Instituto
de Medicina
Molecular

João Lobo
Antunes

Highlights 2018

Instituto de Medicina Molecular | João Lobo Antunes

iMM
Instituto de Medicina Molecular João Lobo Antunes

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Cover
Primary culture of mice muscle fibers.
Credits: Helena Pinheiro, Edgar Gomes Lab, iMM.

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

Design
Botodacruz Creative Studio
www.botodacruz.pt

July 2019

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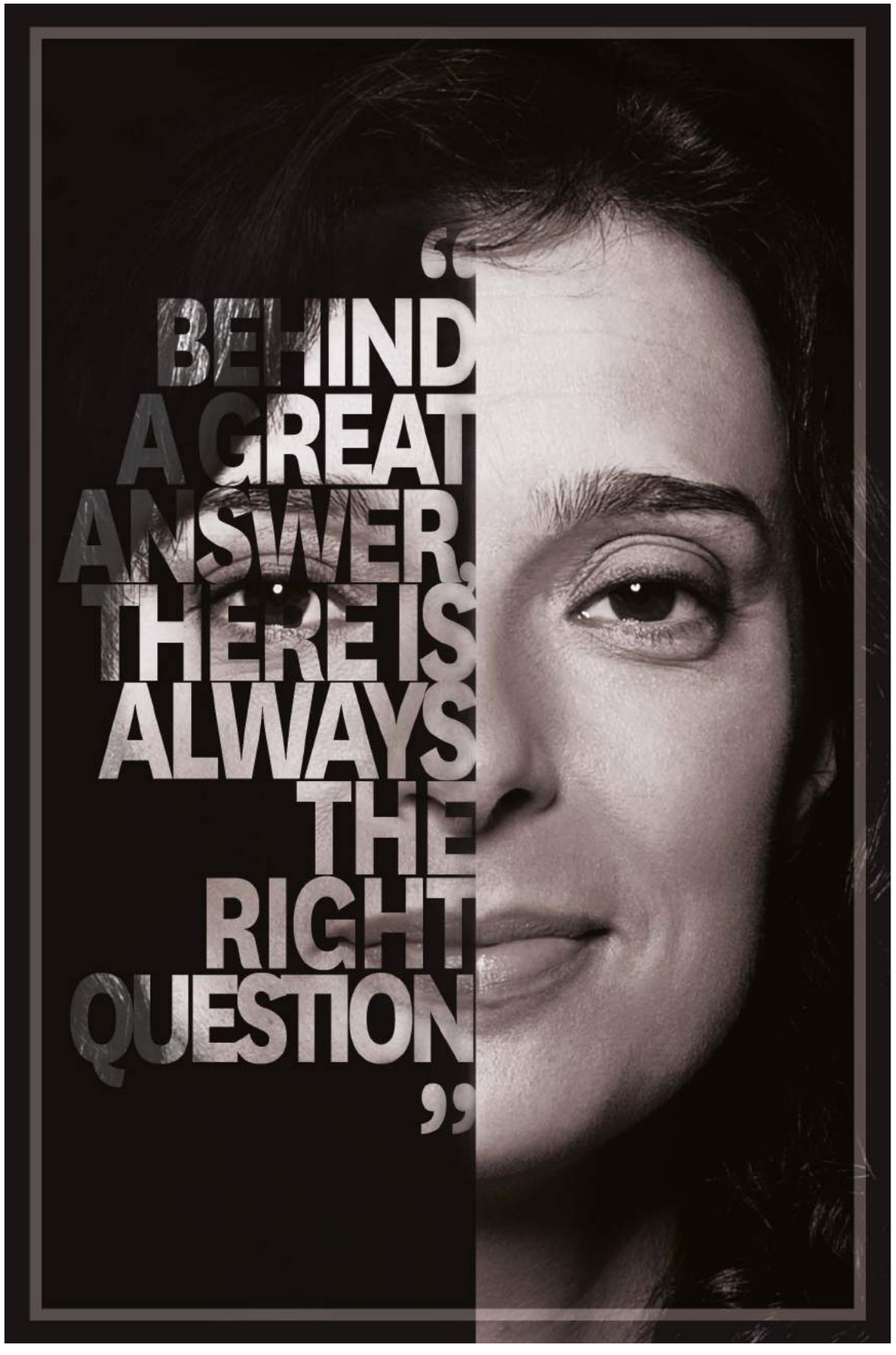

Director's Message

Maria M. Mota | Executive Director

"Futuro" was the word that I picked when I was unexpectedly asked in a live national TV program for a word representing the turning of the year. While it was a totally spontaneous answer, there was a reason behind it. The entire program was dedicated to an analysis of 2018 and at one point I ended up thinking how much time we spend talking about things that obviously have a certain importance in a particular time and space but are just, as we say in Portuguese, "a espuma dos dias" (adapted from the French novel "L'Écume des jours"/ "Froth on the daydream").

For the past 4 years we have been restructuring iMM with the concept that our **overarching mission is the promotion of scientific excellence, leveraged by top quality human resources that are supported by state-of-the-art infrastructures.** We have a strong conviction that we are moving towards a solid and at the same time a genuine environment, excited with the world to discover, as you can witness in the next pages. However, 2018 was the year that we – Bruno Silva-Santos and myself – felt the need to define a more ambitious strategy for iMM in the years to come.

We must aim to foster new and disruptive discoveries, based on **AMBITION**, one of iMM's key values. While **FREEDOM** will continue to be another of those key values, we must **create room for bold initiatives based on interdisciplinary interactions.**

Furthermore, to attract and maintain a vibrant faculty, we must invest in internationalization and enforce a recruitment, evaluation and promotion path based solely on professional excellence.

The success of such a structure also requires us, as community, to be fully committed to train and educate the most promising researchers to succeed in internationally competitive environments of academia, industry and clinical medicine. We should nurture the future leaders. Our MSc, PhD and post-doctoral programs must explore the fundamentals of living systems at all levels, while providing an intensive and demanding period of development of transferable skills. Being in the campus of and belonging to the Lisbon Medical Academic Centre (CAML), which includes the largest medical school (FMUL) and university hospital (HSM) in the country, we must play a unique role in the scientific training of MD interns to **ensure a new generation of Clinician-Scientists** capable of bridging basic and clinical research.

We have no doubts that outstanding science is the motor of groundbreaking applications with societal impact. In that respect, 2018 was a very special year. After 5 years of pioneering research and development, one of iMM start-ups – Lymphact – was acquired in June 2018 by Gamma-Delta Therapeutics, a UK-based company. Lymphact, which was started upon a discovery made by iMM PhD student Daniel Correia in the team led by Bruno Silva-Santos, created a new technology to generate autologous and heterologous cellular immune therapies targeting chemotherapy-resistant cancer cells believed to cause disease recurrence. The iMM team will continue to work now with the UK team to develop their invention – DOT-Cells® – towards clinical application.

This process made clear the need to deploy improved streamlined processes to create a favorable environment to **foster innovation and speed up the development of promising ideas** to improve human life. This environment will ensure a strong interaction between our scientists and key stakeholders in industry, academia and the healthcare system towards clinical translation and commercialization, but always preserving the superior public interest. With that in mind, we have established a new Technology Transfer Office (TTO) fully dedicated to the valorization of iMM research, including the protection of intellectual property, partnering with industry, the promotion of entrepreneurship and the creation of new ventures as a key strategy to drive iMM innovation to the market. Bringing iMM innovation to clinical application will greatly benefit from a close collaboration with our founder HSM, which should reinforce our capacity to promote investigator-initiated trials in our medical research campus.

Last but not the least, while we aim to continue sharing our discoveries and enthusiasm in a range of public events and activities, we now also ambition to **involve the entire society**, contributing constructively to the public debate about the direction, purpose and implications of biomedical research. We are reinforcing iMM's vocation to the service of the society and the pursue of knowledge dissemination in its two distinct but complementary versions: the most visible, which captivates by the results achieved, by the discovery; with the version that precedes it, the first encounter with the question and with the curiosity that is pursued. In this context, 2018 was also very rich.

First, we have created the Societal Advisory Board (SoAB), composed by distinguished members of our society, who will provide advice on public policies that adequately promote the values of iMM to the society. Second, we have launched the first campaign to introduce the iMM to the common non-scientist citizen.

Under the motto "Behind a great answer, there is always the right question" we launched a series of posters in the Lisbon area (with a special focus in the surroundings of the university campus) with questions that we think might be posed by both scientists and non-scientists. Through a QR code in each poster, curious people could access a short video where an iMM scientist provided a simple but rigorous and easy to understand answer. We strongly believe this was just the beginning, as numerous contacts and questions received from the outside will certainly drive us into future adventures.

In the turning of the millennium, Melinda and Bill Gates decided they will help eradicating malaria before they die. Almost twenty years later, and just recently, another philanthropic and younger couple decided to leave an even stronger mark. Priscilla Chan and Mark Zuckerberg have provided 3 billion US dollars for the next 10 years with the ambitious goal to "cure, prevent and manage" all diseases. While such value is incredibly impressive, it is not a huge sum for such an ambitious goal. Notably, Chan and Zuckerberg know they just want to be the spark that triggers a process – to create a long-term global movement to finance science with the support of citizens around the world – that will allow them to achieve their goal. iMM wants to be part of such movement and contribute significantly to improve human health. To that end, in 2018 we have launched João Lobo Antunes Fund where we hope to engage the Portuguese society in supporting iMM scientists to address the most difficult questions, the questions that no one has yet asked or have not been answered yet. More importantly, the questions that have the potential to produce the most relevant answers.

Maria M. Mota

Organization and Structure

The mission of the Instituto de Medicina Molecular João Lobo Antunes (iMM) is to foster basic, clinical and translational biomedical research with the aim of contributing to a better understanding of disease mechanisms, developing novel predictive tests, improving diagnostics tools and developing new therapeutic approaches.

Created in December 2002, iMM is located on the campus of the Faculty of Medicine of the University of Lisbon (FMUL). iMM is mainly supported by national public funds and European Union funds. The research expenditure includes additional funds obtained from peer-reviewed competitive grants, private donations and industrial partnerships.

iMM Associate Members

Universidade de Lisboa
Faculdade de Medicina da Universidade de Lisboa
Hospital de Santa Maria
Associação para a Investigação e o Desenvolvimento da Faculdade de Medicina
Fundação Oriente

Boards of Trustees

The Board of Trustees is composed by representatives of the Associated Members and meets at least once per year to analyze the scientific and finance report and to approve the plan of activities and budget for the next year.

Boards of Directors

The Boards of Directors is responsible for the management of the Institute according to the Plans aprooved by the Trustees.
The Board of Directors is elected by the Trustees.

M. Carmo Fonseca
MD, PhD - President

Maria M. Mota
PhD - Executive Director

Bruno Silva-Santos
PhD - Vice-President

Finance and Operations Director

Fausto Lopo de Carvalho

Scientific Advisory Council

Undertake periodic evaluations to the iMM specific programes and include international experts of scientific fields.

Carlos Caldas
MD, PhD, *Chairman*
Cancer Research UK Cambridge Institute
Cambridge Cancer Center, UK

Philippe Sansonetti
MD, PhD - Pasteur Institute, France

Elaine Mardis
PhD - Institute for Genomic Medicine
at NationWide Children's Hospital

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

Paul Peter Tak
MD, PhD - University of Amsterdam
Netherlands

Societal Advisory Board

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Chairman

Graça Franco

Paula Martinho da Silva

Diogo Lucena

João Filipe Queiró

Henrique Leitão

Pedro Norton

Domítilia dos Santos

Organigram

Assistant to the Board of Directors
Clara Artur

Quality Management Office
Alexandre Jesus

Safety Office
Alexandra Maralhas

Boards of Directors:

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Maria M. Mota
Bruno Silva-Santos

Technical Facilities:

Biobank Unit
Sérgio Dias e Cláudia Faria

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José Rino

Flow Cytometry Unit
José Rino

Histology and Comparative Pathology Unit
Tânia Carvalho

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Pedro Eleutério

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Alexandra Maralhas

Rodents Unit
Pedro Simas

Zebrafish Unit
Leonor Saúde

Laboratory Design
Alexandra Maralhas

Maintenance and Repairs
Sara Santos

Washing Room
Edna Gomes

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Sofia Vicente dos Santos

Career Developement Office
Filipa Nunes

Communication Office
Inês Domingues

Technology Transfer Office
Pedro Silva

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João Barata Lab
Gonçalo Bernardes Lab
Maria Carmo-Fonseca Lab
Miguel Castanho Lab
Luís Costa Lab
Sérgio de Almeida Lab
Mamede de Carvalho Lab
Sérgio Dias Lab
Joaquim Ferreira Lab
José Ferro Lab
Luísa Figueiredo Lab
Paulo Filipe Lab
João Eurico Fonseca Lab
Cláudio Franco Lab
Edgar Gomes Lab
Luís Graça Lab
Domingos Henrique Lab
João Lacerda Lab
Luísa Lopes Lab
Nuno Morais Lab
Vanessa Morais Lab
Maria Mota Lab
Miguel Prudêncio Lab
Mário Ramirez Lab
Miguel Remondes Lab
Carlota Saldanha Lab
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Ana Sebastião Lab
Bruno Silva-Santos Lab
Pedro Simas Lab
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Marc Veldhoen Lab

Finance and Operations Office:

Fausto Lopo de Carvalho

Funding Office
Joana Costa

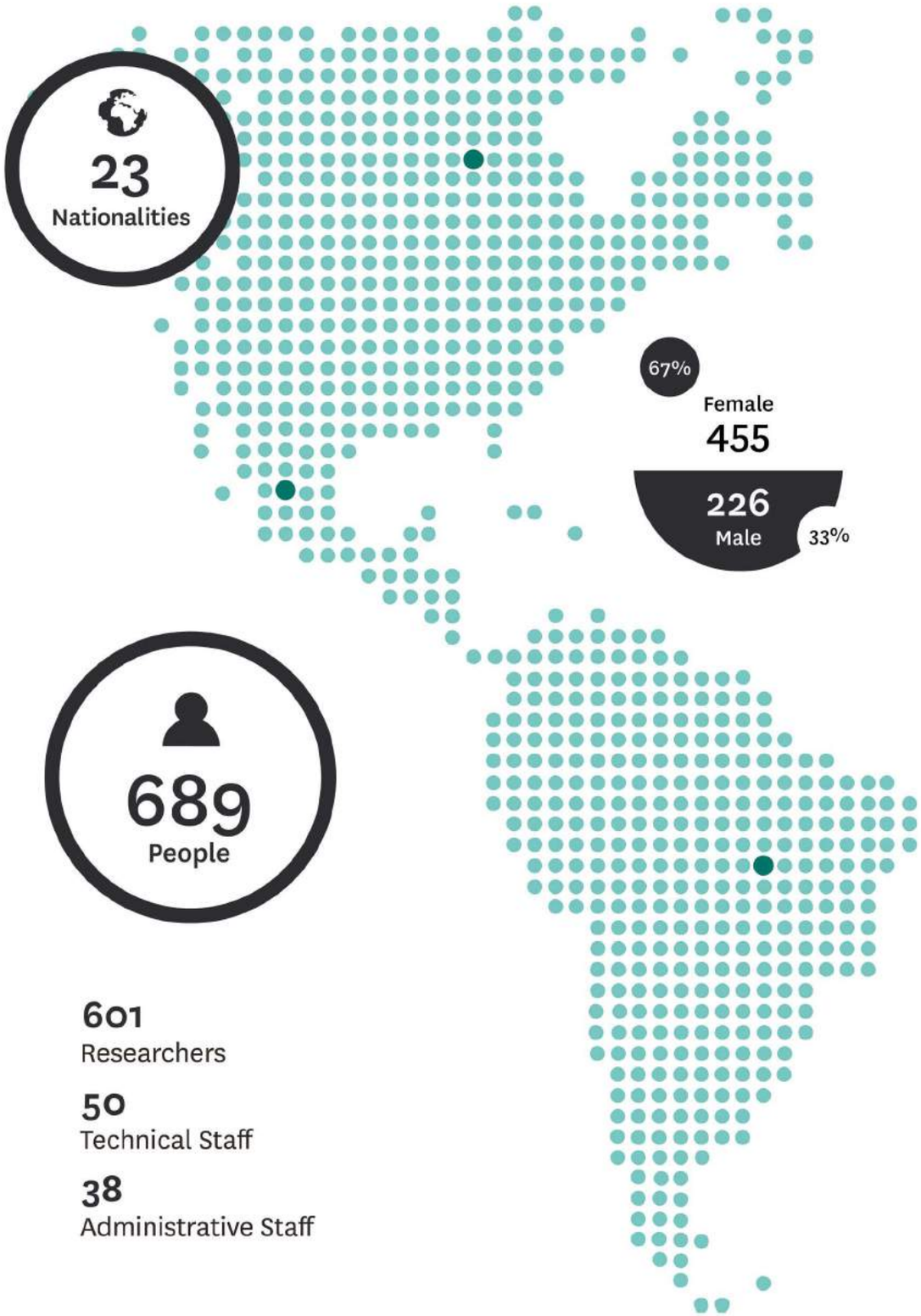
Project Management Accounting
Sandra Duarte

