

Our goal is simple:

To pave the way for groundbreaking science.

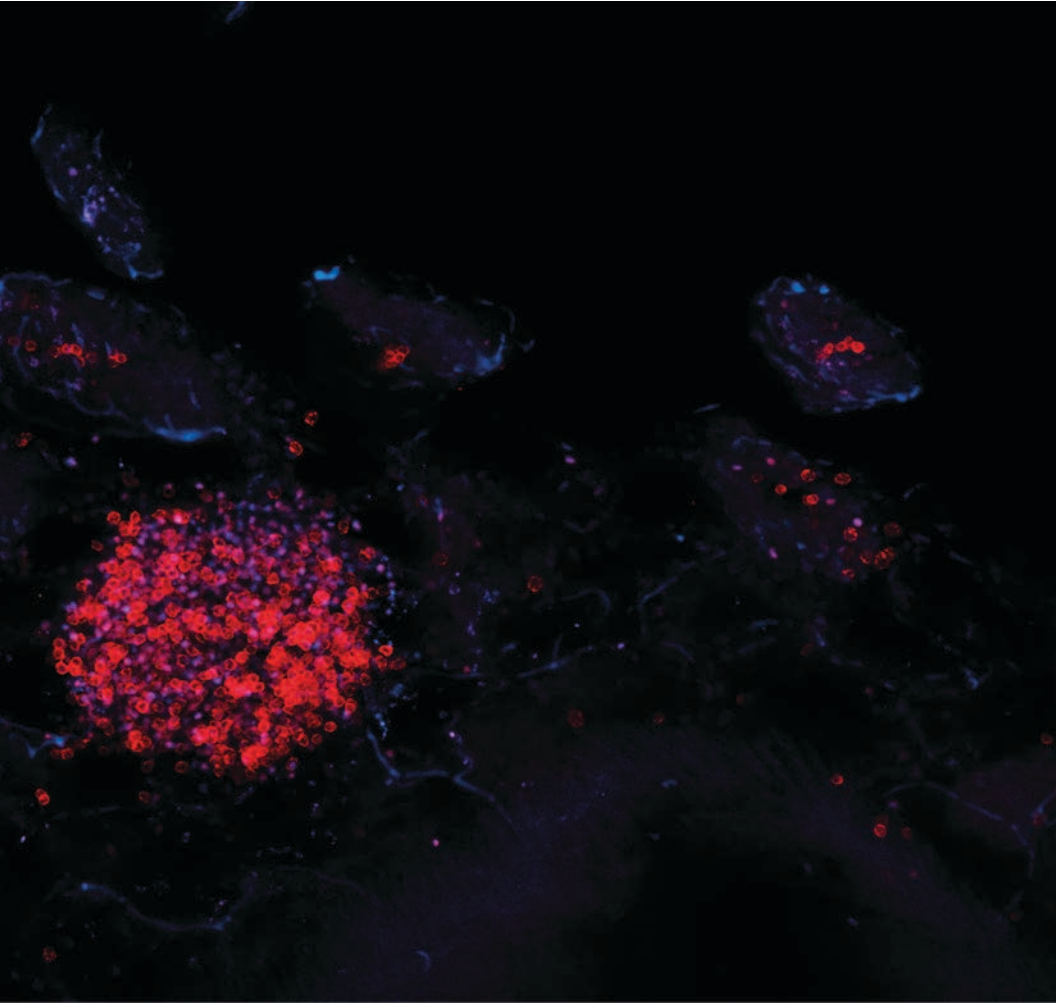


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Director's Message :



Isolated lymphoid follicle from a mouse intestine. | Credits: Carlos Almeida

Director's Message



Dear iMMers,

It has been another good year for iMM... but not a great year – allow me to explain.

I have no doubts we have many reasons to have enormous pride in all our scientific achievements of 2017. The quality of our science has never been higher, as attested by many awards and multiple papers published in top journals from the Nature, Science and Cell groups, among others. Most importantly, many beautiful discoveries have been made during the year. As always, I cannot name them all – a very good sign as they are many – but I would still like to highlight a few.

Luis Graça's team has shown that specific types of immune cells may soon be used as clinical biomarkers to improve the diagnosis of certain autoimmune diseases. Their results published in Science Immunology revealed novel biological features of human follicular helper T cells; and were the basis for their winning application to the first "iMM Innovators" competition. Edgar Gomes's team published in Nature Cell Biology new insights into the mechanism that drives the movement and positioning of nuclei in muscle cells, which may contribute for the formulation of healthier workout strategies aiming to preserve and repair muscle capacity in the aging population as well as in athletes. Luísa Lopes's team published in Nature Neuroscience their discovery of a key mediator of early synaptic impairment, which may constitute a therapeutic target for cognitive defects in Parkinson's disease. And my own team has shown in a study published in Nature that the malaria parasite is able to sense and actively adapt to host nutritional status and as such its replication depends on the calories ingested by the host. And we could not finish the year in a more positive tone for the future – Luísa Figueiredo was awarded an ERC Consolidator Grant.

Thus, from the scientific output perspective, 2017 was undoubtedly an amazing year.


Still, we cannot forget that we have faced some extremely harsh external challenges. iMM was added to the "Perímetro Orçamental do Estado" which, together with the associated "CCPs", created a lot of undesired restrictions on our way of operating. While we have tried to implement all the necessary structural changes to deal with this major hurdle, I know it has affected our daily life enormously. And this is not acceptable in an institute that aims to be at the forefront of biomedical research on an international scale. I know this is still not satisfactory, but I can tell you that a highly qualified team is fully devoted to ameliorate – hopefully to resolve – this situation as soon as possible. Fausto Lopo de Carvalho – appointed the new Finance and Administrative Director in the Spring 2017, replacing Margarida Pinto Gago who retired after her pioneering work at iMM – has been a key element in this fight. His team spirit together

with his energy and creativity are patent in the new processes that are being implemented to make iMM more efficient than ever.

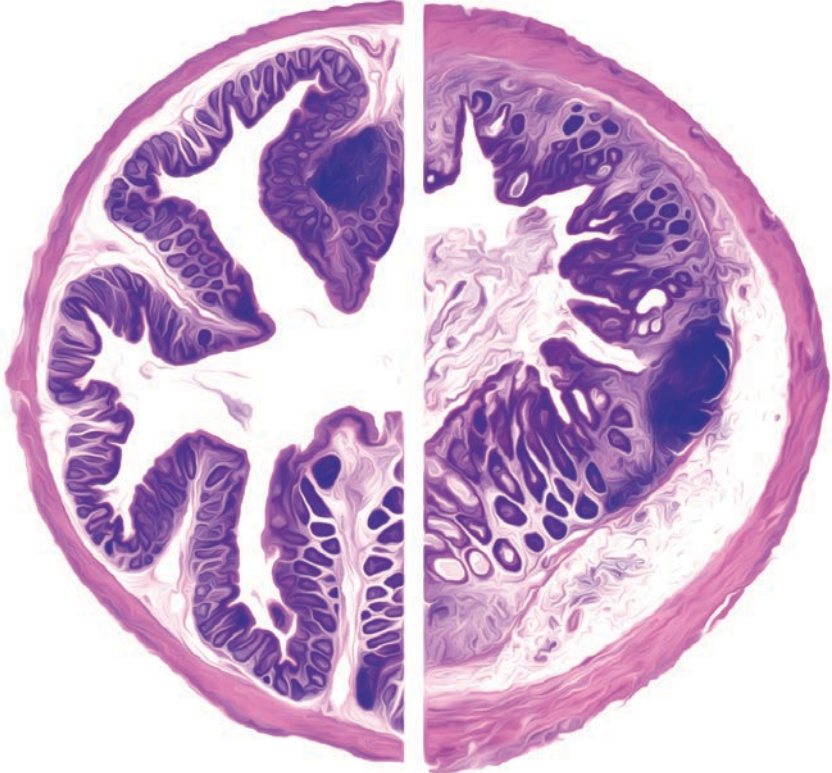
But these were not the only reasons for discontentment. Finishing the year without the results of the FCT grant call, which closed in May after 3 years without any other national call, and without any real outcome of the new FCT "scientific employment strategy", have certainly created undesired levels of anxiety, which hopefully will be resolved during 2018.

While I have started this message in a less optimistic tone than the one that usually characterizes me, I want to assure you that I remain as optimistic as ever. And, in spite of all the external negative pressures, I truly believe iMM is still a great place to work while "chasing questions". And I cannot thank you enough for being part of it and for helping to make the past year so productive. From our side, the Board of Directors can only promise we are fully committed to make our institute an even better place to work in 2018 and the following years. Importantly, our institute now carries the name of our founder, João Lobo Antunes, to lead us on our relentless path of scientific discovery.





Structure and Organisation :



Control versus knockout colon in a mouse colitis model. | Credits: Tânia Carvalho

Board of Directors



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



M. Carmo-Fonseca
MD, PhD – President



Maria M. Mota
PhD – Executive Director



Bruno Silva-Santos
PhD – Vice-President

Financial Director



Fausto Lopo de Carvalho

Scientific Advisory Council



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

Carlos Caldas
MD, PhD – Cambridge Cancer Center, UK

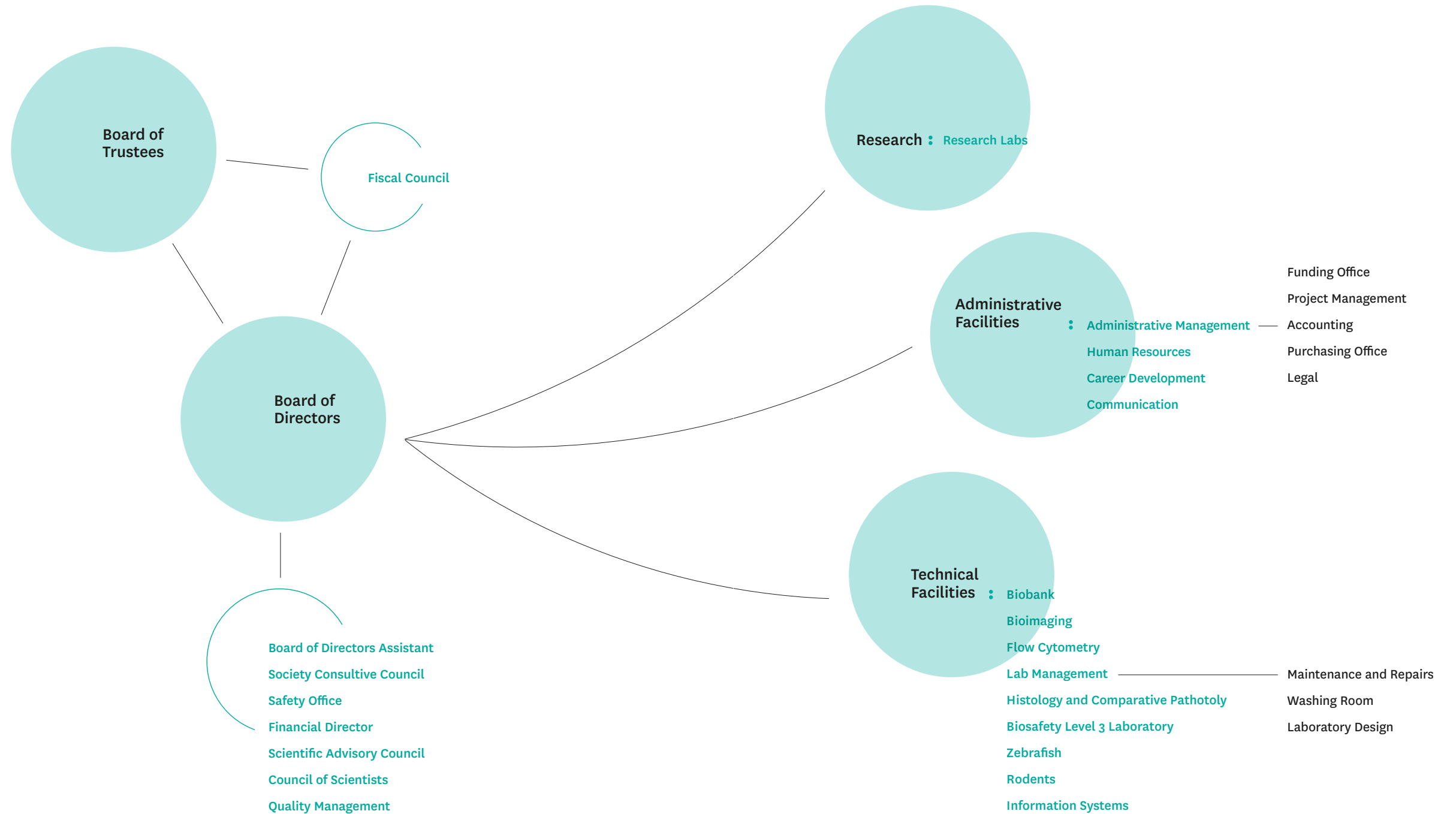
Philippe Sansonetti
MD, PhD – Pasteur Institute, France

Elaine Mardis
PhD – Institute for Genomic Medicine at NationWide Children’s Hospital

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

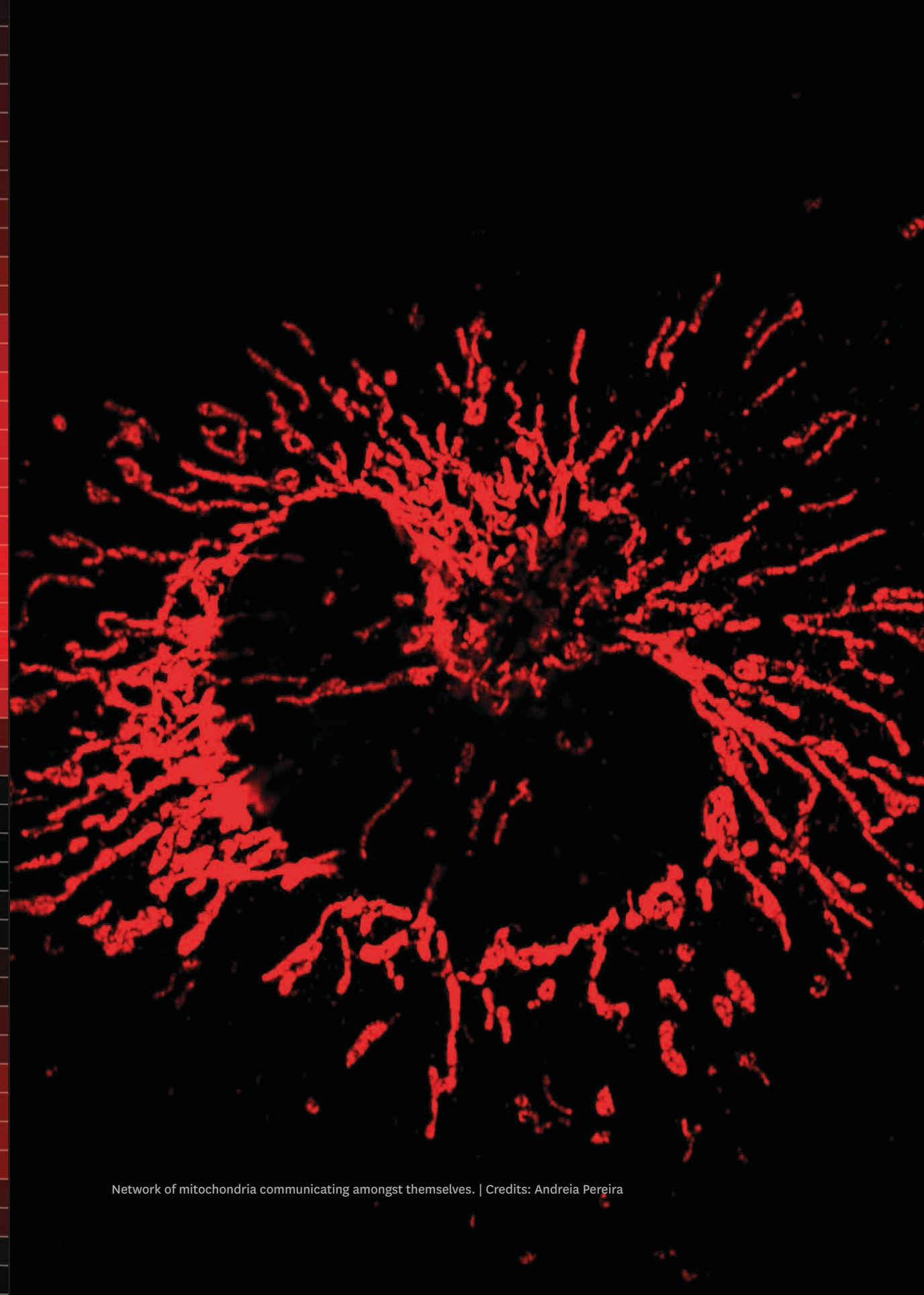
Paul Peter Tak
MD, PhD – University of Amsterdam, Netherlands

Organogram



Funding and Awards :

The research at IMM
is driven by curiosity,
passion and desire
of our researchers
to move forward
the state of the art.



