Highlights 2016

Instituto de Medicina Molecular — iMM Lisboa

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FACULDADE DE MEDICINA LISBOA

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CENTRO ACADÉMICO DE MEDICINA DE LISBOA

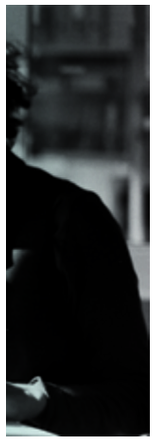
Our goal is simple

To pave the way for groundbreaking science

Contents

Director's message

Maria M. Mota



Our goal is simple – to pave the way for groundbreaking science by providing an environment that fosters freedom to chase key questions and embrace creativity

This is my third yearly "Director's message" and to be honest the most difficult one (until now!). How to find a good beginning? While I am optimistic by nature, after reading last year´s beginning - "Wow... this is quite impressive! After a truly memorable 2014, 2015 also revealed itself to be full of events and achievements." - I realized I cannot do much better than that.

But the truth is that 2016 was again quite a remarkable year. Especially because it was filled with many key discoveries made by many of you. Here I can only mention a few. The laboratory of Gonçalo Bernardes published in Nature Communications a new methodology for the construction of complex protein-antibody conjugates that creates novel possibilities of delivering cytotoxic drugs. My own team also published in Nature Communications a novel malaria parasite iron transporter, curiously one with plant-like features. Henrique Veiga-Fernandes's team presented their discovery that nervous cells are the "eyes and ears" of the immune system in the gut in Nature. Still in the realm of the immune system, the team led by Bruno Silva-Santos published in Nature Immunology that "signal strength" is a major developmental determinant of populations of pro-inflammatory lymphocytes implicated in both immune protection and immune pathology. Nuno Santos and his team used nanotechnology to demonstrate the potential of atomic force microscopy in the identification of cardiovascular problems in an article published in Nature Nanotechnology. And finally Luísa Figueiredo's team made a splash in Cell Host and Microbe publishing their discovery that Trypanosoma brucei, the parasite of sleeping sickness, "hides" in the fat. In spite of sleeping sickness being a truly neglected disease, breaking the dogma that these parasites do not live only in the blood or in the brain was initially difficult but later fully recognized by the community.

These papers, among many others, illustrate once again the diversity of approaches and discoveries portrayed by iMM Lisboa. Notably, this diversity has also been enriched in the past year with the recruitment of two new group leaders – Claus Azzalin and Marc Veldhoen. Marc was recruited as the European Commission-sponsored ERA Chair in Immunity and Infection, after 5 years as a group leader at the Babraham Institute in Cambridge. His team's interests are directed towards understanding the role that cells of the immune system play at the initiation, modulation and resolution of immune responses at epithelial barrier sites such as the intestine, ultimately contributing to the prevention of undesirable immune responses that may result in chronic infections, allergies, autoimmunity and an increased risk of cancer. Claus, on the other hand, moved his laboratory from ETH Zurich, Switzerland, where he started his independent career in 2008. His team focuses on understanding how telomeres execute their protective functions and how telomeric dysfunctions are mechanistically linked to pathological conditions such as cancer and premature aging. Their experiences and niches of research are certain to strengthen both research and training capabilities of our iMM community.

And our community was able to show their amazing ability to interconnect both scientifically and socially in our annual scientific retreat, held in Évora last April. I was extremely proud to see the whole iMM community gathered together in what I truly believe was the first edition of an event that will quickly become a cherished tradition eagerly anticipated by all IMMers.

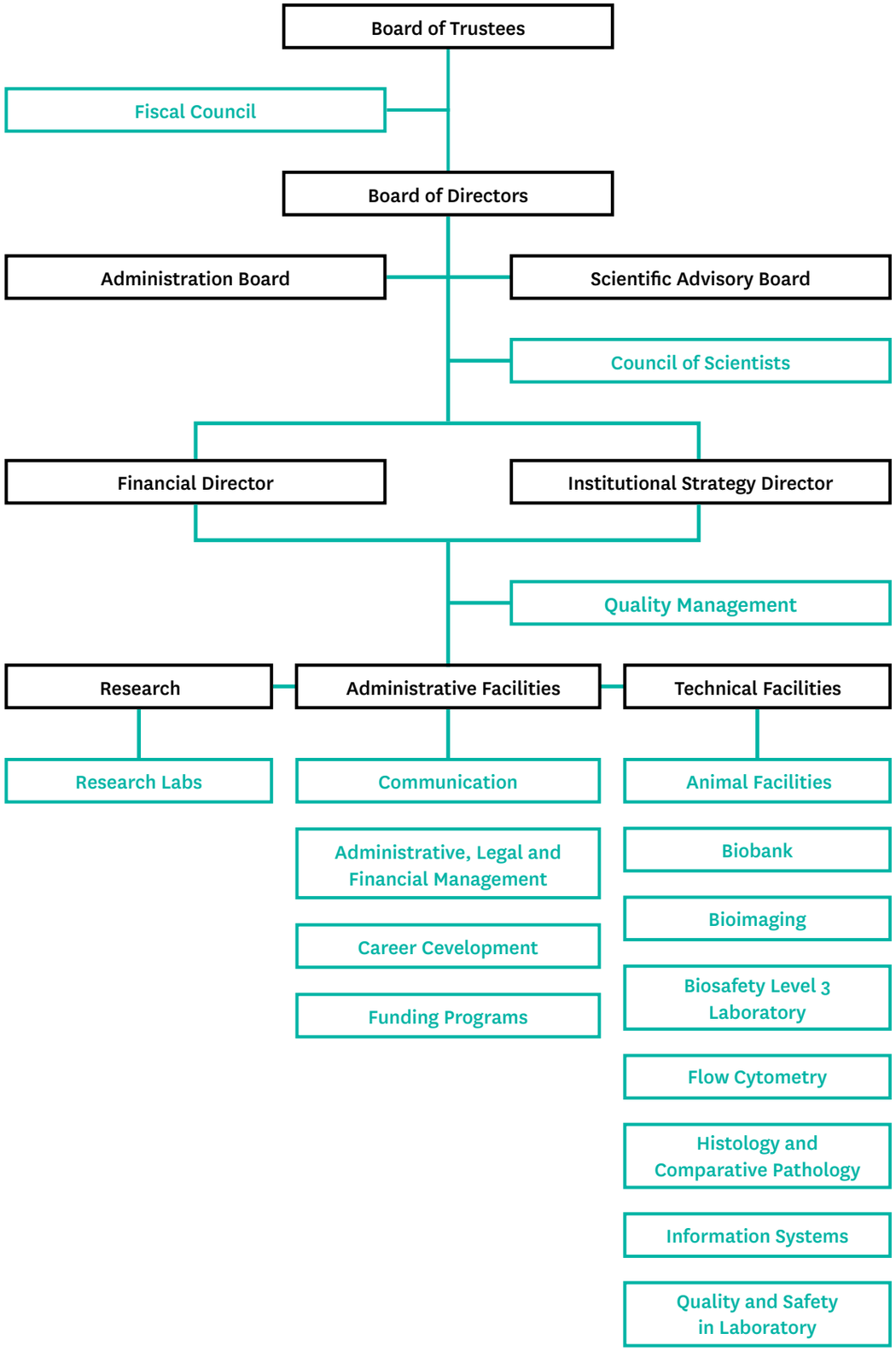
But not everything has been to our advantage in the past year. We also learned that Henrique Veiga-Fernandes will soon move to the Champalimaud Foundation. Henrique has served iMM as a leading researcher (for 8 years) but also as part of the Board of Directors (for 2 years) exceptionally well. And I want to use this opportunity to publicly THANK Henrique on behalf of all of us.

2016 has also been a very challenging year for all of us, with the implementation of the new "ordering rules" following new governmental directives. The Board of Directors is fully aware that these new rules are shaping the way we do science, and unfortunately not in the best way, which is unacceptable.

As Oscar Niemeyer once said:
"Como explicar que cruzar os braços é um problema e que a vida dura só um minuto?"

I can only assure you that we will never fold our arms and we are fully dedicated to finding a much-needed solution to this problem. Our goal is simple – to pave the way for groundbreaking science by providing an environment that fosters freedom to chase key questions and embrace creativity towards the exploration of different fields of science.

Structure and Organisation



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.

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MD, PhD – President

Maria M. Mota
PhD - Executive Director

Bruno Silva-Santos
PhD - Vice-President

Margarida Pinto Gago
Financial Director

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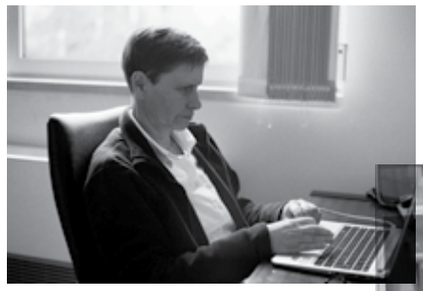
Caetano Reis e Sousa
PhD – Francis Crick Institute, London, UK

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

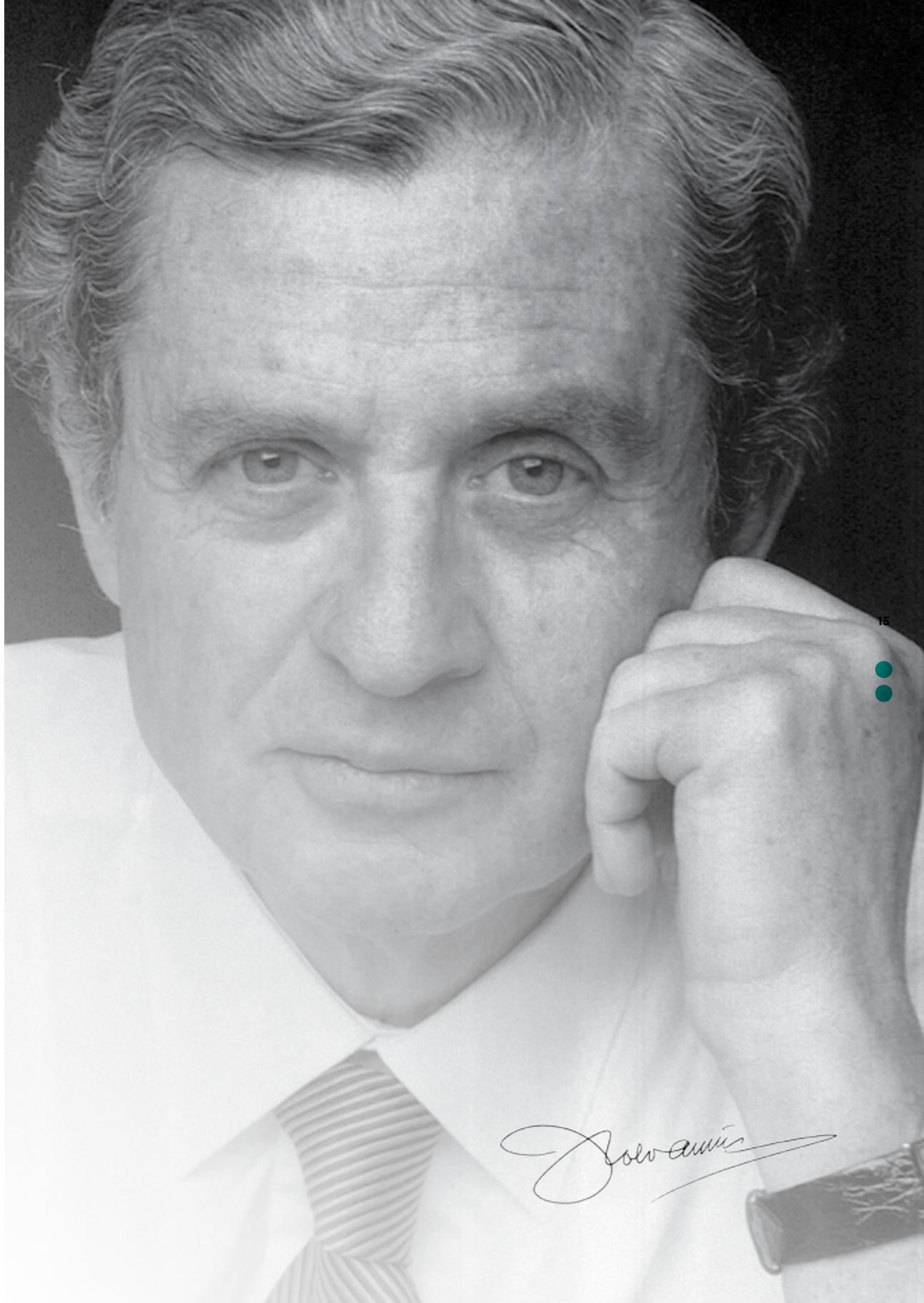

M. Carmo-Fonseca


Maria M. Mota
Bruno Silva-Santos


Margarida Pinto Gago

Homage to João Lobo Antunes

1944 — 2017



On the 27th of November João Lobo Antunes passed away. The Professor was a brilliant multidisciplinar nacional and international academic in the areas of Neurosciences, Ethics, among others. He possessed an invulgar high level of culture and was a distinguished neurosurgeon. He was the founder of iMM Lisboa which he presided for over a decade.

Alongside the Professor, Leonor Parreira was one of the key players involved in the birth and growth of the iMM since day one. A medical doctor and former researcher at iMM Lisboa she is currently a full Professor in the Faculty of Medicine of the University of Lisbon and served as Secretary of State for Science and Technology.

Um salto quântico

Estávamos em 1998. Eu tinha preparado para as minhas provas de agregação uma proposta para uma nova cadeira opcional em Medicina Molecular a incluir no sexto ano do curso de Medicina. Tinha para mim que uma vez na posse de formação clínica, o aluno-médico estaria bem preparado para absorver o impacto da "nova Biologia" na sua prática clínica e com isso colocá-la ao serviço do doente.

