

Annual Report

2022

imed

Research Institute
for Medicines

No Breakthrough
is too small.

2021
— 2022

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for Medicines



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Foreword

message from the coordinator

JOÃO GONÇALVES
Coordinator, imed

Based at the Pharmacy Faculty of the Universidade de Lisboa but on a world-wide mission to spur medicine innovation, we're a group of scientists and students that believe that by overcoming micro challenges we may advance health sciences for the benefit of our community. Therefore, welcome to the Research Institute for Medicines, a research unit funded by Fundação para a Ciência e Tecnologia, where *no breakthrough is too small*.

In a nutshell, 2022 marked the consolidation of the Research Institute for Medicines activities that focused in perfecting the integration between science, technology, translation to advance health sciences. Throughout the year, 101 scientists, 133 PhD students, and 260 master's students collaborated within 30 research laboratories spanning the fields of chemistry, biology, and pharmaceutical sciences. Their daily endeavours were dedicated to developing cutting-edge tools and techniques for the prevention, detection, and treatment of complex human diseases. Notably, these efforts took on significant importance in the response to the COVID-19 pandemic, where imed emerged as a pivotal reference center for diagnosis and information.

At imed, part of our mission is to foster innovation in health sciences and technology by providing an environment conducive to such innovation. To this end, we recognize the essential role of equipping our scientists with state-of-the-art resources. In 2022, we bolstered our bioimaging platform with a Cytex® Aurora full spectrum



flow cytometer, complemented by a workstation running SpectroFlo® software for sample acquisition and data analysis. This new equipment significantly enhances our capacity for more in-depth studies involving unique fluorochrome combinations. In addition to this key investment, we expanded our capabilities for studying complex mixtures and biologics with the acquisition of a Thermo Scientific Orbitrap Exploris mass spectrometry system. This acquisition promises precision data on exact masses and opens the door to exploring proteomics as a valuable tool for uncovering druggable targets and new medicines.

Recognizing the potential for breakthroughs through collaboration, in 2022, we initiated an internal call with a budget of 75,000 euros to foster one-year collaborative projects among IMED laboratories. The IEDA initiative was highly successful, funding 16 research projects aimed at testing novel ideas within the institute.

Despite a challenging ecosystem with reduced national funding, imed scientists achieved remarkable success in fundraising during the year. The institute's budget expanded by 11% compared to 2021, reaching a total of 4.1 million euros. This growth predominantly reflects the achievements of imed scientists in securing funds through highly competitive international calls. The communication of our finding is primarily done in the form of scientific articles. Throughout the year, we published 225 articles, with 61% indexed in the first quartile.

These publications were well-distributed across the Scientific Hub (62%), Technologic Hub (14%), and the Translational Hub (24%).

In 2022, we encountered a multitude of challenges, but it also symbolized a promising new start for our institute, brimming with opportunities for pioneering discoveries that can positively impact everyone.

1. imed Organization

imed structure

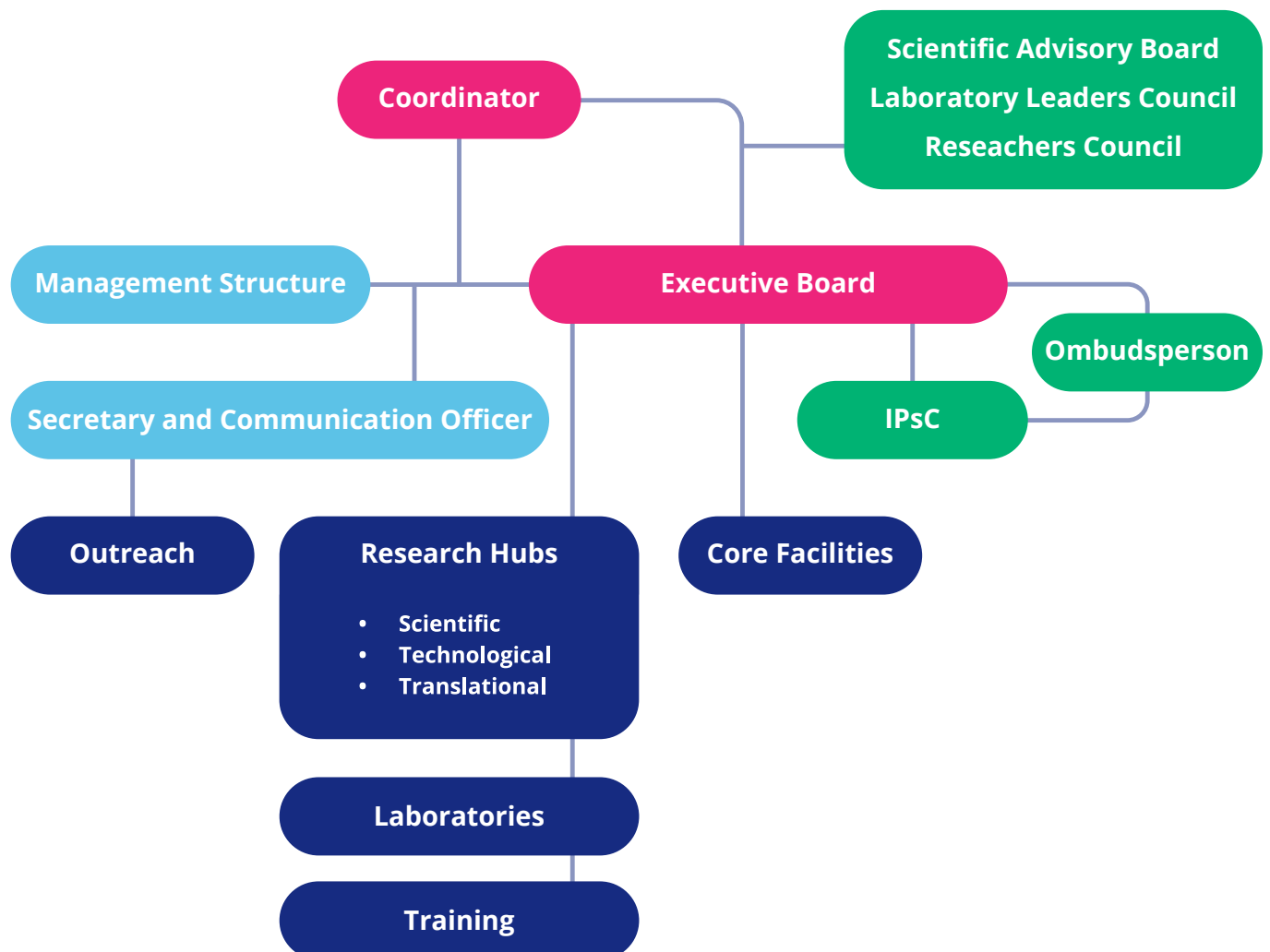
Scientific Advisory Board

imed structure

Our multidisciplinary research unit has 147 researchers that maintain 30 research laboratories covering the fields of chemistry, biology and pharmaceutical sciences. The laboratory leaders, nominated by the laboratory doctors, are responsible for electing the institute coordinator and for supervising the executive board activities.

The executive board (EB) has a critical role in setting the culture and values of the institute. The EB is responsible for overseeing the daily activities of imed and for ensuring the execution of the initiatives proposed in the strategic plan. The EB is coordinated by João Gonçalves that is the main contact point between imed researchers, our host institution (FFUL) and Fundação para a Ciência e Tecnologia.

The coordinator is assisted by Adelaide Fernandes, Helena Florindo, Rui Castro and Pedro Góis that are responsible for coordinating the different research hub activities, for the articulation with imed's post-graduate students commission (ipSC) and for assuring the institute training, communication and outreach activities.



Scientific Advisory Board

imed executive board is constituted by eminent international scientists to ensure that our strategic direction is in the best interest of science and society.



PROF. RONIT SATCHI-FAINARO

Head, Cancer Research and Nanomedicine Laboratory

The Hermann and Kurt Lion Chair in Nanosciences and Nanotechnologies,
Director, Cancer Biology Research Center
Department of Physiology and Pharmacology
Sackler Faculty of Medicine, Sagol School of Neuroscience, Tel Aviv University, Israel



PROF. NUNO MAULIDE

Full Professor of Organic Synthesis at the University of Vienna and adjunct PI at CeMM



DR. PAULO FONTOURA

Global Head and SVP Neuroscience, Immunology, Ophthalmology, Infectious and Rare Diseases at Roche



PROF. NADIM BOU-HABIB

Lecturer at the Nova School of Business and Economics

2. Scientific Structure

Research Hubs & Laboratories
Immunology Laboratories

Research Hubs & Laboratories

Our research model is supported by 30 laboratories who bring the perspectives and tools of disciplines across the fields of chemistry, biology and pharmaceutical sciences to tackle key scientific questions in health sciences. The focus of our team is on discovering molecules, molecular mechanisms and technologies that can be translated into breakthrough healthcare solutions.

Our laboratories have diverse interests and are flexible workspaces that shared knowledge and instrumentation to foster interaction and innovation. Therefore, our capacities cover a wide range of research activities that support our **Scientific, Technological and Translational Hubs**.

Scientific Hub

- Oncology
- Neurodegenerative disorders
- Metabolic diseases
- Infectious diseases

Technological Hub

- Emerging technologies
- Bioorganic and natural products chemistry
- Medicinal and chemical biology
- Pharmaceutical and biotechnology tools and applications

Translational Hub

- Evidence-based interventions
- Regulatory sciences
- Health care sector
- Pharma industry



Scientific Hub

Within the Scientific Hub, we aim at integrating chemistry, biology and pharmaceutical sciences to develop pioneering tools and techniques to prevent, detect and treat cancer, neurodegenerative, metabolic and infectious diseases.

Oncology

In the field of oncology, we work to provide innovative solutions to cancer patients through disruptive advances in fundamental scientific discoveries, guided by a deeper understanding of the molecular basis of this disease. This advanced knowledge drives imed drug discovery program towards the identification of druggable targets that fuel cancer progression. imed cancer research program integrates biochemistry, molecular/cell biology and immunology with chemistry, nanotechnology and biotechnology to translate this fundamental knowledge into novel tools for cancer diagnosis, prevention and therapy.

Leading Laboratories:

- Drug Delivery & Immunoengineering
- Neurovascular
- Natural Products Chemistry
- Medicinal Organic Chemistry
- Computational Medicinal Chemistry

Neurodegenerative disorders

In the field of neurodegenerative disorders, we are studying diseases like Alzheimer, Parkinson, Amyotrophic Lateral Sclerosis or Multiple Sclerosis that are characterized by the progressive degeneration of the structure and function of the central nervous system. Although neurodegenerative diseases are typically defined by specific protein accumulations, regional vulnerability and parenchyma atrophy, these disorders share many fundamental processes associated with inflammation, glial reactivity, neuroimmune interactions and progressive neuronal dysfunction. Therefore, we seek to understand the molecular basis of central nervous system pathogenesis, guiding the rational development of innovative therapeutic approaches for these diseases. Our strategy brings together neuroscientists, biophysicists and chemists to identify novel mechanisms driving disease onset and progression and envision new treatments.

Our long-term vision encompasses the identification of novel, early biomarkers for pre-symptomatic disease diagnosis; the discovery of new targets for pharmacological intervention; as well as innovative strategies to prevent disease occurrence.

Leading Laboratories:

- Central Nervous System, Blood and Peripheral Inflammation
- Neuroinflammation, Signalling and Neurodegeneration
- Stem Cell Bioenergetics and Neurodegeneration
- Toxicology, Biomarkers & Risk Assessment

Metabolic diseases

In the field of metabolic diseases, we recognize the role of metabolism in many different human diseases by affecting the ability of cells to perform critical biochemical reactions that involve the processing or transport of proteins, carbohydrates, or lipids. Therefore, we are studying non-endoplasmic reticulum associated rare inherited diseases and probing novel molecular targets involved in cell function to develop innovative therapeutics for metabolic disorders underlying diabetes, cancer and liver diseases. We perform biochemical and biophysical characterization of enzymes, transporters and channels involved in metabolic pathways, and employ innovative molecular biology techniques on cellular and

animal models of metabolic diseases to identify novel mechanisms of disease pathogenesis that can translate into druggable biological targets. Benefiting from our ties with the pharma industry, we further synthesize and screen putative drugs for identified targets, while working towards the development of novel medical devices with the same goal.

Leading Laboratories:

- Cell Function and Therapeutic Targeting
- Membrane Transporters in Health & Disease
- Metabolism, Genetics and Proteins in Health & Disease
- Liver Disease Diagnostics and Therapeutics

Infectious diseases

In the field of infectious diseases, we work to gain insights into the mechanisms of infection associated to existing and emerging threats, aiming at the development of multipronged approaches capable of targeting host-infectious agent interaction, while controlling disease progression. We aim to develop effective vaccines and treatments to combat the spread of infectious diseases and to improve clinical care. Our coordinated efforts are directed towards the prevention, early detection, and intervention against public health threats, including malaria, HIV and Covid19, as well as tuberculosis, fungal and parasitic diseases.

Leading Laboratories:

- Phage Biology Research and Infection Control
- Host-Pathogen Interactions
- Pathogen Genome Bioinformatics and Computational Biology
- Bacterial Pathogenomics and Drug Resistance
- HIV evolution, epidemiology, and prevention

Technological Hub

Within the Technological Hub, we are highly engaged in translating our advanced scientific knowledge and technologies into breakthrough healthcare solutions that empower societies to live better and healthier.

A vibrant network based on strong partnerships between our scientific community, distinct players within pharmaceutical and biotechnology companies and the Healthcare sector transforms innovative research & technologies into useful everyday products and life-saving medicines.

Emerging technologies

In the field of emerging technologies, recent advances in biology offer a deeper understanding of the molecular basis of complex diseases and unique opportunities to accelerate basic research into healthcare. At imed we are developing emerging technologies based on chemistry, biology and pharmaceutical sciences to facilitate the translation of these findings into new therapeutic options to detect and treat cancer, neurodegenerative, metabolic and infectious diseases.

Leading Laboratories:

- Advanced Technologies for Drug Delivery
- Bioorganic Chemistry
- Advanced Cell Models for Predictive Toxicology & Cell-based Therapies
- Molecular Microbiology and Biotechnology
- Pharmaceutical Bioengineering, Biotechnology & Bioproducts
- Chemical Biology
- Medicinal Chemistry

Translational Hub

Within the Translational Hub we are deeply committed to advance pharmacotherapy innovation and access to it by people living with illness by developing disruptive translational research to benefit human health, by converging our fundamental science discoveries into applied research.

This is driven by the joint efforts of our institute with multiple players within the Healthcare sector, including policy-makers, clinicians and allied healthcare professionals and people living with illness and their representative organizations and associations.

Leading Laboratories:

- Systems Integration Pharmacology, Clinical & Regulatory Science
- Pharmacy Practice & Health Communication

Health Care Sector

The provision of healthcare to patients in the form of new drugs, devices or services is invaluable to support a healthier society. imed scientists strive to empower the healthcare sector with knowledge in the areas of health promotion, disease prevention and medicines optimization.

Leading Laboratories:

- Pharmaceutical Care and Clinical Pharmacy
- Pharmaceutical Development

Pharma Industry

The pharmaceutical industry plays a decisive role in unravelling innovative therapeutic options to prevent diseases and cure or alleviate patients. imed researchers have established strong collaborations with national and international pharma industry to advance innovative research & technologies into the market, aiming to improve patient's health and reducing the social burden of human diseases.

Leading Laboratories:

- Pharmaceutical Engineering and Manufacturing

In line with this program, actions will be intensified to promote interaction between the different areas of knowledge and the intramural collaborations, ensuring that all the PIs and groups can participate in each research line within the new Scientific Strategic Project.

imed Laboratories

Advanced Cell Models for Predictive Toxicology & Cell-based Therapies

We are a multidisciplinary research team, with expertise in cell/tissue engineering, regenerative medicine, toxicology and cancer pharmacology, focused on the use of advanced (3D) in vitro models as tools for developing new cell-based therapeutics and studying drug metabolism and mechanisms of diseases (ex.: liver diseases, skin pathologies, lung cancer).

In 2022 our group developed health and disease in vitro models for evaluating the efficacy and safety of new therapeutics. We showed that the manipulation of glucose homeostasis and glucocorticoid signalling improved MSC-derived hepatic cell energy metabolism, important for implementing relevant hepatic models. Moreover, the efficacy of cisplatin in NSCLC cells was enhanced resorting to the SODm MnTnHex-2-PyP5+.

Leader: Joana Miranda

Advanced Technologies for Drug Delivery

Our major challenge is to deliver bioactive entities at cellular and intracellular target sites using advanced technologies, thus developing new delivery systems for clinically relevant situations, based on conventional and innovative materials, exploring invasive and non-invasive administration routes.

In 2022 we developed new polymeric 3D-scaffolds loaded with antibiotic and antifungal agents that efficiently targeted mixed *S. aureus* and *C. albicans* biofilms and designed rifabutin liposomes with improved activity against MRSA infections.

As part of our activities, we prepared novel anti-cancer agents formulated in liposomes that exhibited higher antitumor effect than current commercial drugs. Finally, we implemented innovative biosafety full testing Array Checklist for AuNPs.