Funding Office Highlights 2017



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

This synergistic effort between IMM researchers and the funding office has been increasingly consolidating and has already proved extremely successful. Indeed, concerning the biggest EU Research and Innovation programme ever – Horizon 2020 - IMM is the only Portuguese Research Institute in the Top-50 Research Organisations in terms of EU funding¹, reaching a total value of €18,84M², and the second top national beneficiary when considering all types of organisations namely universities from all areas of knowledge.

¹ Horizon 2020 Monitoring Report 2014 and 2015

² source: eCORDA DATA update as of October 2017



In fact, the current data brings IMM to a remarkable position within the national Life Sciences landscape regarding several funding schemes of Horizon 2020 as depicted below:

Horizon 2020 Pillar I – Excellent Science

European Research Council (ERC) Grants in Life Sciences in Portugal.

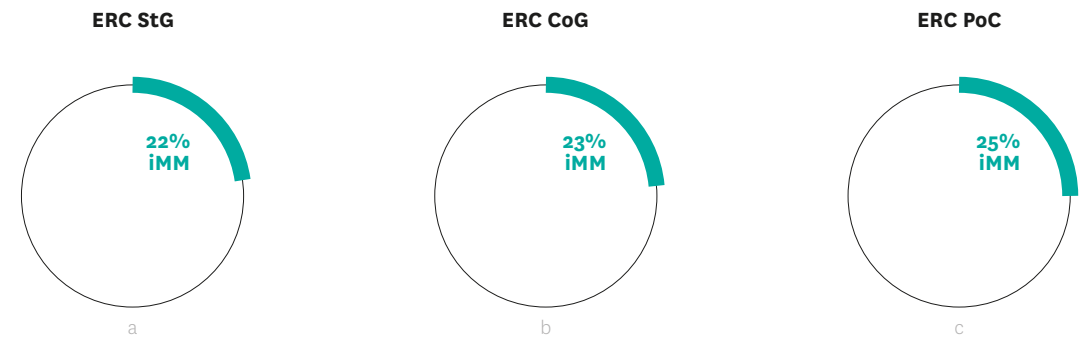


Figure 1: Percentage of secured ERC grants. a) Starting, b) Consolidator, and c) Proof-of-Concept Grants awarded to iMM (dark) and to all other national institutions (light) in the area of Life Sciences.

Marie-Sklodowska-Curie Actions in Life Sciences in Portugal.

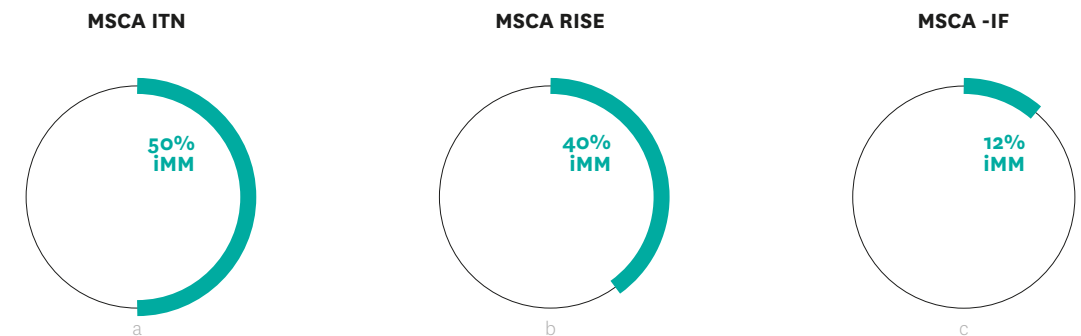


Figure 2: Percentage of Horizon 2020 MSC Actions a) Initial Training Network (ITN); b) Research and Innovation Staff Exchanges (RISE); and c) Individual Fellowships (IF) awarded to iMM (dark) and to all other national institution (light) in the area of Life Sciences.

Horizon 2020 Pillar III – Societal Challenges Health, demographic change and wellbeing

SC1 - Health, demographic change and wellbeing

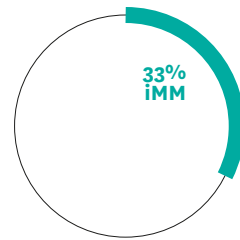


Figure 3: Percentage of H2020 Collaborative Societal Challenge 1 grants in Health, demographic change and wellbeing, coordinated by iMM (dark) and by all other national institutions (light).

Tonalities represent countries with higher number of projects in collaboration with iMM:

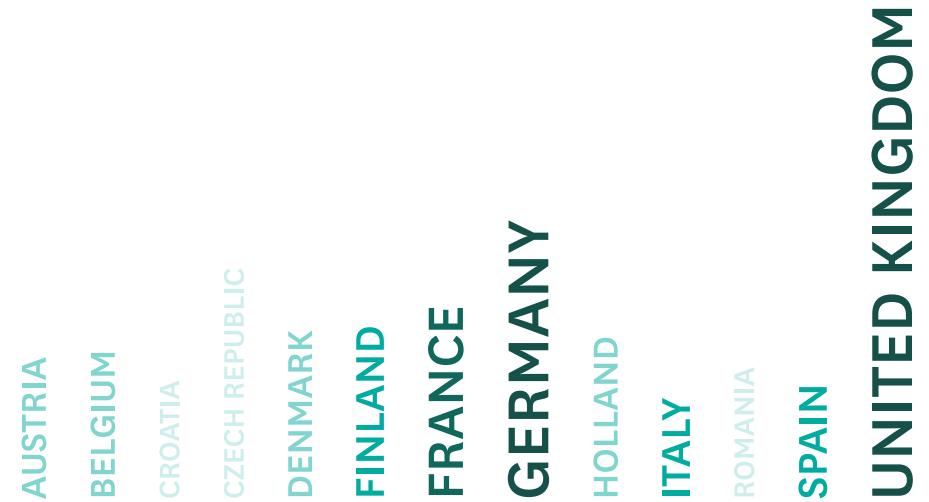


Figure 5: iMM's european partners in Horizon 2020 projects.

H2020 Spreading excellence and widening participation in Life Sciences

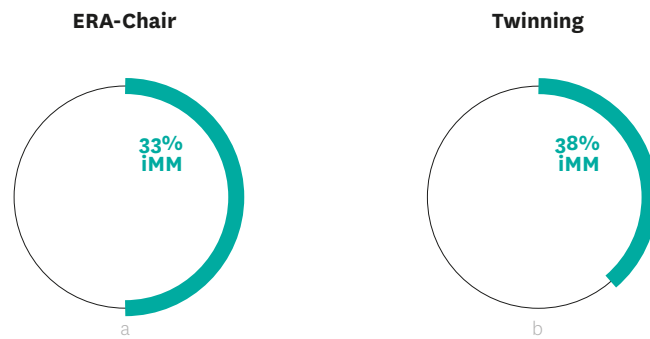


Figure 4: Percentage of H2020 Spreading excellence and widening participation a) ERA-CHAIR and b) Twinning grants awarded to iMM (dark) and to all other national institutions (light) in the area of Life Sciences.

Categories of iMM - Budget 2017

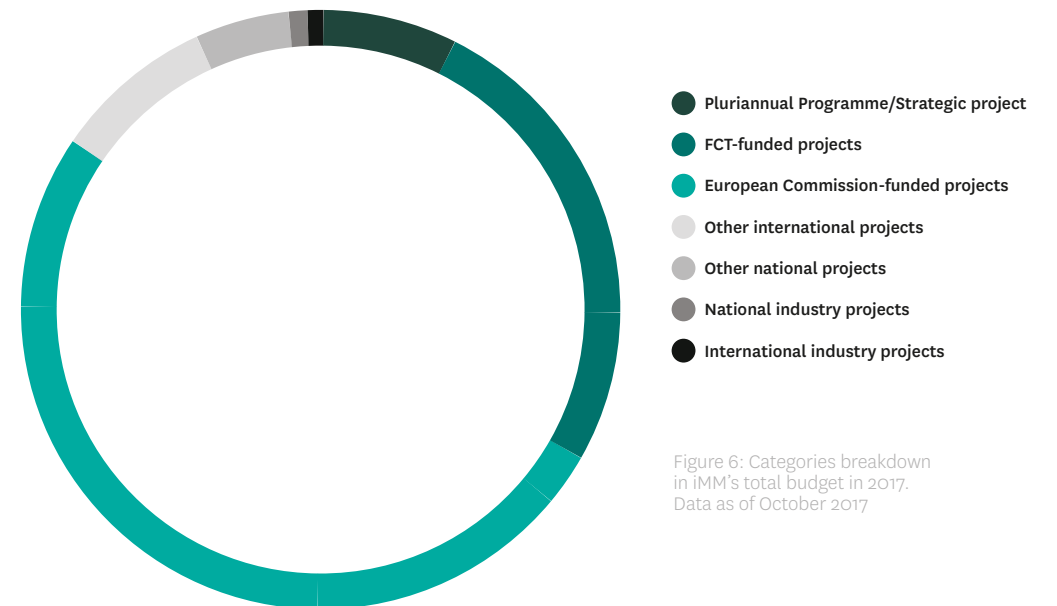


Figure 6: Categories breakdown in iMM's total budget in 2017. Data as of October 2017

This outstanding national performance of iMM in the EU Horizon 2020 has many positive impacts namely in the expansion and consolidation of our scientific network within Europe (Figure 5) and in the relevance in iMM's budget (Figure 6).

Success stories from 2017



In addition to these aspects, IMM was also invited to become member of Vision 2020: The Horizon Network, an Open Innovation platform connecting leading research institutions to innovating businesses fostering access to Horizon 2020 collaborative funding to deliver pioneering projects.

Notwithstanding the importance of EU Research and Innovation Programme, diversification of funding sources is crucial to achieve IMM's scientific goals. Our researchers have certainly embedded this and, in 2017, IMM researchers submitted 215 applications to 42 different International and to 19 different National Funding Programmes.

Last, but not least, during 2017, the Funding team was reinforced with two great professionals – Afonso Duarte and Bárbara Gomes – and integrated in the Management Unit with the goal of streamlining pre- and post-award workflow and strengthening IMM's capacity towards future funding challenges.

iMM was also invited to become a member of Vision 2020: The Horizon Network, an Open Innovation platform connecting leading research institutions to innovating businesses.



H2020 ERC-CoG

Luísa Figueiredo was awarded a €2M ERC Consolidator Grant for her innovative and ground-breaking project FatTryp - Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease. Following her recent discovery of adipose tissue as a novel African trypanosome parasite reservoir, the present project will bring important insights on the understanding of host-parasite interactions namely on aspects related to tissue tropism and adaptive metabolic mechanisms. The state of the art in the field will be pushed forward with important impact in terms of therapy, pathology, relapse and transmission of disease.



Transatlantic Networks of Excellence

Cláudio Franco integrates the team awarded 1 of the 5 Transatlantic Networks of Excellence Grants attributed in 2017 by Fondation Leducq. The team secured €6M for their project ATTRACT - Arterial flow as attractor for endothelial cell migration – a new concept in vascular malformation and stroke regeneration. This collaborative work will pave the way for understanding the rules controlling adaptive and maladaptive endothelial cell movements in blood vessels in health and cardiovascular diseases.



Fundo iMM-Laço 2017

The 2nd edition of Fundo iMM-Laço, a partnership aiming at supporting cutting-edge research at iMM Lisboa on the causes of primary and metastatic breast cancer, distinguished 3 projects based on novelty and impact. Karine Serre will explore a dietary regimen that potentiates anti-tumor immunity enhancing responses to cancer treatments.

Sérgio de Almeida will look to the selective killing of estrogen-dependent breast cancer cells in the context of R-loop suppressor enzymes.

Rui Martinho will work on the hypothesis that yet unidentified components of the DNA repair machinery provide novel targeted therapies for breast cancer.



EMBO Installation Grant

EMBO has awarded Nuno Morais a further 2-year funding for his Installation Grant to continue progressing on the transcriptomic landscapes of cancer focusing on the transcriptional etiology towards personalized therapeutics.



2017 Pfizer Award for Basic Research

Maria Mota and her team were distinguished with the 2017 Pfizer Award for Basic Research in Biomedical Sciences for their work on how Nutrient sensing modulates malaria parasite virulence (Nature Letter, 2017, vol 547, 213). The team's findings reveal a key parasite nutrient-sensing mechanism that is critical to modulate the replication and virulence of malaria parasites.



Santa Casa Neurosciences Award 2017

Maria José Diógenes, senior scientists at Sebastião Lab, was awarded the 2017 Prémio Mantero Belard for her project Novel therapeutic strategy and new biomarker for Alzheimer's Disease based on BDNF receptor cleavage. This work will evaluate a new pharmacological tool to prevent the brain derived neurotrophic factor (BDNF) receptor's cleavage and to validate a novel biomarker for Alzheimer's Disease diagnosis/progression status.

