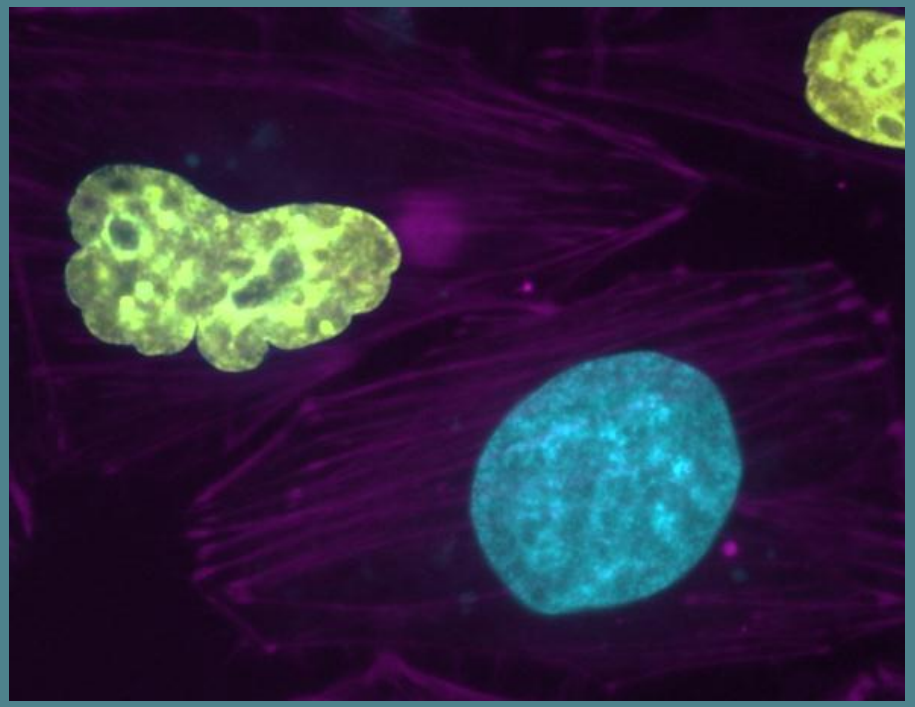

BioISI

Biosystems & Integrative Sciences Institute

Report 2020

BioISI Biosystems and Integrative Sciences Institute

Ciências ULisboa

Front page figure: Overexpression of the transcriptional repressor NKX6-2 (in yellow/green) is frequently associated with aberrant nuclear morphologies. In blue, Hoechst staining shows normal nuclei in cells not expressing NKX6-2. In magenta, the actin network. Image provided by Federico Herrera (FunGP Group, FCUL)

Contents

BioISI Identification

Name of the Research Unit: Biosystems & Integrative Sciences Institute

Unit Acronym: BioISI

Scientific Director: Margarida Sofia Pereira Duarte Amaral

Scientific Areas: Multidisciplinary/Interdisciplinary Research

Molecular Biology & Biomedical Sciences
Biological sciences
Physics
Chemistry

Keywords Multidisciplinary Research

Molecular Systems Biology
Bioinformatics & computational modelling
Integrative Sciences
Quantitative biology

Management Institution:

FCiências.ID – Associação para a Investigação e Desenvolvimento em Ciências

Participating institutions:

Instituto Nacional de Saúde Dr. Ricardo Jorge (INSARJ)

Universidade do Minho (UM)

Universidade de Trás-os-Montes e Alto Douro (UTAD)

Emails: Director: BioISIdirector@fc.ul.pt / Secretariat: BioISInfo@fc.ul.pt | Webpage: http://www.bioisi.pt

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Introduction

Biological systems display complex properties that cannot be predicted from studying isolated parts. Addressing such complexity calls for integrative analyses combining high-throughput Omics with quantitative science and computational tools to describe and predict dynamical behaviours.

Vision

The vision of BioISI, a recent institute created in 2015 (http://www.BioISI.pt) is to pursue cutting-edge research on biosystems and integrative sciences to become the leading centre at the forefront of research in this area in Portugal and internationally.

Goal & Missions

BioISI's goal is to understand and address biological questions using integrative -Systems- approaches at the vanguard of life sciences research. Its researchers benefit from a unique interdisciplinary environment that fosters creative thinking to solve problems through integrative approaches. To achieve its vision BioISI pursues 5 major missions:

1. Research in BioSystems & Integrative Sciences
2. Technology & Instrumentation
3. Facilities and Services
4. Teaching and Training
5. Knowledge/ Technology Transfer

Strategic objectives for 2018-2022

1. Taking a lead role in Biosystems/Integrative Sciences research nationally and internationally
2. Driving research and progress through technology development and innovation
3. Training next generation scientific leaders in Biosystems/Integrative Sciences
4. Providing research facilities and services to BioISI researchers and externally
5. Become a major player in industry partnerships and technology transfer for life sciences

These strategic objectives will be implemented along **BioISI's 5 main Thematic Lines (TLs):**

1. **Biomedicine**: to understand molecular/cellular mechanisms of disease and translate findings into improved diagnoses/prognoses and better personalized therapies.
2. **Biotechnology**: to characterize at systems-level economically relevant plants and microbes to sustainably meet the challenges of global climate changes while safeguarding the environment.
3. **Biological Chemistry**: to develop bioactive molecules (by synthesis or from natural sources) and understand molecular mechanisms of (bio)chemical systems (e.g. molecular/cellular bioenergetics).
4. **Bioinformatics**: to promote digital biology at large, fostering the generation of systems-level knowledge and models to describe and predict the behaviour of complex biological systems.
5. **BioPhysics**: to develop the study of bio-systems using *ad hoc* physical models and tools (e.g. novel simulation approaches to protein (mis)folding, dedicated atomic force microscopy techniques to measure forces in molecules and cells).

BioISI strategy is to cluster its competences in 3 main societal challenges as ´**Flagship projects**´:

1. Crop/product improvement & contributions to bioeconomy: grapevine and wine
2. Systems approaches to rare diseases: Cystic Fibrosis and neurodegeneration
3. Enabling technologies: AFM/FFM tools and innovative computational approaches

BioISI Governance

Research at BioISI focuses on integrative approaches to biological problems at the forefront of life-sciences. In order to benefit from a unique multidisciplinary environment which gathers scientists from diverse areas, BioISI research is organized into 5 Thematic Lines (TLs) each functioning as a collaborative project led by a Coordinator (TLC) and Vice-Coordinator (TLVC), namely:

1) Biomedicine (BioMed): MD Amaral/CM Gomes
2) Biotechnology (BioTech): R Malhó/R Tenreiro
3) BioPhysics (BioPhys): MM Godinho/A Nunes
4) Bioinformatics (BioInf): L Correia/ M Machuqueiro (from October: M Machuqueiro/ A Vicente)
5) Biological Chemistry (BChem): M Pereira /P Costa

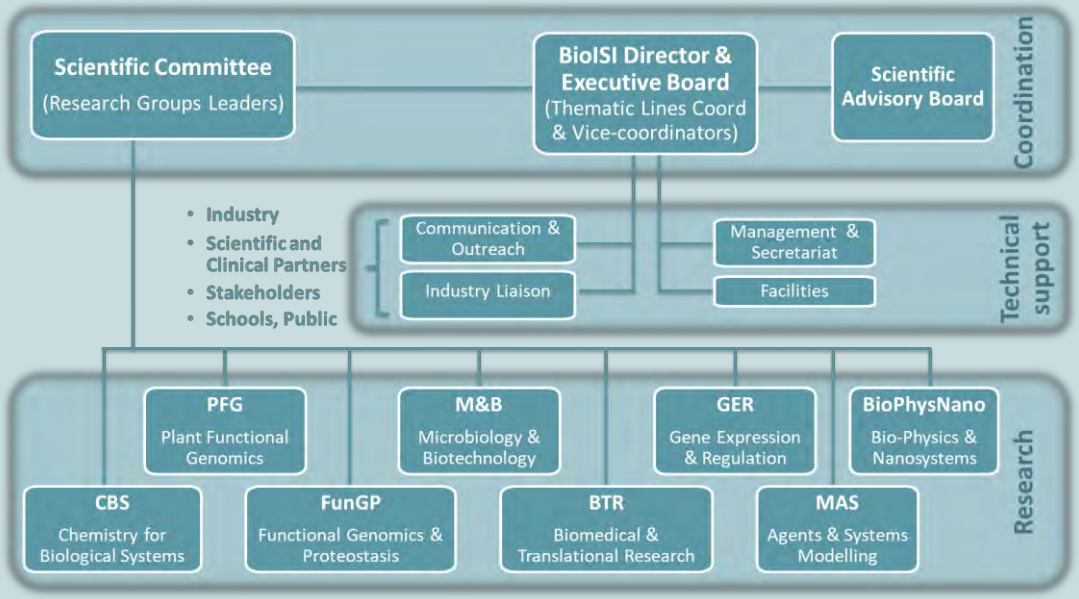
Each TLC is a former centre coordinator with past experience managing internationally funded research, being also a research group leader (RGL). TLCs/VCs promote specific activities and exchange of information to exploit collaborations enhancing multidisciplinary research.

Research groups

BioISI has 8 research groups (RGs) each headed by a RG leader (RGL) and containing multiple teams (headed by PIs).

1. Plant Functional Genomics (PFG): R Malhó
2. Functional Genomics and Proteostasis (FunGP): MD Amaral
3. Microbiology & Biotechnology (M&B): R Tenreiro
4. Biomedical & Translational Research (BTR): AM Vicente
5. Gene Expression and Regulation (GER): M G-Carvalho
6. Bio-Physics & Nanosystems (Bio-PhysNano): MM Godinho
7. Agents and Systems Modelling (MAS): L Correia (Group extinguish Sep 2020)
8. Chemistry for Biological Systems (CBS): M Pereira

Each RGL will coordinate research by the involved teams contributing to different TLs. Each RGL reports progress to the EB (Executive Board). The teams are grouped based on common scientific areas, methodologies and shared technologies.



BioISI Scientific Director (SD)

MD Amaral has significant expertise in leading large international projects. As EMBL alumna, she has a strong vision to promote science of excellence and a high international standing. Activities at EMBL and other top institutions are intensely disseminated and usage of facilities strongly promoted among BioISI researchers. A Vice-Director (R Malhó) assists and replaces the SD, when needed.

Executive Board (EB)

BioISI Director, assisted by the TLCs/VCs, form an Executive Board (EB) who implements BioISI strategic plan and Scientific Advisory Board (SAB) recommendations and proposes strategic guidelines to the Steering Scientific Committee (SSC)

Management Institutions

FCiencias.ID (FC.ID) is BioISI's main managing institution, whereas the participating institution FCUL provides the infrastructures accommodating most of BioISI labs and facilities.

Other BioISI managing institutions (poles) include:

1) **INSARJ:** is the National Institute of Health in Portugal, and its involvement is of high strategic relevance for the impact of BioMed-TL research results. Being within FCUL walking distance, interactions among BioISI researchers at INSARJ and FCUL occur as if they were at FCUL campus.
2) **UTAD & UM:** both in Northern Portugal, involve teams in BioMed & BioTech TLs. Despite being far from FCUL, their involvement in BioISI is of strategic relevance for the establishment of an inter-regional network on specific societal topics. Regular webconferences ensures discussion of progresses among teams involved and joint supervision of internal projects and students strengthens collaborative work.

All managing institutions are responsible for local administrative and financial procedures in coordination with FC.ID to optimize research and avoid hurdles. Each pole has a local project manager and a scientific coordinator ensuring optimal flow of information to and from BioISI director.

BioISI Scientific Advisory Board (SAB)

Rainer Pepperkok Molecular and Cell Biology
EMBL – European Molecular Biology Laboratory, Heidelberg (Germany)

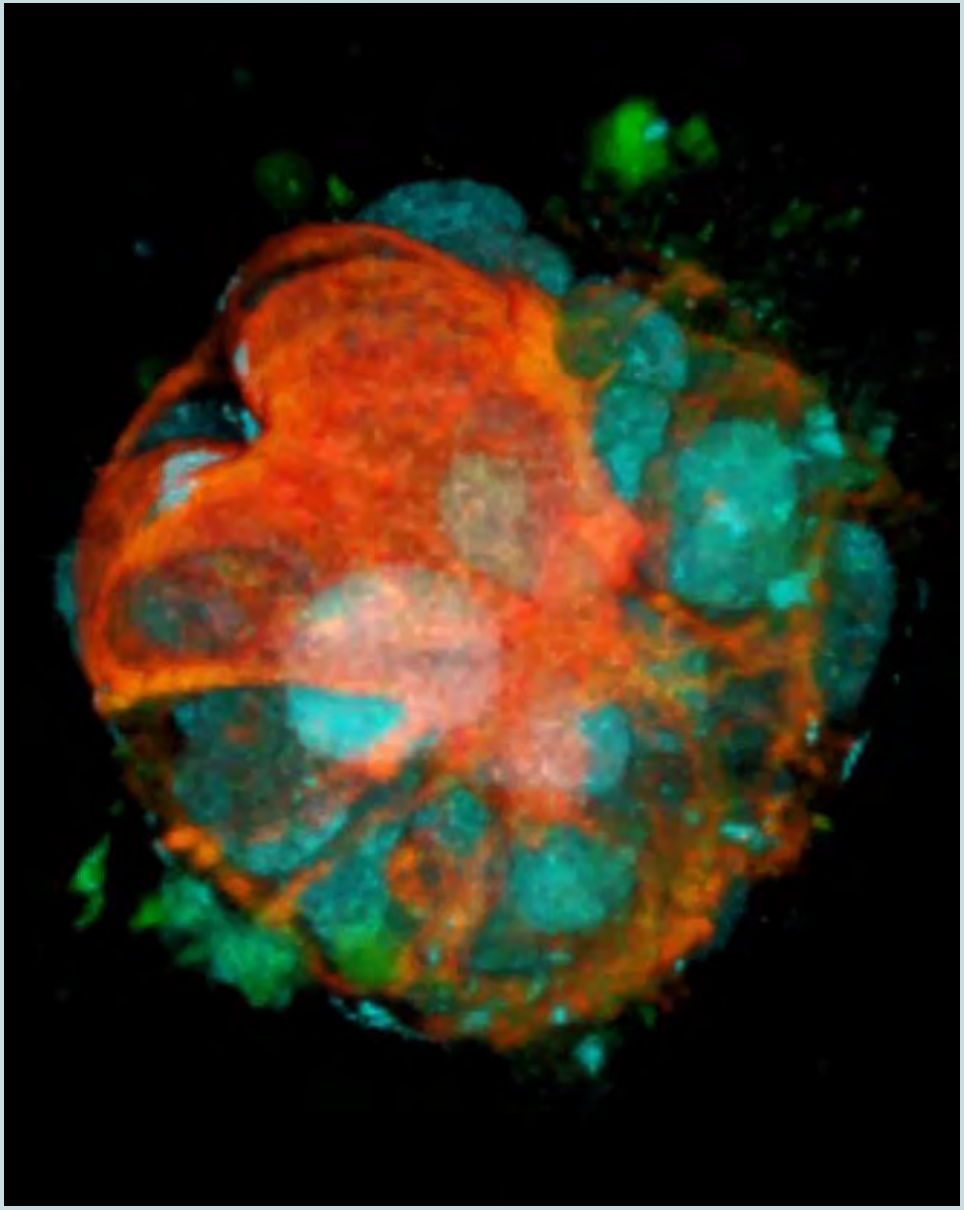
Klaus Palme Plant Molecular and Cell Biology
BIOSS Centre for Biological Signalling Studies, University of Freiburg (Germany)

Juan Valcarcel Juarez Genomics and Systems
CRG – Centre de Regulacio Genomica & ICREA, Barcelona (Spain)

Michael Gill Systems Medicine
Institute of Molecular Medicine, Trinity College Health Sciences Centre, Dublin (Ireland)

Eugene Shakhnovich Physics
Biophysics Laboratory, Harvard University, Cambridge (MA, USA)

Hans Peter Wessel Chemistry
Universidade de Aveiro (Portugal)



BioISI Thematic Lines

Three-dimensional modeling of a human intestinal organoid. Cell nuclei are stained in cyan and the actin cytoskeleton in red.
Image provided by Hugo Botelho, Iris Silva, Violeta Railean (FunGP Group, FCUL).

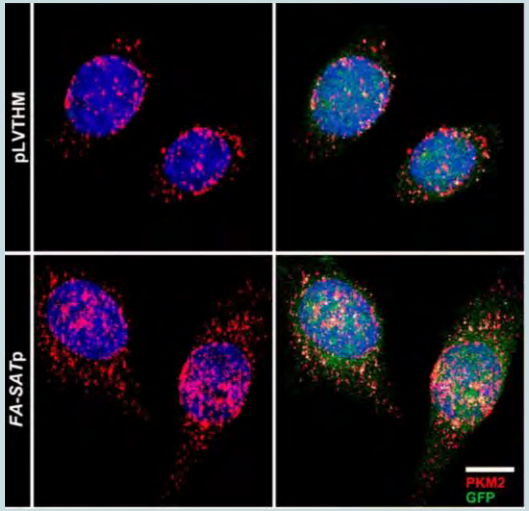
Biomedicine

The BioMed thematic line (TL) aims to establish new approaches to solve health problems at systems-level by identifying the causative pathways/ networks and key disrupted genes/ biomolecules and how these pathways/ networks are impacted by the environment and lifestyle.

The focus of BioMed research is on mechanisms of disease, personalized medicine and new therapies, with a focus on conformational disorders and being the genetic disease Cystic Fibrosis its flagship project. Other relevant areas include cancer, neurological/neurodegenerative and cardiovascular disorders.

BioMed TL involves predominantly scientists from the FunGP, BTR and GER groups who working closely with researchers from other TLs not only to elucidate the mechanisms of human disease at the molecular and cellular levels, but also to uncover the genetic and epigenetic determinants of disease.

Among BioISI projects awarded in 2020, three had a strong component of Biomedicine at the intersection with other TLs, by focusing on familial hypercholesterolaemia and cystic fibrosis.



Institutional Cooperation. To stay at the forefront of innovative research, Biomedicine at BioISI keeps strong international collaborations. For example, BioISI researchers (FunGP) participate in a large EU-H2020 project - HIT-CF - in which they perform drug screens on organoids from individuals with Cystic Fibrosis and rare genetic profiles, to predict their clinical response to these novel drugs in a personalized medicine approach.

BioISI researchers also maintain key collaborations with national hospitals and academic clinical centres.