Leader: António Almeida

Bacterial Pathogenomics and Drug Resistance

Our research is focused on the molecular epidemiology, clinical impact of strain diversity and laboratory diagnosis of infectious diseases caused by bacterial pathogens, namely, mycobacteria and Gram-negative pathogens. Moreover, we also focus on the translation of genomic diversity and in-depth knowledge of resistance mechanisms towards development of novel products and computational tools.

In 2022 our laboratory conducted the largest genome-wide study concerning colistin resistance molecular drivers in *Klebsiella pneumoniae* which, coupled with integration in a high-resolution phylogenetic scenario enabled the identification of clade specific polymorphisms. Moreover, we have identified new polymorphisms associated with colistin resistance as well as structural variation associated with co-resistance between third-generation cephalosporins and colistin. Also, we have been involved in other ongoing efforts that enabled the identification of genomic markers that can inform and assist in the differentiation of hypervirulent *K. pneumoniae* from classical strains and also collaborated in a large international study that establishes and calculates the impact of antimicrobial resistance in Europe.

Regarding ongoing studies on *Mycobacterium tuberculosis*, in 2022 we studied the activity of new compounds with potent activity against tuberculosis, which are presently being evaluated as potential new anti-TB chemotypes and whose mechanisms of action and resistance are presently being studied.

Leader: Isabel Portugal

Bioorganic Chemistry

The Bioorganic Chemistry laboratory is focused on the interface of organic chemistry and biology, aiming at the discovery and process intensification of new more sustainable synthetic methodologies that, in collaboration with biomedical laboratories, can be further explored to tackle important biological problems related with infectious diseases, oncology and inflammation.

In 2022 we developed the synthesis of alpha-enaminones from bio-based cyclopentenones and spiroepoxydienones from salicylaldehydes, under flow conditions. Furthermore, we discovered a new reactivity of photogenerated siloxycarbenes derived from acyl silanes and performed the synthesis of highly functionalized derived structures, using biomass derived furans.

Leader: Carlos Afonso

Cell Function and Therapeutic Targeting

We investigate novel mechanism-based molecular targets to inform drug discovery and biomarker development in inflammation, degenerative and oncogenic diseases. We specifically address cell signalling and the crosstalk with metabolism and interorgan communication, integrating cellular and molecular technologies with multiple preclinical and patient-derived models and samples to facilitate the translation from bench to bedside.

In 2022 we discovered that Ripk3 deficiency restores liver mitochondria bioenergetics and impacts lipid droplet dynamics, suggesting that RIPK3 inhibition is promising in ameliorating non-alcoholic fatty liver disease. During this year, we further showed that adipokines might impact rectal cancer cell stemness and patient prognosis, and that the leptin/STAT3 signalling axis provides the rational for a potential biomarker panel that identifies rectal cancer patients who will not benefit from chemoradiotherapy.

Leader: Cecília Rodrigues

Central Nervous System, Blood and Peripheral Inflammation

The laboratory focuses on the role of inflammation in the emergence or progression of neurodevelopmental and neurodegenerative disorders. We are particularly interested in the interplay between the Central Nervous System (CNS)-centered neuroinflammation and the inflammatory response derived from the periphery.

In 2022 we described a new and improved method – the EAE-Frailty Index - to assess the overall health in the murine model of Multiple Sclerosis, the EAE, that can better detail age-associated changes. Further, we showed that by inhibiting S100B action we could ameliorate the EAE pathogenesis by reducing Central Nervous System demyelination/inflammation and improve regulatory immune cell phenotype.

Leader: Adelaide Fernandes

Chemical Biology

The laboratory focuses on Chemical biology offers unique possibilities to rationally manipulate biological processes and will most certainly play a major role in unravelling solutions for current unmet medical needs. Broadly our laboratory is focusing on discovering innovative chemical technologies that permit the construction of functional molecules, and on applying these technologies to the construction of therapeutic bioconjugates and small molecule probes.

In 2022 we developed innovative chemical methods to modify peptide chains with a particular focus on new reactions that offer control over the site and complexity of the functionalization. In 2022 we developed a proximity driven functionalization of lysine residues and we design multivalent NHS-activated acrylates that permit the orthogonal site-selective functionalisation at cysteine residues and the construction of functional bioconjugates.

Leader: Pedro Gois

Computational Medicinal Chemistry

We design and apply protocols and computational algorithms to gain insight into biological and chemical systems with pharmacological importance and use this knowledge to rationally design and repurpose new potential therapeutic agents that can contribute to the treatment of human diseases. We use a vast range of methods, such as virtual screening, docking, homology and pharmacophore modeling, molecular dynamics, quantum chemistry, cheminformatics and machine learning.

In 2022 we have jointly identified, synthesized, and tested small molecules that could be a more accessible and effective alternative to an antibody that is successfully used to treat a range of cancers.

Leader: Rita Guedes

Drug Delivery & Immunoengineering

Our research is focused on the characterization of the mechanisms of cellular dynamics, cross-talk and networks, to identify new targets that will guide the engineering of translational nanotechnology-based systems for drug delivery, imaging and immunotherapy in specific clinically relevant situations (cancer, inflammation, infectious and genetic diseases).

In 2022 we discovered a new small molecule to target PD-1/PD-L1 pathway as an alternative immunotherapy against cancer. This new small molecule has the potential for oral administration, being, therefore, more accessible to patients, in addition to improving activation against cancer cells. During this year we have established a new fluorescence-based imaging methodology to characterize the diversity and biophysical properties of Lipid Droplets in live cells. Our group has also advanced the state-of-the-art technologies for enzyme delivery using liposomes as dry powders.

Leader: Helena Florindo

HIV evolution, epidemiology, and prevention

Our main areas of activity are: a) Epidemiology, drug resistance and evolution of HIV, HCV and HBV; b) HIV-2 infection (diagnosis, pathogenesis, natural history, neutralizing antibody response); c) Design and pre-clinical evaluation HIV vaccines and microbicides; d) Design and pre-clinical evaluation of antiviral drugs.

In 2022 HIV prevalence among adults in sub-Saharan Africa declined >5% between 2000 and 2018. In people with HIV-1, long-term envelope-C2V3 stimulation by diverse isolates leads to the development of broad and elite antibody neutralisation. In people with HIV+HCV, HCV cure leads to a significant reduction in the HIV reservoir. A new family of spiro-β-lactams with potent activity against HIV has been identified.

Leader: Nuno Taveira

Host-Pathogen Interactions

Microbial pathogens have evolved unique ways to interact with their hosts. It is therefore not surprising that pathogens have developed a large and diverse array of virulence factors well suited to interfere with or stimulate a variety of host-cell responses in order to invade, survive and replicate within their hosts. The understanding of how pathogens interact with their hosts is providing the basis for the development of novel therapeutic approaches as well as a number of very sophisticated tools for probing basic aspects of cellular physiology and immunology. As a result, we are beginning to define not only the molecular details of the host pathogen interactions but also potential targets to be manipulated from the host and the pathogen sides. *Mycobacterium tuberculosis* and other mycobacteria, HIV, Influenza virus, SARS-CoV-2 and other emerging viruses are target pathogens. The group offers expertise to assess the anti-microbial activity of new compounds targeting all these pathogens.

In 2022 we develop drug delivery systems to manipulate cathepsins with significant impact on intracellular killing of multidrug-resistant *Mycobacterium tuberculosis*. We performed a large-scale screening for 172 Mtb clinical isolates allowed the identification of drivers of mycobacterial resistance to peptidoglycan synthesis inhibitors. We studied the contribution of cell signalling driven by cell-to-cell contact as a trigger for HIV viral replication and production of HIV infectious viral particles. Furthermore, the conservation and druggability studies were developed to map interaction hot spots as promising targets for antivirals development against COVID-19 and Influenza.

Leader: Elsa Anes

Liver Disease Diagnostics and Therapeutics

Our laboratory studies the role of microRNAs and other modulators of gene expression in liver disease pathogenesis, while exploring their use in disease diagnosis, treatment, monitoring and prevention.

In 2022 we collaborated in showing that inhibition of RIPK3 is promising in ameliorating NAFLD, by restoring mitochondria bioenergetics and impacting on lipid droplet dynamics; and that aberrant protein NEDDylation contributes to cholangiocarcinogenesis, with its inhibition with pevonedistat representing a potential therapeutic strategy for patients with cholangiocarcinoma.

Leader: Rui Castro

Medicinal Chemistry

Our laboratory focuses on designing molecules technologies to cure human diseases and accelerate drug discovery. Our research programme uses chemistry-centric approaches to interrogate biological systems and to modulate target-ligand interactions that underlie infection, cancer, and neurodegenerative disorders.

In 2022 we applied chemistry-centric approaches to interrogate biological systems and to modulate target-ligand interactions that underlie infection, cancer, and neurodegenerative disorders. In this context, in 2022 we implemented a chemoproteomics protocol that enabled the identification of 4-oxo- β -lactams as efficient inhibitors of dipeptidyl peptidases 8 and 9.

Leader: Rui Moreira

Medicinal Organic Chemistry

To tackle disease unmet needs, Our research is focused on the design and synthesis of small molecules for relevant therapeutic targets. To achieve these goals, novel chemical methodologies are developed and applied to library synthesis, while focusing on structure-activity relationships, metabolic stability studies and identification of the possible metabolites for the most promising leads.

In 2022 we discovered new inhibitors of MDM2/4-p53 PPIs with IC50 values in the nM range. In the area of malaria, we discovered different leads with potent dual-stage activity against *P. falciparum* and *P. berghei*. Our research group was also involved on the development of weak acid derivatives with action against tuberculosis. Modification of the most active esters by amides resulted in a marked increase in activity, with the N-alkyl 3,5 dinitrobenzamides showing similar activity to the first line drug isoniazid. Finally, we designed and synthesised new small molecules, based on the indoloisoquinoline scaffold, to target the DNA G-quadruplex structures in the promoter region of oncogene c-MYC, and we developed a new hybrid molecule of triazene and a tyrosine analogue able to reduce tumour volume and lung metastasis in murine melanoma model.

Leader: Maria M. M. Santos

Metabolism, Genetics and Proteins in Health & Disease

MetGenPro Group research lies at the interface of cell metabolism and gene expression. We focus on molecular genetics and alterations in metabolic pathways or enzyme structure/function in response to drugs, gene variants and disease states. Our studies range from basic biomedical research to translational areas addressing personalized medicine for better diagnosis, prognosis and therapies.

In 2022 we developed better biomarkers that allowed a faster diagnosis and more efficient treatment follow-up of galactosemia, PDC and MSUD patients were found. Based on MCAD:ETF interacting sequence, we used in silico tools to design short-peptides which stabilized in vitro the p.K329E variant (MCADD patients). Advances on biomarkers analyses using targeted metabolomics were achieved, as the in vitro use of stable isotope labelled compounds as tracers of Urea Cycle function.

Leader: Paula Leandro

Membrane Transporters in Health & Disease

Our group investigates membrane transport proteins in living organisms and their potential as new biomarkers and drug targets. We identify mechanisms of regulation and dysfunction leading to disease and discover chemical compounds as modulators, characterizing kinetics and pharmacological potential for therapeutics of metabolic disorders, inflammation and cancer.

In 2022 we developed a new cell-based platform to screen inhibitors of human aquaporins, which will also enable exploring aquaporin interplay with signalling pathways of cancer. We also investigated the role of aquaporins in cancer cell migration and cell-cell adhesion, their impact in membranes mechanical properties and their involvement in cellular oxidative stress and energy homeostasis.

Leader: Graça Soveral

Molecular Microbiology and Biotechnology

The Molecular Microbiology and Biotechnology laboratory aims to develop new strategies of antibody engineering and synthetic biology for the advance of new biopharmaceuticals by interrogating the immune humoral and cellular responses in infectious diseases and biologic therapies.

In 2022 we developed new strategies of CAR-T engineering by synthetic biology for the advance of new advanced therapies and we interrogated the immune humoral and cellular responses in Covid19 disease to understand the protective impact of vaccines in immune depressed populations.

Leader: João Gonçalves

Natural Products Chemistry

The Natural Products Chemistry group is focused on the identification and development of novel hit/lead-drug candidates from natural sources though both isolation and molecular derivatization of novel bioactive chemical scaffolds from plants.

In 2022 we discovered new compounds against the highly aggressive triple-negative breast cancer based on a phytochemical analysis of *Pancratium maritimum*. This study afforded Amaryllidaceae-type alkaloids with different scaffolds that were cable of inducing apoptosis, arrested G2/M cell cycle, and synergized chemotherapeutics. We have also discovered new triterpenoids, from an African medicinal plant, that were capable of reversing multidrug resistance in cancer cells.

Leader: Maria José Umbelino Ferreira

Neuroinflammation, Signaling and Neuroregeneration

Neuro in focus on neurodevelopmental disabilities, genetic susceptibilities, neuroinflammation and ageing causing homeostatic imbalance and predisposing to neurodegeneration. We investigate how glial phenotypes, neuro-immune deregulation, and paracrine distress lead to disease onset/progression. We aim to identify early biomarkers for non-invasive diagnosis, generate patient-specific stratification tools for disease modelling, and improve healthcare.

In 2022 we identified miRNAs (e.g., miR-21/-124/-146a) and alarmins as biomarkers/therapeutic targets for neurodegenerative diseases and aberrant inflammation. With small molecules and miRNA reshaping at secretomes/exosomes we halted pathological progression in multi-Models. Using microfluidic chips and patient engineered neural cells we stratified treatment patterns.

Leader: Dora Brites

Neurovascular

The Neurovascular Lab focuses on the blood-brain barrier in Neuropathology as a source of peripheral biomarkers reflecting brain dysfunction, a target for modulation to prevent disease onset and progression, and an obstacle to overcome to achieve therapeutic concentrations in the brain for treatment of brain disorders.

In 2022 we showed the blood-brain barrier (BBB)-permeation of neuroprotective natural compounds pointing to their use as supplements or nutraceuticals. We found drugs with anti-tumor and BBB-permeant properties as candidates for glioblastoma treatment. We discovered that minocycline averts breast cancer cells-induced BBB disruption pointing to its repurposing for breast cancer brain metastases prevention.

Leader: Maria Alexandra Brito

Pathogen Genome Bioinformatics and Computational Biology

Our lab is focused on genomic studies based on genome sequencing and application of computational and bioinformatics approaches, as well as computation-driven experimental approaches, to comprehend the evolution, epidemiology, virulence, population level genomic variation and phylogeography of pathogens.

In 2022 we identify several phage endolysins with the capability to kill major antibiotic resistant pathogens, namely *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Helicobacter pylori* e *Campylobacter* spp., listed by WHO as priority microorganisms to develop new drugs for. In 2022 we start ascertaining the role of prophages in *H. pylori* pathogenicity and concluded a prophage genomic analysis of a worldwide collection of *H. pylori* genomes.

Leader: Filipa Vale

Phage Biology Research and Infection Control

The PhaBRIC lab addresses key biologic questions concerning the interaction of phages with their bacterial hosts. As a major research topic, the lab seeks to understand the action of phage proteins that disrupt the bacterial cell envelope, and to explore this knowledge to develop innovative strategies to fight antibiotic-resistant bacteria.

In 2022 the PhaBRIC laboratory was involved in studies of antibiotic resistance determinants and of phage lytic functions, aiming at the development of strategies to fight drug-resistant bacteria. We showed that heteromeric, two-polypeptide endolysins are quite common, challenging the established view of the field. We showed that cationic peptides can be used to enhance the enzymatic potential of endolysins.

Leader: Carlos São-José

Pharmacy Practice & Health Communication

The PhP& HC Lab aims to deliver scientific evidence and knowledge on the real-life use of medicines and health technologies, from the societal and population levels to the individual perspectives. In particular, it is meant to evaluate pharmacists' and pharmacy services' contribution to the rational use of medicines, including information and communication fluxes.

In 2022 we established a new consortium with European partner institutions – PoT Pharmacy of Tomorrow which is expected to launch two multinational pharmacy-based studies. Our laboratory is actively cooperating with the International Association for Communication in Healthcare and its research committee (rEACH).

Leader: Afonso Cavaco

Pharmaceutical Care and Clinical Pharmacy

Our laboratory focuses on education, research, and on the implementation of advanced pharmaceutical care, encompassing health promotion, disease prevention and medicines optimization. Specific topics include medication adherence and medication review, early identification of suspects of non-communicable diseases (NCDs), health promotion through pharmacy-based interventions, and development of services to manage inappropriate use of medication.

In 2022 we studied the cardio and cerebrovascular risk of major adverse events following exposure to potentially inappropriate medications and the real-world effectiveness of innovative therapies for the most prevalent cancers in Portugal. In addition to these studies, we have also addressed the decision making for the use of conditionally authorised medicines.

Leader: Filipa Alves da Costa

Pharmaceutical Development

The activities of this specialized group are divided into three main research topics: a) Development of innovative and sustainable drug delivery systems (DDS) and technologies, to be used in the prevention of diseases and optimization of treatments (cosmetics, medical devices and medicines); b) Characterization of the target quality product; c) Safe and efficacy studies – from lab to society.

In 2022 we developed new skin drug delivery systems to treat inflammatory diseases, taking advantage of their ease and speed of use, accessibility, and sustainability. Furthermore, we studied the use of 3D printing technology to produce individualized drug load treatments, adapted in shape and size to the patient.