Awards

January



Cláudia Faria
D. Manuel de Mello Grant



Inês Gomes
Bolsa LPCC/Pfizer



Karine Serre
Fundo IMM-Laço

February

**Ana Martins,
Ivo Martins, Patrícia Carvalho,**
CoHiTec 2016 Program



Diana Prata Lab
CoHiTec 2016 Program



April



Bruno Silva-Santos
Menção Honrosa Prémio Bial 2016

May



Diana Prata
3rd place for the 'Innovation
and Entrepreneurship' category
of the Marie Skłodowska-Curie
Actions 2017 Prizes



Maria M. Mota
Prémio Executiva:
"As 25 mulheres mais influentes"



João Eurico da Fonseca Lab
Fundo de Investigação da Sociedade Portuguesa
de Reumatologia
-
3º lugar Bolsa Pfizer Sociedade Portuguesa
de Reumatologia
-
1º lugar Bolsa JAKIE Sociedade Portuguesa
de Reumatologia

Julho



Joaquim Ferreira
"Prémio na área de Saúde
(Medicina, Medicina Dentária,
Farmácia, Enfermagem)
- Prémios Científicos
Universidade de Lisboa
/Caixa Geral de Depósitos 2017"



Nuno Santos
Prémio na área científica de Biologia,
Engenharia Biológica, Bioquímica e Biotecnologia
- Prémios Científicos Universidade de Lisboa
/Caixa Geral de Depósitos 2017



Luísa Lopes
Menção Honrosa Prémios
Científicos Universidade de Lisboa
/Caixa Geral de Depósitos 2017



Maria José Diógenes
Grant Association Française du Syndrome de Rett

August



Luísa Figueiredo
Welcome Trust Collaborative Grant

October



Diana Prata
The SME Instrument, Horizon 2020
for NeuroPsyCAD spinoff



Luísa Figueiredo
ERC Consolidator Grant

November



Maria M. Mota
Prémio Pfizer: Basic Research



M^a José Diógenes
Prémios Santa Casa
da Misericórdia: Prémio
Mantero Belard




Bruno Miranda
Prémios Santa Casa da Misericórdia:
Prémio João Lobo Antunes

December



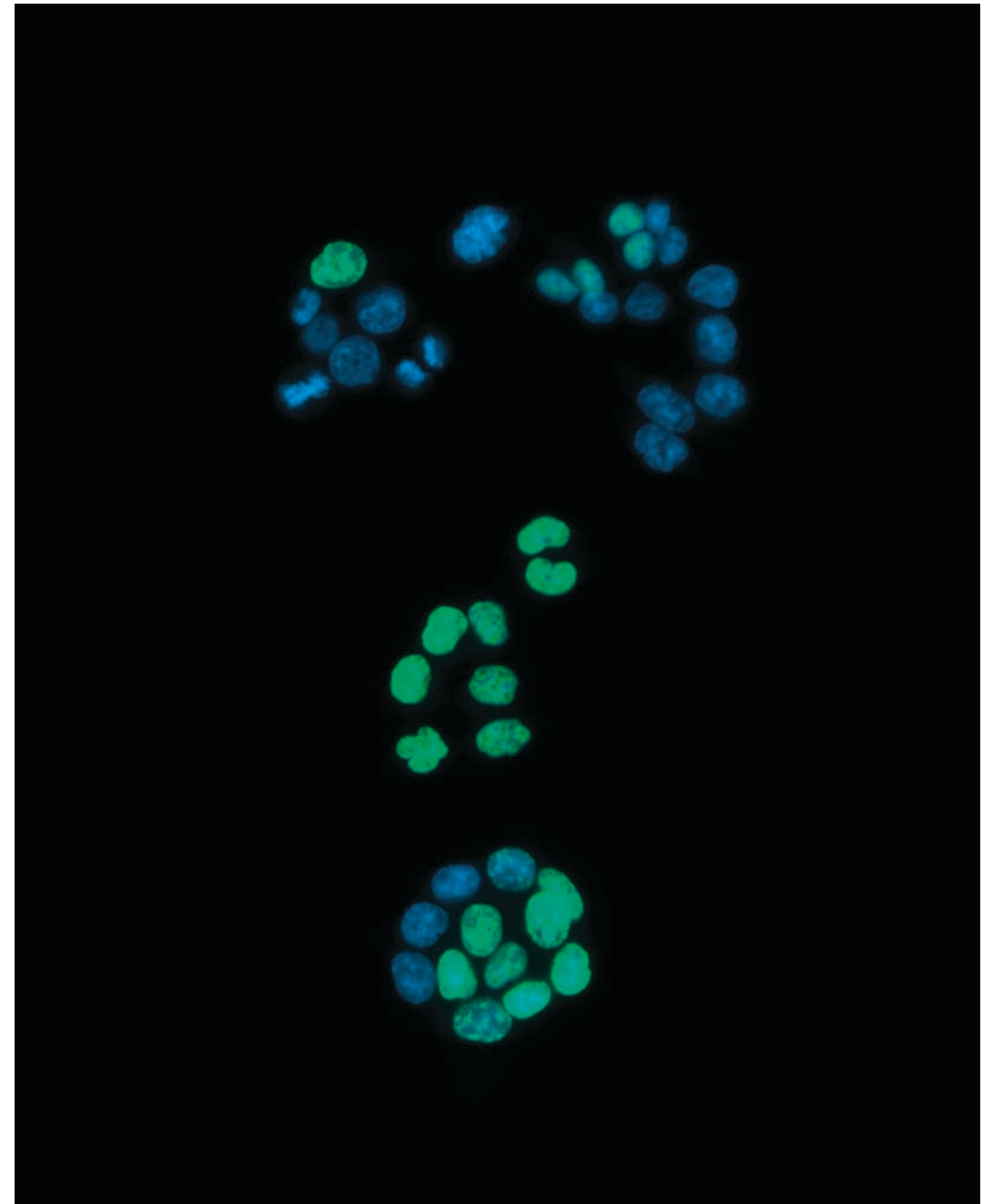
Ana Filipa Guedes
Prémio Pulido Valente Ciência 2017



**We are also among
the most privileged
ones who get to see the
researchers' brand new
and exciting ideas
evolving and getting
a "project shape"**

ERC Symposium :

The ERC
was set up
by the EU
in 2007
to fund
excellent
scientists
and their
most creative
ideas.



Hepatoma tissue culture cells through the lens of a widefield fluorescent microscope.
Credits: José Rino, João Ferreira and Maria Henriques

ERC Symposium



On the 16th of March IMM celebrated the European Research Council's (ERC) 10th anniversary together with several countries around Europe.

After the invitation received by Pablo Amor, ERC's Executive Agency Director, we believed this was an opportunity we could not miss, as over the years IMM has been the home of several ERC grantees.

The ERC was set up by the EU in 2007 to fund excellent scientists and their most creative ideas. It supports cutting-edge research in all fields, and helps Europe keep and attract the best researchers of any nationality. Today, the ERC is a key component of Horizon 2020, the EU's programme for Research and Innovation.

The ERC makes Europe a more attractive place for bright minds, whether they are staying, moving there from afar, or returning to Europe.

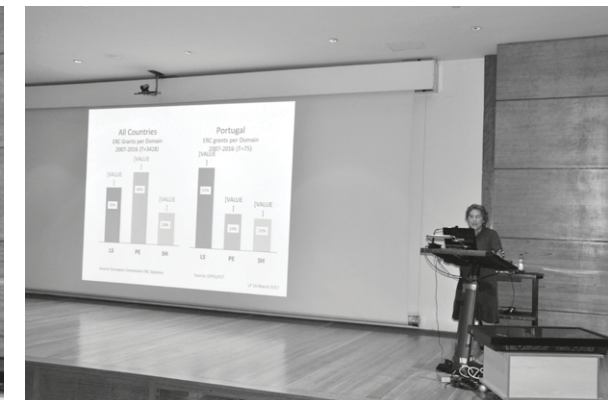
The ERC makes Europe a more attractive place for bright minds, whether they are staying, moving there from afar, or returning to Europe. By creating open and direct competition for funding between the very best researchers in Europe, the ERC enhances aspirations and achievements, enabling the best ideas and talent to be recognised from a larger pool that exists at national level.

"ERC funded projects are responsible for 6 Nobel Prizes, 5 Wolf Prizes and 4 Field Medals. And ERC funded projects have resulted in 100,000 articles being published in scientific journals, including over 5,500 in the 1% most cited scientific journals. That means that for the first time, Europe has surpassed the US in the number of top one percent most cited scientific publications", stated Carlos Moedas, European Commissioner for Research, Science and Innovation, at a speech made during the ERC Grantees Event in Israel.

To celebrate ERC's 10th anniversary, IMM devised a heavy social media campaign with videos from all of IMM ERC grantees and shared them on different social media platforms using the official hashtag #ERC10yrs.

This campaign served its purpose and got people talking, ending up being mentioned by Carlos Moedas himself during his speech at Pavilhão do Conhecimento, Lisboa.

IMM also held an afternoon symposium with Professor M^a Carmo-Fonseca and Professor Leonor Parreira hosting the opening and closing sessions, respectively, and with João Barata, Maria Mota, Bruno Silva-Santos, Vanessa Morais, Cláudio Franco, Edgar Gomes and Henrique Veiga-Fernandes presenting their research projects funded by ERC grants. The Symposium was attended by, amongst several people, the Portuguese Minister for Science and Higher Education Professor Manuel Heitor.





ERC Consolidator Grant :

Lúsa Figueiredo was one of the eight Portuguese researchers who in 2017 received the prestigious European Research Council (ERC) Consolidator Grant, totalling more than 16 million euros of scientific research investment for the country. Lúsa's laboratory received 2 million euros to finance its innovative research projects in areas such as neuroscience, metabolism infection and immunity. The ERC, set up by the European Union in 2007, is the first European funding organisation for excellent frontier research. Every year, it selects and funds the very best, creative researchers of any nationality and age to run projects based in Europe. The ERC Consolidator Grants are awarded to outstanding researchers of any nationality and age and a scientific track record showing great promise. Research must be conducted in a public or private research organisation located in one of the EU Member States or Associated Countries.

Luísa Figueiredo



At IMM, Luísa Figueiredo's team studies the parasite responsible for sleeping sickness. In the terminal phase of this disease, patients suffer from excessive weight loss but the reasons behind this observation remain unknown. Luísa's team recently found that since the initial phase of this disease the parasites occupy and persist in their host's fat. Now, the ERC will allow her team to study the importance of fat tissue "sequestration" for disease development and how it contributes to the observed weight loss. Moreover, the team wants to understand if by hiding within fat the parasite can resist to therapies this way accounting for the common number of relapses observed after treatment.

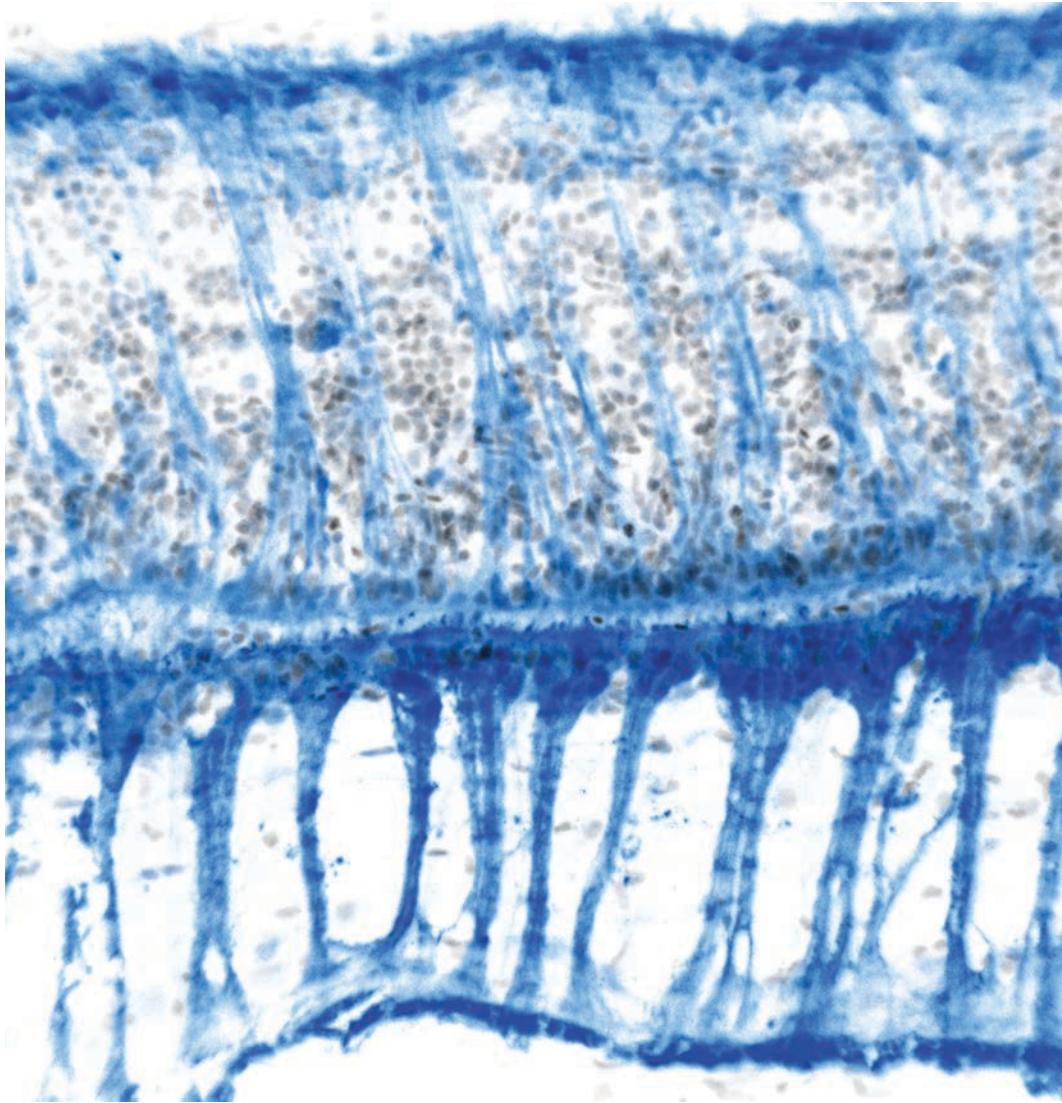
"ERC financing is extremely special because it spans for five years and incentivizes researchers' creativity. This way we are given the appropriate conditions to explore difficult and risky questions that are potentially very innovative," said Luísa.

Carlos Moedas, the European Commissioner for Research, Science and Innovation said that he received these results with "great satisfaction" since another eight Portuguese researchers have now won the prestigious Consolidator Grant. Furthermore, he was even more happy to know that five of them are women, and congratulated every winner stressing they "are examples of the scientific quality developed in Portugal."

The President of the ERC, Professor Jean-Pierre Bourguignon also commented on the occasion: "On behalf of the Scientific Council, I'd like to congratulate the new ERC grant winners. I also express my gratitude to the over 3,000 top scientists and scholars for their pain-staking work, evaluating and identifying the most ambitious proposals submitted to the ERC. The funding will encourage these mid-career scientists to explore further the unknown and develop their most daring ideas at their own initiative. By leaving them freedom, the ERC is enabling breakthroughs. This conditions the capacity of Europe to respond to a number of challenges and to improve the lives of its citizens if the appropriate policies are adopted."

We are sure Luísa and her team will continue to produce state-of-the-art research and we are excited for what the future holds!





Zebrafish spinal cord at the level of the central canal. Ependymal cells send projections that form a palisade. | Credits: Ana Ribeiro



iMM produces cutting-edge scientific research at an incredible speed every year which with the right support can be translated into biomedical products for the benefit of patients and society as a whole.

This is a major challenge for any institution, which requires specific measures and intervention. The EU-funded project TwinntoInfect, of which iMM is a main partner, allowed our institution to have a dedicated budget for a new program focused on innovation and technology transfer, designated “iMM innovators (“iMMi”).

iMMi is aimed at supporting iMM scientists (students, technical staff and researchers, Group Leaders) to develop their ideas, technologies or projects with potential application, with the ultimate goal of commercialization.

We all know that the successful development of entrepreneurial ideas requires time, money and specific skills, all factors for which iMMi will provide institutional support to.

All the involved players



After the first call for innovators with potentially applicable ideas/ technologies, four teams went to competition:

Project 1 João Lacerda's Team

The team intends to develop tailored advanced medical therapy products (ATMP) for the treatment of CMV, EBV and BKV infection occurring in immunocompromised patients. They want to develop a cryobank under GMP standards of third-party pathogen-specific T-cell lines, providing an “off-the-shelf” therapy with the potential to improve survival after allogeneic hematopoietic stem transplantation (allo-HSCT) and also solid organ transplantation and immunodeficiencies.

Project 2 Luís Graça's Team

In the context of autoimmune diseases Luís Graça's team wants to offer a quick and easy blood test that can measure the Tfr/Tfh ratio in the blood of Sjogren's syndrome patients, this way overcoming the need for a liquid biopsy. In addition, they believe this test can also offer companion diagnostics for clinical trials.

Project 3 Gonçalo Bernardes's Team

The team has developed an algorithm using machine learning that can identify drug targets and develop novel drugs against different types of leukemia.

The idea is to leverage the development of a novel drug target (NP) into an efficacious entity to manage and treat acute myeloid leukaemia (AML) and chronic lymphoid leukaemia (CLL), with advantages over the current standard of care. In particular, the targeted delivery of the NP to leukemia cells is mediated through antibodies that have the potential to achieve therapeutic efficacy while circumventing the intrinsic toxicity of the drug. Their machine learning platform has the potential to generate a sustainable product pipeline to answer unmet medical needs with a significant market size.

