Annual Report

2021

imed
Research Institute
for Medicines

No Breakthrough
is too small.

2020
— 2021

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No break—through is too small.*

ANNUAL REPORT 2021

Contents

Foreword

message from the coordinator

JOÃO GONÇALVES
Coordinator, imed

iMed.ULisboa is firmly committed to develop high-quality research that will impact human health and society. Innovative ideas and powerful

technologies are now fuelling breakthroughs in mechanistic biology and medicinal chemistry, which could potentially enable more effective searches of molecules and targets and accelerate success in drug discovery and development, thus tackling complexities underpinning disease prevention, diagnosis and treatment. However, such approaches also raise considerable conceptual, technical and organizational challenges. iMed.ULisboa aims to identify the approaches and technologies that could be implemented robustly, and critically analyse opportunities and challenges for their widespread application. We specifically build on enabling scientific platforms that enhance research inside and outside, providing opportunities to share our science, encouraging collaboration with academic and industry partners, and attracting emerging talents and young students. We value an environment that nurtures and rewards innovative research activities in translational science and technology dedicated to improving human health.

The translation of discoveries to the clinics is speeding with efforts to find more precise ways of managing disease. Since January 2017, iMed.ULisboa leads the POINT4PAC consortium, involving academia, biotech and pharma industry, hospitals, patients and medical associations, supported by European structural funds. POINT4PAC will develop a platform for discovery and early development of innovative technologies, therapies, and solutions for treatment, prevention and control of cancer. We combine complementary state-of-the art resources in phenotypic high-throughput screening and medicinal chemistry, with antibody-drug conjugate technology and nanoparticle-engineered formula- tion for delivery to the right target in the right cell. By involving a large team of researchers at iMed. ULisboa, including young PIs and newly recruited postdoctoral scientists, this project is exemplar for future inclusive multidisciplinarity and leadership.

In 2018, with the new evaluation exercise of the research units ongoing, the individual and institutional support for scientific employment, and the collaborative laboratories to be implemented, iMed.ULisboa looks forward to contributing with coherence, planning and to the extent possible, stability to build an internationally competitive research community.

On behalf of iMed.ULisboa, I would like to thank everyone who has collaborated with us throughout this year. Despite the challenging times, iMed. ULisboa has diversified funding sources and gained visibility in academia, industry and society. We have become a driving force behind interdisciplinary drug discovery and development efforts in Portugal and are seen as attractive partners, thriving for major gains in medical and health sciences, research and training. We look forward to continuing joining forces together in 2018!

1. Introducing imed

Organization and Structure Executive Board

Scientific Advisory Board Researchers

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Organization and Structure

Executive Board

This governing body is led by the coordinator and includes as members leaders of the four strategic program areas; ensures overall development and implementation of coordinated initiatives and activities from the strategic plan.

CECÍLIA M. P. RODRIGUES
Coordinator

BEATRIZ SILVA LIMA
Drug Development Program Leader

JOÃO GONÇALVES
Drug Discovery Program Leader

FERNANDO FERNANDEZ-LLIMOS
Drug Usage Program Leader

RUI MOREIRA
Drug Design Program Leader

Scientific Advisory Board

Independent eminent international scientists ensure that our strategic direction is in the best interest of science and society.

STEPHEN CADDICK
UCL, United Kingdom

ANTONIO ZORZANO
University of Barcelona, Spain

MARK MCALLISTER
Pfizer, United Kingdom

Researchers & Students

4
program groups

14
research groups

288
researchers

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2.
Facts and Numbers

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International Projects

Marie Sklodowska-Curie Innovative Training Networks

A training network for the chemical site-selective modification of proteins: Preparation of the next-generation of therapeutic chemical- ly-defined protein conjugates

Participant: Pedro Góis

Marie Sklodowska-Curie Innovative Training Networks

Bioenergetic remodeling in the pathophysiology and treatment of non-alcoholic fatty liver disease

Participant: Cecília Rodrigues

Marie Sklodowska-Curie Research and Innovation Staff Exchange

Non-invasive profiling of mitochondrial function in NAFLD

Participant: Cecília Rodrigues

Marie Sklodowska-Curie Innovative Training Networks

Bioenergetic remodeling in the pathophysiology and treatment of non-alcoholic fatty liver disease

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Marie Sklodowska-Curie Research and Innovation Staff Exchange

Non-invasive profiling of mitochondrial function in NAFLD

Participant: Cecília Rodrigues

Intercept Pharmaceuticals, Inc.

