



Instituto
de Medicina
Molecular

João
Lobo
Antunes



2019

iMM

Instituto de Medicina Molecular João Lobo Antunes

Avenida Professor Egas Moniz
Edifício Egas Moniz · 1649-028 Lisboa · Portugal

☎ Phone +351 217 999 411 | Fax +351 217 999 412
✉ imm@medicina.ulisboa.pt
f facebook.com/immolecular
t twitter.com/IMMolecular
in linkedin.com/company/instituto-de-medicina-molecular

Cover

Representation of the main areas of research at iMM in the physiological state. In the back cover, the same areas of research are portrayed with signs of dysfunction. This contrast is an allusion to our aim of understanding biological processes always focusing on their implications in disease.

Credits: Helena Pinheiro, iMM.

Project Concept and Management

iMM Communication
imm-communication@medicina.ulisboa.pt

Illustrations

Helena Pinheiro, iMM.

Group photos

Jorge Figanier Castro
<https://www.jorgefiganiercastro.com>

Design

Botodacruz Creative Studio
www.botodacruz.pt

March 2020

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INTERVIEW WITH THE *Board of Directors*

M. CARMO-FONSECA
PRESIDENT

MARIA M. MOTA
EXECUTIVE DIRECTOR

BRUNO SILVA-SANTOS
VICE-DIRECTOR

At IMM, we chase questions. As members of the BoD what have been the main drivers for your work here at IMM?

The thrill of being challenged by the ambitious young scientists that shape the institute. And the prospect of driving IMM to the helm of international biomedical research.

To make this easier to understand by everyone, what is like to run a successful research institute? How have we reached the status that IMM has now?

The success of an institution relies on its people. The status of IMM today results from the cumulative contribution of all the people that work or have worked in the institute since its inception. A key role of the Board of Directors is to select people, from the scientific group leaders to the supporting infrastructure staff; and to provide the environment for them to thrive individually and as a collective. As directors, we strongly believe that we need to combine our strong motivation and commitment to serve the institution with our creativity and passion for Science.

If we look at a typical year at IMM, what would you highlight? And what 2019 has brought new to the institute?

The core business of a research institute is to advance knowledge. Thus, our priority must be to make scientific discoveries and communicate them to our peers and society as a whole. In 2019, besides new exciting discoveries (**page 94**), we have received two new group leaders (**page 72**), established a tech-transfer service (**page 84**) and, most importantly, obtained funding for projects (**page 19**) that will allow us to chase new questions.

The words written in 2019 will follow us at IMM, in the next few years, driving our science, our talent and our place in society. How do you envision the institute in these 3 pillars?

Scientific discovery is a continuum of interconnected steps, each triggered by a lot of hard work and some delightful moments of inspiration. We aim at recruiting the most talented and creative minds and promoting the success of IMMers, while increasing our visibility and involving the society in discussing the future directions of biomedical research.

Questions for the future. What is worth asking?

As a biomedical institute, our societal challenge is to contribute towards better living. We are still far from understanding well enough how disease develops so that effective treatment and prevention strategies may be developed. And in the limit, how can we act on the ultimate threat to live – ageing.

Thinking forward – what will be the main challenges for IMM in the upcoming years?

Sustainability. 2019 was marked by the completion of an international evaluation to all national scientific structures, led by FCT. We were thrilled with the evaluators' enthusiastic feedback in what concerns the evolution of IMM's position in the international arena, but most importantly, our scientific achievements. However, and in spite of this extremely positive evaluation, the budget attributed by FCT was dramatically reduced in comparison to what we had received until 2019. The reversion of this scenario will concentrate much of our energy, while we will continue to explore new funding options that will be critical to expand the range of action and success of IMM in the upcoming years.



**“AS A
BIOMEDICAL
INSTITUTE,
OUR SOCIETAL
challenge
IS TO
CONTRIBUTE
TOWARDS
BETTER
LIVING.”**

ORGANIZATION & 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 Faculdade de Medicina da Universidade de Lisboa (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 Associated 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

Board 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.

Board of Directors

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

M. Carmo-Fonseca

MD, PhD - President

Maria M. Mota

PhD - Executive Director

Bruno Silva-Santos

PhD - Vice-Director

Finance and Operations Director

Fausto Lopo de Carvalho

Industry Advisory Board

The Industry Advisory Board will provide assistance to the Technology Transfer Office team in the definition of a strategy and action plan to drive innovation at iMM.

Daniela Couto

Biogeneration Ventures Fund

David Malta

Vesalius Biocapital

Isabel Ferreira

Versameb

Miguel Forte

Zelluna Immunotherapy

Pascale Redig

Janssen

Scientific Advisory Board

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

Carlos Caldas

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

Caetano Reis e Sousa

PhD - Francis Crick Institute
London, UK

Yasmine Belkaid

PhD - National Institutes of Health, USA

Paul Peter Tak

MD, PhD - University of Amsterdam
Netherlands

Elaine Mardis

PhD - Institute for Genomic Medicine
at NationWide Children's Hospital, USA

Societal Advisory Board

António Barreto

Chairman

João Filipe Queiró

Graça Franco

Henrique Leitão

Paula Martinho da Silva

Pedro Norton

Diogo Lucena

Domília dos Santos

ORGANIGRAM

Board of Directors

M. Carmo-Fonseca
President

Maria M. Mota
Executive Director

Bruno Silva-Santos
Vice-Director

Technical Facilities

Biobank Unit
Sérgio Dias & Cláudia Faria
Bioimaging Unit
José Rino
Comparative Pathology Unit
Tânia Carvalho
Flow Cytometry Unit
José Rino
Information Systems Unit
Pedro Eleutério
Rodents Unit
Pedro Simas
Zebrafish Unit
Leonor Saúde

Administrative Facilities

Communication Office
Inês Domingues
Human Resources Office
Sofia Vicente dos Santos
Technology Transfer Office
Pedro Silva
Training Hub
Filipa Nunes

Research Labs

Claus Azzalin Lab
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
João Lacerda Lab
Luísa Lopes Lab
Nuno Morais Lab
Vanessa Morais Lab

Maria Mota Lab
Joana Neves Lab
Miguel Prudêncio Lab
Mário Ramirez Lab
Miguel Remondes Lab
Nuno Santos Lab
Leonor Saúde Lab
Ana Sebastião Lab
Bruno Silva-Santos Lab
Pedro Simas Lab
Ana Espada Sousa Lab
Pedro Sousa-Víctor Lab
Marc Veldhoen Lab

Finance and Operations Office

Fausto Lopo de Carvalho

Pre-Award
Joana Costa
Project Management
Madalena Reis
Accounting
Sandra Duarte
Purchasing and Procurement
Alexandre Jesus
Legal
Inês Bilé
Safety and Compliance
Sara Santos

People



665
TOTAL



66%

440
FEMALE



34%

225
MALE



22
NATIONALITIES

514
RESEARCHERS

99
TECHNICAL STAFF

52
ADMINISTRATIVE STAFF

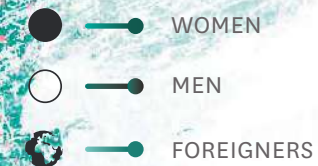
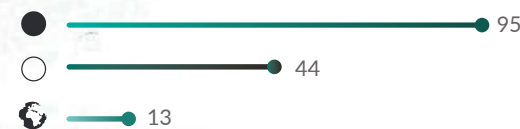
34
GROUP LEADERS



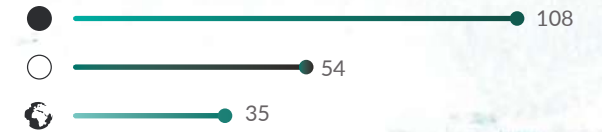
64
MASTER STUDENTS



139
PHD STUDENTS



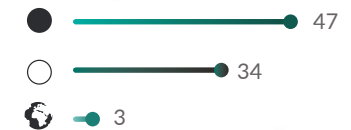
162
POSTDOCS



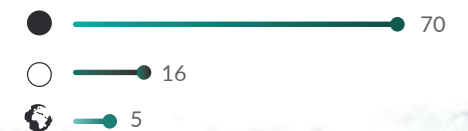
19
TRAINEES



81
CLINICAL RESEARCHER



86
LAB TECHNICIAN
LAB MANAGER
ADMINISTRATIVE TECHNICIAN
JUNIOR PROJECT MANAGER



4

RESEARCH
AREAS

IMMUNOLOGY AND INFECTION
ONCOLOGY
NEUROSCIENCES
CELL BIOLOGY

Productivity AT A GLANCE

2019

435

PUBLICATIONS
IN PEER YEAR
REVIEW

414

INVITED LECTURES
AND SEMINARS

411

COMMUNICATIONS IN
INTERNATIONAL CONFERENCES

102

ORGANIZATION
OF CONFERENCES

374

COMMUNICATIONS IN
NATIONAL CONFERENCES

29

PhD THESIS
COMPLETED

84

MSc THESIS
COMPLETED

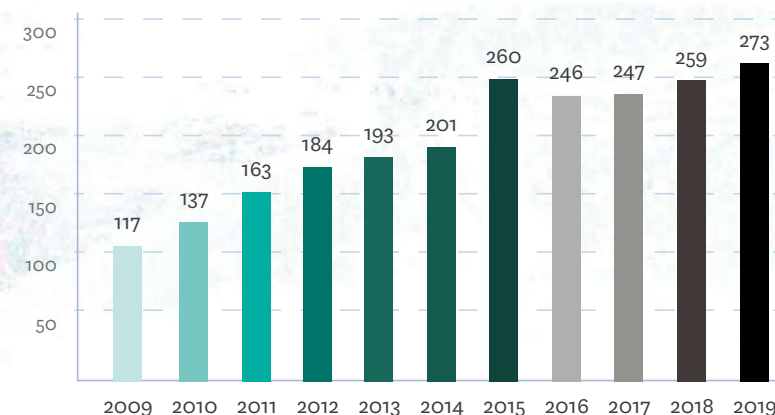
107

PRIZES, HONOURS
AND AWARDS

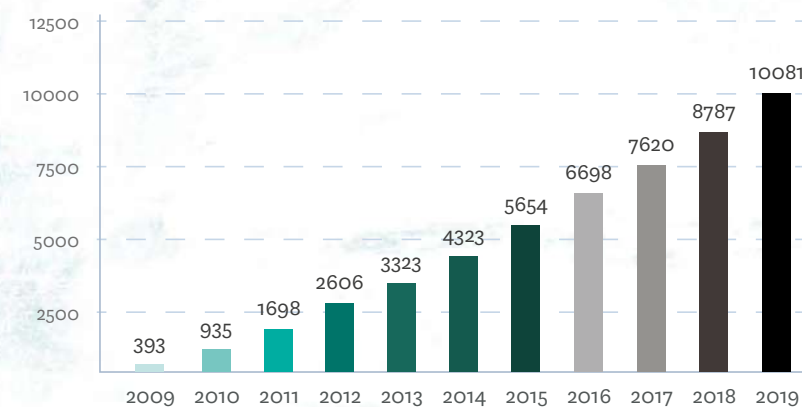
iMM Publications in International Journals

(Source: Web of Science™)

Published Items in Each Year
2009-2019



Citations in Each Year
2008-2018



273

Papers
in 2019

2 280

Papers since
2009

52 745

Sum of the
times cited

22,19

Average citations
per item

91

h-index

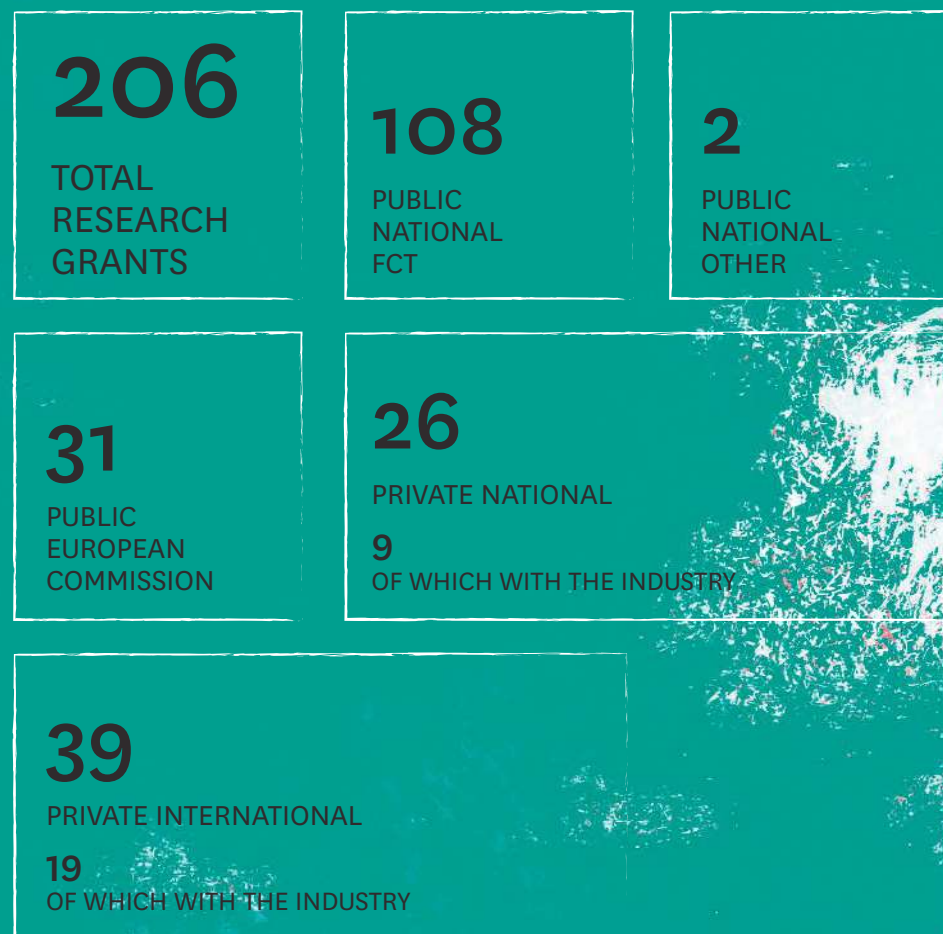


DISCOVER
OUR SCIENCE
IN 2019

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

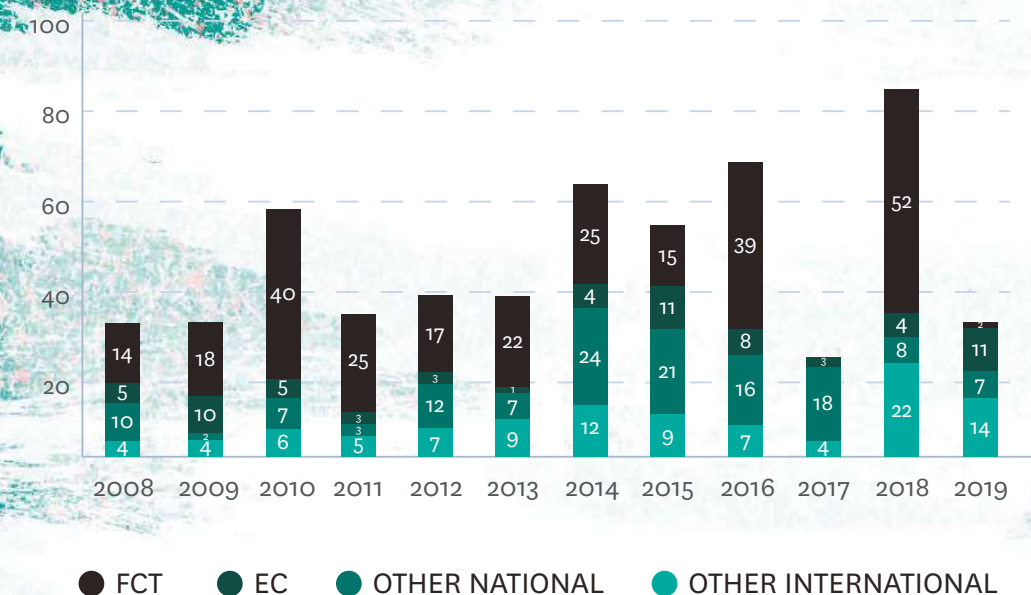
Number of Ongoing Research Grants in 2019



Number of Research Funding Grants in 2019



Number of Research Grants Initiated at IMM from 2008 to 2019



Innovation

We are constantly searching for new ways to improve human life, using the best combination of internal and external collaborations as leverage.