Purchasing and Procurement
Alexandre Jesus

Legal
Inês Bilé

Facts and Figures 2018

People



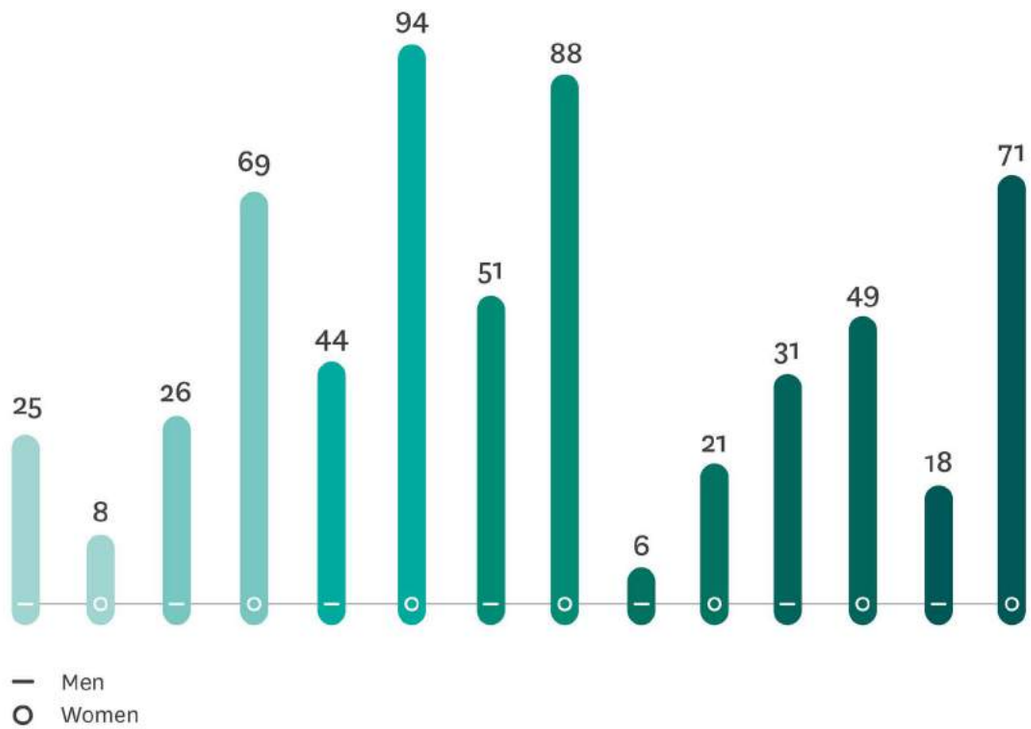
601
Researchers

50
Technical Staff

38
Administrative Staff

Immunology and Infection
Oncology
Neurosciences
Cell Biology

Note: Data presented as of December 2018



33
Group leaders
2 Foreigners

95
Master Students
6 Foreigners

138
PhD Students
21 Foreigners

139
Post-Docs
26 Foreigners

27
Trainees
1 Foreigner

80
Clinical Researcher
2 Foreigners

89
Lab Technician | Lab Manager
Administrative Technician
Junior Project Manager
7 Foreigners

Produtivity at a Glance

254
Total Publications International Journals

53
Publications in Journals with Impact Factor > 10

561
Communications in International Conferences

316
Communications in National Conferences

372
Seminars and Invited Lectures

104
Organisation of Conferences

23
PhD Thesis Completed

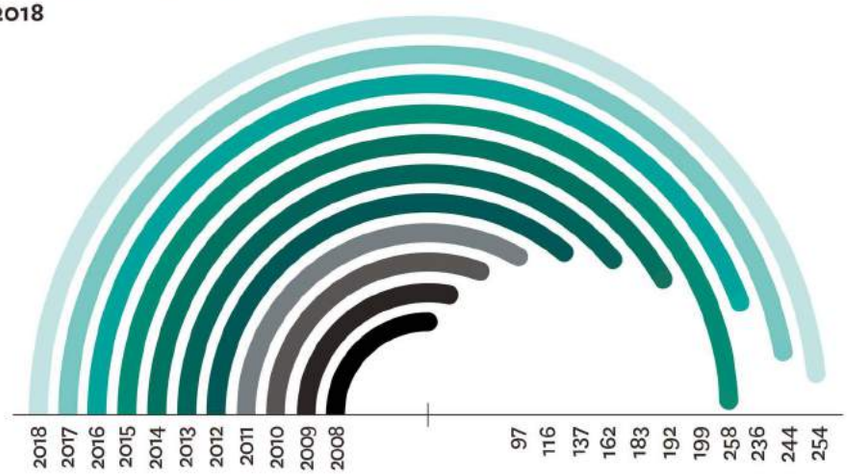
65
MSc Thesis Completed

96
Prizes, Honours and Awards

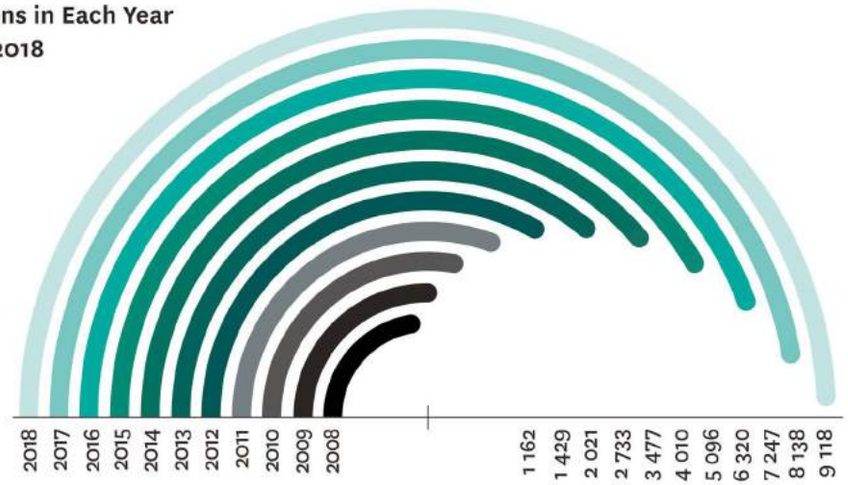
iMM Publications in International Journals

(Source: Web of Science™)

Published Items in Each Year
2008-2018



Citations in Each Year
2008-2018



Papers in 2018 | **Papers since 2008** | **Sum of the times cited** | **Average citations per item** | **h-index**

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

Funding

Number of Ongoing Research Grants in 2018

119
Public National FCT

3
Public National Other

26
Public European Commission

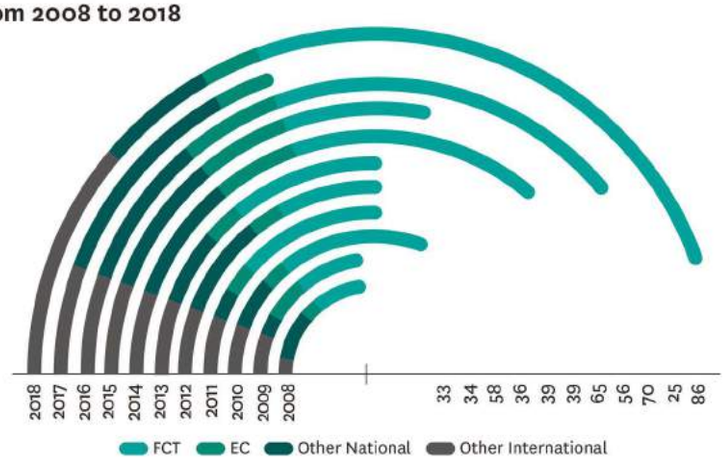
1
Public International Other

19
Private National
12
Of which with the industry

32
Private International
10
Of which with the industry

Number of Research Funding Grants Initiated in 2018

Number of Research Grants Initiated at iMM from 2008 to 2018



2018 in Review

The highlights of the year at iMM including awards, events and grants

January

iMM
Postdoc Day

February

Young Biophysicist 2018
Marta Marques
(Gonçalo Bernardes Lab)

2018 MedChemComm Emerging Investigator Lectureship
Gonçalo Bernardes
(Group Leader)

April

iMM Annual Scientific Retreat in Nazaré

Fundo iMM-Laço:
A Caminho da Cura
(2017 Edition – Announced in April 2018)
Sérgio de Almeida
(Group Leader)
Sofia Mensurado
(Bruno Silva-Santos Lab)
Rui Martinho
(Carmo-Fonseca Lab)

May

Corrida
Saúde+Solidária

Fundo de Investigação da Sociedade Portuguesa de Reumatologia
João Eurico da Fonseca Lab

Janssen Innovation Award – 1st Place
Bruno Silva-Santos
(Group Leader)
Karine Serre e Sofia Mensurado
(Bruno Silva-Santos Lab)

Gilead Génese Programme
Robert Badura
(Ana Espada de Sousa Lab)

Jakie/Sociedade Portuguesa de Reumatologia Grant
João Eurico da Fonseca Lab

June

Launching of Fundo João Lobo Antunes

XII Annual CAML PhD Students' Meeting

July

Nunes Correa Verdades de Faria Award
Mariana Alves
(Joaquim Ferreira Lab)

Nunes Correa Verdades de Faria Award: Honorable Mention
Daniel Caldeira
(Joaquim Ferreira Lab)

la Caixa – Individual Project
Maria Mota
(Group Leader)

Fahraeus Gold Medal Award
Carlota Saldanha
(former Group Leader)

September

H2020 ERC Proof of Concept
Cláudio Franco
(Group Leader)

la Caixa – Collaborative Project
Miguel Castanho
(Group Leader)

H2020 Twinning: ACORN
Gonçalo Bernardes
(Group Leader)

October

ART Diagnostics, EIC-SMEInst-2018-2020 — SME instrument Phase 1
Ivo Martins, Ana Martins e Patrícia Carvalho
(Nuno Santos Lab)

H2020 ERC Synergy Grant
Edgar Gomes
(Group Leader)

November

Scientific Excellence Award in the field of Molecular, Cellular and Immunoparasitology by the American Society of Tropical Medicine and Hygiene
Debanjan Mukherjee
(Maria Mota Lab)

Santa Casa da Misericórdia Awards: Mantero Bellard Award
Luísa Lopes
(Group Leader)

H2020 FETOpen: NOVIRUSES2BRAIN Project
Miguel Castanho
(Group Leader)

Sanofi – Institut Pasteur 2018 Awards: Biomedical Research (International Mid-Career Award)
Maria Mota
(Group Leader)

December

iMM Best Master Thesis Award
Ana Raquel Lopes
(Bruno Silva-Santos Lab)
Cristiana Morgado
(Sérgio de Almeida Lab)
Diana Moita
(Miguel Prudêncio Lab)

BIAL Foundation: Grant for Scientific Research 2018/2019
Luísa Lopes e Miguel Remondes
(Group Leaders)

iMM Christmas Party

Our Science

Labs Highlights

The research at iMM is driven by curiosity, passion and desire of our researchers to move forward the state-of-the-art. Our laboratories develop basic biomedical, clinical, translational and innovation research in these areas, with the aim of contributing to a better understanding of disease mechanisms, to develop new diagnostic or predictive tests as well as new therapies.

Claus Azzalin Lab

Telomeres, long noncoding RNAs and genome stability

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We discovered that the telomeric factor TRF2 promotes invasion of noncoding RNAs into telomeric DNA, leading to the formation of R-loops. When deregulated, this activity compromises telomere and genomic stability. This is the first example of a human DNA-bound factor promoting formation of R-loops in trans and suggests the existence of regulated R-loops, possibly involved in telomere metabolism.

Maria Carmo-Fonseca Lab

RNA & Gene Regulation

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Our lab identified the transcription factor Zeb2 as a novel age-associated barrier to somatic cell reprogramming, and we uncovered an antisense long non-coding RNA as a new target to achieve robust Zeb2 downregulation. In collaboration with the Proudfoot lab in Oxford, we studied nascent RNA complexes in human cells and we unraveled unanticipated dynamic links between RNA Polymerase II and the spliceosome.

João Barata Lab

Signaling in Cancer

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We found that STAT5 is essential for IL-7-mediated viability, growth, and proliferation of T-cell acute lymphoblastic leukemia cells, in part via activation of PIM1. Surprisingly, the STAT5-dependent viability effect of IL-7 occurs in a Bcl-2-independent manner in leukemia cells – in obvious contrast to what happens in normal T cells *(Ribeiro* et al, *Blood Adv 2018)*.

Miguel Castanho Lab

Physical Biochemistry of Drugs & Targets

macastanho@medicina.ulisboa.pt

Our lab was awarded highly competitive and prestigious funding from the European Innovation Council for the significance of the work towards radically new future technologies. In collaboration with an academic and an industrial partner, our lab will lead the development of a unique drug to eradicate multiple viral species simultaneously from the central nervous system.

Gonçalo Bernardes Lab

Chemical Biology & Pharmaceutical Biotechnology

gbernardes@medicina.ulisboa.pt

In contrast to the laborious and time-consuming proteomic approaches, my group has assembled a platform leveraging proprietary machine learning models for drug target identification. Its use has enabled the discovery of new links between drug-macromolecular target-disease that are fueling the development of novel, safer and more efficacious cancer treatments.

Luís Costa Lab

Translational Oncobiology

lcosta@medicina.ulisboa.pt

During 2018, we consolidated our Oncodynamics Biobank, which is a clinically annotated prospective collection of liquid biopsies from breast, prostate, colorectal and melanoma cancer patients, designed to characterize both the host immune response and tumor clonal evolution during cancer progression under therapy. In this last year, we recruited up to 80% of the expected breast cancer cases, which allowed us to start the proposed analyzes.

Sérgio de Almeida Lab

Chromatin & Epigenetics

sergioalmeida@medicina.ulisboa.pt

Using groundbreaking experimental tools, a new study from our lab revealed that DNA breaks alter the reading of the genetic code, originating new messages that may guide novel cellular functions. As DNA breaks are major hallmarks of aging and diseases such as cancer, this study has important physiological implications.

Joaquim Ferreira Lab

Clinical Pharmacology

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We actively participated in a collaborative effort which proposed that LRP10 gene defect is implicated in the development of inherited forms of α-synucleinopathies. This opened new potential biomarkers and therapeutic targets for Parkinson's disease. Additonally, the fruitful collaboration with BIAL in the development program of opicapone, a new COMT-I recently licensed for the treatment of Parkinson's disease.