Para meu desconsolo, a proposta não viria a merecer mais que uns vagos cumprimentos circunstanciais do júri, presidido por João Lobo Antunes, pelo

que antevi de imediato estar destinada ao esquecimento eterno em algum obscuro arquivo nas profundezas da casa.

O que nunca poderia ter previsto foi o que se seguiu. Como sempre fazia, João Lobo Antunes tinha lido com atenção o relatório do curso, em particular a laboriosa argumentação a favor da causa, contida na introdução. Horrorizado por ter tropeçado algures na palavra detestada "holístico" (confesso que nunca mais a usei), não mostrou qualquer entusiasmo pela hipotética nova cadeira. Limitou-se a dizer-me que o importante não era ensinar o que depressa seria esquecido, o importante era, sim, criar as condições para que a medicina molecular fosse praticada de forma sustentada, e ao mais alto nível, na própria Escola. Criar um "Instituto de Medicina Molecular" na Faculdade era o que teria que ser feito, disse ele.

Recordo a estupefação que senti na altura. Era como se estivesse a presenciar um salto quântico, fenómeno que julgava invisível e reservado ao domínio da abstração teórica da Física. E, no entanto, era-o, pelo que representava de descontinuidade abrupta de "estados de energia".

Criou de imediato um pequeno grupo para dar andamento ao assunto. Inicialmente éramos três, Rui Victorino, Domingos Henrique e eu própria, a que se juntaria mais tarde Carmo Fonseca. Foi um tempo interessante e intenso, de análise exaustiva de modelos congéneres internacionais, de conversas com colegas de outros países que há muito tinham vivido experiências semelhantes, de reuniões que ele conduzia com a sua admirável e implacável lucidez.

Recordo a estupefação que senti na altura. Era como se estivesse a presenciar um salto quântico, fenómeno que julgava invisível e reservado ao domínio da abstração teórica da Física. E, no entanto, era-o, pelo que representava de descontinuidade abrupta de "estados de energia".

Havia, contudo, a priori, dois problemas a resolver. O primeiro era, evidentemente, criar as condições operacionais que tornassem possível um Instituto deste tipo. À época, a única forma de o fazer era conseguir aceder ao clube seleto dos Laboratórios Associados ao Ministério da Ciência, estruturas com financiamento público privilegiado, entidades meta-universitárias com regras de gestão ágeis, livres do espartilho burocrático da própria Universidade. Os Laboratórios Associados, contudo, só podiam ver a luz do dia por decisão exclusiva ministerial, pelo que fui encarregue de "sondar" a FCT sobre o assunto. Sondei, e Luís Magalhães, na altura o Presidente da FCT, mostrou desde logo aquilo a que hoje é costume chamar-se de "abertura". Sim, o Ministério veria com bons olhos um novo Laboratório Associado na área biomédica em Lisboa, baseado no "CEBIP", centro FCT criado anos antes por David-Ferreira.

“Conseguiu. Em 2002, o Instituto de Medicina Molecular era formalmente criado como Laboratório Associado e instalava-se no (pouco) espaço que restava no novo edifício Egas Moniz...”

Subsistia o segundo problema – convencer a Escola a acolher no seu seio, sem o rejeitar, um “corpo estranho”, a ela ligado, mas dela independente. Lobo Antunes, negociador tão hábil quanto pragmático, sabia bem o que o esperava. Mas sabia também, que a liberdade, aliada a uma intransigente exigência qualitativa, são os valores que sustentam a boa ciência e, portanto, não são negociáveis.

Conseguiu. Em 2002, o Instituto de Medicina Molecular era formalmente criado como Laboratório Associado e instalava-se no (pouco) espaço que restava no novo edifício Egas Moniz, já (generosamente) ocupado por alguns institutos de ciências básicas da Faculdade.

Sob a sua orientação estratégica, como Presidente, coadjuvado pela mão firme e eficaz da Diretora Executiva Maria do Carmo Fonseca, o Instituto de Medicina Molecular transformou-se rapidamente num ambiente fervilhante de jovens investigadores, alguns deles vindos de percursos internacionais de excelência.

Dez anos depois, quando decide passar o testemunho a Carmo Fonseca e atribuir a nova Direção executiva a Maria Mota, Bruno Silva Santos e Henrique Veiga Fernandes, eles próprios jovens estrelas ascendentes na ciência mundial, o Instituto de Medicina Molecular era já considerado um dos melhores centros de investigação biomédica do país.

Digo “considerado” porque, como sabemos, em ciência o que vale não é a perceção subjetiva e “local” de valor. O valor absoluto e relativo de uma instituição só pode ser determinado por avaliação externa, isenta e competitiva. Assim, a consideração só passaria a inquestionável facto quando, em 2014, o IMM é reconhecido com Excelente por avaliadores internacionais independentes, no âmbito de uma avaliação global de todas as unidades de I&D do país.

O que essa avaliação não podia mostrar, contudo, era o impacto da instituição na própria Universidade. Em Outubro de 2015, estava eu ainda em funções governamentais, Maria Mota convida-me para dizer “umas palavras” numa cerimónia pública de apresentação de uma ERA-CHAIR do IMM (CAML).

Pedi que me fornecessem dados estatísticos desagregados sobre a Universidade de Lisboa, no que respeita à conquista de fundos no Horizonte 2020, o mais competitivo programa europeu de financiamento para a ciência. Confesso a surpresa (minha e de todos): 45% dos cerca de 33 milhões de euros obtidos pela Universidade de Lisboa nos dois primeiros anos daquele Programa (2014 e 2015), tinham sido capturados pelo Instituto de Medicina Molecular.

A que se devia então este singular sucesso? A competitividade internacional em ciência é, obviamente, um proxy de qualidade, e a qualidade, por sua vez, é sempre uma derivada da atividade de indivíduos. Procurei, e a explicação surgiu, cristalina: o Instituto de Medicina Molecular era, à data, o centro de investigação público com mais grantees do European Research Council, e uma das instituições com maior número de Investigadores FCT, eles próprios selecionados por concurso internacional competitivo. O Instituto de Medicina Molecular tinha-se tornado, inequivocamente, um polo atractor de talentos.

Estes números pouco nos dizem, no entanto, sobre a imaterialidade da influência do Instituto na própria Faculdade de Medicina. Não tenho dados que me permitam um juízo objetivo. Sei apenas que o Instituto de Medicina Molecular é hoje motivo de orgulho para a Faculdade, vários dos seus Professores são nele Investigadores principais, os alunos usufruem do contacto com laboratórios e cientistas, a investigação clínica adquire progressivamente a pujança derivada da pesquisa pluridisciplinar. Por seu lado, o Hospital, elemento fundamental da trindade CAML, invoca sistematicamente a “parceria” com o IMM como peça curricular distintiva entre os centros hospitalares nacionais.

A minha perceção, como observadora externa que não pertence ao IMM, é a de que o caminho se tem feito caminhando (y al volver la vista atrás se ve la senda que nunca se ha de volver a pisar), mas o desígnio maior de Lobo Antunes - a fértil e harmoniosa cooperação entre ciência básica e a medicina clínica, alicerçada em impecáveis valores éticos e de ethos institucional – ainda não foi plenamente atingido.

Esse é o desafio, e o imperativo moral, das atuais lideranças nos anos que se aproximam.

Tarefa fácil e de sucesso garantido? Não o é certamente e ele sabia-o, melhor do que ninguém. Mas, como diz Edward O. Wilson, no seu luminoso livro Consilience. The Unity of Knowledge, “The moral imperative of humanism is the endeavor alone, whether successful or not, provided the effort is honorable and failure memorable. If those committed to the quest fail, they will be forgiven. When lost, they will find another way. “

Leonor Parreira
Professora Catedrática, FMUL

Lisboa, 30 de outubro de 2016

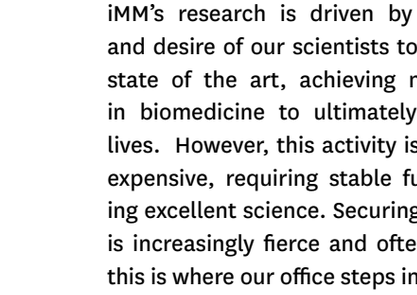

BIOBANCO
IMM


10

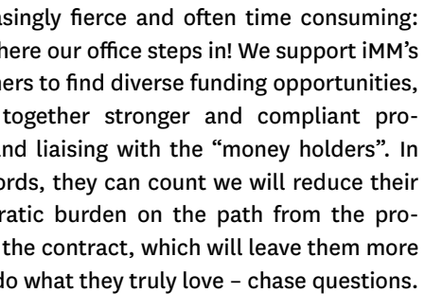
Funding and Awards

Funding Office Highlights 2016

iMM's research is driven by curiosity, passion and desire of our scientists to move towards the state of the art, achieving new breakthroughs in biomedicine to ultimately improve people's lives. However, this activity is as exciting as it is expensive, requiring stable funding for producing excellent science. Securing competitive funds is increasingly fierce and often time consuming: this is where our office steps in! We support iMM's researchers to find diverse funding opportunities, putting together stronger and compliant proposals and liaising with the "money holders". In other words, they can count we will reduce their bureaucratic burden on the path from the proposal to the contract, which will leave them more time to do what they truly love – chase questions. We are also among the most privileged ones who get to see the researchers' brand new and exciting ideas evolving and getting a "project shape". More often than not, preparing applications is a stressful process, with the alarming red deadlines, a sense of relief when pressing the "Submit" button and a burst of excitement and bliss in face of the "Approved" evaluation result.



Marija Garcia



Joana Costa

iMM researchers submitted applications

This synergistic effort between iMM researchers and the funding office has been increasingly consolidating and has already proved extremely successful. Indeed, with regards to the biggest EU Research and Innovation programme ever - H2020 - iMM is the only Portuguese Institution in the Top-50 Research Organizations in terms of EU funding [1], reaching a total value of €17,85M [2].

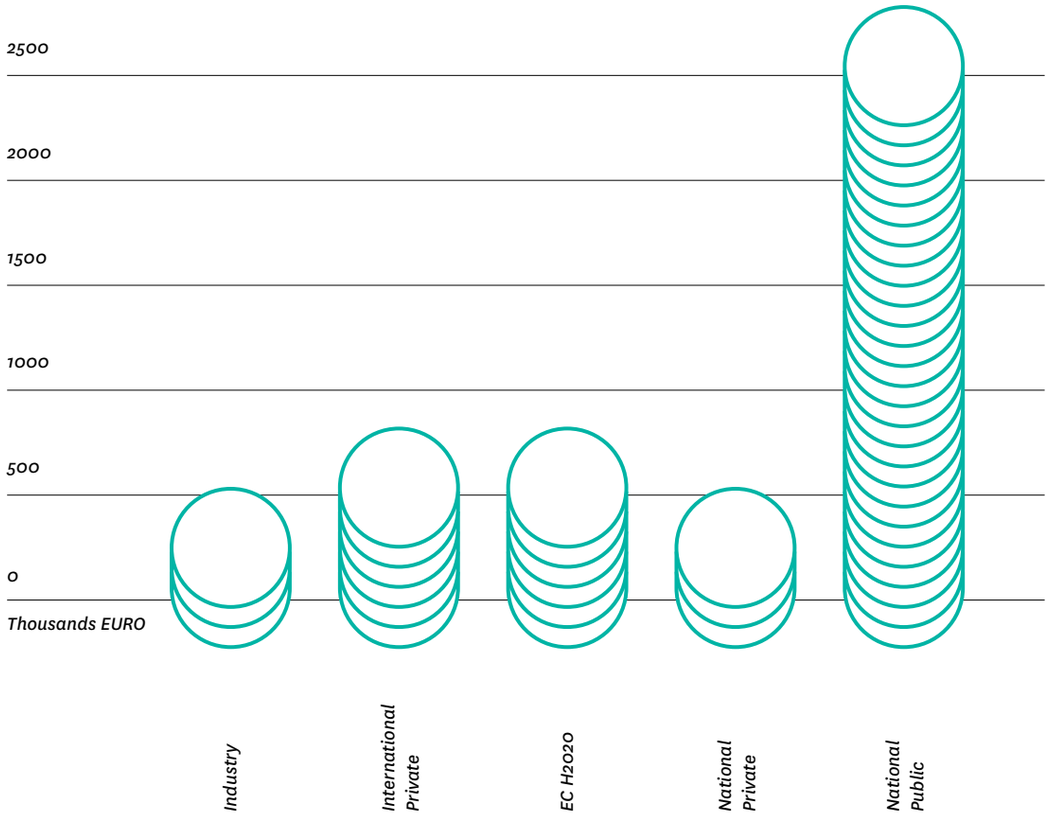
Internationalization and Diversification are crucial aspects in today's R&D funding context and our researchers have certainly embedded this. In 2016, iMM researchers submitted applications to 29 different International and to 19 different National Funding Programmes.

1 Horizon 2020 Monitoring Report 2014 and 2015
2 source: eCORDA DATA update as of September 2016

In the year where the national funding agency for R&D (FCT) omitted to open a call for project grants, iMM exploited the opportunities in the national structural funds programme P2020. Indeed, our research activity of excellence proved to be aligned with the R&I regional and national strategy for smart specialization, having secured nearly €2M for projects tackling important challenges comprised in the Europe 2020 Strategy. The national public funds were actually the larger source of competitive funding in 2016, followed by the EC Framework H2020 and International Private funding agencies [3].

Secured Competitive Funding 2016

40% known results for 2016 applications



3 This snapshot reflects the known results as of December 19, 2016, i.e. only 40% of all submitted applications in 2016.

Success stories from 2016

H2020 MSCA-RISE: LysoMod

Horizon 2020

iMM secured €1.1M to coordinate a project in the area of personalised medicine for disorders linked to lysosomal dysfunction. LysoMod consortium, involving 11 partners from the EU, South America and USA, will implement a mentored staff-exchange program to provide young researchers with high-level training in innovative approaches for exploring biological systems, preparing the next generation of creative researchers with entrepreneurial mindset and wider career prospects either in the private or public health sectors.