20

NEW
INVENTIONS

2

SPIN-
-OFFS

4

MILLION
EUROS

13

PATENTS
FILED



DRUG DISCOVERY
ONCOLOGY



DRUG DISCOVERY
IMMUNE MEDIATED DISEASES

SUPPORT TO
150
COLLABORATIONS
126 WITH INDUSTRY

INSTITUTIONAL *partnerships*



Ablynx
www.ablynx.com

AB Science
www.ab-science.com/

Albumedix
www.albumedix.com

Almirall
www.almirall.com

Alpine Immune Sciences
www.alpineimmunesciences.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

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

European Commission
www.ec.europa.eu/

European Research Council
www.erc.europa.eu/

FairJourney Biologics
www.fjb.pt/

Fluigent
www.fluigent.com

Fundação "la Caixa"
<https://fundacaolacaixa.pt>

Fundação para a Ciência e a Tecnologia
www.fct.pt

Fundo IMM-Laço
www.fundoimmlaco.pt

GammaDelta Therapeutics
www.gammadeltatx.com

Genomed
www.genomed.pt

GSK Vaccines
www.gsk.com

Gilead
www.gilead.com

Health Cluster Portugal
www.healthportugal.com

Hovione
www.hovione.pt

Exogenus Therapeutics
www.exogenus-t.com

Illumina
www.illumina.com

Ionis Pharmaceuticals
www.ionispharma.com

Janssen
www.janssen.pt

Lilly
www.lilly.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

Oxford Biotherapeutics
www.oxfordbiotherapeutics.com

PFIZER
www.pfizer.pt

Pharmakern
www.kernpharma.com

PharmaMar
www.pharmamar.com

Proterris
www.proterris.com

PureTech Health
www.puretechhealth.com

Roche
www.roche.pt

RoPlaVac

Rotary Club
www.rotary.org

TargTex
www.targtex.com

Technophage
<http://www.technophage.pt/>

Theranostics
www.thno.org

Sanofi
www.sanofi.pt

Servier
www.servier.com

Smartfreeze
www.smartfreeze.com

Stryker
www.stryker.com

Synovo
www.synovo.com

UCB Pharma
www.ucb.com

V-Nano
www.vnanocdm.com

2019 in Review

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



Universidade de Lisboa
Caixa Geral de Depósitos
Scientific Award
Miguel Castanho
and **Luís Graça**
(Group Leaders)



L'Oréal-UNESCO For
Women in Science Award
Patricia Reis
(João Eurico da
Fonseca Lab)

SPBf Young
Biophysicist 2019
Tiago Figueira
(Miguel Castanho Lab)

February

January

Horizontes IMM:
Uma Pergunta a Três

iMM
Postdoc Day

Marie Skłodowska-
Curie Actions Individual
Fellowships
**Marie Ouarné, Rosina
Savisaar and Sara Pereira**



March

Fundo iMM-Laço:
A Caminho da Cura
(2018 Edition
Announced in 2019)
Sérgio de Almeida
and **Marc Veldhoen**
(Group Leaders)



April

Human Frontier Science
Program Fellowship
Mariana De Niz
(Luísa Figueiredo Lab)



iMM Annual Scientific
Retreat in Évora



FAZ Ciência Award
Bruno Silva-Santos
and **Noella Lopes**

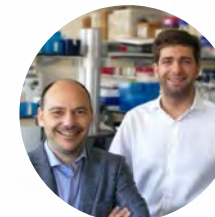


Corrida
Saúde+Solidária



May

Banco Carregosa
SRNOM Award
Luís Graça
(Group Leader)



25 Most Influential
Women of Portugal
(2018 Edition
Announced in 2019)
M. Carmo-Fonseca
(Group Leader)



Aboim Sande
Lemos Award
M. Carmo-Fonseca
(Group Leader)



H2020 ERC Proof
Of Concept
João Barata
(Group Leader)

XIII Annual
CAML PhD
Students'
Meeting



Horizontes iMM:
Uma Pergunta a Três

June

EMBO Member
Bruno Silva-Santos
(Group Leader)



July

August

September

iMM member of EATRIS
(European Infrastructure
for Translational
Medicine)

H2020 ERC
Starting Grant
João Conde

“la Caixa” Foundation
Health and Research
projects
Leonor Saúde
Bruno Silva-Santos
Marc Veldhoen
(Group Leaders)



H2020
Twinning - RiboMed

iMM 15th
Anniversary



October

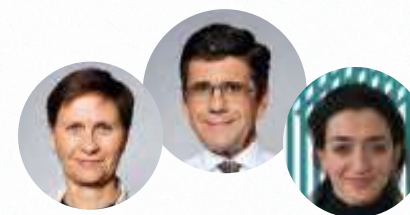
November

December

Chasing
questions :
since 2002

Launching of New
iMM Website

Horizontes iMM:
Uma Pergunta a Três



Gilead Génese Program
M. Carmo-Fonseca,
João Lacerda
(Group Leaders)
and Amelia Trombetta
(Ana Espada Sousa Lab)



H2020
Twinning - SIMICA

Lisbon Area
Postdoc Day



iMM Christmas
Party

iMM Master
Thesis Award
Pedro Ruivo
Catarina Pelicano
Arthur Schneider

HIGHLIGHTS OF *International* PROJECTS



RIBOMED

A new promising influential area in modern biology and medicine is ribonucleic acid (RNA) biology. It has revolutionized molecular biology and will have profound implication for future therapies. The new EU-funded project RiboMed will help IMM establish a strategic collaboration via twinning with partners from already well recognized communities working on RNA biology in the University of Oxford (UK), the Weizmann Institute of Science (Israel) and The Max Delbrück Center for Molecular Medicine (MDC, Germany). In this project, groups organize staff exchanges, experts' visits, common works in laboratories, thematic courses, mentoring, conferences and will work towards translation of basic findings into potential novel biomarkers, RNA-based diagnostic assays and RNA therapeutic targets. This will boost the consolidation of the innovation and entrepreneurship ecosystem at IMM, particularly in the field of RNA biology.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857119.

More information:



SIMICA

Novel aqueous chemistries for the selective modification of proteins have been described in recent years and chemical protein modification has become a key instrument in chemical biology and the drug development processes. The EU-funded project SIMICA is a consortium of IMM with Allcyte (ALLC), an Austrian biotech company, the Leiden University Medical Centre (LUMC), Percuros B.V. (PERC), a Dutch biotech-chemistry company and The University of Cambridge (UCAM). Network will be critical for strengthening the science and technology capacity of IMM in the study of protein drug-conjugates as well as to leverage research excellence and create value. This will be achieved through molecular and chemical innovation with a beneficial outcome for the entire research and development community at IMM.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 852985.

More information:



"la Caixa" FOUNDATION

Bruno Silva-Santos, Leonor Saúde and Marc Veldhoen were three recipients of the four grants awarded in 2019 by "la Caixa" Foundation, in Portugal, under the Health Research Grants program aimed at giving support to groundbreaking projects of scientific excellence, with potential value and a high social impact. IMM scientists will receive up to 1 million euros for three years to develop their research projects in the areas of immunology, regeneration and infectious diseases.

Bruno Silva-Santos, Vice-Director and group leader at IMM, and Professor at Faculdade de Medicina da Universidade de Lisboa, coordinates an Iberian project, in collaboration with the research group of Pablo Menéndez from the Josep Carreras Leukaemia Research Institute, in Barcelona that will receive approximately 1 million euros. This project combines the expertise of the two laboratories to create a novel and more effective approach for the treatment of the deadliest form of blood cancer, the acute myeloid leukemia (AML). This is a cancer where the 5-year survival rate is only 20% and there is an increased need for new therapeutic alternatives to conventional chemotherapy. Immunotherapy, i.e. the manipulation of cells of the immune system, holds great promise to overcome the limitations of these current treatments. By manipulating specific cells of the immune system, the Silva-Santos lab has developed a novel technology based on a specific subtype of anti-tumor T-cells, called Delta One T (DOT) cells which are specific to recognise and kill cancer cells but do not attack the normal host cells even across individuals. These cells have been adequate to be transferred from one healthy donor to cancer patients. Using the additional expertise of the Menendez lab, the project aims to genetically modify these DOT cells by adding a specific antigen receptor to enhance their killing properties and an inducible "safety switch" to guarantee safety. This approach will represent a novel cellular therapy that hopes to be universal, effective and safe for the benefit of AML patients. About the importance of this funding, Bruno Silva-Santos says: "the funding for this project will allow to establish a pre-clinical "proof-of-concept" with concrete applicability in the treatment of a type of cancer that remains a major challenge for current medicine".

Project title: "Next-generation CAR-DOT cells for allogeneic adoptive cancer immunotherapy"

Total Amount: 999,997.00€ | IMM Amount: 500,000.00€

Leonor Saúde, group leader at IMM and Invited Professor at Faculdade de Medicina da Universidade de Lisboa, will receive approximately 450.000 € to coordinate a project that aims to explore the role of senescent cells in spinal cord (SC) regeneration. SC injury in humans renders permanent lesions that have a devastating effect in everyday life due to the lack of SC regeneration. In contrast, there are other species, like the zebrafish, in which SC has the amazing ability to regenerate and recover from injuries, allowing the fish to swim again. It has been shown that both in mammalian and zebrafish, a SC injury promotes proliferation of neural stem cells that reside in the SC. However, in mammals, after a SC injury, the microenvironment around the lesion strongly suppresses regeneration, while in the zebrafish it supports it. In mammals, recent data have shown that senescent cells, which are traditionally associated with cell aging, accumulate in the injured region of the spinal cord, something that does not occur in animals with regenerative capacity such as the zebrafish. Now, the team led by Leonor Saúde wants to explore if this accumulation of senescent cells can be behind the failure of SC regeneration in humans. As Leonor Saúde says: "By the end of the project, we hope to propose the elimination of senescent cells as a new therapy for spinal cord injuries. The cutting-edge technologies and knowledge required for this project will only be possible with this level of funding".

Project title: "SENSe: Targeting induced-senescent cells: a novel approach to promote spinal cord regeneration in mammals"

Total Amount: 444,048.00€ | IMM Amount: 444,048.00€

Marc Veldhoen, group leader at IMM, will receive approximately 500.000 € to coordinate a project that aims to understand and characterize the role of resident lymphocytes, a specific subtype of regulatory cells of the immune system that are located in tissues, not in blood, and which can be important in protecting against infections or tumours. These cells stay at the location of the initial infection and offer swift protection upon reinfection. However, it is still largely unknown how the development of these cells is regulated and how they can contribute to immune protection. Understanding how the presence and function of these lymphocytes residing in tissues can be improved are important questions for the development of new vaccines and can provide valuable insights into immune diseases. The Veldhoen Lab proposes to understand the role of these regulatory cells in the development of tissue lymphocytes and how this knowledge can be used to improve protection (for example, through vaccination) against infections and tumors. About this funding Marc Veldhoen says: “The financing of this project will allow us to investigate the cellular and molecular mechanism that regulates the development of lymphocytes residing in tissues. This will be very important for us to understand how we can better use our own immune system to fight existing and future infections”.

Project title: “ETERNITY: Enhancing Tissue Resident Immunity”

Total Amount: 497,158.00€ | IMM Amount: 497,158.00€





SCIENCE

CHASING OUR
QUESTIONS



Labos **HIGHLIGHTS**



CLAUS AZZALIN LAB

We are interested in understanding how TERRA transcription and chromatin association support telomere elongation in cancer cells. We are also interested in testing the suitability of TERRA and TERRA regulators as novel targets in cancer therapy. This year we focused on how does TERRA associate with chromatin and what molecular mechanisms regulate this association? In this context, we have revealed that a long noncoding RNA can associate with chromatin through invasion of double stranded DNA, independently of ongoing transcription.

Fun facts in 2019

Joint retreat with the laboratories of Teresa Teixeira (IBPC, Paris) and Miguel Godinho Ferreira (IRCAN, Nice) at the Convento da Arrábida (Setúbal).

TELOMERES, LONG NONCODING RNAs AND GENOME STABILITY

cmazzalin@medicina.ulisboa.pt



FIND MORE



JOÃO BARATA LAB

We aim to understand the mechanisms of cancer development and metastasis in order to establish new ways to treat cancer.

We asked how to generate an anti-IL-7RW antibody displaying activity against leukemic cells and we found the answer.

We are now testing new antibodies like this within a European Research Council Proof-of-Concept project.

Fun facts in 2019

All people in the lab love music. So much so that some even released a rock album in 2019.

SIGNALING IN CANCER

joao_barata@medicina.ulisboa.pt



FIND MORE



GONÇALO BERNARDES LAB

We study a range of biological problems through the use of chemistry principles. With an interdisciplinary approach to chemical biology, we develop new reactions that allow to selectively modify proteins for many biological and therapeutic applications.

This year we focused on the development of biorthogonal reactions for the modification and labelling of proteins and the development of new anti-cancer therapies, through the use of chemically-derivatized antibodies and the discovery of new targets of natural products.

Fun facts in 2019

Many achievements for the lab- new babies, postdocs starting new adventures heading new spin out of the lab, or starting as PIs, postdocs getting ERCs, and new exciting discoveries.

CHEMICAL BIOLOGY & PHARMACEUTICAL BIOTECHNOLOGY

gbernardes@medicina.ulisboa.pt

FIND MORE



CARMO FONSECA LAB

We study the role of RNA in the regulation of gene expression in cancer, cardiac and neurological diseases, and we are exploring new therapeutic strategies targeting disease-causing RNA molecules.

This year we focused on further developing the NET-seq methodology to study nascent RNA complexes at genome-wide level.

In parallel, we have been working on stem-cell derived cellular models to study the role of RNA molecules in cancer, cardiac and neurological diseases.

RNA & GENE REGULATION

carmo.fonseca@medicina.ulisboa.pt

FIND MORE





MIGUEL CASTANHO LAB

We study the biophysical principles that govern the interactions of clinically relevant compounds with cell membranes, with the goal of developing new drugs and better understand the mechanism of action of already established ones.

This year marked the kick off of the NOVIRUSES2BRAIN, a project aiming at the development of innovative drugs able to clear several viral species from brain simultaneously, such as Measles, HIV, Dengue, Zika and Chikungunya. Our project INPACT (H2020, MSCA Action, RISE program) was considered a success case model by the funding body, REA – Research Executive Agency, European Commission (Brussels, Belgium).

PHYSICAL BIOCHEMISTRY OF DRUGS & TARGETS

macastanho@medicina.ulisboa.pt

FIND MORE



LUÍS COSTA LAB

We study the most challenging characteristics of metastatic cancer: organotropism, resistance to therapy, and the role of host environment in progression. Our goal is patient-oriented, unravelling new biomarkers and therapeutic options for metastatic cancer.

This year we focused on the analysis of host immune response during metastatic breast cancer treatment and progression. Does (and how) the dynamics of immune cell populations predict/explain progression?

Fun facts in 2019

We found that allowing zebrafish to snack lupine beans (without beer) decreases the size of colorectal tumors!

TRANSLATIONAL ONCOBIOLOGY

lcosta@medicina.ulisboa.pt

FIND MORE





SÉRGIO DE ALMEIDA LAB

We study how cells respond to lesions in their DNA. We use advanced molecular biology and microscopy to dissect the cellular toolbox that heals such lesions, preventing them from causing cancer and other age-associated diseases. Why is a specific group of cells exceptionally resilient to become a cancer cell? Compared with all other cells, these have the extraordinary feature of possessing more than one nucleus.

We therefore aimed at investigating if multi-nucleation is the reason for their cancer resistance. We expect to publish the answer to this question during.

Fun facts in 2019



FIND MORE



MAMEDE DE CARVALHO LAB

We study neurological conditions that affect the brain, spinal cord and the peripheral nerve function, using new tools and testing novel drugs. We aim data integration for extracting new data.

This year we focused on applying new methods for investigating the nervous system, to get original data and finding new associations.