Mamede de Carvalho Lab

Translational Clinical Physiology

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Our unit produced relevant output on dopaminergic role in Tourette Syndrome, learning in Obsessive-Compulsive Disorder, epidemiology of familial amyloid neuropathy (FAP), effect of liver transplantation and tafamidis on FAP, genes epidemiology of amyotrophic lateral sclerosis (ALS) in Portugal, biomarkers in ALS, and transcutaneous direct current stimulation to modulate spinal cord excitability.

José Ferro Lab

Clinical Research in Non-comunicable Neurological Diseases

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Our major achievement in 2018 was to complete the RE-SPECT CVT trial with J.Ferro as the Global Principal Investigator. The trial included 120 patients with cerebral venous thrombosis (CVT) recruited in 36 centers in nine countries. RE-SPECT CVT trial showed that anticoagulant therapy for 6 months, either with dabigatran or warfarin, safely prevented recurrent venous thrombotic events.

Sérgio Dias Lab

Vascular Biology & Cancer Microenvironment

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In 2018, our Lab strengthened its output in the area of cancer metabolism by showing modulation of mitochondrial function by specific signaling pathways reverses leukemia resistance to chemotherapy (Nóbrega-Pereira *et al.*, Cancer Res.) and that a lipid enriched systemic environment has a negative impact in the anti-tumor functions of subsets of lymphocytes. (Rodrigues *et al.*, Cancer Immunology Res).

Luísa Figueiredo Lab

Biology of Parasitism

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In 2018, we published a paper in *Nature Communications* from Filipa Rijo-Ferreira's graduate work describing that mice infected by trypanosomes are continuously jet-lagged, which allowed us to conclude that sleeping sickness is a circadian disorder. In this year, we initiated our ERC-funded period by recruiting three talented post-doctoral fellows that trained in the U.K., Switzerland and U.S.A.

Paulo Filipe Lab

Dermatology Research

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Psoriasis is a common, recurrent, inflammatory skin disease for which no reliable biomarker is currently available. Using high-end mass spectrometry of serum proteins we have identified complement factor H as a putative biomarker of disease severity and response to therapy. We are currently validating these data using larger cohorts of patients undergoing diverse therapeutic modalities.

João Eurico Fonseca Lab

Rheumatology Research

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In 2018, we described (Vidal B, *et al.*, Rheumatology 1;57 (8):1461-1471) in an animal model a bone effect of a JAK-STAT inhibitor that was so far unknown. This merited an editorial and opened new funding opportunities to further understand the clinical implications. The multicentric, double blinded, placebo-controlled GO-DACT TRIAL promoted and fully organized by iMM has tested the first line use of an anti-TNF in the control of dactylitis in psoriatic arthritis patients.

Cláudio Franco Lab

Vascular Morphogenesis

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We discovered that non-canonical Wnt signaling fine-tunes junctional mechanical proprieties during endothelial collective cell migration. Also, we generated a novel double fluorescent reporter mouse line to study front-rear cell polarity in living tissues. We have been awarded an ERC Proof-of-Concept grant and an FCT CEEC junior researcher to identify a novel class of anti-angiogenic drugs.

Edgar Gomes Lab

Cell Architecture

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During skeletal myofiber development, nuclei move from the center to the periphery of the myofiber for proper muscle function. We identified that local activation of integrin by fibronectin secreted by myofibroblasts activates peripheral nuclear positioning in skeletal myofibers. In the future, this work can be basis for the identification of optimal physical exercises to preserve and repair muscle capacity. (Roman, Martins, *et al.*, Dev. Cell, 2018).

Luís Graça Lab

Lymphocyte Regulation

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We study mechanisms underlying induction and maintenance of immune tolerance. In other words, we research methods to reprogram the immune response in situations where the immune system is causing a disease, such as allergy, autoimmunity and transplant rejection. In addition, we are interested in defining the functional properties of lymphocytes that can promote immune tolerance by suppressing pathogenic immune responses. We have been studying how different types of lymphocytes with regulatory function can be induced in the periphery.

Domingos Henrique Lab

Stem Cells & Neurogenesis

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In 2018, activities in our laboratory included the organization of an 8-week course for the LisbonBioMed international PhD Program at iMM and the organization of a 1-week course on Stem Cell Biology for the international PhD Program in Bioengineering – Cell Therapies and Regenerative Medicine.

*Left in December

João Lacerda Lab

Hematology and Transplantaion Immunology

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Our 2018 paper in *Frontiers in Immunology* details the molecular signatures of regulatory T cells (Treg). Hypomethylated CpG sites in the FOXP3 locus, CAMTA1 and FUT7 gene regions were found to distinguish Treg from conventional T cells, describing a new strand-bias hemimethylation in the FOXP3 promoter and TSDR, allowing the identification of Treg subsets in disease settings such as autoimmunity.

Vanessa Morais Lab

Mitochondria Biology & Neurodegeneration

vmorais@medicina.ulisboa.pt

At present, our projects are driving exciting hypotheses and yielding promising targets that now require validation and the exploration of molecular mechanisms. Success in these experiments will address key unanswered questions that will stratify the importance of mitochondrial function for synapse biology, and overall brain homeostasis. Additionally, we are also developing a novel platform for streaming of sequencing data arising from mitochondrial DNA, a unique tool that will enable us to determine mutation burden and heteroplasmy contribution.

Luísa Lopes Lab

Neurobiology of Ageing & Disease

lvlopes@medicina.ulisboa.pt

We have published a new interaction between synaptic proteins -A2AR/mGluR5/NMDAR that control age-related alterations in synaptic plasticity, impacting in memory and relevant for Alzheimer's disease. We were awarded important funding from the Santa Casa da Misericórdia and the BIAL Foundation to develop research projects on novel aging models to study Alzheimer's disease and the role of circadian rhythms in memory.

Maria Mota Lab

Biology & Physiology of Malaria

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Our Lab highlights a discovery made in the past years and published this year - we identified a parasite molecule named UIS3 as a unique and potent mediator of autophagy evasion in *Plasmodium*. The work published in *Nature Microbiology* sets the basis for an undergoing project that explores UIS3 and its interaction with the host-cell autophagy machinery as target for antimalarial drug development.

Nuno Morais Lab

Computational Biology

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We showed the association of a gene signature for the increased number of centrosomes, a "fingerprint" of cancer cells, with genomic alterations and clinical outcome in different cancers. By combining data on chemical perturbations and drug sensitivity, we also identified candidate compounds for selectively targeting cancer cells exhibiting molecular evidence for that abnormality.

Miguel Prudêncio Lab

***Plasmodium* Infection & Anti-malarial Interventions**

mprudencio@medicina.ulisboa.pt

We have established the pre-clinical proof-of-concept of a new vaccination strategy against malaria, and validated the safety of PbVac for human use. We have further carried out the first-in-human evaluation of PbVac in Phase I/IIa clinical trials, which established the vaccine's potent biological effect against a challenge with *P. falciparum*. An International patent application (IPA) on this novel vaccination strategy was granted in Europe and Hong-Kong.

Mário Ramirez Lab

Molecular Microbiology & Infection

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We released a novel plasmid exploration tool: pATLAS. In 2018, we found that covRS mutations are not key determinants of virulence in *S. pyogenes* skin and soft tissue infections. We have also identified serotype 3 vaccine failures among complicated pneumonia cases suggesting lower-vaccine efficacy against this serotype. Also, we found that rises in antimicrobial resistance can be driven by the expansion of a single clone, independent of antimicrobial consumption. Finally, we established a novel *P. falciparum in vitro* culture protocol.

Miguel Remondes Lab

Neural Mechanisms of Perception, Memory & Decision

mremondes@medicina.ulisboa.pt

Memory is a major driver of decision-making, as we decide based on the outcomes of previous decisions. This year we provided a functional characterization of the circuitry connecting the hippocampus with the medial mesocortex *in vitro* and in awake-behaving animals, and responsible for making contextual memories available for decision-making centers in the brain (pre-published DOI: 10.1101/535047, in revision).

Carlota Saldanha Lab

Blood cells recruitment and inflammation

Our lab focused on understanding the cellular and molecular mechanisms underlying acute and recovery of inflammatory responses.

*Retired in September

Nuno Santos Lab

Biomembranes & Nanomedicine

nsantos@medicina.ulisboa.pt

Erythrocyte aggregation has a higher probability to occur in arterial hypertension patients, being directly related with the presence of fibrinogen, especially its gamma' variant, which strongly binds to its receptor on erythrocytes. The transient bridging of two erythrocytes, by the simultaneous binding of fibrinogen to both of them, promoting erythrocyte aggregation, may represent an important cardiovascular risk factor.

Leonor Saúde Lab

Embryonic Development & Regeneration

msaude@medicina.ulisboa.pt

Our PhD students Sara Fernandes and Rita Pinto defended their thesis successfully. Sara demonstrated the importance of gene-specific alternative 3'UTR APA in vertebrate embryonic development. Rita generated genetic tools to identify genes downstream of Dmrt2a. Leonor Saúde and Ana Ribeiro were successful in getting two grants to consolidate our spinal cord regeneration line of research.

Ana Sebastião Lab

Neuronal Communication & Synaptopathies

anaseb@medicina.ulisboa.pt

We identified the cannabinoid actions upon brain connectivity and postnatal neurogenesis. A mechanism of toxicity mediated by β-amyloid and extrasynaptic NMDA receptors to cleave BDNF receptors was disclosed. We have characterized neuroinflammatory markers in epilepsy. Also,a role for astrocytic glycine receptors was identified. Additionally, neuroprotective microreactors mimicking astrocytic functions were fabricated.

Bruno Silva-Santos Lab

T Cell Differentiation & Tumor Targeting

bssantos@medicina.ulisboa.pt

We have characterized a novel crosstalk of tumor-associated neutrophils suppressing the pro-tumoral functions of IL-17-producing γδ T cells. This work was awarded the *Janssen Prize for Innovation 2018*. We identified the first microRNA to control differentiation and function of γδ T cells. In 2018, the spin-off company originated from our lab, Lymphact S.A., was acquired by GammaDelta Therapeutics (UK).

Pedro Simas Lab

Herpesvirus Pathogenesis

psimas@medicina.ulisboa.pt

We utilise murid herpesvirus 4, which causes persistent infection in B-lymphocytes in laboratory mice, as a model to study human gammaherpesvirus pathogenesis, namely Kaposi's sarcoma associated herpesvirus (KSHV). We found that despite 60 million years of evolutionary divergence, KSHV latency-associated nuclear antigen (kLANA) and mLANA act reciprocally on TR DNA and kLANA can rescue mLANA deficient virus to enable chimeric virus to establish latent infection in mice. This system will allow, for the first time, *in vivo* investigation of kLANA in a well-established small animal model of infection.

Ana Espada Sousa Lab

Human Immunodeficiency & Immune Reconstitution

asousa@medicina.ulisboa.pt

We showed for the first time that HIV-2-infected individuals feature no significant loss of mucosal CD4 T-cells and preserve gut integrity. These data provide a possible explanation for the relatively benign course of HIV-2 infection, and suggest new strategies for the design of therapies to foster gut recovery in treated HIV-1-infected subjects.

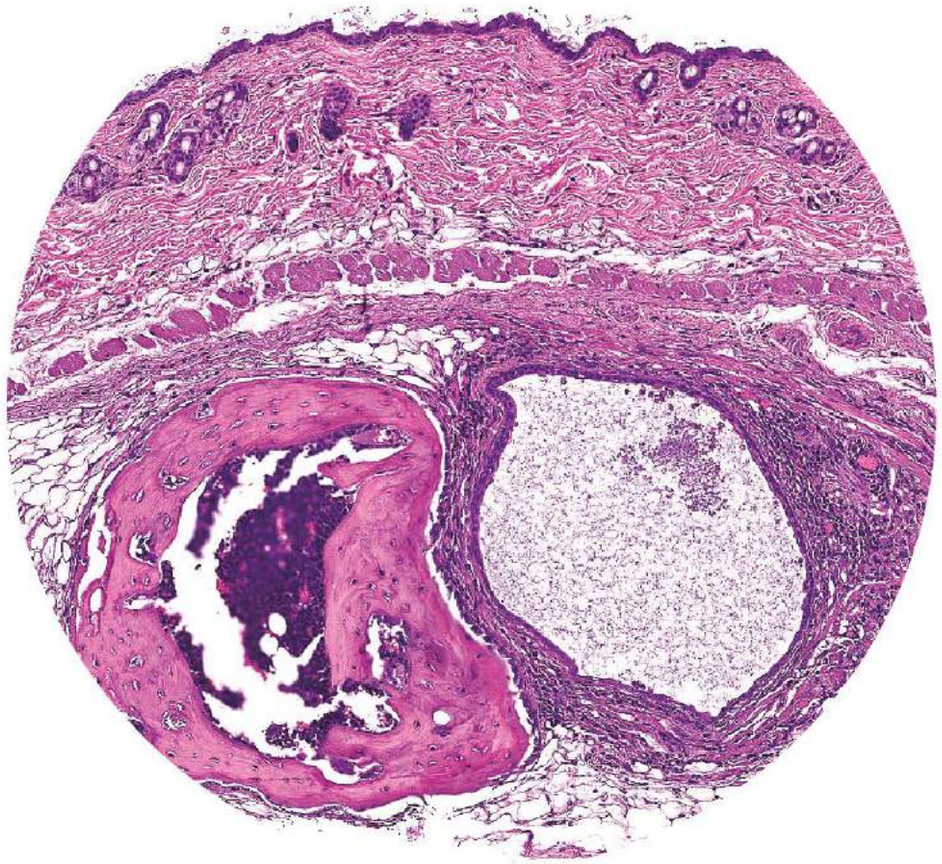
Marc Veldhoen Lab

Immune Regulation

marc.veldhoen@medicina.ulisboa.pt

Our lab has as core interest to understand the development, maintenance and activation of tissue resident T cells. In 2018, we published a paper in *Science Immunology* providing new insights in how gut-resident T cells are maintained in a semi-activated state. We show that alterations in the mitochondrial membranes curtails their metabolic potential and full activation.

Science Stories



Scientists discover molecule that could revert celular ageing

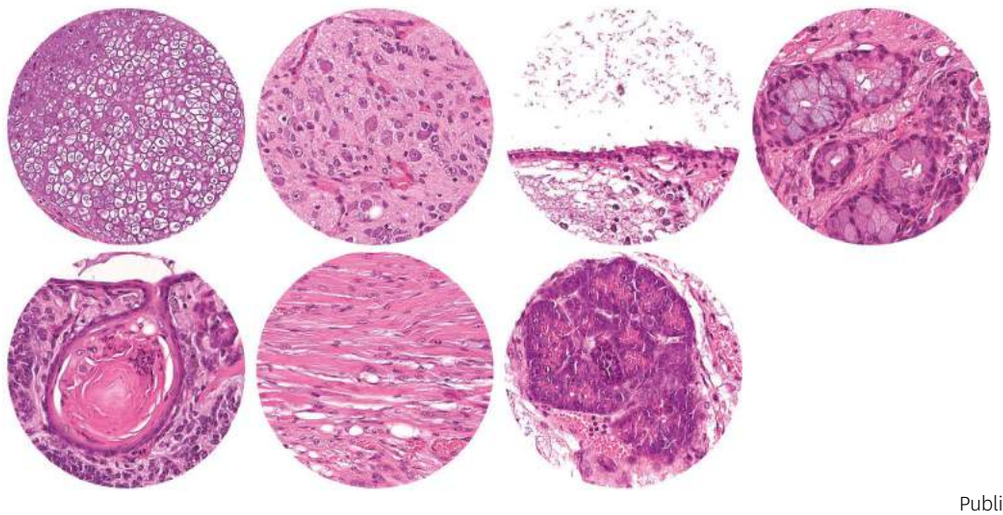
Throughout time all cells age gradually, contributing to the development of several diseases. Inducing cellular regeneration is one of the strategies used to fight diseases associated with cellular ageing. However, aged cells tend to be highly resistant to any type of manipulation intended to induce regeneration. The research group of Maria Carmo-Fonseca found that manipulating a single RNA molecule is enough to revert cellular ageing. Their results were published in *Nature Communications**.