P2020 Programas de Atividades Conjuntas (PAC): PRECISE and ONEIDA

iMM secured €2.5M to coordinate a project aiming at accelerating progress of Portuguese health care toward the new era of precision medicine, by intertwining Medicine (iMM), Bioprocess and Biosystems Engineering (iBB) and Information Systems (INESC-ID). PRECISE aligns with four priority R&D areas at the national level, and represents one of the prime R&D clusters in Lisbon region.

ONEIDA was granted with €2.5M to join three top R&D units in the area of Infectious Diseases and Antimicrobial Resistance in Lisbon region - ITQB, IGC and iMM – and to create an 'omics expertise network which will contribute to more effective prevention and control measures.

EMBO Installation Grant

Claus Azzalin was awarded an EMBO Installation Grant to support his recently established independent laboratory at iMM. The project follows Claus' scientific interest on telomere stability and long noncoding RNAs in the context of healthy aging.

Fundo iMM-Laço 2016

The 1st edition of Fundo iMM-Laço, a partnership aiming at supporting cutting-edge research at iMM Lisboa on the causes of primary and metastatic breast cancer, awarded €100K to support Sérgio Dias and Sandra Casimiro to conduct their translational and clinical research project, respectively.

H2020 ERC Proof of Concept Grants

Horizon 2020

Two €150k ERC Proof of Concept Grants were awarded to verify the innovation potential of ideas arising from previously ERC frontier research projects. With the funded project MUSCLEGUY, Edgar Gomes will advance on a novel muscle disorders 3D in vitro system for drug screening and validation while Maria Mota will expand on drug repurposing for malaria chemoprotection with the funded project REUSE4MALARIA.

ERA Chair joined iMM

Marc Veldhoen has joined iMM as ERA Chair holder of EXCELLtoINNOV H2020 project to study the mechanisms that control the maintenance, activation and function of immune cells located or enriched at mucosal surfaces such as the intestine, ultimately contributing to the prevention of undesirable immune responses that may result in chronic infections, allergies, autoimmunity and an increased risk of cancer. iMM has secured app. €2.5M to leverage the institute's research excellence and innovation potential through the establishment of a translational biomedical research hub anchored in Lisbon that will i) leverage the national potential beyond borders; ii) act as the interface of Europe with America and Africa; iii) effectively contribute to overcome the health and demographic change societal challenges by potentiating major scientific advancements in this research area through worldwide collaborative efforts.

Starting three H2020 Twinning Project

Horizon 2020

iMM secured €3M to implement three Twinning projects to significantly strengthen its S&T capacity in Immunity & Infection, Tumor Biology and Neurosciences through a cohesive and sustainable collaborative network with internationally-leading research institutions.

TwinnToInfect

TwinnToInfect project aims to enhance iMM's research excellence in immunity and infection with its increase in competitiveness and innovation together with its partners Institut Pasteur, France and The Francis Crick Institute Limited, UK.

ReTuBi

ReTuBi project will build up towards outstanding research and training in tumour biology at iMM together with its partners Institut Curie, France and Deutsches Krebsforschungszentrum (DKFZ), Germany.

SynaNet

SynaNet project at iMM will focus on research and training challenges in Neurologic and Psychiatric Disorders together with its partners Itä-Suomen yliopisto, Finland; Università degli Studi di Roma La Sapienza, Italy and Lancaster University, UK.

Awards

Awards

January

ERC Proof-of-Concept
Edgar Gomes

February

Horizon 2020 Marie Curie Individual Fellowship
João Seixas

February

Medalha de Honra L'Oréal Portugal para as Mulheres na Ciência
Ana Catarina Fonseca

March

Gonçalo Bernardes was awarded the Chem Soc Rev Emerging Investigator Lectureship 2016
Gonçalo Bernardes

May

Maria M. Mota was selected an EMBO Member
Maria M. Mota

Gonçalo Bernardes was awarded the Harrison-Meldola Memorial Prize 2016
Gonçalo Bernardes

ERC Proof-of-Concept
Maria M. Mota

July

UL Scientific Awards
Winner *Bruno Silva Santos*
Honourable Mention
Joaquim Ferreira · José Ferro
Carmo Fonseca · Mario Ramirez

November

Pfizer Award in Basic Research
Henrique Veiga-Fernandes

November

BIAL Scientific Grant in Psychophysiology
Diana Prata

December

EMBO installation Grant
Claus Azzalin

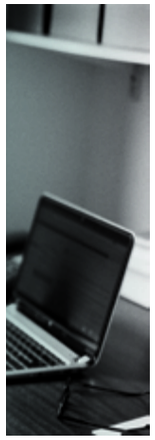
Fundo iMM-Laço
Translational project
Sérgio Dias
Clinical project
Sandra Casimiro

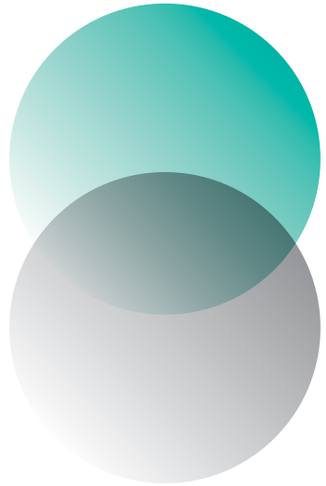
The Forbes Norris Award
Prof. Mamede de Carvalho

PRECISE Project

PRECISE Project

In 2016 the iMM received a 2.5 million euros funding integrated in the Horizon 2020 program, to support scientific research and technological development. The project, called PRECISE, is led by iMM President and researcher Maria do Carmo Fonseca.





What is the *PRECISE* project?

PRECISE is a joint research program that aims to accelerate the progress of Portuguese health care toward the new era of precision medicine. We believe this is the right time to start broadly applying the concept of prevention and treatment strategies that take individual variability into account, so that one day all patients will be offered customized care with treatments that match each individual's molecular profile and personal history.

Who will collaborate in the project and what are the specific contributions each institute will have?

The research program will be implemented by interdisciplinary teams formed across 3 partner institutions with core research programs in Medicine (iMM), Bioprocess and Biosystems Engineering (iBB), and Computers and Information Systems (INESC-ID).

Activities will be executed by 27 highly complementary principal investigators, including physician-scientists specialized in neurology, neurosurgery, oncology, hematology, rheumatology, dermatology, and immunology; basic researchers with expertise in molecular and chemical biology, genomics, synthetic chemistry, oncobiology, and immunology; bioengineers with expertise in biomaterials and bioprocessing of stem cells and their derivatives; and computer scientists specialized in communication networks and information and decision support systems.

What type of data will be available and who can access it?

We will determine cellular, molecular and genetic parameters from biological samples combined with clinical information, and we will build an e-infrastructure to collect, store, consolidate and enrich the resulting data in digital form and to deliver it, in comprehensible ways, to scientists, clinicians and patients.

We will capitalize the excellent IMM biobank infrastructure by creating specific cohorts designed to improve clinical decisions, and we will further develop medical registries as tools that provide feedback to clinical practice in integrated electronic clinical charts and databases.

To develop innovative approaches for cancer treatment, we will develop new diagnostic approaches based on next generation sequencing technologies to genotype fragments of DNA that are shed into the bloodstream by cancer cells undergoing apoptosis or necrosis. We will also develop novel medicinal chemistry approaches for targeted delivery of highly potent cytotoxic drugs into tumor cells, and we will explore targeted manipulations of non-coding RNAs as potential new medicines to control metastasis.

To move Precision Medicine into new disease areas, we will focus on stroke and mitochondrial diseases, as well as on common and rare immune-mediated diseases.

All proposed activities are needs-driven and feature the engagement of future users and patients in the development, testing and scaling of solutions. This makes our activity portfolio highly relevant to societal challenges related to health and the need to move towards more inclusive, innovative and reflective societies.

How do you envision this collaboration can change the way precision medicine is preformed?

The headline goal of *PRECISE* is treatments precisely tailored to specific molecular targets. *PRECISE* will capitalize existing expertise, resources and infrastructure available in the 3 partner institutions to foster the generation of new knowledge and to ensure its rapid translation to the benefit of patients and industry, through the direct involvement of hospitals, patient advocacy groups and the business sector. Although the consortium is located in the Lisbon region, *PRECISE* will have a national impact by effectively involving patients from all over Portugal, providing novel e-infrastructures for the benefit of clinicians throughout the country and reinforcing networks of national collaborations (including participation in 5 projects of the National Roadmap of Infrastructures) and international projects. Finally, *PRECISE* will have a nucleation effect of expertise and resources that will generate critical mass, thus increasing the international competitiveness of Portuguese scientists and innovators in both the public and private sectors.

iMM Laboratories

Azzalin, Claus M.

Telomeres, long noncoding RNAs and genome stability

cmazzalin@medicina.ulisboa.pt

Barata, João T.

Signaling in Cancer

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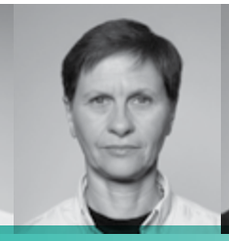

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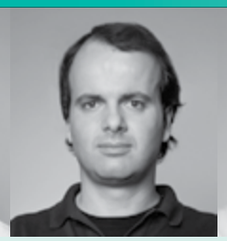

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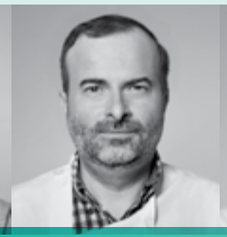

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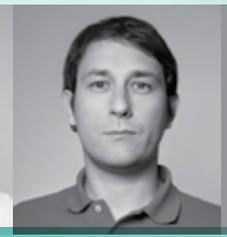

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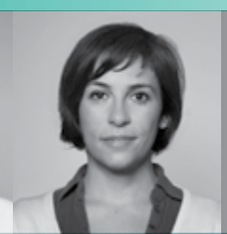

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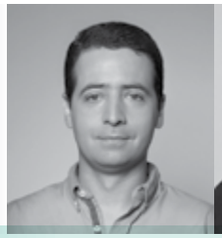

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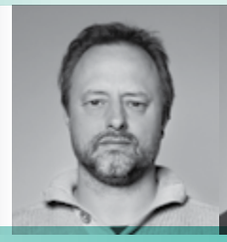

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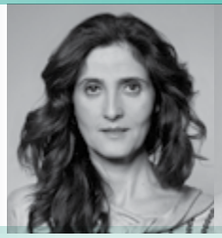

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Interviews

Marc Veldhoen

Marc Veldhoen is a Group leader at iMM Lisboa since 2016. He did his PhD In Molecular Immunology at NIMR, London, UK, where he also worked as a Post-doctoral researcher. He then became a senior investigator scientist at NIMR. After, he served as a Tenure track Group leader at the Babraham Institute, Cambridge, UK, receiving an ERC consolidator grant and an EMBO Young Investigator award, and full tenure in 2015. He is the editor-in- chief of Immunity, Inflammation and Disease, the EFIS open access immunology journal and served on the editorial boards of the European Journal of Immunology, International Journal of Immunology and Frontiers in Immunology. His laboratory studies the role that cells of the immune system play at the initiation, modulation and resolution of immune responses at epithelial barrier sites as well as the homeostatic control of tissues.

What made you establish your laboratory at iMM Lisboa?

I trained at the National Institute for medicine, London, UK. The focus on science, scientific freedom, collaborative efforts had a major impact on my work and success. I found a very similar atmosphere at iMM and hope to be able to contribute to this myself.

What do you study and what questions are you trying to answer in your work?

We mainly try to understand how particular white blood cells, T lymphocytes, are maintained, how they are activated, acquire particular functions and help the host deal appropriately with invading microorganisms as well as how they can contribute to aberrant immunity. In particular, we are currently interested in unconventional T cells that line the top layer of the skin and small intestine, forming part of a first line of defence as well as a specific population enriched in the next layer, called Th17 cells. To study these cells, we use genetically modified mice and infection models ranging from viruses, bacteria to eukaryotic parasites.

How did you become interested in this subject?

As an undergraduate student I became interested in the intricate workings of the immune system. Projects in the departments of parasitology, virology and Immunology were highly enjoyable and strengthened my interest. More by chance than design I did an extracurricular project in an immunology lab, which determined much of my future. The immune system is such an integrated part of an organism that there is always something that can catch one's imagination and interest.

Describe a typical work day for you.

Most days start with very quickly sifting through any e-mails. Right now I rely on data to come in from the Cambridge lab since we are finalising manuscripts and rebutting reviewers' demands. This means that days are filled with rewriting text, sometimes deleting it after a short break, and modifying it with new data coming in. Thinking about the data, potential alternative explanations, other ways to strengthen the mechanistic insights we already have and scanning literature to support data and to get new ideas are taking up a large part of the day. Skype sessions with students and collaborators take place weekly and looking at our mouse colonies is another job I partly do myself. Reviewing papers or grants is something I try and make a little time for but I do keep this very limited on the moment. Going to meetings/presentations, especially in a new environment to get to know the different groups is important and can take quite some time.

Then... whenever I can, I do (at least help) with some experimental work. I look forward to take on some bench work in the new year when the required reagents and equipment is in place. Unfortunately, my bench work is limited to about two days a week.

This leaves time after dinner for some last e-mails or electronic discussions on new data, planning of next experiments and projects before I do try and switch off!

What process do you follow to find answers?

All projects start in either one of two ways: hypothesis driven or question driven ideas. It is normally a progression from previous work, from which we had additional observations and questions, or sometimes it can be the hard way of "I have a brilliant idea"! The first follows a more methodical path, although frequently with additional twists and turns, whereby several experiments are planned to strengthen initial observations, than to gain the important mechanistic insight, followed by physiological relevance. The latter starts with a more direct hypothesis testing; mainly its predictability for the outcome of designed experiments. This is generally where things come tumbling down, but interesting observations are made in the process which eventually become the main project.

What are your expectations for your future work at iMM Lisboa?