Fun facts in 2019

Our Unit has a new young and productive researcher linked to Faculty of Medicine to increase our scientific output.

TRANSLATIONAL CLINICAL PHYSIOLOGY

mamedealves@medicina.ulisboa.pt



FIND MORE



SÉRGIO DIAS LAB

We study cancer as a systemic disease, meaning how a certain cancer interacts with its “host”. In detail, we study the mechanisms involved in blood vessel formation in cancer and also cancer metabolism.

Perhaps the most interesting question this year was: why do alterations in mitochondria dynamics in breast cancer cells exposed to lipids result in more aggressive behavior and metastasis formation?

Fun facts in 2019

We are working in a terrific environment (institutional and personal), an amazing Institute, doing what we love to do (“to understand cancer”), those are the fun facts of 2019.

VASCULAR BIOLOGY & CANCER MICROENVIRONMENT

sergiodias@medicina.ulisboa.pt



JOAQUIM FERREIRA LAB

We study new therapeutic interventions, mainly neurodegenerative diseases, pediatric, rare diseases and orphan indications. This objective is linked to the development of methodologies for new therapeutic interventions, clinical trials design and outcomes.

This year the most interesting finding was the documentation of changes in the ability to swim in patients with Parkinson’s disease. This fact had not been previously documented and was presented for the first time as a possible marker of disease progression for Parkinson’s disease.

Fun facts in 2019

The international impact of our work demonstrating Bipolar patients have a higher risk to develop Parkinson later. A MSc Thesis of a medical student.

CLINICAL PHARMACOLOGY

jferreira@medicina.ulisboa.pt





JOSÉ FERRO LAB

We study the cause and treatment of stroke.

This year we focused on the potential cardiac causes of cryptogenic stroke and treatments to prevent recurrent venous thromboembolism after cerebral venous thrombosis.

CLINICAL RESEARCH IN NON-COMUNICABLE NEUROLOGICAL DISEASES

jmferro@medicina.ulisboa.pt



FIND MORE



LUÍSA FIGUEIREDO LAB

We study the strategies used by parasites to survive in the host for several years. We focus on neglected tropical diseases caused by African trypanosomes.

Our most important finding was that when parasites (Trypanosomes) fail to have a coat made of a single type of protein, they become more susceptible to the host defenses. This finding opens the possibility of new therapeutic interventions.

Fun facts in 2019

The first baby from members of the L Figueiredo lab was born.

BIOLOGY OF PARASITISM

lmf@medicina.ulisboa.pt



FIND MORE



PAULO FILIPE LAB

We study how two types of innate immunity cells, namely macrophages and neutrophils, modulate the inflammatory microenvironment and disease progression in non-melanoma skin cancers and in psoriasis.

This year we focused on the characterization of the inflammatory infiltrate in non-melanoma skin cancers and on the connections between tumor-infiltrating macrophages and angiogenesis.

DERMATOLOGY RESEARCH

pfilipe@medicina.ulisboa.pt



JOÃO EURICO FONSECA LAB

We study inflammatory joint diseases in order to characterize potential tools for early diagnosis, prognosis and potential targets for novel therapies.

Are sphingolipids a biomarker for rheumatoid arthritis?

Fun facts in 2019

This year we concluded a double blind, placebo controlled, multicentric clinical trial, aiming at answering the question of what is the best treatment option for a swelled finger!

RHEUMATOLOGY RESEARCH

jcfonseca@medicina.ulisboa.pt





CLÁUDIO FRANCO LAB

We study how blood vessels form and function in health and disease aiming at finding new ways to stimulate or inhibit vessel growth and function.

This year we focused on how endothelial cells invade into avascular tissues with an actin-centric perspective.

Fun facts in 2019

This year our lab almost graduated two PhD students on the same day.

VASCULAR MORPHOGENESIS

cfranco@medicina.ulisboa.pt



FIND MORE



EDGAR GOMES LAB

We study how cells distribute their organelles spatially. We have been studying how the nucleus, the largest organelle, is positioned inside cells and how this position affects cell function.

This year we focused on why nuclear position is important for muscle function and how cells can prevent unwanted nuclear movement events.

Fun facts in 2019

We built a 3D printed human adult real size arm to spark curiosity and show the complexity and beauty of the muscular system in multiple public sessions.

CELL ARCHITECTURE

edgargomes@medicina.ulisboa.pt



FIND MORE



LUÍS GRAÇA LAB

We study the regulation of the immune system: we need effective defense against pathogens, but not too much aggression that can lead to harmful consequences to our body.

This year we focused on the regulation of antibody production in healthy people, as well as autoimmune patients. We found that there are dedicated systems to prevent damage arising from unregulated antibody production. It may be possible to use this knowledge to differentiate autoimmune patients more likely to respond to certain therapies.

Fun facts in 2019

After hosting several artists, it was very exciting to see artworks initiated in our laboratory being exhibited. Who would say our cells could be an artwork!

LYMPHOCYTE REGULATION

lgraca@medicina.ulisboa.pt



FIND MORE



JOÃO LACERDA LAB

We study the immune system in patients undergoing hematopoietic stem cell transplantation (HSCT), focusing on the most common complications after HSCT: graft-versus-host disease (GVHD) and infection. Our aim is to improve transplantation outcome.

This year we focused on GVHD and Treg, publishing work correlating the occurrence of chronic GVHD with the presence of naïve and stem cell memory T cell populations after HSCT.

HEMATOLOGY AND TRANSPLANTATION IMMUNOLOGY

jlacerda@medicina.ulisboa.pt



FIND MORE



LUÍSA LOPES LAB

We are interested in understanding the genesis of fast versus slow cognitive decline in aging and whether that plays a role on the susceptibility to neurodegeneration.

This year we focused on describing the alterations of synaptic proteins in glutamatergic neurons throughout aging and how that affects memory performance.

Fun facts in 2019

The news of any award or grant this year came always whenever Luisa was away of the lab. So, now every time she travels, we wonder whether there are good news on the way!

NEUROBIOLOGY OF AGING & DISEASE

lvlopes@medicina.ulisboa.pt

FIND MORE



NUNO MORAIS LAB

We study how aging-associated molecular changes in human tissues increase their proneness to diseases like cancer and neurodegenerative disorders, by developing and using computational biology approaches for the analysis of transcriptomic data.

This year we focused on unveiling an atlas of the gene expression alterations that different human tissues undergo as they age. We are particularly interested in finding the molecular signatures of cell senescence and immunosenescence that we hypothesize to be instrumental in pinpointing novel therapeutic candidates for age-associated morbidity.

COMPUTATIONAL BIOLOGY

nmorais@medicina.ulisboa.pt

FIND MORE





VANESSA MORAIS LAB

We are interested in understanding how the energy producing powerhouse of the cell – the organelle mitochondria – regulates the overall function of the neurons, and what happens to brain homeostasis when this organelle goes astray.

This year we focused on understanding how mitochondria, within the same neuron, have different metabolic needs depending on which cellular compartment it resides. Also, we wanted to understand how mitochondria move and arrest within different compartments of the same neuronal cell.

Fun facts in 2019



MITOCHONDRIA BIOLOGY & NEURO- DEGENERATION

vmorais@medicina.ulisboa.pt

FIND MORE



MARIA MOTA LAB

We continue to be amazed with the biology of *Plasmodium*, the causative agent of Malaria. We aim to elucidate the most fundamental and conceptually innovative questions of Host-*Plasmodium* interactions and hopefully to expose its Achilles' heel(s).

Our long-lasting question – What is so special about the liver? – has taken an interesting direction. Specific features of the mammalian liver metabolism seem to be the key to modulate the ability of *Plasmodium* species that infect mammals to achieve extraordinary rates of replication and generate tens of thousands of new parasites.

BIOLOGY & PHYSIOLOGY OF MALARIA

mmota@medicina.ulisboa.pt

FIND MORE





JOANA NEVES LAB

We aim to understand the molecular and cellular basis of the immune modulatory component of tissue repair and how its dysregulation in ageing and disease can be targeted to optimize regenerative medicine-based interventions. This summer we took the challenge of moving our research across the ocean and establishing the Aging and Tissue Repair joint lab at IMM. The central question of 2019 was how the study of the immune environment during regeneration could be integrated with strategies of stem cell rejuvenation to apply regenerative medicine solutions to aging tissues.

Fun facts in 2019

MANF-eating giant macrophages win the prize for most beautiful cell of the year.

AGING & TISSUE REPAIR

joana.neves@medicina.ulisboa.pt



FIND MORE



MIGUEL PRUDÊNCIO LAB

We study the liver stage of infection by *Plasmodium*, the malaria parasite, aiming at harnessing its potential for the development of antimalarial strategies.

This year we focused on: establishing the impact of an ongoing infection by *Trypanosoma* parasites on a subsequent *Plasmodium* infection; establishing a novel 3D hepatic cell platform for *Plasmodium* infection; assessing the transmission-blocking potential of known insecticidal compounds; and elucidating the role of the EXP1 protein during the various stages of the *Plasmodium* life cycle.

PLASMODIUM INFECTION & ANTI-MALARIAL INTERVENTIONS

mprudencio@medicina.ulisboa.pt



FIND MORE



MÁRIO RAMIREZ LAB

We aim to understand the dynamics of populations of bacterial pathogens and how they respond to selective forces. We focus on the effect of antimicrobial use, human vaccination and host diversity on bacterial populations.

By exploring the relationships between commensal and disease-causing populations of the same bacterial pathogen, we hope to identify particularly virulent clones as well as successful colonisers for further characterisation. A strong bioinformatics effort in bacterial genomics, microbial typing data sharing, data analysis and visualisation tools is ongoing. The development of novel laboratory methodologies for the diagnosis of infectious diseases is also an active area of research.

MOLECULAR MICROBIOLOGY & INFECTION

ramirez@medicina.ulisboa.pt



FIND MORE



MIGUEL REMONDES LAB

We model memory acquisition and goal-directed behavior in rodents as behavioral tasks of variable complexity, during which we monitor and manipulate neural activity in the hippocampus and multiple cortical areas, to dissect mechanisms underlying memory formation and function.

This year we focused on how do neurons keep track of elapsed time in a memory episode such that decisions can be accurate and reward maximized?

NEURAL MECHANISMS OF PERCEPTION, MEMORY & DECISION

mremondes@medicina.ulisboa.pt



FIND MORE



NUNO SANTOS LAB

We study the membranes of human cells, as well as virus and bacteria; the assessment of fibrinogen-erythrocyte interaction as a biomarker of cardiovascular risk; and, the pre-clinical development of membrane-active antimicrobial and anticancer peptides.

This year we focused on how does the fibrinogen-erythrocyte interactions could be assessed as a relevant clinical prognosis biomarker for cardiovascular patients?

Fun facts in 2019

All team members got together and participated in a reconstitution of the movie “The Blair Witch Project”, entitled “The PhD Witch Project”, for the “iMM Got-talent”, during the iMM Christmas party.

BIOMEMBRANES & NANOMEDICINE

nsantos@medicina.ulisboa.pt



LEONOR SAÚDE LAB

We study the mechanisms that allow the spinal cord to regenerate after an injury in an animal like the zebrafish and the mechanisms that inhibit its repair in mammals.

This year we raised the question of whether or not we could use the zebrafish larvae to find new therapeutical solutions for spinal cord injury indications.

Fun facts in 2019

In our lab retreat in the Algarve we all tried a vegetarian diet following the current trend of the iMM.

EMBRYONIC DEVELOPMENT & REGENERATION

msaude@medicina.ulisboa.pt





ANA SEBASTIÃO LAB

We study how endogenous modulators and psychoactive compounds affect synaptic signaling, neuronal excitability, neuronal and glial maturation, degeneration, renewal and repair, under normal and pathological conditions, and it impacts upon behavior.

By focusing on the mechanisms involved in synaptic dysfunction that results from cleavage of the receptor (TrkB) of a neurotrophin, we found out that TrkB cleavage may lead gain of toxic function on the top of loss of neuroprotection. Synaptic plasticity mechanisms that lead to prevention of memory deficits by cannabinoids were also under quest.

NEURONAL COMMUNICATION & SYNAPTOPATHIES

anaseb@medicina.ulisboa.pt



BRUNO SILVA-SANTOS LAB

We study immune cells in tissue (patho) physiology, with a particular focus on gamma-delta T cells, from their development in the thymus to their responses in inflamed tissues, such as tumors or infected organs, but also in neurodegeneration.

Why are gamma-delta T cells present in the meninges of the healthy mouse brain? We found they provide basal levels of the cytokine, interleukin 17 (IL-17), to the non-inflamed brain, which stimulate glial cell production of brain-derived neurotrophic factor, required for neuronal synaptic plasticity in the hippocampus in short-term memory formation.

T CELL DIFFERENTIATION & TUMOR TARGETING

bssantos@medicina.ulisboa.pt





PEDRO SIMAS LAB

We are interested in the association of viral infections with lymphoma. Specifically, what are the molecular mechanisms involved in the interaction virus-cell. If one knows the molecular detail it may be able to discover ways to control and treat.

This year we found that vaccine protection against murine herpesvirus-4 is maintained when the priming virus lacks known latency genes. The significance is that this approach of deleting viral latency genes could be applied to generate safe and effective vaccines against human disease.

HERPESVIRUS PATHOGENESIS

psimas@medicina.ulisboa.pt



ANA ESPADA SOUSA LAB

We study human T-cell homeostasis and immune regulation with the ultimate goal of identifying new strategies for immune reconstitution, using as main clinical models are HIV-2 infection, an attenuated form of HIV disease, and primary immunodeficiency.

This year we asked whether follicular helper CD4 T-cells, a critical subset for the mounting of effective antibody responses, support productive HIV-2 infection. Our results opened new perspectives on the generation of protective germinal center responses that may inform HIV vaccine development.

HUMAN IMMUNODEFICIENCY & IMMUNE RECONSTITUTION

asousa@medicina.ulisboa.pt





PEDRO SOUSA-VÍCTOR LAB

We are interested in understanding the mechanisms of stem cell aging and rejuvenation. Our goal is to devise novel approaches to improve stem-cell based therapies for muscle rejuvenation.

This year we established the Aging and Tissue Repair lab at IMM, a joint venture of two independent group leaders studying stem cell function and immune modulatory mechanisms in an integrated manner. We questioned how a combined approach to the problem of tissue repair could lead to new strategies for the use of stem-cell based therapies in aging.

Fun facts in 2019

100 genetically unique fruit flies and 3 new mouse models traveled land and sea across the US and the Atlantic Ocean to find a new home at IMM.

AGING & TISSUE REPAIR

psvictor@medicina.ulisboa.pt



MARC VELDHOEN LAB

We study how immune cells adapt to environmental changes, such as encountered in tissues and upon infection.

This year we focused on how tissue resident memory T cells are generated in non-lymphoid tissues and how these cells are maintained in these tissues.

IMMUNE REGULATION

marc.veldhoen@medicina.ulisboa.pt



INTERVIEW WITH THE NEW *group* LEADERS:

JOANA NEVES

PEDRO SOUSA-VÍCTOR



Briefly, what are your main scientific interests?

We are interested in the process of aging and the potential use of regenerative medicine as a rejuvenating intervention. Our approach to this problem involves an integrated perspective of the biology of tissue repair, achieved through the collaborative efforts in our joint lab, which includes a simultaneous focus on the mechanisms of stem cell aging (Pedro Sousa-Victor) and on the molecular and cellular changes that occur in the tissue environment of aged organisms (Joana Neves). At this moment, we are using muscle repair as a paradigm to tackle this problem with the hope of developing novel treatments for Sarcopenia, the age-related loss of muscle mass and force that greatly affects the health of the elderly population.

At IMM, we chase questions. What will be the most interesting questions you will chase at IMM?

The overarching question that drives the research in the lab is whether we can use stem cells to rejuvenate old organs. Designing effective strategies to achieve this goal requires us to answer smaller questions: Do stem cells have an aging “memory” and can it be reset? How can we apply immune modulatory interventions to improve regenerative therapies in aged organs? Can we use the integrated knowledge on the process of tissue repair to identify new therapeutic molecules with pro-repair activity?