Project 4 Lina Páez's Team

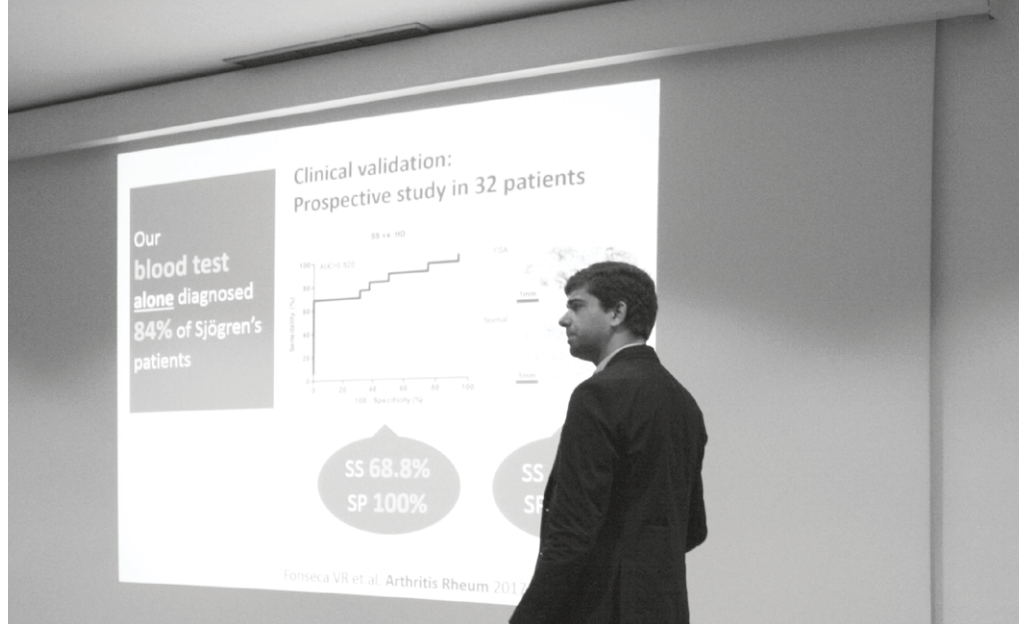
The team has developed a strategy, based on the bioinformatics analysis of publicly available genetic information of Colorectal carcinoma (CRC) tumour samples to develop a novel algorithm for CRC prognosis and/ or prediction. This algorithm is based on the balance between different products of the same gene and allows the detection of tumor malignancy at an earlier stage of development. Moreover, it provides a better guidance regarding the best treatment for each patient and it is doctor friendly to define prognosis and response to treatment.

Winners

After an intense round of presentations and much deliberation, the jury formed by Richard Hampson from Thelial, Cristina Simões and Ana Filipa Bernardo from Cohitec, Paulo Osswald from Movente, Mallory Perrin-Wolff and Nicolas Torno from Institut Pasteur, Veronique Birault from the Crick Institute, Pedro Moura from Merck and António Dinis from Hovione, deliberated that Válder Fonseca from Luís Graça lab were the winners of the first iMM innovators competition!

The researchers will now receive financial support and expertise guidance to develop their ideas towards application in human health care.

Researchers presented their work to all the members of the jury



iMMi

Lina Páez's Team



Luís Graça's Team

João Lacerda's Team

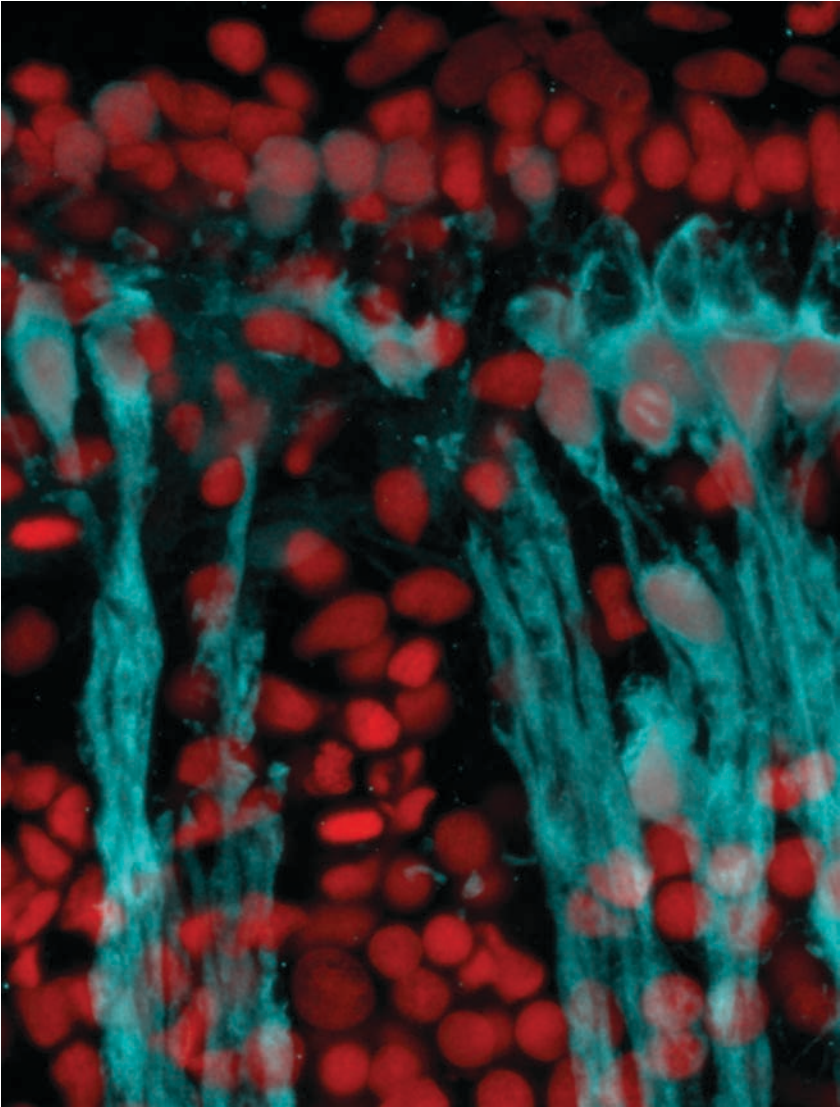


Gonçalo Bernarde's Team

The winning team represented by Valter Fonseca, from Luís Graça's Lab



iMM Laboratories :



Ependymal cells in the zebrafish spinal cord. | Credits: Ana Ribeiro

iMM Laboratories



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Cláudio Franco
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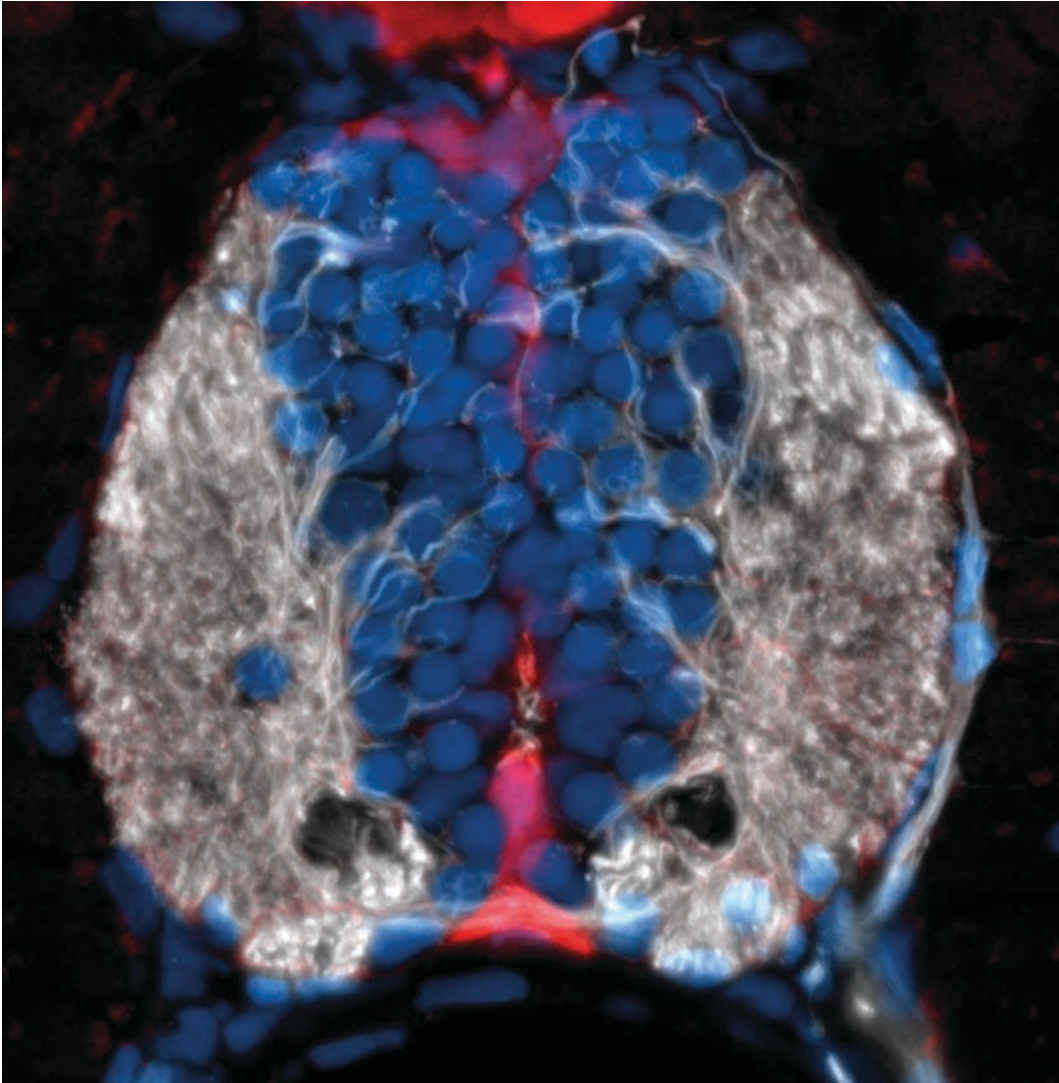
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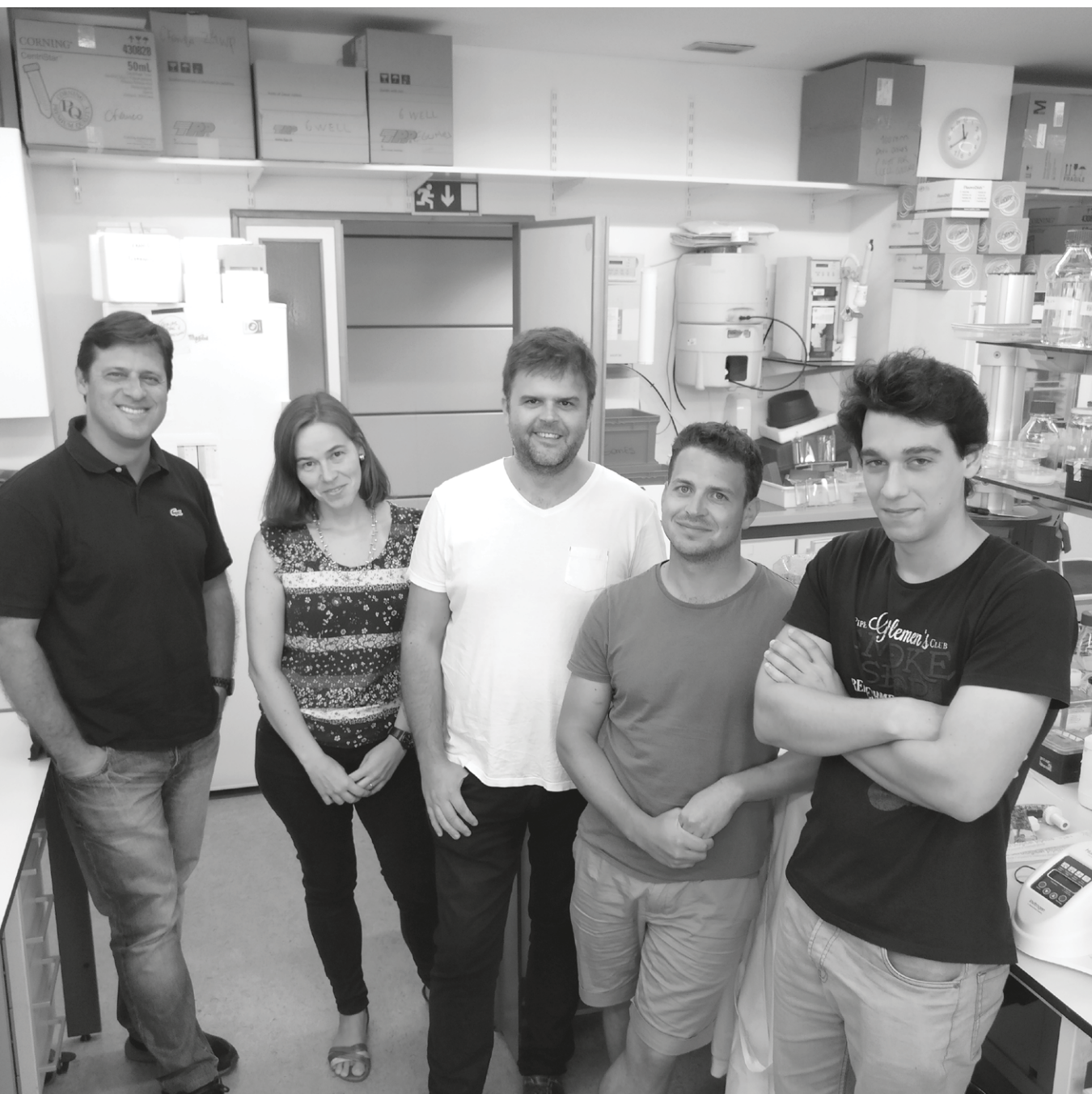
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Publication Highlights :



Zebrafish embryonic spinal cord, showing dorsal and ventral cells in red and axonal projections in white. | Credits: Ana Ribeiro

Muscle nuclei: may the force be with you



Edgar Gomes and his team have revealed the mechanism by which cellular nuclei reach their position within muscle cells. The discovery published in *Nature Cell Biology* can have important implications in therapeutic strategies to treat muscular diseases.

Muscular diseases can range from genetic disorders to aging muscles. Muscle loss affects the entire segment of the aged population. This increases the risk of severe mobility limitations, hospitalization and mortality. These numbers will all be inflated by the growing aging population. It is estimated that by 2050 the world's population above 60 year's old will double reaching around 2 billion world-wide. This generalized aging poses a series of challenges for society.

A hallmark of muscle cells is the unique position of their nuclei at the cellular periphery. In multiple muscle diseases, this nuclear positioning fails to occur. Although the severity of symptoms varies amongst affected individuals, these diseases result in a gradual loss of muscle function that leads to a loss of autonomy.

The team studies nuclear positioning during muscle formation, in particular how nuclei move from an initial central position to the periphery of muscle cells.

"Throughout my PhD I heard scientists commenting on nuclear positioning as an indicator for muscle diseases without knowing how nuclei are positioned. It was therefore exhilarating to uncover how this process occurred; now we have to understand why", said the study's first author William Roman.

Researchers devised a unique protocol that allowed them to design a theoretical model to explain this natural phenomenon. The model was then tested in the laboratory and led to the identification of the forces involved in nuclear movement at a molecular level.

"It was fascinating to observe for the first time how nuclei are positioned at the periphery of the muscle fibers. We expect that this discovery will be important to develop novel treatments for different muscle disorders and for sport-induced muscle injuries", said Edgar Gomes.

This work, which also involved teams at the Crick Institute in London, and Center for Research in Myology in Paris, identifies both the mechanism and the molecular pathways involved in nuclear positioning in muscle. Since nuclear positioning is disrupted in most muscle disorders, these discoveries can become targets for novel therapeutic strategies.

In the future, this work can be basis for the identification of optimal physical exercises to preserve and repair muscle capacity. Formulating workout strategies not only for aging population but also for athletes would promote a healthier lifestyle.

Roman et al. Myofibril contraction and crosslinking drive nuclear movement to the periphery of skeletal muscle. *Nature Cell Biology* 2017

Tick tock: Time to sleep? Sleeping parasite has own internal clock ●



Luísa Figueiredo and her team, in collaboration with Joe Takahashi's group from Southwestern University, have shown for the first time that the parasite responsible for sleeping sickness, *Trypanosoma brucei*, has its own internal clock, which allows it to anticipate daytime alterations of its surrounding environment and become more virulent.

The article, published in *Nature Microbiology*, reveals that the parasites slightly alter their composition and functions in a highly predictable manner, according to the different hours of the day. One of the consequences of such alterations is that parasites become more sensitive to a certain drug in the evening rather than in the morning.