Targeting the NAFLD-HCC continuum with dual FXR/TGR5 agonists and miRNAs

Principal Investigator: Rui Castro

ERANet-LAC Latin America Caribbean and European Union

Integrated valorization of lignocellulosic agroindustrial waste to furan based building blocks

Participant: Carlos Afonso

European Society of Clinical Microbiology and Infectious Diseases

Transcriptomic profiling of clinical Mycobacterium tuberculosis strains: global transcriptomic response towards drug exposure and meta- bolic shift towards latency

Principal Investigator: João Perdigão

ERANet JPco-fuND EU Joint Programme|Neurodegenerative Disease Research

Generation of Improved cellular and animal models for identification of disease phenotype and new therapeutic targets of Alzheimer's Disease

Participant: Dora Brites

Marie Sklodowska-Curie Innovative Training Networks

A training network for the chemical site-selective modification of proteins: Preparation of the next-generation of therapeutic chemical- ly-defined protein conjugates

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Marie Sklodowska-Curie Research and Innovation Staff Exchange

Non-invasive profiling of mitochondrial function in NAFLD

Participant: Cecília Rodrigues

Research Scholars Program in Liver Diseases|Gilead Sciences

International Role of mitofusin 2 in NAFLD and targeting by miRNAs

Principal Investigator: Rui Castro

R&D Projects Joint Call|TÜBITAK

The use of exosomes derived from umbilical cord tissue mesenchymal stromal cells for the treatment of open cutaneous wounds (UCX®)

Principal Investigator: Joana Miranda

Intercept Pharmaceuticals, Inc.

Targeting the NAFLD-HCC continuum with dual FXR/TGR5 agonists and miRNAs

Principal Investigator: Rui Castro

ERANet-LAC Latin America Caribbean and European Union

Integrated valorization of lignocellulosic agroindustrial waste to furan based building blocks

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European Society of Clinical Microbiology and Infectious Diseases

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Participant: Dora Brites

3. Research Highlights

Drug Discovery

Cellular Function and Therapeutic Targeting Host-Pathogen

Interactions

Metabolism and Genetics

Molecular Microbiology and Biotechnology Neuron-Glia

Biology in Health and Disease

Drug Design

Bioorganic Chemistry Medicinal Chemistry Natural Products

Chemistry

Drug Development

Chemical Biology and Toxicology

BioNanoSciences - Drug Delivery and Immunotherapy

Nanostructured Systems for Overcoming Biological Barriers

Pharmacological and Regulatory Sciences

Drug Usage

HIV Evolution, Epidemiology and Prevention

Pharmacoepidemiology and Social Pharmacy

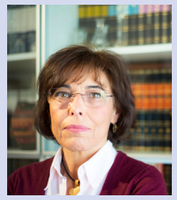
Translational Hub

JOÃO GONÇALVES
Programme Leader

Research Groups

CECÍLIA RODRIGUES
Cellular Function and Therapeutic Targeting

ELSA ANES
Host-Pathogen Interactions



PAULA LEANDRO
Metabolism and Genetics

JOÃO GONÇALVES
Molecular Microbiology and Biotechnology

DORA BRITES
Neuron Glia Biology in Health and Disease

The Drug Discovery Programme is a multidisciplinary effort that closely links research on cellular function, metabolism and genetics, with cancer, infectious diseases and neurological disorders. We are committed to spin innovative research on drug targets and biomarkers into therapeutic strategies, exploring their feasibility in preclinical models. The alliances with the Drug Design, Development and Usage Programmes at iMed.ULisboa are fundamental to raise pertinent scientific questions and offer unique opportunities to foster bench to bedside drug discovery in a highly collaborative environment. To incorporate iMed.ULisboa vision into the Drug Discovery, our broad strategic lines are:

1. Genetic, molecular and cellular research to find new therapeutic interventions in cancer and metabolic diseases.

We aim to an integrated view on cellular function and how it changes during disease. Genetic, cellular and metabolic approaches will identify key signalling and metabolic pathways that can be targeted with high-throughput drug screening and protein engineering and biochemistry, or that can give rise to better biomarkers of disease.

2. Neurobiology research to dissect new treatment strategies in neurodegenerative and age-related disorders.

The impact of neuron-glia-vascular interactions is of crucial value to provide new answers to neurodegenerative diseases. A variety of in vitro and in vivo systems are used to discover innovative strategies of understanding and ameliorating neurological disorders and aging.

3. Host-pathogen interaction to exploit infectious agents as a source of drug targets.

The molecular biology and epidemiology of mycobacteria, virus and phages aims to realise how these agents interact with host and how they explore their structural peculiarities to optimal replication. With this understanding we aim to develop novel anti- infective strategies and new biopharmaceutical drugs.

The Drug Discovery Programme drives a culture of technology transfer to hospitals, biotech and pharma industry. Funding for research is supported by competitive national and international sources both from public (H2020, IMI and FCT) and private institutions (Pharma and non-profit organizations) reaching more than 4 M€ in 2017 ongoing projects. As result, the track record during 2013-2017 shows also impactful publications and respectful international recognition of our science. Given the attractiveness of Drug Discovery areas to young scientists, ca. 40 PhD students finished their graduation during 2013- 2017 and equivalent numbers are currently enrolled in the PhD Programme in Pharmacy, based in FCT and Marie Currie funded training in Medicines and Pharmaceutical Innovation, Medical Biochemistry and Biophysics, and Advanced Integrated Microsystems. Specific scientific platforms provide access to state-of- the-art facilities capable of performing protein, cellular and animal studies at single and high-throughput assessment.

Cellular Function and Therapeutic Targeting

CECÍLIA M. P. RODRIGUES
Group Leader

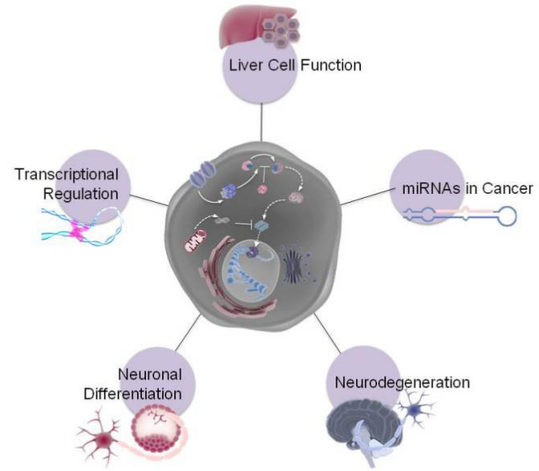
PhD (1996) in Pharmacy (Biochemistry), Universidade de Lisboa. Postdoctoral research at University of Minnesota, USA. Full Professor, Biochemistry and Human Biology, Faculdade de Farmácia UL.

Achievements

Hepatic fibrosis is the wound-healing response of the liver to many causes of chronic injury, of which non-alcoholic steatohepatitis (NASH) is the most common. Hepatocellular car- cinoma (HCC) is rising in incidence worldwide and is a major cause of liver-related death in patients with cirrhosis. The transition from benign steato- sis to NASH and HCC occurs through yet unclear mechanisms. A lack of tractable non-invasive biomarkers is hampering the diagnosis, risk strat- ification and monitoring of patients, with many remaining undiagnosed and presenting with advanced disease. We have recently profiled miR- NAs and the microbiome in murine and human tissues and identified several changes with dis ease. As disease progresses and cell death and inflammation settle, miR-21 increases, aggra- vating NASH and, eventually, promoting HCC. Our work in the field has been recognized by EU H2020 IMI2, funding the LITMUS consortium with the overarching aim to develop, robustly validate and advance towards regulatory qualification biomarkers that diagnose and risk stratify NAFLD/ NASH progression and fibrosis. We will specifi- cally work on developing consensus on preclinical models of NAFLD/NASH and then back-translate biomarkers for validation.