Facilities. Biomedicine benefits from the facility of high-throughput screening (applying to become a node of EU-OpenScreen) and also of the Mass Spec (soon open for Proteomics. It also benefits from the Genomics facility (Biotechnology TL) which recently joined the national Genome network.

Future plans:

- Understand the regulatory networks underlying traffic disorders, namely Cystic Fibrosis;
- Carry out tests in patients own cells/tissues towards personalized medicine, namely in Cystic Fibrosis;
- Further unravel the role that CFTR (the protein mutated in Cystic Fibrosis) plays in cellular epithelial differentiation and when dysfunctional in cancer;
- Elucidate the role of RNA metabolism in disease, and to develop novel diagnostic and therapeutic strategies based on this knowledge;
- Unravel cell signalling mechanisms related to cancer;
- Use bioinformatic integrative analyses of large genetic and environmental datasets for improved diagnosis and clinical intervention in autism;
- Explain mechanisms of Alzheimer's disease (AD) by *in vitro* studies of self-assembly and amyloid formation of proteins involved in AD.

"Flagship" project: Cystic Fibrosis

Biophysics

The broad goal of BioPhys TL is to boost interdisciplinary research rooted in Physics. Model building, computational approaches and high-resolution experimental techniques are combined to help solve a variety of biological problems, in close collaboration with other BioISI groups. The expertise of the physics team in AFM and magnetic studies is crucial to probe and manipulate biosystems at the smallest scales. Theoretical understanding at these and at larger scales involves physical models and computational approaches that are also part of the team's expertise.

Protein folding physics

Development of models and computational approaches to study protein folding under confined environments; integrated view on the early stage of b2-microglobulin aggregation mechanism by combining protein folding and docking simulations – preliminary study of the pre-fibrilar phase (dimers and tetramers) of the aggregation mechanism, in the framework of the project, "PhysBD", which involves a collaboration with the BChem TL. Expertise of the PBS physics team was used in the effort to fight Covid-19: Project 131_596787873 "Making the way out: model-based evaluation of exit strategies from the COVID-19 lock-down in Portugal" (FCT Call Research 4 Covid-19).

Nanostructured magnetic systems

Development of magnetic nanoparticle (MNP) systems for biomedical applications encompassing: synthesis, structural/microstructural and magnetic properties assessment of coated iron oxide nanoparticles; preparation of stable biocompatible ferrofluids and evaluation of specific loss power performance; improvement of organized magnetic nanoparticles aggregates using gels and polymers hosts; analysis of the aggregation/orientation effect of combined ac/dc external magnetic fields; collaboration with FunGP, concerning the evaluation of MNP uptake and toxicity in human cell lines.

AFM/FFM methodologies

Home-made FFM was completed in 2019 (M.Vitorino, PhD Eng.Physics) becoming fully operational for studies on biological systems; the new equipment was used to assess the mechanical properties of CFBE cells, a study framed by a collaboration with C. Farinha (FunGP) and to perform preliminary force-indentation curves on glioma cells, a study proposed by F. Herrera (FunGP),both to develop in Conventional AFM was used for studies on: the influence of metal ions (Ca2+,Zn2+) on Tau protein aggregation targeting the understanding of molecular mechanisms in AD (steady collaboration with Protein Folding/Misfolding Lab); surface/morphology analysis of prokaryotic membranes and respiratory complexes in membrane mimicking systems, a collaboration work with M. Pereira (CBS group) launched by a 2019 BioISI project .

Future plans:

- Further assessment of public health strategies for the Covid-19 pandemic, focussing on Portugal (fast track FCT funding).
- Study of nanostructured magnetic systems, to develop methodologies with potential application on biomedical devices;
- Development of AFM/FFM methodologies for nanomechanical properties studies & biological interactions assessment;
- Biomimetic photosynthesis and molecular solar energy storage.

Expertise/facilities of the physics team in optical techniques and software development were used in the production of a phenotyping platform prototype (InterPheno project, PFG/FCT grant); a PostDoc (M. Vitorino) was hired to install the sensors, develop data acquisition/image processing and prototype control software.; Squid magnetometry and 57Fe Mossbauer spectroscopy physics infrastructures were extensively used in the study of chemical complexes with magnetic centres displaying spin crossover (SCO) transitions to characterize the behaviour, strength, thermal hysteresis and time evolution of SCO (Squid), and to probe the valence states (oxidation/spin states) and atomic environment of iron compounds, in the frame of a long standing collaboration with P. Martinho (CBS group).

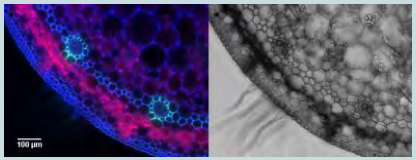
Biotechnology

The research performed in the Biotech-TL was conducted to acquire knowledge that will enable responses to societal challenges, such as the emergence of new plant or diet-related diseases, the emergence of new environmental conditions or the impact assessment of new bio-based products.

Key Actions and major achievements

Plant health

- Characterization of *Plasmopara viticola* isolates with contrasting aggressiveness towards grapevine.
- Transcriptomic profiling of drought response mechanisms in the mediterranean conifer *Pinus pinaster*.
- Characterization of secondary metabolism genes involved in the plant defense to *Phytophthora cinnamomi*.

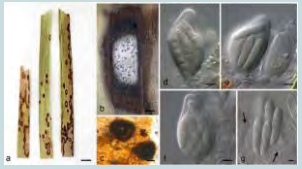


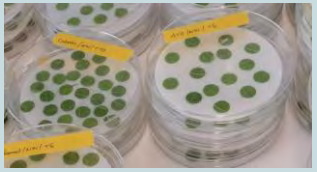
Interdisciplinary funded project *– Fostering High-Throughput Plant Phenotyping (Interpheno).*

Crop improvement and security

- Impact of plant genotype and plant habitat in shaping bacterial pathobiome using olive tree as case study.
- Enabling reusability of plant phenomic datasets with MIAPPE 1.1.
- Portuguese wild grapevine genome re-sequencing.
- Genome-wide transcriptomic analysis of novel regulators of cork formation in cork oak.

Networking activities of PFG (plant functional analysis), M&B (symbiotic and pathogen interaction), BioPhys-Nano (phenotypic analysis – cell wall AFM imaging) and MAS (systems networks).

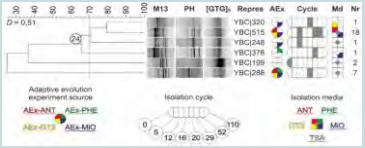




Microbial pharmacogenomics

- Identification of bioactives from deep-sea marine bacteria with anti-cancer potential.
- MarCODE: Development and application of biochemical tools for marine commercial product tracking.

Internal funded project – *Identification of biotechnological potential on genomic nonfunctionalized orthologs elements.*



Wine biotechnology

- The role of yeasts and lactic acid bacteria on the metabolism of organic acids during winemaking.
- Phenotypic and transcriptional analysis of *Saccharomyces cerevisiae* during wine fermentation.

*Networking between PFG, M&B and GER - Management of a unique dedicated computational infrastructure for processing genomic data in real-time (**BioISI Genomics**).*

CNOIV awards – "Enology distinction" [to Barrias et al.] and "Viticulture distinction" [to Laureano et al.]

Microbial biotechnology

- Microalgal cell disruption: Effect on the bioactivity and rheology of wheat bread.
- Integrated selection and identification of bacteria from polluted sites for biodegradation of lipids.
- Selection of a portfolio of wine yeasts for biocontrol of non-biotrophic grapevine fungi

"Fight against COVID" - *Implementation of "Centro de Testes de Ciências ULisboa" (CT Ciências ULisboa), infrastruture dedicated to Biological Risk Management currently focused on SARS-CoV-2 testing and mitigation; Collaboration in the Portuguese network for SARS-CoV-2 genomics.*

BioInformatics

The main scientific goals of the BioInformatics thematic line (BioInf TL) is to promote the development and use of methods and software tools for understanding large datasets, fostering the generation of molecular and systems-level models that help to describe and predict the behaviour of complex biological systems.

The BioInf-TL integrative approach aggregates BioISI research on molecular, biophysical, biological, and biomedical systems, nurturing the development of computational methods and tools that bridge all thematic lines.

Several BioISI research groups have activities that converge into BioInf-TL. In common, all work with numerical and algorithmic models of molecular or living systems for which computational implementations are fundamental.

Key Actions:

- Computing & storage common infrastructure set up;
- Development of new methods to help model and interpret biological data;
- Preprocessing pipelines for data analysis;
- Development of new computational tools to manage, integrate and interpret data;
- Meetings on computation for life sciences with invited experts.

Actions in 2020

The computing facilities usage has been improved and we continue to take advantage of the national (INCD) and European (EGI) computational infrastructures for large dataset processing and heavy computing tasks.

Future Plans:

- To develop novel computational tools for multilevel data integration and modelling;
- Knowledge discovery from Nanopore-based devices with Innovative algorithms;
- Implementation of models of gene regulatory networks in signalling and protein-protein interactions.
- Creation of a public server for the PypKa tool and its integration with a PostgreSQL database to store pK_a values of the complete PDB databank.

Major achievements in flagship projects

Usability results of an intelligent virtual assistant for promoting behaviour change and self-care in older people with type 2 diabetes, as a result of project VA-SelfCare.

A new tool (PypKa) has been developed to predict pK_a values in proteins. Its competitive accuracy and speed, together with a simple easy-to-use Python API make it a suitable candidate for a wide variety of applications.

Biological Chemistry

The Biological Chemistry (BChem) thematic line embraces multiple aspects of chemistry in the biological context. BChem aims at developing bioactive compounds by synthesis or extraction from natural sources, understanding molecular mechanisms of (bio)chemical systems, from small molecules, to proteins, membranes, and cells, and widening the knowledge of molecular and cellular bioenergetics. BChem expertise contributes directly to BioISI flagship projects "Systems approaches to rare diseases: Cystic Fibrosis and neurodegeneration" and "Enabling Technologies for Cutting-edge Research". We employ symbiotic approaches that combine computational and experimental methodologies to tackle health and/or environmental safety problems, either directly (e.g., new leads), indirectly (studying mechanisms or designing eco-friendly molecules and processes), or by unravelling pathogens bioenergetics. Profiting from the nurturing environment at BioISI and expertise of other BioISI members, we aim at contributing to the discovery new drugs acting at the core of human diseases, create innovative computational approaches and optimize nano-methods for bio-measurements and biodevices.

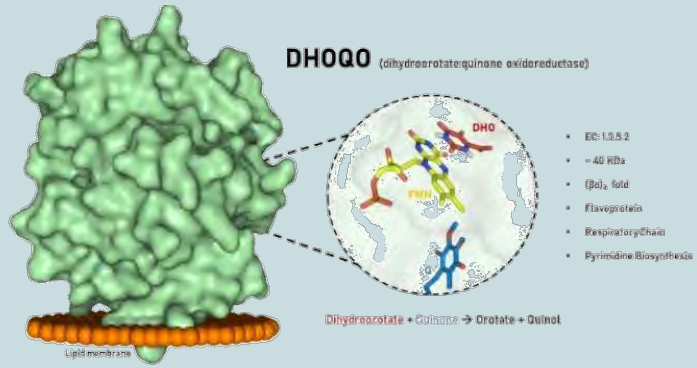
Key Actions and major achievements

BioISI Projects

Three out of five awarded BioISI projects involved the Biological Chemistry thematic line. Namely the projects "*Multidisciplinary approach to study post-translational modifications in metabolic enzymes*", "*Exploring the impact of Staphylococcus aureus on Cystic Fibrosis epithelial cell inflammation, differentiation and epithelial repair*" and "*VALHealth- Valorisation of ALgae for Health: Bioactive Compounds from Marine Bioresources by Membrane Technology*".

Organization of Meetings

We are engaged with the organization of the 7th IIBC - 2021 (Iberian International Biophysical Congress) and FEBS2022 Congress.

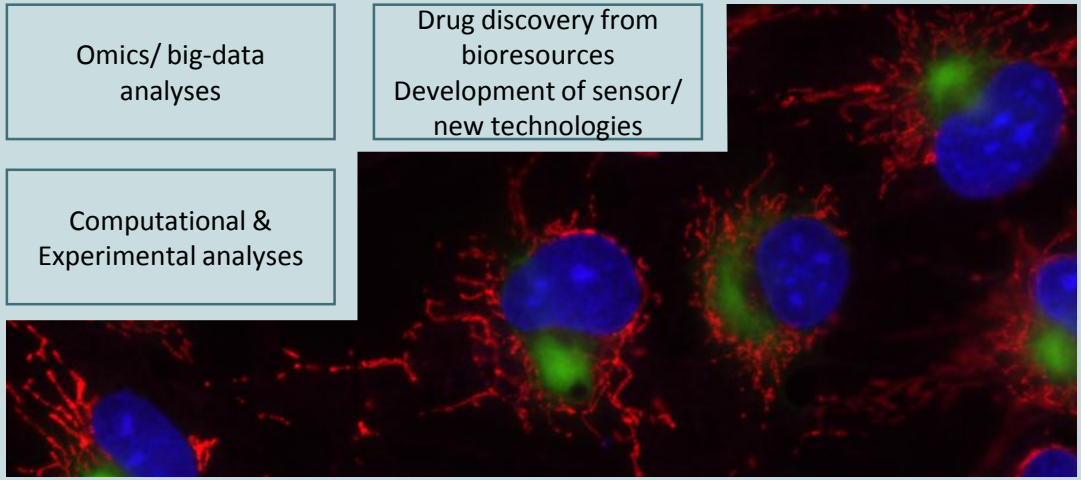


Facilities. Biological Chemistry is involved in the maintenance and development of the computing/bioinformatics facility, enabling BioISI scientists to run calculations and simulations in (bio)chemical systems. Biological Chemistry benefits from the facility of high-throughput screening (BioMed TL) and Atomic Force Microscopy (AFM) related techniques facility (BioPhys TL).

Future Plans. We will keep investing in the identification and purification of bioactive single molecules that are active in the context of CF-therapy. Efforts will be made to finalize the deconvolution and identify the pure active compounds. We shall also continue to investigate membranes proteins from bacteria with impact in human health in frame with the BioISI strategic program.

Integrated Research

	BioPhysics	Bioinformatics	Biological Chemistry	Biotechnology
Biomedicine	Development of new enabling technologies/ biomedical devices	Omics/ big-data analyses	Drug development	Drug discovery from bioresources
Biotechnology	Developing of enabling technologies/field devices	Omics/ big-data analyses	Drug discovery from bioresources Development of sensor/ new technologies	
Biological Chemistry	Development of sensors/ new technologies	Computational & Experimental analyses		
Bioinformatics	Innovative modelling/ computational approaches			



Pestalotiopsis pini sp. nov., a novel fungal species described as an emerging pathogen causing shoot blight and trunk necrosis on *Pinus pinea* in Portugal., 279 Conidia. Scale bars: 10 µm. Image provided by Helena Bragança, Eugénio Diogo, and Joana Henriques (M&B Group, INIAV).

BioISI Projects

For the 5th year, BioISI opened a call for projects of 1-year duration. These projects aimed to develop activities strongly related to BioISI Thematic Lines and BioISI's Strategic Project. This call required the involvement of PIs from two different BioISI groups from different areas, and were evaluated by their scientific excellence, originality and impact and relation to BioISI strategic program.

In 2020 these included 5 projects:

1. Multidisciplinary approach to study post-translational modifications in metabolic enzymes

PIs: Bárbara Henriques | Bruno L. Victor

Thematic Lines involved: Biomedicine | Biological Chemistry

2. Exploring the impact of *Staphylococcus aureus* on Cystic Fibrosis epithelial cell inflammation, differentiation and epithelial repair

PIs: Inna Uliyakina | Ines Pankonien

Thematic Lines involved: Biomedicine | Biophysics | Biological Chemistry

3. Restoring NKX6-2 function by protein complementation: a proof-of-concept

PIs: Federico Herrera | Luísa Romão | Margarida Gama Carvalho

Thematic Lines involved: Biomedicine | Bioinformatics

4. Novel mechanisms causing Familial Hypercholesterolaemia: Functional characterization of variants in the regulatory regions of PCSK9 and LDLR genes

PIs: Ana Catarina Alves | Juliane Menezes

Thematic Lines involved: Biomedicine

5. Valorisation of ALgae for Health: Bioactive Compounds from Marine Bioresources by Membrane Technology

PIs: Rita Pacheco | Hugo M. Botelho

Thematic Lines involved: Biomedicine | Biotechnology | Biological Chemistry

Multidisciplinary approach to study post-translational modifications in metabolic enzymes

PIs – Bárbara Henriques | Bruno L. Victor

Biomedicine | Biological Chemistry

Post-translational modifications (PTMs) of mitochondrial enzymes are major modifiers of the metabolism. One example of nonenzymatic PTMs are acylations, which are caused by the accumulation of acyl-metabolites, with implications in pathophysiological conditions. Despite of the current available animal/cellular models, the molecular mechanisms underlying these regulatory functions, which are likely critical in disease states, remain to be elucidated.

Here, we aim to clarify this issue with a multidisciplinary approach combining *in vitro* and *in silico* methods to study the effects of protein acylation on a critical mitochondrial enzyme, the electron transfer flavoprotein (ETF). We will use biochemical and biophysical methods and different computational molecular modelling approaches to a) study the effects of acylations on the enzyme structure, stability and function; b) identify ETF relevant modification sites; and c) validate the identified sites and show their *in vivo* relevance.

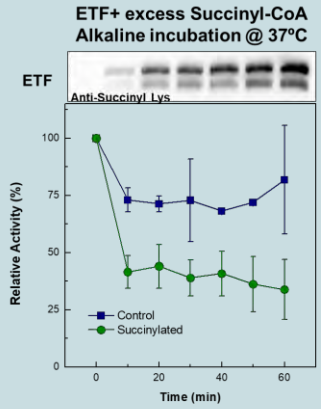


Figure 1 – ETF succinylation Left panel, *in vitro* succinylation profile at 37°C. Top, western blot detection using anti-succinyl lysine antibody at different time points during 1H. Bottom, ETF enzymatic activity using a couple assay with MCAD protein.

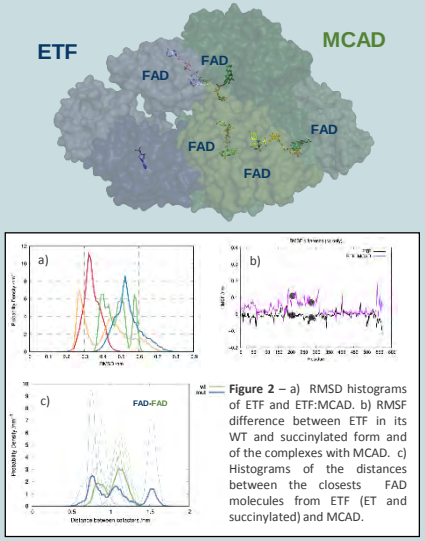


Figure 2 – a) RMSD histograms of ETF and ETF:MCAD. b) RMSF difference between ETF in its WT and succinylated form and of the complexes with MCAD. c) Histograms of the distances between the closests FAD molecules from ETF (ET and succinylated) and MCAD.