We all have our own internal clock that allow us to know the time of day even without looking at our clock. When we travel to countries with a big time difference from our original timezone, we get 'Jet-lagged', precisely because our body 'thinks' it is still a certain time of the day.

This internal clock, also known as circadian clock, allows living organisms to be adjusted and anticipate daytime variations.

The team already knew that the parasite interferes with the internal clock of its host, however it was not known that the parasite had its own clock.

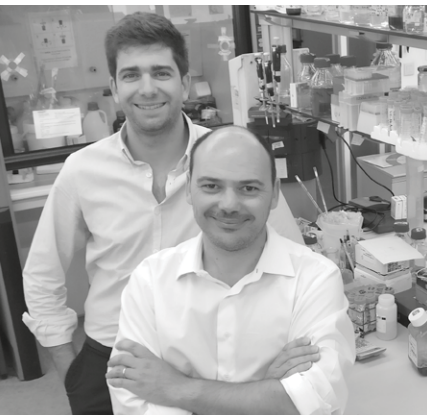
This was a highly risky project! But it was worth it because ultimately it worked," said Filipa Rijo-Ferreira, a PhD student who led the project.

The team identified a way to synchronize all parasites to the same time of the day and from then they sequenced their transcriptome, a type of genetic fingerprint. With the help of bioinformatics, they found a pattern of daytime variation which meant there are processes within the parasite that oscillate throughout the day.

For the treatment of patients with sleeping sickness "in the future we can administer this drug at certain hours of the day because now we know that it will be more efficient. This concept of administering a therapy at a specific hour, known as chronotherapy, is already applied to other pathologies, namely asthma and cancer. However, it has never been applied in the treatment of infectious diseases," concluded Luísa Figueiredo.

Sleeping sickness is an infectious disease that is fatal in the majority of cases. It is transmitted by the tsetse fly and and such it only exists in Sub-Saharan Africa. There are currently no vaccines against this disease and most treatments carry several problems like toxicity and difficulty to administer. There are currently approximately 7000 disease cases every year with the World Health Organization (WHO) intending to eliminate the disease until 2020.

Researchers find new type of blood cells that work as indicators of autoimmunity along with a key mechanism to control antibody production



Luis Graça and his team have found a cellular mechanism that underlies the development of autoimmune diseases.

The immune system is responsible for our body's defence against infections. However, an inefficient and uncontrolled defence can lead to certain lesions and result in autoimmunity.

The study, published in Nature Communications, builds on previous observations from the same team who found that a specific type of cells regulate antibody production. They hypothesized there was probably a marked division of tasks between different cells of the immune system: those that help the production of antibodies (T follicular helper) and those that stop the production of antibodies against our own tissues (T follicular regulatory).

The team developed experimental methodologies which allowed them to identify the molecular targets that lead to the formation of antibodies in both helper and regulatory cells.

The development of autoantibodies is one of the key factors for the development of several autoimmune diseases, such as lupus or rheumatoid arthritis.

As such, to be able to identify the specific cells that regulate the production of antibodies and that suppress the actions of the immune system may lead to the development of novel forms of diagnostic or treatment, including more efficient vaccines.

Throughout 2017 Luis Graça and his team have published two studies demonstrating how the process that leads to the production of antibodies is regulated.

Deregulation in this type of process can lead to the development of autoimmune diseases. In one of the studies published in Nature Communications, the team showed that cells that promote antibody production (T_{fh}) coexist with another type of cells (T_{fr}) that stop these same antibodies from reacting against proteins of our own bodies.

In the other study, published in Science Immunology, the team analysed blood samples from Sjögren syndrome patients, an autoimmune disease that affects the mucous membranes and moisture-secreting glands of the eyes and mouth, and found that these patients have a significant increase in a specific type of immune cells called T follicular regulatory cells (T_{fr}).

These cells are usually found in lymphoid tissues where they regulate antibody production. It was a surprise to find an increase of these type of cells in patients with excessive antibody production. In fact, the results were the opposite of what the team was expecting.

To understand the reason behind such unexpected results the researchers studied different biological samples. For instance, comparing T_{fr} cells in the blood and in the tissues where antibodies are produced (tonsils obtained from children subjected to tonsillectomies), provided evidence that blood T_{fr} cells are immature, not able to fully suppress antibody production. Such immaturity was confirmed by studying blood samples from other patients with genetic defects. Furthermore, exposure of healthy volunteers to flu vaccine led to an increase in blood T_{fr} cells, in line with their generation during immune responses with antibody production.

Blood circulating T_{fr} cells are distinguished from other circulating lymphocytes by two molecular markers, CXCR5 and FOXP3, the first of which endows these cells with the ability to migrate into specific zones of lymph nodes where they may complete maturation and regulate antibody production.

The team is now trying to understand what happens to these cells in other autoimmune diseases to evaluate their potential not only for diagnostic but also to identify which patients may benefit with medicines that interfere with the production of harmful antibodies.

Maceiras et al. T follicular helper and T follicular regulatory cells have different TCR specificity. Nature Communications, 2017

Fonseca et al. Human blood T_{fr} cells are indicators of ongoing humoral activity not fully licensed with suppressive function. Science Immunology, 2017

Novel protein interactions explain memory deficits in Parkinson's disease



Luísa Lopes and her team, along with colleagues from University Medical Center Goettingen, Germany and CEDOC – Nova Medical School Lisbon, have shown that abnormal forms of Parkinson's disease (PD)-associated protein alpha-synuclein interact with the prion protein (PrP), triggering a cascade of events that culminates in neuronal dysfunction, causing cognitive defects that are reminiscent of those in PD.

"This is the follow up of a previous study initiated in my laboratory, where we found that particular forms of the protein alpha-synuclein cause dysfunction of neuronal circuits involved in memory formation. We did not know how this was happening, and in this new study we have detailed the molecular mechanisms involved, which suggests we now have new targets for therapeutic intervention" – explains Tiago Outeiro, a former Group leader of iMM now in Germany and at CEDOC, who coordinated the study together with Luísa Lopes, a Group Leader at iMM.

Using pharmacology and genetics, the team has now defined a series of molecular events that explains the memory defects observed in animals that model some important aspects of PD.

Luísa Lopes adds: "We used a mouse model of PD in which human alpha-synuclein is produced and found that by blocking this interaction with PrP using a caffeine analogue, reverted the abnormal neuronal activity and memory deficits. This study links nicely with our previous work on Alzheimer's disease, further suggesting that molecules like caffeine may indeed have potential benefits against memory deficits upon neurodegeneration".

Parkinson's disease is a devastating disorder affecting millions of people worldwide. Current therapies are only symptomatic, and treat only some of the motor symptoms of the disease. "We now know that PD is much more than just a motor disease, and there is a great demand for novel therapies, especially those capable of modulating disease progression or, ideally, capable of preventing the onset of the disease" - explains Tiago Outeiro.

"We are very excited with the findings of our collaboration, and this study demonstrates that when we pull together our complementary expertise we can make important discoveries that can impact the lives of the millions of people (patients and families) affected by these terrible disorders" – concludes Luísa Lopes.

Ferreira et al. α -Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B.

Nature Neuroscience 2017

Less is better: Malaria parasites able to sense their hosts calorie intake



Even though malaria still kills one child every minute, the vast majority of those infected still survive, with roughly 200 million new infections every year.

Maria Mota and her team have shown that the infectious agent responsible for malaria, the *Plasmodium* parasite, is able to sense and actively adapt to the host's nutritional status.

Using mouse models of malaria infection, scientists found that mice who ate 30% fewer calories had a significantly lower parasite load.

Plasmodium parasites reproduce inside red blood cells every 48 hours. The study in *Nature* reveals for the first time that the parasite's rate of replication depends on the calories ingested by the host. This may ultimately dictate the outcome of a malaria infection: survival or death.

"This finding alters our understanding of the dynamics of malaria infections in the field and might be highly relevant facing the alarming trend of global increased overweight versus underweight populations, including in malaria endemic regions", says Maria M. Mota.

Initial findings were greeted with some surprise. "For several months I was stunned by how quickly these parasites adapt," says Liliana Mancio-Silva, the study's first author. "It was very exciting."

There were two possibilities to explain the surprising observation: either the parasite was actively adapting when changed to a host with lower calorie intake, or instead was struggling to replicate due to the fact that some key nutrients were missing.

Researchers controlled the food intake of mice before infection with different *Plasmodium* parasites and studied their response. They found that parasites that were missing an enzyme called KIN had an impaired response to decreased nutrient availability, and replicated at the same speed, regardless of the food available to the mice.

“This is one of the best examples demonstrating that malaria parasites sense and adapt to their host’s metabolic environment through transcriptional and developmental changes,” said Manuel Llinás, professor of biochemistry and molecular biology at Penn State University and an author of the paper. “Discovering precisely how this occurs may lead to new therapeutic intervention strategies to significantly reduce parasite burden.”

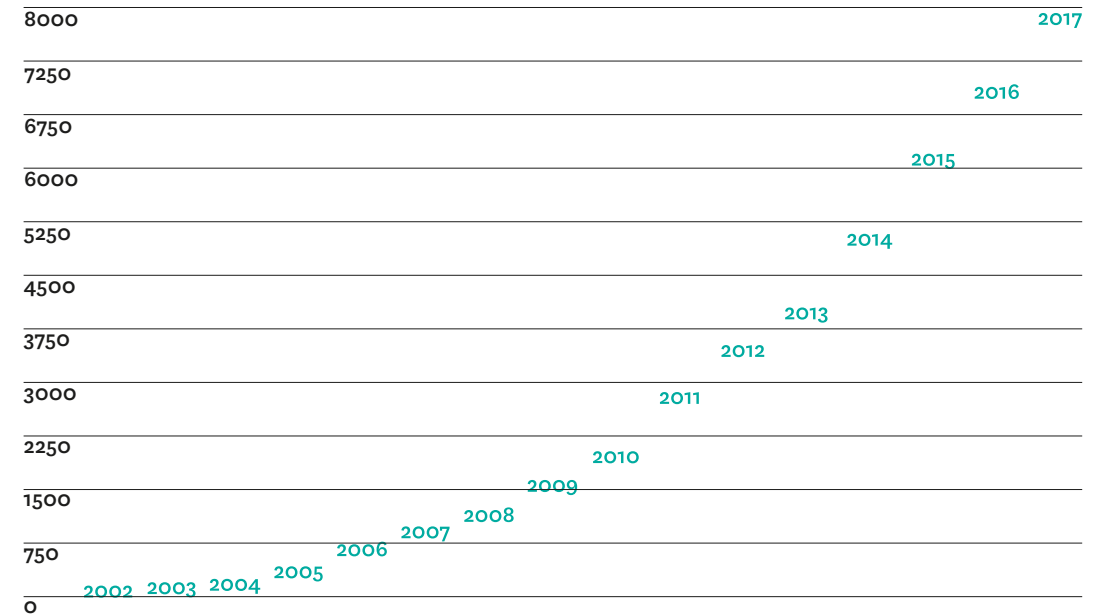
These results imply that KIN acts as a nutrient sensor and major regulator of parasites’ ability to respond to nutritional changes, and that the malaria parasites adapt actively.

Dr Oliver Billker, a collaborator on the research from the Wellcome Trust Sanger Institute, said: “This is the first time that anyone has seen that a parasite can actively restrict its growth to the environment and completely changes the way we look at parasite growth. While future research is still necessary to understand the full extent of these findings, it may well have implications not just for malaria, but also for other infectious diseases.”

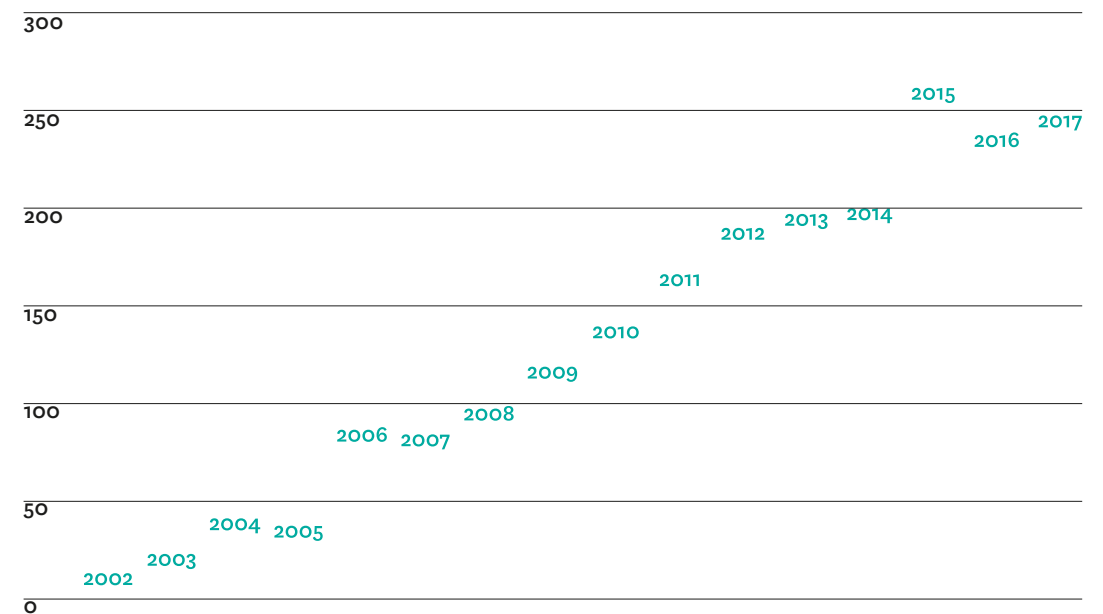
The data was also surprising in the context that KIN does not have many of the expected features of other nutrient sensor molecules shared between yeast, plants and mammals. As such, these findings are just the tip of the iceberg. Future studies in parasite adaptation to host nutritional states will investigate how KIN is controlled and what are its partners.

A better understanding of this system may help researchers design strategies that trick the parasite into slowing its replication to make it easier to control.

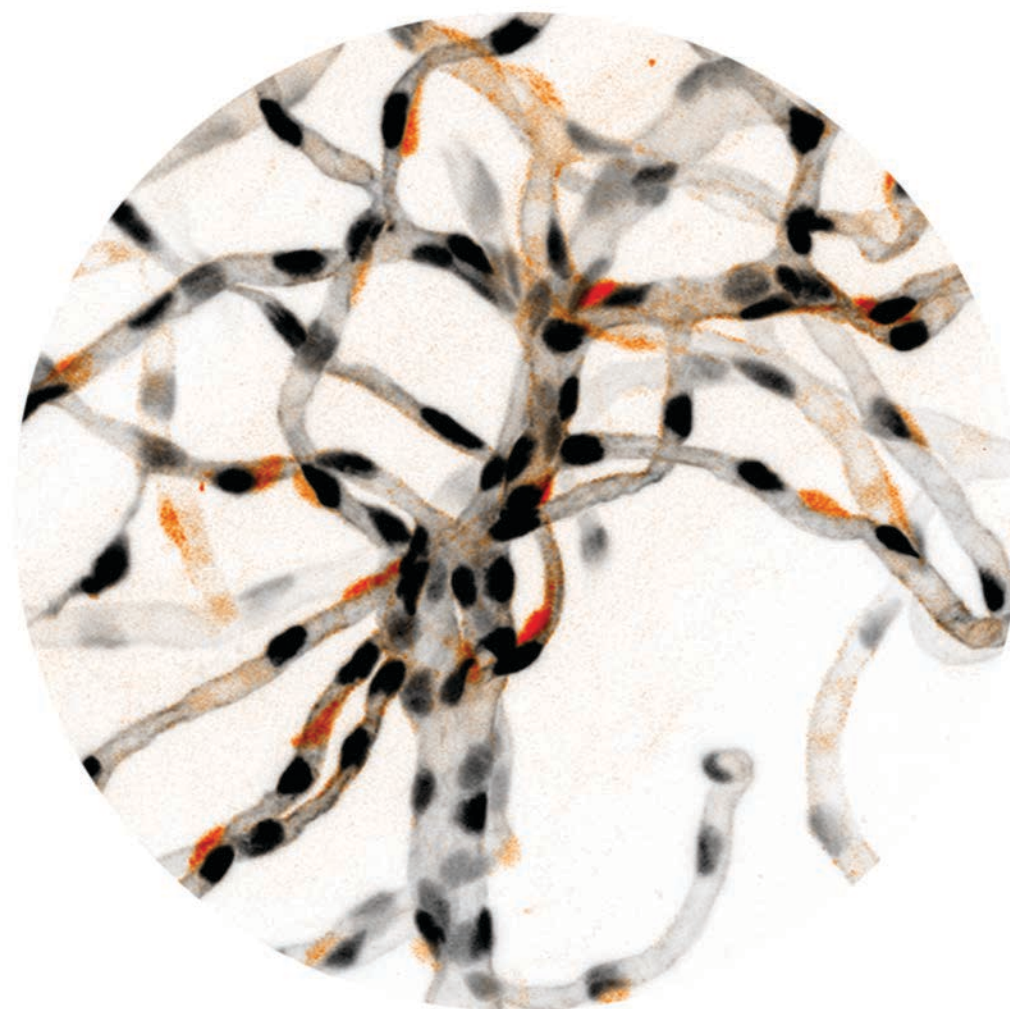
Citations in each year



Publications in each year



Malaria Vaccine Clinical Trial :



The spinal cord vasculature in zebrafish, with endothelial cells in black and pericytes in orange. | Credits: Ana Ribeiro

Miguel Prudêncio



In the beginning of 2010 Miguel Prudêncio and his team received the first Bill & Melinda Gates Foundation (BMGF) grant attributed to a Portuguese project, as a part of their Grand Challenges Explorations (GCE) program. In 2012, the team submitted the first report containing the results obtained with the initial 100.000 dollars and later in 2013 they received the second funding of the GCE program, something that only happens to roughly 10% of all projects funded in the initial stages of the program and that accounted for a total of 1.5 million dollars.