Leader: Joana Marto

Pharmaceutical Engineering and Manufacturing

The PhEMLab is focused on the underpinning sciences related with the design, optimization and manufacturing of bulk pharmaceutical dosage forms. The PhEMLab is oriented for pharmaceutical materials characterization (solid-state), particle engineering, drug products manufacturing process development (including continuous and 3D printing), modelling and advanced real-time high-throughput monitoring. The PhEMLab operates in strong collaboration with the pharmaceutical industry.

In 2022 we focused on the particle design of drugs, particularly in what concerns the solid-state properties addressing a demand from pharmaceutical laboratories. Major innovation was achieved in both the modelling and prediction of crystalline structures of co-crystals and in the manufacturing of stable co-amorphous drug systems suitable for industrial processing. In 2022, the PhEMLab contributed not only to advances in pharmaceutical technology but also to several different areas, as for example culture heritage (mechanisms of degradation of culture heritage objects), once more demonstrating the multidisciplinary nature of the research performed at the PhEMLab. PhEMLab received funds for R&D activities in 2022 from Merck (Germany), Hovione, Basi, Medinfar, Hikma and Bial, through signed protocols.

Leader: João Almeida Lopes

Pharmaceutical Bioengineering, Biotechnology & Bioproducts

PharmaBB aims at developing innovative research, exploring bioengineering & biotechnology, to disease prevention, health promotion and well-being. Our Group brings together different areas of expertise, contributing to achieve a higher knowledge based on the manufacturing of bioactive compounds using green technologies, biofabrication of (bio)materials and gene/drug delivery platforms towards (bio)therapeutics (against infectious, cancer or neuroprotection), medical devices, biomedical and food applications.

In 2022 we developed innovative covalently functionalized medical-grade polydimethylsiloxane (PDMS) with antimicrobial rhamnolipids, inhibiting dual-species biofilms and ensuring biocompatible surfaces. Additionally, reduced cell adhesion and positive tissue implant results make it ideal for medical devices and infection prevention. Furthermore, we gained valuable insights into (multi) enzyme immobilization, evaluating methods, carriers, metrics, and sustainable biocatalytic applications.

Leader: Maria H. Ribeiro

Stem Cell Bioenergetics and Neuroregeneration

Our laboratory is interested in understanding and exploiting the contribution of bioenergetics to neural stem cell fate in the adult brain. By bridging areas of stem cell biology and metabolism, we aim to discover checkpoint mechanisms and promising molecules capable of improving the neuroregenerative potential of these cells throughout adulthood.

In 2022 we reported the mechanism by which a mitochondrial antioxidant protein cooperates with lipid metabolism to safeguard adult neurogenesis in ageing and Depression. We also explored how different systemic cues, including metabolic regulators and insults, influence the regenerative properties of adult neurogenic niches. At last, we started to assess the interplay between microglia and neural stem cells in models of Aniridia.

Leader: Susana Solá

Systems Integration Pharmacology, Clinical & Regulatory Science

Our group aims to support integrative systems pharmacological research focusing in developing innovative pharmacological tools to be used both in a non-clinical and clinical development pipeline, while predicting and modelling preventive or therapeutic clinical effects in a translational approach, profoundly anchored in state-of-the-art principles and guidance of Regulatory Science.

In 2022 we focused on designing more effective and ethical uses of registry data to support patient-centred regulatory decision-making and on accelerate drug repurposing for rare neurological, neurometabolic and neuromuscular disorders by exploiting similarities in clinical and molecular pathology. Using EMA rules for assessment for highly variable drug products, we proposed a new approach for the statistical assessment of bioequivalence between two products of a narrow therapeutic drug.

Building on the different expertise of the group, we successfully published papers in the area of clinical and non-clinical study of the pathological and therapeutical approaches on several diseases (septic shock, inflammatory bowel diseases, colorectal cancer, diabetes), using several medicine development strategies (repurposed medicines, new synthetic substances and herbal or food preparations/substances).

Leader: João Rocha

Toxicology, Biomarkers & Risk Assessment

Our laboratory works on exposure assessment and environmental occurrence of xenobiotics that are considered worldwide concerns to Environment and Public Health. We study the toxicants and drugs' mode of action to identify new biomarkers to support Human and Environmental Risk Assessment processes and develop innovative technologies and therapies.

In 2022 we continued the study of redox-selenoproteins inhibition by mercury compounds and we discovered that thimerosal and its metabolite ethylmercury were more effective than Temozolamide that is the first-line option in Oncology. During this year we have also studied food-contaminants in and water-contaminants and developed the use of Powdered Activated Carbon, to improve pharmaceuticals treated-wastewater and sludge quality.

Leader: Cristina Carvalho





3. imed Training Structure

Undergraduate course

Master program

Doctoral students

Committed with the training of the next generation of scientists working at the interface of chemistry, biology and pharmaceutical sciences, imed researchers provide extensive training activities for undergraduate students but also at the master, doctoral and post-doctoral levels.

Undergraduate course

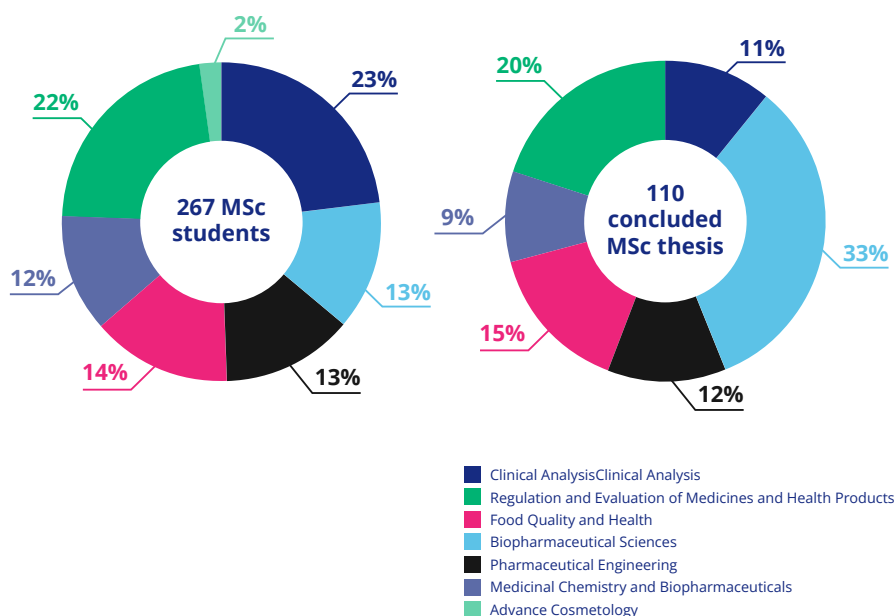
Most of imed researchers participate in the teaching activities of the pharmaceutical sciences and medicines department and the Pharmacy, pharmacology and health technologies department of the Faculty of Pharmacy at the Universidade de Lisboa. In this context, the teaching activities of

imed researchers spread over the many different disciplines of the integrated master of pharmaceutical sciences. Furthermore, most of imed laboratories offer positions for undergraduate students and in 2022, over 30 undergraduate students initiated their scientific careers in imed laboratories.

Master program

In addition to this responsibilities, imed scientists are also leading most of the faculty master courses. This involvement encompasses teaching of individual courses but also the supervision of thesis. In 2022, 110 master students concluded their studies under the supervision of imed scientists.

Over this year, imed scientists coordinated the following master courses that were attended by 260 students.



Advance Cosmetology

Coordinator: Helena Margarida Ribeiro and Joana Marto

The MCA covers a general view of cosmetics, from regulation aspects to the development, production, control, and counselling for all categories of these products. It is a sector of high economical value and high technical-scientific and regulatory complexity, which involves researchers, manufacturers, users, and regulatory entities, and with an important role in the healthcare. The MCA objective is to prepare students for the skills demanded by the society: teamwork, selection knowledge, relate and summarize information, critical and initiative skills in problem solving. Thus, the learning allows diversifying and adapting strategies, putting the students in cognitive contexts appropriate for the proposed objectives.

Biopharmaceutical Sciences

Coordinator: Cecília Rodrigues

Enlarge the classical concept of biopharmaceutical sciences by providing scientific, multidisciplinary background on the discovery phase of the drug development process. Study molecular mechanisms of disease, targets, biomarkers and advanced therapies. Train graduates to equate and solve problems, while motivating students. Prepare creative and independent investigators and knowledgeable professionals, encouraging the debate of recent topics and the use of advanced experimental technologies.

Food Quality and Health

Coordinator: Maria Eduardo Figueira

This course aims to contribute to the acquisition and / or updating of professional and scientific skills in the area, to improve the Quality and Food Safety in Portugal, indispensable in the guarantor of public health, in line with the requirements of the European Community.

Laboratory Medicine

Coordinator: Maria Cristina Marques

To provide a solid and up-to-date training in different scientific domains of the clinical analysis, guaranteeing a comprehensive laboratory component to confer skills for the achievement of laboratory techniques applicable to the prevention, diagnosis and monitoring of the disease, as well as to ensure a professional specialization.

To promote the academic training necessary to follow studies of higher cycle in different scientific areas of the clinical analyses.

Medicinal and Biopharmaceutical Chemistry

Coordinator: Maria José Umbelino

Pharmaceutical Chemistry, a core subject of Pharmaceutical Sciences, is essential for a comprehensive understanding of the drug discovery and development pathway. Named Medicinal Chemistry in the Anglo-Saxon and Northern Europe and Pharmaceutical Chemistry in the countries of southern and central Europe, it is internationally recognized as a transversal subject able to integrate many knowledge areas as Chemistry, Biology or Pharmacology, aiming at the development of new therapeutic agents based on their mechanisms of action and molecular targets.

Pharmaceutical Engineering

Coordinator: António Almeida

To train professionals with competence in the most modern tools for the design and operation of processes for manufacturing, managing and quality control of the product throughout its life cycle (including active substances of chemical or biological origin, drug products and health products) and capable of contributing significantly to technological innovation, improvement of industrial competitiveness and leadership in certain pharmaceutical areas, as well as to the resolution of public health problems in current or emerging therapeutic areas.

Regulation and Evaluation of Medicines and Health Product

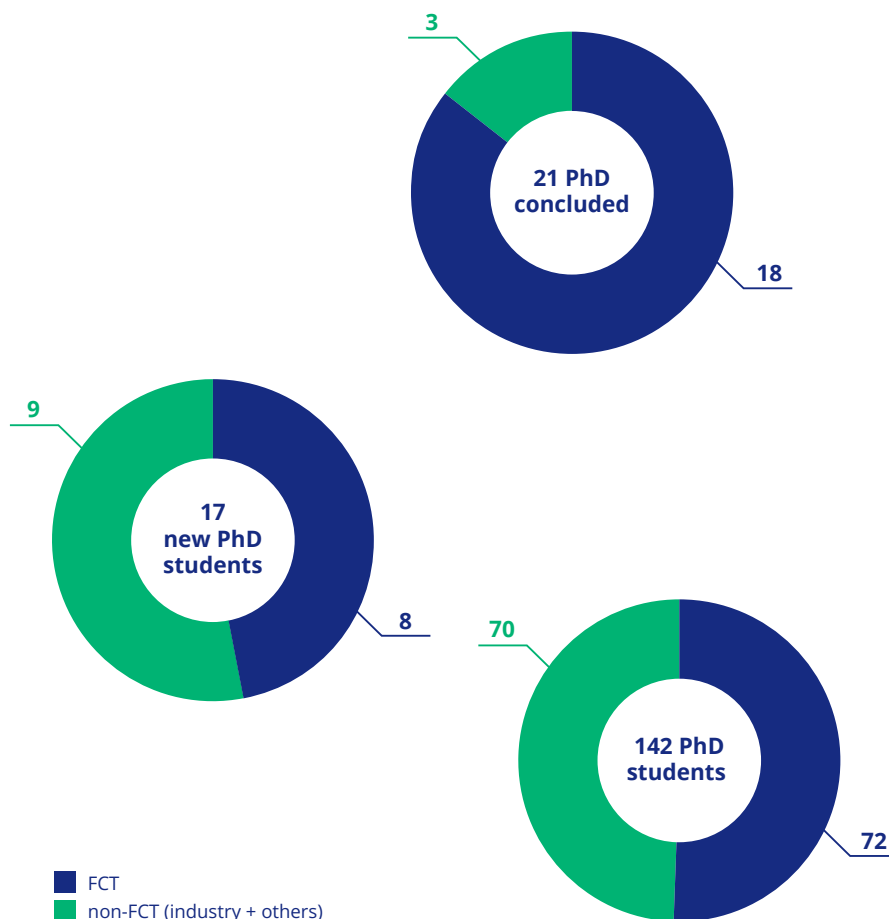
Coordinator: Maria Beatriz da Silva Lima

This course aims to increase knowledge on all the regulatory aspects, laws and directives, science based approaches on the Marketing authorisation in European Union for Medicinal Human Medicines and Veterinary Medicines. Furthermore, this course will include legislation in Health Products based on Medicinal Plants, Medical Devices as well as patent laws, price regulation and others.

Doctoral students

imed scientists contribute intensely for the PhD in Pharmacy at the Faculty of Pharmacy, University of Lisbon with the direct supervision of PhD candidates and with the organization of post-graduate courses. In 2022, imed scientist recruited 17 new PhD students and 21 concluded their studies. Currently, 142 students are engaged in the PhD program at the Pharmacy Faculty that are funded by FCT (72) and other schemes that include collaborations with the industry and patient associations (70).

imed scientists are actively involved in training activities at the post-graduate level and offer the following advanced doctoral programs:



Advanced Research Methods in Health and Pharmacy Practice

Coordinator: Afonso Miguel Cavaco;
Filipa Alves da Costa

Laboratory: Pharmacy Practice & Health Communication; Public Health & Medicines Use

Pharmacy practice is an area of study within health services research that focuses on the role of pharmacists in promoting the safe and effective use of medicines and medical devices. Therefore, pharmacy practice research studies come to play and can adopt varied formats, resorting to methodologies used initially in epidemiology, including observational and experimental studies, whilst combining these with methods primarily used in the social sciences. These methodologies enable a more person-centred approach to understanding the experience of people living with illness and relying on medication and medical devices to maintain their health and well-being.

Gaining in-depth knowledge in health services research is essential for pharmacy doctorates to develop their research projects by selecting the most appropriate methodologies for reviewing state of the art in their areas of interest, selecting suitable study designs, collecting and analysing data emerging and producing high-quality evidence that supports the advancement of this area of practice.

Advanced Topics in Medicinal Chemistry and chemical biology

Coordinator: Rui Moreira

Laboratory: Medicinal Chemistry

The advanced specialization course in Medicinal Chemistry and Chemistry Biology is intended to frame the training of students who have been admitted to the PhD program in Pharmacy. It is a highly flexible programme covering a wide range of courses taught by chemists, pharmacists, biologists and industrial medicinal chemists.

It provides a strong foundation in core chemistry, supplemented by specialist knowledge of medicinal chemistry and chemical biology.

Advanced Drug Delivery

Coordinator: António Almeida; Helena Florindo

Laboratory: Advanced Technologies for Drug Delivery; Drug Delivery & Immunoengineering

Advanced Drug Delivery is part of the PhD Programme in Pharmacy, trains students in the development of advanced medicinal products, covering crucial aspects that determine the fate of drugs in the human or animal body, from their fundamentals to the advanced strategies to overcome the physiological barriers, including innovative technological and therapeutic applications. The course will be held at the Research Institute for Medicines (iMed.ULisboa), Faculdade de Farmácia, Universidade de Lisboa, in Lisbon. The training program is aimed at PhD students but welcomes the participation of external academic and scientific community members. Registration is free but mandatory. The course intends to improve PhD students' knowledge in the discovery of potential biotherapeutics, the improvement of production and monitoring of drugs and the translation of these drugs to the clinics.

Advanced Analytical Tools: Multiple Applications for Mass Spectrometry

Coordinator: Maria Rosário Bronze; Noélia Duarte

Laboratory: Natural Products Chemistry

Mass Spectrometry (MS) is an advanced analytical technique that has reached an outstanding position due to its unique characteristics: high selectivity, low detection limits, speed and a large diversity of applications. During the last two decades, MS has progressed rapidly through the advances on ionization methods and mass analysers that have led to the advent of new equipment.

This progress has allowed the development of new applications mostly oriented towards health promoting areas such as proteomics, lipidomics, metabolomics, foodomics, drug discovery, pollution control and forensic and toxicological sciences. This course aims to give an overview on basic MS fundamentals and instrumentation highlighting several recent applications.

Multidisciplinary Project-based Learning in Pharmacy

Coordinator: André Santos; Isabel Rivera; Maria M.M Santos

Laboratory: Cell Function and Therapeutic Targeting; Bacterial Pathogenomics and Drug Resistance; Medicinal Organic Chemistry

The **Multidisciplinary Project-Based Learning in Pharmacy** course is part of the Doctor of Pharmacy Program, and trains students to embrace new ways of thinking, outside their comfort zone, to generate a new approach to solving a real-world based problem (e.g., a pandemic disease). To achieve this goal, mixed groups of students (with backgrounds in chemistry, biology, or pharmaceutical sciences) will provide the starting point for productive discussions that will culminate in the development of a project capable of answering the proposed problem. Understanding how to integrate multi- and translational disciplines will facilitate students in strengthening their critical thinking, communication skills, and peer networking. The course is held at the Institute for Medicines Research (iMed.ULisboa), Faculty of Pharmacy, University of Lisbon, in Lisbon, is a key tool to develop a scientific personality, crucial for the next years of their PhD programs.