In 2019, you moved from the US directly to IMM to start your lab – why have you chose IMM?

While abroad for 14 years, we followed closely the progress of scientific research in Portugal and witnessed the development of IMM into the excellent institution that it is today. When we visited in 2018 we felt like a perfect fit. The strategic vision for the institute driven by excellence in research and anchored in scientific freedom and independence was the ideal setting to start our lab. This was topped up by excellent supporting facilities and a vibrant scientific community where we envisioned future collaborations to develop. Finally, pushing forward the translational potential of our work was something we were determined to pursue in our new lab and we felt that in IMM we could have the right kind of support for that next step. We were determined to return to Lisbon, and IMM felt like home.

How does a scientist start a lab?

For us, this is still an ongoing process, but also a natural progression of the ideas and research lines we established in the US. It was back in 2017, while we were writing a review article on rejuvenating interventions for stem-cell based therapies in aging, when we decided that we wanted to have a joint lab that would look at the biology of tissue repair in an integrated manner. We were convinced that this was the best strategy we could follow to have an impact on aging and in the design of successful rejuvenating

interventions. We were fortunate to have a lot of freedom and independence and the opportunity to create a small team and together built on our joint expertise to create the knowledge and tools that became the foundation of what our lab is today. At this point we had the main pillars of a future lab: our question, our innovative approach and our own tools to develop independent projects. Some challenges come after that: packing our flies and mice, moving already established protocols and systems, transposing our ideas to a new environment, ship everything half way across the world and unwrap them to build the Aging & Tissue Repair Lab at IMM.

How will your research impact the institute?

One of our objectives when returning to Lisbon was to contribute to the expansion of research on aging in Portugal. We were lucky to have worked in the vibrant aging research community in the San Francisco Bay Area, and we are convinced that this is going to become a transversal topic

in biomedical research in the coming years. Ultimately, at some point, the question will arise on how aging affects the biological process or disease that you are studying. We hope that the research tools and expertise in our lab will make it easier for other scientists to pose those questions and that our discoveries will drive further interest in the biology of aging. On a different angle, we also envision the application of our discoveries to fields other than aging. It is likely that the new mechanisms of immune modulation and stem cell biology that we are pursuing could be applied in other physiological and pathological contexts giving rise to new collaborations with other IMM scientists.

Questions for the future. What is worth asking?

One interesting aspect about scientific research is that you are never certain of what your next question is going to be. It is the answer to the questions that we are posing today that will create the questions for the future.

“At this point we had the main pillars of a future lab: our question, our innovative approach and our own tools to develop independent projects.”



FINANCE AND *operations* OFFICE

The Finance and Operations Office main purpose is to maintain an extremely agile structure to give the best possible support to the scientific community, viewed as internal clients. The six areas working collaboratively, allow for a unified 360° view of the full science management loop, starting with **pre-award** writing, counselling and application revision to post-award financial and operational follow-up, coordinated by the **project management** team in proximity with the **procurement and purchases** team responsible for maintaining full compliance in procurement alongside with internal **legal** counseling. The

process ends with the **accounting** booking processes and reporting executed by the accounting team.

Finally, all **safety and compliance** procedures regarding lab management are dully integrated in this process as a vital part of IMM's operations infrastructure.

The Finance and Operations Office is also responsible for all audit processes coordination and to assure the liaison with all financing bodies and develops, upon request, specific studies on relevant matters with nationwide impact for the Portuguese scientific landscape.



Finance and Operations Office

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

PRE-AWARD



EXPERTISE

New expertise building on RRI and “Broader impact” - Preparation actions to put in place regarding the starting year of HEU in 2021.

PROJECT MANAGEMENT



EXECUTION

Generate Internal control procedures for budget execution focusing on project long term planning and forecasting.

PURCHASING AND PROCUREMENT



SUSTAINABILITY

Build sustainable long term relationships with main suppliers to become a trusted partner leading to ideal cost/service deals.

ACCOUNTING



COMPLIANCE

Ensure compliance with shorter closing periods and dashboard build-up including a new document management system.

LEGAL



SPECIALIZATION

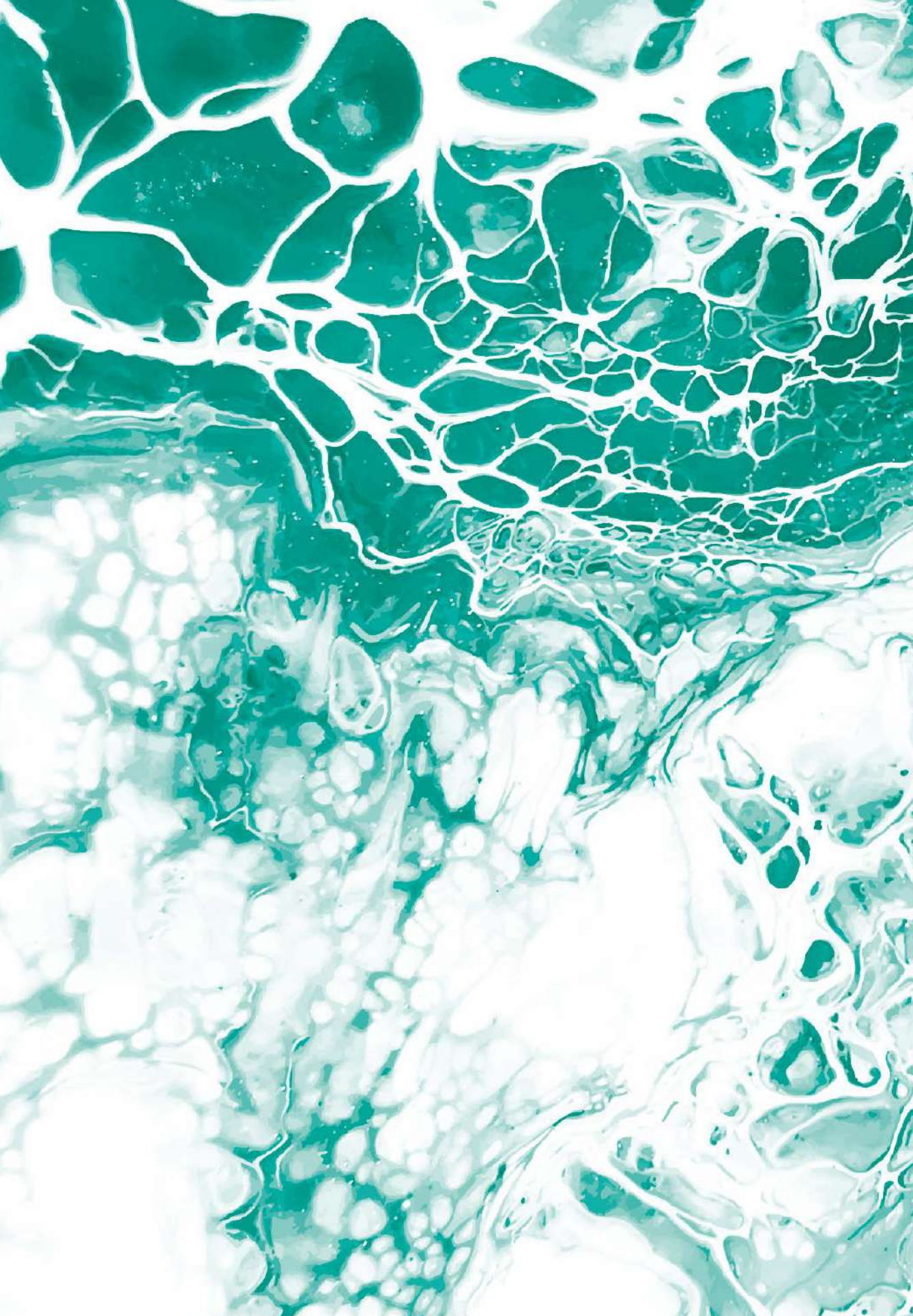
Evolve to a specialization model while streamline the legal process flow focusing on operational precision.

SAFETY & COMPLIANCE

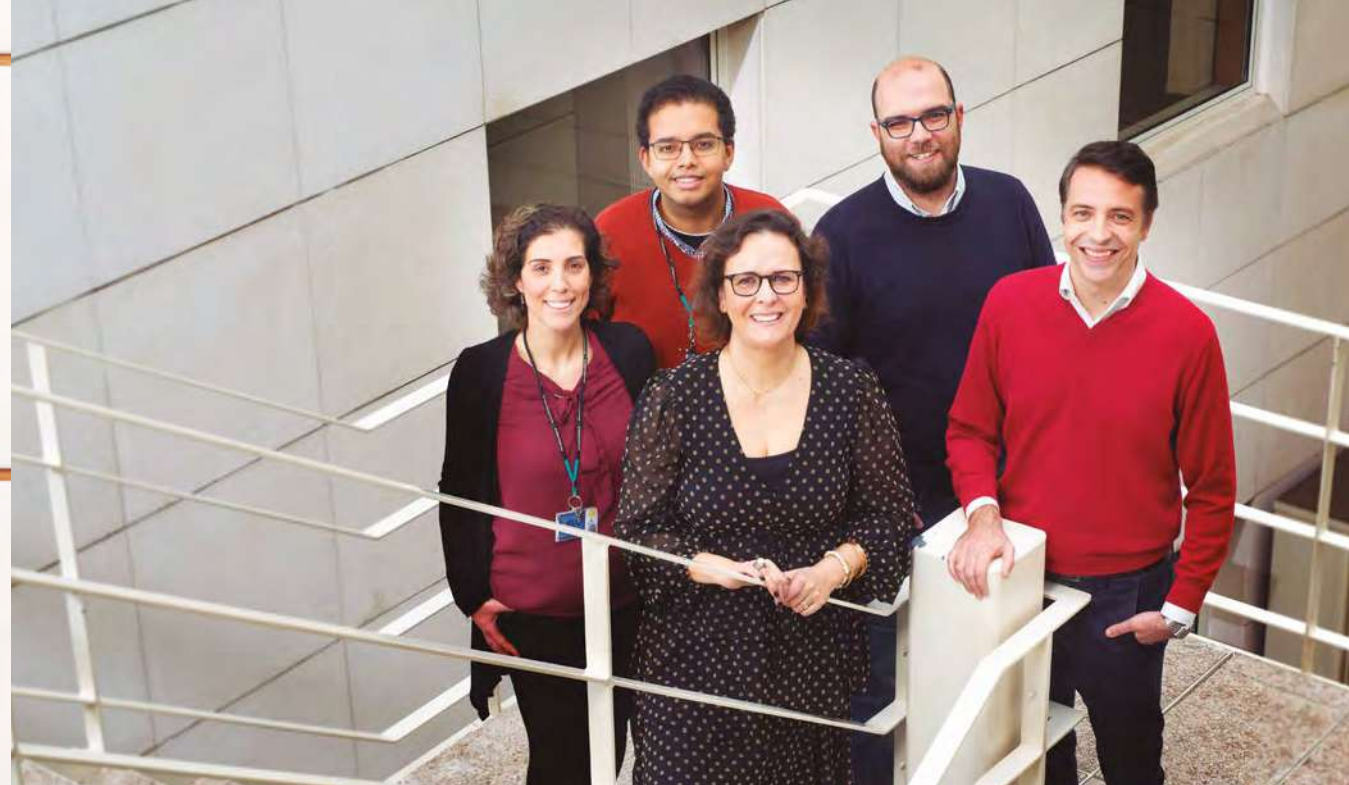


SAFETY

Planning and execution of legal demands on lab safety while ensuring coordination of new equipment set up and lab fit-out works.



Facilities **HIGHLIGHTS**



COMMUNICATION OFFICE

Our mission

Our 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.

What we offer?

We are responsible for the overall image of IMM, our day-to-day activities encompass Media Relations, Science & Society Outreach, Conferences & Events,

Institutional Visits, Awareness Campaigns, Social Media, Internal Communication and Public Affairs Training.

Fun facts about us?

This year we received more than 2430 visitors during school visits, public outreach events, open days and others. For a 1 minute conversation we spoke more than 364 000 words, which represents 7,8% of all the words one can speak on average in a lifetime.

FIND MORE



HUMAN RESOURCES OFFICE

Our mission

Pursuing the goal of becoming an international research center of excellence, our mission is to provide effective human resource management through the development and implementation of policies, programs and services that contribute to the accomplishment of IMM's Vision: "to promote individual freedom and ambition, not a culture of individuality.

What we offer?

Administrative Management; Payroll; Recruitment; Follow-up interviews;

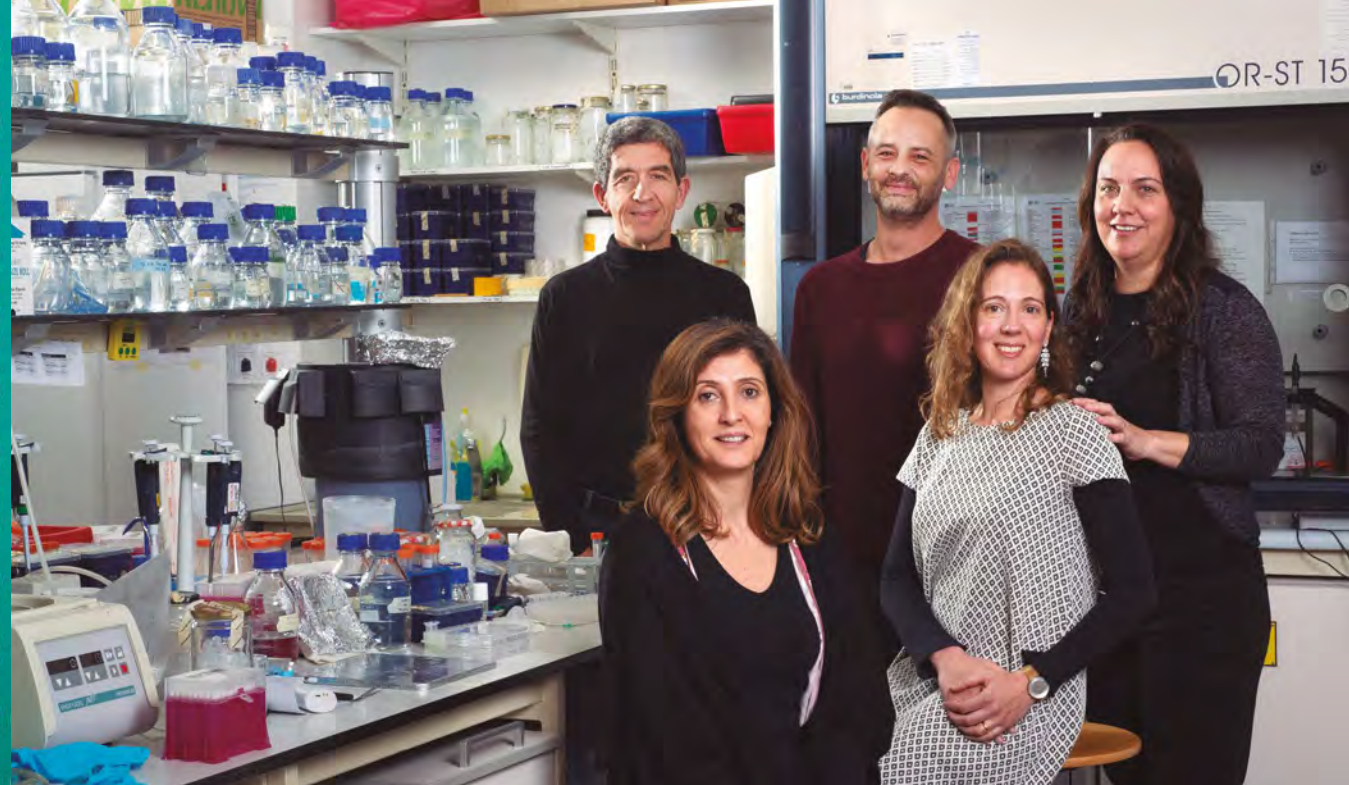
Career Development; Exit interviews; Job interviews and/or oral presentations/ pitches preparation; Conflict resolution; Mentoring; Training.

Fun facts about us?

Throughout 2019, the implementation of All Aboard lunches allowed us to get to mingle with Group Leaders, Heads of Facility and talk about their team's quirks. Truly a memorable and awesome experience!