The lack of biomarkers has also hampered drug development and conduct of clinical trials. We have shown that miR-21 ablation in com- bination with FXR activation strongly impairs NASH development and should be regarded as a prospective therapeutic option for NAFLD. Interestingly, we have also shown that liver damage and RIPK3-dependent necroptosis are prevented in bile duct-ligated miR-21 KO mice, via specific targets. More recently, we found that both miR-21 and RIPK3 ablation prevent long- term inflammation, fibrosis, proliferation and resistance to cell death, and should entailing therapeutic potential. We have recently attracted funds to support collaborative development of precise therapies/technologies (EU COMPETE 2020 POINT4PAC; FCT; Intercept Pharma; Gilead), and European network training (ETN FOIE GRAS).

Consistent with the growing role that cell metabolism may play in neurodegeneration, we have used in vitro and in vivo experimental models and strategies to show that mitoprotective targeting attenuates neurodegeneration and influences lineage stem cell fate decision. We have also dissected the molecular mechanisms involved in restoration of brain cholesterol homeostasis as a therapeutic strategy to treat neurodegenerative disorders. Arising from our work, global coverage patents have been licensed, and partnerships have been established with AstraZeneca (UK), in phenotypic high throughput screening and with the biotech Brainvectis (France), in gene therapy.



Keywords

Molecular targets, Biomakers and Therapeutics. Signalling pathways of cell proliferation, differentiation and death. Cell systems, Murine models and human Biological samples. Liver, Gut and Brain diseases.

Selected References

Afonso MB, Rodrigues PM, Simão A, Gaspar M, Carvalho T, Nunes P, Banales J, Castro RE, Rodrigues CM. miRNA-21 is overexpressed in primary biliary cholangitis and contributes to liver injury and necroptosis in bile duct-ligated mice. Cell Death Differ. 2018; 25: 857-872.

Soares R, Ribeiro FF, Xapelli S, Genebra T, Ribeiro MF, Sebastião AM, Rodrigues CMP, Solá. Tauroursodeoxycholic acid enhances mitochondrial biogenesis, neural stem cell pool, and early neurogenesis in adult rats. Mol Neurobiol. 2018; 55: 3725-3738.

Rosa AI, Duarte-Silva S, Silva-Fernandes A, Nunes MJ, Neves Carvalho A, Rodrigues E, Gama MJ, Rodrigues CMP, Maciel P, Castro-Caldas M. Tauroursodeoxycholic acid improves motor symptoms in a mouse model of Parkinson's disease. Mol Neurobiol. 2018; 55: 9139-9155.

Mueller M, Castro RE, Thorell A, Marschall H-U, Auer N, Herac M, Rodrigues CM, Trauner M. Ursodeoxycholic acid: Effects on hepatic unfolded protein response, apoptosis and oxidative stress in morbidly obese patients. Liver Int. 2018; 38: 523-531.

Rodrigues PM, Afonso MB, Simão AL, Carvalho CC, Trindade A, Duarte A, Borralho PM, Machado MV, Cortez-Pinto H, Rodrigues CMP, Castro RE. miR-21 ablation and obeticholic acid ameliorate non-alcoholic steatohepatitis in mice.

Cell Death Dis. 2017; 8: e2748.