In 2015, BMGF considered the project was promising enough to continue into the Malaria Vaccine Initiative (MVI), an entity that coordinates the development of malaria vaccines around the world. This major step led to an additional funding of 250.000 dollars to pursue the necessary studies that would eventually lead to the development of a vaccine candidate.

In 2017 Miguel's team together with the Radboud University Medical Center (RUMC), Netherlands, saw their request for a clinical trial approved.

The trial, which began in May, is a Phase 1, first-in-human clinical trial, followed by a Phase 2a trial to evaluate protection against Controlled Human Malaria Infection (CHMI).

The concept being tested is similar to that used by Edward Jenner to develop a vaccine against smallpox, the only disease affecting humans that has ever been eradicated. Jenner used cowpox – a similar but much less dangerous bovine version of the disease – to inoculate people against smallpox. The trial, based on data from earlier studies in rabbits conducted by Miguel's lab, will use a rodent version of the malaria-causing parasite (known as *Plasmodium berghei*) to induce protection against the human form of the disease.

The team has modified the genes of the rodent parasite using a protein from *Plasmodium falciparum*, the deadliest version of the parasite known to cause malaria in humans. By modifying the genes of *P. berghei*, the protective efficacy of the vaccine formulation, known as Pb(PfCS@UIS4), will hopefully be increased.



As security measures that need to be undertaken before a clinical trial of this nature can be initiated, the team created a parasite's "Master Cell Bank" (MCB), which means a stock of Pb(PfCS@UIS4) that was extensively characterized at the genetic and microbiological level to account for any possible fault that could compromise the trial. Moreover, the team developed a detection assay to allow for Pb(PfCS@UIS4)'s detection in the blood of vaccinated volunteers along with a pharmacological study to identify drugs with 100% efficacy to eliminate the parasite, in the unlikely event it infects their red blood cells.

The trial will be conducted in two phases at RUMC in the Netherlands. In the first phase, eighteen healthy adult volunteers will be recruited across three groups, and exposed to varying numbers of bites from mosquitoes infected with the genetically modified parasite. If all goes well in phase 1, volunteers will enter into the second phase of the study to assess the protective efficacy of Pb(PfCS@UIS4).

The trial will be conducted in two phases at RUMC in the Netherlands. In the first phase, eighteen healthy adult volunteers will be recruited across three groups, and exposed to varying numbers of bites from mosquitoes infected with the genetically modified parasite. If all goes well in phase 1, volunteers will enter into the second phase of the study to assess the protective efficacy of Pb(PfCS@UIS4).

Pb(PfCS@UIS4) is considered a whole organism approach to vaccine development, meaning that the entire parasite that causes malaria is used to develop the vaccine and induce an immune response in the vaccinee. Though this is the first trial of a malaria vaccine using a genetically modified version of the parasite, other similar approaches have yielded high levels of protective efficacy in early-stage clinical trials. The goal of the malaria vaccine community is to develop a vaccine with 80 percent efficacy for more than one year to help eliminate and ultimately eradicate this disease.



iMM Insectarium :

iMM Inaugurates New Insectarium

In 2017 the iMM inaugurated its new Insectarium thanks to the financial support of the Rotary Club of Oeiras, the Calouste Gulbenkian Foundation and Merck KGaA.

Throughout the years the Rotary Foundation has faced several challenges that have allowed the improvement of the life of different communities that benefit from its involvement.

One of the Foundation's major challenges has been the eradication of Poliomyelitis, which began upon the vaccination of 6 million children in the Philippines. Throughout the years, and as a consequence of the several efforts made in that direction, this disease is practically nonexistent nowadays. As such, the Rotary Foundation took on board two new projects in the areas of Alzheimer and Malaria.

Malaria is currently responsible for the death of 400.000 people every year of which more than 85% are children younger than 5 years of age. The Rotary Club of Oeiras has a close connection to the Rotary Club of Lobito, Angola, making it even more sensitive to this serious infectious disease.

During the Rotary International Convention of 2013, iMM Director Maria Mota presented the project "Let's put an end to malaria" which allowed the Foundation to get to know the work developed by not only the researcher but her fellow iMM colleagues, sparking the interest of Rotary Club of Oeiras.

During 2015 an investment of over 160.000 USD was approved for the acquisition of all the necessary equipment to build a state-of-the-art insectarium, one of the few in available in Europe and worldwide, that can replicate *Plasmodium falciparum*'s life cycle in a laboratory context, the main agent responsible for malaria mortality in human beings.

“The generous contribution of the Rotaries from eleven different countries, the Calouste Gulbenkian Foundation and Merck KGaA has allowed iMM to have a resource with a great potential for the development of novel strategies in the fight against Malaria”, said Miguel Prudêncio, iMM researcher and responsible for the Plasmodium Infection & Anti-Malarial Interventions.



“Once more, the Rotary Club of Oeiras shows us the importance of the involvement of society in the quest for solutions for some of the most pertinent problems we face”, said iMM’s Director and head of the Biology & Physiology of Malaria lab, Maria Mota.

**Technical and
Administrative
Facilities :**

Administrative Facilities



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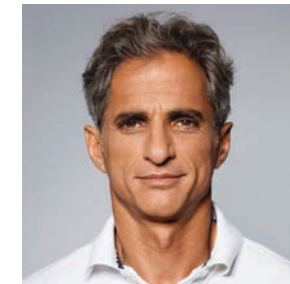
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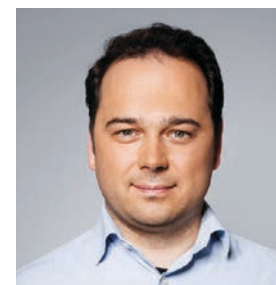


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We want a society that understands what we are doing in IMM. Our dreams, our concerns, our worries in relation to the future.



Interviews :



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For how long has IMM been certified?

We have been certified since 2014 and we've had 8 audits regarding our quality system.

What do you do as the Quality Manager?

I try to make myself useful to facilities by helping them create ways to standardize what we can, this way allowing them to focus on their own objectives while having innovative ideas, always making sure that we comply with the standards and our own rules.

I'm also responsible for managing suggestions and complaints and I accompany and respond to audits.

The main objective of a Quality Manager is to stop being needed and I'm glad to say that all facilities have started to incorporate the ISO in their way of thinking, this way becoming their own quality managers.

What were the main difficulties in creating such a system?

The main difficulty is creating a system that takes into account the fact that we have different facilities with different workflows and requirements they must comply to satisfy researchers:

- some facilities have less users and so they have more of a "family" sense, with less enforced rules;
- some facilities rely more on digital information than others;
- some facilities live more in the back-office and rarely contact with researchers.

And so, to create a uniform system that adapts to all of this mix without creating multiple systems that would by themselves be hard to maintain, is a tough balancing act!

What are the main difficulties going forward?

IMM is still growing and changing and there have been a lot of changes imposed on us. However, we have to keep our culture and face all these changes head on.

And those are the same difficulties that the Quality Management System faces, to be able to accompany everything that is happening, to maintain itself current and useful and sometimes to implement these changes to standardise what we can and to continue to have space for innovation. And that is a challenge for all facilities: how to maintain an excellent service to all researchers, respond to their needs while at the same time innovate and try new things.

Interview with Fausto Lopo de Carvalho



In the beginning of 2017 Fausto Lopo de Carvalho joined IMM to become its Financial and Administrative Director. Although Fausto has a background in Civil Engineering he received an MBA in Finance and has since then developed his career in this area. We talked with him to know more about the man behind the name.



Could you tell us a little bit about yourself?

Sure! I'm a proud father of two amazing kids with whom I learn every day, I'm very positive by nature and with a strong attachment to natural landscapes and outdoor activities. At a professional level, after some years of doubt, I'm now sure that engineering is cool! Very transversal in scope and very good to generate curiosity and brain agility. I support the theory that curiosity drives knowledge and that there are no age limits to gain knowledge on any specific subject from arts to music to science or even... to Finance! I also believe that hard work is the cornerstone for excellence. If I'm allowed to have a "sun tzu cliché moment", I choose the famous quote: "the only place where success comes before work is in the dictionary".

How do you perceive IMM in the context of national and international research?

I think there's no doubt that among the scientific community, both national and international, and for a slice of the general public that shows interest in knowing more about institutions that make our country progress, IMM has the "excellence stamp". Nevertheless, I think IMM has the potential and the need to grow in brand awareness.

What do you think are IMM's main strengths?

If I would dare to comment on the scientific process, I would say that the main strength resides on the transversal reach of the several lines of investigation. Having a broad scope allows researchers to pursue an extremely diverse set of questions! As for the organization itself, the main strength, from my point of view, lays in the freedom of thought and the attitude of continuously pushing IMM forward, aiming high.

What do you believe can be your main contribution(s) towards IMM's future development?

My goal is simple to state - create an organizational structure backed by extremely accurate and agile processes to serve in the best possible way IMM's scientific community. It's ambitious, I'm aware. But I also like to aim high! That's why I'm happy to work here.

Finally, do you have any hobbies? How do you spend your free time?

Well, back in the days I used to be a good tennis player. I pretty much like everything related to outdoor activities. I will climb the Kilimanjaro one day! I also like to laugh and look younger than my kids when walking our misleadingly agile basset hound. I like Ansel Adams photography, Philip Roth novels, Miles Davis Trumpet, a combo of The Deer Hunter + Godfather 1,2 and 3 and, of course, I have the dream of seeing Benfica win the champions league once more.

**How We
Communicate iMM :**

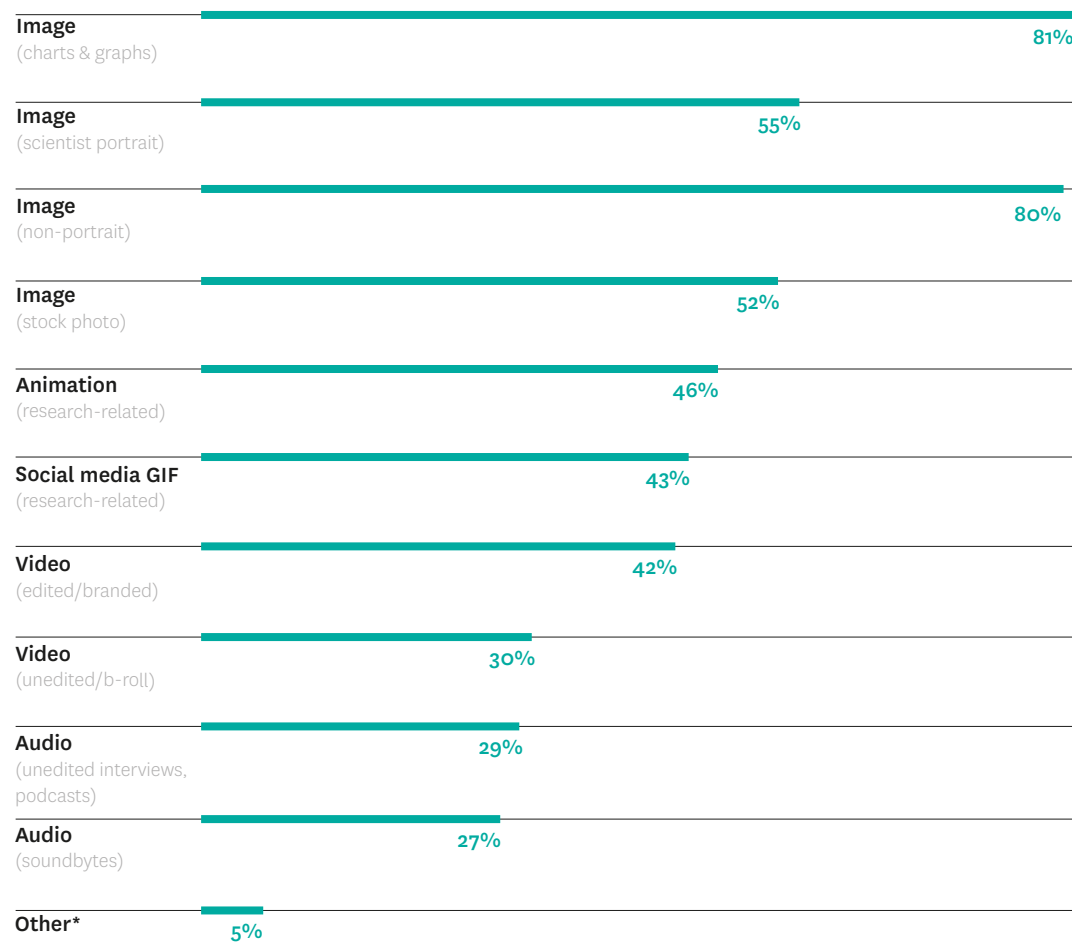


Figure 3. What multimedia formats are useful to science reporters' news-gathering efforts

2017 was also the year where IMM created a digital marketing strategy aligned with the institute's vision to promote and increase its research visibility while promoting science education for the general public.

The rapid development of social media has changed the way people interact with one another, access and share information and has created networked communication channels that facilitate interactions, allowing information to proliferate within professional academic communities as well as in informal social circumstances².

Social media platforms are the way modern society is networking and communicating. It is through these platforms that we share information with friends, colleagues and acquaintances.

Contrary to traditional forms of media, social media facilitates two-way interaction and allows information to proliferate within an electronic community that is constantly evolving on a daily basis.

2. Collins et al., How are scientists using social media in the workplace? PlosOne 2016

There is evidence that scientists are increasingly using social media for communicating not only specific aspects of their research but also science in general, as a means of outreach to increase engagement and science literacy. In fact, the American Association for the Advancement of Science (AAAS) surveyed its members in 2015 and found that 47% of them had used social media to discuss or follow science³.

Several studies have also shown there is a connection between public communication, increased research visibility and a greater number of citations^{4,5}. Furthermore, scientists who engage in public communication tend to be more academically productive⁶.

The Communication Department has taken several actions throughout the last year towards innovation, using a new approach with an emphasis in the digital universe. We wanted to create a space of multi-directional conversation where IMM would always be the central key player. To reach that goal, we created different contents that fed directly from the groundbreaking science that takes place everyday at IMM, this way generating indoor conversations within IMM's collaborators, enhance IMM's presence and notoriety amongst its peers, media and civil society whose relation with science is mainly inexistent.

Some of these include videos series, like our monthly "coffee break" where we interview international speakers that pass by our institution, animations to deconstruct and explain state-of-the-art research and several outreach videos (Fig 4).