Molecular Biomarkers and Technologies

Coordinator: Elsa Rodrigues

Laboratory: Cell Function and Therapeutic Targeting

Biomarkers are now an integral part of the drug discovery and development process, acting as indicators of drug mechanism of action, efficacy, safety and disease progression, as well as assisting in disease diagnosis, patient selection and clinical trial design. Biomarkers also offer the potential to inform treatment decisions and bring personalized medicine into clinical practice. Latest advances in clinical and translational biomarkers will be covered, including patient selection and predicting response to therapy, liquid biopsy and cell free DNA, companion diagnostics and personalized medicine, biomarker assay development and validation, and biomarker-based clinical trials. The new frontier of digital health and its impact on drug and diagnostic development will be explored, covering emerging digital biomarkers and their utility in clinical trials, advances in biosensors and wearables as clinical endpoints, integration of mobile health into drug development, and the latest applications in point-of-care testing and remote patient monitoring.

Advances in Neuropharmaceutics

Coordinator: Adelaide Fernandes

Laboratory: Central Nervous System, Blood, and Peripheral Inflammation; Neuroinflammation, Signaling and Neuroregeneration; Neurovascular

Neuropharmaceutics focuses on the identification of therapeutic targets in nervous system diseases, and then translating those discoveries into drug and therapy development. Neurological disorders have a crucial impact on our society accounting for increased health costs, while drug development to central nervous system (CNS) disorders represents the second investment priority of the pharmaceutical industry, following cancer. Thus, advances in neuropharmaceutics is a key area for students of a PhD programme aiming to target discovery, drug design, medicine development and usage.

Pathogen Multiomics and Bioinformatics

Coordinator: João Perdigão

Laboratory: Bacterial Pathogenomics and Drug Resistance

The Pathogen Multiomics and Bioinformatics advanced course is structured around six distinct modules that spans the entire spectrum from the introduction to NGS data and quality control to genome-wide association studies applied to different pathogens. While the course comprehends a solid theoretical component that underpins the learning and execution of the different analytical stages in the practical sessions which comprise most of the course. It is intended that the participants apprehend the concepts and fundamentals of the analytical procedures that are necessary to translate the large data volumes generated by NGS platforms while systematically consolidating the theoretical basis of this knowledge.

Redox Signaling and Redox Systems in Health and Disease: implications for drug design and development

Coordinator: Vasco Branco

Laboratory: Toxicology, Biomarkers & Risk Assessment

Redox signalling achieved by reactive oxygen species (ROS) is a key aspect of signal transduction in various cellular processes such as cell death, differentiation and inflammation. However, the line separating redox signalling from oxidative stress is a thin one and redox homeostasis is reliant on the action of redox active systems. These systems are complex arrays of enzymes controlling ROS levels but also the oxidation-reduction cycle of critical protein residues (e.g. cysteines) that enable signal transduction. Disruption of redox signalling has been implicated in the aetiology of several pathologies including cancer and neurodegenerative diseases. Moreover, redox enzymes have very reactive residues (cysteines and selenocysteines) and are, therefore, candidate targets for inhibition by electrophilic compounds, creating opportunities for therapeutic strategies.

This Advanced Course will approach these aspects in detail which are of widespread interest for many PhD candidates in Pharmacy.

Stem Cell Technologies

Coordinator: Susana Solá

Laboratory: Stem Cell Bioenergetics and Neuroregeneration

Stem cell-based therapies are thriving. In fact, pharmaceutical companies are increasingly investing in stem cell technology to develop innovative and potentially valuable new treatments for severe human diseases, including cancer and neurological disorders, such as multiple sclerosis, Alzheimer's and Parkinson's disease, mood disorders, brain tumours and even stroke. Moreover, although seminal advances have occurred in understanding stem cell biology, further work is still needed to bridge the current gap between stem cell technologies and effective treatments in brain-related disorders. Stimulating the scientific interest on the topic will certainly accelerate and improve the successful transfer of stem cell-based discoveries from the bench to the bedside.

Topical and Transdermal Delivery

Coordinator: Sandra Simões

Laboratory: Advanced Technologies for Drug Delivery

Topical and transdermal drug delivery systems are designed to support the development of new and effective therapeutics. The human stratum corneum acting as a barrier for the permeation of active substances has limited the number of molecules commercially available as transcutaneous delivery systems. Several strategies have been employed over the past few decades to optimize drug delivery across the skin of several poorly permeable compounds. However, passive techniques present limited potential to facilitate the delivery of macromolecules. Topical and transdermal delivery is therefore an area of research with many challenging objectives but also with great opportunities to work envisaging the patient compliance as it refers to a convenient painless non-invasive drug administration route.

4. Resources

Facilities

New equipment

imed research ecosystem is supported by 30 laboratories across the fields of chemistry, biology and pharmaceutical sciences. All research groups benefit from laboratory facilities and shared scientific platforms that include:

Facilities

imed state-of-the-art facilities and world-class services provide an ideal environment for the discovery and development of new medical treatments and for generating breakthroughs in health sciences. Our facilities are equipped with the latest equipments and state-of-the-art technologies, allowing us to conduct research and provide services that are at the forefront of modern science. In parallel, we offer a wide range of services, including research and development of new drugs and therapies, and advanced imaging and flow cytometry.

We are committed to advancing healthcare through innovation, research, and collaboration, and our facilities are open to the scientific and health community, as well as the pharma and industry sector.

Animal Facility

Head: Maria Manuela Gaspar

Laboratory: Advanced Technologies
for Drug Delivery

The Animal Facility supports the discovery and development of innovative medicines for the benefit of humans and animals. This Facility consists of several rooms for animal maintenance with housing capacity of around 500 small rodents (rats and mice) and rooms for experimental procedures (small surgeries and dissections). Metabolic cages are also available. Support rooms are used for cleaning, washing and sterilization of cages and other equipment, food, and bedding. Several rodent models are established and typically available, including models of infection, acute and chronic inflammation, xenograft or metastatic tumors, non-alcoholic fatty liver disease, neurodegenerative diseases as well as biodistribution and toxicity studies. Upon request and contract, these or other animal models may be provided to external entities. The Animal Facility provides technical and scientific support to investigators on protocol development, refinement of experimental procedures, small surgery techniques, and services of husbandry and routine daily care (feeding, watering, and cage changing).

The Animal Facility is licensed by “Direção Geral de Alimentação e Veterinária” (DGAV), the competent national authority responsible for implementing the legislation for the protection of animals for scientific purposes. All animal experiments conducted in the Animal Facility are subject to rigorous review and must be previously submitted to the Animal Welfare Board (ORBEA – Orgão de Bem-Estar Animal) at the Faculty of Pharmacy, University of Lisbon (Regulamento 806/2016), and then approved by DGAV. Together, they ensure that research animals are used only when necessary and under humane conditions. Personnel and users are certified researchers for conducting animal experimentation. All procedures are performed according to the EU Directive (2010/63/UE) and Portuguese laws (DR 113/2013, 2880/2015, Portaria 260/2016 and 1/2019).

imed is committed to following the 3Rs, Replacement, Reduction and Refinement, and carrying out research of the highest quality and providing animals used in research with the best care available. Alternatives to animal use, which include computer modeling, cell culture and bacterial systems, are available and used whenever possible.

Biosafety Level 3

Head: Quirina Santos Costa

Laboratory: Host-Pathogen Interactions

The Biosafety Level 3 Facility is specifically dedicated to research involving biological pathogens of level 3 security. It was designed to minimize the risk of personnel and environmental exposure to potential hazardous agents according to European and Portuguese legislation. All users must undergo specific biosafety level 3 training and must follow strict rules and guidelines while working in the facility.

Consists of an anteroom for material and personnel preparation, and a main procedure room equipped with three vertical laminar flow chambers (type A2 and type B2), three CO₂ incubators (Hera Cell), one regular incubator, two benchtop centrifuges (Eppendorff), a benchtop ultracentrifuge (Beckman), an aerosol-tight microfuge (Eppendorff), a Tecan infinite 200 multimode microplate reader, water baths, freezers, refrigerators, optical and inverted phase-contrast microscopes (Leica), and a dedicated double door pass-through autoclave (Matachana).

Cell Culture

Head: Joana Amaral; Rui Silva

Laboratory: Cell Function
and Therapeutic Targeting;
Neuroinflammation, Signalling
and Neuroregeneration

The Cell Culture Facility comprises dedicated cell culture rooms equipped with the required environment and equipment for a wide range of cell and tissue culture procedures, from maintenance and manipulation of cell lines and tissue samples to cell observation and data analysis. In addition, the facility provides routine mycoplasma detection testing for mammalian cell lines. Consists of laminar flow hoods (Esco, Class II Type A2), CO2 incubators (Hera Cell), inverted microscopes (Zeiss) coupled to an imaging system (Leica), and support equipment (automated cell counter, centrifuges, water baths, refrigerators, freezers). Fluorescence and bright-field microscopes (Zeiss) with dedicated cameras (Leica) and imaging and acquisition systems are available, including an Invitrogen EVOS™ FL Auto 2 fully automated, inverted, multi-channel fluorescence and transmitted light imaging system.

Additional dedicated equipment provides cell analysis high-throughput capabilities with Multidrop Combi Reagent Dispenser (Thermo Scientific) for 6 to 1536-well plates; GloMax®-Multi+Microplate Multimode Reader (Promega), accepting 6 to 384-well plates, and accommodating luminometer, fluorescence, and visible/UV absorbance modules and dual injector system for 6 to 96-well plate formats; and xCELLigence RTCA SP (ACEA Biosciences) for real-time label free impedance-based cell analysis in 96-well format.

The facility provides biological evaluation of cell function, routinely determining the role of transgenes and the cytotoxic and cytoprotective activities of synthetic and natural compounds in multiple cell models, including immortalized cells (human, monkey, rat, mouse), embryonic stem cells (rat and mouse), primary cultures (rat and mouse liver, brain), and organotypic cultures.

Confocal Microscopy

Head: Liana Silva

Laboratory: Drug Delivery & Immunoengineering

The confocal microscopy facility supports the highest level of research aimed by providing confocal imaging training, services and bioimage analysis. Activities are divided among three key areas: sample preparation, confocal microscope image acquisition and data analysis with Aivia, a powerful artificial intelligence-guided image analysis software.

The Leica TCS SP8 laser scanning confocal microscope is a fully motorized high-resolution inverted confocal microscope for fluorescence imaging. The DMI8 fluorescence microscope is equipped with a fully motorized stage, fast z movement (Leica Super Z Galvo stage), 4 solid state lasers (405, 488, 552, 638 nm), four detectors (one HyD high-sensitivity and three PMT), a transmitted light detector with CCD camera, three dry objectives (5x, 10x and 20x) and two oil immersion objectives (40x and 63x).

The advantage over conventional widefield light microscopy is that the optics of this confocal microscope remove scattered light and light originating from outside the focal plane of interest, thus generating a high contrast “optical section”. Moreover, this microscope allows several types of image acquisition, such as 2D, z-stack, multi-positions, tile scanning/image stitching of large samples and time-lapse.

Computer Assisted Drug Design

Head: Rita Guedes

Laboratory: Computational Medicinal Chemistry

The Computer Assisted Drug Design Facility consists of a Linux-based high performance computer cluster with 424 CPU cores, 4 to 8GB per CPU/GPU and 2 TB per node with a specific implementation of state-of-the-art software for molecular modeling, molecular dynamics, virtual screening, and de novo design. Provides technical support ranging from advice in experimental design to data analysis.

Flow Cytometry

Head: Catarina Godinho Santos

Staff: Miguel Cardoso

Laboratory: Molecular Microbiology
and Biotechnology

The cytometry system at imed consists of the Cytex® Aurora full spectrum flow cytometer and a computer workstation running SpectroFlo® software for sample acquisition and data analysis. This spectral flow cytometry system allows unique fluorochrome combinations in comparison to conventional flow cytometry and enables analysis of cells with high autofluorescence.

The cytometer is an air-cooled, compact benchtop instrument. It is equipped with 4 lasers (Violet, Blue, Yellow-Green and Red), 48 detection channels for fluorescence, and three channels for scatter (blue laser FSC, blue laser SSC, and violet laser SSC). High-throughput sample loaders are available to automate sample delivery and acquisition and currently are compatible with 96-well plates.

An independent workstation for analysis of flow cytometry data is available upon booking, where SpectroFlo® and FCS Express™ 7 softwares can be used.

Technical support in panel design, experimental planning, sample preparation, sample acquisition and data analysis can be requested.

Gene and Protein Expression

Head: Rui Castro

Laboratory: Liver Disease Diagnostics and Therapeutics

The Gene and Protein Expression Facility at imed is equipped with cutting-edge technologies that allow for high-throughput, accurate and sensitive measurements of gene and protein expression levels, enabling researchers to gain a deeper understanding of the molecular mechanisms underlying biological processes.

Consists of equipment for sample quality monitoring and quantification, including a Qubit 4 fluorometer and a NanoDrop 2000c spectrophotometer (ThermoFisher Scientific); and microplate readers, including a Multiskan FC and a Varioskan LUX multimode reader (ThermoFisher Scientific), equipped with a flexible range of measurement technologies including Absorbance, Fluorescence Intensity, Luminescence, AlphaScreen, and Time-Resolved Fluorescence.

Protein Electrophoresis & Western Blotting equipment includes standard and mini-gel electrophoresis systems (Bio-Rad and ThermoFisher Scientific); Trans-Blot Turbo (Bio-Rad) and iBlot 2 (ThermoFisher Scientific) transfer systems; and the Chemidoc MP (Bio-Rad), iBright CL750 and iBright FL1500 (ThermoFisher Scientific) Imaging Systems, supporting imaging applications of fluorescent,

chemiluminescent, and colorimetric western blots, in addition to fluorescent stained nucleic acid gels, fluorescent stained protein gels, colorimetric stained protein gels, and colorimetric membrane stains.

Gene expression equipment encompasses end-point thermocyclers (Bio-Rad and ThermoFisher Scientific) and real time PCR systems, including the Applied Biosystems 7300 and state-of-the-art QuantStudio 7 Flex Real-Time PCR Systems. The later enables high-throughput, quantitative gene expression, combining 384-well microfluidic gene expression, predesigned or customized card arrays, with multiplexing (21 filter combinations), and fast real-time capabilities.

The facility provides personalized guidance and training to researchers in designing and conducting experiments, data analysis and interpretation; and provides a wide range of services, including protein and RNA isolation, quantification and quality control, protein and gene expression profiling, and data analysis.

Mass Spectrometry

Head: Maria do Rosário Bronze and Fábio Santos

Laboratory: Chemical Biology

The Mass Spectrometry Facility is part of the National Mass Spectrometry Network.

Consists of a Triple Quadrupole mass spectrometer (Micromass Quattro Micro API, Waters) with electrospray ionization (ESI) atmospheric pressure chemical ionization (APCI) ion sources. This facility is also equipped with an Ion-Trap (LCQ-Fleet, Thermo) mass spectrometer dedicated to the characterization of proteins and biological conjugates.

Provides identification and quantification of small molecules in complex matrices, as biological fluids, and extracts of natural products. Services are available for users on a "do-it-yourself" basis or self-service, for long-term studies, upon initial training requirements. A technician is also available for a full-service.

Molecular BioScreening

Head: Vanda Marques and Cecília Rodrigues

Laboratory: Cell Function and Therapeutic Targeting

The Molecular BioScreening facility at imed offers an innovative and integrated approach of cell-based medium- to high-throughput assays for screening small molecules (natural or synthetic) and biologics. It provides cell-based assays, including untargeted phenotypic assay approaches, using human and non-human cell lines, primary cells, stem cells and organoids that recapitulate human biology.

Primary screens are designed and optimized to deliver solutions that help achieve specific experimental goals; and are available for adherent and 3D cell cultures, optimized for 96-well and/or 384-well formats, include IC50 and EC50 determination, drug interaction evaluation, or cell death arrays (apoptosis, necroptosis and ferroptosis).

The facility is equipped with instrumentation, automation, and software for running medium- to high-throughput screens using a variety of assay technologies, including an automatic liquid handling platform for 6 to 1536-well plates (Thermo Scientific); multi-label plate readers; and real-time label free impedance-based cell analysis (xCELLigence RTCA SP – ACEA Biosciences)

The Molecular BioScreening unit is available to both internal and external researchers. Inquiries regarding other specific assays are welcome from academia, biotechnology and pharmaceutical industries seeking solutions in bioscreening.

The facility is core for many researchers at imed, as it combines the power of relevant cell models, phenotypic screens, and live cell functional assays to ultimately lead to the discovery of new therapeutic agents.