Ribonucleic acid, or RNA, is responsible for protein synthesis inside cells. However, a specific type of molecule named non-coding RNA is never translated into protein. In fact, since the mapping of the human genome in 2001 it is known that only about 2% is actually translated into proteins.

In this study, the team led by Bruno de Jesus and Maria Carmo-Fonseca, used a genetically modified mouse model to study cellular ageing and regeneration. They found that cells derived from the skin of old mice produced higher amounts of a long non-coding RNA molecule named Zeb2-NAT when compared to cells from young mice. By reducing the amount of this specific RNA molecule, it was possible to efficiently regenerate old cells.

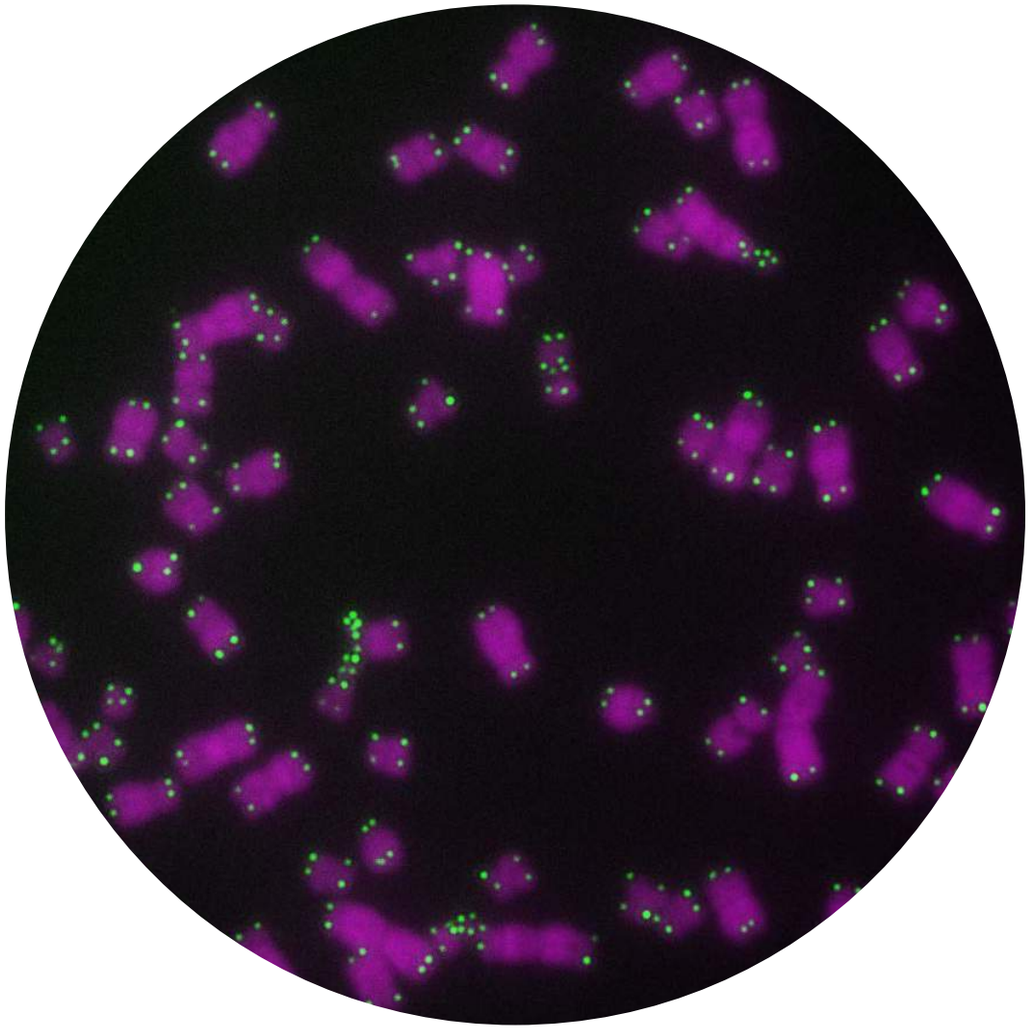
"These results are an important step to be able to regenerate diseased tissues in older people," said Bruno de Jesus.

Jesus, B.B., Marinho, S.P., Barros, S., Sousa-Franco, A., Alves-Vale, C., Carvalho, T., Carmo-Fonseca, M. (2018) Silencing of the lncRNA Zeb2-NAT facilitates reprogramming of aged fibroblasts and safeguards stem cell pluripotency. **Nature Communications**, *9:94.*



Figures: Histology sections of mouse iPS teratoma.
Depicted are the several mature tissues (bone, cartilage, muscle, glandular) that iPS cells differentiate into.
Credits: Tânia Carvalho, iMM.

Publication



Ground Control to Major Tom: Scientists find novel mechanisms to avoid chromosome instability found in cancer and aging cells

Group leader Claus Azzalin and his research group have found that a functional component of telomeres called TERRA has to constantly be kept in check to prevent chromosomal instability, one of the underlying anomalies associated with cancer. These discoveries published in *Nature Structural & Molecular Biology**, help to understand the molecular basis of chromosomal instabilities associated with cancer development and age-associated diseases, possibly paving the way for new therapeutic approaches.

Telomeres, the very ends of chromosomes, protect the stability of the genome by preventing erosion of genetic material and fusion of independent chromosomes. When telomeres are dysfunctional, severe genomic instability arises as often observed in cancer cells as well as in aged cells, for example from old individuals. Telomeres are therefore genomic structures composed of protein, DNA and RNA molecules including the 'telomeric repeat-containing RNA' (TERRA).

In this study, the team led by Claus Azzalin wanted to understand what happens when the RNA component TERRA is not properly preserved in cells.

Using an extensive combination of molecular biology, cellular biology, microscopy and biochemistry, they found a new interplay between three key telomeric molecules that results in the fine-tuned activity of TERRA. The results show that this component needs to be constantly regulated to serve their protective functions. Indeed, a lack of such fine regulation leads to severe telomere (and chromosomal) instability commonly found in cancer and aging cells.

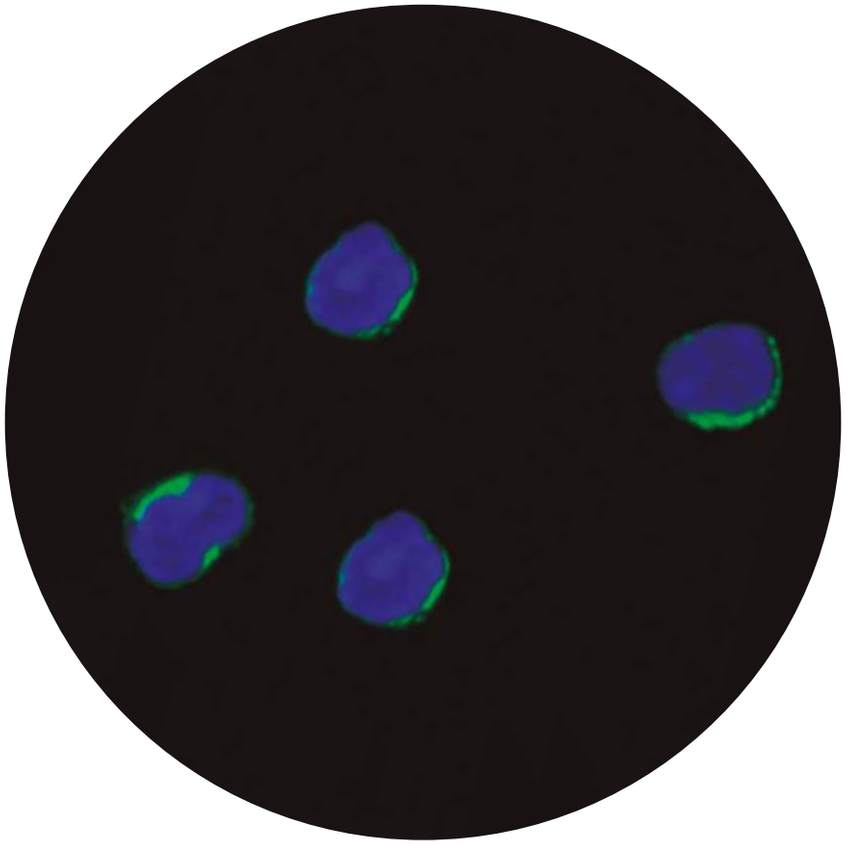
"I'm excited at the idea that our work could illuminate novel avenues for therapeutic intervention based on modulation of RNA in cells", said Claus Azzalin.

"I expect this study will open a new window on our understanding of genome stability and ultimately help in the development of aging and cancer therapies", said the study's first author Yong Woo Lee.

Lee, Y.W., Arora, R., Wischnewski, H., Azzalin, C.M. (2018). TRF1 participates in chromosome end protection by averting TRF2-dependent telomeric R loops. **Nature Structural & Molecular Biology**, *25:147–153.*

Publication

Figure: Human metaphase chromosomes (magenta) showing telomeres (green) at the tip of each arm.



When low batteries are a good thing: New study shows how gut immune cells are kept in control

Every day the human gut works on a fine-tuned balance that ensures the retention of essential nutrients while it prevents the entrance of potential armful microbes. Contributing to this surveillance system is a specialised group of immune cells that are held back due to unknown reasons although they have many characteristics of activated cells. A new study led by Marc Veldhoen shows how these cells are kept under control.

The work published in *Science Immunology**, reveals that the "batteries" of these cells have a different composition that reduces their capacity of producing energy, keeping them in a controlled activated mode.

This knowledge can give rise to new diagnostics and treatments for conditions affecting the digestive track such as gut inflammations or infections.

The outer layer of our bodies, the skin and intestine, contains a special population of white blood cells, called intraepithelial lymphocytes. It is largely unknown how the activity of these cells is controlled, not fully activated nor at rest. Using imaging and biochemical experiments, the research group led by Marc Veldhoen has now shown this is, at least in part, due to differences in the cells' "batteries" – the mitochondria. These energy-producing structures are present inside our cells regulate the cell's power. "We hypothesised that these gut-resident white blood cells may use energy in a different way. It was surprising to see that the detection of mitochondria gave a very different picture than seen in other white blood cells, forming the basis of a new hypothesis that the mitochondria themselves are different in these cells", explains Marc Veldhoen.

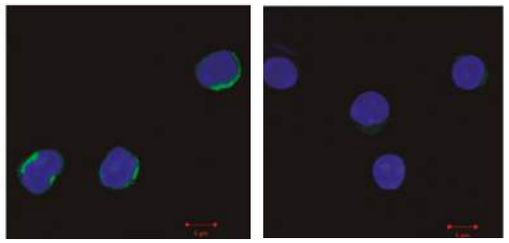
Using high magnification electron microscopy, the researchers observed that the mitochondria were present in abundance but seem to be different upon staining for light microscopy. Next, they studied the functionality of these batteries. "When we analyzed in detail these structures, we found changes in the lipids that form a layer separating the mitochondria from the rest of the cell", says Špela Konjar, first author of the study, adding that "these changes make the "batteries" work differently, as if they are in a "low energy mode".

When the lipid landscape was purposely altered, the researchers confirmed a change in the activation potential of the cells. "Our results showed that lipids in the mitochondria of these cells could alter their metabolic state and change their activity. When the mitochondrial lipids could not be arranged similar to those found in other white blood cells, the cells could not be properly activated when needed", explains Marc Veldhoen.

The researcher further explains: "This knowledge allows us to investigate how we can inhibit these cells when they are too active and cause damage, such as in gut inflammations, or how we can activate them more in cases of gut infections. Furthermore, the detection of mitochondria could be a diagnostic marker for the activation state of intestinal white blood cells".

This work was performed at the iMM (Portugal) and at the Babraham Institute (UK) with collaborations at Chicago University (USA). It was funded by the European Research Council, the Biotechnology and Biological Sciences Research Council, Horizon 2020 "EXCELLtoINNOV", National Institutes of Health, FEDER through POR Lisboa 2020-Programa Operacional Regional de Lisboa, PORTUGAL 2020, and Fundação para a Ciência e a Tecnologia.

Konjar, S., Frising, U.C., Ferreira, C., Hinterleitner, R., Mayassi, T., Zhang, Q., Blankenhaus, B., Haberman, N., Loo, Y., Guedes, J., Baptista, M., Innocentin, S., Stange, J., Strathdee, D., Jabri, B., Veldhoen, M. (2018) Mitochondria maintain controlled activation state of epithelial-resident T lymphocytes.* **Science Immunology. *3: eaan2543.*



Figures: In circulating white blood cells (left side) the "batteries" or mitochondria (in green) have a stronger signal – than in intestinal white blood cells, that are in a "low energy mode" (right side). Blue indicates the cell's nucleus.
Credits: Špela Konjar, iMM.

Publication

New approach on the use of big data in clinical decision support

A new computational approach that allows the identification of molecular alterations associated with prognosis and resistance to therapy of different types of cancer was developed by the research group led by Nuno Barbosa Morais, and published open access in *Nucleic Acids Research**.

Cancer cells are characterised by perturbations in the regulation of genes and, in particular, by alterations in alternative splicing, a process by which the same gene can originate different proteins. Some of those alterations are associated with different malignant features of cancer and its resistance to treatment but vary from tumour to tumour. "Each patient hosts a different cancer, so that scientists and clinicians need molecular information about many individuals to, supported by data, understand disease mechanisms, assess prognosis and make predictions on the best treatment for each patient based on their tumour's molecular profile", explains Nuno Barbosa Morais.

"We have created a software that, by analyzing large databases with clinical and splicing information for thousands of tumours, detects patterns of similarities between different cases and allows, for instance, to identify the relation of each molecular alteration with patient survival, for more than thirty types of cancer. In practice, the program allows to quickly convert a lot of genome-wide data into biological information with clinical potential", explains Nuno Saraiva Agostinho, first author of the study and student of the PhD program CAML (Centro Académico de Medicina de Lisboa, da Faculdade de Medicina da Universidade Lisboa).

"Thanks to this approach, we have already identified a possible mechanism of resistance to chemotherapy in colorectal cancer that we are now investigating, in an international collaboration that we are leading. We have also identified a new prognostic marker in breast cancer that we will now study, teaming up with other iMM colleagues", highlights Nuno Barbosa Morais, who leads the lab and has supervised the study.

This work was funded by the European Molecular Biology Organization (EMBO) and the Portuguese Fundação para a Ciência e a Tecnologia (FCT).

Saraiva-Agostinho, N, Barbosa-Morais, N.L. (2018) psichomics: graphical application for alternative splicing quantification and analysis. **Nucleic Acids Research**. *gky888.*

Figure: Adapted detail of data analysis using *psichomics*.
Credits: Nuno Agostinho, iMM.

Publication

Facilities & Finance and Operations Office

iMM offers a vibrant scientific environment and state-of-the-art infrastructures, providing an ideal setting to nurture new ideas with the mission of improving human health.

The support infrastructure is composed of different technical facilities that combine excellent instrumentation and dedicated staff to assist in experimental design, develop experimental assays and promote training activities.

These technical facilities support internal but also external scientists and other institutions.

The administrative facilities support the human resources, career development, communication and tech transfer activities of the institute.