Technological Hub

Research Groups

PEDRO M. P. GÓIS
Bioorganic Chemistry

RUI MOREIRA
Medicinal Chemistry

MARIA J. U. FERREIRA
Natural Products Chemistry

RUI MOREIRA
Programme Leader

The Drug Design Programme offers a chemistry-centred platform oriented to the discovery of biologically active chemical entities that target specific proteins or nucleic acid structures, with the ultimate goal of optimizing their therapeutic properties and value. Working in concert with other groups at iMed.ULisboa, Drug Design researchers develop solutions for cancer, infectious diseases and neurological disorders. The broad strategic lines that intersect all Drug Design groups are:

1. Innovative chemistry for innovative drugs.

The development of bio-inspired and sustainable synthetic methodologies for the preparation of small molecule modulators of proteins identified as key therapeutic targets of important diseases is core to this programme, and one of the cornerstones of our technology transfer platform.

2. Tools for chemical biology, biotherapeutics and drug targeting.

We provide unique chemistry-led solutions to manipulate molecules in order to interrogate and intervene in biological systems. This includes the development of probes to decipher the complex machinery of the proteome of diseases and to identify targets of therapeutic value. Cell-targeting is also addressed, e.g. by developing synthetic methods to modify a broad range of proteins and to construct therapeutically useful bioconjugates, or by using prodrug chemistry to develop site- specific drug delivery systems.

3. Medicinal chemistry solutions for lead generation.

Our work focus on the druggability of protein and protein-protein interactions within multi-subunit protein complexes through innovative use of synergic computer aided drug design and synthetic approaches campaigns to identify new hits and optimize more effective leads that can modulate important cellular responses in cancer, infectious and neurodegenerative disorders, bringing hope to future cures.

4. Natural products for drug discovery.

Natural products remain an invaluable source of therapeutic agents. The Drug Design groups are committed in identifying novel chemotypes from natural sources and to develop new synthetic methods for the valorisation of natural resources.

Entrepreneurship is a hallmark of programme, with out-of-the-box solutions and methodologies contributing significantly to the patents portfolio of iMed.ULisboa. Training new generations of innovative scientists is also at the core of our mission. With stringent criteria of selection, we recruit the best students for the PhD Programme in Pharmacy, based in FCT and Marie Curie funded Medicinal Chemistry training.

From 2013 to 2017, 22 students successfully completed their thesis in this scientific area, while 35 are currently enrolled in PhD Programme in Pharmacy. The required state- of-the-art facilities are in place to perform high-level computational studies, chemical synthesis, isolation and purification of compounds from natural sources, production of protein conjugates, and preclinical ADME studies.

Medicinal Chemistry

RUI MOREIRA
Group Leader

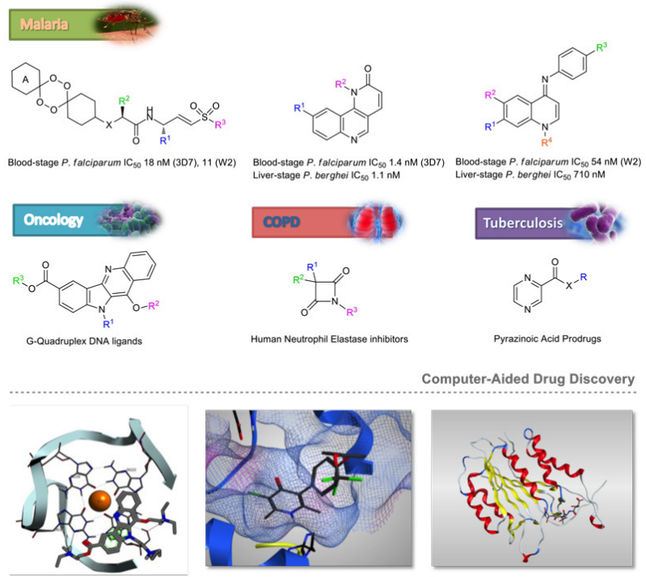
PhD (1991) in Pharmacy (Pharmaceutical Chemistry), Universidade de Lisboa. Full Professor, Pharmaceutical Chemistry and Therapeutics, Faculdade de Farmácia, Universidade de Lisboa.