Nuclear Magnetic Spectroscopy

Head: Noélia Duarte

Laboratory: Natural Products Chemistry

Nuclear magnetic resonance (NMR) spectroscopy is an advanced analytical technique that has reached an outstanding position in several scientific areas, including chemistry, biochemistry, medicine, physics, material sciences and geology. At imed, the NMR facility is equipped with a Bruker® - Biospin Fourier 300 MHz (7.1 T) spectrometer, with a ^1H & ^{13}C (5 mm) probe and autosampler SampleXpress Lite. The equipment is used to support R&D projects and advanced training activities. 1D and 2D-NMR experiments are routinely carried out to elucidate the structure of small molecules obtained both from synthesis or natural sources; and kinetic studies to elucidate reaction mechanisms.

Additional applications include metabolic studies (for instance, metabolite identification), and compound quantification in drug development studies. Basic training of users (students or researchers) for in-house data collection and processing, as well as external services for academia and pharmaceutical industries are also provided.



New equipment

In 2022, we strength our capacity to study complex mixtures and biologics with the acquisition of a Thermo Scientific Orbitrap Exploris mass spectrometry. This is a quantitative high-resolution, accurate-mass (HRAM) liquid chromatography mass spectrometry (LC-MS) with record-setting performance. We expect that this new equipment will deliver precision data on exact masses and the possibility to start exploring proteomics as a tool to unravel druggable targets and new medicines.

5. Scientific Development

Human resources

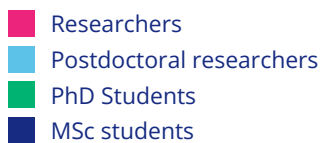
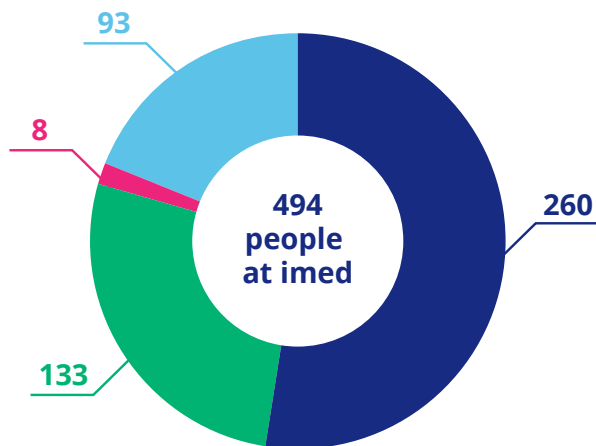
Research funding

Research outputs & actions

Internationalization

imed joint seminars

Human resources



In December 2022, more than 419 people were working at imed: 93 Research, 8 postdoctoral researchers, 133 PhD students, 260 MSc students.

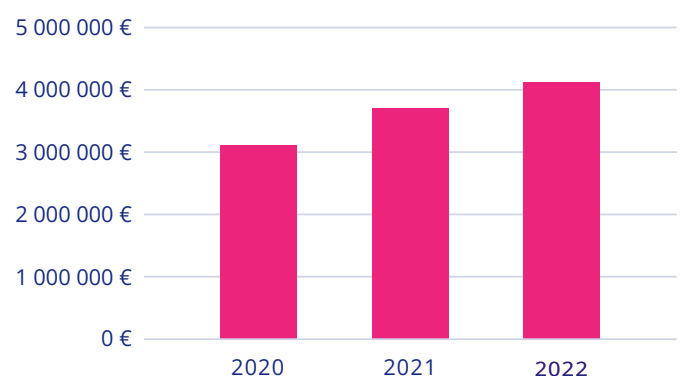
Recruitment policy

At imed we aim to establish an organic environment that leads to breakthroughs in health sciences for the benefit of all. This can only be achieved with the best researchers working together. Therefore, as a research centre of the Pharmacy Faculty of the Universidade de Lisboa, imed recruiting strategy is aligned with the host institution policy, which during this year, was able to recruit 23 (10 FFUL + 13 FARMID) new researchers that are now fully integrated in imed. Finally, taking advantage of the Fundação para a Ciência e Tecnologia - Scientific Employment Stimulus- we were able to recruit 2 new researchers in the highly competitive individual call.

Research funding

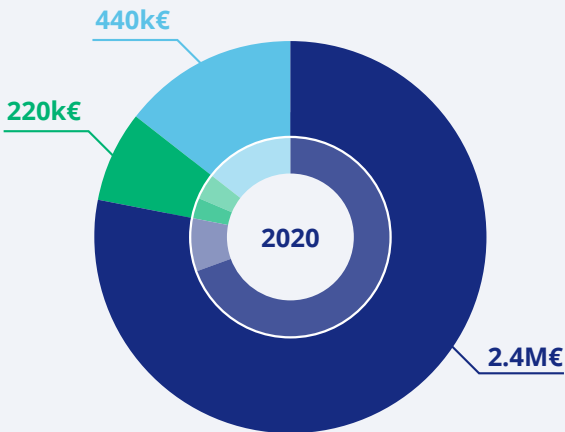
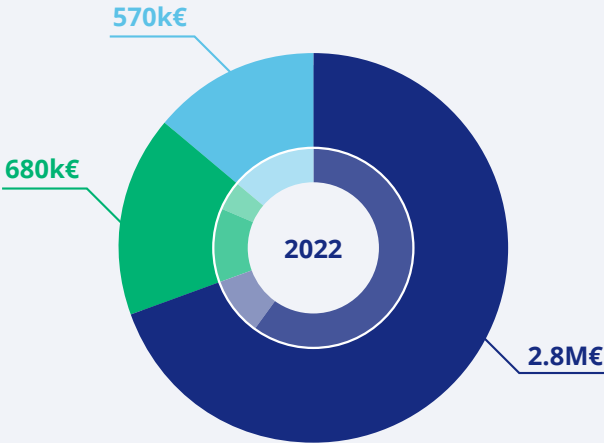
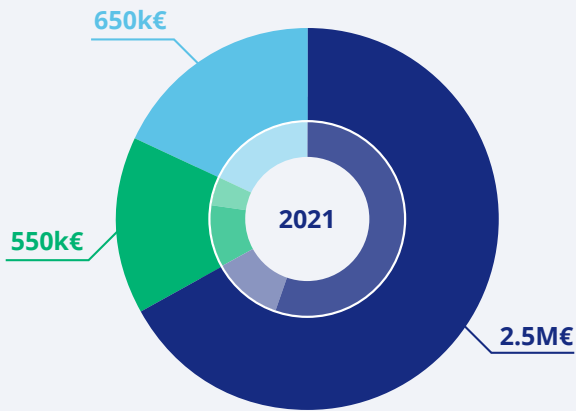
imed scientist have been quite successful in securing competitive funds despite the difficult financial circumstances experienced in 2022. The institute funds increased 11%, comparing with the available budgeted of 2021, and reached a global value of 4.1 MEuros.

Total available funding

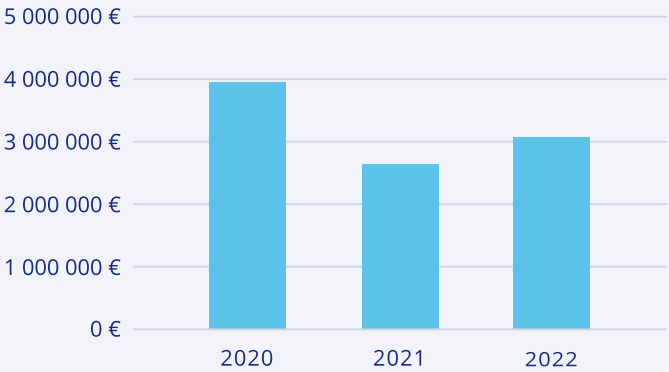


These positive numbers were possible because our scientists were particularly successful in securing funds both through national (2.8 MEuros) and international competitive calls (680 kEuros), as well as from projects with industry and contracted research services (570 kEuros) following our commitment to strengthen our knowledge transfer capacity.

Globally our figures as at 31st of December 2022, show 54 (coordinator)+ 24 (partner) active national projects, 8 (coordinator)+ 4 (partner) international projects, and 7 funded contracts with the private sector. The overall budget of imed also considers Fundação para a Ciência e Tecnologia support in the form of: R&D Unit Pluriannual funding; contracts of researchers with PhD and PhD and other scholarships.



Total awarded funding



List of projects starting in 2022

National projects

SmartBox: Development of the first generation of ROS-sensitive ADCs

Foundation for Science and Technology (PTDC/QUI-OUT/3989/2021)

PI: Pedro Góis

NanoMetBrain - Multifunctional nano-immunotherapy for the treatment of melanoma brain metastases

Foundation for Science and Technology (PTDC/BTM-SAL/4350/2021)

PI: Helena Florindo

ANIMATE - Analysis of neuroimmune dysregulation in Alzheimer's disease for therapy with miRNAs carried by exosomes

Foundation for Science and Technology (PTDC/MED-NEU/2382/2021)

PI: Dora Brites

ImmuneMScognit - The interaction between the innate and acquired immune response as a basis for the cognitive deficit present in Multiple Sclerosis

Foundation for Science and Technology (PTDC/MED-PAT/2582/2021)

PI: Adelaide Fernandes

RIPliver - Translating RIPK3 signaling for application in metabolic liver disease

Foundation for Science and Technology (PTDC/MED-FAR/3492/2021)

PI: Cecília Maria Pereira Rodrigues

Potential of nitrobenzoic acid derivatives as anti-tuberculosis drugs. Insights into the mechanism of action

Fundação para a Ciência e Tecnologia (EXPL/SAU-INF/1097/2021)

PI: Luis Constantino

Potential of nitrobenzoic acid derivatives as antituberculosis drugs. Insights into the mechanism of action

Foundation for Science and Technology (EXPL/MED-OUT/1317/2021)

PI: Pedro Rodrigues

NxGNanoTher - Next-generation nanomaterials to sensitize breast cancer to immunotherapy

Programa University of Texas at Austin Portugal - 2021 (UTAP-EXPL/NPN/0041/2021)

PI: Helena Florindo

Pro2Liver - Role of Limosylactobacillus D-lactate in the treatment of NAFLD

Foundation for Science and Technology (EXPL/MED-OUT/0688/2021)

PI: André Anastácio Santos

TB3D - Development and validation of a 3D cell culture model of the tuberculosis granuloma for application in studies of new drug research and the host cellular response in the context of latent infection and a multicellular response

Foundation for Science and Technology (EXPL/SAU-INF/0742/2021)

PI: David Pires

TB3D - Development and validation of a 3D cell culture model of the tuberculosis granuloma for application in studies of new drug research and the host cellular response in the context of latent infection and a multicellular response

Foundation for Science and Technology (EXPL/SAU-INF/0742/2021)

PI: David Pires

REMIND - Modulation of mitochondrial dysfunction by redox signaling via post-translational modifications

Foundation for Science and Technology (EXPL/BIA-BQM/0793/2021)

PI: Andreia Carvalho

miR2myelin@obMS - Role of obesity in multiple sclerosis: identification of microRNAs related to oligodendrocyte development as novel therapeutic targets to promote remyelination

Foundation for Science and Technology (EXPL/MED-NEU/1033/2021)

PI: Andreia Barateiro

ChemSlotProtein - A new tool to promote investment in new molecular targets by medicinal chemists

Foundation for Science and Technology (EXPL/QUI-OUT/1288/2021)

PI: Rita Guedes

SM-UnLOCK - Immunomodulator Small Molecules in Cancer: Discovery, Development and Application in Immuno-oncology

Foundation for Science and Technology (EXPL/MED-QUI/1316/2021)

PI: Rita Acúrsio

International projects

Multifunctional nano-immunotherapy against breast brain metastases

Health Research - La Caixa

PI: Helena Florindo

Iron-triggered technologies as a novel targeted therapy for cancer

La Caixa Validate- La Caixa

PI: Diogo Silva

COST Action: 16205 – UNGAP

H2020 (GA 951996)

PI: Nuno Silva/Paulo Paixão

OncoProTools - Protease-guided tumor targeting tools to revolutionize cancer diagnosis and treatment

HORIZON-MSCA-2021-DN-01 (101073231)

PI: Maria MM Santos/Rui Moreira

Industry and contracted research

Pipeline for discovery of CDK4/6 inhibitors for metastatic breast cancer treatment

Pfizer Inc. (68977633)

PI: Alexandra Brito

Covi-Vac: The response of immunocompromised people to COVID-19 vaccine

AstraZeneca

PI: Joao B. Gonçalves

FUJIFILM Covid-19 Ag Test, a highly-sensitive and rapid antigen test kit for the detection of SARS-CoV-2-infection

PI: Joao Gonçalves

Contracted research with different institutions

PI: Various

Research outputs & actions

Continuing our mission to strengthen multidisciplinary and collaborative science, in 2022 we launched an internal call with a 75Keuros budget for 1-year collaborative projects between internal laboratories. The IEDA action was quite successful and funded the following research projects to test new ideas within the institute.

Small organic molecules targeting aquaporins as a novel therapeutic approach to pancreatic cancer

Laboratories: Membrane Transporters in Health & Disease - Bioorganic Chemistry

Development of mutant p53 binding assays for screening indole-based molecules

Laboratories: Medicinal Organic Chemistry - Metabolism, Genetics and Proteins in Health & Disease

External signals neuronal stem cells to deliver regenerative micro RNAs in their secretome

Laboratories: Stem cells Bioenergetics and Neuroregeneration - Liver Disease Diagnostics and Therapeutics

Determining the mechanism of antiviral action of spiro-beta-lactam compounds

Laboratories: Molecular Microbiology and biotechnology - HIV Epidemiology, Evolution and Prevention

Nitrobenzamides active against M. tuberculosis

Laboratories: Host-Pathogen Interactions - Medicinal Organic Chemistry

Periadvac: Breaking the link between periodontitis and Alzheimer's diseases

Laboratories: Advanced Technologies for Drug Delivery – Central Nervous System, Blood and Peripheral Inflammation

Plant derived compounds for targeting resistant *Helicobacter pylori*

Laboratories: Natural Product Chemistry – Pathogen Genome Bioinformatics and Computational Biology

Phage4Wound – Phage-based wound dressings

Laboratories: Pharmaceutical Development – Phage Biology and Infection Control

miRNA-Exosomes as a therapy for AD

Laboratories: Neuroinflammation, Signaling and Neurogeneration

Developing a screening assay to identify compounds targeting the energy metabolism of the *Mycobacterium tuberculosis*

Laboratories: Medicinal Chemistry – Bacterial Pathogenomics and Drug Resistance

Treatment of breast cancer brain metastases: from a drug screening to a drug delivery system development

Laboratories: Neurovascular – Drug Delivery and Immunoengineering

EXO-BASHY a novel fluorescent platform for drug delivery

Laboratories: Advanced Cell Models for Predictive Toxicology & Cell-based Therapies -Chemical Biology

Unravelling biotechnology to improve the bioactivity of dietary polyphenols: the role of gut microbiome in the bioavailability

Laboratories: Pharmaceutical Bioengineering & Bioproducts – Systems Integration Pharmacology, Clinical & regulatory Science

In-silico support for the bioavailability enhancement of pharmaceutical drugs via crystal engineering

Laboratories: Pharmaceutical Engineering and Manufacturing – Computational Medicinal Chemistry

Automated batch analysis algorithm development for the characterization of NPC cell models based on confocal fluorescence imaging

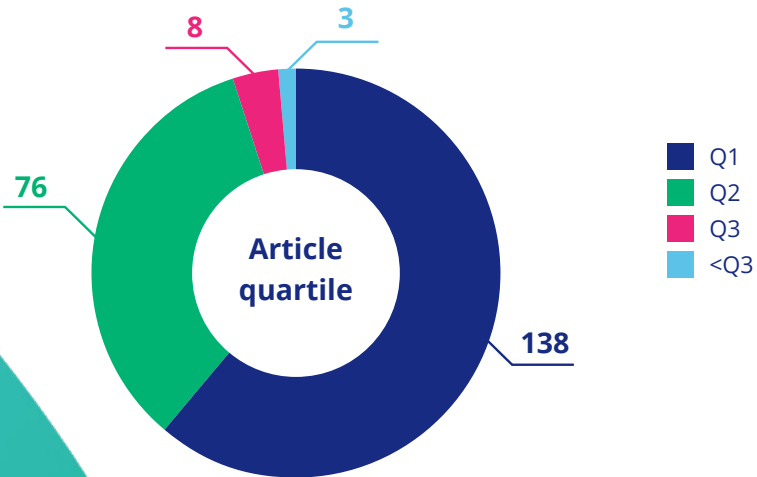
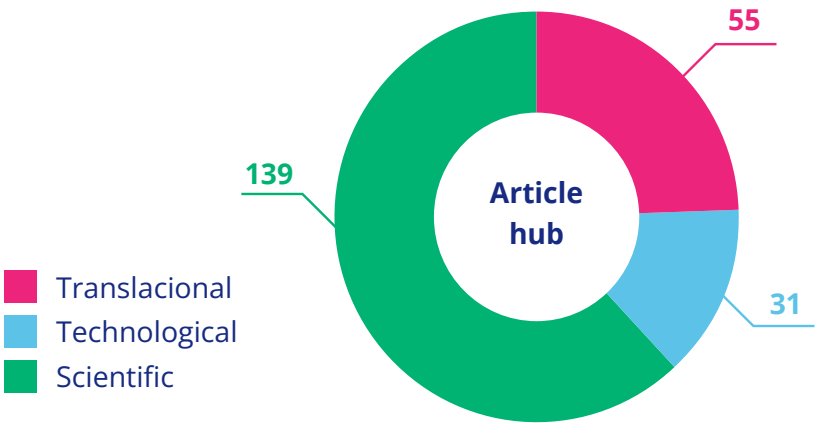
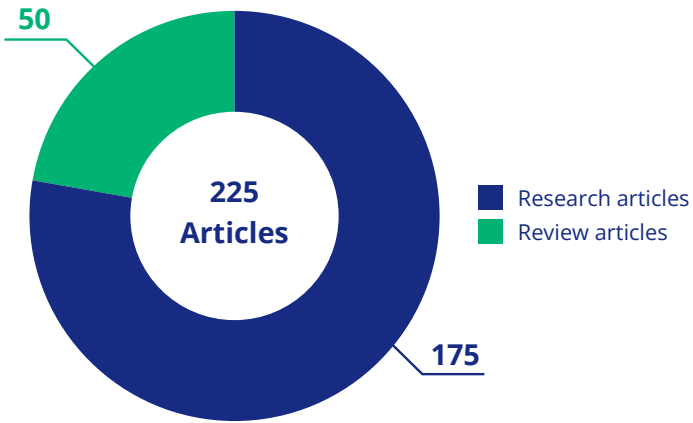
Laboratories: Cell Function and Therapeutic Targeting - Pharmaceutical Engineering and Manufacturing