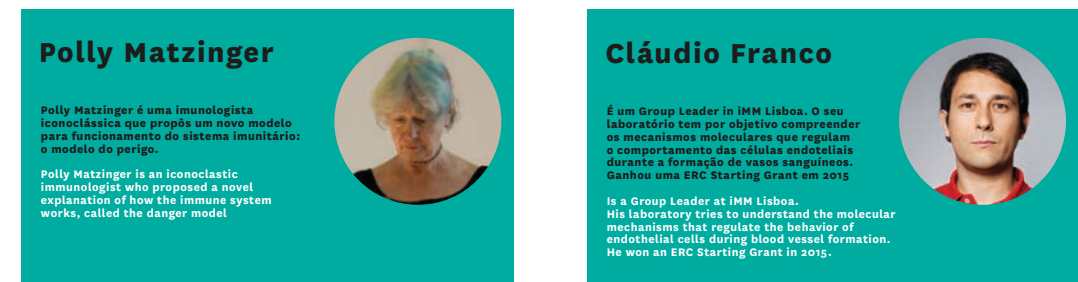


Figure 4. Some of the multimedia initiatives throughout 2017.

Throughout the year our analysis has been very positive, especially within the scientific community - team spirit and fair-play within departments and laboratories is IMM's strong point and there is clearly a correlation between mutual respect with other research institutions and even the media.

Since the beginning of 2017, IMM's facebook community grew more than 15.2%, however the number of weekly active engaged users grew by an impressive 80%. It's important to note that the publications with bigger engagement in this social platform always contained multimedia content.

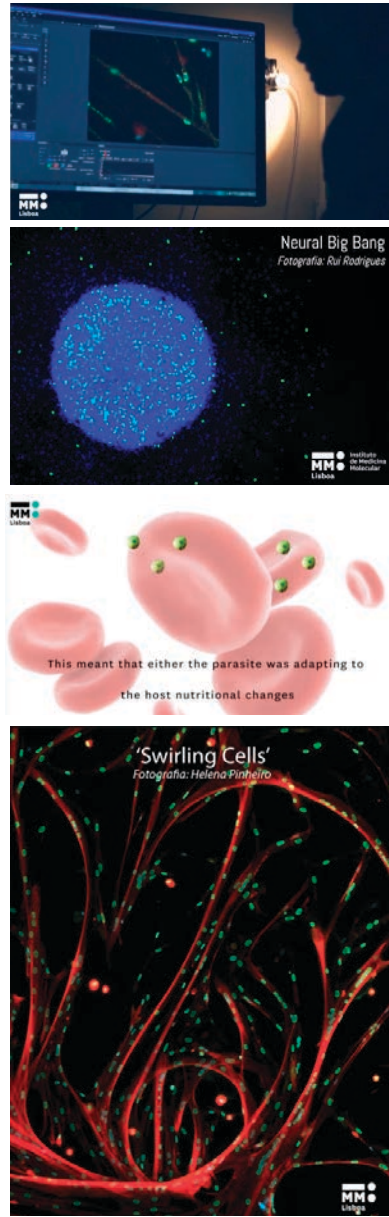
Also in Twitter, IMM's community grew significantly month after month in terms of followers, profile visits, mentions and impressions (tweets sent that actually generate interaction or replies from others online). Finally, the number of visits in LinkedIn are now four times higher than last year, publications obtain more than the triple of impressions and the number of followers is increasingly constantly at not only a national, but also international level (Fig 5).

3. Brossard D. New media landscapes and the science information consumer. PNAS 2013

4. Thelwall et al., Do Altmetrics Work? Twitter and Ten Other Social Web Services. PlosOne 2013

5. Lian et al., Building Buzz: (Scientists) Communicating Science in New Media Environments. Journalism Mass Comm Quarterly 2014

6. Jensen et al., Scientists who engage with society perform better academically. Sci Public Policy 2008



Watch our multimedia initiatives throughout 2017. Use your phone to scan the code.

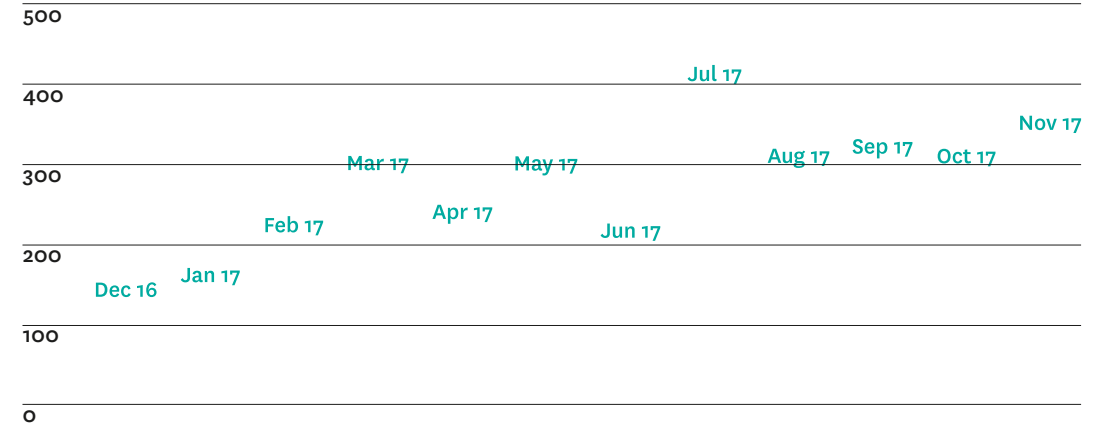


Importantly, we have been actively working on our visual language. We believe it is crucial to maintain a coherent image that people can easily associate with IMM. When we show our image to the outside world, it makes a difference in the way we connect with people.

Facebook:



LinkedIn:



Twitter:



Figure 5. IMM's growth on different social media channels

2017 was also marked by a significant presence of IMM in the media. The institution has been establishing itself as one of the strong names when it comes to scientific research which can be translated in the growing number of media appearances (Fig 6).

Media appearances:

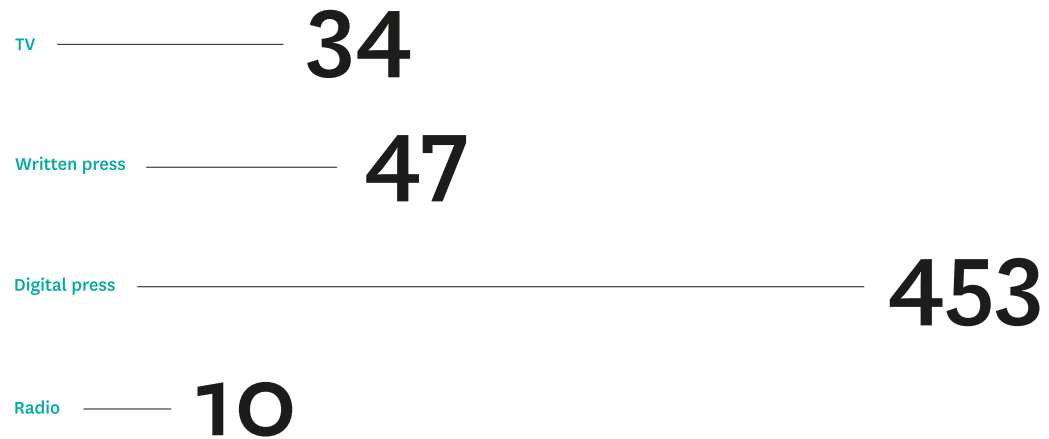


Figure 6. IMM media appearances during 2017

In the era of information technologies the evolution of science communication is rapid and demanding. It is visible that IMM is growing and it is important to keep up the pace while developing novel and efficient strategies that communicate its essence to the outside world.

**Career Development
and Advanced Training :**

Career Development



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

LisbonBioMed 2017 Class (4th Edition)

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

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



Carlos Labão-Almeida

My enthralment for the unknown and commitment to learning is what led me to pursue a career in science. Throughout my academic path, I became increasingly fascinated by the field of Immunology, which prompted me to proceed my MSc degree in Medical Biochemistry. I was fortunate enough to work in an Immunology-focused research group at Instituto de Medicina Molecular (iMM), in Lisbon, Portugal. I decided to apply to the LisbonBioMed International PhD Programme, because I found that the given opportunity of working in a top-class research institute as iMM would provide me the possibility of not only broadening my theoretical and experimental knowledge in a broad range of research areas but also to thrive as an academic scientist.



Eunice Paisana

Ever since I was very young, I knew I had to pursue a career related to Biology, which drove me, later on in life, to apply and complete a degree in Molecular and Cellular Biology at *Faculdade de Ciências e Tecnologia (Universidade Nova de Lisboa)*. My experience on different research environments made me very keen on Biomedical Research, with a more translational approach, leading me to enrol and graduate as a MSc in Cancer Immunology and Biotechnology at the University of Nottingham.

Between both my previous academic experiences, I got in touch with the research done at iMM, working as an intern. The great work environment together with the advantage of a close interaction between the Institute, the Hospital and the Medical School, lead me to see the iMM as the perfect place to develop my PhD project. During the first eight weeks of the LisbonBioMed we had the opportunity to get in touch with the different fields of the research done at the Institute, allowing us to make an informed decision on which group we should integrate and the project to embrace for the next four years of our PhD. I am very glad I got the opportunity to belong to the LisbonBioMed PhD program, an experience that has been one of the most amazing and challenging in my academic life.



João Sabino

I am a recently graduated engineer that just decided to pursue a path in science. At first, it was the eagerness to understand the hidden laws underneath every single phenomenon around us that led me to Instituto Superior Técnico, where I studied Biological Engineering for 5 years. Once I got the chance to contact with biomedical research, as part of my master thesis internship at iMM, I became fascinated by a particular elementary “code” of nature and a cornerstone of life itself: the genome. I believe that a deep knowledge of our genetic regulation, such as how it coordinates diverse cellular functions, shapes environmental and time-dependent adaptations, and ultimately dictates cell fate, is the key to unravel some of the leading biomedical questions of our time. Therefore, joining LisbonBioMed PhD program came as a natural step for me to take, in order to develop my work on a top-notch scientific institute, supported by outstanding facilities and surrounded by exciting and challenging minds. Regarding non-scientific subjects, I am an easy-going person and an animal lover, committed to raise awareness about animal rights. Besides, I enjoy meeting new people and exploring unexpected places.



Henrique Machado

I come from Braga in northern Portugal, where I've spent most of my time before moving to Lisbon. As far as I can recall I've always been a curious person and especially fond of natural sciences. Upon completing my graduation in Biochemistry at the University of Minho, I realized that what I really wanted to do was to keep on learning and being able to think and answer my own questions. Thus, doing research seemed to be the most fulfilling option. Accordingly, I enrolled a research oriented MSc program in Health Sciences at the ICVS. There, I grew increasingly interested in the interactions between host and pathogens, largely from an immunological standpoint. After a couple of short research fellowships I was fortunate enough to be granted a position in the LisbonBioMed PhD program. So far it has been a blast! The initial eight weeks training module fosters an amazing environment for scientific discussion which really helped me identify the current gaps of knowledge in a wide variety of research areas. This really helps you find a research project that you are passionate about, and chances are, you might find yourself switching to a new research field altogether. Indeed, the LisbonBioMed program and the IMM are ideal for young researchers who wish to thrive amidst a great scientific community.



Helena Pinheiro

I believe that I naturally pursued a scientific career due to my inquisitive nature: my Biochemistry degree allowed me to observe the surrounding world with an extra layer of complexity and to perceive how basic biological mechanisms orchestrated such intricate processes. Later, I joined the Biomedical Research master in Coimbra, where I had the opportunity to study the effects of antenatal glucocorticoids in brain structure and development and their putative implications in brain pathology.

Currently, I have the opportunity to develop my PhD under the supervision of Dr Edgar Gomes in the exciting IMM scientific environment and surrounded by amazing and motivating colleagues from the LisbonBioMed program.



Luís Monteiro

Being an MD currently attending the residency of Clinical Hematology in Hospital dos Capuchos, I soon understood how challenging cancer biology is. But lately, I also started to feel frustrated by realizing how little is known and applied in my everyday practice. The gap that exists between the clinical and the research fields is undoubtedly a big setback in our patients' hope and this has to change... Personally, I found the need to deepen my knowledge in cancer, with a particular focus in Leukemia, and I saw the LisbonBioMed PhD program as a great chance to do so. By integrating a team with a different background but that shares the same main interest, I think I will improve as a doctor, as a scientist and ultimately as a person, developing a set of skills that will hopefully be useful in the fight against leukemia. Even though my background constrained my personal choices within the IMM labs, the LisbonBioMed PhD program exposes us to newer and broader horizons on a daily basis, teasing our curiosity for different scientific fields, and developing this ultimate characteristic that a Scientist needs – a curious mind.



Marcin Makowski

I felt in love with the secrets of nature very early in my childhood. In fact, my deepest desire was to become a Naturalist. Fortunately for me (and unfortunately for many tadpoles), my parents and I seized every opportunity to escape the rush of the big city to our little cottage in the countryside. This provided the perfect scenario to pursue my dream of becoming a new Attenborough. Not surprisingly, many years later I entered the faculty of Biology at Universidad Autónoma de Madrid. These years consolidated my love for biology and showed me what being a biologist is. To try to solve the never ending puzzle posed by the most fascinating natural force: evolution. My path led me to study a master's degree in microbiology in Lisbon. During my master's thesis (at the IMM) I got to come across an extremely interesting group of molecules: antimicrobial peptides. Because my curiosity on this matter was still far from being fulfilled, I took the decision to further pursue a PhD. I considered the LisbonBioMed PhD program a great opportunity, in a renowned institution with an extremely good scientific environment. And in a great city!

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



Marco Cavaco

I graduated in Pharmaceutical Sciences at the Faculty of Pharmacy, University of Lisbon. During the course of my degree, I had a chance to join different labs and develop different projects. Thus, the interest for science was growing and I realized that I would like to pursue my career in research. Applied immunology, therapeutic proteins development, and nanomedicines were my main areas of interest, so I decided to look for an Institute where I could develop my PhD project in one or more of these areas. The Instituto de Medicina Molecular soon popped out as the place where I wanted to be. The research developed in this institute was always extremely exciting to me and the incredible facilities that it has is a plus that I would like to explore. Then, I saw that the LisbonBioMed program was perfect for my interests. The interdisciplinarity of the program, the opportunity to discuss science with all the investigators in a relaxed environment, and the incredible support that is given to the new ones are key features of the program. Since I am here, all my expectations are being confirmed and the more I know about both the Institute and the PhD program, the more I realize that I made a good choice. I can only hope that this big family continues to grow and that all of us continue to do what we want to do – Science with Quality.

Master Program @ iMM:

In 2017, the Career Development service implemented a new program targeted to the master students, aiming to provide specific training opportunities towards a successful scientific career, and to attract the best master students to the iMM labs.

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

Open Afternoon for Master Students

iMM Lisboa invites all
1st year Master students
to the
“Open Afternoon at iMM Lisboa”

Do you want to do your Master project at iMM?
Then come and check out what iMM has to offer you!
Tuesday 7th MAR'17 — 14:30h – 17:00h

iMM Lisboa Instituto de Medicina Molecular

Venue Instituto de Medicina Molecular (iMM Lisboa)
Registration <https://goo.gl/E6m6Xs> until 27th FEB'17
Organization iMM Career Development Service
imm-careerdev@medicina.utlisboa.pt

“Best Master Thesis” Awards



1st Prize:
Tiago Rebelo
(Luisa Figueiredo Lab)

2nd Prize:
Bernardo Almeida
(Nuno Morais Lab)

3rd Prize:
Raquel Duarte
(Luis Costa Lab)

PhD Students' Activities

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

PhD Students' Representatives for 2017

Marie Bordone (Nuno Morais Lab) and Margarida Vaz (Miguel Prudêncio / Luisa Figueiredo Labs) are the elected PhD students' representatives

PhD Students Annual Meeting

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



PhD Students Annual Retreat

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



PhD Students Workshops

The 2017 PhD Students' Committee organized the II Workshops Series to fulfill their need to have more training aimed at improving their soft skills.



