence of common helper innate lymphoid cell precursors. **Cell Reports** 10:2043-54. (Citations: 14)

— van de Pavert, S. A., M. Ferreira, R. G. Domingues, H. Ribeiro, R. Molenaar, L. Moreira-Santos, F. F. Almeida, S. Ibiza, I. Barbosa, G. Goverse, C. Labao-Almeida, C. Godinho-Silva, T. Konijn, D. Schooneman, T. O'Toole, M. R. Mizee, Y. Habani, E. Haak, F. R. Santori, D. R. Littman, S. Schulte- Merker, E. Dzierzak, J. P. Simas, R. E. Mebius, and Veiga-Fernandes, H. (2014). Maternal retinoids control type 3 innate lymphoid cells and set the offspring immunity. **Nature** 508:123-127. (Citations: 63)

— Fonseca-Pereira, D., Arroz-Madeira, S., Rodrigues-Campos, M., Barbosa, I., Domingues, R.G., Bento, T., Almeida, A.R.M., Ribeiro, H., Potocnik, A., Enomoto, H. and Veiga-Fernandes, H. (2014). The neurotrophic factor receptor RET drives haematopoietic stem cell survival and function. **Nature** 514:98-101. (Citations: 5)

— Klose, C. S., M. Flach, L. Mohle, L. Rogell, T. Hoyler, K. Ebert, C. Fabiunke, D. Pfeifer, V. Sexl, D. Fonseca-Pereira, R. G. Domingues, H. Veiga-Fernandes, S. J. Arnold, M. Busslinger, I. R. Dunay, Y. Tanriver, and A. Diefenbach (2014). Differentiation of Type 1 ILCs from a Common Progenitor to All Helper-like Innate Lymphoid Cell Lineages. **Cell** 157:340-356. (Citations: 120)

— Patel, A, Harker, N, Moreira-Santos, L, Ferreira, M, Alden, K, Timmis, J, Foster, K, Garefalaki, A, Pachnis, P, Andrews, P, Enomoto, H, Milbrandt, J, Pachnis, V, Coles, M, Kioussis, D, Veiga- Fernandes, H. (2012). Differential RET Signaling Pathways Drive Development of the Enteric Lymphoid and Nervous Systems. **Science Signaling** 5 (235), ra55. (Citations: 13)

Technical Facilities

Zeiss Axiovert 200M

© Photo by *Bioimaging Facility*

Animal Facility

Joana Marques, PhD
Head of facility
joanammarques@medicina.ulisboa.pt

The rodent facility of the iMM Lisboa aims to support state-of-the-art animal research. For that purpose we provide the best housing and care of laboratory rodents and support training and education in Laboratory Animal Science.

Biobank

Sérgio Dias, PhD and Joaquim Polido Pereira, MD, PhD
Head of facility
biobanco-imm@medicina.ulisboa.pt

Biobanco-iMM is a structure created by the Instituto de Medicina Molecular (iMM Lisboa), which receives and stores a wide collection of biological samples donated voluntarily and its correspondent clinical information in order to foster biomedical research.

Biobanco-iMM aims to achieve sustainable growth, focused on improving quality, not only in samples but also in data management. We are working on several aspects of serum and DNA quality control parameters. Other strategic goals are to promote national biobanking networking with standardized procedures and established synergies as well as international integration of biobanking networks.

Zebra Fish Facility

Leonor Saúde, PhD
Head of facility
msaude@medicina.ulisboa.pt

Provide a fully functional facility to be used by the iMM research labs. Provide technical assistance to facilitate the use of zebrafish in a wide range of experimentation sets.

Bioimaging

José Rino, PhD
Head of facility
joserino@medicina.ulisboa.pt

The Bioimaging Facility acts as a support structure to carry out and nurture research done with Light Microscopy inside the institute. Besides managing resources, the Facility provides iMM Lisboa scientists and visitors with excellence in scientific know-how and expertise in using light microscopy methods for their research. We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques and foster interactions and collaborations between microscopy users at the iMM Lisboa.

Biosafety Level 3 Laboratory

Miguel Prudêncio, PhD
Head of facility
mprudencio@medicina.ulisboa.pt

The iMM Lisboa houses a 70 m2 BSL3 Facility meeting the highest safety standards as defined by European and International guidelines. The purpose of this facility is to enable researchers to carry out work with infectious agents that require BSL3 or ABSL3 containment conditions.

The Facility is available to iMM Lisboa internal and affiliated researchers, and, with the exception of ABSL3, to external researchers from academia, pharma and biotech. Work in the BSL3 Lab follows SOPs defined in the Facility's Rules and Guidelines Manual.