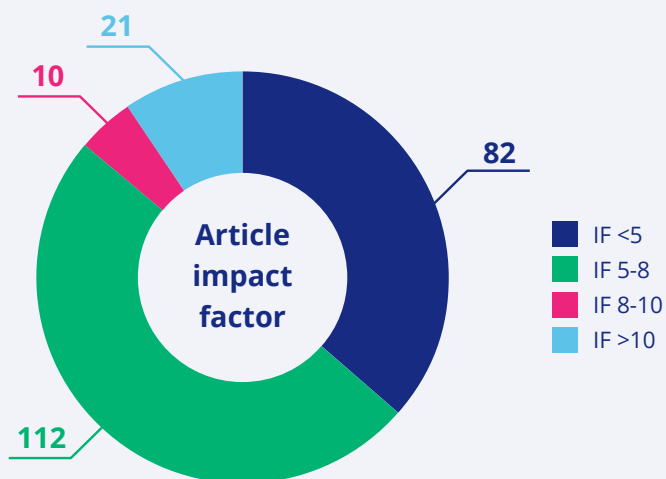
Selenium and selenoproteins in pregnant women

Laboratories: Toxicology, Biomarkers & Risk assessment – Pharmacy & Health Communication

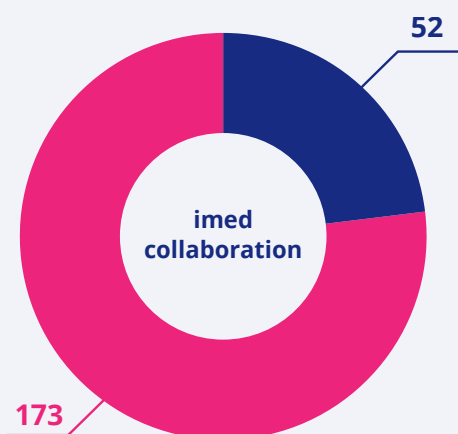
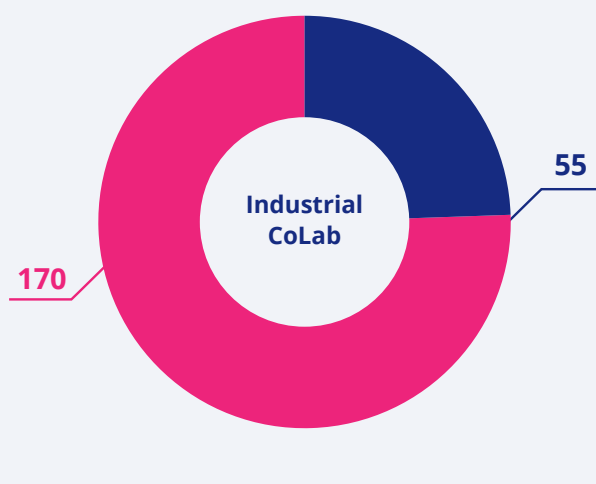
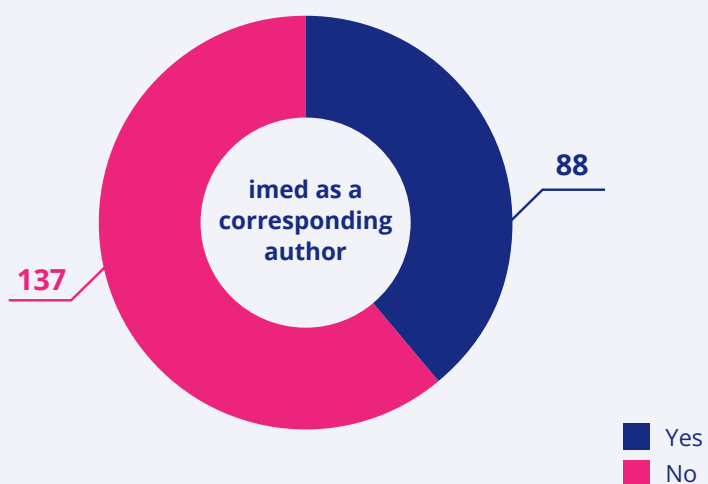
Scientific publications and actions

In 2022 imed maintained a good record of scientific contributions, with 225 articles published in Journal Citation Reports (JCR) referenced Journals. These 175 research papers and 50 reviews are a main output of the institute recently created research Hubs. 62% of these articles are a contribute from the Scientific Hub, 14% from the Technologic Hub and 24% from the translational Hub. 61% of imed JCR articles were published in journals indexed in the first quartile (Q1) and, more importantly, 9% in the first decile (D1) of their respective thematic areas of the Web of Science database (WoS). 39% of all articles have imed scientists as corresponding authors and 24% result from collaborative efforts of imed laboratories.





Furthermore, imed researchers achieved a sharp increase in the number of publications in top-ranked journals namely 21 papers with IF>10. It is very important to note that many of the publications in top journals are the result of research lead by imed researchers, which demonstrates that imed PIs can themselves be highly competitive.



Research highlights

imed's research program aims at discovering molecules, mechanisms and technologies that can be translated into breakthrough healthcare solutions. Our research methodology combines the expertise of disciplines across the fields of chemistry, biology, and pharmaceutical sciences to tackle key scientific questions in health sciences. The institute capacities cover a wide range of research activities that support our **Scientific, Technological and Translational Hubs**.

Scientific Hub

Within the Scientific Hub, we integrate chemistry, biology, and pharmaceutical sciences to develop new tools and techniques to prevent, detect and treat cancer, neurodegenerative, metabolic and infectious diseases.

Selected publications from the Scientific Hub

RIPK3 dampens mitochondrial bioenergetics and lipid droplet dynamics in metabolic liver disease

Hepatology 2023, 77, 1319

<https://doi.org/10.1002/hep.32756>

Laboratory: Cell Function and Therapeutic

Research area: Metabolic diseases

Chemoproteomics-Enabled Identification of 4-Oxo- β -Lactams as Inhibitors of Dipeptidyl Peptidases 8 and 9

Angew. Chem.Int. Ed. 2022, 61, e2022104

<https://doi.org/10.1002/anie.202210498>

Laboratory: Medicinal Chemistry

Research area: Oncology

A phylogenomic approach for the analysis of colistin resistance-associated genes in *Klebsiella pneumoniae*, its mutational diversity and implications for phenotypic resistance

Int. J. of Antimicrobial Agents 2022, 59, 106581

<https://doi.org/10.1016/j.ijantimicag.2022.106581>

Laboratory: Bacterial Pathogenomics and Drug Resistance

Research area: Infectious Diseases

Therapeutic targeting of PD-1/PD-L1 blockade by novel small-molecule inhibitors recruits cytotoxic T cells into solid tumor microenvironment

J. Immunother Cancer 2022, 10, e004695

<https://doi.org/10.1136/jitc-2022-004695>

Laboratory: Drug Delivery & Immunoengineering

Research area: Oncology

Long-Term and Low-Level Envelope C2V3 Stimulation by Highly Diverse Virus Isolates Leads to Frequent Development of Broad and Elite Antibody Neutralization in HIV-1-Infected Individuals

Microbiology Spectrum 2022, 10, e0163422

<https://doi.org/10.1128/spectrum.01634-22>

Laboratory: HIV Evolution, Epidemiology and prevention

Research area: Infectious Diseases

Technological Hub

Within the Technological Hub, we are highly engaged in advancing our scientific knowledge into innovative chemical, biotechnological and pharmaceutical technologies that may lead to breakthrough healthcare solutions.

Selected publications from the Technological Hub

3D-MSCs A151 ODN-loaded exosomes are immunomodulatory and reveal a proteomic cargo that sustains wound resolution

Journal of Advanced Research 2022, 41, 113

<https://doi.org/10.1016/j.jare.2022.01.013>

Laboratory: Advanced Cell Models for Predictive Toxicology & Cell-based Therapies

Research area: Emerging Technologies

A direct Diels-Alder reaction of chitin derived 3-acetamido-5-acetylfuran

Green Chem. 2022, 24, 7131

<https://doi.org/10.1039/d2gc00253a>

Laboratory: Bioorganic Chemistry

Research area: Emerging technologies

Long-Term and Low-Level Envelope C2V3 Stimulation by Highly Diverse Virus Isolates Leads to Frequent Development of Broad and Elite Antibody Neutralization in HIV-1-Infected Individuals

Microbiology Spectrum 2022, 10, e0163422

<https://doi.org/10.1128/spectrum.01634-22>

Laboratory: HIV Evolution, Epidemiology and prevention

Research area: Infectious Diseases

Tandem Thio-Michael Addition/ Remote Lactone Activation of 5-Hydroxymethylfurfural-Derived δ -Lactone-Fused Cyclopentenones

ChemSusChem 2022, 15, e202102204

<https://doi.org/10.1002/cssc.202102204>

Laboratory: Bioorganic Chemistry

Research area: Emerging technologies

Discovery of MDM2-p53 and MDM4-p53 protein-protein interactions small molecule dual inhibitors

European J. of Med. Chem. 2022, 241, 114637

<https://doi.org/10.1016/j.ejmech.2022.114637>

Laboratory: Medicinal Organic Chemistry

Research area: Emerging technologies

Translational Hub

Within the Translational Hub we are deeply committed to advance pharmacotherapy innovation and access to it by people living with illness by developing disruptive translational research to benefit human health, by converging our fundamental science discoveries into applied research. This is driven by the joint efforts of our institute with multiple players within the Healthcare sector, including policy-makers, clinicians and allied healthcare professionals and people living with illness and their representative organizations and associations.

Selected publications from the Translational Hub

Preclinical validation of a new hybrid molecule loaded in liposomes for melanoma management

Biomedicine & Pharmacotherapy
2023, 157, 114021

<https://doi.org/10.1016/j.biopha.2022.114021>

Laboratory: Advanced Technologies for Drug Delivery

Research area: Evidence-based interventions

Neurotoxic Astrocytes Directly Converted from Sporadic and Familial ALS Patient Fibroblasts Reveal Signature Diversities and miR-146a Theragnostic Potential in Specific Subtypes

Cells 2022, 11, 1186

<https://doi.org/10.3390/cells11071186>

Laboratory: Neuroinflammation, Signaling and Neuroregeneration

Research area: Evidence-based interventions

Efficacy and safety of erythropoietin in a chronic model of Inflammatory Bowel Disease

Biomedicine & Pharmacotherapy
2022, 156, 113944

<https://doi.org/10.1016/j.biopha.2022.113944>

Laboratory: Systems Integration Pharmacology, Clinical & Regulatory Science

Research area: Evidence-based interventions

Selenium and Redox Enzyme Activity in Pregnant Women Exposed to Methylmercury

Antioxidants 2022, 11, 2291

<https://doi.org/10.3390/antiox11112291>

Laboratory: Pharmacy Practice & Health Communication

Research area: Evidence-based interventions

Formulation of spray dried enzymes for dry powder inhalers: An integrated methodology

Int. J. of Pharmaceutics 2022, 615, 121492

<https://doi.org/10.1016/j.ijpharm.2022.121492>

Laboratory: Metabolism, Genetics and Proteins in Health & Disease

Research area: Pharma Industry

imed scientists contributed in with 50 reviews and perspectives articles on the most advanced areas of research across the different imed hubs. The following list highlights some of these contributions.

Evaluation guidelines for machine learning tools in the chemical sciences

Nature Reviews Chemistry 2022, 6, 428

<https://doi.org/10.1038/s41570-022-00391-9>

Laboratory: Medicinal Chemistry

Research area: Emerging Technologies

Spatial localization of cathepsins: Implications in immune activation and resolution during infections

Front Immunol. 2022, 13, 955407

<https://doi.org/10.3389/fimmu.2022.955407>

Laboratory: Host-Pathogen Interactions

Research area: Infectious Diseases

Microglia states and nomenclature: A field at its crossroads

Neuron. 2022

<https://doi.org/10.1016/j.neuron.2022.10.020>

Laboratory: Neuroinflammation, signaling and neuroregeneration

Research area: Neurodegenerative disorders

Momordica balsamina: phytochemistry and pharmacological potential of a gifted species

Phytochemistry Reviews 2022, 21, 617

<https://doi.org/10.1007/s11101-022-09802-7>

Laboratory: Natural Products Chemistry

Research area: Oncology

Semi-continuous and continuous processes for enantiomeric separation

Green Chem. 2022, 24, 4328

<https://doi.org/10.1039/D1GC03668H>

Laboratory: Bioorganic Chemistry

Research area: Pharma Industry

Intellectual property

Intellectual property protection as patents is critical to fostering innovation and to build a strong alliance with the private sector. At imed we aim at translating our findings commercially valuable technologies and/or products. Therefore, in 2022 we filled 8 national and 11 international patent requests.

PT118237 – A Biomaterial with enhanced antimicrobial properties, its preparation method and use in a medical device or prosthesis for in vivo medical applications. Submitted 30/09/2022

Ana Bettencourt and co-workers

PT117765 - Fluvoxamine for treatment of psoriasis. Submitted 02/2022

Martins AMTBS, Ribeiro HMOM, Marto JM, Gonçalves LMD, Simões SID

PT118152 - One-pot method for the synthesis of 3-acetylamido-furfural from N-acetylglucosamine. Submitted 09/12/2022

Bruno M. F. Gonçalves, Rafael F. T. A. Gomes, Carlos A. M. Afonso

PT11728 (PT117644)
-1,2,4,5-Tetraoxane compounds, a drug delivery system based in said compounds useful in diagnosis and therapy, and methods thereof. Submitted 16/12/2021

Diogo Silva and co-workers

PT118236 - Nitrobenzamide compounds, methods and uses thereof. Pub. Date: 12/12/2022

Luis Filipe Vicente Constantino, João Pedro Almeida Pais, Tiago Alexandre Duarte Delgado, Olha Antoniuk, Raquel Martins Da Silva, Elsa Maria Ribeiro Dos Santos Anes, David Alexandre Rodrigues Pires

PT118234 - Benzoic acid derivatives, methods and uses thereof. 12/12/2022

Luis Filipe Vicente Constantino, João Pedro Almeida Pais, Tiago Alexandre Duarte Delgado, Olha Antoniuk, Elsa Maria Ribeiro Dos Santos Anes, David Alexandre Rodrigues Pires

PT118464 - Instituto Nacional de Propriedade Industrial (INPI). Compostos tioesteres, métodos de obtenção e seu uso.

Luis Filipe Vicente Constantino, João Pedro Almeida Pais, Olha Antoniuk, Duarte Manuel Moura da Silva Figueiredo Antunes, Tiago Alexandre Duarte Delgado, Elsa Maria Ribeiro Dos Santos Anes, David Alexandre Rodrigues Pires

EP4069305 - Nanostructured drug delivery system as a multifunctional platform for therapy. Submitted 12/10/2022

Vitorino CS, Pais AACC, Sousa JJ, Ferreira AC, Fortuna AC, Cova, TF, Nunes SC, Torres JD, Almeida AJ, Mendes MM, Gonçalves LMD

EP22199255. Nitrobenzamide compounds, methods and uses thereof. 12/12/202.

Luis Filipe Vicente Constantino, João Pedro Almeida Pais, Tiago Alexandre Duarte Delgado, Olha Antoniuk, Raquel Martins Da Silva, Elsa Maria Ribeiro Dos Santos Anes, David Alexandre Rodrigues Pires.