FIND MORE





TECHNOLOGY TRANSFER OFFICE

Our mission

We stimulate the creation of a favorable environment to foster innovation and speed up the development of promising ideas to improve human life.

What we offer?

We support IMM researchers in bringing their discoveries and inventions to the market.

We support entrepreneurship and start-up creation. We support industry to get access to IMM knowledge and IP.

Fun facts about us?

We struggle to communicate what we do to family, friends (and sometimes scientists too). Any help?



TRAINING HUB

Our mission

Our mission is to provide training opportunities for a successful science-related career to researchers at different career stages (Master/PhD students and Postdocs).

What we offer?

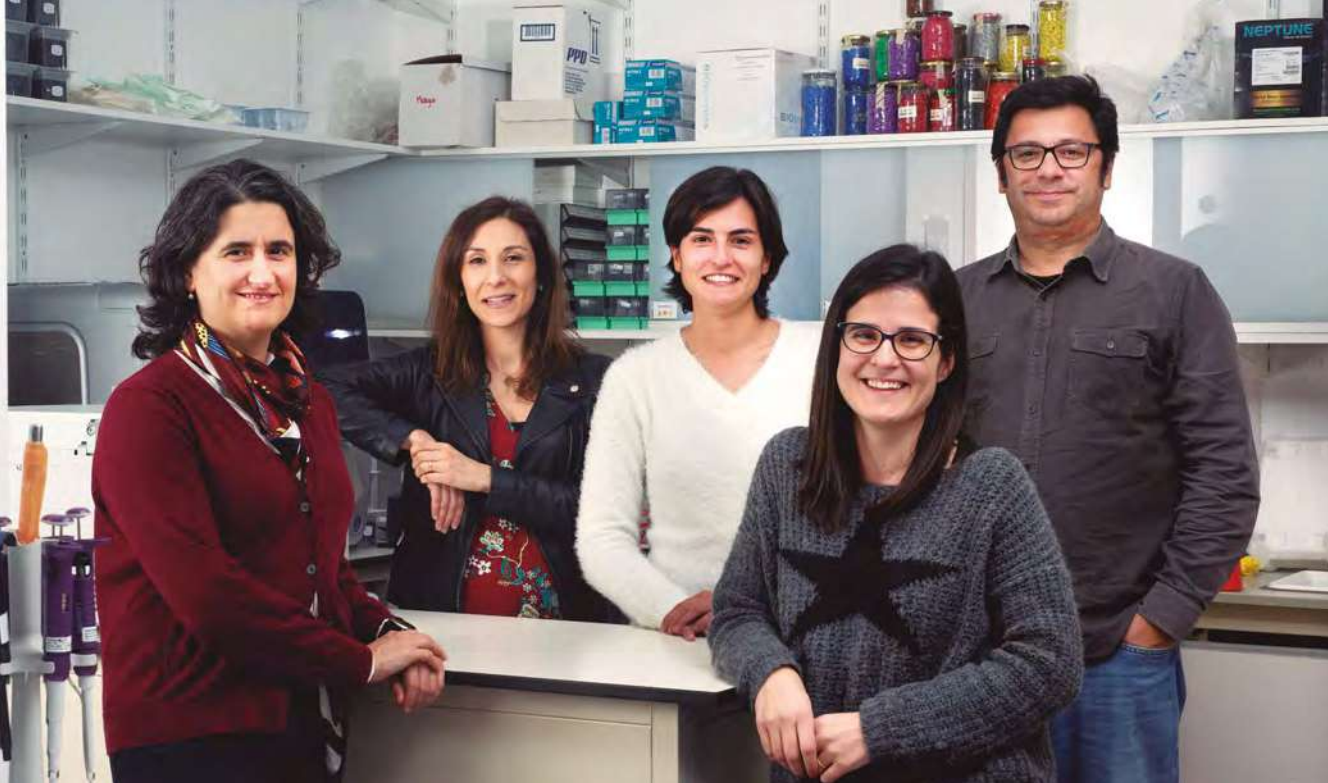
We offer support in the organization of training activities tailored to the needs of IMM researchers, and personalized

reviewing of full applications for doctoral, postdoctoral, and group leader positions.

Fun facts about us?

We serve a community of around 400 researchers – almost 60% of all people at IMM.





BIOBANK UNIT

Our mission

We aim to collect and store a wide variety of biospecimens with clinical information, in order to promote research in diseases with a major impact in health.

What we offer?

- Sample processing according to Good Laboratory Practice (GLP) and Standard Operating Procedures (SOP)
- Nucleic Acid extraction

- Blood Cells (PBMC) Isolation
- Primary cell culture

Fun facts about us?

According to our healthy donor's registry, women (70%) are more generous than men (30%) regarding blood donations.



FIND MORE

BIOIMAGING UNIT

Our mission

We act as a support structure to help and nurture research done with Light Microscopy at the IMM, training and assisting users with excellence in scientific know-how and expertise in Microscopy.

What we offer?

From project planning and experiment design to publishing microscopy data, we offer training and assistance in image

acquisition and analysis, organize courses, perform maintenance and quality control.

Fun facts about us?

We are a multidisciplinary team with biologists, chemists and a physicist. In 2019 our top user spent 1787.5h using microscopes.



FIND MORE



COMPARATIVE PATHOLOGY UNIT

Our mission

We provide histology, transmission electron microscopy and pathology support to scientists investigating animal models of human disease, and scientists/physicians investigating human disease.

What we offer?

We transform fresh and fixed biological samples (cells, tissue biopsies, organs) into thin and ultra-thin sections to be

viewed under a microscope, electron or optical.

Fun facts about us?

We consume alcohol at the rate of 680 beers/year; and paraffin enough to shape a candle the size of Burj Khalifa.



FLOW CYTOMETRY UNIT

Our mission

We aim to provide a state-of-the-art Flow Cytometry service, train users in the adequate use of instruments, on flow cytometry principles, experiment planning, data analysis and interpretation.

What we offer?

Besides providing training in flow cytometry and support to users, from experiment planning to equipment

operation and data analysis, we offer a cell sorting service and maintain all systems.

Fun facts about us?

In one year, approximately 80 billion cells are analyzed in our flow cytometers, one by one, at an average rate of 5000 cells per second. 30 billion of them in the two sorters we operate.





INFORMATION SYSTEMS UNIT

Our mission

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

What we offer?

We offer IT support to iMMers, managing the infrastructure that stores, processes and protects research data, and taking

care of information systems to facilitate scientific and management processes.

Fun facts about us?

We registered a total of 3018 support request tickets in 2019.

We play football every day after lunch.



RODENTS UNIT

Our mission

To support scientific projects associated with animal experimentation, working towards a state-of-the-art animal-based research while maintaining the highest standards of animal welfare.

What we offer?

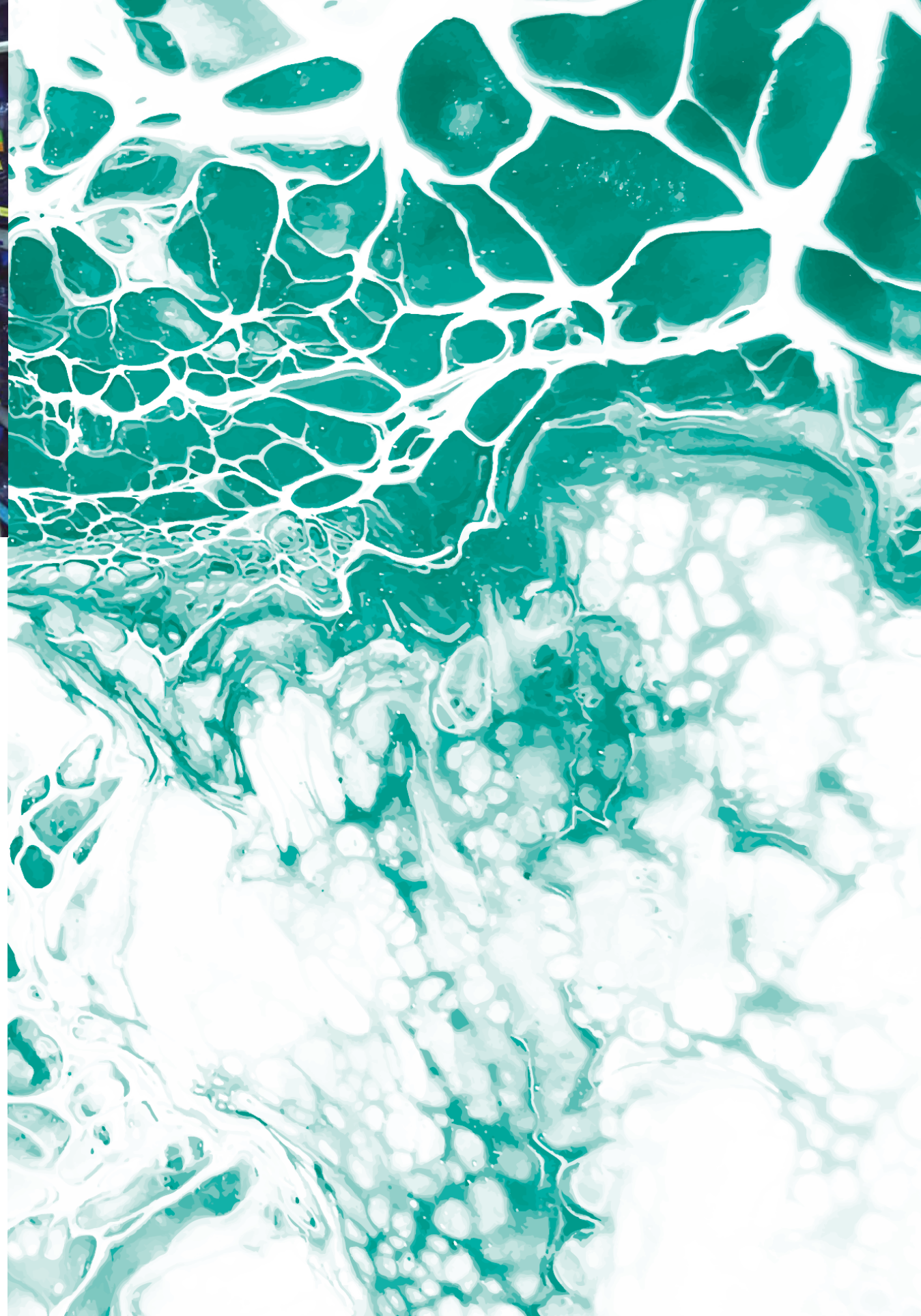
Housing and care of laboratory rodents, training and education in Laboratory Animal Science, sperm cryopreservation

services, colony management and experimental support for ongoing projects.

Fun facts about us?

We are a multicultural team, with people from five nationalities.





ZEBRAFISH UNIT

Our mission

We provide scientific and technical support to researchers on the use of zebrafish (at larval or adult stages) for biomedical studies.

What we offer?

We provide regular maintenance of the aquarium systems. We provide the necessary tools and technical support for

any internal or external research group to develop a research project.

Fun facts about us?

Imagine 46m² at 24°C with 7500 fish swimming around... No!!! you are not in Mexico!!! You are in the fantastic iMM Zebrafish Facility!!!





STORIES OF *Science*

HOW TO GET YOUR *communication* SKILLS ALIGNED

NEW STUDY SHEDS LIGHT ON PHYSICAL COMMUNICATION IN BLOOD VESSELS

A proper network of blood vessels is essential for life, and its organization is normally aberrant in several diseases including cancer, retinopathies, and arteriovenous malformations. A key element to generate a functional vascular system is the collective migration of endothelial cells that form the inner lining of blood vessels. Yet, it is still largely unknown how this collective behavior is regulated. Now, a study led by Cláudio Franco, group leader at IMM has found that a molecule named Wnt5a promotes the collective migration of endothelial cells by strengthening the physical communication between cells. The study published in March in the open access journal *eLife**, sheds light on how endothelial cells behave in the context of health and disease.

“We are interested in studying how chemical and physical signals are interacting and how they regulate each other

in order to guide the migration of endothelial cells towards a given direction”, says Cláudio Franco. Previous studies had shown that Wnt5a is important for the orientation of endothelial cells. “However, we still did not know the exact mechanisms behind it. Now, we found that this mechanism operates at specialized sites in cells, the cellular junctions, which are structures that can be found in regions where cells establish physical interactions (contacts?) with each other”, explains Joana Carvalho, first author of the paper. The team has demonstrated that Wnt5a promotes an efficient transmission of physical information between cells by reinforcing cell junctions.

These results contribute to understand how blood vessels develop and the origins of some forms of vascular mis-organization. “We found a novel pathway that regulates the growth of blood vessels. Now, we hope to use this information

to modulate angiogenesis in pathological conditions”, states Cláudio Franco.

This work was developed at IMM, in collaboration with the lab of Nuno Santos also at IMM and funded by H2020 European Research Council Starting Grant, Fundação para a Ciência e a Tecnologia, Fondation Leducq and H2020 Spreading Excellence and Widening Participation.

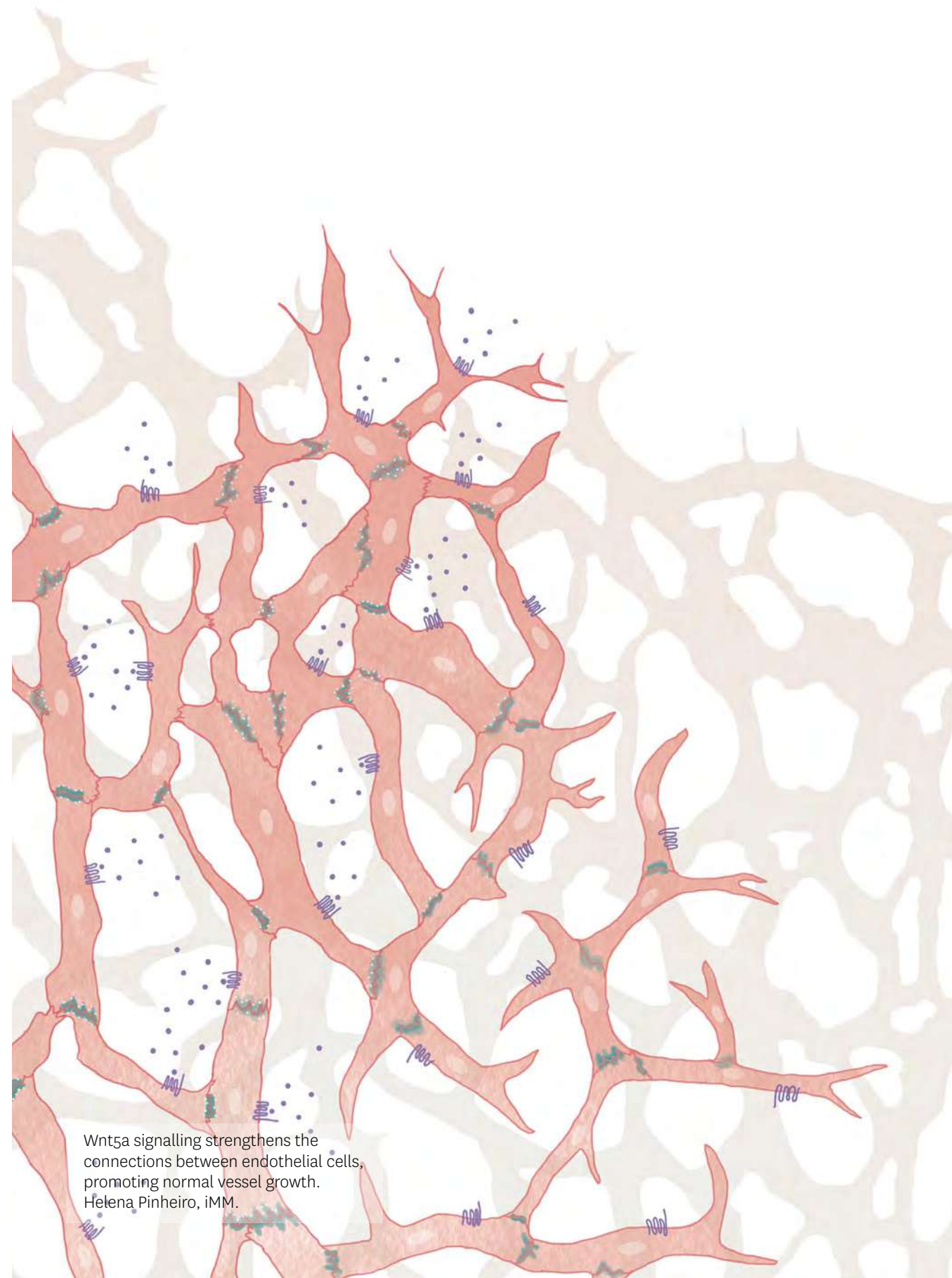
*Joana R Carvalho, Isabela C Fortunato, Catarina G Fonseca, Anna Pezzarossa, Pedro Barbacena, Maria A Dominguez-Cejudo, Francisca F Vasconcelos, Nuno C Santos, Filomena A Carvalho, Cláudio A Franco. (2019) *Non-canonical Wnt signaling regulates junctional mechanocoupling during angiogenic collective cell migration.*

eLife, 8: e45853.