I see an opportunity to push our data and interest in different directions via the influence of my new colleagues. Similarly, some of my background and knowledge can hopefully make a contribution to the iMM community. This means the future is both uncertain and exciting! In addition, a potential more clinical direction would be welcomed. This is not something that can be established very quickly, but hopefully it will be a reality in the future.

And of course, I would like to contribute towards the ongoing internationalization of the iMM, this way increasing the exchange of ideas and people.

Compared to other national and international renowned institutes, where do you position iMM Lisboa in terms of scientific excellence?

It is very difficult to do this as every place has its quirks. As far as equipment, energy and opportunity is concerned, iMM is doing very well and can rank above a lot of European universities, the publications and grants awarded speak for themselves. The horizontal setup, the absence of a strict hierarchal departmental structure is something I like very much.

It does not have the reputation of Cambridge and does not find itself very central in Europe (I have noted my flights suddenly take a lot longer). But with continued efforts Lisbon and iMM are certainly drawing attention as a place to watch where things are happening.

What do you enjoy most about being a scientist?

The freedom, the moving into truly novel areas with the potential to discover something novel and exciting. The ever increasing paper burden can take some of the joy away, so does the financial absence of long term planning due to sort term funding cycles. But, getting data that substantiate a hypothesis or are making inroads into something truly novel still outweighs that.

Do you have any hobbies outside of science?

There is generally limited time, but reading is something I enjoy. Most free time goes to family life, and having just moved into a new country and city, there is a lot to explore in the weekends.

Claus M. Azzalin

Claus M. Azzalin is a group leader at iMM Lisboa since 2016. He did his PhD in Genetics and Molecular Biology at 'Università degli Studi di Pavia' in Italy. He then became a Post-Doctoral Researcher at the Memorial Sloan-Kettering Cancer Center, New York, USA and successively at the Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland. In 2008, he became a Group Leader at Eidgenössische Technische Hochschule Zürich, Switzerland and the following year a SNSF/ETHZ Assistant Professor at Eidgenössische Technische Hochschule Zürich, Switzerland.

His research focuses on how telomeres execute their protective functions and how telomeric dysfunctions are mechanistically linked to pathological conditions. Specifically, his team studies how the telomeric long noncoding RNA TERRA participates in maintaining proper telomere structure and functions in both normal and diseased human cells.

What made you establish your laboratory at iMM Lisboa?

I visited several institutions in Europe and overseas and very rarely witnessed such a vibrant and exciting atmosphere as at iMM Lisboa. This, together with the strong sense of community that I felt every time I was at iMM Lisboa, made me decide that it was the right place for me. I do not deny that Portuguese food and life style had a say in my decision.

What do you study and what questions are you trying to answer in your work?

We study how telomeres, the end of linear eukaryotic chromosomes, support genome stability. We are particularly interested in how telomeric chromatin is established and maintained and we hope to contribute significant milestones to anti cancer therapeutic approaches based on the inhibition of cell immortality by interfering with telomere maintenance.

How did you become interested in this subject?

Contrarily to what people think, I have always been a 'DNA person'. RNA has drawn my interest only later during my scientific career. I have always been fascinated by how cells prevent accumulation of DNA damage and how they manage to repair breaks that accidentally occur throughout their genome. A telomere is just nothing more than one end of a constitutively protected break on our chromosomes. That's absolutely captivating!

Describe a typical workday for you.

I do not really have a typical work day... science and less fun duties decide my schedule.

What process do you follow to find answers?

The way we do it is quite straightforward: we ask questions and we use/develop the most suitable tools to answer those questions. And of course new answers pose new questions, it's a loop.

What are your expectations for your future work at iMM Lisboa?

My big expectation (hope) is to ultimately be able to cross the bridge between basic science and the clinics.

Compared to other national and international renowned institutes, where do you position iMM Lisboa in terms of scientific excellence?

Definitely very high up, that's one of the factors that made me decide to join.

What do you enjoy most about being a scientist?

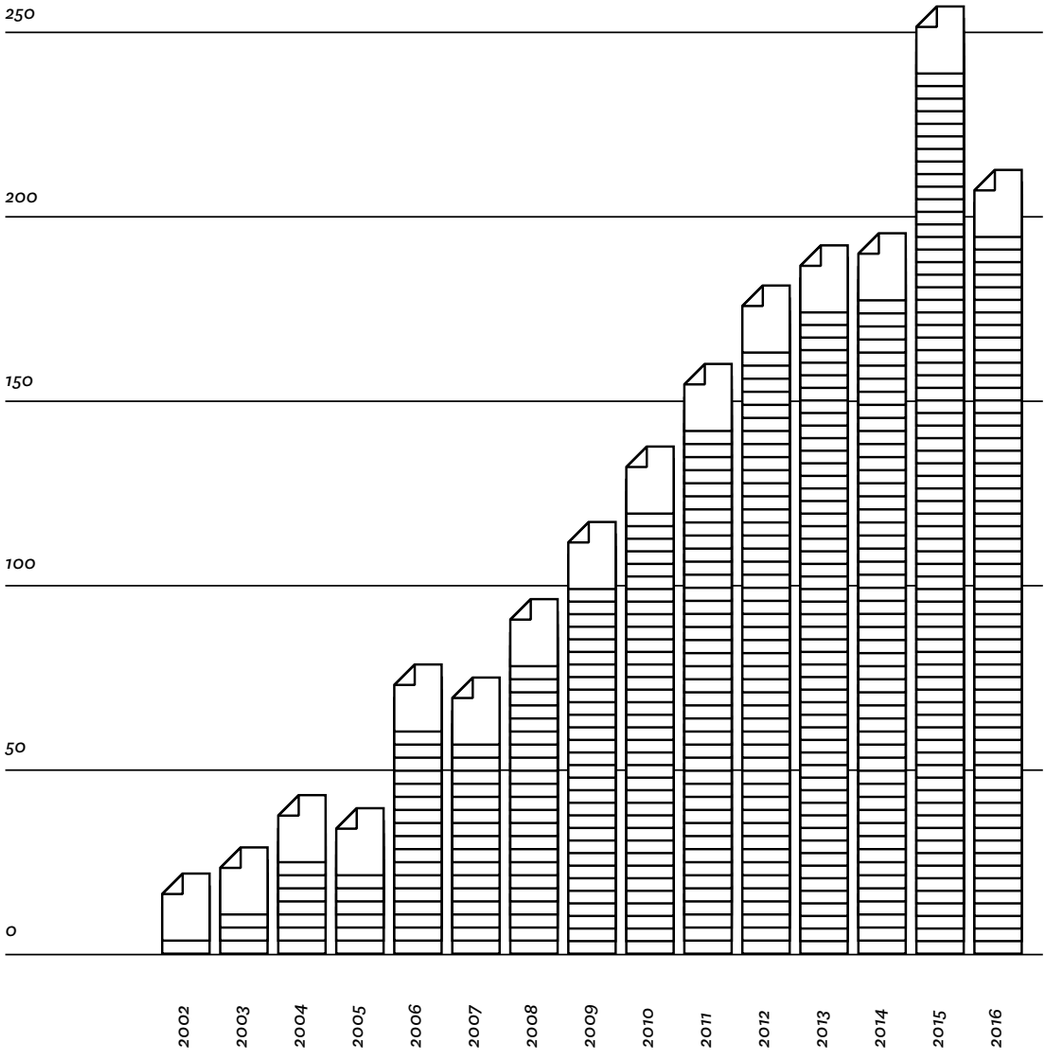
Intellectual stimulation, independence and mentoring.

Do you have any hobbies outside of science?

Travelling, although I mostly do it for my job. Need to work on better ones.

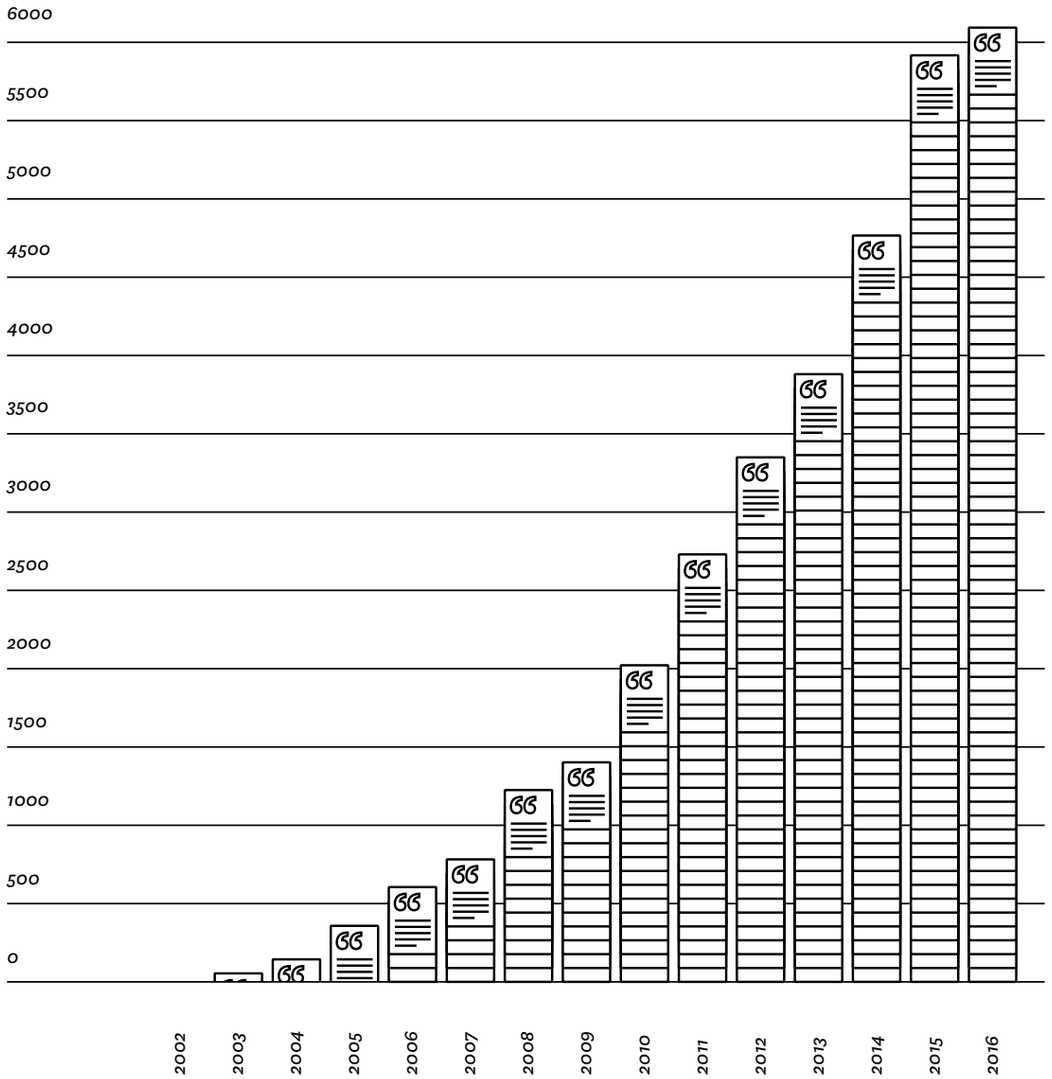
Publication Highlights 2016

Published Items in Each Year



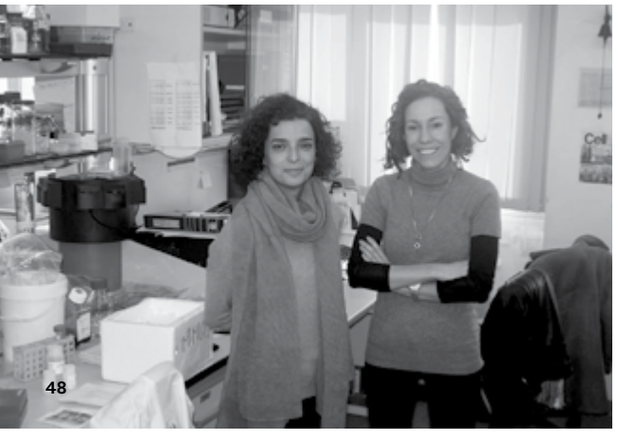
The latest 20 years are displayed

Citations in Each Year



The latest 20 years are displayed

Baker's yeast used to discover malaria pathway that could improve drug treatment



New anti-malarial drugs could be developed after researchers discovered a major transport pathway used by the malaria parasite when it infects humans.

Experts from St George's, University of London and the Instituto de Medicina Molecular (iMM Lisboa), University of Lisbon have exploited baker's yeast to discover how iron is controlled by the malaria parasite within the human body, providing the first detailed characterisation of an important iron transport pathway.

Malaria is a massive global health burden, with a current WHO estimate of around 600,000 deaths annually, although this figure could rise sharply if treatment failures associated with drug-combination therapies become widespread.

Dr Henry Staines, a senior research fellow at St George's, University of London said iron is essential to a malaria parasite's survival but can also be toxic at high levels.

He explained that iron is also critical to the effectiveness of important antimalarial drugs such as chloroquine and the artemisinins.

"This research will not only allow us to identify new ways to attack the parasite but will help us to understand how our current arsenal of antimalarial drugs work," he said.

"This is important because antimalarial drugs such as artemisinin-based combination therapies are not as effective as they were in South East Asia, which is a worrying trend."

The researchers used a mutant baker's yeast, in which the sequence for a specific iron transport protein is removed from the yeast's DNA. "With the yeast mutant unable to make this iron transport protein, it loses the ability to grow when iron is present. We thought a protein from the malaria parasite might perform the same iron transporting role, as the one lacking in the mutant yeast," Dr Staines said.

"To confirm our hypothesis, we introduced the DNA sequence for the malaria parasite protein into the mutant yeast and showed that the yeast regained their ability to grow in the presence of iron," explains Dr Ksenija Slavic from Instituto de Medicina Molecular Lisboa. "A mutant malaria parasite was also created by removing the iron transporter's gene, which resulted in reduced numbers of parasites in the liver, where they first multiply, and subsequently in the blood, at which point patients become ill", Dr. Slavic said.