Results:

- Succinylation diminishes ETF enzymatic function by changing the overall net charge of the protein, probably by impacting the redox potential of ETF's FAD cofactor and/or the way it interacts with its biological partners;
- The mutation of K283 to a glutamate at ETF-α subunit has a negative impact in enzyme function, similarly to Succinylation;
- MD simulations of succinylated ETF's show that this PTM also influences the way it interacts with MCAD, one of its functional partners;
- The region of the structure of succinylated ETF which is most affected when interacting with MCAD is the region where K283 is found.

Conclusion:

Further studies are currently being developed to further characterize the effect succinylation has on ETF's function.

Exploring the impact of *Staphylococcus aureus* on Cystic Fibrosis epithelial cell inflammation, differentiation and epithelial repair

PIs – Inna Uliyakina | Ines Pankonien

Biomedicine | Biophysics | Biological Chemistry

Cystic Fibrosis (CF), which is caused by mutations in the CF Transmembrane Conductance Regulator (CFTR) gene, is characterized by multiple manifestations in different organs, but the disease is dominated by the respiratory symptoms, the main cause of morbidity and mortality. The very thick mucus that is produced because of CFTR dysfunction leads to inefficient mucociliary clearance, airway clogging and recurrent bacterial infections and chronic inflammation, altogether contributing to progressive loss of lung function. Individuals with CF are predominantly infected by *S. aureus* and *P. aeruginosa*. However, their roles in the pathogenesis in CF airways are not completely understood. Recently, *S. aureus* has been shown to release extracellular vesicles (SEVs) that are able to transport a variety of biologically active cargos, such as proteins, lipids, DNA and RNA, among other molecules. Furthermore, SEVs have been shown to mediate pathophysiological functions by inducing cellular inflammation and evoking death in the host cell. We are investigating which role SEVs play during the infection of CF airway epithelial cells with focus on inflammation, differentiation and repair.

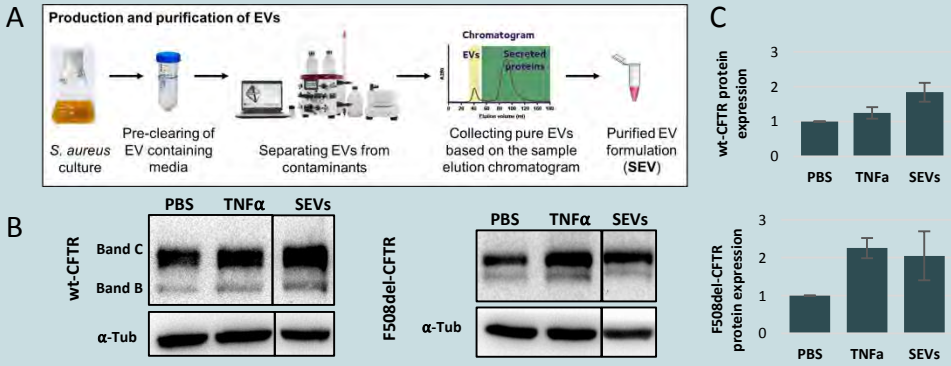


Figure 1 – (A) Isolation and purification process for *S. aureus* secreted extracellular vesicles (SEVs). (B) Western Blot analysis showing CFTR expression (wt-CFTR left panel, F508del-CFTR right panel) after treatment with TNFα (positive control) and SEVs. (C) Western Blot quantification (number of independent experiments=3).

Results:

- Optimized method for isolation and purification of *S. aureus* derived extracellular vesicles (SEVs) was developed;
- SEVs significantly increase CFTR and ICAM1 (Intercellular Adhesion Molecule 1) expression in both wt- and F508del-CFTR stably expressing Human Bronchial Epithelial cells.

Conclusion:

***S. aureus* secreted extracellular vesicles seem to play an important role in the host-pathogen interaction.**

Restoring NKX6-2 function by protein complementation: a proof-of-concept

PIs – Federico Herrera | Luísa Romão | Margarida Gama Carvalho

Biomedicine | Bioinformatics

Nonsense or frameshift mutations in the transcriptional repressor NKX6-2 produce a rare neurodegenerative disorder known as SPAX8. Most of the mRNAs carrying these mutations are degraded by nonsense-mediated RNA decay (NMD) and the surviving mRNA molecules produce truncated, dysfunctional NKX6-2 proteins. The final aim of this project is to restore the function of the NKX6-2 protein by means of a Protein Complementation (PC) approach. PC is a property of proteins by which they can be split in two or more fragments that are not functional, but that recover their function when they are brought back together by non-covalent bonds. In theory, truncated NKX6-2 function could be restored by simply adding the C-terminal fragments that are missing. However, we need enough truncated NKX6-2 protein to be produced, and therefore we must circumvent NMD. We are trying to establish the proof-of-concept for a combined strategy based on simultaneous NMD inhibition and PC with NKX6-2 fragments.

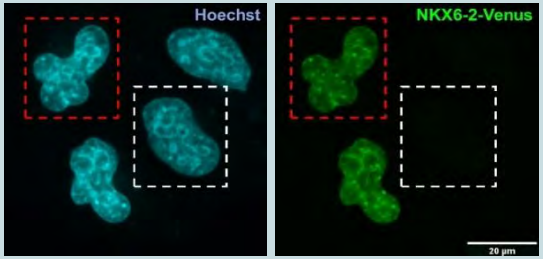


Figure 1 – NKX6-2 overexpression changes the nuclear morphology of HeLa cells. HeLa cells were transfected with the full-length, wild-type NKX6-2-Venus constructs (in green), and imaged 24 hours later after counterstaining of nuclei with Hoechst 33342 (in blue). Our preliminary results indicate that NKX6-2 expression levels are related to a higher frequency of nuclear blebbing (red square). Scale bar, 20 µm.

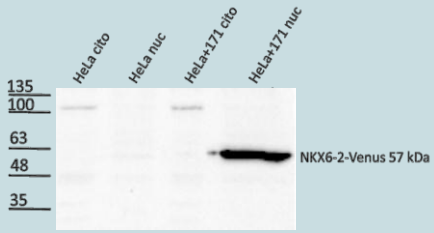


Figure 2 – NKX6-2 expression is fundamentally nuclear. We validated the NKX6-2 antibody in cytosolic and nuclear protein extracts isolated from non-transfected and transfected HeLa cells (171 is the NKX6-2-Venus construct). As expected, overexpression of NKX6-2 produced a massive increase of the chimeric protein (57 KDa) in the nuclear fraction, but not in the cytosol.

Results:

- Production of 2 novel constructs carrying a NKX6-2-Venus chimera and the NKX6-2 minigene. These will be used to produce SPAX8 models based on mutations found in patients;
- Overexpression of NKX6-2 in HeLa cells produced aberrant nuclear morphologies. A possible role of NKX6-2 on nuclear structure is under study;
- Endogenous expression of NKX6-2 is negligible in HeLa cells.

Conclusion:

We will produce 4-8 unprecendented celular models of SPAX8, shed some light on NKX6-2 obscure biological functions, and establish a proof-of-concept for a combined NMD/PC therapy for SPAX8

Outputs:

Ferreira-Peralta P., Letra-Vilela R., Gama-Carvalho M., Romão L., Herrera F. (2020) The role of nonsense-mediated mRNA decay on NKX6-2-associated spastic ataxia 8. Poster will be presented at the XXI meeting of the Portuguese Society of Biochemistry (March 2021).

Novel mechanisms causing Familial Hypercholesterolaemia: Functional characterization of variants in the regulatory regions of PCSK9 and LDLR genes

PIs – Ana Catarina Alves | Juliane Menezes

Biomedicine

Familial hypercholesterolemia (FH) is the most common genetic disorder conferring an increased cardiovascular risk due to cholesterol accumulation since birth. Most patients with FH phenotype have mutations in *LDLR*, *APOB* or *PCSK9* genes. In about 50% of patients a variant causing disease has not been possible to find. The 5' and 3' untranslated regions (UTRs) and promoter of these genes is poorly studied. Consequently, few variants were detected in these locations and functional validation is lacking for the ones described. The aim of this project is to define the 5'UTR and promoter regions of the *PCSK9*, as well as, to perform an in vitro characterization of variants in *LDLR* and *PCSK9* genes in the regulatory region.

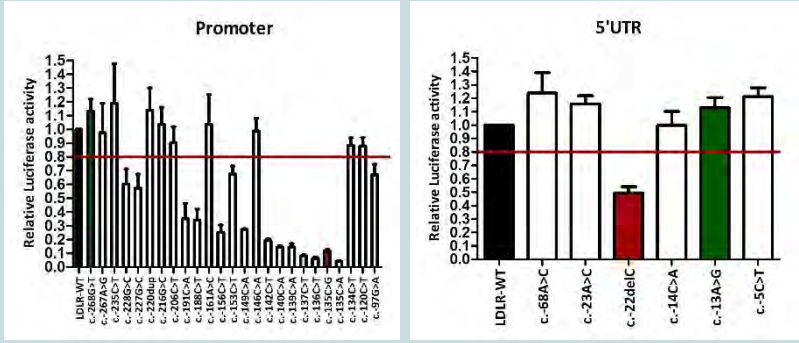


Figure 1: Measurement of (A) promoter and (B) 5'UTR activities using luciferase assay. Fragments containing the wild-type and mutants were cloned into the pGL4.10 (Firefly) plasmid and co-transfected with pRL-TK (*Renilla*) into *CHO-ldlA7* cells line. Ratio is the unit of Firefly luciferase after normalized with *Renilla* luciferase, and each value was derived from, at least, three independent experiments. The ratio of all variants was compared to the counterpart wild-type (LDLR-WT), arbitrarily set to 1. Results are expressed as mean ± standard deviation. Black bars are the wild-type controls, the green ones are the silent variants used as a positive control, and the red ones are the described functional variants, used as a negative control.

Results:

- We studied 23 variants in the promoter region of the *LDLR* gene described in ClinVar. From these 23 variants, 57% resulted in reduction of promoter strength compared to the wild-type. Most of these abnormal variants occurred within the sterol regulatory element in repeat 3 (Fig 1A);
- We also studied 4 variants in the 5'UTR region of *LDLR* but none were shown to have an abnormal effect. Only c.-22delC (the negative control), which creates a new ATG codon has been demonstrated to produce an abnormal effect (Fig 1B);
- Using 5'RACE, we were able to define *PCSK9* 5'UTR region. The promoter and 5'UTR of *PCSK9* were cloned into pGL4.10 plasmid and by site-directed mutagenesis we obtained the 17 variants that we are going to be study in *PCSK9* in the next months.

Conclusion: Our results emphasize the necessity of functional analysis of new variants in the *LDLR* promoter with the objective of determining their biological effect and possible influence on FH phenotype, allowing the correct diagnosis of the disease.

Valorisation of ALgae for Health: Bioactive Compounds from Marine Bioresources by Membrane Technology

PIs – Rita Pacheco | Hugo M. Botelho

Biomedicine | Biotechnology | Biological Chemistry

Algae are valuable marine renewable resources rich in bioactive compounds (BC), which are scarcely explored. The main aim of this project is to value algae bioactive compounds targeting Cardiovascular Disorders (CVD) and Cystic Fibrosis (CF). CVD are the top cause of death worldwide, which may be prevented by reducing blood cholesterol levels. CF is the most common life-shortening autosomal recessive disease, caused by mutations in the gene encoding the CFTR anion channel. Current drugs targeting the most common F508del-CFTR mutant do not fully restore the most severe CF hallmark: lung disease. Also, altered lipid metabolism and dyslipidemia frequently occur in CF, often correlated with alterations in intestinal cholesterol and lipid absorption. In this project we envisage the identification of novel bioactive seaweed compounds modulating cholesterol permeation in intestinal lining cells and CFTR trafficking and function in bronchial epithelial cells.

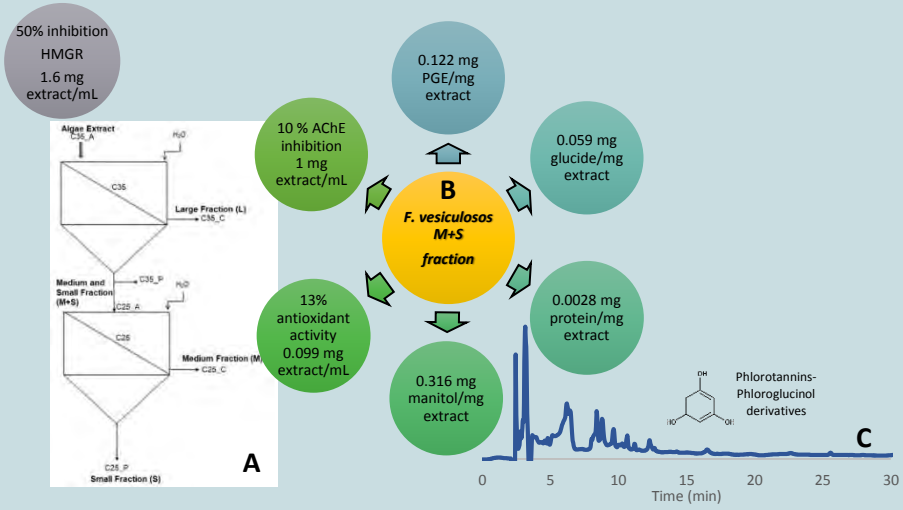


Figure 1 – A. Membrane technology flowchart to obtain fractions with bioactive compounds (BC) from *Fucus vesiculosus* extract. HMG-CoA reductase inhibition activity of the extract is presented. B Characterization of M+S fraction which holds the most BC and C. M+S fraction RP-HPLC-DAD chromatogram. (M+S- medium and small size compounds, PGE- Phloroglucinol equivalent)

Results:

- Development of a diafiltration methodology for obtaining *F. vesiculosos* seaweed fractions enriched with BC. Characterization of the extract and fractions;
- Extraction and analysis of bioactive compounds from *Eisenia bicyclis*. *Porphyra tenera* extractions in progress;
- Screening assays focusing on CVD and CF in progress;
- Analysis on cellular metabolomic profiles in progress.

Conclusion:

Seaweeds are rich in bioactive compounds mostly phlorotannins, which demonstrated potential to target CVD.

BioISI Research Units (Groups)

Mutant Arabidopsis flower expressing Castanea resistance gene to *Phytophtora cinnamomi*.
Image provided by Susana Serrazina (PFG Group, FCUL)

PFG Group
Plant Functional Genomics

http://bioisi.pt/pfg/

Research topic - Study of multiple aspects of plant growth and development with emphasis on functional aspects aiming biotechnological applications:

- Characterization of signaling and secretory pathways regulating growth and morphogenesis;
- Omics profiling of plant (and fruit) development and responses to biotic interaction (parasitic and symbiotic) and abiotic stresses;
- Food authenticity and traceability;
- Plant genetic diversity assessment/screening;
- Genome editing of relevant crops and cultivars for better traits and increased resilience.

Major Achievements:

- Development of High-Throughput Real-Time PCR Assays for pathogen detection on fruits and food derivatives;
- Genome-Wide Identification of Epigenetic Regulators in *Quercus suber*;
- Photobiological and lipidic responses upon biotic (pathogen attach) and abiotic (drought) stresses;
- Impact of plant genotype and plant habitat in shaping bacterial and fungal soil microbiome;
- Functional characterization of cork oak and chestnut genes involved in defense mechanisms against pathogen attack;
- Development and improvement of phenomic metadata sets for the plant phenotyping domain.
- Genome re-sequencing of portuguese wild grapevine (*Vitis vinifera sylvestris*);

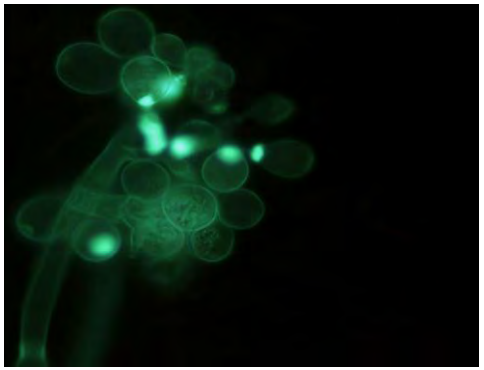


Figure 1. Sporangiophore and sporangium structures of *Plasmopara viticola*, the downy mildew causing pathogen.

Figure 3: Mutant Arabidopsis flower expressing Castanea resistance gene to P*hytophtora cinnamomi.*

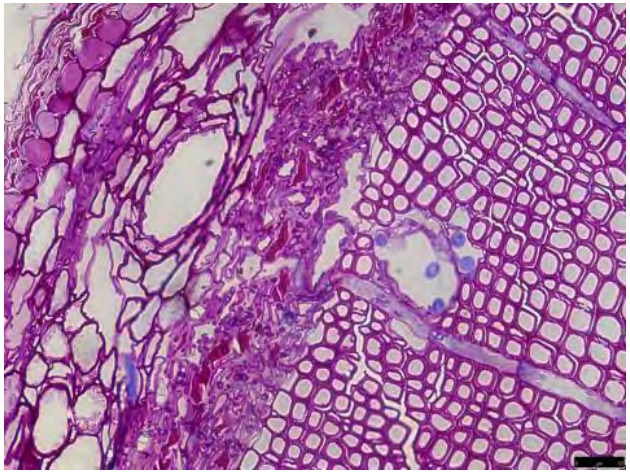


Figure 2: PAS/Schiff-Comassie Brilliant Blue-double stained stem cross sections of *Pinus pinaster* inoculated tree with pinewood nematode (PWN) showing the presence of PWN and the internal stem tissues destruction in inoculated pines.