In 2018, the Finance and Operations Office was created and constitutes now one of the main pillars of the iMM organizational structure.

Finance and Operations Office

Fausto Lopo de Carvalho
Head
fausto.carvalho@medicina.ulisboa.pt

After combined efforts the status of iMM was reviewed and iMM was excluded from the government institutional sector. A new organizational structure was put in place allowing for a more agile structure and for a clear understanding of the higher purpose we serve at iMM. As a result, iMM had an active voice in the change of the public procurement code and is recognized for the implementation of good management practices.

The results of a new organization with more collaborative and agile process were very visible not only in iMM internal procedures but also in the relationship of iMM with the main financing bodies and ministerial entities. Due to its own nature, the former called Management Unit is now called Finance and Operations Office and it is now one of the four main pillars of iMM organizational structure (Research Labs, Technical Facilities, Administrative Facilities and Finance and Operations Office).

Administrative Facilities

Career Development Office

Filipa Nunes, PhD
Executive Manager
imm-careerdev@medicina.ulisboa.pt

The Career Development Office provides training opportunities for success in science to researchers at different stages in their careers.

Human Resources Office

Sofia Vicente dos Santos
Head
imm-hr@medicina.ulisboa.pt

The purpose of the Human Resources Office is to develop, implement and support programs and processes that add value to iMM and its employees, leading to improvements in employee well-being, empowerment and growth, while committed to key iMM activity: Research.

Communication Office

Inês Domingues, PhD
Head
imm-communication@medicina.ulisboa.pt

The Communication Office is iMM's first line of interaction with society providing updated, reliable and relevant information on all of iMM's thematic areas, as well as promoting the very best scientific successes made by its research teams. With the firm belief that science should inform decisions because it impacts everyone's lives, our projects and activities target a wide range of audiences (schools, academia, industry, media, patients' associations, medical societies, policy makers, public opinion, among others).

Technology Transfer Office

Pedro Silva
Head
imm-techtransfer@medicina.ulisboa.pt

The Technology Transfer Office at iMM was established in May 2018 with the main goal of stimulating the valorisation of knowledge at iMM through:

- The creation of a favourable internal environment to foster innovation and speed up the translation of promising ideas and results into new medical solutions;
- The protection and licensing of intellectual property;
- The promotion of entrepreneurship and the creation of start-ups;
- A closer interaction with industry (at national and international level) leading to new collaborations;
- The participation in relevant European networks and initiatives related with translational research, open innovation and business acceleration.

Technical Facilities

Biobank Unit

Cláudia Faria, MD, PhD
Sérgio Dias, PhD
Head
imm-biobank@medicina.ulisboa.pt

The Biobanco-iMM Centro Académico de Medicina de Lisboa (CAML) was created in 2012 by the Instituto de Medicina Molecular João Lobo Antunes (iMM), and since then it has received, processed and stored a wide variety of clinically annotated biological samples, donated voluntarily, and aiming at foster biomedical research.

Currently with thousands of human biospecimens, including blood, serum, saliva, urine, cerebrospinal fluid, and tumour tissue, representative of 60 different human diseases, the Biobanco-iMM CAML is a unique platform to support national and international scientific research, with potential high impact on public health and on the advance of patient care.

Histology & Comparative Pathology Unit

Tânia Carvalho, DMV, PhD
Head
imm-histology@medicina.ulisboa.pt

Our mission is to achieve the highest level of quality in supporting researchers through: (1) training dissection skills and basic recording of macroscopic findings; (2) preparing the samples through state of the art histology and transmission electron microscopy services, including routine technique, paraffin, resin and cryo-embedding and sectioning, special stains, immunohistochemistry and immuno-EM; and (3) creating meaningful data from gross pathology observations and histopathology, with pathology reporting and document review for pathology content.

José Rino, PhD
Head

Bioimaging Unit

imm-bioimaging@medicina.ulisboa.pt

The Bioimaging Unit acts as a support structure to carry out and nurture research done with Light Microscopy inside the institute. We assist in planning microscopy-oriented projects, choosing materials and equipment, analyzing experimental results, processing acquired images and presenting data. Together with continuous training of new users, we organize regular courses to introduce users to the most recent microscopy techniques and foster interactions and collaborations between microscopy users at the iMM.

Flow Cytometry Unit

imm-flowcytometry@medicina.ulisboa.pt

The Flow Cytometry Facility provides a state-of-the-art flow cytometry service to iMM researchers as well as external groups from other research institutes. We aim at training researchers in the adequate use of the instruments and also on flow cytometry principles, experiment planning, as well as data analysis and interpretation.

Information Systems Unit

Pedro Eleutério
Head
imm-itsupport@medicina.ulisboa.pt

Our mission is to help researchers reach their maximum productivity by using adequate Information Technology resources.
We provide state-of-the-art information technology infrastructure and support services, contributing to improve the productivity and facilitate and optimise management business processes.

Rodents Unit

Pedro Simas, PhD
Head
imm-rodent@medicina.ulisboa.pt

The Rodent facility supports state-of-the-art animal research. We provide housing and care of laboratory rodents. We also support training and education in Laboratory Animal Science. The Rodent Facility strictly follows Portuguese and international laws and recommendations governing good practices and animal welfare. Namely, we follow 3R's principles, i.e., Replacement, whenever possible, of the animal model by alternative methods, Reduction of the number of animals used and, Refinement of experimental methodologies and animal care procedures.

Lab Management Unit

Alexandra Maralhas
Head
imm-labmanagement@medicina.ulisboa.pt

Our team is responsible for laboratory design, equipment management and equipment and infrastructure maintenance, including repairs and the organization of specific training courses. Our team offers a specialized service of washing, sterilising, preparing and storing of materials.

Zebrafish Unit

Leonor Saúde, PhD
Head
imm-fish@medicina.ulisboa.pt

Our unit provides a fully functional service to be used by the iMM research units. We provide technical assistance to facilitate the use of zebrafish in a wide range of experimentation sets.

International Projects

Three Successful Twinning Projects

ReTuBi
SynaNet
TwinnToInfect

ReTuBi:
Research and Training in Tumour Biology

For the last 3 years, scientists at iMM combined efforts with scientists at Institut Curie in France and the German Cancer Research Centre (DKFZ) in Germany to establish and promote a network of interactions and collaborations aiming at reinforcing its capacity for outstanding pre-clinical and translation research in the field of cancer biology.

Some of the highlights of this project:

- **45 Staff Exchanges**
- **29 Experts visits to iMM**
- **21 Scholarship Conference Awards**
- **5 Joint Lab Retreats** with a total of 186 participants
- **4 Workshops on Microscopy and Soft Skills** with a total of 109 participants
- **1 Summer School** with a total of 38 participants
- **6 Conferences and Symposia** with a total of 418 participants
- **2 ReTuBi events** with a total of 185 participants

Website: http://www.tumourbiology.eu/

Project video

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 692322.

SynaNet

A collaborative multidisciplinary and translational research project, from synapses to networks in Neurologic and Psychiatric Disorders between iMM at the Faculty of Medicine of University of Lisbon, the University of Eastern Finland, the University of Rome, La Sapienza and Lancaster University. For the past 3 years this project has been enhancing effective knowledge transfer, exchange of best research practices, and the mobility of early stage scientists.

Some of the highlights of this project:

- 19 labs and 26 Principal Investigators from the 4 institutions
- 38 Short-term missions
- 424 students attending summer schools and workshops
- 364 participants in the annual meetings
- 14 students participated in the European Researchers' Night 2017-2018

More information: https://www.synanet2020.com/

Project video

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 692340.

TwinnToInfect

A collaborative project between iMM, The Francis Crick Institute in the UK and the Institut Pasteur in France to unleash iMM's research excellence in immunity and infection that for the past 3 years has been increasing iMM's competitiveness and innovation.

Some of the highlights of this project:

- 21 Group leaders
- 51 Staff exchanges
- 19 On-site Training
- 2 Summer schools on Infection & Immunity and Ethics in Science with 90 participants
- 2 Technology Transfer events with 120 participants
- 15 Travel awards

More information: https://twinntoinfect.eu/

Project video

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 692022.

Four Horizon 2020 new projects

ERC | Synergy
FETOPEN | NOVIRUSES2BRAIN
FETOPEN | MyoChip
ACORN

Ten million euros to study the development and structure of the cytoskeleton

Pilar I | Excellence Science | European Research Council

Edgar Gomes, group leader at iMM integrates a consortium of 3 European laboratories with Carolyn Moores (Birkbeck College, University of London, UK) and coordinated by Michael Way (The Francis Crick Institute, UK) that together received an ERC Synergy Grant awarded by the European Research Council (ERC) worth 10 million euros for six years. The three research teams will join efforts to study the fundamental processes of development, structure and muscle physiology.

"The dynamics of the cell skeleton, critical to the integrated processes of development, operation and sustainability of the human body is conferred by a complex of molecules called the Arp2 / 3 complex," explains Edgar Gomes. His and Michael Way's laboratories have previously shown that this complex is essential for proper muscle development. The goal now is to expand this knowledge and determine the role of these molecules not only in the development process, but in muscle structure and physiology.

"This ERC Synergy funding scheme provides a unique opportunity for us to work together. Our close collaboration will allow us to understand how cells regulate not only their form, but how they interact with each other, giving clues to a wide range of diseases.", say the researchers about the importance of this funding.

Development of "One size fits all" unique drug to eradicate multiple viruses receives 4.2 million euros

Pilar I | Excellence Science | FETOPEN

Miguel Castanho, group leader at iMM and Professor of the Faculty of Medicine of the University of Lisbon leads the NOVIRUSES2BRAIN project that was selected by the European funding mechanism FETOPEN, under Horizon 2020, worth 4.2 million euros. In collaboration with researchers from the Pompeu Fabra University (Spain) and the German company SYNOVO GMBH, the team led by Miguel Castanho aims to develop innovative drugs that can fight viruses carried by the *Aedes* mosquito, such as Measles, HIV, Dengue, Zika and Chikungunya.

"Viruses that inflict the brain and other parts of the central nervous system are a major worldwide threat. In this project we want to finding and selecting drug leads that are both efficacious and able to translocate the blood-placental and blood-brain barriers so that Zika, Dengue, Chikungunya and other viruses can be targeted across barriers, including during pregnancy", explains Miguel Castanho. The project gathers the expertise of medicinal chemists, biochemists, drug development specialists and virologists to create drug leads able to clear all viral species from brain simultaneously.

A functional muscle on a chip: the MyoChip project

Pilar I | Excellence Science | FETOPEN

The MyoChip project, with a total funding of 3.2 million euros, is coordinated by iMM group leaders Edgar Gomes and Cláudio Franco and postdoctoral fellow William Roman, in collaboration with Institut Curie (France), University of Edinburgh (UK) and Fluigent (France).

The aim of this project is to develop a functional human muscle *in vitro*, irrigated by blood vessels and innervated by neurons. This system with architecture and functionality similar to that found in humans will have several possible applications, such as a better characterization of the structure and aging of the muscle, to serve as a "test tube" for the screening of new drugs and the application in prosthetic and robotics.

"This project will allow the study of the functioning of the muscle to a level never achieved before, as we will create human muscle and test new therapies. It is a very high-risk project involving for the first time the best specialists in a European multidisciplinary team", explains Edgar Gomes.

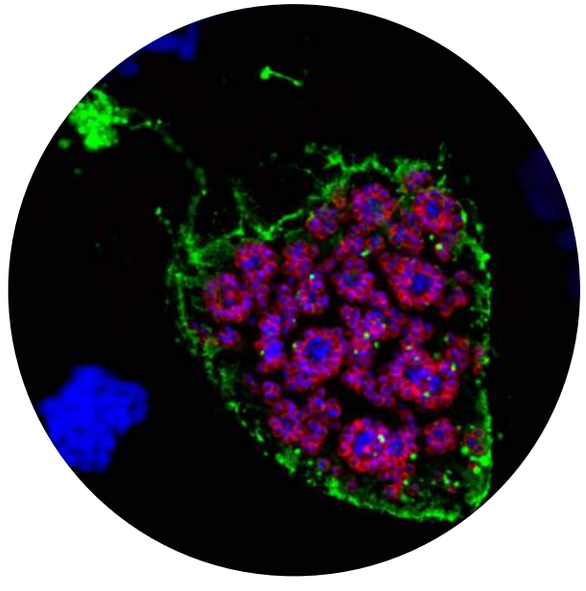
Given the various diseases of the muscular system that affect society, such as Duchenne dystrophy, sports injuries and the degenerative loss of muscle mass as a result of aging, it is essential to study the functioning of the muscle so that this knowledge may have a direct application to people's quality of life.

Carbon monoxide in health and disease: the ACORN project

Widening Program

Started in September 2018, ACORN is a Twinning project funded with 1 million euros for 3 years by the European Union's Horizon 2020 research and innovation program, aiming at placing iMM within the core of a European network of laboratories and pharma/biotech companies that seek to produce cutting-edge research in the field of gaseous signalling molecules (gasotransmitters).

Partnering with the University of Cambridge (UK), Leiden University Medical Center (The Netherlands), Pilotality and Percuros B.V., two Dutch biotech companies, and Veronica de Marchis, a SME, the project aims to develop a sustainable network that will allow iMM to contribute and be part of the leading pack of institutions that could unravel the role of carbon monoxide in health and disease and to the development of a new class of therapeutic agents.



Our Talent

Master Program

The Career Development service coordinates a new program at iMM targeted to master students, aiming to provide specific training opportunities towards a successful scientific career, and to attract the best master students to the iMM labs.

This program includes the dissemination of iMM's master projects/vacancies in an "Open Afternoon", and the attribution of the "Best Master Thesis" Awards.

Instituto de Medicina Molecular | João Lobo Antunes

iMM João Lobo Antunes invites all

1st year Master Students

to the

"Open Afternoon at iMM"

Do you want to do your Master project at iMM?
Then come and check out what iMM has to offer you!

Wednesday 18th APR'18 — 14:30h - 17:30h

Venue Instituto de Medicina Molecular (iMM)

Registration https://goo.gl/E6m6Xs until 6th APR'18

Organisation iMM Career Development Service | imm-careerdev@medicina.ulisboa.pt

"Best Master Thesis" Awards

The winners won a scholarship to visit the Institut Curie, in Paris.

1st Prize
Diana Moita
(Miguel Prudêncio Lab)

2nd Prize
Raquel Lopes
(Bruno Silva-Santos Lab)

3rd Prize
Cristiana Morgado
(Sérgio de Almeida Lab)

LisbonBioMed PhD Program

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.

LisbonBioMed 2018 Class | 5th Edition

Bárbara Pinto Correia

My enthusiasm for knowledge and the human biology led me to pursue a career in science. I started my studies in human biology and found my passion in the research field of neurosciences. When it was time to choose my PhD, I knew I wanted to keep doing reserach in neurosciences, in a top institute.

LisbonBioMed allowed me to increase my knowledge in several fields for two months while I could get to know labs of my interest before committing to a final choice. I am glad I can keep pursuing my academic career at iMM - it is a top European institute with great scientists and a great working environment.

Carlos Ramos

When I graduated as a Pharmacist, from the University of Coimbra, I knew I wanted to contribute to the philosophy “From the bench to the bedside”. This led me to the Research & Development department of the Tecnimede Group. However, I soon realized most current treatments are merely symptomatic, and we know very little about the pathological mechanisms of most diseases. Therefore, it was time to embrace academic research and I saw in the LisbonBioMed PhD program an excellent opportunity to do so. During the first 8 weeks, my colleagues and I were exposed to all the research areas of iMM, but we were also stimulated to get out of our comfort zone through an essay, debates and projects’ design. This created in us a sceptic attitude towards Science and life in general, which unravelled this passion to ask questions and to generate novel hypothesis to answer them. Besides, the scientifically vibrant atmosphere present at iMM, makes it the ideal place to do my PhD. I couldn’t be happier with my decision to apply to this PhD program!