"Inside liver cells, iron binding chemicals that remove iron improved how well the mutant parasites grew," adds Dr. Maria Mota from Instituto de Medicina Molecular in Lisbon, one of the senior authors of the study.

"Inside red blood cells, we found that these mutant parasites contained an increased amount of iron that could be potentially toxic, explaining the reduced numbers. Both findings imply that the gene helps the parasite to tolerate iron. This greater understanding of iron regulation in the malaria parasite could lead to urgently needed new treatment strategies."

Next up, the researchers will be looking into how the mutant parasites are impacted by anti-malarial drugs that use iron.

Slavic K, Krishna S, Lahree A, Bouyer G., Hanson KK, Vera I, Pittman JK, Staines HM, Mota MM. A vacuolar iron-transporter homologue acts as a detoxifier in Plasmodium. *Nat Commun*. 2016 Jan 20;7:10403.

The molecular strength required for immune protection also causes fatal pathology

An iMM team led by Bruno Silva-Santos has uncovered "signal strength" as a major developmental determinant of populations of pro-inflammatory lymphocytes implicated in both immune protection (against tumors) and immune pathology (as in cerebral malaria). The research, funded by the European Research Council, was published in Nature Immunology (Muñoz-Ruiz, Ribot et al. 2016).

γδ T lymphocytes are white blood cells with potent pro-inflammatory functions based on the secretion of soluble molecules (alike hormones) called cytokines, such as interferon-γ (IFN-γ) and interleukin-17 (IL-17). These cytokines can be highly protective against intracellular bacteria, viruses and tumors (IFN-γ); or extracellular bacteria and fungi (IL-17). However, when deregulated these cytokines can promote the severe pathology associated with diseases like multiple sclerosis, psoriasis, diabetes or Crohn's disease.

The Silva-Santos team had previously characterized two distinct subsets of γδ T cells producing either IFN-γ or IL-17 (Ribot, DeBarros et al. Nature Immunology 2009). "Now we dissected the molecular requirements of the development of these subsets in the thymus, namely the role of the T cell receptor (TCR) complex that characterizes γδ T cells", says Silva-Santos. They generated a mouse model with reduced expression of that signature TCRγδ complex, by genetically interfering with associated CD3 molecules required for the assembly and surface expression of TCRγδ. "The result was a clear-cut loss of the population of γδ thymocytes that normally expresses the very highest levels of IFN-γ, which

was absent in the thymus and in the peripheral lymphoid organs of the mutant mice", said Silva-Santos.

Through a detailed characterization of the mutant mice it became apparent that the low expression of TCRγδ meant reduced intracellular signaling events (such as protein phosphorylation or calcium release) and various changes at the gene expression level, including failure to upregulate the transcription factors required for the IFN-γ expression program, whereas the molecular determinants of IL-17 production were unaltered.

It was then important to analyze the physiological implications of these developmental phenotypes. "We assessed the impact on cancer and infection, especially infection-driven pathology", said Silva-Santos. "The cerebral malaria phenotype of the mutant mice was particularly striking: this is an inflammatory syndrome, dependent on IFN-γ, that affects the brain as a result of the potent immune response to Plasmodium infection. Whereas the control mice succumbed to pathology, the mutant mice were essentially devoid of cerebral malaria".

Silva-Santos believes this new mouse model will be highly valuable to test the role of IFN-γ-producing γδ T cells in many other diseases. They already observed their importance for protection against tumor development, which is the basis of follow-up investigations aimed at developing an innovative immunotherapy for cancer.

The work was the result of a very fruitful collaboration with the Complutense University in Madrid, through a Spanish PhD student, Miguel Muñoz-Ruiz, supervised at iMM by Bruno Silva-Santos and his group's senior staff scientist, Julie Ribot.

Muñoz-Ruiz M, Ribot JC, Grosso AR, Gonçalves-Sousa N, Pamplona A, Pennington DJ, Regueiro JR, Fernández-Malavé E, Silva-Santos B. TCR signal strength controls thymic differentiation of discrete proinflammatory γδ T cell subsets. Nat Immunol. 2016 Jun;17(6):721-7.

Potential of Atomic force microscopy to identify patients with higher risk of cardiovascular disease

Researchers led by Nuno C. Santos, from iMM Lisboa have published their work in the prestigious journal *Nature Nanotechnology*, focusing on the link between nanotechnology (technology that manipulates particles that are a million times smaller than a millimeter) and the identification of cardiovascular problems.

Currently, cardiovascular diseases are the leading cause of mortality worldwide, accounting for about one third of all deaths. The biomarkers for assessing

cardiovascular risk still have a limited applicability. High levels of fibrinogen, a protein essential for the blood clotting process, have been identified as a potential risk factor for these diseases.

This study, published in collaboration with clinicians from the Department of Cardiology at Hospital Pulido Valente (Centro Hospitalar Lisboa Norte), evaluated the interaction between fibrinogen and red blood cells from patients with chronic heart failure, understanding how fibrinogen influences the aggregation of these cells.

"Using atomic force microscopy (AFM), a nanotechnology technique, we were able to use a single fibrinogen molecule as "bait" to "fish" its receptor on the surface of red blood cells", said Nuno C. Santos. "We found out that the force required to break the binding between fibrinogen (the "bait") and red blood cell (the "fish") is higher in patients with chronic heart failure than in healthy donors". Red blood cells from these patients also showed changes in their elasticity and behavior while in the blood stream.

"Subsequently, during a one-year clinical follow-up, we saw that patients where a higher force was initially required to release the "bait" (fibrinogen) from the red blood cells were more likely to be hospitalized due to cardiovascular complications in the following 12 months", Santos added.

This study demonstrates the potential of atomic force microscopy in identifying patients with higher risk of cardiovascular diseases, proving to be an important advance in the field of Nanomedicine for medical prognosis, with applicability in Cardiology.

Guedes AF, Carvalho FA, Malho I, Lousada N, Sargento L, Santos NC. Atomic force microscopy as a tool to evaluate the risk of cardiovascular diseases in patients. *Nat Nanotechnol*. 2016 Aug;11(8):687-92.

The parasite of sleeping sickness is hidden in fat

Luísa Figueiredo and her team at iMM Lisboa have published their work on sleeping sickness in the prestigious journal *Cell Host & Microbe*.

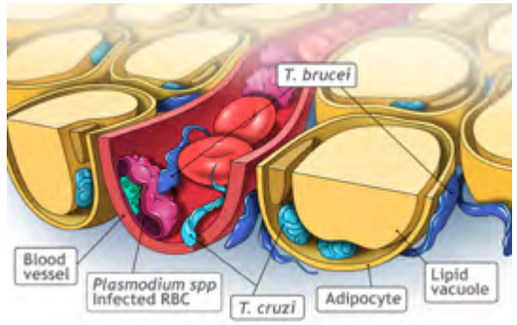
The study, which led to the discovery of fat as a reservoir for parasites, may open new treatment avenues for this disease, which infects the host through the bite of the Tsetse fly and puts at risk more than 60 million people in Africa. Without treatment, the disease is typically fatal. In addition to humans, other animals such as cows and horses can also get this disease, having a devastating economic impact and contributing to poverty in many African countries.

Sleeping sickness is caused by a parasite (*Trypanosoma brucei*), which was thought to live in the blood of infected mammalian hosts. However, the treatment of patients frequently appeared effective in an initial stage but it was subsequently found that even after all the parasites in the blood were eliminated the disease persisted. Given these observations, doctors and

scientists have been questioning "Where could the parasites that have not been eliminated by the drug be?"

In the work published by Luísa Figueiredo and her team, the researchers unraveled that the parasites are found in large quantities in adipose tissue (more commonly known as fat). "*This work initially met a lot of skepticism because the dogma in the field was that trypanosomes lived in the blood or in the brain*", said Luísa Figueiredo.

In this fat, the parasites undergo a major transformation. Although the morphology is unaltered, the genetic program of the parasites that live in the blood and in the fat is quite different. As an example, blood parasites only use sugar as an energy source, whereas parasites in the adipose tissue use lipids as well. "*This was a very exciting discovery, because for years, the field believed that trypanosomes were not capable of using lipids as an energy source. We broke this dogma*", Luísa FIgueiredo added.



The discovery of fat as a parasite reservoir may open new treatment avenues for sleeping sickness. This study suggests that a suitable drug will be able to penetrate the adipose tissue and be active in targeting parasites residing either in the blood or fat. Further studies are now needed to explore novel and effective therapeutic approaches.

Trindade S, Rijo-Ferreira F, Carvalho T, Pinto-Neves D, Guegan F, Aresta-Branco F, Bento F, Young SA, Pinto A, Van Den Abbeele J, Ribeiro RM, Dias S, Smith TK, Figueiredo LM. Trypanosoma brucei Parasites Occupy and Functionally Adapt to the Adipose Tissue in Mice. Cell Host Microbe. 2016 Jun 8;19(6):837-48.

Nervous cells in the gut are the 'eyes and ears' of the immune system

The sheer size of the network of nervous cells that reside in the vertebrate gut has earned it the nickname of the "eyes and ears" of the immune system. And judging by the research led by Henrique Veiga-Fernandes at iMM Lisboa, it appears that it is actually a well-deserved one. The results were published in *Nature* magazine.

"Our study reveals that the nervous system acts as the 'eyes and ears' of the immune system", said Veiga-Fernandes. Nervous cells receive alerts from the gut and then give specific instructions to the immune system to repair the damage."

It is already known that there is a relationship, a dialog, between neurons in the gut and the immune system. In particular, a study published very recently by a team at Rockefeller University (USA) showed that certain neurons can induce a type of immune cells (macrophages) to produce substances that protect the gut.

But Veiga-Fernandes' team went further: "What is totally new in our work", he said, "is that not only did we discover the phenomenon, but we also described the molecular mechanisms at play".

It all started when he and his colleagues identified the presence of a receptor protein, called Ret, on the surface of a type of immune cells called innate lymphocytes (lymphocytes are white blood cells), which are among the most important regulators of inflammation and infection at mucous membranes. Ret acts, in fact, as a switch which can be turned on or off by the signals it receives.

Lymphocytes parading as neurons

Scientists also knew that the same Ret protein is present on the surface of nervous cells in the gut, where it regulates the function of these cells by picking up, as if it were an antenna, chemical signals (called neurotrophic factors) coming from outside the cells. "Suddenly, we were seeing a type of lymphocytes parading as neurons", said Veiga-Fernandes. "This was a big surprise. What was the Ret protein doing on those lymphocytes?"

To try to elucidate this enigma, the team started by locating the innate lymphocytes that expressed the Ret receptor in the gut of laboratory mice, which had been genetically modified so that their cells glowed green when carrying Ret on their surface. And they discovered that, immediately beneath the intestinal mucosa, there are, in fact, thousands of cellular clusters, each containing 100 to 200 innate lymphocytes expressing Ret.

The next step consisted in determining what could be the function of the protein in those lymphocytes. "We then showed that the Ret

protein controls the production, by the innate lymphocytes in the gut, of interleukin-22 (IL-22), a molecule that is extraordinarily important for the repair of the gut epithelium [or wall]", said Veiga-Fernandes.

In fact, they confirmed that transgenic mice which did not express Ret on their innate lymphocytes had an altered intestinal epithelium that was less able to regenerate and to express the genes that promote repair.

These results led to another idea: proving that those animals, given their altered epithelium, were prone to various inflammatory pathologies and infections of the gut. "We tested this idea in mice infected with gut bacteria or in which we had induced a chronic bowel inflammation", said Veiga-Fernandes. "And what we saw was that the animals that did not express Ret were highly susceptible to both things and died very quickly."

On the other hand, transgenic mice in which the expression of Ret had been boosted to higher-than-normal levels proved to be "totally resistant" to these pathologies.

The next step was to figure out how Ret is activated in the innate lymphocytes. In other words, to identify the cells that send the necessary neuroregulatory signals to the Ret proteins on the innate lymphocytes, thus inducing these immune cells to produce the key molecule of intestinal repair IL-22. To answer this question, the team used high-resolution microscopy to search for cells in the vicinity of the innate lymphocytes that could be responsible for turning on the Ret switch.

Multi-cellular troika

"We then discovered that all the cluster of innate lymphocytes were very close to glial cells, a type of nervous system cell", explained Veiga-Fernandes. "In fact, these are the cells that make the neurotrophic factors that activate the Ret protein on the innate lymphocytes." Glial cells are not neurons, but they are a crucial component of the nervous system.

Next question: how do glial cells detect intestinal threats in order to activate Ret in the innate lymphocytes at the right time?

"Actually, what enables the glial cells to make these Ret activators is the fact that they are able to detect signals of bacterial presence and of damage to intestinal tissue", said Veiga-Fernandes. "These signals are either produced by bacteria or substances called alarmins, which are signals that are emitted by any cell when it is in trouble."

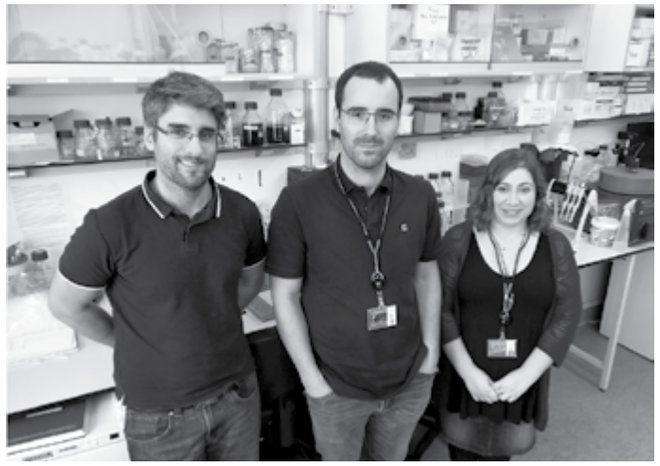
"To summarize, we identified a multi-cellular 'troika' [innate lymphocytes, glial cells, gut epithelial cells], orchestrated by neurotrophic factors, that protects the intestine", the researcher added. "And we found that changes in this cellular and molecular axis lead to intestinal inflammatory disease and to the incapacity of eliminating intestinal infections."