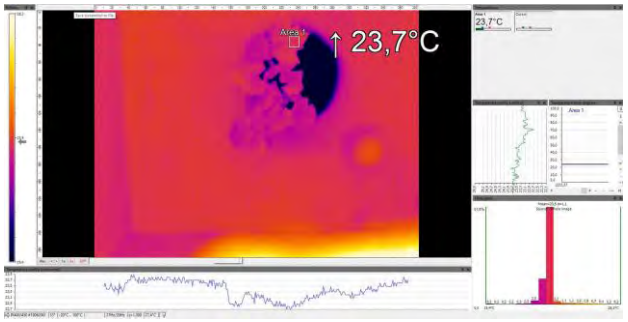


Figure 4: Termographic image of leaf from *Vitis vinifera* (Touriga Nacional)

Group Members

PhD & MSc Students Vanessa Azevedo, Catarina Gouveia, Diana Pimentel, Flávio Soares, Teresa Braga, Gonçalo Laureano, Marisa Maia, Joana Figueiredo, Helena Santos, Susana Lopes, Bruno Costa, Inês Modesto, Hamilton Chiango, Ana Rita Cavaco, Pedro Correia, Inês Diniz, Ana Rita Santos, Rui Nascimento, Ana Alves, Sara Barrias, Francisca Reis, Daniela Costa, Laura Nascimento, Dario Marchese, João Mina, Ana Alhinho, Marlene Santos, Gonçalo Pereira, Luis Sousa, Giovanna Calvão, Alexandra Lino, Catarina Lino, Rute Amaro, Tomás Werner, Ana Catarina Marques, Ana Pereira, Ana Rita Amaral, Cláudia Teixeira

Selected Publications

1. Papoutsoglou *et al.* (2020). Enabling reusability of plant phenomic datasets with MIAPPE 1.1. *New Phytologist* 227: 260-273. doi: 10.1111/nph.16544.

2. Mina *et al.* (2020). Impact of plant genotype and plant habitat in shaping bacterial pathobiome: a comparative study in olive tree. *Scientific Reports,* 10: 1-11. doi: 10.1038/s41598-020-60596-0

3. Azevedo-Nogueira *et al.* (2020). Development of High-Throughput Real-Time PCR Assays for the *Colletotrichum acutatum* Detection on Infected Olive Fruits and Olive Oils. *Food Chemistry*, 317: 126417. doi: 10.1016/j.foodchem.2020.126417

Key Funded Projects

vWISE – Vine and Wine Innovation through Scientific Exchange, H2020-MSCA-RISE, 874.000€. Partners, 37K€.

PINASTER-PWN – Development of molecular markers for resistance to pine wilt disease in *Pinus pinaster*, PTDC/BAA-MOL/28379/2017. Coordination, 239.613€.

GRAVITAS – Grapevine immunity: the innovative role of subtilisin-like proteases. PTDC/BIA-BQM/28539/2017. Coordination, 235.767€.

FunGP Group

Functional Genomics and Proteostasis

http://bioisi.pt/fungp/

The focus of FunGP research is on Biomedicine in Cystic Fibrosis, neurological disorders and malaria:

1. Translational science into personalized medicine and therapeutic strategies in Cystic Fibrosis.
2. Molecular and cellular mechanisms of secretory traffic of CFTR and CF-related ion channels (anoctamins, SLC26A9).
3. Systems approaches to tackle mechanisms of disease: Cystic Fibrosis and neurodegeneration.
4. Relating protein structural changes to disease states in Alzheimer's Disease (AD) and in mitochondrial rare diseases.
5. Pharmacology of drug resistance and pharmacogenetics, having *Plasmodium falciparum* (malaria) as the main model.

Major Achievements:

Cystic Fibrosis

- Characterization of the macromolecular complexes interacting with CFTR at the plasma membrane and of their regulatory role.
- Establishment of organoids as a personalized medicine tool for ultra-rare mutations in Cystic Fibrosis.
- Mechanism of action of a novel corrector compound rescuing the most frequent Cystic Fibrosis mutant to the cell surface.
- Unveiling the mechanisms of dedifferentiation in Cystic Fibrosis that lead to high cancer propensity.

Neurological disorders

- Discovery of asymmetric post-translational modifications have a major influence in the behavior of protein homodimers.
- 20 new constructs were deposited in a public repository for the study of signaling pathways involved in astrogliosis.
- Establishment of in vitro and in cell models to investigate regulation and mechanisms of aggregation in Alzheimer's Disease and definition of novel anti-aggregation chaperone activities of S100 alarmins.
- Molecular insights into potential beneficial effects of riboflavin supplementation in glutaric aciduria-type I patients.

Malaria

- Identification of a molecular marker for post-treatment protection collapse effect by dihydroartemisinin-piperaquine, a global antimalarial drug.

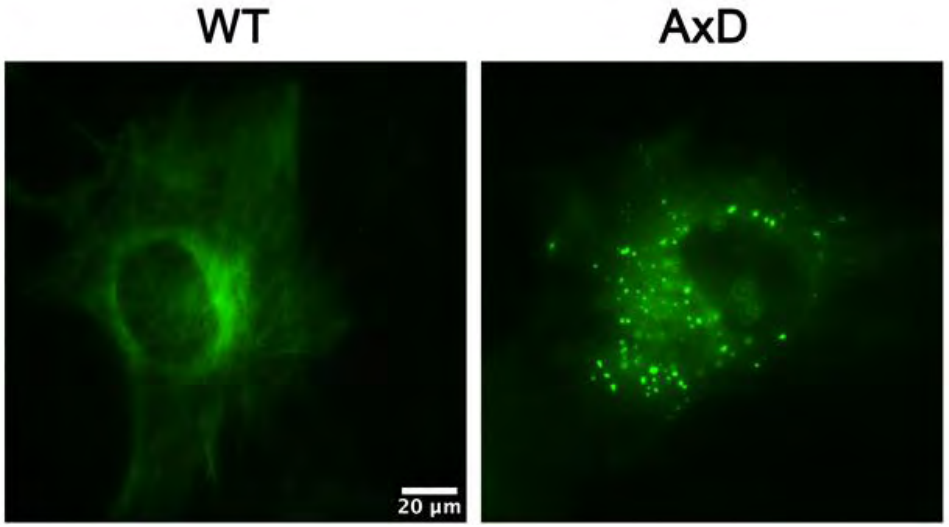


Figure 1: New tools for the visualization of the glial fibrillary acidic protein (GFAP) in living cells. GFAP is an intermediate filament typically found in astroglia, and its mutation causes a neurodegenerative disorder called Alexander´s disease (AxD). GFAP is very reluctant to accept tags in its N- or C-termini, making it very difficult to visualize it in living cells. Using a transposon strategy, we successfully introduced the fluorescent protein EGFP in the middle of the GFAP amino acid sequence. Wild type GFAP-EGFP fusion proteins (WT) produce normal intermediate filament networks, while AxD-related mutation R239C (AxD) produces GFAP aggregation. These new constructs will be extremely useful for the understanding of GFAP function. [In:Letra-Vilela et al (2020) *Experimental Results* **1**: E4. doi:10.1017/exp.2020.1.

Group Members

GL: Margarida D. Amaral

PI's:


Bárbara Henriques


Carlos Farinha


Cláudio Gomes


Hugo Botelho


Federico Herrera


José-Pedro Gil


Luka Clarke


Miquéias Lopes-Pacheco

Post Docs: Andrea Gutierrez | Arthur Kmit | Filipa S. Carvalho | Ines Pankonien | Iris Silva | Mafalda Bacalhau | Mickael Diallo | Patrícia Barros | Sónia Zacarias | Ulrika Morris

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BI Researchers: Cláudia Rodrigues | Guilherme G. Moreira | Joana Serralha

Technicians: Sofia Correia

Selected Publications

1. Santos JD, Pinto FR, Amaral MD, Zaccolo M, Farinha CM (2020). Cytoskeleton regulators CAPZA2 and INF2 associate with CFTR to control its membrane levels under EPAC1 activation. *Biochem J* 477: 2561-2580. doi: 10.1042/BCJ20200287.

2. Quaresma MC, Pankonien I, Clarke LA, Sousa LS, Silva IAL, Railean V, Doušová T, Fuxe J, Amaral MD (2020). Mutant CFTR Drives TWIST1 Mediated Epithelial-Mesenchymal Transition. *Cell Death & Dis* 11: 920. doi: 10.1038/s41419-020-03119-z

3. Ribeiro JV, Gomes CM, Henriques BJ (2020). Functional Recovery of a GCDH Variant Associated to Severe Deflavinylation-Molecular Insights into Potential Beneficial Effects of Riboflavin Supplementation in Glutaric Aciduria-Type I Patients. *Int J Mol Sci* 21: 7063. doi: 10.3390/ijms21197063.

Key Funded Projects

HIT-CF – Personalised Treatment for Cystic Fibrosis Patients with Ultra-rare CFTR Mutations (and Beyond). FCUL budget: 257K€; 5 yrs. PI: K Van der Ent, University Medical Centre Utrecht, (Netherlands). FCUL PI: MD Amaral.

Mechanistic and Optogenetic Control of Astroglia for Neural Repair. Budget: 239K€; 3 yrs. PI: F Herrera; Co-PI: C Santos

ProDysMITO - Mechanisms of Protein Dysfunction in mitochondrial Disease. Budget: 219K €. PI: BJ Henriques; Co-PI: CM Gomes.

MALANGO – Malaria Drug Resistance: Treatment Alternatives and Optimization – a Project Strengthening a National Reference Centre for Anti-Malarial Clinical Trials and Capacity Building in Angola. Budget: 286K€; 2yrs. PI: JP Gil.

M&B Group

Microbiology & Biotechnology

http://bioisi.pt/mb/

M&B-BioISI focused on innovative integrated approaches in M&B areas and on linking group know-how and expertise with SMEs and industry.
R&D translation to society was further achieved through nurturing and promotion of new start-ups, participation of PhD members in SMART FARM CoLAB (with Torres Vedras Municipality), networks of key value chains, partnerships established with SMEs, association with FabLab Lisboa (Lisbon Municipality) and co-involvement in outreach events like Science Days and 2020 International Microorganism Day.
Furthermore, a massive investment was made to participate in COVID-19 pandemics combat by the setting-up and management of a Central Test Center in FCUL (CTC COVID FCUL| Coordinator: R Dias), that also uses part of the Lab Bugworkers|M&B-BioISI facilities, as well as by the participation of some M&B-BioISI members in the Portuguese network for SARS-CoV-2 genomics.

Major Achievements:

Yellow and White M&B

- Selection and integrative analysis of Saccharomyces and non-Saccharomyces yeasts (natural and adaptively evolved) as novel starters for food and wine industry.
- Whole genome sequencing and comparative genomics of non-Saccharomyces yeasts to broaden their application in wine industry and other bio-industries in which they could be explored as cell factories.
- Demonstration of the involvement of other pathways in wine yeast response and adaptation to SO2 beyond SSU1-FZF1 axis
- Atribution of the first biological function to the poorly characterized yeast transcription factor COM2
- Selection of a portfolio of wine yeasts for biocontrol of non-biotrophic grapevine fungi.
- Development of a flow-cytometry assisted method to evaluate the impact of the controlled microalgae cell disruption on the bioavailability of microalgae contents.

Gold and Red M&B

- Management of an unique dedicated computational infrastructure for processing genomic data in real-time (BioISI Genomics) under the cooordination of R Dias.
- Intelligent Decision Support Systems for personalized prevention and clinical management of infectious diseases.
- Intelligent Decision Support Systems for early warning system of SARS-CoV-2 outbreaks.
- Implementation of "Centro de Testes de Ciências ULisboa" (CT Ciências ULisboa), infrastruture dedicated to Biological Risk Management currently focused on SARS-CoV-2 testing and mitigation.
- Collaboration in the Portuguese network for SARS-CoV-2 genomics.
- Identification of biotechnological potential on genomic nonfunctionalized orthologs elements from microbial origin.
- Development and upgrading of the 1st comprehensive annotation pipeline on Microbial Genomic Dark-Matter.
- Extending of yeast STN genetic tools set for biomedical research.
- Surveillance of Aedes albopictus mosquito (dengue vector) in Portugal within the vector surveillance network REVIVE.
- Assessment of genetic relationships in Aedes albopictus populations introduced in Portugal and of their likely route of invasion.
- Development of a new method based on fluorescent in situ hybridization coupled with flow cytometry (FISH-FC) to identify and assess viability of Mycobacterium bovis in environmental matrices.

Blue and Grey M&B

- Nomination of a group member (H Vieira) as General Director of Sea Policy (DGPM).
- Assessment of stakeholder's challenges, implementable actions and business models towards marine bioresources development and blue bioeconomy.
- Identification of bioactives from deep-sea marine bacteria with anti-cancer potential.
- Development of a molecular method for differential identification of oyster species Crassostrea angulata and C. gigas.
- Novel adaptively evolved bacterial strains for biodegradation of FOG (fat, oils and grease) and PAH (polycyclic aromatic hydrocarbons) residues.

Green M&B

- Major contributions in the field of Ascomycete systematics, with with introduction of new families, genera and species.
- Botryosphaeriales web site was launched https://botryosphaeriales.org/ and is now being populated.
- Novel optimized protocol for in situ quantification of relative H2O2 concentrations in infected plant leaves.
- Description of volatile organic compounds produced by pines fed by Monochamus galloprovincialis associated with Pine Wilt Disease.
- First report of Sydowia polyspora associated with associated with current season needle necrosis in Pinus pinea and description of a new species, Pestalotiopsis pini, an emerging pathogen on Pinus pinea.
- Evaluation of the dispersion of the charcoal canker disease caused by the fungi Biscogniauxia mediterranea in cork oaks in different forests in Algeria.
- Development and validation of a novel immune flow cytometric (IFC) method for in planta detection of Erwinia amylovora (causative agent of pear fire blight disease).
- Genomic characterization of emergent and endophytic bacteria associated to forests in Portugal.
- Isolation of phytopathogenic bacteria affecting endangered Olea maderensis endemic of Madeira islands.
- Phylogenetic characterization of Pseudomonas syringae species complex affecting stone fruits in Portugal.
- Validation of RNAseq analysis of differential virulence gene expression in Xanthomonas campestris affecting Brassicaceae.
- Identification of turf-grass diseases through Green Project phytopathology service.

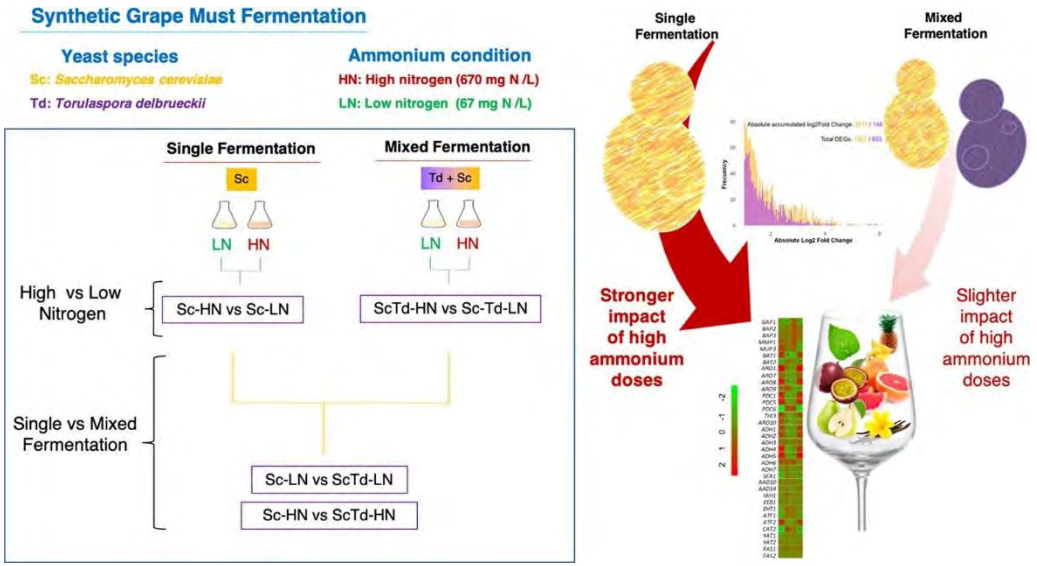

Figure 1: Phenotypic and transcriptional analysis of Saccharomyces cerevisiae during wine fermentation in response to nitrogen nutrition and co-inoculation with *Torulaspora delbrueckii.* .(Graphical Abstract)

.

Group Members

Established Scientists: Ana Reis | João Baptista Ferreira | Abdelhak Lemsaddek | Bruno Jesus | Cristina Houghton | Filipe Costa | Margarida Barata | Maria Helena Bargança | Mónica Cunha | Patrick Freire | Sandra Chaves | Teresa Lemsaddek

PhD Early Scientists: Ana Cristina Inácio | Joana Cruz | Joana Henriques | Patrícia Lage | Daniela Pinto

PhD Students: Pablo Vaglini |Pedro Escudeiro | Tiago Silva | Eugénio Diogo | Isabel Seixas | Marcos Esteves | Ana Cristina Reis | André Pereira | Pedro Teixeira | Diogo Pereira

MSc Students: Sara Filipa Pimpão Cabeça

CLO: Filipa Silva

Selected Publications

1. Giovani B, Blumel S, Lopian R, Teulon D, Bloem S, Martínez C, Montoya CB, Morales C, Dharmapuri S, Timote V, Horn N, Chouibani M, M'Ella J, Herrera V, Castinel A, Goletsos C, Moeller C, Naumann I, Stancanelli G, Bronzwaer S, Tramontini S, MacDonald P, Matheson L, Anthoine G, De Jonghe K, Schenk M, Steinmöller S, Rodriguez E, Cruz ML, Luck J, Fraser G, Brunel S, Montuori M, Fedchock C, Steel E, Pennington H, Rossi JP, Xia J (2020). Science diplomacy for plant health. *Nature Plants* 6, 902–905. doi: 10.1038/s41477-020-0744-x.

2. Phukhamsakda C, McKenzie EHC, Phillips AJL, Gareth Jones EB, Bhat DJ, Stadler M, Bhunjun CS, Wanasinghe DN, Thongbai B, Camporesi E, Ertz D, Jayawardena RS, Perera RH, Ekanayake AH, Tibpromma S, Doilom M, Xu J, Hyde KD (2020). Microfungi associated with Clematis (Ranunculaceae) with an integrated approach to delimiting species boundaries. *Fungal Diversity* 102, 1–203, doi: 10.1007/s13225-020-00448-4.

3. Ruiz J, de Celis M, de Toro M, Mendes-Ferreira A, Rauhut D, Santos A, Belda I (2020). Phenotypic and transcriptional analysis of Saccharomyces cerevisiae during wine fermentation in response to nitrogen nutrition and co-inoculation with *Torulaspora delbrueckii*. *Food Research International* 137, 109663. doi: 10.1016/j.foodres.2020.109663.