Catarina Tomé

After being forced to give up from my non-talented artistic vein and pursue the scientific academic pathway, I became increasingly fascinated to understand how life works. Both biological and psychological components of life have always been areas of high interest. However, considering it more challenging, I decided to study Biochemistry at the University of Coimbra (Portugal), where I obtained my Bachelor and Master degree. During my academic pathway, initially marked by a huge interest in neurosciences, I became aware of my incapacity to deal with animal experimentation. Therefore, in my master thesis, I went to a group where I could directly study humans and thus I discovered that better than perceiving how life works was to realize how it is kept. Thereby, my passion for immunology emerged. Then, I applied to the LisbonBioMed PhD program at iMM where I had the privilege to be accepted and I am very glad to belong to. Currently, I am developing my PhD project in the Lab, in the clinical immunology field, in order to decipher the interplay between T follicular cells and B cells in early arthritis. At iMM, I have found an excellent scientific environment full of amazing scientists with different backgrounds and so, my experience has been very challenging and enriching .

Cláudia Afonso

I decided to pursue a PhD because I am interested in the process of acquiring and later applying scientific knowledge to solve a specific problem. Being involved in research at a doctoral level also gives me an opportunity to exchange ideas and collaborate with other people, which is important for me to keep moving forward in my training. During my education, I have learned techniques from both chemistry and biology and I consider iMM to represent an ideal place to undertake a PhD precisely due to the integration of many research groups within the same institution, each one contributing with different technical expertise in the wider field of biomedical science.

Filipa Ribeiro

My interest about science during high school prompted me to graduate in Biochemistry at the University of Coimbra. During this time, the passion about research in biomedical sciences kept growing , and I started a MSc in Biomedical and Molecular Sciences Research in King's College London. After this enriching experience, I became absolutely certain that I wanted to pursue a research career in biomedical sciences, where I could make meaningful contributions to human health. However, although it was a great experience in London, I wanted to come back to Portugal and undoubtedly iMM was the best place to enroll in a PhD program. iMM not only provides an excellent training in biomedical research, but also encourages the interplay between basic and clinical science which is aligned with my career prospects.

Inês Faleiro

I did not know that I wanted to be a scientist while growing up but watching my mom and aunt doing science experiments inscreased my curiosity about this exciting field. Driven by the wish to pursue a scientific career, I decided to take a bachelor's degree in Molecular and Cellular Biology from the NOVA University of Lisbon and later a MSc degree in Biopharmaceutical Sciences from the Faculty of Pharmacy of the Lisbon University. The idea of learning something new every day and contribute for the creation of knowledge could not be more thrilling and stimulating for me. The decision to pursue a PhD came as a natural next step to continue the search for answers to the biological questions that intrigue me the most. The dynamic and highly productive research environment of the iMM was enough to convince me that it is the ideal place to achieve my goals.

Joana Ribeiro

After completing my Master's in Cell and Molecular Biology at University of Porto, I became aware of how limited my scientific knowledge still was. I also realized I truly liked neurosciences. So, I decided to embark on the PhD adventure, to continue learning about the brain, but keeping in mind the possibility of exploring other fields in biomedical research, I decided to embark on the PhD adventure. When trying to decide which programs to apply for, the LisbonBioMed PhD program appeared at the perfect timing. The program got my attention due to its multidisciplinary and flexible nature, promoting contacts with a multitude of renowned scientists from inside and outside of iMM and allowing students to define their career path in accordance with their scientific interests. And so far, it has lived up to the expectations. I have had the opportunity to listen and talk to brilliant minds in a variety of biological and clinical fields, I reinforced my interest in neurosciences and was fortunate enough to design my own PhD project, under clever guidance from my supervisors. I have also encountered some fantastic colleagues and friends with whom I share work, ideas, interests, disappointments, failures, and good-quality free time. Being a PhD student is an arduous journey, but if you are put in the right environment and surround yourself with intelligent, supportive, hard-working, and humble minds, you can most definitely achieve your career and personal goals.

"I have also encountered some fantastic colleagues and friends with whom I share work, ideas, interests, disappointments, failures, and good-quality free time."

Joana Ribeiro

Joana Saraiva

What truly motivates me is to ask new questions and contribute to exciting findings in biomedicine. That is why I did my BSc in Biochemistry and then the MSc degree in Cellular and Molecular Biology, at the University of Coimbra and CNC, where I have received strong research-oriented training. During my master's thesis, I became extremely interested in gene therapy, a field that I continued to pursue afterwards, by working as a research assistant at the Oxford University. Altogether, these experiences gave me the reassurance that the next challenge I wanted to address was to complete a PhD in biomedical research, particularly focused in neurosciences. I realized that the Lisbon Biomed would be the ideal PhD program for me, considering its flexible curricular structure and the stimulating work environment at iMM. So far, this has been an excellent experience. During the first months of the program I got to know several iMM scientists from a wide range of research areas, thus expanding my scientific knowledge and curiosity. Finally, by the end of this module, I joined the group where I am currently developing my PhD work and was given the freedom to design a research project that really motivates me. Therefore, I am glad to have joined the Lisbon Biomed program and to be now part of the iMM inspiring scientific community.

"I joined the group where I am currently developing my PhD work and was given the freedom to design a research project that really motivates me." *Joana Saraiva*

Marta Fernandes

Throughout my years of study, I have become fascinated by biomedicine research as I learned more about the intriguing biological mechanisms responsible for orchestrating life homeostasis or instability. My academic path began with a bachelor's degree in Biochemistry followed by a master thesis on metabolism and neurogenesis, which culminated in a master's degree in Molecular Genetics and Biomedicine. Unraveling the molecular network behind the discovery of new targets for more efficient therapeutic approaches, truly stimulates my mind and kept me striving for a career in Science in connection to translational research. So, the opportunity to unite my interests and a cutting-edge research in an institute of top quality made me step forward to apply for this PhD program. The LisbonBioMed PhD program embraces us with versatility, new challenges and freedom to choose our own scientific path. I am really happy to work on the subjects that ignite my curiosity the most, surrounded by a lot of amazing people and confident that I will get the tools that I need to be a Scientist.

Pedro Ávila Ribeiro

As a medical student at Faculdade de Medicina da Universidade de Lisboa, I soon learnt about iMM and my interest in biomedical research grew, leading me to choose a rheumatology residency at Centro Hospitalar Lisboa Norte. I find rheumatology a thrilling field, where diseases with a complex, not completely understood pathophysiology and a systemic burden bring basic and clinical research into the forefront of clinical activity. Further, new drugs and new data coming from clinical research are changing much of patient care even in a short time span. Being already involved in clinical and translational research at JEFonseca lab, I found the LisbonBioMed program a unique opportunity to devote full-time to research and pursue a PhD project. In particular, I appreciated the interactive, broad-range initial module on critical thinking, where we also met the work of most groups at iMM. As a result, opportunities to collaborate with other labs emerged and I hope this will lead to innovative projects, making the most of the resources available at the Lisbon Academic Medical Center. At iMM, I also found a very supportive group of colleagues, bound by a common goal of developing science but similarly committed to enjoy and making enjoyable our life at iMM.

LisbonBioMed Scientific Retreat

The 2nd LisbonBioMed Scientific Retreat gathered all the PhD students from the 5 editions of the program. During the 2-day retreat, students made a progress report of their PhD work to the Board of Directors and to the External Advisory Board. Presentations included chalk talks from the 1st year PhD students, posters pitch from the 3rd/4th year PhD students, and oral communications from the 2nd/5th year PhD students.

There was time for discussion with our guest Carolina Perdigoto (Associate Editor, *Nature Communications*) about "Scientific Publishing" and "Careers in Science".

LisbonBioMed PhD Vivas

"Kyotorphin and its derivatives: Unveiling routes and targets"
Juliana Rodrigues Perazzo (Miguel Castanho Lab), 23rd January

"Adenosine A2AR in cognitive decline - decoding the molecular shift towards neurodegeneration"
Mariana Temido Ferreira (Luisa Lopes Lab), 29th October

"Reciprocal Regulatory links between Transcription and DNA Damage Response"
Alexandra Coitos Vitor (Sérgio de Almeida Lab), 19th December

PhD Students Activities

PhD Students at iMM 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

The PhD Students' Committee 2018/2019 is composed by 33 PhD students who elected **Mariana Oliveira** (João Barata Lab) and **Elvira Leites** (Vanessa Morais Lab) as the PhD Students' Representatives for 2018/2019.

PhD Students Annual Meeting

The PhD Students annual meeting is the place by excellence where students present and discuss their work with the overall iMM community during three days. Oral presentations are given by students from the 1st and 4th year, while students from the 2nd and 3rd year present a poster. Moreover, students have the opportunity to gain further insight and inspiration for their PhD work from renowned scientists. In 2018, there were four keynote speakers:

Maria Blasco (Telomeres & Telomerase Group, CNIO, Spain)
Thomas Pradeu (CNRS & University of Bordeaux, France)
Suzana Houzel-Herculano (Vanderbilt University, USA)
António Almeida (Hospital da Luz & IPO Lisboa, Portugal)

PhD Students Annual Retreat

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

PhD Students Workshops

The Workshop series is aimed to nurture the acquisition/consolidation of scientific and transversal competences, as well as to explore the diversity of career paths for PhD-holders.

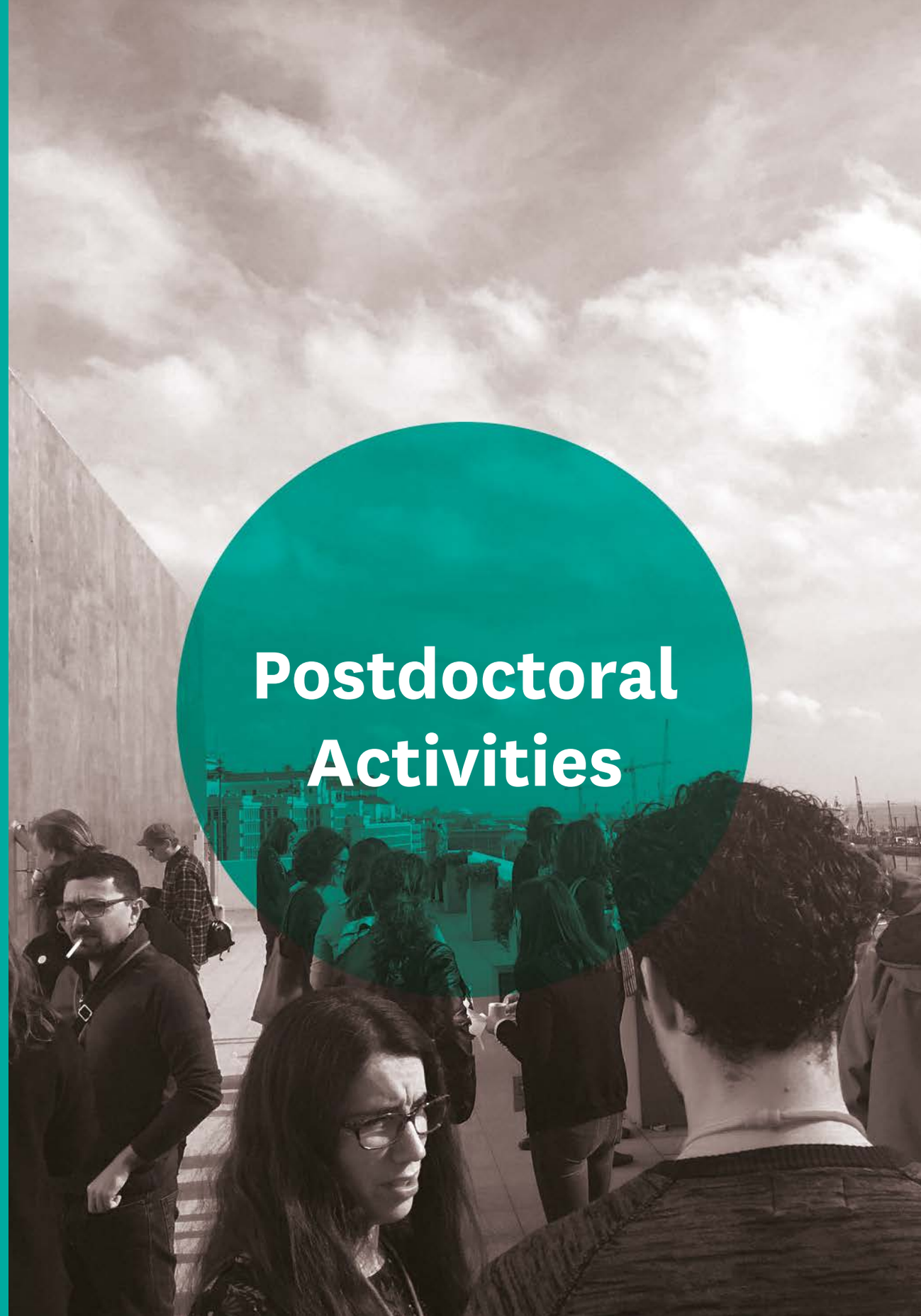
"Graphical design: How to tell a story with a picture" by Gil Costa

"LINK yourself INto the online job market" by Jean Branan (The Scripps Research Institute)

PhD Students Job Shadowing

In 2018, 8 PhD Students had the opportunity to "shadow" a professional in his/her daily tasks in 3 different work environments:

NOVARTIS Bial Daiichi-Sankyo



Postdoctoral Activities

iMM Postdoctoral Association (PDA)

The iMM PDA aims to build community among the institute's Postdoctoral 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 2018:

Bruno Cardoso (João Barata Lab)
Filipa Carvalho (Vanessa Morais Lab)
Helena Nunes Cabaço (Miguel Prudêncio Lab)
Rita Cascão (João Barata Lab)
Sandra Vaz (Ana Sebastião Lab)

Annual Postdoctoral Day

In 2018, this event was organized as a two-day event, in which the first day was totally dedicated to career development workshops:

"Mentoring for career success - mentoring skills"
by Colby Benari (UCL)

"Mentoring for career success - finding a mentor in your network" by Colby Benari (UCL)

"Different techniques of Mentoring"
by Ivo Boneca (Institut Pasteur)

"Science Communication"
by Ana Godinho (CERN)

"How to write a Career development plan"
by Filipa Nunes (iMM)