EP22199251. European Patent Office (EPO). Benzoic acid derivatives, methods and uses thereof. 12/12/2022

Luis Filipe Vicente Constantino, João Pedro Almeida Pais, Tiago Alexandre Duarte Delgado, Olha Antoniuk, Elsa Maria Ribeiro Dos Santos Anes, David Alexandre Rodrigues Pires

US20220387620 - Nanostructured drug delivery system as a multifunctional platform for therapy. Submitted 08/12/2022

Vitorino CS, Pais AACC, Sousa JJ, Ferreira AC, Fortuna AC, Cova, TF, Nunes SC, Torres JD, Almeida AJ, Mendes MM, Gonçalves LMD

PCT/IB2022/06210 - Drug delivery systems based on endoperoxides useful in diagnosis and therapy, and methods thereof, 2022

Diogo Silva and co-workers

PCT/IL/2022/050366 - Nanovaccines for treatment of viral diseases. Patent Application: US Provisional Patent Application No. 63/172,144. Submitted 8/04/2022

Satchi-Fainaro R, Florindo HF.

PCT/PT2023/050002 - Fluvoxamine for treatment of psoriasis, submitted 28/01/2022

Joana Marto and co-workers

PCT/IB2022/057408 - One-pot method for the synthesis of 3-acetylamido-furfural from N-acetylglucosamine. Submitted 09/12/2022

Bruno M. F. Gonçalves, Rafael F. T. A. Gomes, Carlos A. M. Afonso

PCT/IB2021/057430 - Air quality enhancement system based on fluid mechanics and integrated uv emission. Pub. Date: 17/02/2022; WO/2022/034530A1

Elsa Anes, and co-workers

WO/2022/175955 - Modulators of pd-l1/pd-1 interaction and uses thereof. Patent Application: US Provisional Patent Application No. 63/150,643. Filed on February 18, 2021. PCT/IL2022/050195 international filing date 18 February 2022. Publication date 25.08.2022,

Satchi-Fainaro R, Florindo HF, Guedes R, Acúrcio R

Book chapters

Book chapters are an important tool to organize and disclosed scientific information for a broad audience. Therefore, imed scientists participated in these efforts and in 2022 contributed with 13 book chapters in a wide range of important topics for the development of innovative medicines.

M. P. Guerreiro, I. B. Félix., J. Balsa, M. B. Carmo, M. A. Henriques, A. Cavaco, A. P. Cláudio. (2022) "Contribution of an intelligent virtual assistant to healthy ageing in adults with type 2 diabetes" in Research Anthology on Supporting Healthy Aging in a Digital Society, Ed. M. Khosrow-Pour, S. Clarke, M. E. Jennex, A-V. Anttiroiko, IGI Global. ISBN: 978-166845296-7.

M. Afonso, M. A. Brito MA (2022) "Tumor Cell Signaling Pathways" in Scholarly Community Encyclopaedia. Available online: <https://encyclopedia.pub/entry/24295>.

Faria-Silva AC, Mota AL, Costa AM, Silva AM, Ascenso A, Reis C, Marto J, Ribeiro HM, Carvalheiro M, Simões S. (2022) "Application of natural raw materials for development of cosmetics through nanotechnology" in: Mohd Setapar SH, Ahmad A, Jawaid M (eds) Nanotechnology for the Preparation of Cosmetics using Plant-based Extracts. Elsevier Science. Paperback ISBN: 9780128229675. Chapter 7, pp. 157-201.

Anjos I, Bettencourt A, Ribeiro, IAC (2022) "Antimicrobial biosurfactants towards the inhibition of biofilm formation" in: Federico Soria et al (eds) Urinary Stents. Springer Nature Switzerland AG. ISBN: 978-3-031-04483-0, 509991. Chapter 23.

Costa J, Portugal J, Neves C, Franco M, Alves N, Santos C, Bettencourt A (2022) "Structural characterization of a drug delivery system based on reline resins" in: Belinha et al (eds) Advances and Current Trends in Biomechanics. CRC Press. ISBN – 978-1-032-10806-3. 1st edition, pp. 308-312. doi: 10.1201/9781003217152-68.

Bettencourt A, Gonçalves L (2022) "Trends in the design and evaluation of polymeric nanocarriers: the in vitro nano-bio interactions" in: Louro H, Silva MJ (eds) Nanotoxicology in the safety assessment of nanomaterials. Advances in Experimental Medicine and Biology, Springer Nature Switzerland AG. eBook ISBN 978-3-030-88071-2. Doi: 10.1007/978-3-030-88071;

J. C. David, M. B. Afonso, C. M. P. Rodrigues (2022) "Metabolic alterations of hepatocellular cancer stem cells" in *Interdisciplinary Cancer Research*. Springer Cham. https://doi.org/10.1007/16833_2022_43

CMM Almeida (2022) "An Age-Old Problem: Sulfites in Meat Preparations" in *Advances in Chemistry Research*, Chapter 7". Nova Science Publishers, Volume 75, Edited by James C. Taylor, New York, 2022. ISBN: 979-8-88697-259-7

Silva R. F. M., Pogačnik L., Eds. *Dietary Polyphenols and Neuroprotection*. MDPI 2022. ISBN 978-3-0365-2883-0 (hardback); ISBN 978-3-0365-2882-3.

Vale, F. F., Tanoeiro, L., & Marques, A. T. "16S Genomics for Diagnosing Invasive Bacterial Infection" in *Encyclopedia of Infection and Immunity* (pp. 287–300), Ed. Nima Rezaei. Elsevier 2022. ISBN: 9780323903035. <https://doi.org/10.1016/b978-0-12-818731-9.00213-5>

A.C. Faria-Silva, A. Mota, A.M. Costa, A.M. Silva, A. Ascenso, C. Reis, J. Marto, H.M. Ribeiro, M. Carvalheiro, S. Simões "Application of natural raw materials for development of cosmetics through nanotechnology" in *Micro and Nano Technologies, Nanotechnology for the Preparation of Cosmetics Using Plant-Based Extracts*, Setapar, S. et al. (eds.), Elsevier 2022. ISBN: 9780128229675

M. H. Ribeiro, S. L. Martins "Bioencapsulation of Proteins in Therapeutics" in *Micro and Nano Technologies, Smart Nanomaterials for Bioencapsulation*, Ed. G. R. Castro, A. Kumar, T. A. Nguyen, S. Sharma, R. Gupta, Elsevier 2022. ISBN: 9780323912297. DOI: 10.1016/B978-0-323-91229-7.00005-2

M. H. Ribeiro, E. Fahr, S. Lopes "From Glycolipids Biosynthesis to Biological Activity Toward Therapeutic Application" in *Biomolecules from Natural Sources: Advances and Applications*, Ed. V. K. Gupta, S. D. Sarker, M. Sharma, M. Elida Pirovani, Z. Usmani, C. Jayabaskaran, John Wiley & Sons. 2022. ISBN: 9781119769576. DOI: 10.1002/9781119769576

Internationalization

Addressing current health problems requires a multidisciplinary approach which often implies the constitution of highly collaborative international teams. imed researchers have demonstrated their commitment with internationalization, both in funding and publications.

International collaborations

Over the year imed researchers have established a strong network of collaborations with prestigious international institutions. The following list highlights some of the international institutions that had active collaboration with imed scientist throughout 2022.

Cambridge University, UK
University of Oxford, UK
Max Plank Institute for Polymer Science, Germany
University of Vienna, Austria
Chimie Paristech, France
CIC bioGUNE-Ciberehd, Spain
Finland Helsinki Institute of Life Science (HiLIFE), Finland
Infitiny-INSERM, France
Karolinska Institutet, Sweden
Medical University Lodz, Poland
University of Lausanne, Swiss
University of Michigan, USA
Stanford University, USA
Penn State University, USA
Weizmann Institute of Science, Israel

Participation in international projects

LiVERRip - RIPK3 biology and targeting in metabolic liver disease

"la Caixa" Banking Foundation (HR21-00793)

PI: Cecilia Rodrigues

EnzIL - Biofriendly Decontamination of Chemical Warfare Agents

SPS-Nato (SPS G5713)

PI: Carlos A. M. Afonso

Biomass4Synthons - Straightening training, research and innovation capacities in the valorization of bio-renewable resource

H2020 (GA 951996)

PI: Carlos A. M. Afonso

Rifabutin liposomes: a novel nanotechnological strategy for effective treatment of systemic methicilin-resistant staphylococcus aureus infections

Phospholipid Research Center, Heidelberg, Germany (MMG-2021-092/1-1)

PI: Manuela Gaspar

DRUGS4ALS - Targeting TDP-43 with protein kinase inhibitors: a effective and measurable therapy for ALS

"la Caixa" Banking Foundation (HR21-00931)

PI: Dora Brites

BREAST-BRAIN-N-BBB - Protecting the brain from metastatic breast cancer

"la Caixa" Banking Foundation (HR21-00605)

PI: João B. Gonçalves

Rifabutin liposomes: a novel nanotechnological strategy for effective treatment of systemic methicilin-resistant staphylococcus aureus infections

Phospholipid Research Center, Heidelberg, Germany (MMG-2021-092/1-1)

PI: M. Manuela Gaspar

Participation in international networks

imed scientists participate in an extensive number of international networks that strength transnational collaboration with the objective of addressing important scientific problems. The following list highlights some of the networks that include imed scientists in 2022.

EU-OPENSREEN

In 2022, imed became a partner site of the EU-openscreen, which is the most extensive European high-performance screening network. This network collaboratively develops novel molecular tool compounds and early therapeutic candidate molecules together with external users from various disciplines of the life sciences.

VectorB2B

imed become a founding member of VectorB2B that aims provide services to drug development programs via CDMO/CRO integrated services. This is a non-profit association that resulted from the shared initiative of seven entities: iMed.Lisboa - Faculty of Pharmacy, University of Lisbon, Faculty of Medicine, University of Lisbon, Faculty of Veterinary Medicine, University of Lisbon, University of Coimbra, Medinfar, BeVaG and TechnoPhage. These shareholders are a strong and complementary set of academic partners and biotech companies renowned in the health sector in Portugal. Together, they form a robust asset of knowledge and innovation, particularly in the domain of biological therapeutics, across the whole chain of development with focus on drug discovery, toxicology, chemistry manufacturing and controls (CMC) and CRO.

Marie Skłodowska-Curie Innovative Training Networks (MSCA ITN)

HORIZON-MSCA-2021-DN-01 — MSCA Doctoral Networks 2021. Targeting Circadian Clock Dysfunction for Alzheimer's Disease (TClock4AD) (2022-2027). 101072895

imed: Rita Guedes

ONCOPROTOOLS - Protease-guided tumor targeting tools to revolutionize cancer diagnosis and treatment (MSCA Doctoral Network) 2022-2026

imed: Maria M. M. Santos

H2020 MSCA-ITN-ETN - FOIEGRAS - Bioenergetic remodeling in the pathophysiology and treatment of non-alcoholic fatty liver disease 2016-22

imed: Cecilia Rodrigues

H2020 MSCA-RISE 2016 - mitoFOIEGRAS - Non-invasive profiling of mitochondrial function in non-alcoholic fatty liver disease 2016-22

imed: Cecilia Rodrigues

European Innovative Medicines Initiative 2

EU H2020 IMI-RIA - Litmus - Liver Investigation: Testing Marker Utility in Steatohepatitis 2017-23

imed: Cecilia Rodrigues

European & Developing Countries Clinical Trials Partnership (EDCTP), EU

RIA2016MC-1615- LIFE study (Neonatal HIV early infant diagnosis (EID) versus standard of care EID – Long term Impact on inFant hEalth: a feasibility study of point-of care testing at birth versus at 6 weeks of age, on the uptake of ART and infant prophylaxis, and on rates of infant survival, morbidity and retention in care). 2018-2024

imed: Nuno Taveira, Rute Marcelino

European Cooperation in Science and Technology (COST) actions

CA 21147 - ENOTTA - European Network on Optimizing Treatment with Therapeutic Antibodies in chronic inflammatory diseases, 2022-2026

imed: Paulo Paixão

CA21108 - European Network for Skin Engineering and Modeling, 2022-2026

imed: Sandra Simões, Manuela Carvalheiro

CA20121 – BenBedPhar: Bench to bedside transition for pharmacological regulation of NRF2 in noncommunicable diseases, 2021-25

imed: Joana Miranda

CA19124 - Rethinking Packaging for Circular and Sustainable Food supply chains of the Future (CIRCUL-A-BILITY), 2021-25

imed: Ana F. Bettencourt

CA19144 - Venon: European Venom Network, 2020-24

imed: Joana Miranda

CA18117 - European network for Gynaecological Rare Cancer research: From Concept to Cure, 2019-23

imed: Maria Santos

CA 18127 - International Nucleome Consortium, 2019-23

imed: Maria Santos

CA18122 - European Cholangiocarcinoma Network, 2019-23

imed: Rui Castro, André Santos, André Simão, Vanda Marques, Marta Afonso, Cecília Rodrigues

CA16217 - ENIUS - European network of multidisciplinary research to improve the urinary stents, 2019-23

imed: Ana F. Bettencourt

CA18116 - Aniridia: networking to address an unmet medical, scientific, and societal challenge, 2019-23

imed: Susana Solá

CA 17104 - Multidrug Resistance in Cancer, 2018-22

imed: Maria Santos

CA17112 - Pro-Euro Dili Network: Prospective European Drug-Induced Liver Injury Network, 2018-22

imed: Joana Miranda

CA17104 - New diagnostic and therapeutic tools against multidrug resistant tumors, 2019-22

imed: Maria José U. Ferreira

CA19140 - Focused Ion Technology for Nanomaterials

imed: Catarina Reis

CA18125 - Advanced Engineering and Research of aeroGels for Environment and Life Sciences

imed: Catarina Reis

CA17140 - Nano2Clinic. Cancer Nanomedicine – from the Bench to the Bedside, 2018-2023

imed: Maria Manuela Gaspar

CA21154 - Translational control in Cancer European Network

imed: Graça Soveral

CA21145 - European Network for diagnosis and treatment of antibiotic-resistant bacterial infections

imed: Maria Santos

CA18127 - International Nucleome Consortium

imed: Alexandra Paulo

Other EU funded projects and networks

HORIZON-HLTH-2022-STAYHLTH-02-01 – Halt-ROIN- Halt-chRONic Inflammation: Discovering chronic inflammation biomarkers that define key stages in the Healthy-to-NASH (nonalcoholic steatohepatitis) transition to inform early prevention and treatment strategies 2022-2027

imed: Joana Miranda

Research and Innovation Framework Programme: CSA-LSP-101017408

H2020 - Planning the Future of Research & Innovation in the European University Alliance UNITE! - Open Science and Innovation 2020-23

imed: Maria H. Ribeiro

Erasmus+ KA2 – European University

Science with and for Society UNITE! 2019-2022

imed: Maria H. Ribeiro

Erasmus+ 2020-1-SE01-KA226-HE-092578

Erasmus+ JPROV project – Joint Programmes: Embedding Virtual Exchange 2021-2023

imed: Maria H. Ribeiro

The HEPCOVivac Registry - Immunological response in patients with liver disease vaccinated against COVID-19

imed: Rui Castro

Publication with international teams

28% of imed publications result from ongoing projects involving international collaborators. The following examples, reflect some of the outputs in 2022 of these collaborations.

Targeting NAE1-mediated protein hyper-NEDDylation halts cholangiocarcinogenesis and impacts on tumors-stroma crosstalk in experimental models

J Hepatol. 2022, 77, 177

With Instituto de Investigación Sanitaria Biodonostia, Italy, and others

<https://doi.org/10.1016/j.jhep.2022.02.007>

Laboratory: Liver Disease Diagnostics and Therapeutics

Research area: Oncology

Repeated out-of-Africa expansions of *Helicobacter pylori* driven by replacement of deleterious mutations

Nat Commun. 2022, 13, 6842

With the Hellenic Pasteur Institute, Athens, Greece and others

<https://doi.org/10.1038/s41467-022-34475-3>

Laboratory: Pathogen Genome Bioinformatics and Computational Biology

Research area: Infectious diseases

Cysteine-Assisted Click-Chemistry for Proximity-Driven, Site-Specific Acetylation of Histones

Angew. Chem.Int. Ed.2022,61, e2022085

With the University of Cambridge

<https://doi.org/10.1002/anie.202208543>

Laboratory: Chemical Biology

Research area: Emerging technologies

Discovery of XL01126: A Potent, Fast, Cooperative, Selective, Orally Bioavailable, and Blood-Brain Barrier Penetrant PROTAC Degradator of Leucine-Rich Repeat Kinase 2

J. Am. Chem. Soc. 2022, 37, 16930

With the University of Dundee, United Kingdom

<https://doi.org/10.1073/pnas.2206327119>

Laboratory: Medicinal Chemistry

Research area: Neurodegenerative diseases

Brain Endothelial STING1 Activation by Plasmodium-Sequestered Heme Promotes Cerebral Malaria via Type I IFN Response

Proc Natl Acad Sci USA 2022, 119, e2206327119

With the Helmholtz Centre for Infection Research and the Hannover Medical School, 30625 Hannover, Germany

<https://doi.org/10.1073/pnas.2206327119>

Laboratory: Computational Medicinal Chemistry

Research area: Infectious diseases

imed Joint Seminars

Following the success of the Joint Seminars series initiated in 2021 and organized with the Universidade Federal do Rio de Janeiro and the Max Plank Institute for Polymer Science, in 2022 we organized a Joint Seminar with CIQUS of the University of Santiago de Compostela.

imed-CICUS joint seminars

May 2022

Protein engineering and synthetic biology towards the development of new biodrugs

Prof. João Gonçalves, iMed.Ulisboa Pharmacy Faculty, Universidade de Lisboa

Merging Metal Catalysis with Chemical Biology

Prof. Jose Luis Mascareñas, CIQUS in the University of Santiago de Compostela

Dendritic Nanostructures for Biomedical Applications

Prof. Eduardo Fernandez-Megía, CIQUS in the University of Santiago de Compostela

Active Nanomaterials for Live Cell Applications

Dr. Pablo del Pino, CIQUS in the University of Santiago de Compostela

6. Leadership & Recognition

Participation in national & international institutions

Prizes and recognitions

Participation in national & international institutions

imed scientist have been actively involved in the governing bodies of national and international institutions. The following list highlights some of these activities.