Achievements

Multitargeting strategies for malaria drug discovery - Elimination of malaria has been set as one of the WHO's Sustainable Development Goals for 2030. This effort re- quires novel agents active against all stages of the parasite complex life-cycle, and preferably acting on underex- ploited targets. Our program focused on iden- tifying compounds with multistage antimalarial activity was one of the first to provide preclinical proof-of-concept that hybrid drugs with a mul- titarget profile can block the development of all forms of malaria parasites. The Indian Society of Chemists and Biologists recognized the contribu- tion of the hybrid- multi-stage concept to malaria elimination, nominating Moreira as Honorary Life Fellow in 2015. The hybrid approach has evolved to highly potent modular small molecules, and one chemotype that fulfils the target candidate profile criteria for targeting asexual parasites and hepatic schizonts and is now under evaluation by the Medicines for Malaria Venture (MMV).

Chemistry-led approaches to target cancer cells - Oncogenes and oncoproteins remain some of the few poorly druggable targets in cancer. Wild- type p53 is a tumor suppressor gene that is inac- tivated in most human cancers, either by nega- tive regulation or by mutation. Our group has been actively involved in the development of novel chemical families to reactivate the p53 pathway, and very promising compounds emerged as non-genotoxic, displaying potent in vivo anti- tu- mor activity with no apparent toxic side effects, repre- senting novel anticancer drug candidates in cancers where the p53 pathway is inactivated (patent). These findings have been recognized by the Portuguese Chemical Society, which awarded Santos with the prize of best young organic chem- ist in 2016, and by the Portuguese Association for Cancer Investigation, a patient association. Most recently, we suc- cessfully expanded the hybrid drug concept to cancer, by developing agents capable of targeting DNA and HDACs (epigene- tic regulation) for the treatment of glioblasto- ma (GBM), the most common and aggressive type of brain tumor in adults. Remarkably, these hybrids did not enhance the expression of drug resistance proteins, a major issue in the treatment of GBM.

Biological applications of activity-based probes (ABPs) - ABPs are tools with a reactive chemical group that covalent- ly interacts with the active site residues of mechanistically related enzymes and a tag that enables the detection and/ or enrich- ment of probe-labeled enzymes. The medicinal chemistry group has developed ABPs tailored for serine or cysteine hydrolases by appropriate modulation of the reac- tivity and molecular recog- nition structural features. This approach yielded not only low-molecular weight ABPs to identify enzymes that are biomarkers in disease (Fulbright award to Carvalho), but also novel chemical tools to inhibit poorly understood targets associated to neurodegenerative diseases.



Keywords

Medicinal chemistry; In silico drug discovery; Drug targeting; Target identification.

Selected References

Capela R, Magalhaes J, Miranda D, Machado M, Sanches-Vaz M, Albuquerque IS, Sharma M, Gut J, Rosenthal PJ, Frade R, Perry MJ, Moreira R, Prudencio M, Lopes F. Endoperoxide-8-aminoquinoline hybrids as dual-stage antimalarial agents with enhanced metabolic stability. Eur J Med Chem. 2018;149: 69-78.

Acurcio RC, Scomparin A, Conniot J, Salvador JAR, Satchi-Fainaro R, Florindo HF, Guedes RC. Structure-function analysis of immune checkpoint receptors to guide emerging anticancer immunotherapy. J Med Chem. 2018; 61: 10957-75.

Raimundo L, Espadinha M, Soares J, Loureiro JB, Alves MG, Santos MMM, Saraiva L. Improving anticancer activity towards colon cancer cells with a new p53-activating agent. British J Pharmacol. 2018; 175: 3947 - 62.

Yosipof A, Guedes RC, Garcia-Sosa AT. Data mining and machine learning models for predicting drug likeness and their disease or organ category. Front Chem. 2018; 6: 162.

Florindo PR, Pereira DM, Borralho PM, Piedade MFM, Oliveira MC, Dias AM, Rodrigues CMP, Fernandes AC. Organoruthenium(II) nucleoside conjugates as colon cytotoxic agents. New J Chem. 2019; 43: 1195-1201.