READ MORE

Wnt5a signalling strengthens the connections between endothelial cells, promoting normal vessel growth. Helena Pinheiro, IMM.



NEW STUDY DEVELOPS PROOF OF CONCEPT FOR TARGETED *therapy* AGAINST T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Two IMM research groups led by Gonalo Bernardes and Joo Taborda Barata together with international partners, collaborated on the development of an antibody-based treatment against T-cell acute lymphoblastic leukemia (T-ALL). The study, in which Padma Akkapeddi, a PhD student at CAML is the first author, was published in March in the scientific journal *Leukemia* and is the proof of concept for the development of new targeted therapies in T-ALL and other diseases where IL-7R has a pathological role.

T-ALL is an aggressive hematological cancer that results from the transformation of thymic T-cell precursors and that affects mostly children. Although chemotherapy is effective in over 80% of pediatric cases (adult success rate drops by half), patients who relapse or do not respond have a poor prognosis, while those who respond well to therapy usually suffer from

long term side effects such as propensity for obesity, heart problems and growth retardation. Therefore, specific therapies associated to fewer negative effects are needed.

The lymphatic system faces many changes throughout the development and growth of a child, involving a frequent exposure to new antigens, a complex network of signals and maturation processes. Interleukin 7 (IL-7), a surface molecule called cytokine that is produced in the thymus, bone marrow, and other tissues, and its receptor (IL-7R) are essential for normal lymphoid development. However, the IL-7/ IL-7R axis can also play a significant role in leukemogenesis and studies have shown that IL-7 accelerates human T-ALL development *in vivo*. IMM scientists have developed an antibody that recognizes interleukin 7 receptor (IL-7R), a surface molecule on leukemic cells that is essential for their

survival but is also involved in the normal development of the lymphoid tissue.

This work demonstrates that such antibodies (alone or in conjunction with a drug that helps killing cancer cells) are able to slow tumor development and may therefore be a valid strategy for treating T-ALL and other pathological conditions in which IL-7 and IL-7R have a role.

*Padma Akkapeddi, Rita Fragoso, Julie A. Hixon, Ana Sofia Ramalho, Mariana L. Oliveira, Tnia Carvalho, Andreas Gloger, Mattia Matasci, Francisco Corzana, Scott K. Durum, Dario Neri, Gonalo J. L. Bernardes & Joo T. Barata. (2019) *A fully human anti-IL-7R α antibody promotes antitumor activity against T-cell acute lymphoblastic leukemia*. *Leukemia*, 33: 2155-2168.

READ MORE



An antibody targeting IL-7 receptor sensitises T-cells to anti-tumoral drugs in T-cell acute lymphoblastic leukemia, indicating its potential as a therapeutic approach. Helena Pinheiro, IMM.

IS BIPOLAR DISORDER ASSOCIATED WITH *increased* RISK OF PARKINSON'S DISEASE?

A SYSTEMATIC REVIEW AND META-ANALYSIS
SHOW EVIDENCE FOR AN ASSOCIATION

READ MORE



A systematic review indicates that
people with bipolar disorder have higher
risk of developing Parkinson's disease.
Helena Pinheiro, IMM.

Parkinson's disease (PD) is characterized by motor and nonmotor symptoms attributed to a loss of dopaminergic neurons. PD might be preceded by mood disorders for more than a decade. Bipolar disorder (BD) is a mood disorder characterized by cyclic episodes of depression and mania or hypomania.

Now, a new study led by Joaquim Ferreira, neurologist and group leader at IMM, has performed a systematic review and meta-analysis to establish a potential association between BD and a later diagnosis of PD. Previous studies have shown an association between the dopaminergic system and BD.

There is evidence that altered levels of both dopamine or dopamine receptors can lead to mood switches in patients with BD. Additionally, few studies have shown that BD may be more common in patients with PD compared with the general population. Now, the research team combined the results of 7 studies with more than 4.3 million participants and analyzed the potential association between BD and a later diagnosis of PD. The results published in October in *JAMA Neurology** suggest that patients with BD have a significantly increased risk of developing PD compared with the general population,

highlighting that BD may be associated with a later development of PD. "Overall, these results are clinically relevant and sustain the importance of the differential diagnosis of parkinsonism features in people with BD. Based on the results obtained in this study, new projects are being developed to assess the biological link between the two diseases, both in terms of basic research and in terms of the methodologies we use", reveals Joaquim Ferreira.

This work was developed in a collaboration between IMM, Faculdade de Medicina da Universidade de Lisboa, Hospital Santa Maria, CNS at Torres Vedras, Hospital Beatriz Angelo, the Università di Verona, Italy, and the University College of London, UK.

*Patrícia R. Faustino, Gonçalo S. Duarte, Inês Chendo, Ana Castro Caldas, Sofia Reimão, Ricardo M. Fernandes, José Vale, Michele Tinazzi, Kailash Bhatia, Joaquim J. Ferreira (2019) *Risk of Developing Parkinson Disease in Bipolar Disorder. A Systematic Review and Meta-analysis*. *JAMA Neurol.* doi: 10.1001/jamaneurol.2019.3446. [Epub ahead of print]

IMMUNE MEDIATORS AFFECT *cognitive* FUNCTION

A STUDY SHOWS THE ROLE OF MENINGEAL $\gamma\delta$ T CELLS—DERIVED IL-17 IN SHORT-TERM MEMORY AND SYNAPTIC PLASTICITY

There is increasing evidence that explores the crosstalk between the nervous and the immune system. Although the production of interleukin-17 (IL-17) in the brain has been typically associated with immunopathology and inflammatory disease progression, IMM researchers have shown that IL-17 supports important normal neurophysiological roles.

In a recent study published in *Science Immunology**, a research team led by Bruno Silva-Santos has analyzed immune infiltrates in the meningeal spaces of mice and identified a population of meningeal gamma-delta T cells ($\gamma\delta$ T cells) that were involved in IL-17 production. They have shown that these IL-17-producing $\gamma\delta$ T cells represented a non-inflammatory subset of $\gamma\delta$ T cells that populates the meninges in the perinatal period and persist throughout life. Animals lacking these cells displayed deficient short-term

memory but did not exhibit any motor deficit or changes in long-term memory. Further analysis has shown that IL-17 influences the plasticity of glutamatergic synapses during short-term learning. Also, the team found that IL-17 stimulates glial cells to secrete brain-derived neurotrophic factor in mouse brains, which could be the molecular link between $\gamma\delta$ T cells and synaptic plasticity.

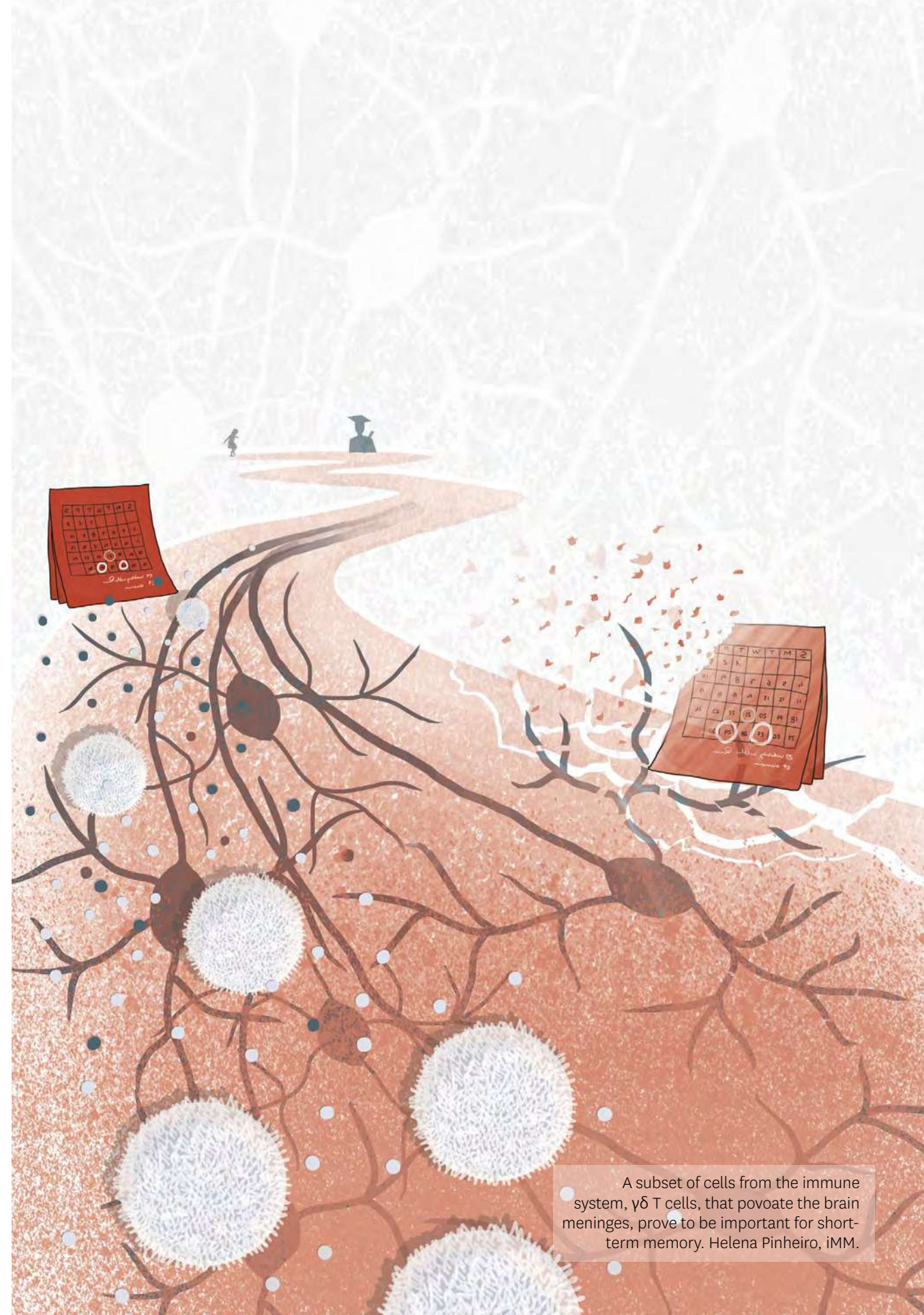
This study suggests that IL-17-producing $\gamma\delta$ T cells may impact neurophysiological roles like learning and memory, providing clues on the evolutionary and functional link between the immune and nervous systems.

This work was developed at IMM in collaboration with Luísa Lopes Lab, in collaboration with Centre National de la Recherche Scientifique, Université de Côte d'Azur, France, the Institute for Molecular Medicine, University Medical Center of the Johannes Gutenberg-University Mainz, Germany,

the Center for Neuroscience and Cell Biology and Institute for Interdisciplinary Research at Universidade de Coimbra, Portugal; and the Francis Crick Institute, UK.

*Miguel Ribeiro, Helena C. Brigas, Mariana Temido-Ferreira, Paula A. Pousinha, Tommy Regen, Cátia Santa, Joana E. Coelho, Inês Marques-Morgado, Cláudia A. Valente, Sara Omenetti, Brigitta Stockinger, Ari Waisman, Bruno Manadas, Luísa V. Lopes, Bruno Silva-Santos, Julie C. Ribot. (2019). *Meningeal $\gamma\delta$ T cell-derived IL-17 controls synaptic plasticity and short-term memory*. *Science Immunology*, 4(40).

READ MORE



A subset of cells from the immune system, $\gamma\delta$ T cells, that populate the brain meninges, prove to be important for short-term memory. Helena Pinheiro, IMM.

TRYPANOSOMES MORE *vulnerable* TO THE IMMUNE SYSTEM

A STUDY SUGGESTS INVOLVEMENT OF CELL-SURFACE PROTEINS VSGs

The lab of Luísa Figueiredo at IMM studies *Trypanosoma brucei*, a unicellular parasite responsible for the vector-borne disease sleeping sickness, a fatal disease in humans, in Sub-Saharan Africa. To avoid being eliminated by the immune system, trypanosomes use antigenic variation, a process that consists in periodically switching the major cell-surface protein, the variant surface glycoprotein (VSG). These changes in VSGs may also account for the survival of this parasite in different hosts, since during its life cycle *Trypanosoma brucei* shifts between a mammalian host and the tsetse fly vector.

An interesting characteristic is that only one VSG is transcribed at any time in bloodstream forms. In a study published in the scientific journal *PNAS**, the team led by Luísa Figueiredo has shown that *Trypanosome* parasites expressing several coat proteins are more easily

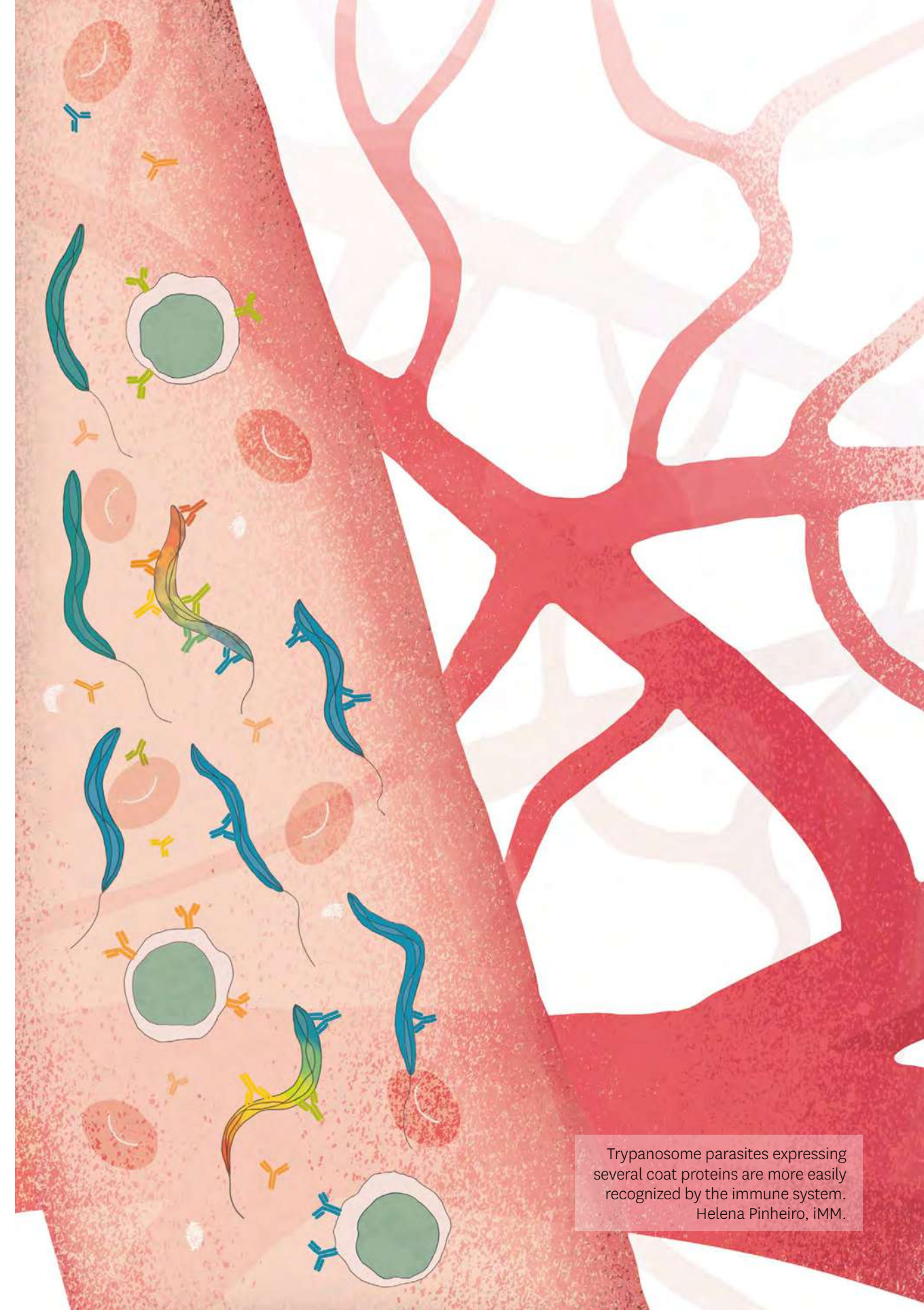
recognized by the immune system. In a series of genetic experiments, researchers were able to generate viable and healthy parasites expressing multiple distinct VSGs, meaning that these parasites “wore” mixed VSG coats. Animals infected with these parasites mounted a multi-VSG antibody response and nearly 90% survived with undetectable parasitemia after 30 days of infection.