Key Funded Projects

MarCODE – Development and application of biochemical tools for marine commercial product tracking. Project PO MAR 2020. 2020-2023. Proponent: FCUL (PI: B Duarte |MARE). Partners: DocaPesca, IPMA. Total funding: 1.257 M€. M&B-BioISI funding: 335 k€. M&B-BioISI Team: A Tenreiro (FCUL), R Tenreiro (FCUL) and R Dias (FCUL).

ABCyeasts – A portfolio of antagonist yeasts for biocontrol of phytopathogenic agents in a sustainable winemaking. Project 39793 - FEDER through N2020. 2019-2022. Promotor: Proenol Indústria Biotecnológica SA. Co-Promotors: UTAD and ADVID (Associação para o Desenvolvimento da Viticultura Duriense). Partner: Sogrape Vinhos SA. Total funding: 1.007 M€. UTAD/BioISI funding: 453 K€. M&B-BioISI Team: A Mendes-Ferreira (UTAD), A Mendes-Faia (UTAD), A Tenreiro (FCUL) and R Tenreiro (FCUL).

Predikt – Predicting Infectious Disease Outbreaks and Patients at Risk. Portugal 2020. 2020-2021. Promotor: MaxData. Funding: undisclosed. M&B Team: R Dias (FCUL).

BTR Group

Biomedical and Translational Research

http://bioisi.pt/btr/

Understanding how genetic, epigenetic, clinical, lifestyle and environmental determinants and modulators interact to influence health, disease and treatment efficacy; integrating large human datasets and translating findings into personalized medicine tools for improved diagnosis and intervention using systems Medicine frameworks.

Major Achievements:

- An update of the results of the Portuguese FH Study was published and novel genes contributing to the FH phenotype are being characterized. A very interesting population sample of 134 homozygous familial hypercholesterolemia (HoFH) individuals from Iberoamerica (71 adults and 63 children) was analyzed, showing a high frequency of cardiovascular disease, even in children. Phenotype and cardiovascular complications were heterogeneous and associated with the type of molecular defect.
- We continued to study biomarkers for ARHL and Tinnitus in an older Portuguese population, to identify associations between these conditions and genetic and inflammatory markers. Our results reinforce the idea that inflammatory mechanisms are involved in hearing loss pathogenesis but also in Tinnitus with IL10 levels appearing to be significantly altered in tinnitus but not in hearing loss.
- Analysing large databases of genomic data for individuals with Autism Spectrum Disorder we identified potentially pathogenic genetic variants in regulatory processes mediated by regulatory RNAs, including miRNAs, lncRNAs, and NMD-mediated decay. . In the context of GEnvIA project, we identified several genes involved in the regulation of the body's permeability to xenobiotics responsible for gene-environmental interactions.
- In the context of the 1+Million Genome initiative, we were awarded the CSA Beyond 1 Million Genomes, and initiated the development of activities to facilitate the implementation of Genomic Medicine and data sharing across borders in Europe.
- With the International Consortium of Personalised Medicine, we developed a vision for Personalised Medicine in 2030, focusing on the perspectives for citizens, health professionals, health systems, information and data, and economic value (https://www.icpermed.eu/en/activities-vision-paper.php)
- Contributing to the scientific effort for the COVID-19 pandemic, we collaborated in the development and data analysis of a mental health survey for the study SM-COVID – Mental Health in pandemic times. This study highlighted the increased anxiety and psychological distress of the population in general and, in particular, of healthcare professionals treating COVID-19 patients.

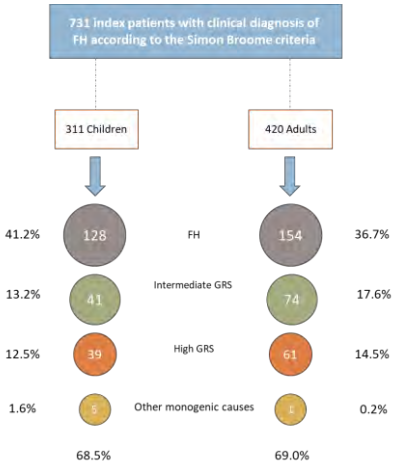

Figure 1 – Number of index cases, children and adults, referred to the Portuguese Familial Hypercholesterolaemia (FH) Study with Simon Broome FH clinical criteria divided by the different causes of the FH phenotype and percentages of identification rate by group and total. FH refers to patients with pathogenic or likely pathogenic variants in either LDLR, APOB or PCSK9, intermediate GRS (genetic risk score) to patients with a LDL-C GRS between P25th and P75th, high GRS to patients with GRS above P75th.

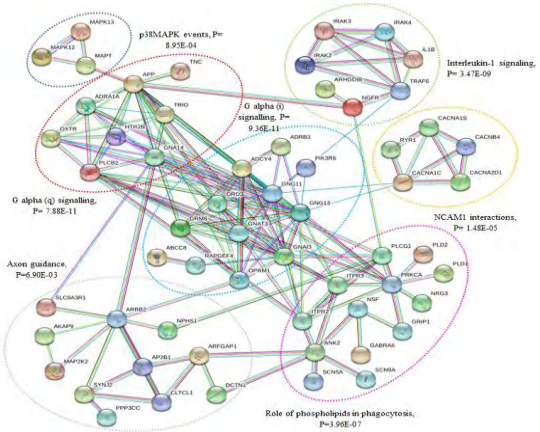

Figure 2 Protein-protein interaction network of Neurotranmissor and Synaptic genes targeted by ultra-rare SNVs. Each biological community is highlighted with a circle in a specific colour. Pathways with best p-value are indicated near the correspondent community.

Group Members

GL: Astrid Vicente

PI's:


João Lavinha


Helena Caria


Helena Mota Vieira


Mafalda Bourbon

Post Docs: Ana Catarina Alves | Celia Rasga | Cláudia Branco | Tiago Matos |Renato Pires | Hugo Martiniano | Sonija Luzi | Maria Luis Cardoso

PhD Students: Ana Margarida Medeiros|Ana Rita Marques (BioSYS) Joana Chora | João Pedro Santos (BioSYS) | Niccolo Rosi (BioSYS)| Marta Correia (BioSYS) | Rafael Graça (BioSYS)| Joana Vilela (BioSYS) |João Albuquerque | Nilda Tatiana Ramos

Master students: Micaela Santos

Technicians: Joana Duarte| Lisa M Esteves | Maria Luis Cardoso (PhD)

Selected Publications

1. Alves AC, Alonso R, Diaz-Diaz JL, Medeiros AM, Jannes CE, Merchan A, Vasques-Cardenas NA, Cuevas A, Chacra AP, Krieger JE, Arroyo R, Arrieta F, Schreier L, Corral P, Bañares VG, Araujo MB, Bustos P, Asenjo S, Stoll M, Dell'Oca N, Reyes M, Ressia A, Campo R, Magaña-Torres MT, Metha R, Aguilar-Salinas CA, Ceballos-Macias JJ, Morales ÁJR, Mata P, Bourbon M, Santos RD (2020). Phenotypical, Clinical, and Molecular Aspects of Adults and Children With Homozygous Familial Hypercholesterolemia in Iberoamerica. *Arterioscler Thromb Vasc Biol*. 40(10):2508-2515. doi: 10.1161/ATVBAHA.120.313722.

2. Mariano C, Alves AC, Medeiros AM, Chora JR, Antunes M, Futema M, Humphries SE, Bourbon M (2020). The familial hypercholesterolaemia phenotype: Monogenic familial hypercholesterolaemia, polygenic hypercholesterolaemia and other causes. *Clin Genet.* 97(3):457-466. doi: 10.1111/cge.13697.

3. Rosa J, Gaspar-Silva P, Pacheco P, Silva C, Branco CC, Vieira BS, Carreiro A Gonçalves J Mota-Vieira L (2020). A comprehensive overview of the cystic fibrosis on the island of São Miguel (Azores, Portugal). *BMC Pediatrics* 20(1) doi: 10.1186/s12887-019-1903-y

Key Funded Projects

Beyond 1+M Genomes (BMG) Coordinating and Support Action Funded by DG-CONNECT Total Budget €4M, Budget INSA €257148 WP leader Astrid Vicente, Collaborator Mafalda Bourbon, Maria Luis Cardoso

Saúde Mental em Tempos de Pandemia COVID-19 (SM-COVID19). Funded by FCT, Special support applications from the RESEARCH4COVID19 Program. Ref nº 279_596885124, total budget 29.500,00€, Collaborator Astrid Vicente, Célia Rasga, Hugo Martiniano

GER Group

Gene Expression and Regulation

http://bioisi.pt/ger/

GER aims to generate a mechanistic and quantitative understanding of gene expression processes at the molecular, cellular and systems level that can be harnessed to predict and manipulate the behaviour of biological systems for useful applications, namely in human health and disease.

Major Achievements:

- **Non-coding genome:** Development and adaptation of sequencing, molecular and bioinformatics methodologies for the study of Sat DNAs and their transcripts, following the concept of 'chromosomics'.
- **RNA processing, translation & decay:** Demonstration that the uORF-mediated translational regulation of PERK is involved in cell homeostasis and human disease; and that uORFs regulate the translation of the human ABCE1 transcript.
- **Modelling of Biological Systems:** Completion of an extensive model of ENaC regulation, including the metabolic network of phosphoinositide metabolism and ASL dynamics. Development of models for the classification of monogenic and polygenic/environmental dyslipidaemias using new blood biomarkers through the application of machine learning approaches.
- **Signaling Pathways:** The phosphorylation of splicing factor SRSF1 by kinase SRPK1 and subsequent nuclear translocation is controlled by a WNK1/GSK3β complex and inhibited by the drug ibuprofen.
- **miRNAs in disease:** Demonstration that the host miRNA machinery can be hijacked by parasites to modulate the immune response. Identification of predictive and prognostic profiles of circulating tumour cell associated microRNAs in advanced rectal cancer.
- **Regulation of neuronal function:** elucidating the role of VIP expressing interneurons and VIP receptors in the regulation of hippocampal synaptic plasticity. Mapping of common gene functional modules affected in Amyotrophic Lateral Sclerosis and Spinal Muscular Atrophy.
- **Network Biology:** Benchmark comparison of network disease module overlap prediction methods across multiple biological networks.

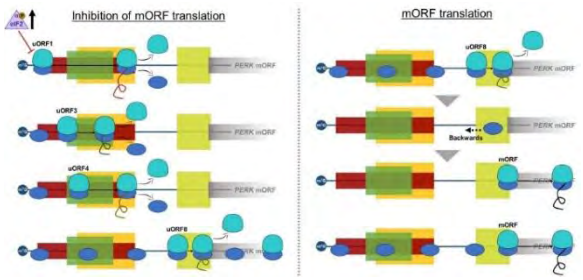

Figure 1. Working model for PERK uORF-mediated translational regulation.

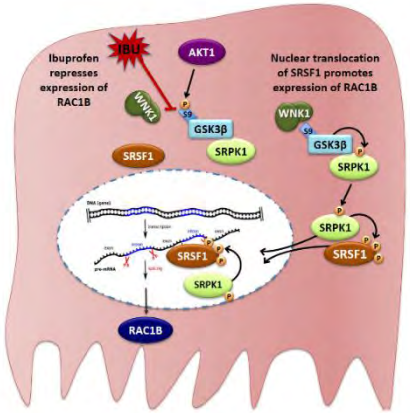

Figure 2: Proposed model for how ibuprofen inhbits the expression of alternative splicing variant RAC1B

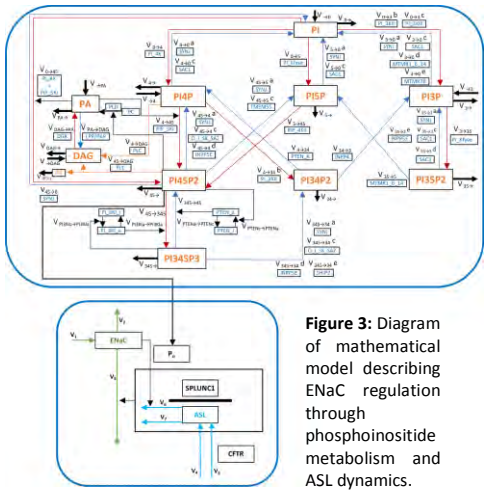

Figure 3: Diagram of mathematical model describing ENaC regulation through phosphoinositide metabolism and ASL dynamics.

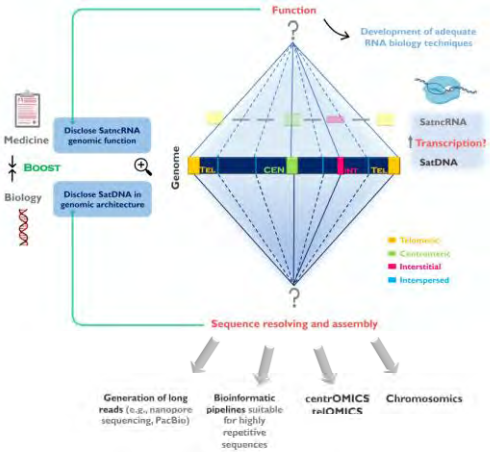

Figure 4: Technical challenges in the study of Sat-DNAs.

Selected Publications

1. Louzada S, Lopes M, Ferreira D, Adega F, Escudeiro A, Gama-Carvalho M, Chaves R (2020). Decoding the Role of Satellite DNA in Genome Architecture and Plasticity—An Evolutionary and Clinical Affair. *Genes* 11(1), 72. doi: 10.3390/genes11010072.

2. Gonçalves V, Henriques AFA, Matos P, Jordan P (2020). Ibuprofen disrupts a WNK1/GSK3β/SRPK1 protein complex required for expression of tumor-related splice variant RAC1B in colorectal cells. *Oncotarget* 11:4421-4437. doi: 10.18632/oncotarget.27816.

3. Loureiro CA, Pinto FR, Barros P, Matos P, Jordan P (2020). A novel SYK/SHC1 pathway regulating the amount of CFTR in the plasma membrane. *Cellular and Molecular Life Sciences* 77, 4997–5015. doi: 10.1007/s00018-020-03448-4.

Group Members

GL: Margarida Gama-Carvalho

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Other researchers: Cláudia Estima | Sofia Conceição | Fábio Resende | Daniel Eleutério| Diogo Lucas | Juliana Miranda | Ana Rocha | Joana Niza | José Rosa | Maria Silva | Rita Marques | Telma Rosado | Filipa Pereira | Fiviano Santos | Inês Costa | Cláudia Costa | Filipa Rita | Maria Neto | Margarida Pedro | Mariana Almeida | Ana Queiroz

Key Funded Projects

miRiAD - Exploring the role of microRNAs in T cell function and anti-HIV defense PTDC/BIA-CEL/29257/2017, October 2018-September 2021 Budget: 240K€

Microenvironmental effects on alternative splicing in malignant progression of colorectal tumor cells induced by an inflammatory microenvironment PTDC/BIA-MOL/28386/2017, October 2018-September 2021 Budget: 240K€

PulmaGene - Análise genética ao sangue para guiar a terapia de pacientes com carcinoma do pulmão de não pequenas células (CPNPC) - NORTE-01-0247-FEDER-033533. Financiado pelo Portugal2020. Promoter: STABVida Budget: 680.902,52€.

CBS Group

Chemistry for Biological Systems

http://bioisi.pt/cbs/

CBS research embraces several complementary topics namely: a) synthesis of molecules for applications in catalysts, in magnetic systems for spintronics, and in green systems for artificial photosynthesis or antifouling; b) discovery of drug leads or bioactive compounds from marine organisms, algae, food components, industrial waste, and medicinal herbs; c) in silico prediction and interpretation of reaction mechanisms and magnetic or photochemical properties); d) development of simulation methods to study solvation and solubility effects, the pH effect in drugs, peptides, proteins, and lipid bilayers, or to explore molecular recognition phenomena; e) elucidation of processes of energy transduction, with specific emphasis on the molecular mechanisms of electron transfer, ion translocation and their coupling.

Major Achievements:

- We expanded the research on carbon dioxide conversion by establishing partnerships with Industrial companies and European consortia, and developed an eco-friendly antifouling coating strategy against multi-resistant bacteria;
- We developed a new scalable python-based method to easily calculate pKa values in proteins and a computational protocol to identify potential membrane PAINS which are compounds that influence the function of membrane proteins by non-specific perturbation;
- We showed that hydration entropy, scaled by the solvent accessible surface area, is a universal property for small aliphatic and aromatic hydrocarbons, but not for similar size/shape amphiphilic solutes, due to long range electrostatic interactions.
- Using a metabolomics approach, we showed that *Fucus vesiculosus*, an edible brown alga, affects the lipid metabolism mainly by changes introduced in the fatty acids' amides and n-acylethanolamines, and demonstrated, by MD simulations, that membrane-ligand interactions can be mediated by halogen bonds, a mechanism previously overlooked in drug-design;
- We validated of a GC-MS methodology for the detection of psychoactive cathinones in blood and showed how substituents play a role in photo-switching rates in azobenzene derivatives;
- We performed a thorough bioinformatics approach on the structural conservation and taxonomic distribution of dihydroorotate:quinone oxidoreductases which are key enzymes in both the de novo pyrimidine biosynthetic pathway as well as in energy metabolism.

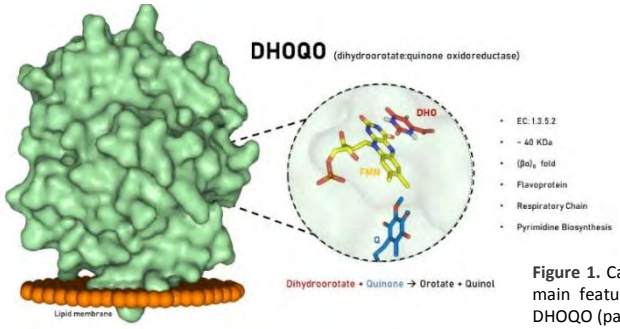

Figure 1. Cartoon illustrating the structure, reaction and main features of the DHOQO protein family. *E. coli*'s DHOQO (pale green), lipid membrane (orange), DHO (red sticks), FMN (yellow), and quinone (blue).

Figure 2. Spin lability is highly affected by the ligand design and external

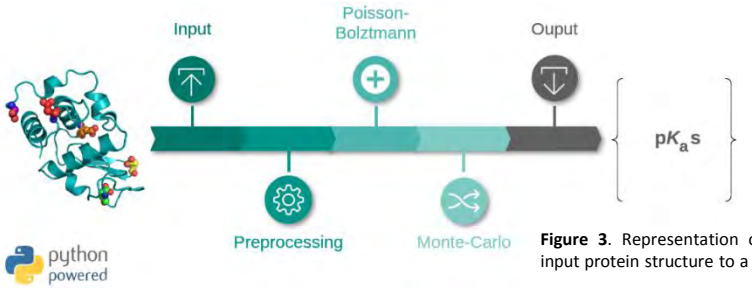

Figure 3. Representation of PypKa's pipeline from an input protein structure to a final set of pKa values..