National

Cecília Rodrigues

Univerisidade de Lisboa Vice-Rector for research, inovation and development

<https://www.ulisboa.pt/membro-equipa/cecilia-maria-pereira-rodrigues>

Graça Soveral

President of the Portuguese Biochemistry Society, 2018-22

<https://www.spb.pt/Governance.html>

João A. Lopes

President of the Sociedade Portuguesa de Ciências Farmacêuticas (SPCF) and President of the Analytical Chemistry Division of the Portuguese Chemistry Society (SPQ)

<http://socportcienfarm.weebly.com>

<https://www.spq.pt/associates/divisions>

Pedro Gois

General secretary (adjunct) of the Portuguese Chemical Society

<https://www.spq.pt/>

Adelaide Fernandes

Member of the Executive Committee of Portuguese Glial Network

<https://redegial.weebly.com/about.html>

Afonso Cavaco

Governing body of the Portuguese Society for Clinical Communication in Health Care

<https://sp3cs.org/>

Maria Alexandra Brito

Member of the Fiscal Council of the Portuguese Anatomical Society

<https://sociedadeanatomica.pt/sap-aap/corpos-sociais/>

António J. Almeida

Member of the steering committee of the National Laboratory for Medicines, representing the Ministry of Science, Technology and Higher Education

<https://lm.exercito.pt>

Maria Manuela Gaspar

Presidente da Mesa de Assembleia da Sociedade Portuguesa Ciências em Animais de Laboratório

<https://www.spcal.pt/en/page/8>

Joana Miranda

President of the Fiscal council of Portuguese Society of Pharmacology (SPF) and Coordinator of the Portuguese Register of Toxicologists (ERT)

<https://pttoxicologyregister.webs.com>

<http://www.spfarmacologia.pt/index.php/a-spf/orgaos-sociais>

Dora Brites

Member of the Coordinator Council and Executive Director of Mind-Brain College

<https://colegiomento-cerebro.ulisboa.pt/>

Founder and Member of the Executive Committee, Rede Glial Portuguesa, Portugal

<https://redegial.weebly.com/>

José Miguel Azevedo Pereira

Direction board member of the Portuguese Society for Virology

<https://fems-microbiology.org/member-societies/portuguese-society-microbiology-spm/>

Maria José U. Ferreira

Vice-president of executive committee of the Phytochemical Society of Europe

<https://new.phytochemicalsociety.org/pse-committee-2020/>

Isabel Rivera

President of the General Assembly of Sociedade Portuguesa de Doenças Metabólicas

<https://www.spdm.org.pt/>

Paula Leandro

President of the Supervisory Board of Sociedade Portuguesa de Doenças Metabólicas

<https://www.spdm.org.pt/>

International

Rui Moreira

President and member of the executive commission of the European Federation for Medicinal Chemistry and Chemical Biology

<https://www.efmc.info/>

Cecília Rodrigues

Associate editor, Hepatology journal 2021-24

Função desempenhada na organização: Associate editor

<https://aasldpubs.onlinelibrary.wiley.com/hub/journal/15273350/editorial-board/editorial-board>

Cecília Rodrigues

Executive editor, Journal of Physiology and Biochemistry 2020-2024

<https://aasldpubs.onlinelibrary.wiley.com/hub/journal/15273350/editorial-board/editorial-board>

Filipa Alves da Costa

Executive Committee Board Member, International Society for Medication Adherence (ESPACOMP)

<https://www.espacomp.eu/>

Filipa Alves da Costa

Vice-President, Social and Administrative Pharmacy Section, International Pharmaceutical Federation

<https://www.fip.org/>

Helena F. Florindo

Chair: Controlled Release Society – Focus Group Nanomedicine and Nanoscale delivery and President, Spanish-Portuguese Local Chapter of the Controlled Release Society

<https://www.controlledreleasesociety.org/focus-groups/nanomedicine-and-nanoscale-delivery-nnd>

<https://www.splc-crs.org/about-us/board>

Joana Miranda

Chair of the Communication Subcommittee of the European Society of Toxicology (EUROTOX)

<https://www.eurotox.com>

Rita Guedes

Coordinator member Paul Ehrlich MedChem Euro-PhD Network

<http://www.pehrlichmedchem.eu/>

Bruno Sepodes

Vice-Chair of the Committee or Human Medicinal Products (CHMP) European Medicines Agency

<https://www.ema.europa.eu/en/committees/chmp/members>

Co-Chair of the Emergency Task Force (ETF)

European Medicines Agency

https://www.ema.europa.eu/en/documents/other/composition-emergency-task-force-etf-therapeutic-response-covid-19-monkeypox-public-health_en.pdf

Beatriz Silva Lima

Member of Advisory Board of AICIB - Agency for Clinical Research and Biomedical Innovation

<https://aicib.pt/en/inicio-aicib-english-2/>

Rui Castro

European Medicines Agency (EMA) Healthcare Professionals' Working Party (HCPWP) UEG representative member

<https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/healthcare-professionals-working-party>

Maria M. M. Santos

Member of the International Advisory Board of ChemMedChem (Wiley).

<https://chemistry-europe.onlinelibrary.wiley.com/journal/18607187>

Alexandra Paulo

Member of Editorial Board of Scientific Reports

<https://www.nature.com/srep/about/editors>

Prizes & recognitions

imed scientists have been awarded several distinctions for that scientific and social activities. The following list highlights some of these awards.

Cecília Rodrigues

Sir Hans Krebs medal

Federation of European Biochemistry Societies (FEBS), 2022

<https://www.febs.org/other-activities/prizes/febs-medals/>

Pedro Gois

Nominated as a Pioneering Investigator

Chemical Communications of the Royal Society of Chemistry

<https://pubs.rsc.org/en/journals/articlecollectionlanding?sercode=cc&themeid=112a127b-716f-49bc-9582-cffb7e2820aa>

Dora Brites

Medal of Honor - Ordem dos Farmacêuticos

<https://ordemfarmaceuticos.pt/pt/noticias/cinco-novos-medalhados-de-honra/>

Helena Rebelo de Andrade**Praise from the Directorate-General of Health**

Issued by the Director of the Department of Quality in Health, 5th September 2022

Contribution to evidence-based health decision support for the promotion of adequate, safe, humanised and person-centred health care throughout the health system

<https://www.dgs.pt/>

Helena F. Florindo

International Teaching Award. "New English Course" Nanotechnology for Cancer Immunotherapy. As part of the Sackler Faculty of Medicine School of Graduate Studies, Tel Aviv University, Israel.

<https://english.tau.ac.il/>

Joana Marques Marto

Menção Honrosa do Prémio "Prof. Doutor Aluísio Marques Leal – Investigação e Inovação em Farmácia Clínica"

Associação Portuguesa de Farmacêuticos Hospitalares, 2022

<https://www.apfh.pt/>

António J. Almeida, Catarina P. Reis, Cecília Rodrigues, Joana Marques Marto

World's Top 2% Scientists - Updated science-wide author databases of standardized citation indicators, J. Baas, K. Boyack e J. P.A. Ioannidis, University of Stanford, 2022.

<https://elsevier.digitalcommonsdata.com/datasets/btchxktzyw/5>

Ana Rita Garcia**Fulbright Fellowship**

<https://www.fulbright.pt/fulbrighters/bolseiros/ano-academico-2022-2023/ana-rita-garcia/>

Filipa Alves da Costa

Research Fellow, for continuing excellence in Clinical Pharmacy research and practice and long-lasting contributions to the European Society of Clinical Pharmacy

European Society of Clinical Pharmacy, 2022

<https://escpweb.org/>

Margarida Espadinha**EFMC-YMCS PUBLIC CHOICE AWARD**

– Design, Synthesis and Biological Evaluation of Novel p53 Activators by Targeting p53 Protein-Protein Interactions, EFMC-YMCS 2022, sponsored by Roche

Best PhD Thesis in Medicinal Chemistry 2021 Award, Medicinal Chemistry Division of the Portuguese Chemical Society

<https://www.efmc.info/>

<https://www.spq.pt/>

Inês Bártoło, Paloma Gonçalves and Nuno Taveira

First prize, R2 Value 2022 Edition Course Pitch session, NOVAID, Faculty of Science and Technology, UNOVA, Portugal

<https://www.novaidfct.pt/r2value/>



7. Communication, Dissemination & Outreach

Communication & dissemination of results

Outreach activities

Other selected activities

imed on the news

The European Charter for Researchers clearly states that researchers have the duty to actively engage in the communication of science to the public. imed is deeply committed with this goal and we have actively engaged in different communication, dissemination, and public outreach activities during 2022.

Communication & dissemination of results

Website and social media

imed website (<https://imed.ulisboa.pt/>) is our primary mechanism of communication with the public. The website is frequently updated with information about research areas, scientific production, research groups, facilities, job offers, training programs and comprehensive information about the institute's activities and research outputs. The institute communication is further complemented with activity on social networks like Facebook, LinkedIn, Twitter.

Conferences

imed communicates with the scientific community mainly by publishing in peer-reviewed journals, though, scientific results are also disseminated through the participation in international conferences as well as local scientific meetings. In 2022 imed scientists delivered more than 160 oral communications in national and international meetings.

Imed post-graduate students (iPsc)

The institute post-graduate students are also actively contributing to the institute communication and dissemination of results namely by organizing the 14th iMed.ULisboa Meeting on 26 and 27th of June 2022. This event counted with the active participation of over 100 post-graduate students which contributed with oral and poster presentations, and the following plenary lectures:

Antibiotic mechanisms and resistance

Prof. Luiz Pedro Carvalho, The Francis Crick Institute, London UK

How science, health and economics can help Portugal

Nadim Habib, Nova School of Business and Economics, Lisboa Portugal (*imed SAB member*)

Outreach activities

imed aims to connect with the society by sharing the knowledge produced by us researchers with the public and by encouraging the venue of young students and scientific curious citizens to our labs to discover our most recent breakthroughs. In 2022, iMed participated in several outreach activities including “Brain awareness week-2022” created by the Dana Foundation, USA, which aims to raise awareness among the general public, particularly students, of the progress and benefit of brain study by lectures at High School and venue of students to iMed. Also, in close collaboration with CienciaViva imed participated in “Ciência Viva no Laboratório - Ocupação Científica de Jovens nas Férias”, where imed received 20 high school students in 10 different activities, with the main objective of opening the paths to convergence with the principles of promoting experimental science teaching and attracting scientific careers among secondary school students.

And also with the activity entitled “Era uma vez o medicamento...” during “Semana da Ciência e Tecnologia”, aiming to open Scientific Institutions and Universities to the general public in order to provide the population with opportunities for scientific observation and personal contact with specialists from different areas of knowledge. Furthermore, several iMed researchers that are also Professors at the FFULisboa have participated in the annual ULisboa outreach event for the high school students “O dia aberto da FFULisboa” and “Verão na ULisboa”, where the Pharmaceutical Sciences course from the FFULisboa is publicized.

Other selected activities

Sunset Skin Summit – 2ª Edição: Sustentabilidade no tratamento e cuidado da pele (2022)

26-27, October

Farmacêuticos “farmacêutico para além da arte da farmacêutica, a olhar o futuro”

November 2022 (Elsa Anes)

Semana Internacional do Cérebro 2022 - Os Neurocientistas vão às Escolas, Ciência Viva, “Explorando o Cérebro”; “Disfrutar das Neurociências na Escola”

March 10-14, 2022 (Adelaide Fernandes e Rui Silva)

“HIV, AIDS, diagnosis and treatment”, Emídio Navarro Secondary School, Almada

May 2022, (JM Azevedo Pereira)

Programa Cientificamente Provável Atividade “Era uma vez o medicamento”, FFUL

May 20, 2022. (Adelaide Fernandes, Ana Rita Vaz, Ana Paula Francisco, Filipa Siopa, Maria de Jesus Rocha, Manuela Gaspar, Sandra Simões)

“As células estaminais na regeneração da pele - o elixir da juventude?” with the participation of 108 students from the secondary level

October 12, 2022 (Sergio Camões)

50 years celebration of Ordem dos

imed on the news

Sistema imunitário, um mecanismo de defesa que também envelhece, *Jornal Farmácia Distribuição* nº 359, 2022 (Elsa Anes).

Helena Florindo work on the development of a small molecule targeting PD-L1 immune suppression marker featured in the international press:

Radio International Paris interview

<https://www.rfi.fr/pt/programas/ciencia/20221030-cientistas-portuguesas-descobrem-mol%C3%A9cula-eficaz-no-combate-ao-cancro>

Drug target review website

https://www.drugtargetreview.com/news/104648/researchers-develop-a-small-molecule-that-makes-immunotherapy-available-to-all-cancer-patients/?utm_content=bufferd26dd&utm_medium=social&utm_source=linkedin.com&utm_campaign=buffer

Scitechdaily website

<https://scitechdaily.com/small-molecule-developed-that-makes-immunotherapy-available-to-all-cancer-patients/>



8. Entrepreneurial activities

At imed we create scientific knowledge and technologies that we aim to translate to society in the form of breakthrough healthcare solutions, therefore we are actively engage in entrepreneurial activities, the following list highlights some companies founded by imed scientists.

Nuno Taveira

Founder and Chief Executive Officer (CEO) of BSL Pharmaceuticals, Lda. <https://www.linkedin.com/in/nuno-taveira-7a905b106/?originalSubdomain=pt>

Tiago Rodrigues

Founder of TargTex, Lda. <https://targtex.com/>

João Gonçalves

Founder of Technophage SA
<http://technophage.pt/>

João Gonçalves

Founder of T-oncology AG
<http://technophage.pt/technophage-s-a-announces-spin-off-of-t-oncology-ag/>

9. imed in society

COVID response

Metabolism disorders

imed is deeply committed to work with the community and providing services that may help patients and public health services.

COVID response

Early in the pandemic, efforts at iMed.Ulisboa proved the utility of research labs performing large, wide-scale testing in their communities. Our research labs applied the expertise and capabilities to test more than 70 000 people for COVID-19. As nonmedical academic scientists we provided the scientific and technological knowledge that supported public health and helped to develop diagnostic kits, vaccines, and therapeutics. Our effort during the pandemic supported with talent, technology, determination, partnerships, and logistical capability to serve the community and state during a crisis. We were able to implement and use our scientific equipment for Covid testing and promoted multiple interactions with health and public organizations to provide massive testing.

Health research systems were already under strain when COVID-19 brought significant challenges, and at imed we wanted to show that health research systems can be more visible and significant. In this context, our research efforts at iMed.Ulisboa were able to help in: a) manage and control the epidemic, b) prevent future epidemics, c) be more prepared in the event of the outbreak of such crises. At iMed.Ulisboa we realized that to control and manage the COVID-19 epidemic, and to effectively prevent and respond to future epidemics there are knowledge gaps that need to be addressed in various fields, and a wide range of research in basic sciences, clinical sciences, public health sciences, implementation science, and policy and system studies is needed to fill these gaps.

Metabolism disorders

The Metabolism and Genetics Laboratory (MetGen Lab) has been involved in the study of Inborn Metabolic Disorders of intermediary metabolism working in close collaboration with clinicians and pediatric units of central hospitals (e.g. Santa Maria and D. Estefânia). The MetGen Lab performed biochemical and molecular diagnosis (metabolic profiles, enzymatic activities, DNA analysis) as well as treatment follow-up (disease biomarkers monitoring) on ≈2600 patients/year. The MetGen Lab is also involved in clinical-based studies supported by pharmaceutical industry such as BioMarin Pharmaceutical”.

Liver Dysfunction and Brain Biopathology lab

Our scientific activity began in 1976 following the Hospital D. Estefânia request, to identify jaundiced newborns and hereditary hyperbilirubinemias (e.g., Gilbert and Crigler Najjar syndromes) at risk of bilirubin encephalopathy (kernicterus). This led us to analyze the serum (Bilirubin Metabolic Study) and bile bilirubin fractions, and to advance in the mechanisms of bilirubin-induced neurotoxicity/glial cell immunostimulation. Later (1980), we extended our evaluations to the differential diagnosis of jaundice-associated cholestasis, including the intrahepatic cholestasis of pregnancy, by assessing the Serum Bile Acid Profile. This determination has been crucial in the prognosis of cholestatic liver diseases and efficacy of therapeutic options, such as the ursodeoxycholic acid oral administration. We are unique in performing such metabolic studies in the country, working close to clinicians at public hospitals and private clinics from all Continental and Autonomous Regions of Portugal. Our goal is to improve Public Health by responding to increasing demands and creating new knowledge in Liver-Brain axis failure.

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