Scientific Hub

BEATRIZ SILVA LIMA
Programme Leader

The Drug Development Programme is designed and implemented synergistically with other iMed.ULisboa programmes, validating newly identified products, targets, biomarkers or methods, with the goal of transforming drug leads into clinical candidates and ultimate facilitating patient access to innovation in health. Our research uses innovative technological platforms for formulation and targeted delivery of drugs and diagnostic agents, and addresses related safety concerns. Preclinical development further guarantees proof-of-concept and safety. Covering therapeutic areas, including cancer, genetic disorders and infection, strategic lines of our activity are:

1. Innovative targeting strategies.

Innovation in polymer synthesis, formulation and targeting strategies are exploited for the delivery of synthetic- and natural-based candidate therapeutics to their specific site of action. At the frontiers between materials science and biology, these strategies aim to overcome biological barriers and modulate cellular checkpoints and gene regulators, including those crucial for cancer immune evasion.

2. Tools to test clinical candidates and diagnostic systems.

Aiming at clinical translation of therapeutic and diagnostic agents with improved efficiency and reduced toxicity, we use in sillico modelling approaches, molecular biophysics, 3D-multicellular-based systems and mouse models of disease to predict and study pharmacology, biodistribution and pharmacokinetics, and toxicology. We also implement process analytical technology tools at early research stages to enable establishing critical process parameters and critical processes attributes for pharmaceutical products, reinforcing batch-to-batch reproducibility and cost-effectiveness, which are vital for progressing from bench-to-bedside translation.

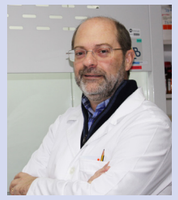
3. Regulatory science.

Our research follows and promotes existing regulatory requirements to maximize the translational value of results from in vitro or in vivo tools into first-in-human research and beyond, including dedicated actions addressing specific regulatory questions.

Research Groups

MARIA H. L. RIBEIRO
Chemical Biology and Toxicology

HELENA F. FLORINDO
BioNanoSciences – Drug Delivery and Immunotherapy



ANTÓNIO J. ALMEIDA
Nanostructured Systems for Overcoming Biological Barriers

BEATRIZ SILVA-LIMA
Pharmacological and Regulatory Sciences

Recognising the importance for scientific community and society to understand scientific and regulatory basis of medicines development, the Drug Development Programme is involved in international training initiatives for researchers, regulators and patients. From 2013 to 2017, ca. 30 students successfully completed their thesis in Drug Development areas, while 28 are currently enrolled. Strategic collaborations with the European Medicines Agency, Portuguese regulator INFARMED, and the Innovative Medicines Initiative and specific support from Horizon 2020 ERA-NET and COST schemes strengthen the quality of our research and training outputs. Training initiatives for patients occur within the European Patients Academy for Technical Innovation and its Portuguese platform.

BioNanoSciences – Drug Delivery and Immunotherapy

HELENA F. FLORINDO
Group Leader

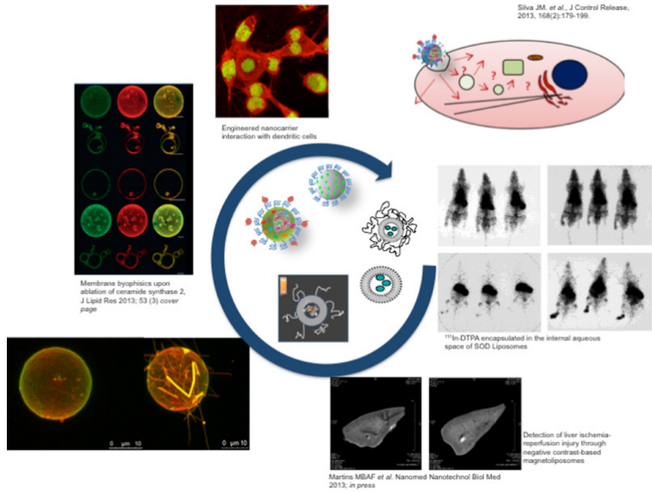
PhD (2008) in Pharmaceutical Technology, Universidade de Lisboa. Assistant Professor, Galenic Pharmacy and Pharmaceutical Technology, Faculdade de Farmácia, Universidade de Lisboa.