Selected Publications

1. Antunes M, Sequeira M, Pereira MC, Caldeira MJ, Santos S, Franco J, Barroso M, Gaspar H (2020). Determination of Selected Cathinones in Blood by Solid-Phase Extraction and GC–MS. J. *Anal. Toxicol*., bkaa074. doi: 10.1093/jat/bkaa074.

2. Ferreira O, Rijo P, Gomes JF, Santos R, Monteiro S, Vilas-Boas C, da Silva MC, Almada S, Alves LG, Bordado JC, Silva ER (2020). Biofouling Inhibition with Grafted Econea Biocide: Toward a Nonreleasing Eco-Friendly Multiresistant Antifouling Coating. *ACS Sustainable Chem. Eng.* 8(1) 12–17. doi: 10.1021/acssuschemeng.9b04550.

3. Reis PBPS, Vila-Viçosa D, Rocchia W, Machuqueiro M (2020). PypKa: a flexible Python module for Poisson–Boltzmann based pKa calculations. *J. Chem. Inf. Model*. 60(10), 4442-4448. doi: 10.1021/acs.jcim.0c00718.

Group Members

GL: Manuela M. Pereira

PI's:


Paulo Costa


Mª Luísa Serralheiro


Miguel Machuqueiro


Bruno Victor


Helena Gaspar


Paulo Martinho


Vukosava Torres


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Nuno Galamba

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PhD Students: Diogo Silva | Filipa Sena | Filipe Sousa | Jiawei Wang | Joana Matos | Olga Ferreira | Pedro Reis | Rafael Nunes | Rebeca André | Tomás Silva

MsC Students: Andreia Fortuna | Bárbara Correia | Beatriz Lopes | Bernardo Henriques | Diogo Reis | Filipe Rodrigues | Jéssica Catarino | Jéssica Marques | João Vitorino | José Dias | Marcos Bento | Constança Lorena | Nuno Oliveira | Pedro Suzano | Rafaela Marques | Sara Ferreira | Beatriz Farinha | Raquel Ferro | Mariana Coelho | Ana Duarte | Sofia Pinto | Vanessa Esteves

Key Funded Projects

Uncovering blind spots in halogen bonding applications, PTDC/QUI-QFI/28455/2017. Total Funding: 239 399.61 € (PI: P. J. Costa)

Deal with PAINS: strategies to identify membrane modulators, PTDC/BIA-BFS/28419/2017. Total Funding: 239 399.61 € (PI: Bruno L. Victor; Co-PI: Miguel Machuqueiro)

Metabolic odyssey of Staphylococcus aureus, PTDC/BIA-BQM/28827/2017. Total Funding: 233 254.12 € (PI: M. Pereira)

Molecules for Health: cholesterol absorption, and expression of its transporter proteins, interactions with drugs, PTDC/BIA-BQM/28355/2017 . Total Funding: € 232 723.40 (PI: L. Serralheiro)

Novel eco-friendly Antifouling Strategies based on Cyanobacterial bioactive Metabolites, PTDC/BTA-BTA/31422/2017. Total Funding: € 232 723.40 (PI: E. Silva)

Bio-PhysNano Group
Bio-Physics & Nanosystems

http://bioisi.pt/biophysnano/

The main goal of the Bio-PhysNano group is to understand and to improve the characterization of biosystems by studying them as physical systems, and to develop adequate instrumentation and theoretical tools. The group comprises 2 teams:

- **MagNano** (Magnetism and Nanosystems) team develops experimental/theoretical research centred in the study of nanostructured systems electronic properties and nanoscale experiments using atomic force microscopy techniques.
- At **PBS** (Physics of Biological Systems) the main focus is protein physics. Innovative methods are developed for a theoretical, physics based approach to the understanding of proteins, as well as other quantum and classical complex systems.

Major Achievements:

- Protein physics: review of the early phase of β2-microglobulin aggregation focusing on the monomers triggering aggregation and the initial small oligomers formed in the nucleation phase, based on results from molecular simulations [Loureiro Rui J. S., et al, Frontiers in Molecular Biosciences 7: 278, 2020]; review on knotted proteins highlighting the contributions in the scope of lattice Gō models in the context of experimental/theoretical results and other computational approaches [Nunes, A., et al. Contemporary Mathematics 746:155-184 2020]
- AFM/FFM: the Force Feeback Microscope was used to advantage in the study of human bronchial epithelial cells (wt-CFTR and F508del-CFTR) mechanical properties [A.P. Carapeto, et al., Int. J. Mol. Sci. 21(8), 2916, 2020]; using the FFM technique a new set of mechanobiology experiments on glioma cells was launched; AFM analysis of the membrane surface mechanical properties in response to abiotic stresses (Arabidopsis taliana secondary roots-wt, single ateca4 and cap1 mutant lines) planned for 2020, was severely hindered by the confinement restrictions and equipment failure.
- Magnetic nanoparticles for biomedical applications: water-based ferrofluids of biopolymer-coated iron oxide nanoparticles were produced; synthesis/coating parameters were varied to infer the impact on nanoparticle size, size distribution and water dispersibility; pectin-containing coatings systems have shown enhanced quality concerning magnetic fluid hyperthermia applications - corresponding biocompatibility studies have been initiated; anisotropic magnetic nanoparticles aiming at improved heating efficiency, were produced and characterised.
- Atomic/electronic structure: theoretical results for the magnetic shielding of protonated/unprotonated nitrogens of eumelanin building blocks, in gas phase and water, using Monte Carlo statistical mechanics sampling combined with quantum mechanics calculations [Leonardo B.A. Oliveira, et al, Molecules 25, 3616, 2020]; new theoretical and empirical values of average L shell fluorescence yields of elements with $23 \leq Z \leq 96$. [[Y. Sahoune, et al, Rad. Phys. Chem. 166, 108495 2020]

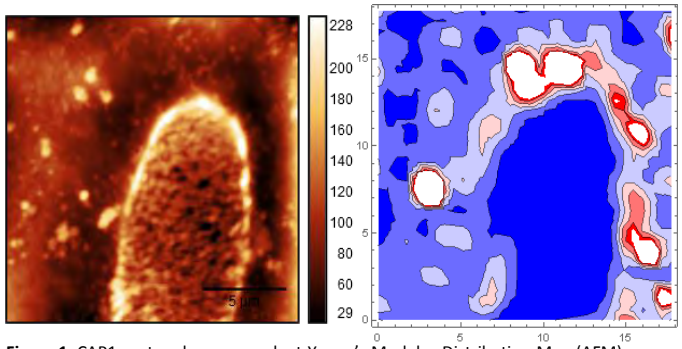

Figure 1. CAP1 root and correspondent Young's Modulus Distribution Map (AFM)

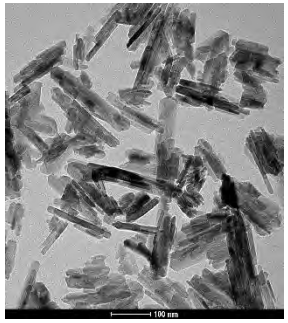

Figure 2. TEM image of goethite nanoparticles as precursors to high aspect ratio magnetite

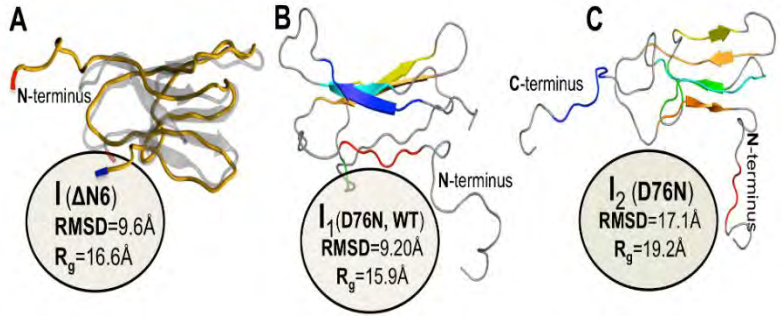

Figure 3. Aggregation prone intermediate states of b2m

Group Members

GL: Maria Margarida Godinho

PI's:

Ana Nunes

M.M. Cruz

José Pires Marques

Benedito Cabral

Liliana Ferreira

Patrícia Faísca

Mário Rodrigues

Post Docs: Ana Carapeto | Jules Morand | Miguel Vitorino |Bernardo Cardoso

Other integrated members: Margarida Pires | António Casaca | M. Estrela M. Jorge | Tânia Ramos | Abdollah Hajalilou (until Oct.2020)) | Gabriel Martins

PhD Students: João P Santos (BioSYS, with BTR, ongoing) | João Especial | Cíntia Veiga

Master Students: **João Freitas** (Eng. Fsica, concluded Sept 20) | Ana Sofia Fonseca (Eng. Fiisca) ongoing

Other Collaborators: T. P. Gasche | Fernando Parente | Andrea Parisi | Ganna Rozhnova | Tomás Aquino

Selected Publications

1. Loureiro RJS, Faísca PFN (2020). The Early Phase of β2-Microglobulin Aggregation: Perspectives From Molecular Simulations. *Frontiers in Molecular Biosciences* 7: 278. doi: 10.3389/fmolb.2020.578433.

2. Cristóvão J, Figueira A, Carapeto AP, Rodrigues MS, Cardoso I, Gomes CM (2020). The S100B alarmin is a dual-function chaperone suppressing Aβ oligomerization through combined zinc chelation and inhibition of protein aggregation. *ACS Chemical Neuroscience* 11(17), 2753–2760. doi: 10.1021/acschemneuro.0c00392.

3. Besenhard MO, LaGrow AP, Hodzic A, Kriechbaum M, Panariello L, Bais G, Loizou K, Damilos S, Cruz MM, Thanh NTK, Gavriilidis A (2020). Co-precipitation synthesis of stable iron oxide nanoparticles with NaOH: New insights and continuous production via flow chemistry. *Chemical Engineering Journal* 399, 125740. doi: 10.1016/j.cej.2020.125740.

Key Funded Projects

FCT Call Research 4 Covid-19 131_596787873 – "Making the way out: model-based evaluation of exit strategies from the COVID-19 lock-down in Portugal"; Total amount of the project: 17.490€; PI:G. Rozhnova

The Physical Basis of Disease: The case of dialysis related amyloidosis, FCT project grant, start date: 04/10/2018 – 3 years; Total amount - 195.145€; BioISI total amount – 195.145€; PI: P. Faísca

Organized Magnetic Nanoparticles, FCT project grant, start date: 01/09/2018 – 3 years; Total amount - 232.888€; BioISI total amount – 215.145€; PI: M.M. Cruz

Theoretical design of molecular machines with applications in organic photovoltaics and solar thermal storage, FCT project grant, start date:01/08/2018 – 3 years; Total amount : 232.675€; BioISI total amount - 232.675€; PI: B.J. Cabral

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MAS Group
Agent and Systems Modelling

http://bioisi.pt/mas/

MAS research focuses on three main themes in the area of artificial intelligence:

- Data mining and knowledge discovery
- Agent and multi-agents systems, which includes research in mobile robotics, artificial life, and natural language
- Complex multi-agent systems, including agent visualisation and animation, and social simulation

Major Achievements:

- Two PhDs completed, António Manso (Comp. Sci.), Nuno Henriques (Cog. Sci.)
- Coelho, H. 2 Décadas de Progresso da IA: Novos Desafios, (invited talk) ENEI 2020, Fevereiro 24, Braga, 2020.
- New results in combinatorial game theory, J. Neto

This report refers to 9 months of activity due to the extintion of MAS Group on September 2020

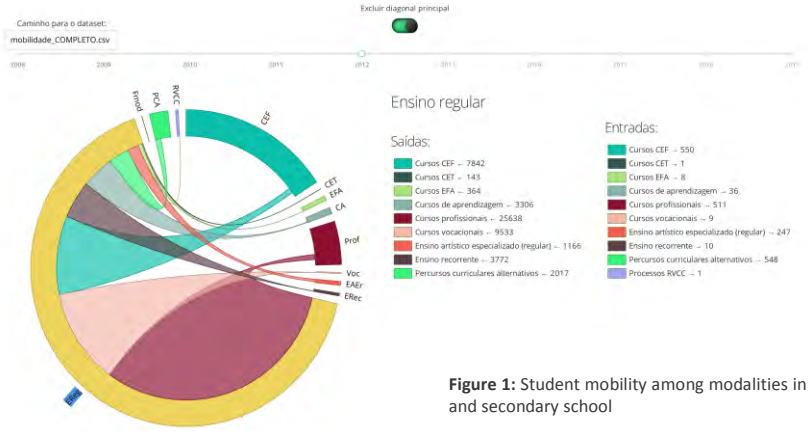


Figure 1: Student mobility among modalities in the basic and secondary school

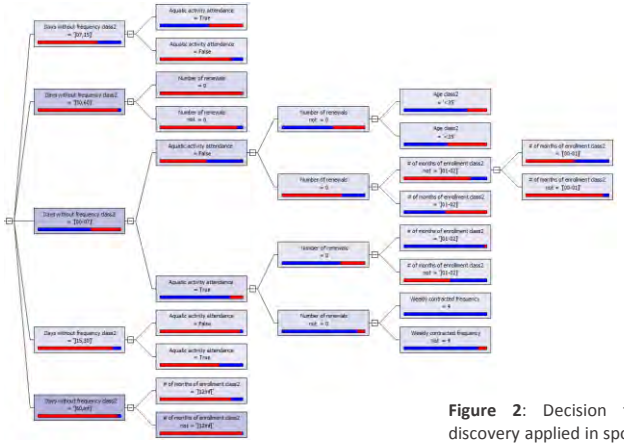


Figure 2: Decision tree of actionable knowledge discovery applied in sports services

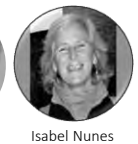
Group Members

GL: Luís Correia

PI's:

Ana Paula Cláudio

Hélder Coelho



Isabel Nunes

Beatriz Carmo

Luís Cavique

Pedro Mariano

João Neto

Graça Gaspar

Post Docs: Paulo P. Matos

PhD Students: Cláudio Reginaldo | Davide Nunes | Nuno Henriques | António Manso | Carlos Geraldes

Selected Publications

1. Cruz-Filipe L, Gaspar G, Nunes I (2020). Hypothetical answers to continuous queries over data streams. *Proceedings of AAAI*, 2798-2805.

2. Balsa J, Félix I, Cláudio AP, Carmo MB, Costa e Silva I, Guerreiro A, Guedes M, Henriques A, Pereira Guerreiro M (2020). Usability of an Intelligent Virtual Assistant for Promoting Behavior Change and Self-Care in Older People with Type 2 Diabetes. *Journal of Medical Systems* 44, 130. doi: 10.1007/s10916-020-01583-w.

3. Marques da Silva J, Figueiredo A, Cunha J, Eiras-Dias JE, Silva S, Vanneschi L, Mariano P (2020). Using Rapid Chlorophyll Fluorescence Transients to Classify *Vitis* Genotypes. *Plants* 9(2), 174. doi: 10.3390/plants9020174.

Key Funded Projects

Train4Health - Improving healthcare students' competences for behaviour change to effectively support self-care in chronic diseases. Start Sep 2019, duration 3 years, funded by Agência Nacional Erasmus+ Educação e Formação. Total amount for BioISI: 43.400,00€. BioISI team PI: A.P. Cláudio

ModEst - Student flow modelling in the Portuguese educational system. Start: Jan 2019, duration 3 yrs. Proj. nr. DSAIPA/DS/0039/2018, funded by FCT. Total amount for BioISI: 247 k€. Project PI: L. Correia

INTERPHENO - An interdisciplinary approach to high throuput phenotyping in plants. Start: Sep 2018, duration 3 yrs. Proj. nr. PTDC/ASP-PLA/28726/2017, funded by FCT. Total amount for BioISI: 173 k€ (w/ PFG). Project co-PI: P. Mariano

At BioISI, facilities are an important instrument to recruit the most talented young scientists and significantly contribute to advanced training: PhD, MSc students, workshops. In 2018-2022, resources will be applied to maintain, update, and support BioISI facilities with expert staff, so that their usage can be applied to maximize expertise and technologies to solve specific biological problems.

Main Goals:

1. Providing excellent services with state-of-the-art equipment, user support and appropriate computational infrastructure;
2. Turning BioISI into a key player in the operation of the next generation of biological research infrastructures within ULisboa;
3. Open labs to society initiatives (FabLabs as proposed by the PRP-National Reform Plan for Portugal) by which citizens, companies, researchers and public institutions work together (in co-creation) to innovate faster and more effectively.

High-Throughput Screening Facility

http://fculmf.campus.ciencias.ulisboa.pt

Coordinator: Hugo Botelho

The High-Throughput Screening Facility is a research infrastructure for spectroscopy and image-based screening. It provides services, technical support and training on Automated Microscopy, High-Content Screening, plate reader-based assays, bioimage analysis and data processing. The Facility integrates two research infrastructures in the national roadmap: PT-OPENSCREEN (National Infrastructure for Genetic and Chemical Biology) and PPBI (Portuguese Platform of Bioimaging). It is also part of the Portuguese node of Euro-BioImaging ERIC.

Major Projects

- High-throughput screening of genes, compounds and natural products regulating the secretory traffic of the CFTR protein.
- Screening of genes affecting cell proliferation and differentiation in cystic fibrosis.
- Identification of drug-responsive individuals to inform therapeutic intervention in cystic fibrosis (forskolin-induced swelling of intestinal organoids).
- High-Content data analysis pipelines.