The iMM Lisboa BSL3 Facility comprises two fully equipped tissue culture rooms and one animal experimentation room for rodents. Available equipment includes incubators, benchtop centrifuges, refrigerators and freezers, microscopes, a -80 freezer, and an ultracentrifuge.

Flow Cytometry

Ana Vieira
Facility Manager
ivieira@medicina.ulisboa.pt

The Flow Cytometry facility provides support and training to iMM Lisboa and external researchers who require this technology in their research projects. The facility is equipped with 4 cell analysers (1 FACSCalibur, 2 BD LSR Fortessa and 1 BD Accuri C6) and 2 cell sorters (FACSAria IIu and FACSAria III). One LSR Fortessa is equipped with High Throughput Sampler, which allows the automated acquisition of samples from 96 and 384 well plates. A substantial part of our work is to provide training in flow cytometry concepts, experiment planning, experimental controls, instrument operation and data analysis. Our staff further ensures quality control and maintenance procedures on all instruments and the implementation of the Quality Management System, according to ISO 9000.

Histology & Comparative Pathology Laboratory

Tânia Carvalho, PhD
Head of facility
taniacarvalho@medicina.ulisboa.pt

The Histology and Comparative Pathology Laboratory aims at providing histology and comparative pathology support to iMM scientists investigating animal models of human disease, and scientists/physicians investigating human disease. Services are also available for extramural investigators.

Services include HISTOLOGY (tissue processing for paraffin-embedding; gelatin/OCT-embedding and cryosectioning; histochemistry), IMMUNOHISTOCHEMISTRY, TRANSMISSION ELECTRON MICROSCOPY and VETERINARY PATHOLOGY. We also provide assistance in study design and procedural training for researchers (necropsy, tissue harvesting).

Information Systems

José Braga, PhD
Head of facility
josebraga@medicina.ulisboa.pt

The Information Systems mission is to help researchers reach their maximum productivity by using adequate Information Technology resources.

Our aims are:

1. Provide state-of-the-art information technology infrastructure and support services.
2. Contribute to improve productivity of researchers and research outcomes.
3. Facilitate and optimize management business processes.

USI intervenes mainly in the following areas:

1. Information Technology (IT) support to iMM users.
2. Planning, implementation and maintenance of the infrastructure that stores, processes and protects research data.
3. Design, implement and integrate information systems to facilitate scientific and management processes.

Quality and Safety in Laboratory

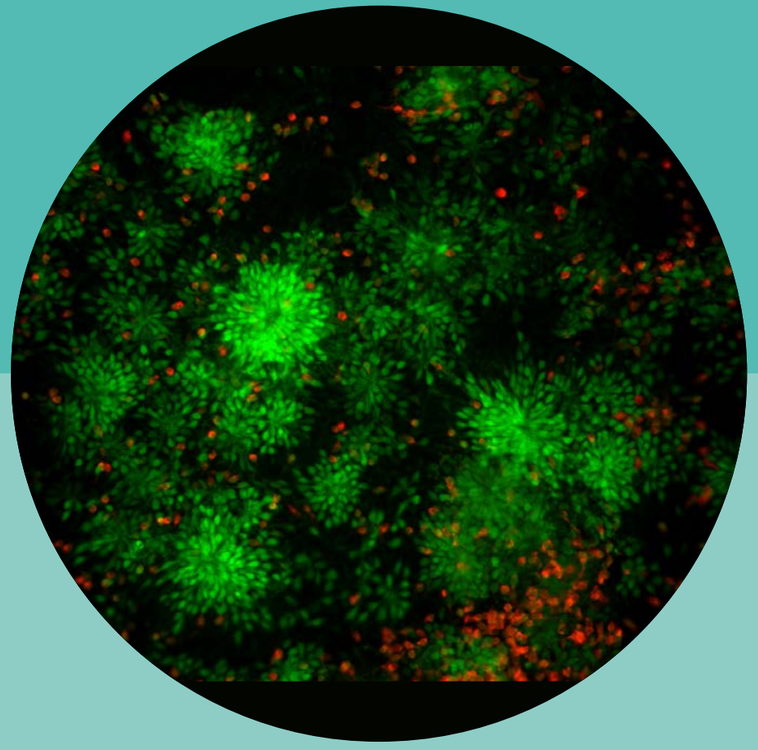
Alexandra Maralhas
Head of facility
amaralhas@medicina.ulisboa.pt

The Lab Management Facility is divided in three different areas, each one dedicated to improve the quality of research of the Institute and comply with National and International guidelines and best practices.

The Washing Room is responsible for the cleaning and sterilization of lab material, both common and specific of all research labs. The Purchasing Office centralizes all the Institute acquisitions, namely products, services and equipments and provides important information related to prices and ongoing promotions to all research labs.