Workshop: Communication - Turn yourself into a successful speaker, by Dr. Malcolm Love

Post-Doctoral Activities

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

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

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

PDA Executive Committee for 2017



Joana Coelho (Luisa Lopes Lab), William Roman (Edgar Gomes Lab), Susana Lobo (Gonçalo Bernardes Lab, left in March), Elisabete Martins (Mário Ramirez Lab), Inês Bento (Maria Mota Lab), Marco Domingues (Nuno Santos Lab), Maria Dominguez-Cejudo (Cláudio Franco Lab, started in April)

MasterClass: Fundamentals of Innovation and Tech Transfer, by Dr. Marta Ribeiro

Workshop: Graphic Design for Scientists, by Dr. Gil Costa



Annual Retreat (Cross-Institutional Meeting)

Postdoctoral researchers from IMM, CEDOC, IBET, and ITQB jointly organized a Scientific Symposium and Job Fair - Career Opportunities for PostDoctoral Researchers in Life Sciences. This event aimed to promote the unique career brand of PhD holders, and stimulate the networking inside and outside academia.

During the Scientific Symposium postdoctoral researchers had the opportunity to present and discuss their work while establishing strategic collaborations with their peers from academia. On the other hand, the Job Fair, open to the public, was a great chance to meet a variety of organizations that actively offer positions for PhD holders. There were also parallel sessions with several workshops and career discussion tables.



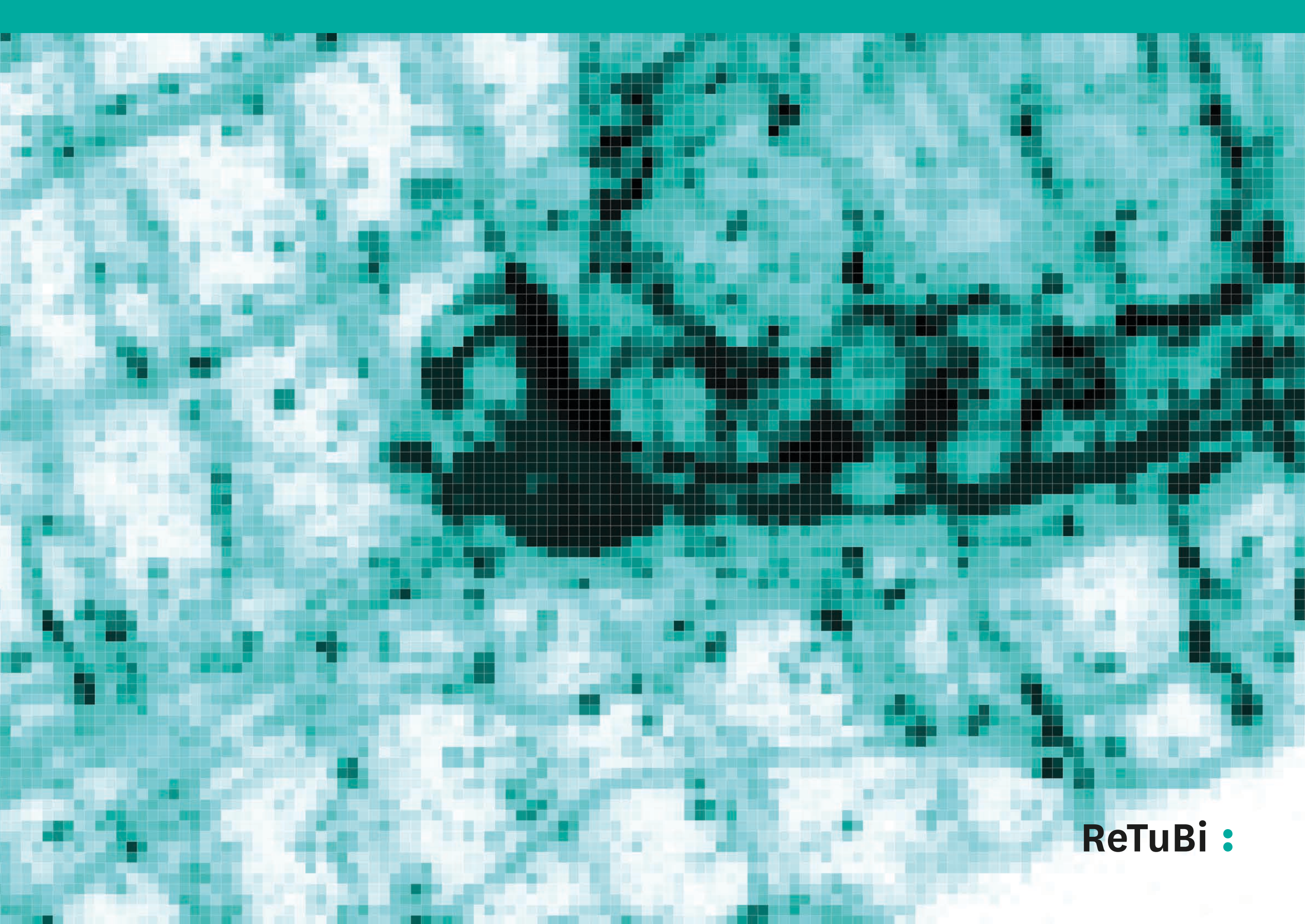
Picnic

A moment of relaxed interaction and fun, open to all IMMers and their beloved ones.



Beer Hour





ReTuBi :

ReTuBi First Joint Summer School (29-31 May 2017) and Signal Transduction Meeting (1-2 June 2017)

By organizing these two events together, the ReTuBi project maximize its impact in the IMM and Lisbon scientific community. These events also promoted an extensive dynamic network of interactions that provided a channel of knowledge transfer to potentiate the already existent scientific and innovative capacity within IMM.



Educational sessions in Cancer Biology

ReTuBi IMM researchers led educational sessions about tumour biology in Secondary schools in Lisbon during May 2017, to 250 students from Biology courses with the main objective to spread the ReTuBi project and the importance of this network in the cancer research area.



Oncology: Talking with Scientists

This event specially dedicated to the Portuguese cancer patients' associations was held at IMM on November 13th 2017. This event was focus on the relationship between science and cancer patients and on the role of immunotherapy in the cancer treatment. An exhibition of the work of some IMM labs/facilities was also organized to disseminate IMM research.

By promoting these activities, the ReTuBi will therefore contribute to the development of cancer and tumour biology research, focused on four main scientific axes: cancer stem cells; cancer signalling; tumour angiogenesis and cancer invasion and metastasis. Through the ReTuBi network, IMM aims to create a significant improvement in the overall scientific and innovation capacity in the tumour biology research field and will contribute to research excellence and value creation in health at National and European level.



ReTuBi in a Nutshell:

Title: *Towards outstanding REsearch and training in TUmour Biology at IMM*

Consortium: Instituto de Medicina Molecular – João Lobo Antunes (Portugal), Institut Curie (France) and The German Cancer Research Centre - DKFZ (Germany)

Total investment: EUR 999.975.00

Dates: 01st January 2016 – 31st December 2018

Project coordinator: Edgar Gomes (IMM)

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

Fundraising :

The Brain Tumor Team creating a circle of hope



In 2011, Adelaide Passos published the book “O céu pode esperar”, telling the story of one of her grandchild who was fighting a brain cancer. She decided that she wanted to help other children with brain tumors by creating awareness and by fundraising for brain tumor research. She spoke to Professor João Lobo Antunes about her dream and a few months later the *Centro de Investigação de Tumores Cerebrais* (CITC) was created. Since then many companies and individuals have sponsored the CITC with great generosity and enthusiasm.

The Fundação Millennium bcp is one of the most relevant sponsors and it has been determinant to take our project further. Besides supporting brain tumor research at IMM, Fundação Millennium bcp led the development of a cooperation protocol between the Lisbon Academic Medical Centre (CAML) and the *Hospital Central de Maputo* (Mozambique) to promote the training of medical doctors in Pediatric Neurosurgery and to develop pediatric brain tumor research. The first mission occurred in May 2017 and it was very successful, particularly in the training of local neurosurgeons, pediatricians and nurses.

In keeping with this spirit, we have started organizing and participating in fundraising events for cancer research at IMM.

The **Brain Tumor Team (BTT)** was formed in 2014 to create awareness and to fundraise for cancer research. The BTT has participated in all editions of *Corrida Saúde + Solidária*, an event organized by the students of the Lisbon Medical School (AEFML), with an increasing number of participants. In the last edition of *Corrida Saúde + Solidária*, held in May 7th 2017, we have joined “David Vaz Associação”, created in memory of a young man who passed away with a malignant brain tumor. David was a joyful person and an amazing athlete. “David Vaz Associação” is committed to create awareness and to fundraise for cancer research through sports events. The BTT team gathered over 500 participants from diverse hospitals and research institutes in Lisbon! More importantly, patients, their families and friends participated in the event, spreading the word and helping us creating a circle of hope for those who fight with a brain tumor. With the donations received we have acquired equipment for cancer research at IMM.

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



Fundo iMM-Laço: On the Way to a Cure

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 every year.



The Fundo iMM-Laço aims to support at least 3 new projects every year with grants of 25.000€ for each successful proposal. Throughout the year, the Fundo iMM-Laço organizes initiatives with sponsors and the general public to raise the money to fund these grants. Part of the Fundo's mission is to communicate the importance of science for health so in addition to generating over 75 mentions in newspaper, magazine and online articles and on TV in 2017, the Fundo offers free workshops for high schools, companies and other organizations in which scientists help explain the role of research in looking for a cure for breast cancer. In 2017, there were 11 workshops attended by over 750 people. The Fundo also participated in seminars with ASPIC and ReTuBi. Information about all of the activities of the Fundo can be found on the Facebook page: [Facebook.com/fundoimmlaco](https://www.facebook.com/fundoimmlaco) and the new site: www.fundoimmlaco.pt

Currently, there are four ongoing projects at iMM supported by Fundo iMM-Laço, one carried forward from 2015 and 3 from the 2016 Call. Two of these projects investigate the immune system and its role in the inhibition of tumor growth and metastases formation and how it can inhibit tumoral progression. Two other projects investigate tumor genetics: one tries to understand what leads tumors to metastasize in the bone and the other focuses on the genetic analysis of tumor cells to predict their response to chemotherapy in women with early stage breast cancer, as well as identify which types of tumors have a higher level of metastatic risk.

In July 2017, the annual internal Call was launched for new projects focused on the causes of breast cancer or the mechanisms of metastases and the deadline for applications was October 30th.



Sérgio Dias

Group Leader, Vascular Biology & Cancer Microenvironment Lab

Every day starts and ends with studying all kinds of cells, from blood vessels to tumors to the immune system. Sérgio's group is trying to understand how these different components communicate and how they allow or even encourage tumor growth. We all have innate immunity and adaptive immunity. There are blood vessels which form during the growth of tumors which are different from regular vessels and have different molecular markers. Sérgio's group is studying how these vessels communicate with the other elements of the tumor environment. The objective is to identify the molecular marker which favors or inhibits tumor growth by modifying the vessels which feed the tumor or by altering the immune response of the host cells which could lead to clinical therapies to inhibit tumor growth much earlier on.



Karine Serre

FCT Researcher, Bruno Silva-Santos Lab, T cell Differentiation & Tumor Targeting

Karine's project aims to harness the immune system to inhibit tumor growth. Her group is studying myeloid cells (specifically macrophages and neutrophils) which are manipulated by tumors to create an environment that favors tumor growth. This project is trying to reeducate the myeloid cells such that they recognize tumor cells as invasive and stop helping them. The financial support from the Fundo is allowing the researchers to isolate the myeloid cells and analyze their expressed genes to identify which proteins are being expressed by these cells. In this way they hope to understand the mechanisms which regulate the cell action and identify elements which could be used to create myeloid cells that stop tumor growth, reduce tumor size and even possibly eliminate tumors altogether.



Sandra Casimiro

Post-Doctoral Researcher, Luís Costa Lab, Translational Oncobiology

Sandra has been studying the RANK protein (the receptor activator for the NF κ B pathway) since 2007. It is the principal control mechanism for the activity of the cells which can create new bone. Approximately 30% of all breast cancer patients will develop metastases, the most common location being the bones. The RANK protein is associated with metastases in the bone in addition to being linked to the mammary glands and breast cancer. There are mammary gland cells which have increased levels of RANK protein and there is a correlation between high levels of RANK protein and the development of triple negative tumors so it is already understood that mutations in the RANK protein influence the type of breast cancer and its prognosis. The objective of this project is to correlate mutations in the RANK protein with outcomes of patients in terms of both bone metastases and overall survival in the hope of using existing treatments to stop bone metastases.



Célia Carvalho

Auxiliary Professor at the Faculty of Medicine of the Universidade de Lisboa and Researcher, Lab Maria Carmo-Fonseca, RNA & Gene Regulation| Ph.D. Student at GenoMed-iMM

Célia and Catarina have been working together on two different breast cancer research projects for one year now. Hopefully, their results will provide clinicians with some important tools for patient management. One project aims to develop a molecular classification for early stage low risk breast cancer that will distinguish which cancers have a lower risk of relapse and can avoid aggressive treatments like chemotherapy.



Catarina Silveira

Catarina is optimizing the molecular analysis of “liquid biopsies” which are done just using circulating tumor DNA in the blood thus avoiding traditional biopsies. Using Next Generation Sequencing, she is looking for actionable mutations that could help clinicians with decision making in the choice of targeted therapies. This is the kind of research that can bring us a step closer to truly personalized medicine.

If you would like to know more about Fundo iMM-Laço you can visit the website at www.fundoimmlaco.pt

Events :

iMM Scientific Retreat

The iMM annual scientific retreat took place on the 08-10th of April 2017 at the University of Évora who kindly hosted 266 iMM staff and four members of our Scientific Advisory Board (SAB): Caetano Reis e Sousa, Carlos Caldas, Gustave Moonen and Philippe Sansonetti. The iMM community got together for a privileged forum of scientific discussion and social interaction. There were talks by 12 group leaders and a talk session by PhD Students or Post-Doctoral Fellows from 12 research groups. The group leaders, PhD Students and Post-Doctoral Fellows also had the opportunity to have direct interaction with SAB members.





European Researchers' Night

29th September – Museum of Natural History and Science, Lisbon





Management Retreat



16th November – Quinta da Alorna, Santarém



Christmas Party



15th December – Instituto de Medicina Molecular João Lobo Antunes, Lisbon



Institutional Partnerships



Ablynx: www.ablynx.com
Albumedix: www.albumedix.com
Almirall: www.almirall.com
AMGEN: www.amgen.com
Astellas Farma: www.astellas.com.pt
AstraZeneca: www.astrazeneca.pt
BAYER: www.bayer.com
Bristol-Myers Squibb: www.bms.com
Bial: www.bial.com/pt
Budapest University of Technology and Economics: www.bme.hu
Celgene: www.celgene.com
Centro Académico de Medicina de Lisboa
Centro Hospitalar Lisboa Norte/ Hospital de Santa Maria: www.chln.min-saude.pt
CHDI Foundation: www.chdifoundation.org
Cytokinetics: www.cytokinetics.com
EHDN: www.ehdn.org
EMBO: www.embo.org
Fundo IMM- Laço: www.fundoimmlaco.pt
Genomed: www.genomed.pt
Harvard Medical School - Portugal Program: www.hms.harvard.edu
Health Cluster Portugal: www.healthportugal.com
Hovione: www.hovione.pt
iBET: www.ibet.pt
Janssen: www.janssen.pt
Liga Portuguesa Contra o Cancro: www.ligacontracancro.pt
Lymphact
Malaria Vaccine Initiative (MVI): www.malariavaccine.org
Medtronic: www.medtronic.pt
Merck: www.merck.com
Merck Sharp & Dohme: www.msd.pt
NOVARTIS: www.novartis.com
Otsuka Pharmaceutical Co, Ltd: www.otsuka.co.jp
PFIZER: www.pfizer.pt
PureTech Health: www.puretechhealth.com
Roche: www.roche.pt
RoPlavac
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UCB Pharma: www.ucb.com
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