Main Publications:

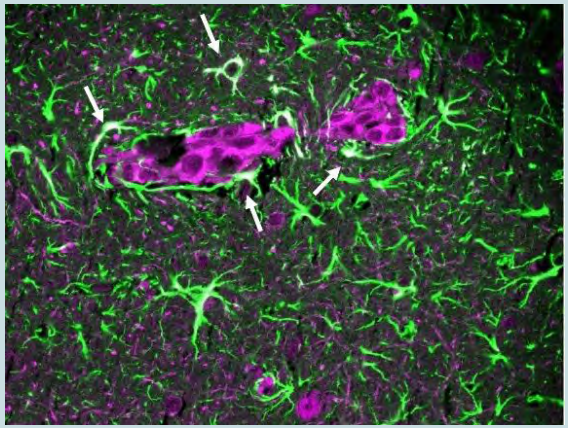
- Biochem Pharmacol (2020) 180, 114133 - Characterization of the mechanism of action of RDR01752, a novel corrector of F508del-CFTR (Lopes-Pacheco *et al*)
- Int J Mol Sci (2020) 21,6717 - Impact of KLF4 on Cell Proliferation and Epithelial Differentiation in the Context of Cystic Fibrosis (Sousa *et al*)
- Cells (2020) 9, 1607 - KLF4 Acts as a wt-CFTR Suppressor through an AKT-Mediated Pathway (Sousa *et al*)
- Biochim Biophys Acta Mol Basis Dis (2020) 1866(11):165905 - Organoids as a personalized medicine tool for ultra-rare mutations in cystic fibrosis: The case of S955P and 1717-2A > G (Silva *et al*)
- Cell Death Dis (2020) 11(10):920 - Mutant CFTR Drives TWIST1 mediated epithelial–mesenchymal transition (Quaresma *et al*)

Technicians: Luís Marques | Aires Duarte

(BioISI/FCUL) Microscopy Facility

http://fculmf.campus.ciencias.ulisboa.pt/

Coordinator: Rui Malhó; Co-coordinator: Hugo Botelho



BioISI Microscopy Facility is a research and training infrastructure for microscopy and bioimaging integrated in the FCUL campus. The facility is also a node of the Portuguese Platform of Bioimaging.
BioISI Microscopy Facility functions as a service provider and technical support hub on stereo, widefield fluorescence, confocal and electron microscopy. It also supports its users in image analysis and quantification.

Major Projects

- Three-dimensional imaging of human tissue: characterization of protein expression, tissue architecture and pathological changes.
- Live imaging of fluorescent dyes and molecular constructs in plant cells for the functional characterization of signaling pathways – analysis of protein, lipid and ion dynamics.
- Ultrastructural characterization of plant tissues with scanning electron microscopy.

Main Publications:

- Front Cell Dev Biol (2020) 12(8): 337 - Liquid-ordered phase formation by mammalian and yeast sterols: a common feature with organizational differences (Khmelinskaia *et al*)
- Mol Oncol (2020) 14(3):520-538 - Downregulation of circulating miR 802-5p and miR 194-5p and upregulation of brain MEF2C along breast cancer brain metastasization (Sereno *et al*)
- Int J Mol Sci (2020) 21, 6717 - Impact of KLF4 on Cell Proliferation and Epithelial Differentiation in the Context of Cystic Fibrosis (Sousa *et al*)

Technicians: Luís Marques | Telmo Nunes

BioISI Genomics
Biosystems and Integrative Sciences Institute
Bringing Knowledge to you: anyTime anyWhere

BioISIGenomics

http://bioisi.pt/services-and-facilities | genomics@bioisi.pt

Coordinators: Ricardo Dias & Margarida Gama-Carvalho

Vision: The BioISI Genomics Facility Vision is to deliver innovative knowledge production from biological systems to research and industry through state-of-the-art biomolecular sensing, following the motto 'anything, anywhere'. The implementation of BioISIGenomics aims to support and consolidate the concept of Biology 4.0 and to empower the scientific community in the development path towards the fields of Digitization of Life and Synthetic Biology.

Mission: The Facility's Mission is centered around the multi-site production of high-quality omics data from multiple biological sources based on biomolecular nanopore sensing technologies. The facility functions both as a basic infrastructure support for the research activities developed at BioISI/FCUL and as a provider of external services to the global research community and industry partners, constituting an International Refence Hub for innovation and development in the field of molecular genomics. The deliverables are the knowledge generated by the data analysis and integration.

Activities & Achievements:

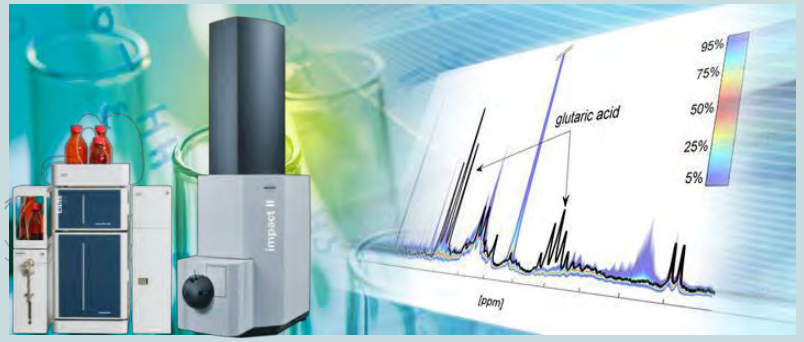
- Development of protocols and workflows for a set of novel services (ISIGen Services) focusing on:
  - Metataxonomic, metagenomic and functional classification;
  - Real-time detection of pathogenic organisms in plants and humans;
  - Analysis of SARS-CoV-2 gene variants;
  - Fast genome assembly platform for Nanopore genomic sequencing data.
- External dissemination of advantages of nanopore sensing technologies and available services;
- Active participation in the main national & international funding programs;
- Generation of the first whole human genome sequencing datasets from native DNA in Portugal;
- Affiliation as Full member at the GenomePT – National Infrastructure for Genome Sequencing and Analysis.

Technicians: Mariana Nascimento | Marcelo Pereira | Pedro Pascoal

Mass Spectrometry Facility

Coordinator: Maria Luisa Serralheiro

BioISI Mass Spectrometry Facility is a research infrastructure for mass spectrometry analyses integrated in the FCUL campus.
BioISI Mass Spectrometry Facility major functions concern the fields of metabolomics and proteomics. It works as a service provider (academic environment and industry) for sample analysis through UPLC-MS/MS (QToF) and/or FIA (flow injection analysis).



Major Projects:

- Screening, identification and quantification of several compounds, *food chemistry* (e.g. algae, cholesterol).
- Effect of algae compounds in *cells metabolomics* (different processes of extraction).
- Analysis of the degradation process of several compounds, *the environmental chemistry*.
- Screening and identification of several compounds throughout the fermentation process of wine samples, *wine metabolomics*.
- Screening of several compounds, *forensic chemistry*.
- Exact mass determination in synthetic chemistry

Academic and Industry Analysis:

- Academic Analysis: 271 (BioISI); 8 (Outside)
- Industrial Analysis: 3

Outputs:

- Papers in peer rev journals: 4 (published); 3 (submitted); 2 (metabolomics in preparation);
- MSc Thesis: 2
- Scholar reports: 1

Technician: Rita Guedes

Physics

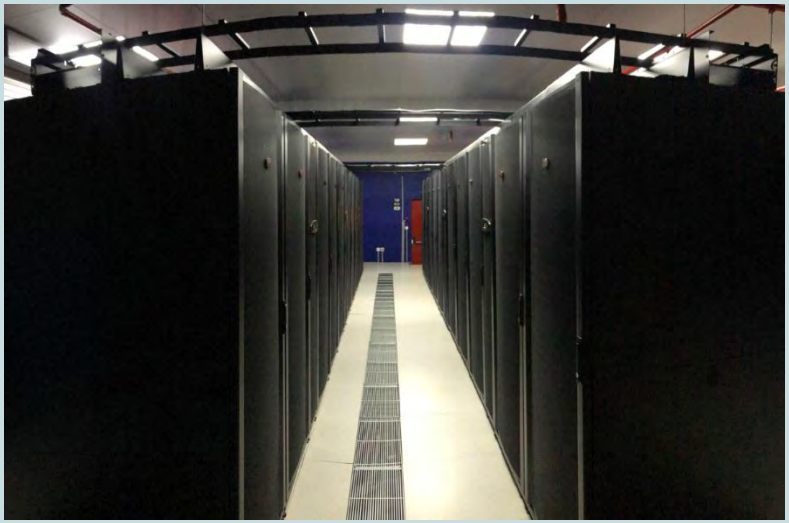
The Atomic Force Microscopy and Related Techniques Laboratory (AFM-RT Laboratory) serves both scientists and students.

There are 3 microscopes: one commercial AFM, one commercial AFM converted into an FFM and one home developed Force Feedback Microscope (FFM). The main activities of this laboratory are:

1. Research
   a) Imaging: protein structures, cells, DNA, surfaces in general
   b) Mechanical properties of cells
   c) Instrumentation: development of new instruments, software and experimental strategies that support our research activity
   d) Study of nanotribology and nanofluidics by AFM and similar techniques
2. Education: AFM training classes for graduate students
3. Outreach: Visits from high school students and displays for the general public.

Computing

In terms of computing and data storage facilities, BioISI has currently access to an in-house managed HPC cluster with 2500 cores and 160 TB storage in equipment used by all groups. Several servers and workstations are now also equipped with GPU processing units, providing an important boost in their computing abilities. We also use facilities available nationwide and at European level, INCD and EGI, respectively.

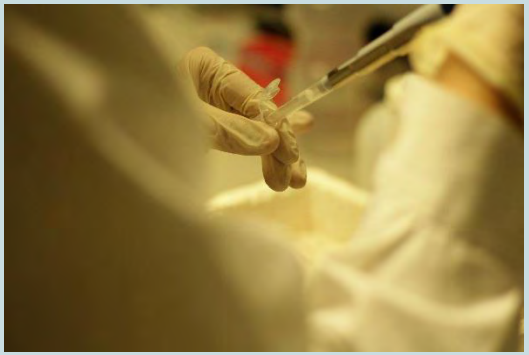


Infrastructures

Plant House

The Plant House Facility has specialized plant growth chambers and provides support to research groups.

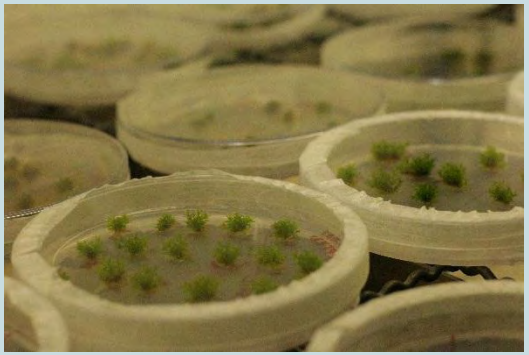
Several chambers are capable of providing stressful environmental conditions i.e. low temperature (chilling), high temperature, different light intensities and different relative humidity, allowing precise environmental simulation across different climate zones.



Mammalian Cell Culture

This facility provides expertise and advice in advanced methodologies for mammalian cell culture. Mammalian cell culture facility services include:

a) Expert consultation for researchers regarding primary cultures of human cells and organoids;
b) General cell culture (media and experimental design);
c) Large-scale production of cells;
d) Cryopreservation of cell lines;
e) Mycoplasma screening;
f) Training in usage of environmental and safety of laminar flow hoods, incubators, cell seeder and microporator.



Teaching & Training

BioISI offers also advanced training to external visitors in the scope of collaborations or to use its facilities and through the organization of international workshops that were canceled in 2020 due to the pandemic strike.

One of the BioISI missions is to share knowledge with the scientific community and society. To achieve this goal BioISI invites many international experts on their working areas which resulted in several Senior Research Seminars and others.

BioISI contributes to advanced training, as it hosts the multidisciplinary BioSys PhD program and participates in two more PhD programs.

BioSYS PhD Programme

BioSys - PhD Program in Biological Systems, Functional & Integrative Genomics, is a multidisciplinary PhD Programme in the framework of the FCT PhD Programmes Call.
BioSys was awarded with 11 PhD scholarships for each edition of the Programme for a total of 5 editions. BioSys has already enrolled 55 highly promising young scientists from 6 different countries. In total BioSYS received more than 500 applications from all around the world.
Our International PhD Programme offers a post-graduate training during the first semester involving mainly international experts in different fields that bring their own experience to the discussion. This will allow each student to contact with internationally recognized researchers and make contacts and collaborations with them. The following 3 ½ years are devoted to research in either national or international laboratories.

BioSYS 1 - Enrolled Students

- **Ana Margarida Matos** - Search for new modulators of Phe508del-CFTR retention at the plasma membrane of epithelial cells | Supervisor - Paulo Matos (FCUL), Co-supervisor - Rainer Pepperkok (EMBL) | Defense date: 18.9.2018 | Approved with distinction | http://hdl.handle.net/10451/36933 *
- **Cibelle Costa** - Biochemical and molecular characterisation of the dyslipidaemia in Portugal | Supervisor - Marília Antunes (FCUL), Co-supervisor - Mafalda Bourbon (FCUL) | Defense date: 17.5.2018 | Approved with distinction | http://hdl.handle.net/10451/35136
- **Cláudia Loureiro** - Regulation of epithelial chloride transport by phospho-tyrosine-initiated protein networks | Supervisor - Luka Clarke (FCUL), Co-supervisor - Peter Jordan (FCUL) | Defense date: 3.5.2019 | Approved with distinction | http://hdl.handle.net/10451/42299
- **Daniel Olivença** - A mathematical model of the phosphoinositide pathway in human pulmonary epithelial cells | Supervisor - Francisco Pinto (FCUL), Co-supervisor - Eberhard Voit (Georgia Institute of Technology) | Defense date: 3.10.2018 | Approved with distinction and honors | http://hdl.handle.net/10451/35920 *
- **Hugo Santos** - Gene networks for motor neuron degeneration: from disease model transcriptomes to cellular systems | Supervisor - Margarida Gama-Carvalho (FCUL), Co-supervisor - David Van Vactor (Harvard Medical School) *
- **Joana Lérias** - Anoctamin 1 – A Member of A Novel Family of Ion Channels with Extended Functions and Significance in Disease | Supervisor - Margarida Amaral (FCUL), Co-supervisor - Karl Kunzelmann (Univ Regensburg) | Defense date: 1.3.2018 | Approved with distinction | http://hdl.handle.net/10451/35037 *
- **Muhammad Asif** - A System medicine approach to study autism spectrum disorder, based on genomic, and clinical data | Supervisor - Francisco Couto (FCUL), Co-supervisor - Astrid Vicente (FCUL) | Defense date: 2.10.2018 | Approved with distinction | http://hdl.handle.net/10451/35761
- **Nikhil Awatade** - Using a systems approach to identify the mechanism of action of correctors | Supervisor - Margarida Amaral (FCUL), Co-supervisor - Rainer Pepperkok (EMBL) | Defense date: 1.3.2018 | Approved | http://hdl.handle.net/10451/34859 *
- **Paulo Costa** - The human mRNA decay machinery : an unexpected role for DIS3L2 over nonsense -mediated decay targets | Supervisor - Luísa Romão (FCUL), Co-supervisor - Margarida Gama-Carvalho (FCUL) | Defense date: 12.10.2018 | Approved with distinction | http://hdl.handle.net/10451/35913
- **Rita Catarino** - Functional studies of members of the matrix-plasma membrane-actin cytoskeleton continuum and responses to abiotic stress, Supervisor - Rui Malhó (FCUL), Co-supervisor - Patrick Hussey (Univ Durham) *
- **Sara Canato** - The endoplasmic reticulum quality control : dissecting protein networks in Cystic Fibrosis | Supervisor - Carlos Farinha (FCUL), Co-supervisor - André Falcão (FCUL) | Defense date: 8.5.2018 | Approved with distinction | http://hdl.handle.net/10451/34856

*International / mixed scholarships

BioSYS 2 - Enrolled Students

- **Ana Marques** - Neuropsychiatric disease clustering in families with Autism Spectrum Disorder (ASD): genetic, epigenetic and environmental issues | Supervisor - Astrid Vicente (FCUL), Co-supervisor - Luísa Romão (FCUL)
- **André Lamúrias** - Development of a Text Mining Approach to Disease Network Discovery | Supervisor - Francisco Couto (FCUL), Co-supervisor - Luka Clarke (FCUL) | Defense date: 8.2.2019 | Approved with distinction and honors | http://hdl.handle.net/10451/42317
- **Andreia Henriques** - Regulation of glucose uptake in mammalian cells by protein phosphorylation networks | Supervisor - Luka Clarke, Co-supervisor - Peter Jordan (FCUL) | Defense date: 20.9.2019 | Approved with distinction | http://hdl.handle.net/10451/42767
- **Joana Silva** - Analysis of translation of 5' untranslated regions in cancer | Supervisor - Luísa Romão (FCUL), Co-supervisor - Augusto Luchessi (Univ. de Campinas) | Defense date: 22.11.2019 | Approved with distinction | http://hdl.handle.net/10451/42783 *
- **João Santos** - Regulation of CFTR trafficking and membrane anchoring: new insights into cAMP signalling | Supervisor - Carlos Farinha (FCUL), Co-supervisor - Manuela Zaccolo (Univ. de Oxford) | Defense date: 23.5.2019 | Approved with distinction and honors | http://hdl.handle.net/10451/42281 *
- **Luís Sousa** - Role of CFTR in epithelial differentiation by functional genomics | Supervisor - Margarida Amaral (FCUL), Co-supervisor - Marc Chanson (Univ Geneva) | Defense date: 25.11.2020 | Approved with distinction and honors *
- **Niccolò Rossi** - Tackling the molecular basis of lipid metabolism: from candidate genes testing in a disease cohort to multi-omics approaches in unselected populations | Supervisor - Mafalda Bourbon (FCUL), Co-supervisor - Mario Falchi (Univ País Vasco) | Defense date: 25.11.2019 | Approved with distinction and honors | http://hdl.handle.net/10451/42771 *
- **Nuno Domingues** - sncRNA regulatory networks in T cell activation and viral response | Supervisor - Margarida Gama-Carvalho (FCUL), Co-supervisor - Francisco Pinto (FCUL)
- **Rui João Loureiro** - Disclosing the aggregation mechanism of β2-microglobulin in amyloid disease| Supervisor - Patrícia Faísca (FCUL), Co-supervisor - Eugene Shakhnovich (Univ Harvard) | Defense date: 26.11.2019 | Approved with distinction | http://hdl.handle.net/10451/42784 *
- **Samina Kausar** - Computational approaches to virtual screening in human central nervous system therapeutic targets | Supervisor - André Falcão (FCUL), Co-supervisor - Rita Guedes (Fac Farmácia - ULisboa) | Defense date: 17.7.2019 | Approved with distinction | http://hdl.handle.net/10451/42764