A future application of these results may be the development of new preventive and therapeutic strategies against chronic bowel inflammations - such as Crohn disease and ulcerative colitis - and even against intestinal cancer, according to Veiga-Fernandes.

The team is now exploring ways of activating the innate lymphocytes directly, without the help of glial cells. "We want to manage to do the glial cells' job in their place", Veiga-Fernandes concluded.

Ibiza S, García-Cassani B, Ribeiro H, Carvalho T, Almeida L, Marques R, Misic AM, Bartow-McKenney C, Larson DM, Pavan WJ, Eberl G, Grice EA, Veiga-Fernandes H. Glial-cell-derived neuroregulators control type 3 innate lymphoid cells and gut defence. *Nature*. 2016 Jul 21;535(7612):440-3

New class of antibody-drug bio-conjugates



A group of researchers led by Gonçalo Bernardes have developed a new site-selective method for the construction of complex protein/antibody conjugates.

The scientists have designed a new class of carbonylacrylic cysteine-selective reagents that may vastly improve the effectiveness of targeted drug delivery while cutting problems of low efficacy and side-toxicity associated with current methods.

The team, located in Cambridge and Portugal, use very small amounts of carbonylacrylic derivatives bearing a drug or fluorophore that react irreversibly with cysteine residues to produce chemically defined protein and antibody conjugates.

Current methods of antibody-drug bioconjugation are based on maleimide chemistry. But the resulting conjugates often undergo thiol-exchange reactions while in circulation, which leads to the premature release of the drug. Gonçalo said: "If this happens, the drug is released prematurely which not only limits the efficacy of the treatment but also leads to side-toxicity".

Therapeutic protein/antibody-drug conjugates built using carbonylacrylic derivatives that selectively modify cysteine residues are highly stable in plasma. "By making antibody-drug conjugates more stable in the circulation we know the drug is only going to be delivered in the site of disease," said Gonçalo Bernardes. The work, published in *Nature Communications*, raises important questions and possibilities regarding the delivery of cytotoxic drugs, particularly during cancer treatments or therapy.

Barbara Bernardim, Pedro M.S.D. Cal, Maria J. Matos, Bruno L. Oliveira, Nuria Martínez-Sáez, Inês S. Albuquerque, Elizabeth Perkins, Francisco Corzana, Antonio C.B. Burtoloso, Gonzalo Jiménez-Osés & Gonçalo J. L. Bernardes. Stoichiometric and irreversible cysteine-selective protein modification using carbonylacrylic reagents. *Nature Communications*. 2016 Oct 26;7:13128

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Joaquim Polido Pereira


Sérgio Dias


Leonor Saúde


Tânia Carvalho


Pedro Eleutério

The Histology and Comparative Pathology Laboratory

Bent over a computer screen, scrolling over a scanned glass slide of a mouse lung, Drs. Cláudia Faria and Tânia Carvalho stare intently at a small group of cells. It's a lung metastasis, derived from a tumor that was surgically removed from the brain of a lung cancer patient, and immediately implanted in the back of a mouse, weeks earlier. Claudia, a neurosurgeon at Hospital de Santa Maria and researcher at the iMM, has a question: what drives tumor cells from the lung, breast, colon, skin, to invade the central nervous system, the core of our self, our sense, our commander? And how can we stop them? As they inspect the tissue sample, Tânia, veterinary pathologist and head of Histology and Comparative Pathology Laboratory at the iMM, directs Cláudia's gaze to the tumor cells that appear completed adapted to that lung microenvironment, highly proliferative, suggesting that they probably know where they came from in the patient, what their place of origin is; it is the true meaning of tumor *homing*, and this case in particular was a home run! "We need to understand what drives these cells to disseminate, to invade the brain, so that we know how to block that process," Cláudia said. "That requires us to examine how the patients' tumor behaves *in vivo*, in a model organism that we can manipulate, challenge. Having a facility that is able to help me design and interpret these experiments, take the most out of the animal model, has been a major asset to these studies. I could not do this easily without their support."

In this quest, to be partners in your research, 2016 was an amazing year for the Lab, culminating with the engagement in medical diagnosis (Primary Ciliary Dyskinesia) and the publication of much of the research work that we were engaged in over the past few years. Cancer, sleeping sickness, inflammatory bowel disease, malaria, aging, are just a few examples, and from these we would like to focus on one in particular, the *special one*; because it utterly illustrates the power of collaboration, multidisciplinarity and trust in science; because it proves the power of anatomic pathology and of these *old* methodologies, often portrait as outdated, in making unexpected, exciting and novel discoveries. The paper: Trypanosoma brucei Parasites Occupy and Functionally Adapt to the Adipose Tissue in Mice (Trindade et al., Cell Host & Microbe, Volume 19, Issue 6, 2016); and the praises and titles of the highlight and preview articles unravel its content: African trypanosomes find a fat haven (Cell Host and Microbe); trypanosomes chew the fat (Nature Reviews Microbiology); unexpectedly the sleeping sickness parasite lives in fat (Público). Histological analysis, immunohistochemistry and transmission electron microscopy were crucial in this work and, truthfully, we weren't even looking for the adipose tissue, we were focused on the brain. Serendipity! Were we lucky? Maybe. Or maybe we carefully planned the experiments in order to minimize missing [unexpected] phenotypes. Maybe we simply love what we do and curiosity always gets the best of us, even when were told to look some other way.

As Plato said, *science is nothing but perception*.

Who we are. What we do

Currently we have one veterinary pathologist with expertise is pathology analysis and in animal models of disease; and three biomedical scientists specialists in various histological techniques, immunohistochemistry and transmission electron microscopy; and in the era of precision medicine, we aim at providing precision histology and experimental pathology, with customization of cell, tissue, organ, and organism analysis, tailored to the individual researcher, to the scientific question.

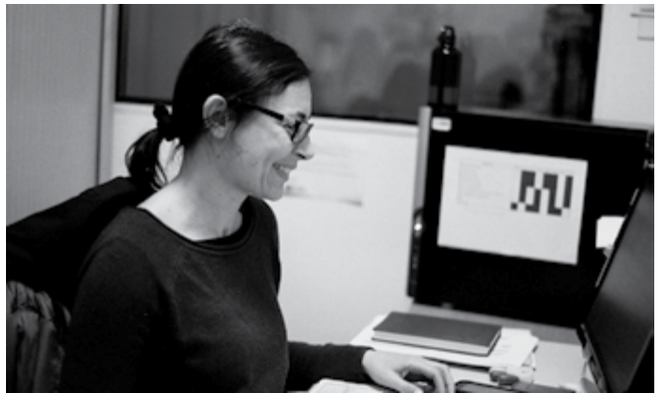
Publications

BOOKS *Manual de Necrópsia Veterinária*. M Peleteiro, (...), T Carvalho, *et al.*. Lisboa: LIDEL. **PAPERS 1.** *Activation of necroptosis in human and experimental cholestasis*. MB Afonso *et al.*, Cell Death and Disease. **2.** *MiR-146b negatively regulates migration and delays progression of T-cell acute lymphoblastic leukemia*. NC Correia *et al.*, Scientific Reports. **3.** *Glial cell-derived neuroregulators control type 3 innate lymphoid cells and gut defense*. Ibiza *et al.*, Nature. **4.** *Trypanosoma brucei parasites functionally adapt to host adipose tissue*. Trindade *et al.*, Cell Host & Microbe. **5.** *MEK5/ERK5 signaling inhibition increases colon cancer cell sensitivity to 5-fluorouracil through a p53-dependent mechanism*. DM Pereira *et al.*, Oncotarget. **6.** *Short Telomeres in Key Tissues Initiate Local and Systemic Aging in Zebrafish*. M Carneiro *et al.*, PLoS Genetics.

Animal Facility

"The best laid schemes o' Mice an' Men,
Gang aft agley.
An' lea'e us nought but grief an' pain,
For promis'd joy!
(*To A Mouse*)" *Robert Burns*

The iMM's Rodent Facility is a dynamic facility which is constantly striving to improve the quality of the services provided. For this reason, we are always changing and expanding. This year was no exception, with major achievements including the employment of an Animal Welfare Officer, facilitating iMM's membership into the European Animal Research Association (EARA) and merging the rodent facility with the Biosafety Level 3 (BSL-3) Laboratory.



Animal Welfare Officer

While the use of animals as a way to get scientific knowledge goes back to ancient Greece, ethical and animal welfare concerns are relatively recent and have been gaining importance as of lately, becoming integrated in the current legislation and recommendations.

In 2010, the EU Directive 2010/63 was passed. This regulation harmonizes European animal laboratory standards, and requires the implementation of several new requirements aiming to ensure the welfare of animals used in research.

Some countries, such as the UK, have a long tradition of professionals dedicated to ensuring animal welfare – Animal Welfare Officers. In Portugal, these positions were so far inexistent. To be able to fully implement the legal requirements brought up by the directive, the rodent facility decided to hire a dedicated person – an Animal Welfare Officer. This is the first position of its sort in Portugal and we believe other institutions will soon follow our lead.

The rodent facility facilitates iMM's membership to EARA

Animal research is a 'hot topic' and being transparent about animal use is not always easy. While being transparent is important to counteract the effects of fallacious campaigns, speaking up is often perceived as risky by potentially damaging the institution's image and increasing its vulnerability.

EARA – the European Animal Research Association – is an organization that communicates and advocates animal research by providing accurate and evidence-based information. EARA works with research institutions to better inform and educate audiences on matters related with the responsible use of animals in biomedical research. It supports researchers and trains them to be able to communicate efficiently.

In September 2016, the rodent facility, supported by the iMM communications office, promoted a seminar by EARA's executive director – Kirk Leech. Kirk spoke to researchers about EARA's activities and how it supports institutions in matters related to animal research.

Following the seminar, Kirk met with iMM's Directors to deliver a membership invitation. This invitation was later accepted and the iMM, as a member of EARA, will now be able to adopt a more proactive and transparent approach to animal use.

Merging of Rodent facility with BSL-3 Lab

As a strategy to optimize the use and management of the Biosafety level 3 laboratory, this facility was merged with the rodent facility, allowing for an optimal use of human resources, as well as the standardization of logistics, administrative procedures and general organization and routines. We hope in time these changes will result in an increased quality of the services provided to our researchers.

Zebrafish Facility

We work every day with a small fish with stripes giving them all the care and attention they deserve because they are AWESOME biomedical animal models!

In 2016 we were very happy to be able to contribute to the successful ending of the project of two of our PhD students studying fundamental aspects of embryonic development; one will tell us how asymmetric positioning of the internal organs is achieved and the other will reveal the complex world of Fgf8 function.

An important characteristic of the zebrafish is its capacity to regenerate all its organs. So several researchers try hard to understand how is the zebrafish able to regenerate a spinal cord, either dissecting the molecular and cellular mechanisms

or identifying drugs that could improve motor function recovery.

Our zebrafish colonies met their new fish friends that arrived this year to help us in the study of vascular morphogenesis. These special fish are very colourful, with green blood vessels and red Golgi apparatus inside their cells.

A major challenge in our facility was the implementation of a new set of technical procedures that allowed a group of researchers to start two projects that are extremely relevant for human prevalent diseases, like diabetes and myocardium infarction.

Our zebrafish are very sociable and like to be the centre of attention! So we have used them to create awareness of the importance of science and this year was particularly busy: we hosted several visits from secondary schools, political decision makers, pharmaceutical companies, medical students and international invited speakers.

As part of our training mission, we hosted an ERASMUS-supported researcher and a rodent facility manager that wanted to start a zebrafish facility in Trieste-Italy and in Rio Grande do Sul-Brazil, respectively.

Who we are. What we do.

We are the "*fish*" people: one zebrafish developmental biologist, one marine biologist and one technician with aquariophilia expertise. We aim at providing all the training necessary to start working with this wonderful animal model and to help researchers in their daily experiments.

The Bioimaging Facility

Ah, a spot! Do you see it?" It's a tiny spot, just a few pixels on the computer screen. We can measure its width, not more than 350 nm. That's what a single mRNA molecule tagged with about 40 GFP molecules looks like when imaged in our spinning disk confocal microscope: a 350 nm spot. In reality it is much smaller than that, smaller than the optical resolution of the microscope. But the goal is not to measure the size of mRNA molecules. The goal is to image single mRNAs being created in living cells and to find out how long they take to be processed at the transcription site. They need to be imaged as fast as possible, as gentle as possible, while keeping cells alive and making them express fluorescent proteins that will bind to the nascent mRNAs. A spinning disk confocal microscope is the tool for the job.

No matter how many spots they have seen already, Prof. Carmo-Fonseca and Dr. José Rino are not able to look away from the computer screen. Single mRNA molecules imaged inside living cells! A feat only possible with the combination of genetic engineering, fluorescent protein tagging and high speed confocal microscopy. By imaging single mRNA molecules, we can measure in real time the dynamics of mRNA biogenesis. Understanding what happens in those particular cells being imaged, where the gene sequence encoding for the target mRNA was mutated, could provide clues into how aberrant mRNA processing can lead to disease. But imaging hundreds of cells and thousands of mRNAs is not enough. Additional tools are required to extract quantitative parameters and to make sense of all the imaging data.