Achievements

A stepwise approach elucidated the effect of nano-vaccine composition and method of antigen association on the different steps involved on the development of the anti-cancer immune response: i) nanocarrier uptake by APC; ii) expression of activation/maturation markers at DC surface; iii) effect on T cell activation and expansion; iv) activation of T cell memory fundamental to protect patients against recurrence. Final proof of concept was evidenced regard- ing the immune therapeutic effect of our novel nano-vaccine on melanoma and Her2-specific breast carcinoma models. Those studies are of particular importance to evidence the potential of nano- vaccines to trigger a broad immune response against a breast carcinoma better resembling the human disease, namely the lower expression of cancer associated antigens. These mechanistic approaches provided further understanding of nanocarrier mechanisms of cellular dynamics of outmost importance to guide the design of optimized cancer vaccines.

Biological membranes are complex entities organized into compositionally and functionally distinct membrane domains that ensure physical separation of biological events and regulation of cell function. Current models support the concept of fluidity in biological membranes as original proposed by the fluid mosaic model. Our observations challenge this dogma, and demonstrate that sphingolipid-domains display biophysical features typical of the gel phase. This discovery defines a new paradigm for biological membranes, proposing the exis- tence of biologically-relevant gel domains in cellular membranes. Understanding the bio- physical and biological properties of these novel gel domains will open unprecedented opportunities to modulate membrane-associated cellular events and may lead to the identification of new therapeutic targets.

It was proved the feasibility of laminar extrudates to deliver small to large molecular weight active pharmaceutical ingredients (APIs) to patients either by oral individualize therapy to patients.



Keywords

Translational Nanotechnology; Cell Membrane Interactions; Immune Modulation; Process Analytical Technologies (PAT); Imaging in Diagnostic & Therapeutic.

Selected References

Zupančič E, Curato C, Kim J-S, Yeini E, Porat Z, Viana AS, Globerson-Levin A, Waks T, Zelig E, Moreira JN, Satchi-Fainaro R, Eisenbach L, Jung S, Florindo HF. Nanoparticulate vaccine inhibits tumor growth via improved T cell recruitment into melanoma and huHER2 breast cancer. Nanomedicine. 2018; 14: 835-847.*

Sainz V, Moura LIF, Peres C, Matos AI, Viana AS, Wagner AM, Vela Ramirez JE, S Barata T, Gaspar M, Brocchini S, Zloh M, Peppas NA, Satchi-Fainaro R, F Florindo H. α-Galactosylceramide and peptide-based nano-vaccine synergistically induced a strong tumor suppressive effect in melanoma. Acta Biomater. 2018; 76: 193-207.

Catelani TA, Santos JR, Páscoa RNMJ, Pezza L, Pezza HR, Lopes JA. Real-time monitoring of a coffee roasting process with near infrared spectroscopy using multivariate statistical analysis: A feasibility study. Talanta. 2018; 179: 292-299

Marcelino P, Marinho HS, Campos MC, Neves AR, Real C, Fontes FS, Carvalho A, Feio G, Martins MBF, Corvo ML. Therapeutic activity of superoxide dismutase-containing enzymosomes on rat liver ischaemia-reperfusion injury followed by magnetic resonance microscopy. Eur J Pharm Sci. 2017; 109: 464-471.

Paisana MC, Wahl MA, Pinto JF. An insight into the impact of polymers on the hydrate conversion of olanzapine form I in aqueous suspensions. J Pharm Sci. 2017; 106: 1786-1794.

4.
Facilities and Services

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NAME SURNAME
Group Leader

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MIGUEL TAVARES
Group Leader

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