The Lab Management is responsible for the adequate selection and installation of new equipment, the preventive and corrective maintenance of common equipment; design/renewal of laboratory infrastructures; advisory and authority regarding safety with products, equipment and infrastructure.

Administrative Facilities



Neural progenitors in culture, organized as rosetttes

Communication

Andreia Machado
Communication Manager
imm-communication@medicina.ulisboa.pt

The Communication is iMM's first line of interaction with society providing updated, reliable and relevant information on all of iMM's thematic areas, as well as promoting the very best scientific successes made by its research teams. Its mission is to support the internal and external communication of iMM's activities as well to advise iMM Direction on Public Affairs issues. With the firm belief that science should inform decisions because it impacts everyone's lives, the Communication targets a wide range of audiences (policy makers, public opinion, patients associations, medical societies, schools, academia, industry, media, arts, amongst others). It serves as spokesman for the institute and it's responsible to manage iMM's image aligned with the institute values and mission.

Management

Margarida Pinto Gago
Head of facility
mpintogago@medicina.ulisboa.pt

iMM legal, Human Resources and general administrative and financial matters:

- **Accounts** — iMM statutory accounts and tax returns; cost accounting;
- **Projects Management** — from contractual start until final report submission; related support to researchers;
- **Human Resources** — contracts and salaries; performance assessment;
- **Legal** – Institutional and researchers support: namely on intellectual property and consortium agreements;
- **Quality Management System**
- **General Administrative and financial support**

The Management facility also gives support to the Executive Director and the other Statutory Boards in relation to organizational issues, inter-institutional collaborations, financial and budget management strategy.

Education & Advanced Training

Filipa Moraes, PhD
Manager
imm-advancedtraining@medicina.ulisboa.pt

General Aim
Provide training opportunities for success in science to researchers at different stages in their careers.

Ongoing Activities

- Ensure full running of ongoing PhD (CAML, LisbonBioMed) and Postdoctoral Programs: Launch Calls; Administrative execution; Managerial Support to PhD and Postdoctoral fellows activities; Support PhD and Postdoctoral Fellows throughout their training. Update Webpage within new iMM site.
- Run Advanced Courses, scheduled upon CAML & LisbonBioMed Scientific Boards approval; cover all organizational aspects.

New Programs

- Launch & implementation of Mindthegap — Postdoctoral Training Program approved for funding under Marie Curie Actions;
- Join EMBL- lead international consortium for Horizon 2020 application: outreach as post-graduate training.

Funding Programs

Joana Lamego, PhD
Head of facility
jlamego@medicina.ulisboa.pt

Initially created in 2008 the Funding Programs Office has been restructured in September 2015. With the vision of becoming the strategic front door for funding at iMM, aiming its sustainable growth and its placement as scientific excellence leader and societal influencer, the Office develops its core activities in two main pillars: i) to support the securing of funding at iMM (by disseminating funding opportunities, supporting the preparation & submission of applications, and supporting the negotiation of funded projects); ii) to increase the competitiveness of iMM in the long-term attraction of funding (by developing new and improving existing tools and processes, and diversifying funding sources).

Ongoing Partnerships

Centro Académico de Medicina de Lisboa
CAML

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 consortium aiming to promote the academic dimension in clinical practice, renewing the teaching hospital concept.

Harvard Medical School
Portugal programme

IMM is also a partner of the Harvard Medical School – Portugal programme, sponsored by the Portuguese Foundation for Science and Technology. This programme, directed by M. Carmo-Fonseca (IMM/FMUL), results from a Memorandum of Understanding between Portuguese Ministry of Education and Science 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 is associated with the Doctoral Programme for Physicians, PFMA, supported by the Gulbenkian and Champalimaud Foundations, the Ministry of Health and the Portuguese Foundation for Science and Technology.

Genomed
Technophage
Lymphact
RoPlaVac
StemCell2Max

iMM Lisboa 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 Lisboa: Genomed, Technophage, Lymphact, RoPlaVac and StemCell2Max.

Health Cluster Portugal

IMM is one of the leading founders of the Health Cluster Portugal, a consortium that promotes initiatives and research projects to increase the national competitiveness, innovation and technology and encourages cooperation between companies, organizations, universities and public entities, seeking to expand economic areas related to health and to the improvement of health care.

Institutional Partnerships

www.bayer.com
www.smd.qmul.ac.uk
www.biogen.com
www.bioportugal.pt
www.bms.com
www.celgene.com

www.embo.org
www.janssen.pt
www.laco.pt
www.ligacontracancro.pt
www.lilly.pt
www.linde.pt

www.medtronic.pt
www.millenniumbcp.pt
www.novartis.com
www.omega-pharma.pt
www.pfizer.pt
www.roche.pt

www.servier.com
www.taper.pt
www.chln.min-saude.pt

imm.medicina.ulisboa.pt