Besides managing and providing training in iMM's microscopy systems, the Bioimaging Facility also develops image processing and analysis software in collaboration with research labs with challenging questions. The year of 2016 saw the publication of a research article on the software we developed to automatically track and quantify single mRNAs in living cells (Rino et al, Methods, volume 98, 2016). This and other software tools are now freely available to the scientific community through the Bioimaging Wiki Page (https://imm.medicina.ulisboa.pt/facility/bioimaging/doku.php), our comprehensive reference site for everything related with the Facility. Besides software tools, you can also find information on the courses we organize, such as the ReTuBi Microscopy Workshop (October 2016) and on the microscopy systems that are currently available. In this regard, 2016 was an exceptional year for the Facility, as the iMM acquired three new microscopy systems: a lightsheet microscope, a confocal microscope and a widefield microscope. These and other systems were used in 2016 by 150 users from 34 research labs. We also have users from outside the iMM and provide in depth knowledge and support to the scientific community on a national and international level: the Bioimaging Facility is one of the nodes of the Portuguese Platform for Bioimaging and a Zeiss labs@location Partner.

Who we are. What we do.

The Bioimaging team includes a Physics engineer that shifted from solid state Physics to Biology and got a PhD in Biophysics spending hundreds of hours on a confocal microscope, a Master in Evolutionary and Developmental Biology that switched from Medicine to live zebrafish and mouse imaging and a Master in Biochemistry that started in Flow Cytometry before becoming a microscopist. We provide support in everything related with optical microscopy, from project planning to microscope training and support, software development and data analysis for iMM scientists and visitors.

2016 Publications

STaQTool: Spot tracking and quantification tool for monitoring splicing of single pre-mRNA molecules in living cells, Rino J, de Jesus AC, Carmo-Fonseca M. Methods 98:143-9, 2016 (PMID: 26855377); Single-Molecule Live-Cell Visualization of Pre-mRNA Splicing, Martin RM, Rino J, de Jesus AC, Carmo-Fonseca M. Methods Mol Biol 1358:335-50, 2016 (PMID: 26463395).

The Flow Cytometry Facility

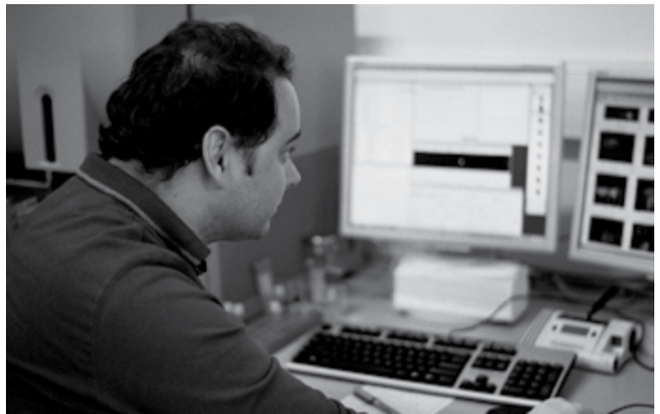
In 2016 approximately 80 billion cells were analyzed in our flow cytometers. Thirty billion of them in the BD FACSAria III and FACSAria IIu, the two cell sorters operated by the Flow Cytometry staff. Analyzed one by one and sorted by electrostatic deflection at an average rate of 5,000 per second, cells that corresponded to populations of interest were collected for further studies. Mostly lymphocytes but also other cell types such as neurons or stem cells, tagged with specific fluorescently labeled antibodies or expressing fluorescent proteins. Some of these samples could contain infectious agents that might pose a threat for operators. To provide protection from harmful agents and avoid contaminations, a Class II biological safety cabinet was installed in 2016 to house the FACSAria III cell sorter.

A total of 148 users from 34 research labs, 5 of them from outside the iMM, used the Flow Cytometry Facility in 2016. The total usage of our 10-color BD LSR Fortessa analyzers alone exceeded 3200 hours. To overcome problems in the analyzers availability and the need for 16-color analysis, the iMM decided to acquire a new BD LSR Fortessa X-20 which will be installed in 2017, significantly upgrading the Flow Cytometry services.

In addition, funding from the EXCELLtoINNOV project from the European Union's Horizon 2020 research and innovation programme allowed the acquisition of a state of the art imaging equipment that suits the scientific needs of iMM's ERA chair holder and potentiates the research of several labs at iMM. Negotiations for the acquisition of a new generation ImageStream Mark II imaging flow cytometer, which combines the high throughput of flow cytometry with optical microscopy imaging, were concluded in 2016. The first 12-color imaging flow cytometer equipped with 20x, 40x and 60x objectives to be made available to the national scientific community will thus be installed in early 2017.

Who we are. What we do.

The Flow Cytometry team includes three technicians and a new Head of Facility that started in October. Besides providing training in flow cytometry and support to all users, from experiment planning to equipment operation and data analysis, our staff ensures regular maintenance and quality control on all systems. We also provide a cell sorting service using two high-speed cell sorters, which are operated by dedicated staff.



Career Development

The Career Development facility consists of a set of integrated Programs, offered under the Career Development hub, aim at providing the best training for success in science to researchers, at different stages in their careers.

Lisbon Biomed

The Lisbon Biomedical and Clinical Research PhD Program (LisbonBioMed) provides privileged education and training to generate PhDs in areas encompassing the full spectrum of biomedicine, based on the principle that science informs and shapes medicine while human diseases provide critical clues for basic biological research.

The LisbonBioMed PhD Program encourages young basic and clinical researchers to work together, and to apply and produce new knowledge in the interplay between laboratory and clinical practice, acquiring a unique skill-set to succeed in international careers within the broad scope of Biomedicine.

Ana Filipa Cardoso

My name is Ana Filipa Cardoso and my interest in Science has accompanied me for as long as I can recall, driving me to graduate in biochemistry at the University of Minho. During the course of my undergraduate studies I became particularly interested on the complexity of the biological pathways that enable homeostasis in humans, specifically the metabolic, physiological and immunological pathways. In line with my interests, I chose to perform my Master's in Health Sciences at ICVS in immunology. After this stimulating experience, I became absolutely certain that pursuing a career in science would be the best decision to make. Accordingly, I enrolled the LisbonBioMed PhD program since my main research interest lies on immunology, and IMM is be the perfect place for me to pursue this topic during my PhD.

Andreia Pereira

My name is Andreia Pereira and I come from Ponte de Lima. It was during my graduation in Biology that I had the opportunity to do an internship in cancer epigenetics at IPO Porto. There I realized how important basic research is for medicine and decided to come to Lisbon and pursue an MSc in Molecular Biology and Genetics. During that time I had the opportunity to work with embryonic stem cells and was exposed to the intriguing world of Developmental Biology and Regenerative Medicine at the iMM. Realizing the importance of multidisciplinarity, crucial for biomedical sciences, when the time came to decide my next step I realized that iMM was where I wanted to do my PhD. The vibrant scientific atmosphere, the incessant search for answers (and questions!), the top-notch research areas and the cutting-edge resources made me choose this institute. I am currently deciphering the distinctive features of mitochondria that localize on neuronal synapses surrounded by creative and enthusiastic people and working in one of the best research institutes.

Daniel Martins

My name is Daniel Martins and I am a medical doctor from "Faculdade de Medicina da Universidade do Porto" (MD, MsC). Parallel to medical school, I began my research career as a trainee at the Department of Experimental Biology (FMUP)/ IBMC – Isaura Tavares's lab (2010 – 2015). Inspired by the motto "The doctor that only knows medicine, does not even know medicine…" I am now complementing my clinical skills with an experience on basic and translational research as a LisbonBioMed16 PhD student at Diana Prata's Lab and at the Neuropharmacology lab (Centre for Neuroimaging studies, Institute of Psychiatry, Kings College London). My research focuses on the neurobiological basis underpinning human social behavior and its dysfunction during mental illness (schizophrenia).

Julia Skalska

My name is Julia Skalska, from Poland and I graduated in Biotechnology at the Warsaw University of Technology. During my Bachelor I was working in the International Institute of Molecular and Cell Biology, with one of the leading groups studying mitochondrial biogenesis. Thanks to the invaluable experience gained under the supervision of world-class researchers I had an opportunity to pursue my scientific adventure in a research program for Master students at The University of Chicago, during which I realized that science is not only (not at all) Nobel Prizes and spectacular discoveries, but a painstaking work full of frustrations. However, the beauty and significance, of even small achievements gives you a priceless satisfaction, which compensate all the hardships. Looking for a PhD I was focused on applicable aspects of research, which directly contribute to the issue of human health. That is why the very close collaboration between the iMM and Hospital Santa Maria together with the international environment of LisbonBioMed PhD program seemed like the perfect scenario to continue my studies."

Maria Helena Brigas

My name is Maria Helena Brigas and I am a graduate in Cellular and Molecular Biology at the University of Porto, Portugal. Previously I devoted my research to basic molecular biology and tumor immunology. Driven by my fascination with how immune cells can interact to promote or counteract different diseases I decided to continue my studies and pursue a PhD. The outstanding scientific quality of iMM, promoting synergies from relevant and complementary areas of science and linking basic science to clinical research drove me to join the LisbonBioMed program. The diverse background of all of my colleagues has kept this experience both challenging and enthusiastic. Personally, this experience is a unique opportunity to improve personal knowledge and skills and to expand my research horizons.

Mariana Oliveira

My name is Mariana Oliveira and I am 24 years old. I became fascinated with biology and developed a great interest in science during high school. I graduated in Cell and Molecular Biology at Universidade Nova de Lisboa. After that, and to explore a more translational research with clinical implications for patients, I got my Master's degree in Oncobiology at Universidade de Lisboa. As I wanted to continue to specialize in Cancer research and to proceed further in my studies, I found that the LisbonBioMed PhD program was perfect for my research interests and future goals. First of all, iMM is a leading national biomedical institute which provides an excellent scientific environment with great people. Secondly, this program gives the possibility of learning from excellent internal and international teachers, and thinking on a wide range of scientific topics. I am so glad I was selected to be part of this amazing group of people.

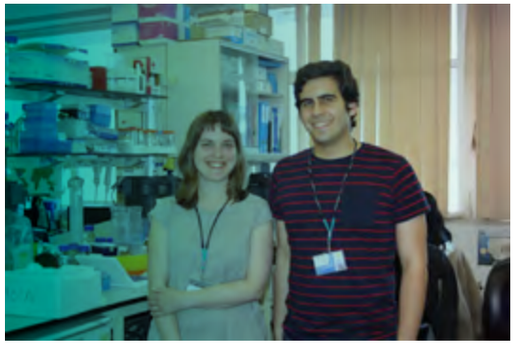
Sofia Mensurado Santos

My name is Sofia Mensurado Santos and ever since I can remember I am curious about human biology. In general, answers tend to lead me to more and more questions, which made me realize that research was what would fulfill me. To pursue my interest in biomedicine I studied Health Sciences at Universidade de Lisboa and soon developed an interest in immunology. I then pursued a MSc in Biochemistry, and developed my thesis at iMM in tumour immunology. This experience at iMM made me feel very privileged not only due to the outstanding scientific community but also due to the truly collaborative environment. As such, the LisbonBioMed program was a natural choice for me as it combines a great scientific environment with a multidisciplinary program, which I believe is the best recipe to do top quality biomedical research.

PhD Students' Activities

PhD Students at iMM Lisboa are challenged to actively suggest activities to foster both scientific and social networking among the research community. These activities are organized by the PhD Students' Committee.

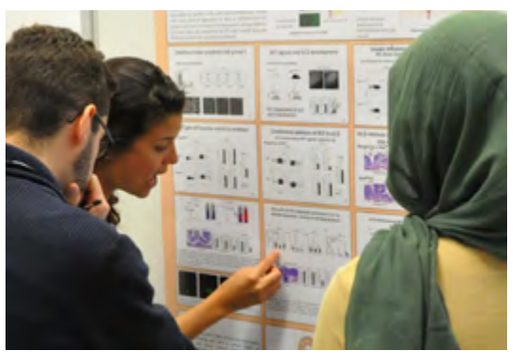
PhD Students' Committee



PhD Students' Representatives for 2016
Sílvia Arroz Madeira (HVeiga-Fernandes Lab) and João Mello Vieira (MMota Lab) are the elected PhD students' representatives

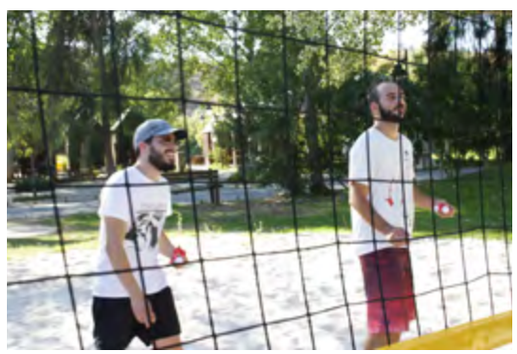
PhD Students Annual Meeting X iMM CAML PhD meeting

The PhD Students' annual meeting is the place by excellence where students present and discuss their work with the overall iMM community during two and a half days. Oral presentations are given by students from the 1st and 4th year, while students from the 2nd and 3rd year present a scientific poster. Moreover, students have the opportunity to gain further insight and inspiration for their PhD work from four excellent keynote speakers.



PhD Students Annual Retreat

During this two-day retreat, PhD students engage in scientific and group activities fostering team spirit and social interaction.



PhD Students Workshops

For the first year, the 2016 PhD Students' Committee organized a Workshop series to fulfill their need to have more training aimed at improving their soft skills.

Workshop
Communication:
How to present in a scientific congress
by Dr. Malcolm Love

Workshop
Graphic Design in Science
by Dr. Gil Costa

Workshop
Exploring Different Career Paths

Post-Doctoral Activities

iMM Post-Doctoral Association (PDA)

The iMM Post-Doctoral Training Program format and content are defined together by the overall Post-Doctoral community, the iMM Post-Doctoral Association (PDA) and the iMM Career Development team.

The PDA aims to build a community among the Institute's Post-Doctoral fellows and its mission includes:

- Developing activities centered around communication and networking;
- Organizing a series of professional enrichment activities and career development events.