Lisbon Area Postdoctoral Meeting | PDA

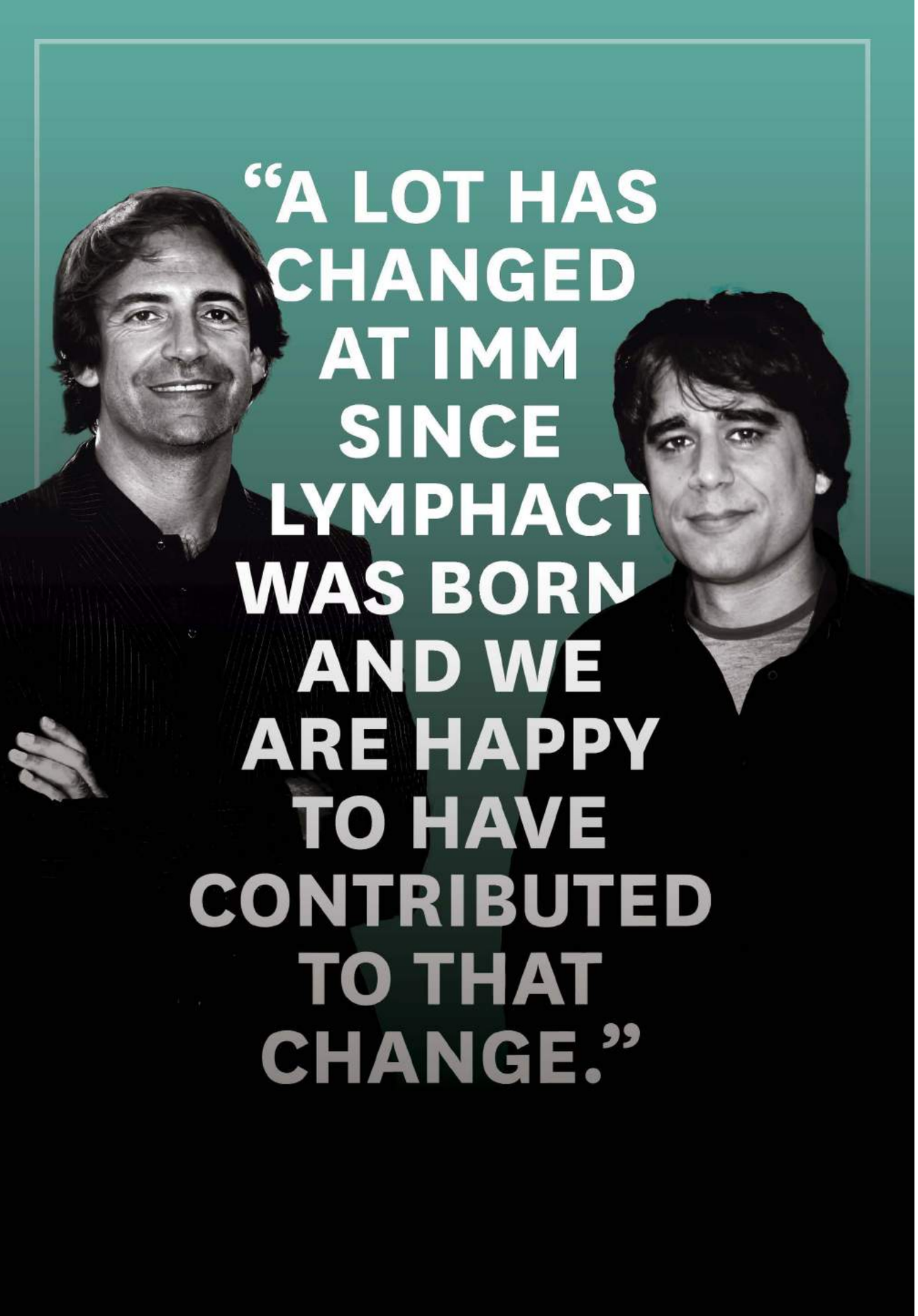
(Annual Cross-Institutional Meeting)

The Lisbon Area Postdoctoral Meeting, at Museu do Oriente, joined almost 80 postdocs from iMM, Champalimaud Foundation, ITQB and UCIBIO/Requimte (FCT-NOVA).
During this one-day meeting postdoctoral researchers had the opportunity to present and discuss their work while establishing strategic collaborations with their peers.

Our Science with and for Society

Innovation at iMM

iMM is a fertile milieu for innovation in its essence. Our strategic positioning in the largest medical research campus in the country gives us the unique capacity of bringing promising biomedical discoveries from bench to bedside. Brilliant scientists work together with leading clinical investigators to understand and treat the most threatening diseases. Our scientific excellence and research infrastructure enable us to nurture innovative ideas at discovery stage and develop them into medical solutions through to a clinical development stage. These conditions also make iMM a very attractive partner to external organizations developing novel medical solutions in industry and academia. All in all, the one and only driver for innovation at iMM is its constant search for new ways of improving human life, using the best combination of internal and external collaborations.



Lymphact

Lymphact's research derived from Bruno Silva-Santos's laboratory at iMM, more specifically from Daniel Correia's PhD studies that led to the initial discoveries of a new type of tumour-killing lymphocytes, later baptized as DOT-Cells. The two scientists founded Lymphact back in 2013, teaming up with Diogo R. Anjos, MBA, an IE Business School graduate. In 2018, Lymphact was acquired by the British company GammaDelta Therapeutics.

What were the fundamental questions that you were chasing when you found this new type of tumour-killing lymphocytes, later baptized as DOT-Cells?

We were investigating one of the multiple strategies used by cancer cells to evade our immune system. We had recently observed that leukaemia and lymphoma cells often stop exposing certain important molecules ("ligands") on their external membranes, so that they become "invisible" to our tumour-killing γδ T lymphocytes that express receptor(s) for those ligands. This leads to the selection of γδ T cell-resistant tumour variants, so we were looking for new ways to improve the tumour targeting by γδ T cells in vitro and in mice, hoping to generate new strategies that could help increase their therapeutic efficacy in clinical trials. With some luck and a lot of work (we tested 2,488 experimental conditions!) we ended up establishing a new protocol for the expansion and differentiation of a new type of γδ T cells ("Delta One T", aka DOT, cells) expressing additional tumour-recognition receptors that were capable of eliminating previously resistant tumours, thus making them a very promising tool for cancer immunotherapy.

How have you decided to start a company using this knowledge and what were the main challenges found in those initial steps, particularly for you as scientists?

We thought of starting a company after we realized we had gathered the most important building blocks: solid data supporting our initial discovery (a solution for an important medical need); having it published in a prestigious scientific journal; having filed a provisional patent application (describing the novel cell type); owing a vast knowledge in the field and excellent track-record; and of course, benefiting from the IMM/FMUL reputation. The final critical element (provided by Daniel), was a strong motivation to pursue a career in entrepreneurship. Daniel had just finished his PhD and left iMM; he being supported by his family. At that time, our scientific activities had stopped; our primary concern was to maintain or patent "alive" – a battle against time to secure the necessary funds.

We lacked expertise in business and financial areas, so it was urgent for Daniel to participate in an Entrepreneurship course at ISCTE (COHiTEC), in Lisbon. The classes were excellent, teaching how to write an actual

Business Plan. However, it was impossible to proceed without someone fully dedicated to the business side, and that was how Diogo Anjos – a team member at the COHiTEC course – joined us (on his way to becoming Lymphact's CEO). Our major difficulty then was to get investors for Lymphact amid a huge international financial crisis (2012-2013)! Thanks to the close collaboration between Lymphact and iMM, we managed to get competitive funding for a project, which allowed us to continue to do research on DOT-cells. When we finally received a positive assessment from Portugal Ventures (P.V., a Venture Capital company), we faced another challenge: the need to find substantial co-investment, which was finally solved with the help of a group of private investors ("Busy Angels", BA). This finally allowed us to guarantee our first seed investment from P.V., together with BA, who became Lymphact shareholders and followed the project until the acquisition on 31st May 2018.

Briefly what was the scientific progress you had since the company has started (in the last 5 years)?

We initially identified a new subset of immune cells with improved anti-tumor properties. However, we had used a rudimentary method to generate those cells. For a feasible industrial application, it was necessary to optimize the methodology as to produce billions of DOT-cells in a large-scale, clinical-grade compatible cell culture system. It took us another 2 years of intense work in the lab (and the above-mentioned 2,488 experimental conditions!) to achieve this, leading to a second patent on the process of DOT-cell production. At the same time, our colleague Afonso Almeida (then working for Lymphact, now in João Barata's lab) performed (and published) the seminal pre-clinical Proof-of-Concept studies in vivo, i.e. using immunodeficient mice bearing human leukaemia and treated (or not) with DOT-cells. This was followed by more *in vitro* and *in vivo* work on other leukaemia types by André Simões, again published in a top journal in the field. Finally, we transferred our technology to GammaDelta Therapeutics (upon their acquisition of Lymphact), aiming for the clinical application of DOT-cells in cancer patients.

What will be the next challenges for Lymphact?

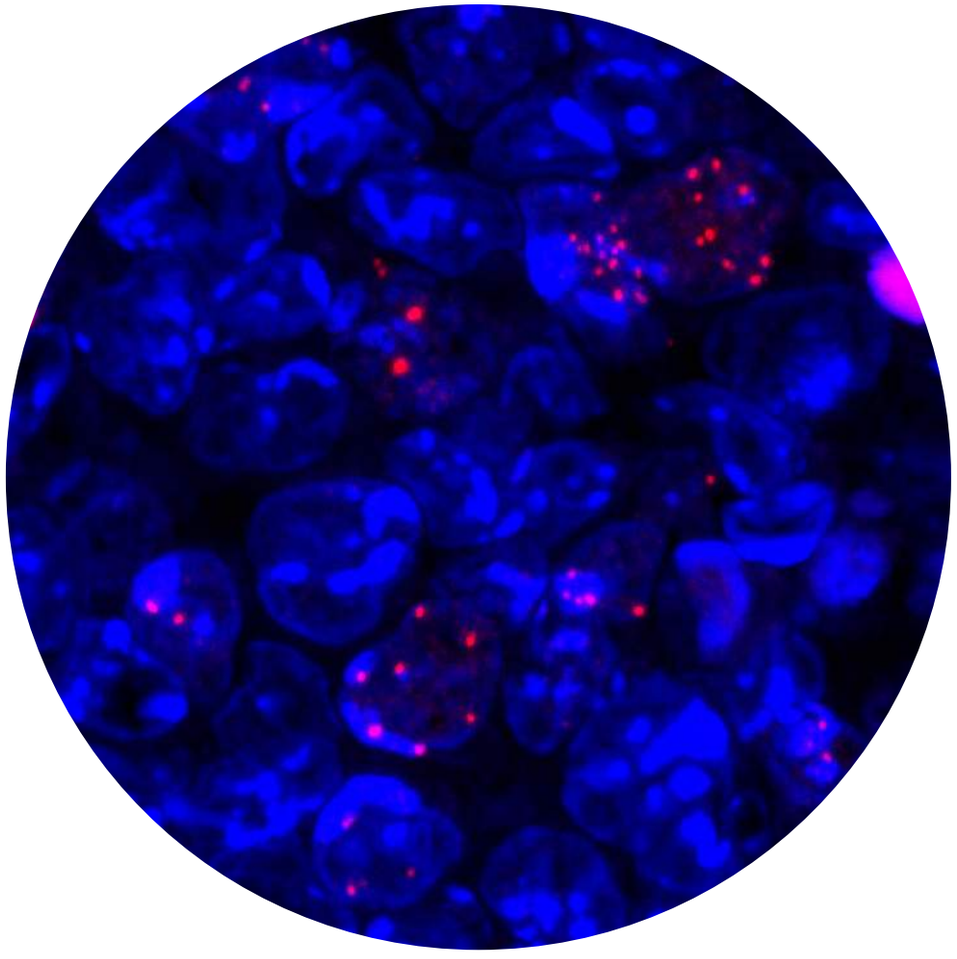
Lymphact was fully acquired by GammaDelta Therapeutics and is no longer under our direct control. GammaDelta Therapeutics must to continue the process development, obtain regulatory approvals and perform clinical trials in cancer (initially leukaemia) patients. Testing the potential of using DOT-cells against solid (instead of haematological) tumours is also in the pipeline.

When and how do you think this technology will help cancer patients?

That decision will be made by GammaDelta Therapeutics. At its current stage of development, our technology could be ready for clinical trials in less than 1 year. Depending on the indication, the therapy could be in the market in 5 to 10 years.

How is iMM using (or could use) Lymphact as an example to foster innovation?

A lot has changed at iMM since Lymphact was born, and we are happy to have contributed to that change. We posed new challenges to iMM, encouraging the creation of new solutions and procedures that are now (to be) used by others. Our success should represent a clear example that it pays off to invest in spin-off startups. To foster more innovation, iMM should adopt a more ambitious and interventive position (now greatly promoted by the recruitment of a Technology Transfer Officer, Pedro Silva), selecting their target teams and supporting start-ups in their early days. This strategy will produce a far more intimate and profitable relationship with its spin-off companies.



A new Technology Transfer Office at iMM

In 2018, a new Tech Transfer Office was created at iMM. Pedro Silva, head of this new structure is starting an ambitious program to boost innovation in the institute.

What are the main challenges and new approaches to be initiated at the institute?

Starting the Technology Transfer Office (TTO) at iMM is an exciting challenge that I was fortunate to be trusted with, and shows the commitment of the Board of Directors to increase the impact of iMM in society.

I came in time to help with the negotiation of the license agreements and research agreement with Lymphact, in parallel with its acquisition by Gamma Delta Therapeutics, a landmark for the Portuguese biomedical industry. You could not wish for a better start than this as a TTO.

Even if I was presented with this important case to kick off, I must confess that I initially thought that my first challenge would be to motivate the research community for technology transfer. The outcome of the interviews with group leaders and heads of facilities was very surprising in this regard, and I could immediately detect several technology transfer cases to work on.

As a completely new function in the institute, our first priorities were focused on 1) establishing professional technology transfer operations, including standard processes, procedures and templates; 2) raising awareness and engaging community in technology transfer activities; 3) assessing individual capacities, motivations and potential for technology transfer; 4) finding sources to fund and grow the TTO structure and activity. I think it is fair to say that since we started in May, most of our efforts have targeted the internal community.

After creating the necessary internal conditions to start the TTO activity, we could focus on the main challenge that we face - to bring discoveries that are mostly at very early stages of development closer to the market. We have to acknowledge that the chances to bring biomedical innovation to market are very small, and that the process of moving early stage discoveries to market is particularly risky, complex and costly. Very few organizations are capable of doing it alone. This challenge is even greater in Portugal with the absence of a strong pharma and biotech industry.

To face this challenge adequately we have to act at both internal and external level. At an internal level, we are working on reinforcing our relationship with our shareholders and partners - the Faculty of Medicine of the University of Lisbon (FMUL) and Hospital de Santa Maria, with a view at creating an integrated innovation environment. Specific measures to create a continuum between basic and clinical research should also increase our capacity to bring innovation closer to market. In addition, we need to be able to identify, protect (whenever possible) and develop the

most promising ideas for new therapeutic or diagnostic solutions.

At an external level, we are actively working under an open innovation approach to tap into the necessary resources needed to move our internal innovation faster to the market, on one hand, and to identify opportunities to collaborate in innovation programs led by external organizations, on the other hand.

The participation in leading EU innovation and translational research platforms is key to these aims. We are now a member of EATRIS, the European Infrastructure for Translational Medicine, and a full partner in the first Open Innovation Test Bed funded by the EC to support nanomedicine development. This participation will position ourselves as a partner of industry in the preclinical and clinical development of new medical solutions.

Opportunities to partner industry are also facilitated by our presence in the most important international biotech industry partnering events. Last year we attended BIO-Europe and MedFIT to identify and discuss new collaboration opportunities.

At a National level, we are building stronger links with the local pharma and biotech industry, as well as with investors, accelerators and trade and investment agencies active on life sciences.

And new plans and future perspectives for innovation at iMM?

Besides our ongoing work to bring active cases closer to market and to start new collaborations with external organizations in industry and academia, our immediate plans for the future include improving the technology transfer policies (including intellectual property and start-ups) and making sure that these policies are known and understood by everybody.