Overall, these results show that simultaneous exposure of multiple VSGs is highly detrimental to the parasite, thus suggesting that in the future trypanosome infections may be treated using drugs that generate parasites with multi-VSG coats.

This work was developed at IMM in collaboration with the Division of Immune Diversity and the Division of Structural Biology of Infection and Immunity at the German

Cancer Research Center, and the Institute of Molecular Biology at Johannes Gutenberg Universität, Germany.

*Francisco Aresta-Branco, Margarida Sanches-Vaz, Fabio Bento, João A. Rodrigues, and Luisa M. Figueiredo (2019). *African trypanosomes expressing multiple VSGs are rapidly eliminated by the host immune system*. Proceedings of the National Academy of Sciences of the United States of America (PNAS), 116 (41): 20725-20735.



Trypanosome parasites expressing several coat proteins are more easily recognized by the immune system.
Helena Pinheiro, IMM.

TALENT.

**TRAINING
A NEW
GENERATION
OF SCIENTIFIC
MINDS**

OUR Programs

We work closely with the MSc students, PhD students, and Postdoctoral researchers to maximize their career prospects through specific programs and activities:

MASTER PROGRAM

A MSc Program aimed at selecting and awarding the best master students at IMM. Yearly, an Open Afternoon is organized to welcome prospective students and to share the research projects available. In 2019, 58 students were developing their Master thesis at IMM.

AN INTERNATIONAL PhD PROGRAM - LISBONBIOMED

In 2019, all PhD students who are developing their doctorate studies at IMM are under the umbrella of LisbonBioMed - an international PhD Program with a flexible and tailored curricular structure, offering excellent opportunities for young basic and clinical researchers to work together. Together with Faculdade de Medicina da Universidade de Lisboa (FMUL) and with Hospital de Santa Maria (HSM), IMM is part of the Lisbon Academic Medical Center (CAML), a consortium that provides an integrated form of education and training in Biomedicine and Clinical Research, combining multidisciplinary and internationalization. Besides CAML PhD students,

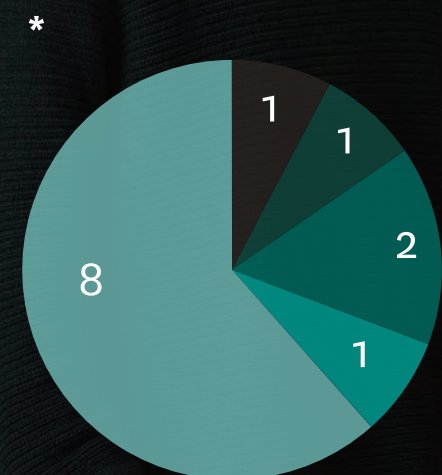
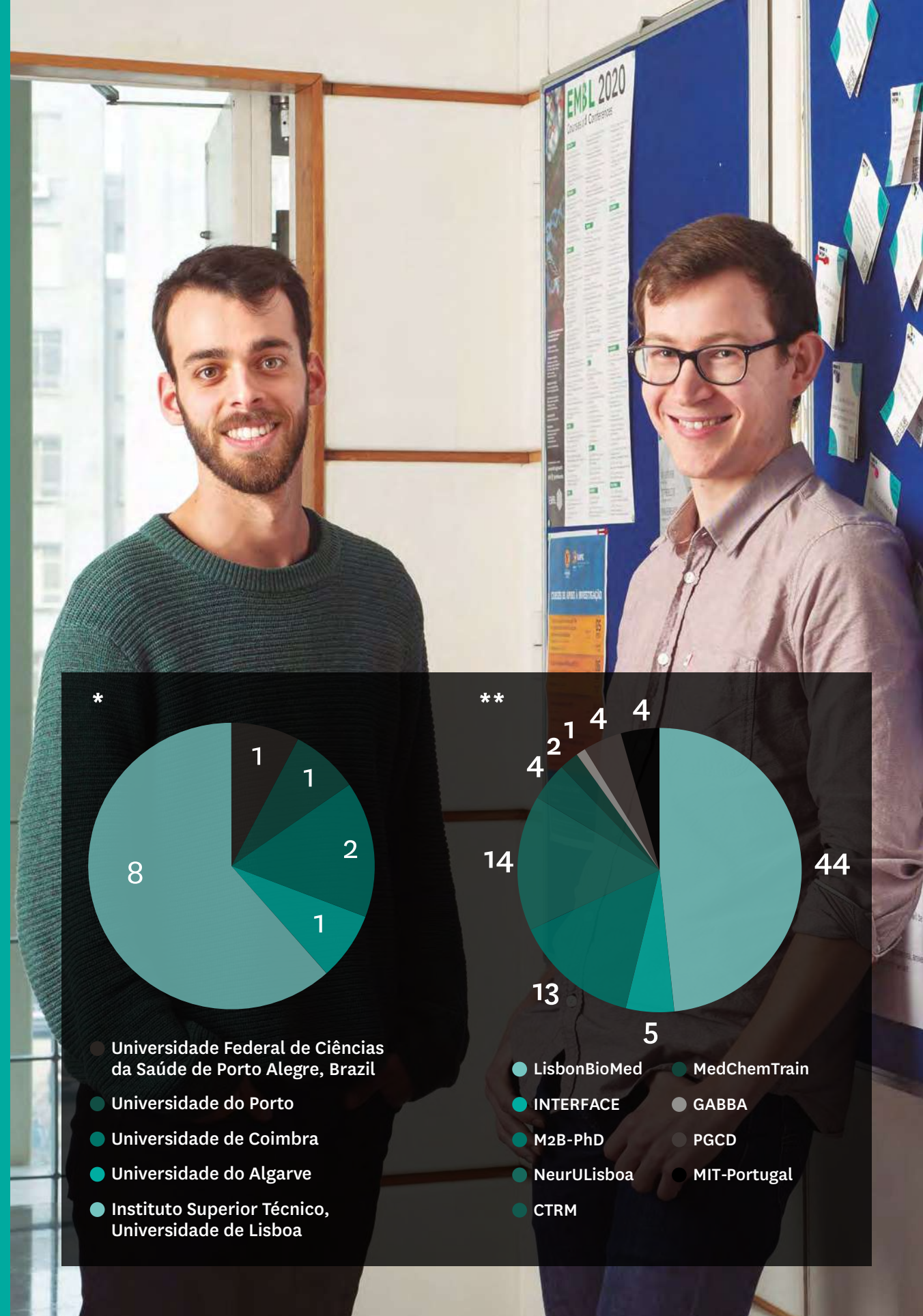
iMM hosted 13 PhD students from other Institutions/Universities*. Students enrolled in 9 different FCT PhD Programs are developing their research projects at iMM**. In the 2019 FCT Call for PhD Scholarships, 19 doctoral fellowships were granted to iMM as host institution. Through the "la Caixa" Foundation INPhINIT - Incoming doctoral fellowship program, one PhD student has chosen iMM as host institution.

Three Innovative Training Networks (ITN) from the European Commission program Marie Skłodowska-Curie Actions (MSCA) brought 4 PhD students to iMM.

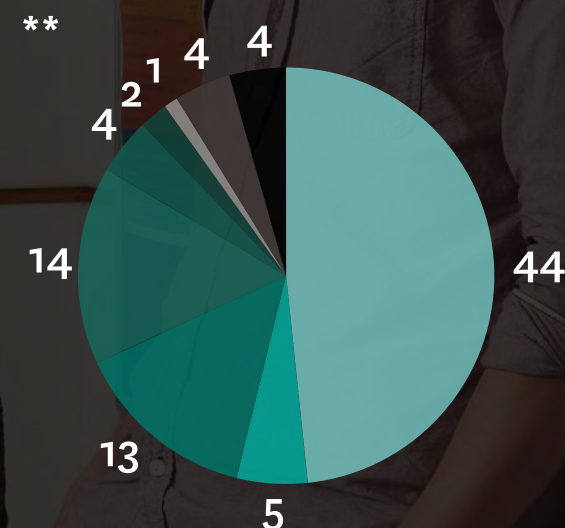
POSTDOCTORAL TRAINING PROGRAM

A Postdoctoral Training Program, structured around specific actions that promote scientific discussions and sharing of experiences, in academia and beyond. The postdoctoral community at iMM has 154 members, as of 2019.

Pedro Ruivo (left side), Arthur Schneider (right side) and Catarina Pelicano were the awardees of the Best Master Thesis at IMM in 2019. Watch here their videos:



- Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil
- Universidade do Porto
- Universidade de Coimbra
- Universidade do Algarve
- Instituto Superior Técnico, Universidade de Lisboa



- LisbonBioMed
- MedChemTrain
- GABBA
- PGCD
- MIT-Portugal
- INTERFACE
- M2B-PhD
- NeurULisboa
- CTRM

BEING A PhD *student* AT IMM

Being a PhD student is one of the most rewarding experiences we have had so far. A great part of this success comes from being a PhD student at Instituto de Medicina Molecular João Lobo Antunes. Here we have access to several formal and informal scientific talks, fostering our interaction with junior and senior scientists, increasing our critical thinking. We believe these discussions are a great fuel for students' creativity and important scientific breakthroughs.

As PhD students, we have to deal with failure and insecurities, which can become a setback in our scientific progress. The great support system provided by the institute and the great sense of community are certainly important to overcome these situations. There is always someone willing to spare their time to help and discuss, just at the distance of an email or across the corridor.

IMM is an outstanding biomedical research institution, composed by researchers from different research areas, providing a unique multidisciplinary environment. Moreover, the close location of IMM to Hospital de

Santa Maria, CHULN, and the Faculty of Medicine, provides a clinical environment and a close contact with patients, their perspectives and samples for translational research. Becoming a student at IMM gives us the opportunity to use our top knowledge facilities, starting at Biobank, where 193 653 samples are already stored, to Histology and Comparative Pathology, Flow Cytometry, Bioimaging, Zebrafish and Rodent facilities. All these infrastructures and human resources are a precious help during our PhD projects, giving us not only technical tools, but also specialized discussions.

IMM has a great team spirit, mainly due to a variety of social events. Particularly, the PhD student's community is very strong at IMM as a result of our motivation, enthusiasm and dedication. Alongside our scientific paths, we join a variety of committees that are responsible for organizing, very successfully, the PhD Meeting and Retreat, Pizza seminars, Workshops, among others. All in all, IMM provides us with an exceptional scientific and social environment to be a PhD student.



Elvira Leites (left side) from the Vanessa Morais Lab and Eunice Paisana (right side) from the João Barata Lab are the PhD representatives for the period 2019-2020.

”A *sketch* OF MY PhD THESIS”



A new video series launched as part of a joint initiative between the Training Hub and the Communication Office, aimed to highlight the work developed by our PhD students as they finish their PhD theses. In these videos the students talk about their PhD work with the aid of sketches.

Vânia Cardoso

Henrique Veiga-Fernandes Lab

1st February

Control of mucosal defense and innate immunity by neuroregulators

Padma Akkapeddi

Gonçalo Bernardes Lab

6th February

Antibody based therapy for T-cell acute lymphoblastic leukemia: Targeting IL-7 receptor

Diana Fernandes

João Eurico Fonseca Lab

20th February

Coupling of atherosclerosis progression and bone disturbances in inflammatory rheumatic diseases

Mafalda Pimentel

Edgar Gomes Lab

8th March

The role of nuclear positioning in muscle function

PhD VIVAS IN 2019

Andreia das Neves Horácio

Mário Ramirez Lab

15th March

Characteristics of pneumococci causing disease in adults in Portugal in a time of private use of pneumococcal conjugate vaccines in children

Mafalda Matos

Sérgio de Almeida Lab

23rd May

A systematic pan-cancer analysis of somatic variants reveals epigenetic drivers of intratumor heterogeneity

Margherita Fabbri

Joaquim Ferreira Lab

30th May

Multimodal response to levodopa treatment in advanced and late Parkinson's Disease

Tiago Nascimento Figueira

Miguel Castanho Lab

5th June

Targeting enveloped virus entry into cells: Self-delivery and other strategies against HIV and Measles virus

Anna Braga

Mamede de Carvalho Lab

27th June

Amyotrophic Lateral Sclerosis: exercise and disease progression

Joana Bettencourt Gesta

João Lacerda Lab

1st July

Expansion and in-depth characterization of antigen-specific regulatory T cells *in vitro* for subsequent clinical translation

Biagio Di Lorenzo

Bruno Silva-Santos Lab

9th July

Characterization of the Vδ1+T Cell receptor repertoire during early and adult human life: implication of clonal diversity for cancer immunotherapy

Annabel Kitowski

Gonçalo Bernardes Lab

10th September

Bio-orthogonal site-selective labelling of carbohydrates and proteins

Pedro Papotto

Bruno Silva-Santos Lab

10th September

Homeostasis and response of IL-17-producing Gamma Delta T Cells in peripheral tissues

Jorge Miranda

Mário Ramirez Lab

1st October

Understanding pherotype specificity and its influence on the genetic structure of *Streptococcus pneumoniae*

Sofia Fernandes

Mamede de Carvalho Lab

7th October

Transcutaneous spiral direct current stimulation: modelling the spiral electric field distribution and clinical relevance

Pedro Barbacena

Cláudio Franco Lab

4th November

Molecular mechanisms regulating endothelial cell axial polarity during vascular morphogenesis

Raquel de Freitas

Luís Graça Lab

4th November

The impact of CD6 targeting in T cell function and immunopathology

Joana Carvalho

Cláudio Franco Lab

7th November

Force transmission and endothelial cell rearrangements during vascular remodeling

Neidy Rodrigues

Sérgio Dias Lab

27th November

Impact of metabolic resources and infiltrating immune cells on protective responses against solid tumors

Charlotte Baker

Gonçalo Bernardes Lab

16th December

Selective cancer therapies: Targeting TRP channels in glioblastoma and prostate cancer

Tiago Amado

Bruno Silva-Santos Lab

16th December

MicroRNAs in the functional differentiation of T cells

Elsa de Sousa

João Eurico Fonseca Lab

20th December

New perspectives on Tumor Necrosis Factor inhibition for the treatment of Psoriatic Arthritis

PhD Student's 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.

ANNUAL MEETING

Is the place by excellence where students present and discuss their work with the overall IMM community during three days.

In 2019 the three keynote speakers were:

Marino Zerial

(Max Planck Institute of Molecular Cell Biology and Genetics, Germany)

Miguel Nicolelis

(Duke University Medical Center, USA)

Fátima Carneiro

(Faculdade Medicina & Hospital São João & Ipatimup, Portugal)

ANNUAL RETREAT

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

PIZZA SEMINARS

PhD students' presentation in an informal atmosphere. Happens every other Tuesday.