PDA Executive Committee for 2016

Marta Marques (NSantos Lab), Eleonora Aquilini (LFigueiredo Lab), Patrícia Costa (EGomes Lab), Sales Ibiza (HVeiga-Fernandes Lab), Isaura Martins (LSaúde Lab), Lina Páez (NMorais Lab), Vanessa Luis (MMota Lab)

Workshop
Science Communication
"Mastering the art of presentation"
by Dr. Adria LeBoeuf

Course
Leadership and Management skills for Postdocs

Annual Retreat (Cross-Institutional Meeting of Young Researchers)

The Third Joint Meeting of Young Researchers aims to bring together postdoctoral fellows of four leading biosciences research institutes in Portugal: Instituto Gulbenkian de Ciência (IGC), Instituto de Medicina Molecular (iMM), Instituto de Tecnologia Química e Biológica António Xavier (ITQB Nova) and Champalimaud Foundation Research (CR).

The main goal of the initiative is to go beyond fostering a common dialogue between these communities of young researchers, and establish a starting point for strategic cooperation between these four hubs of scientific excellence.

Additionally, the initiative aims to draw attention to, and constructively discuss challenges and policy making that influence professional lives of postdoctoral fellows.

Beer hours

Lisbon Academic Medical Center (CAML)

The Lisbon Academic Medical Center 2016

The Lisbon Academic Medical Center (AMC) is a consortium composed of the iMM, the Lisbon University Medical School and the Santa Maria University Hospital. It was created in 2009 with the goal of contributing for an innovative and efficient environment facilitating education, research and patient care. In line with AMCs mission throughout the world, the Lisbon Center sets out to offer patients the latest discoveries in medicine, more opportunities to participate in clinical trials, and extended help for unusual or rare conditions. The consortium shares its members' responsibilities of training the next generation of physicians, expanding health care knowledge, and evaluating novel ideas rigorously from a medical ethics perspective. Accordingly, the Center runs a common Ethics Committee and a common PhD program. An important milestone of the Lisbon AMC was the foundation of a biobanking operation that started in 2012. In this regard, the Center is currently participating in research initiatives aiming at the development of database resources for collecting, tracking, and annotating thousands of specimens. In parallel, the Center is studying international management models for the long-term sustainability of large academic biorepositories. An additional milestone of the Lisbon AMC was the creation in 2016 of a clinical trials' unit composed of centralized shared resources to assist in the design and coordination of clinical trials in campus. Indeed, it is well demonstrated that clinical researchers who have access to a supporting research infrastructure are able to increase their knowledge development, improve healthcare delivery and more easily integrate these elements into clinical practice. The Lisbon AMC is also well aware that clinical research should innovate beyond clinical trials. To explore new research areas and technologies, as well as to foster innovative career paths, it is critical to work in multidisciplinary teams composed of faculty and students educated in different areas of knowledge ranging from medicine, biomedical sciences and engineering. Moreover, it is necessary to develop and implement innovative training concepts in the fields of academic nursing and health technicians. Today, human knowledge allegedly doubles every 12 months, so it is no longer possible for a scientist to be an expert in all aspects of research. Recognizing the value of collaboration, the Lisbon AMC thought to establish strategic partnerships with the vision of creating a hub for interdisciplinary health research in the Lisbon region. Accordingly, in 2016 the Lisbon AMC consortium has expanded to include the Engineering and Pharmacy Schools of the University of Lisbon, the National Cancer Institute Hospital in Lisbon, and the Nursing and Health Technologies Schools of the Lisbon Polytechnic Institute. Multiple collaborative inter-institutional research projects have already been submitted and approved for funding in 2016. Namely, research groups from Instituto de Medicina Molecular and Instituto Superior Técnico are partners in the "Discoveries Centre for Regenerative and Precision Medicine", a project funded by the H2020 Teaming Program, as well as in a collaborative project on Precision Medicine funded by POR2020 and Fundação para a Ciência e Tecnologia.

CENTRO ACADÉMICO DE MEDICINA DE LISBOA

iMM Retreat

The iMM annual scientific retreat took place on the 11-13th of April 2016 at the University of Évora who kindly hosted 175 iMM staff and three members of our Scientific Advisory Board (SAB): Carlos Caldas, Gustave Moonen and Caetano Reis e Sousa. Following up on previous (more restricted) iMM retreats, this was the first time that the whole iMM community got together for a privileged forum of scientific discussion and social interaction. There were talks by 10 group leaders and poster presentations by PhD students or post-doctoral fellows from other 11 research groups. There was also time for direct interactions between SAB members and group leaders, on one hand; and PhD students and post-doctoral fellows, on the other. The overwhelming feeling was one of cohesion: the retreat definitely fostered pride in being an "iMMer"!

Carlos Caldas

Carlos Caldas leads a team in the prestigious Cancer Research UK Cambridge Institute. His work focuses on the identification of gene faults and variations that are important to predict the success or failure of cancer treatments. He currently serves as Professor of Cancer Medicine, Director of the Cambridge Breast Cancer Research Unit, Honorary Consultant in Medical Oncology and chairs iMM's Scientific Advisory Board together with Philippe Sansonetti, MD, PhD (Pasteur Institute), Gustave Moonen, MD, PhD (Université de Liége), Caetano Reis e Sousa (Francis Crick Institute), PhD, and Paul Peter Tak, MD, PhD (University of Amsterdam).

In your opinion, how important is the Scientific Retreat iMM Lisboa for the development of an institutional identity?

The annual retreat should be the highlight event of the IMM. And it already is! The 'tissue' of an Institute is constituted by its scientists. The coming together at the retreat ensures healthy homeostasis! An open forum where students, postdocs, core facilities and PIs come together is therefore essential. The retreat is also the opportunity for the SAC that I chair to interact with IMM and if you want 'take the pulse' of the place.

How can the retreat promote iMM's growth?

Any Institute that is not constantly questioning what it does is destined to commit to apoptosis! Growth is based on tacking stock of what you do: discussing stopping what you either do not do well or is no longer relevant to the mission of the Institute. Then to try to gaze at the future. Are there new technologies emerging, what are the most important unanswered questions in biomedicine, who should we recruit, etc? That is what the retreat is there for. Not that you should not do the above very day of the life of the Institute, but the retreat provides a focus to that constant quizzing!

Is iMM Lisboa a key hub for scientific career development?

IMM is part of a Medical School and University. It should be (and today already is!) an hub of excitement for discovery, and hence curiosity-driven research. But its integration into a Medical School and University gives it added 'responsibilities', a crucial one being training the new generation (students and postdocs). It should also be the place where young scientists seeking the first independent position as group leaders find a nurturing environment to be succesful. That means the most important decision the Director and Board need to make is not about tenure (important as that is), it is about whom to hire as a new GL! The second important responsibility is its focus in biomedicine.

How can a relevant scientific critical mass, like the one that constitutes iMM's Scientific Advisory Board, guarantee and maintain the quality and level of scientific discussion among researchers?

The SAC is there to support the Director with constructive critical advice. It is also there to foster the younger generation. Finally, it is a 'guarantor' of the only thing that matters for the IMM to have a future: doing excellent science!

How do you perceive iMM's technical facilities? How crucial are they to develop a high level of scientific excellence?

In my view advancement in science has two main drivers: 1- asking the right questions; 2- having the means to address those questions. Technology is therefore key and core facilities are there to constantly probe the boundaries (what is the next method or model that is empowering new discoveries?); and to provide precise measurements (e.g. NSG, high-resolution microscopy, proteomics, etc) and reliable models (e.g. GEMMs and other model organisms, primary human tissue explants, etc). So to succeed IMM needs to continue to invest and innovate its core facilities.

How do you envision IMM's future?

The future of IMM is the one its scientists will make! I have no prescient powers (you are glad to hear!!) but the future should be bright if IMM remains engaged in doing excellent curiosity-driven science and if it continues to play a major role within the Clinical School and the University. It can only do that if it keeps its scientific independence.

Fundraising

Fundo iMM-Laço: Towards a Cure

FUNDO iMM - LAÇO
A CAMINHO DA CURA

Since 2000, Associação Laço has promoted breast cancer awareness and supported projects that impact on prevention, early diagnosis and treatment of breast cancer in Portugal. In 2013, Laço began to support scientific research. After awarding 5 grants, Associação Laço and the Instituto de Medicina Molecular (iMM Lisbon) joined efforts to investigate breast cancer on a more permanent basis. In 2015, the **Fundo iMM-Laço: A Caminho da Cura**, was created to support the development of projects that work towards the discovery of the causes underlying breast cancer development and metastasis and have as an ultimate goal the reduction of breast cancer incidence.

With the support of Fundo iMM-Laço: A Caminho da Cura an innovative study is currently being developed for the first time in Portugal that aims to contribute to a more accurate breat cancer treatment. In 2016, 100.000€ were distributed between two breast cancer research projects.

As of 2016, Sandra Lopes, previously Associação Laço's communication officer, is now the communication officer of Fundo iMM-Laço: A Caminho da Cura and she thanks everyone who has contributed to this cause and challenges them to take another step on the road to breast cancer cure.

Lynne Archibald, *founder & president of Laço*

Centro de Investigação de Tumores Cerebrais

CENTRO
DE INVESTIGAÇÃO
DE TUMORES
CEREBRAIS

In 2011, Adelaide Passos published the book "O céu pode esperar"("Heaven can wait"), telling the story of one of her grandchildren who was fighting a brain cancer. She decided at that time that she wanted to help other children with brain tumors by creating awareness and by fundraising for brain tumor research. She spoke to Professor João Lobo Antunes about her dream and a few months later the *Centro de Investigação de Tumores Cerebrais* (CITC) was created.

The main goal of CITC is to understand the molecular mechanisms of brain tumor formation and dissemination, with a special focus in the pediatric population. We aim to identify novel and less toxic therapeutic targets to improve patients' quality of life.

Our team includes health care professionals from Hospital de Santa Maria (CHLN), particularly from the Department of Neurosurgery, and scientists from iMM, in a true collaborative effort to develop translational research projects to study the most common brain tumors.

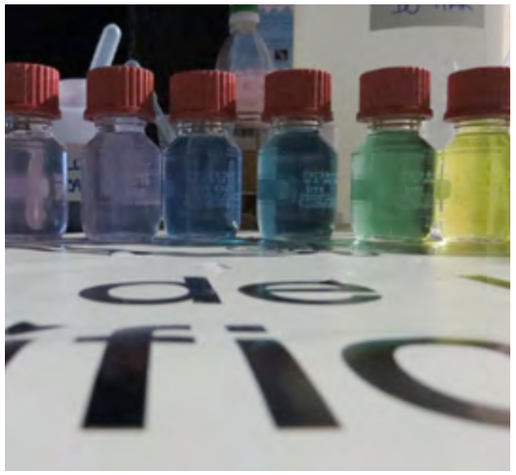
In 2012 we started collecting biological samples (including tumor tissue, blood and cerebrospinal fluid) from patients with brain tumors at Biobanco-iMM. Initially, brain tumor samples were mainly collected from the Department of Neurosurgery at Hospital de Santa Maria. Nowadays we receive biological samples from patients treated in several public and private hospitals at the Lisbon area but also at other cities of Portugal. The Brain Tumor Bank at Biobanco-iMM harbors biological samples from over 1000 patients with detailed clinical information, and represents the largest collection of its kind in the country. This allowed us to participate in national and international collaboration projects for the study of several brain tumor types including medulloblastoma, ependymoma, pilocytic astrocytoma, glioblastoma and brain metastases.

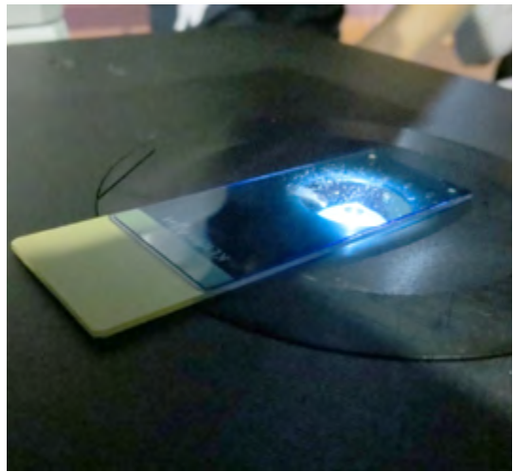
In keeping with the spirit of Adelaide Passos, we have started organizing fundraising events for cancer research at iMM. The Brain Tumor Team (BTT) was formed in 2014 to create awareness and to fundraise for cancer research. The BTT has participated in *Corrida Saúde + Solidária*, an event organized by the students of the Lisbon Medical School (AEFML), with an increasing number of participants. Last May 8th 2016 our team gathered over 500 participants from diverse hospitals and research institutes in Lisbon! With the donations received we have acquired equipment for research at iMM.

The CITC was supported by Fundação Millennium bcp from the beginning and it was determinant to take our goals further. Besides supporting brain tumor research at iMM, Fundação Millennium bcp led the development of a cooperation protocol between the Lisbon Academic Medical Centre (CAML) and the Hospital Central de Maputo (Mozambique) to promote the training of medical doctors in Pediatric Neurosurgery and to develop pediatric brain tumor research.

Social Events

European Researchers Night





Christmas Party

Ongoing and Institutional Partnerships

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

Amgen www.amgen.com
Bayer www.bayer.com
Budapest University of Technology and Economics www.bme.hu
Bristol-Myers Squibb www.bms.com
Celgene www.celgene.com
Centro Hospitalar Lisboa Norte, ETE www.chln.min-saude.pt
EMBO www.embo.org
Cytokinetics cytokinetics.com
Janssen www.janssen.pt
Laço www.laco.pt
Liga Contra Cancro www.ligacontracancro.pt
Medtronic www.medtronic.pt
Merck Sharp & Dohme msd.pt
MVI www.malariavaccine.org
Millennium bcp www.millenniumbcp.pt
Novartis www.novartis.com
Otsuka Pharmaceutical Co, Ltd www.otsuka.co.jp
Pfizer www.pfizer.pt
Roche www.roche.pt
Rotary Club www.rotary.org
Servier www.servier.com
Technophage www.technophage.pt
Theranostics
UCB Pharma www.ucb.com
Universidade de Aveiro www.ua.pt