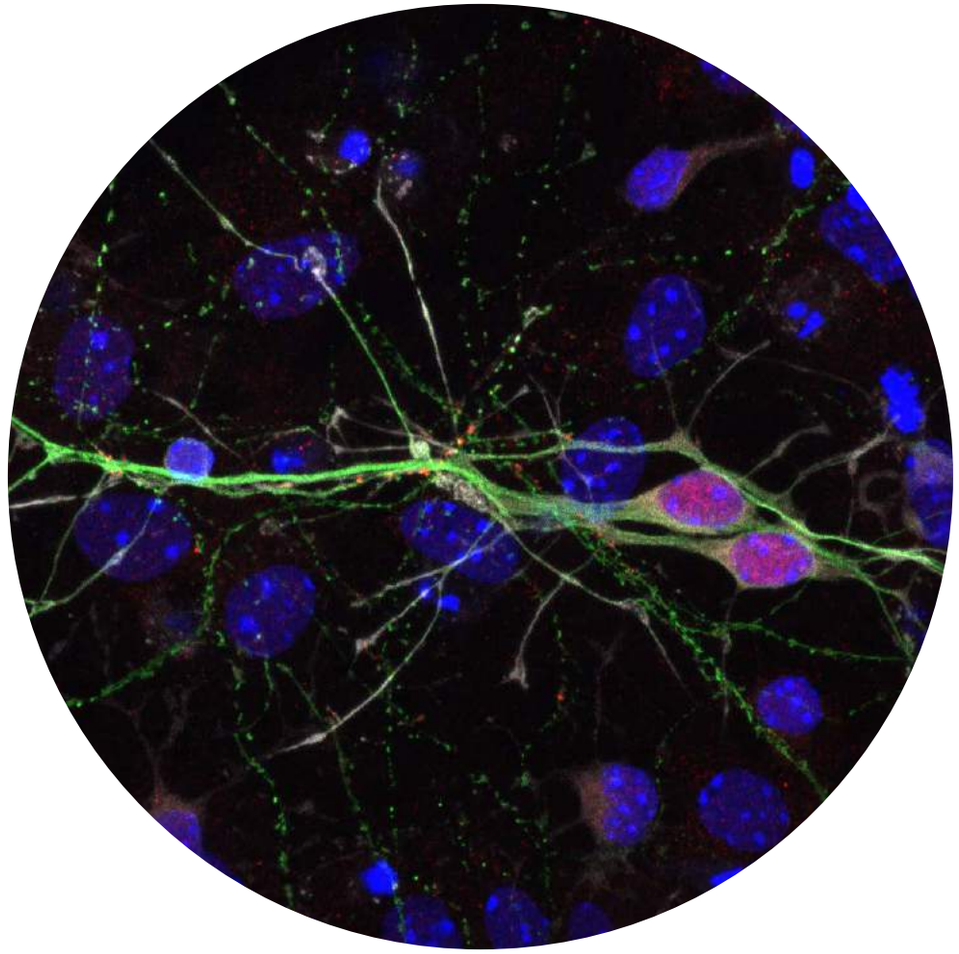
We also plan to organize more technology transfer events to not only foster innovation and entrepreneurship, but also to increase the awareness regarding important technology transfer issues. To increase our attractiveness to industry and other external partners, we also plan to complete the mapping of our research capacities in 2019. This action will result in a catalogue of capacities following industry standards, meaning that capacities will be listed according to the main stages of development and therapeutic areas.

Our participation in EU innovation support platforms is expected to grow with our involvement as a full partner of the European Nanomedicine Characterization Laboratory (EUNCL), the key reference infrastructure supporting nanomedicine developers at preclinical stage. Similarly to the Open Innovation Test Bed, the TTO will lead the business development activity of EUNCL. The participation in these platforms helps us to grow and fund our team and operations too.

Longer term we have ambitious plans to improve our capacity to foster innovation. We want to be able to increase our capacity to fund and run successful proof-of-concept programs to bring our promising ideas to investment-ready stage.

Our future perspectives are very positive.

Our IP portfolio is growing steadily with 19 new inventions identified, 26 patents filed (in 13 different countries), and 6 patents licensed to companies. 6 start-up companies are being formed to exploit IP assets, and we are very excited to intensify our support to some of them through equity positions. To bring iMM ideas and capacities closer to the market, 57 collaborations with external organizations were supported, including 49 collaborations with industry. As a result, 23 collaborations are already active.



iMM Summit

iMM Summit is an event to bring iMM science and research closer to the market. iMM Summit is a networking event that wants to match scientific and research capabilities with market needs. Industry have the opportunity to learn more about the exciting science performed at iMM, whereas our research community is exposed to market trends and partnering opportunities offered by industry.

The first edition of the iMM Summit, organized in November 2018 had the participation of 138 people and the presence of 14 companies. During two days, iMM scientists and entrepreneurs, industry representatives and policy makers had the opportunity to share ideas and discuss possible partnerships.

"The goal of these events is to enable the discussion of new partnerships between our research community and industry. Since Portugal has a very small pharma and biotech industry, and the decision centres of big pharma are not in Portugal unfortunately, we thought that it would be important to organize an event to bring people from the global innovation centres to Portugal. Having direct access to this people should increase our chances of establishing strong long-term partnerships with industry." – Pedro Silva, TTO.

iMM Summit

Building partnerships between science and industry

Institutional partnerships

Ablynx
www.ablynx.com

Albumedix
www.albumedix.com

Almirall
www.almirall.com

AMGEN
www.amgen.com

Astellas Farma
www.astellas.com.pt/

Astrazeneca
www.astrazeneca.pt/

BAYER
www.bayer.com

Bristol-Myers Squibb
www.bms.com

Bial
www.bial.com/pt

Budapest University of Technology and Economics
www.bme.hu

Celgene:
www.celgene.com

Centro Académico de Medicina de Lisboa

Centro Hospitalar Lisboa Norte/Hospital de Santa Maria
www.chln.min-saude.pt

CHDI Foundation
www.chdifoundation.org

Cytokinetics
www.cytokinetics.com

EHDN
www.ehdn.org

EMBO
www.embo.org

Fundo iMM-Laço
www.fundoimmlaco.pt

Genomed
www.genomed.pt

Harvard Medical School - Portugal Program
www.hms.harvard.edu

Health Cluster Portugal
www.healthportugal.com

Hovione
www.hovione.pt

iBET
www.ibet.pt

Janssen
www.janssen.pt

Liga Portuguesa Contra o Cancro
www.ligacontracancro.pt

Lymphact

Malaria Vaccine Initiative (MVI)
www.malariavaccine.org

Medtronic
www.medtronic.pt

Merck
www.merck.com

Merck Sharp & Dohme
www.msd.pt

NOVARTIS
www.novartis.com

Otsuka Pharmaceutical Co, Ltd
www.otsuka.co.jp

PFIZER
www.pfizer.pt

PureTech Health
www.puretechhealth.com

Roche
www.roche.pt

RoPlaVac

Rotary Club
www.rotary.org

Technophage
http://www.technophage.pt/

Theranostics
www.thno.org

Servier
www.servier.com

UCB Pharma
www.ucb.com

Universidade de Aveiro
www.ua.pt

Outreach

Scientists at iMM work in areas important to human health, such as oncology, infectious diseases, neurodegenerative diseases, among many others and they are keen to understand the mechanisms that lead to these diseases, finding clues to better diagnosis and new treatments. Since these themes are absolutely relevant to society it is of the outmost importance to make the research developed at iMM more perceptible and increase the involvement of people with science. A structured program promoting a two-way communication between scientists and citizens is currently being developed and implemented at iMM.

Let's take science to the streets!

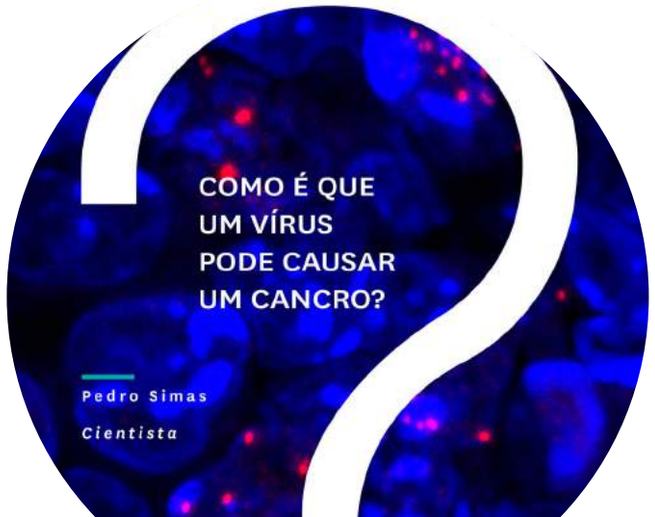
iMM Scientists and their questions invaded the city of Lisbon with an awareness campaign

In 2018, it was developed a major public awareness campaign with the motto "There is no great question without a great answer", that focused on the continuous chasing of questions that scientists at iMM pursue. This campaign targeting the general public was divided in several actions disseminated in newspapers, national television, social media, and locally in the Lisbon area as a mean to create a proximity to the local, national and international community. "Why is there still no vaccine against malaria?", "How does breast cancer appear?", "What does chocolate do to our brains?" were some of the questions included in the graphical artworks produced to illustrate the research outputs of the scientists and the ongoing international projects at iMM. The artworks were disseminated through the 49 digital advertising billboards present in the streets and metro stations of the city of Lisbon. During four weeks, the citizens and visitors of Lisbon were able to visualize and interact with these signs. Simultaneously, the videos and graphical outputs were disseminated through the institutional social media channels. "Unleashing curiosity about the images of science and the questions we are working on were the starting point for bringing scientists closer to the common citizen. Each outdoor had a specific QR Code linking scientific images to short videos with our scientists", explains Maria M. Mota, Executive Director at iMM. Together with this, a multimedia spot hired on prime time of two Portuguese national TV channels reaching.

This campaign was also highlighted in the Portuguese media, including the magazines Briefing, Meios e Publicidade, the TV news programs Edição da Manhã SIC, Diário da Manhã TVI, and a radio show Prova Oral Antena 3, increasing the reach and impact of these actions.

Also, a Societal box was created. This box includes some of the graphical materials used for the campaign and has been distributed to representatives of different stakeholders (patients associations, industry, teachers and students, civil organizations, politicians). This combined approach optimised the resources available and increased the global benefits of the campaign, creating tools that promote the visibility of the research done at iMM.

It was the first time that a campaign of this kind was launched in Portugal, impacting the perception of the public on the work of scientists.



Science in Schools and Events

Schools:

School visits to promote the science developed at iMM and to create awareness about the importance of the work of scientists to a younger audience. In 2018, 209 students and 22 teachers from 11 schools visited the iMM.

Outreach Events:

iMM has participated in the European Researchers' Night 2018 at National Museum of Natural History and Science in Lisbon with a joint activity of 6 research groups and 1 technical facility (João Barata Lab; Gonçalo Bernandes Lab, Miguel Castanho Lab, Vanessa Morais Lab, Luisa Lopes Lab, Maria Mota Lab and the Bioimaging Unit)- A city called "Cell". We cannot imagine a city without hospitals, post offices, courts, firemen, police, theaters and cinema and a transport network. Similarly, a cell cannot exist without its basic structures: the nucleus, the cytoplasm, the mitochondria and the cell membrane. In this activity, visitors observed different cells and the structures that compose them under the microscope. Visitors also bet their luck in a game that travelled within this city and discovered how the cell's energy center works - the mitochondria, how neurons communicate, what happens when something stops working, as in cancer and how chemical compounds are mixed to produce drugs.

Fundraising

Science is the engine of our society's development and discoveries are always at a specific question of distance. This is the driving force of our scientists and together we shall leave a legacy for the future. It is our ambition to involve the society towards a future with science.

Fundo iMM-Laço

On the Way to a Cure

Breast cancer is the most common cancer in women around the world. Each year, there are more than 6 000 new cases of breast cancer, only in Portugal.

In 2015, the Fundo iMM-Laço: On the Way to a Cure was created to support breast cancer research projects and bring hope to thousands of women who are diagnosed with metastatic breast cancer. Also, Fundo iMM-Laço provides information about metastatic breast cancer through its website, social media and through awareness campaigns. The fund annually supports new research projects, each worth € 25,000.

100% of the funds come from fundraising campaigns and donations to Fundo iMM-Laço, including the contribution of individual citizens and the support of partner entities. The existence of this fund is only possible as a result of the numerous initiatives that take place throughout the year and that allow raising funds for this cause.

Since 2015, eight of the iMM scientists were supported by the Fundo iMM-Laço Annual Grant.

In 2018, three new research projects were supported by Fundo iMM-Laço:

Sofia Mensurado | PhD Student
at Bruno Silva-Santos Lab

Manipulation of methionine intake to promote the effectiveness of immunotherapy in breast cancer

T lymphocytes are the cells of the immune system with the greatest ability to kill tumor cells. However, the tumor is able to render them ineffective through the action of inhibitory molecules that function as “breaks” of the T lymphocytes. These blockers are now used, which allows the T lymphocytes to re-kill cells tumor. This therapy has revolutionized the treatment of cancers such as lung and melanoma, however, in patients with breast cancer its effectiveness is greatly reduced. This project aims to realize how diet can improve the performance of the immune system in response to breast tumors, especially in combination with blockers of inhibitory molecules. Preliminary results show that its efficacy improves substantially when the diet is supplemented with an amino acid-methionine. Funding from the iMM-Laço Fund will allow us to see if this phenomenon happens only with this component of the diet or with others, and what the cellular and molecular target of this combination therapy. We hope to find a diet that helps improve the response of breast cancer patients to established therapies.

Rui Martinho | Visiting Scientist
at Maria Carmo-Fonseca Lab

Accelerating the development of new therapeutic strategies for the treatment of breast cancer

The stability of a cell’s genetic information is essential to its proper functioning. Mutations in the mechanisms of revision and repair of the DNA molecule (where the genetic information is stored) increase the rate of errors, facilitating the development of cancer. It turns out that these mutations also present as a true Achilles heel of this disease, since tumor cells may be especially sensitive to drugs capable of further decreasing the integrity of their genetic information. This project aims to use a model organism (vinegar fly) to identify genes whose inhibition can lead to the specific death of tumor cells, thereby accelerating the future development of new therapies for breast cancer.

Sérgio Almeida | Group Leader

Inducing the selective death of breast cancer cells through the increase of DNA damage

About two-thirds of breast cancers rely on estrogen to develop. However, to activate genes that promote tumor growth, estrogen causes damage to the genome that can culminate in cell death. To avoid this fate, tumor cells have developed the ability to repair these damages extremely efficiently. The goal of this project is to inhibit this ability to repair using specific drugs, so as to induce the death of tumor cells. As estrogen does not induce a significant amount of lesions in the genome of the remaining cells of the organism, we anticipate that our therapeutic strategy is extremely selective, causing only the death of the tumor cells. To test our hypothesis we will use different drugs in cultured breast cancer cells in vitro. Drugs that show the most promising results will then be tested in vivo in animal models of the disease.

The Brain Tumor Team

Running for science

The Brain Tumor Team (BTT) was formed in 2014 to create awareness and to fundraise for cancer research. The BTT has participated in all editions of Corrida Saúde + Solidária, an event organized by the students of the Lisbon Medical School (AEFML), with an increasing number of participants. This year, the BTT team gathered 381 participants that run together the Corrida Saúde + Solidária, held in May 5th. Scientists, physicians, patients, their families and friends participated in the event, running for a cause – the Centro de Investigação de Tumores Cerebrais – a research unit dedicated to brain tumor research.

The donations received in this event enable to acquire equipment for cancer research at iMM.

The scientific community at iMM is deeply grateful to all who have generously supported our initiatives and research projects.

Fundo

João Lobo Antunes

iMM was created in 2002 based on the vision of João Lobo Antunes to nurture the exchange of ideas between those who produce knowledge at the bench and the ones who practice medicine. We believe it is fundamental to include the society in a commitment to the research of excellence developed in iMM. To this end, it was created in June 2018, the Fundo João Lobo Antunes with the aim of attract and retain the best scientists in Portugal, supported by an infrastructure of excellence, competitive internationally, and dedicated to improving the human health.

This is the mission of the Fundo - to engage the society towards a future with science.

Fun moments

Beer Hour

Scientific Retreat

Picnic

Christmas Party