WORKSHOPS

Aimed at improving scientific and transversal competences, as well as to explore the diversity of career paths for PhD-holders.

•“**Basics of programming (First Steps in R for Data Science)**”, by Filipe Cadete

•“**Graphic Design - Creating Figures for Publications**”, by Samuel Hertig

•“**Communication: Turn Yourself into a Successful Speaker**”, by Michael Daniels

•“**Network yourself into the scientific world**”, by Nuno Afonso

•“**How to represent your data**”, by Tracey Weissgerber

•“**Science Careers**”, by Filipa Robalo and Inês Lopes





POSTDOCS: A CAREER AS A *Scientist* STARTS AT IMM

What is like to be a postdoc at IMM?

Being a postdoc at IMM means belonging to a great scientific community. Through the PDA activities, IMM offers to its postdocs relevant scientific and social events, which promote cohesion and interchange of ideas between peers. In addition, IMM organizes regular seminars with invited top researchers, and give us the possibility to join productive discussions over lunch. Of ultimate importance, IMM really supports postdoctoral work, by having on its organizational structure several lab managers and technical/administrative staff, which activities enables each postdoc to mainly focus on their research projects.

On the other hand, we also feel that as a scientific community, we do not know enough about each other's work, due to the lack of opportunities to present our work inside IMM. PDA is on top of this topic, and we are proposing to the IMM Board of Directors the creation of a postdoc seminar series, in order to fulfill the need of our community to present and discuss their work internally.

What is the IMM-Postdoc Association and how does it contribute/help to the career of a postdoc at IMM?

The PDA is a group of motivated (volunteer) postdocs with an active role in the IMM community. We try to identify the main concerns of our peers and work within the IMM organization towards a solution. In addition, the PDA is the liaison between the postdoc community and the IMM Board of Directors. We communicate their opinions and problems to the Board and participate in the generation of solutions. The PDA organizes several activities throughout the year, which are important complements to the postdoc career (seminars, postdoc day, scientific retreats, workshops, etc.).

Why should a Postdoc choose IMM?

IMM is unique in the biomedical research scene, not only in Portugal but also in all European context. IMM brings together top researchers distributed in ~30 research groups with partial overlapping interests and with increasing translational research. Moreover, IMM records an outstanding record of projects funded by international / EU agencies and a growing network of facilities. Altogether, IMM is a fantastic place to develop top-notch science.

IMM is a good environment for informal discussions and potential collaborations with a handful of weekly seminars, courses and PDA-driven activities, together with friendly and helpful PIs. IMM is also a friendly workplace, with regular opportunities to socialize, either with the monthly beer-hour, some get-together events or the IMM retreat.

What is the best part of your community?

IMM has a straight relationship with the clinicians and researchers at the Hospital Santa Maria, which increases the chance of developing great translational research projects, with privileged access to patients' data and biological samples. In addition, every year, IMM postdocs have a day fully dedicated to present their work and attend exceptional seminars/workshops, with special attention to fruitful discussions between their peers. Furthermore, every year postdocs working in the research institutes from the great Lisbon area meet for a retreat to foster new collaborations between institutions, and this way, bring together what each place has to offer to their projects and careers.

Postdocs ACTIVITIES

The IMM Postdoctoral Association (PDA) organizes several activities centered around communication and networking, aimed to build community among the institute's postdoctoral researchers.

ANNUAL POSTDOC DAY

In 2019, the program included oral presentations and graphical abstracts showcase from the IMM postdocs, and a round table with current and former IMM researchers about "Canonical and Non-canonical Research Paths".

LISBON AREA POSTDOCTORAL MEETING (Annual Cross-Institutional Meeting)

The LAPD Meeting 2019 joined postdocs from IMM, Champalimaud Foundation, ITQB, CEDOC, iMed.Ulisboa, and UCIBIO/Requimte (FCT-NOVA). During this two-day meeting postdoctoral researchers had the opportunity to present/discuss their science, to network, to find partners, to build collaborations, and also to discuss other issues that relate to a scientific career, including topics such as: Science Policy, Career Planning, Funding Schemes, Laboratory Sustainability,

Science Communication and Outreach. Sessions devoted to soft and technical skills and a variety of social activities were also featured.

WORKSHOP

"Sustainable Science and Green Lab Workshop", by Martin Farley, UCL, King's College London, Green Lab Associates

BEER HOURS

Happens every 1st Thursday of the month.



SOCIETY:

**WHAT IS
WORTH
ASKING?**

SCIENCE *Outreach* AT IMM

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. We are implementing a structured program promoting a two-way communication between scientists and citizens.

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 2019, 689 students and 52 teachers from 26 schools visited the IMM. Also, we have organized an Open Afternoon for teachers aimed at promoting a closer interaction with scientists and to jointly re-shape the school visits program for 2019-2020.

Outreach Events:

During 2019, we have organized and participated in several outreach events, that brought to different publics the science developed at IMM:

IMMUNOLOGY DAY

The Immunology Day is celebrated internationally on the 29th of April, and at IMM we opened doors to 70 visitors, mostly high school students and their teachers. They have interacted with 27 IMMers working in different areas of immunology

research through hands-on activities, speed-dating chats and lab tours.

MICRODIA

On the 22nd of May, several research institutions in Portugal, have organized specific activities to bring microscopy and the wonders of the micro world closer to schools. At IMM, we have received 51 students that participated in different hands-on activities coordinated by the Bioimaging Facility.

LITTLE IMMERS

An afternoon of open doors for a very special crowd: children, relatives and friends of all IMMers. Ten labs and facilities were involved in the organization of hands-on activities tailored for different age groups and other activities that included lab visits and informal chats with scientists. We received 63 children and 34 adults that were able to learn more about the daily work of their parents, children and friends.

EUROPEAN RESEARCHERS' NIGHT 2019

iMM has participated in the European Researchers' Night 2019 at National Museum of Natural History and Science in Lisbon with a joint activity of 9 research groups and 1 international project (João Barata Lab, Miguel Castanho Lab, Sérgio Dias Lab, Edgar Gomes Lab, Vanessa Morais Lab, Miguel Prudêncio Lab, Ana Sebastião Lab, Bruno Silva-Santos Lab, MyoChip)- "Our Body is our City". Through different activities, visitors explored the functioning of organisms and how these are affected in different diseases. More than 750 visitors have interacted with our scientists and learnt more about the research developed at IMM.



HORIZONTES iMM: UMA *pergunta* A TRÊS



During 2019, iMM launched the first series of public talks that join a scientist, a medical doctor and a patient around one same question, in collaboration with Fundação Belmiro de Azevedo. These talks based on discoveries made by iMM researchers were organized with the aim of bridging the gap between science and society, involving citizens in favour and facilitating a real dialogue for health literacy.

Four sessions took place between February and October 2019 at the Grande Auditório João Lobo Antunes and brought together over 700 participants. All the sessions are available on iMM website and YouTube channel.

“Why does cancer escape us?” was the first question discussed on February 20th by Fernando Rosas (former deputy of the Bloco de Esquerda, the patient), Luís Costa (the doctor) and Bruno Silva-Santos (the scientist) and moderated by Graça Franco (journalist, Director of Rádio Renascença, and member of the Societal Advisory Board at iMM). The advances in research and treatment of cancer were debated within different perspectives.

“Why do muscles fail to obey?” on March 20th brought together Pedro Souto (President of APELA, the patient), Mamede de Carvalho (the doctor) and Edgar Gomes (the scientist) with Graça Franco as moderator. The motto for this session was Amyotrophic Lateral Sclerosis (ALS), a neuromuscular disease, the same that affected Stephen Hawking and Zeca Afonso. The molecular mechanisms that underlie muscle formation were discussed as well as the different perspectives on the understanding and follow-up of this disease.



FIND MORE

“Why does the brain stop communicating with the body?” held on June 19th, was dedicated to Parkinson’s disease. Paulo Teixeira Pinto (former politician and Chairman of Banco Comercial Português, the patient), Joaquim Ferreira (the doctor) and Luísa Lopes (the scientist) discussed this neurodegenerative disease that affects 20 000 patients in Portugal. António Barreto (social scientist and member of the Societal Advisory Board at iMM) moderated the session where the breakthroughs on research and treatment of Parkinson’s disease were discussed along with the valuable testimony of Paulo Teixeira Pinto.

“Why doesn’t the spinal cord regenerate?” with Salvador Mendes de Almeida (Founder of Salvador Association, the patient), António Francisco (the doctor) and Leonor Saúde (the scientist). The last session of the year held on October 16th was again moderated by António Barreto and covered the differences associated with spinal cord regeneration in mammals and other species. Did you know that in the zebrafish there is a total recovery after a spinal cord injury? The inspired testimony of Salvador Mendes de Almeida added to the valuable comments of the other participants made this closing conference a success.

“Horizontes iMM: Uma pergunta a três” will continue in 2020, promoting a closer relationship between Science and Society in a real dialogue involving citizens and scientists on behalf of Health Literacy.

OUTREACH OF INTERNATIONAL *Projects*

NOVIRUSES2BRAIN

This is a project that aims at 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. 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. An important component of this project is the organization of specific science outreach activities, which in 2019 included:

International Day of Climate Action

On 24th October, 65 high school students and 7 teachers had the opportunity to interact with researchers and to visit the biophysics and biochemistry laboratory, where they participated in hands-on activities to understand how to develop drugs that can cross the blood-brain barrier and inactivate viruses in the brain.

Seminar at António Damásio Secondary School, Lisbon

On 3rd December, more than 100 high school students were present in a seminar dedicated to HIV and to the importance of science and technology for our daily lives.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 828774.

More information about the project:



MYOCHIP

The aim of the MyoChip project is to build a 3D human skeletal muscle irrigated by vasculature and innervated by neurons. The reconstituted 3D muscle will mirror the architecture and function found *in vivo*, namely in shape, contractility and microenvironment, while irrigation by a vascular network and innervation by human motor neurons will bring additional physiologic pertinence to it. This organ-on-a-chip technology will have numerous applications including but not limited to research on muscle building and aging, drug testing and screening, as well as prosthetics and biorobotics. The feasibility of the project relies on the interdisciplinary approach which joins a team of cell biologists, material engineers, experts in microfluidics and mathematical modelers.

Bringing this knowledge closer to the society is a major goal for this project and in 2019 the MyoChip team of cell biologists collaborated with designers and artists from MILL (Makers In Little Lisbon) and built a 3D printed real size arm and myofiber with structural and functional details. In partnership with Science4You, 6 smart microscopes will be used in several outreach activities throughout the project. The outreach activities in 2019 included school visits to IMM and showcasing the work developed by the team in one of the sessions on *Horizontes IMM: Uma pergunta a três*. Several illustrated bookmarks that highlight the main components of the muscle were also developed.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 801423.

More information about the project:



Fundo iMM-LAÇO

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, in Portugal alone.

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. Additionally, Fundo iMM-Laço provides information about metastatic breast cancer through its website, social media and through awareness campaigns. The fund annually supports two 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, twelve of our scientists were supported by the Fundo iMM-Laço Annual Grant.

We are deeply grateful to all the entities and anonymous who have generously supported our initiatives and research projects in 2019:

BSK

Clinica Médica Dentária Dr. Magno

Dama de Copas

Fitness Nestlé

GhD

Hard Rock Lisboa

Hard Rock Porto

Hoteis Real

ISDIN

Jean Louis David

Kayan

Pioneer | The Navigator Company

Savana Calçados SA

Sorisa

Women' Secret | TEDAM

In 2019, two new research projects were supported by Fundo iMM-Laço:

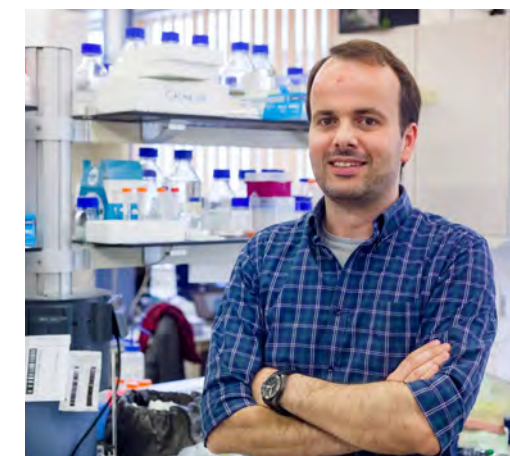


Marc Veldhoen | Group Leader

** Project fully supported by Pioneer | The Navigator Company*

In recent years, immunotherapy using immune checkpoint inhibitors, such as antibodies against PD-1 and CTLA4 (awarded the Nobel Prize 2018) has promoted cancer-free survival. In addition, therapies using the patient's own white blood cells that are transferred back to attack tumor tissue, have achieved very promising results. However, questions remain whether these approaches will be sufficiently effective against solid tumors, as breast cancer, in which, durable responses are only achieved in a fraction of patients. A subset of white blood cells, termed tissue resident T cells, have unique attributes that allow them to penetrate deep into tissues. These cells are equipped with anti-tumor activity and indeed, their numbers in tumor tissue correlate positively with patient survival. However, the conditions under which these cells are generated are unknown.

We have novel data that provides insights into the mechanisms that determine the generation of tissue resident T cells. Now, with the support of Fundo iMM-Laço we will explore if we can apply these to improve anti-tumor therapies.



Sérgio de Almeida | Group Leader

Cancer is a genetic disease characterized by the presence of several DNA mutations. These mutations are mostly driven by DNA damage, which can be caused by both endogenous (e.g. metabolites) and exogenous (e.g. UV light or radiation) sources. Not surprisingly, DNA damage is considered a major driver of cancer. However, a number of recent studies disclosed a puzzling but physiologically relevant and apparently innocuous role for DNA damage in gene expression regulation. In this project we aim at developing a completely novel approach using state-of-the-art genome editing tools to exploit DNA damage as a tool to modulate the expression levels of tumor suppressor genes in cancer cells.

Funding from Fundo iMM-Laço will support the research aimed at providing the proof of concept for a completely novel anti-cancer approach.

Information about all of the activities of the Fundo can be found on the website:



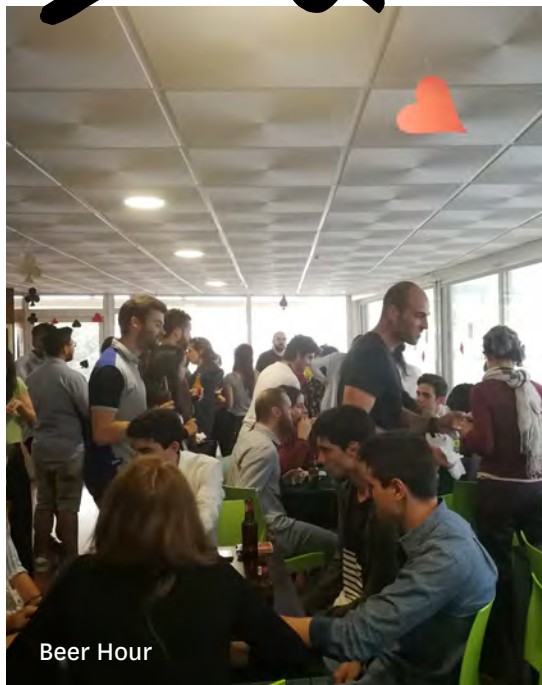


THE BRAIN *tumor* TEAM

RUNNING FOR SCIENCE

The Brain Tumor Team (BTT) was formed in 2014 to create awareness and to fundraise for cancer research. The BTT participates annually in the Corrida Saúde + Solidária, an event organized by the students of the Lisbon Medical School (AEFML) that aims to raise funds for specific causes. In 2019, the BTT team gathered 194 participants that run together the Corrida Saúde + Solidária, held in April 28th. Scientists, physicians, patients, their families and friends participated in the event, running for a cause – the Fundo João Lobo Antunes – a fundraising initiative for science launched at IMM, in 2018. The donations received in this event enable to acquire equipment for research developed at IMM.

Life AT iMM



Beer Hour



Get2Gether Treasure Hunt



iMM 15th Anniversary



iMM Scientific Retreat 2019, Évora



iMM Scientific Retreat 2019, Évora



iMM Scientific Retreat 2019, Évora



iMM Christmas Party



iMM Christmas Party



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