BioSYS 3 - Enrolled Students

- **Daniel Cruz** - Regulation of the TGF-B1 signaling in cystic fibrosis: the role of LMTK2 | Supervisor - Carlos Farinha (FCUL), Co-supervisor - Agnieszka Swiatecka-Urban (UPitt) | Defense date: 30.3.2020 | Approved with distinction and honors *
- **Diana Pimentel** - Functional Genomics applied to the study of resistance against powdery mildew in grapevine | Supervisor - Ana Margarida Fortes (FCUL), Co-supervisor - Antonio Granell | Defense date: 1.5.2020 | Approved with distinction and honors *
- **João Pedro Santos** - Gene-Environment interactions in Autism Spectrum Disorders (ASD) | Supervisor - Astrid Vicente (FCUL), Co-supervisor - Ana Nunes
- **Madalena Pinto** - Anoctamin 6 - A novel ion channel regulator with extended functions and significance in disease | Supervisor - Karl Kunzelmann (UReg/FCUL), Co-supervisor - Margarida Amaral (FCUL) *
- **Márcia Faria** - Targeting Rac1-signaling to enhance iodide-related therapy in breast cancer | Supervisor - Paulo Matos (FCUL), Co-supervisor - Rune Matthiesen (INSARJ)
- **Margarida Quaresma** - Role of CFTR in epithelial mesenchymal transition (EMT) by functional genomics | Supervisor - Margarida Amaral (FCUL), Co-supervisor - Jonas Fuxe (I Karolinska) *
- **Maria Teresa Braga** - Functional studies of plant cytoskeleton and membrane trafficking in responses to abiotic stress | Supervisor - Rui Malhó (FCUL), Co-supervisor - Patrick Hussey (Univ Durham) *
- **Mariana Romão** - S100 Proteins as novel modifiers of proteostasis in cancer and neurodegeneration | Supervisor - Cláudio Gomes (FCUL), Co-supervisor - Frederic Rousseau
- **Marina Luque** - A systems approach to the mechanisms of neurodegeneration | Supervisor - Margarida Gama-Carvalho (FCUL), Co-supervisor - Javier De Las Rivas (USalamanca) *
- **Marta Correia** - LiPID - Lipid profile ID - Identification of novel biomarkers to distinguish polygenic and monogenic dyslipidemia by a system biology approach | Supervisor - Mafalda Bourbon , Co-supervisor - Margarida Gama-Carvalho (FCUL)
- **Rafael Fernandes** - Regulation of nonsense-mediated mRNA decay (NMD) and the transcriptome: implications for physiology and myocardial infarction | Supervisor - Luísa Romão (FCUL), Co-supervisor - Mafalda Bourbon (FCUL) | Defense date: 09.11.2020 | Approved with distinction and honors

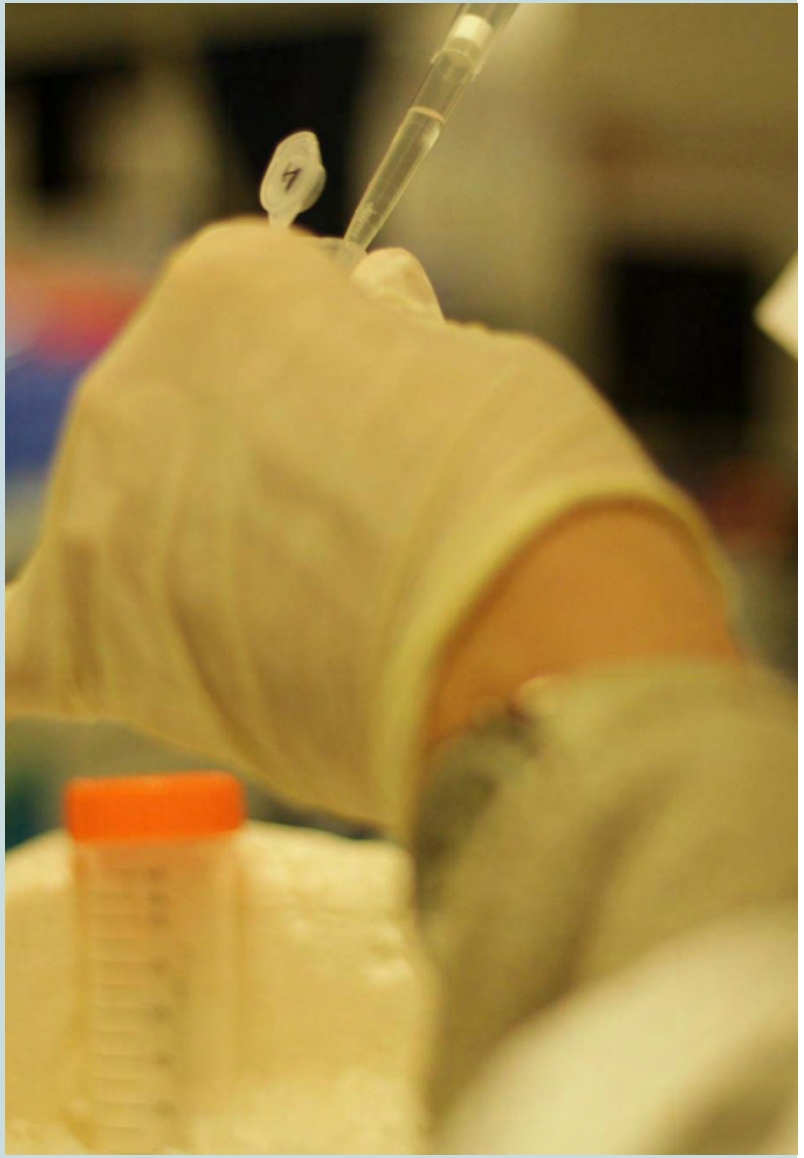
BioSYS 4 - Enrolled Students

- **Ana Rita Mendes Cavaco** - Lipid signaling in grapevine resistance against fungal pathogens | Supervisor - Andreia Figueiredo (FCUL), Co-supervisor - Ana Rita Matos (FCUL)
- **Filipa Simões** - Functional characterization of complexes regulating chloride and mucus transport and their significance in disease | Supervisor - Karl Kunzelmann, Co-supervisor - Margarida Amaral (FCUL) *
- **Flávio Soares** - Functional analysis of VviPAT6 and orthologous SlGRAS10: role in non-climacteric and climacteric fruit ripening | Supervisor - Ana Margarida Fortes (FCUL), Co-supervisor - Serge Delrot *
- **Gonçalo Nogueira** - The interplay between the mechanisms of PTC definition, mRNA translation, and NMD | Supervisor - Luísa Romão (FCUL), Co-supervisor - Francisco Pinto (FCUL)
- **Pedro Escudeiro** - Identification of biotechnological potential on genomic nonfunctionalized orthologs elements | Supervisor - Ricardo Dias (FCUL), Co-supervisor - Christopher Henry *
- **Joana Vilela** - Regulatory RNAs in Autism Spectrum Disorder – modulation of genomic variant effects on clinical phenotype and brain structure and function | Supervisor - Astrid Vicente (FCUL), Co-supervisor - Guiomar Oliveira (U Coimbra)
- **Lúcia Santos** - CFTR orphan mutations in Cystic Fibrosis – towards a detailed understanding of disease mechanisms | Supervisor - Carlos Farinha (FCUL), Co-supervisor - Patrick T Harrison *
- **Pedro Correia** - Feeding 10 Billion: building upon plant systems biology to understand grain productivity in a warming climate | Supervisor - Jorge Marques da Silva (FCUL), Co-supervisor - Elizabete Carmo-Silva
- **Rafael Graça** - Functional genomics in familial dyslipidaemia | Supervisor - Mafalda Bourbon (FCUL), Co-supervisor - Rainer Pepperkok (EMBL) *
- **Cartarina Pereira** - Systems-wide Identification of Cystic Fibrosis Disease Map | Supervisor - André Falcão (FCUL), Co-supervisor - Margarida Amaral (FCUL) and Alexander Mazein *

*International / mixed scholarships

BioSYS 5 - Enrolled Students

- **Catarina Gouveia** - Grapevine resistance to downy mildew: the innovative role of subtilisin-like proteases | Supervisor - Andreia Figueiredo (BioISI), Co-supervisor - Gunther Buchholz, Institute for Plant Research (Germany)
- **Guillem Santamaria** - Metabolomics and genomics of microbial infections and gut microbiome dynamics in patients undergoing allogeneic hematopoietic stem cell transplantation | Supervisor - Francisco Pinto (BioISI), Co-supervisor - João Xavier, Memorial Sloan Kettering Cancer Center
- **Helena Santos** - Remodelling of grape cell wall upon infection with biotrophic and necrotrophic pathogens | Supervisor - Ana Margarida Fortes (BioISI), Co-supervisor - John Moore (Stellenbosch University, South Africa)
- **Juan Fernández García-Moreno** - The involvement of DIS3L2 in nonsense-mediated mRNA decay and its functional networks in colorectal cancer | Supervisor - Luísa Romão (BioISI), Co-supervisor - Paulo Matos (BioISI)
- **Leyre Pernaute Lau –** Resistance to antimalarials - a pharmacogenomics approach for both parasite and human host | Supervisor - José Pedro Gil (BioISI/Karolinska Institutet), Co-supervisor - Volker M. Lauschke (Karolinska Institutet)
- **Rebeca André** - Molecules for Health: cholesterol absorption and transporter proteins expression under the effect of bioactive molecules | Supervisor - Maria Luísa Serralheiro (BioISI), Co-supervisor - Mafalda Bourbon (BioISI)
- **Romina Lopes Coelho** - The role of secondary modification of S100B in protein aggregation and its influence on Alzheimer's disease pathology | Supervisor - Cláudio Gomes (BioISI), Co-supervisor - Andreas Grabrucker (Ulimerick, Ireland)
- **Sofia Ramalho** - Orphan CFTR mutations – from disease mechanisms to novel therapeutic opportunities | Supervisor - Carlos Farinha (BioISI), Co-supervisor - Margarida Amaral, (BioISI) and André Falcão (BioISI)
- **Tânia Marques** - An integrative approach to tissue-specific effects of microRNA regulatory networks | Supervisor - Margarida Gama-Carvalho (BioISI), Co-supervisor - Nham Tran (UTS)
- **Vanessa Azevedo** - Determination of epigenetic marks of grapevine genes in the early response to *Plasmopara viticola*: immunity related subtilisin-like proteases as a case study |Supervisor - Andreia Figueiredo (BioISI), Co-supervisor - Fiammetta Alagna (CREA, Italy); Rui Malhó (BioISI)



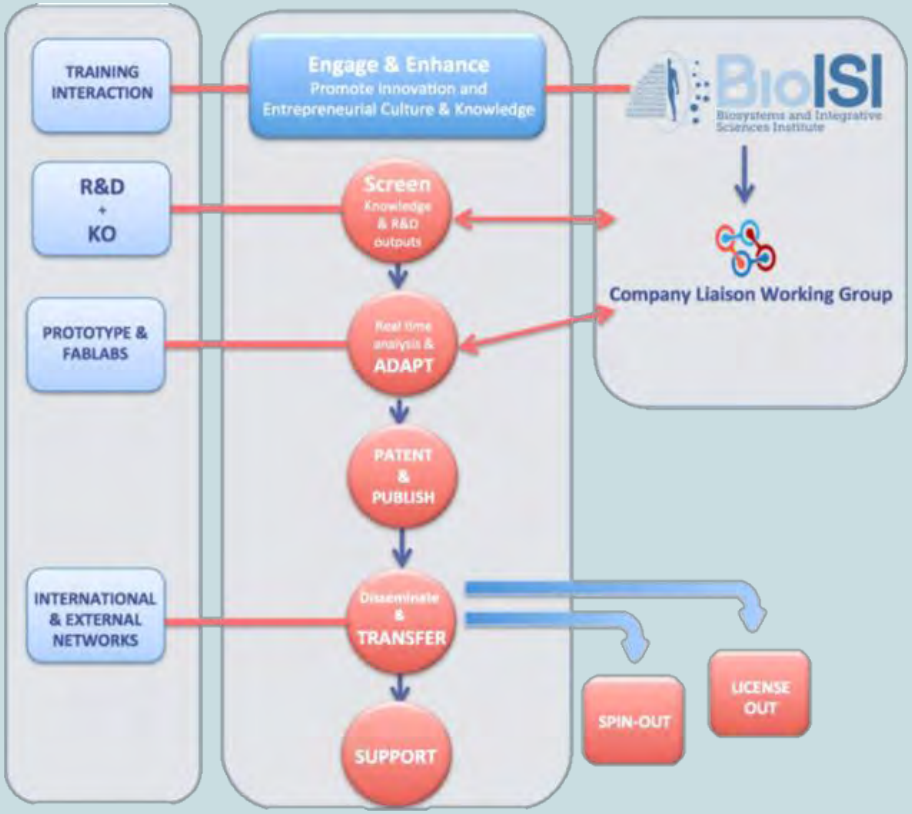
BioISI - KTT
Knowledge & Technology Transfer

BIOISI's team believes deeply in the concept of science contributing back to society. That is the principle behind the KTT concept of BIOISI – Knowledge & Technology Transfer. BioISI is actively engaged in developing its scientific and technological discoveries to benefit society, as indeed 25% of BioISI activities are on applied research. Thus, interacting with the socio-economic environment is an important BioISI aim.

To achieve such goal the centre has created the BioISI Company Liaison Working Group (CL-WG) which will help PIs to screen, develop and promote R&D knowledge outputs and support their market valorisation and industry interaction, given its privileged links to industry. A strategic KTT activities within the centre comprise, amongst other:

- internal and external awareness activities for the current KTT thematic realities, opportunities and challenges
- promote other activities, like service providing, contract R&D, project collaborations, Fablabs, etc, that can lead to economic valorisation of the knowledge outputs generated by the centre
- promote intergroup extended collaborations and strengthen international and external reach activities and outputs

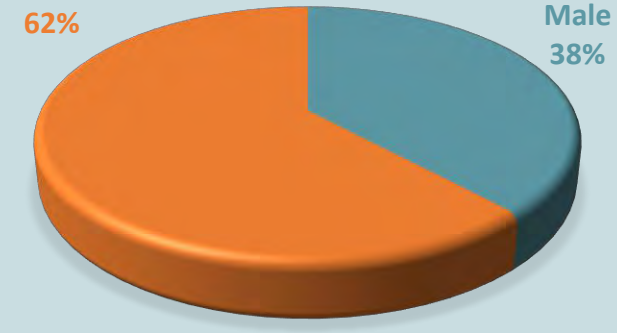
The management of KTT within BioISI will be under the responsibility of each PI who will communicate on commercially valuable results to the UL-INOVAR, after which they will work closely with CL-WG and external IP experts to identify and develop all necessary steps for IP protection and commercial exploitation deals.



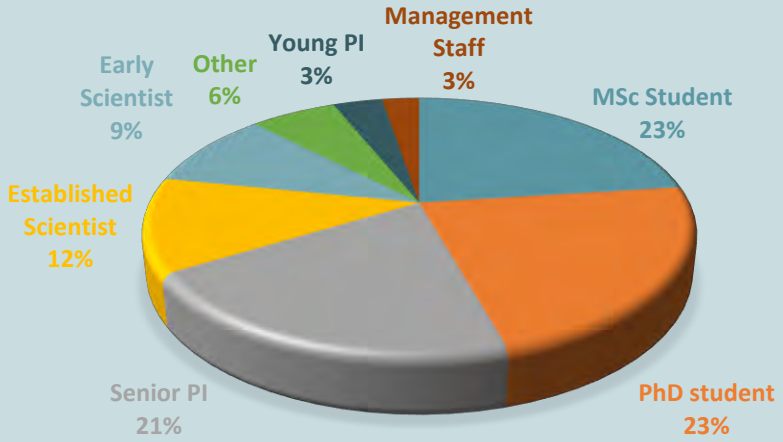
BioISI in Numbers

Members:

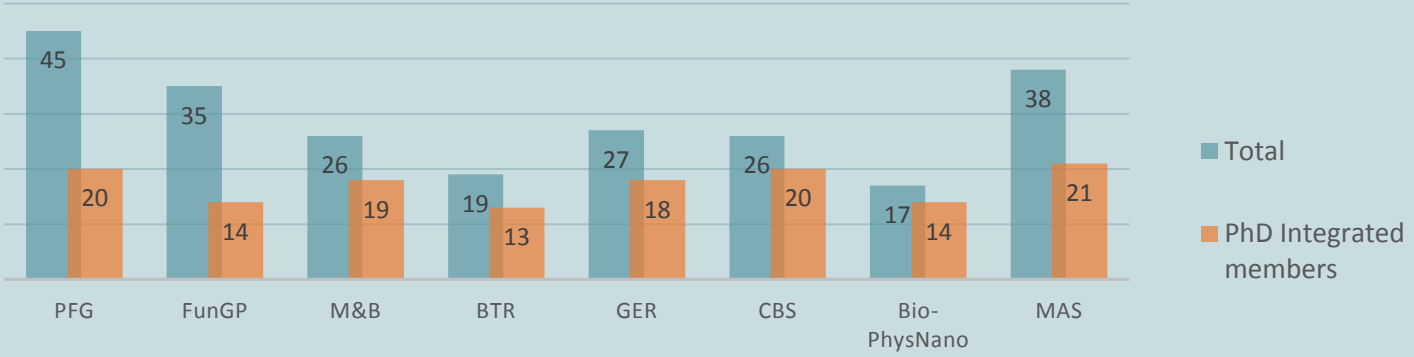
BioISI Gender Distribution



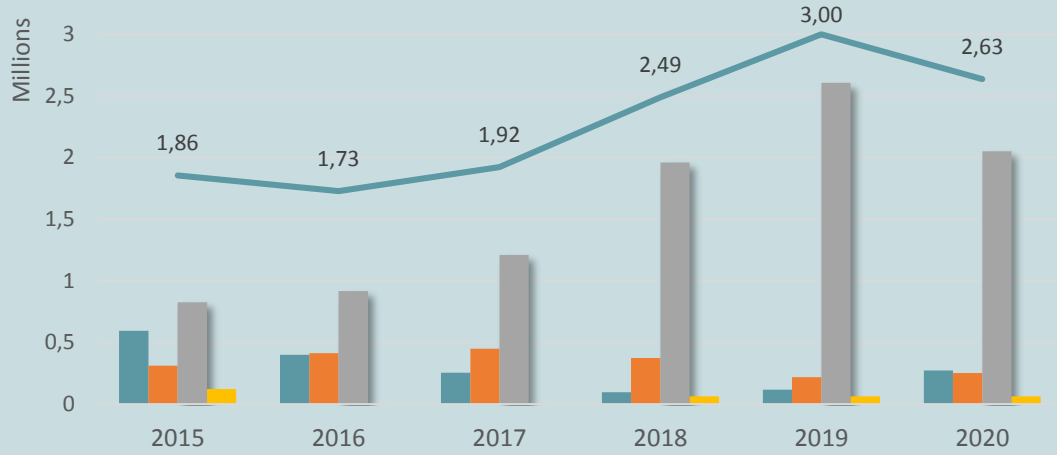
BioISI Members per Position, Total 344



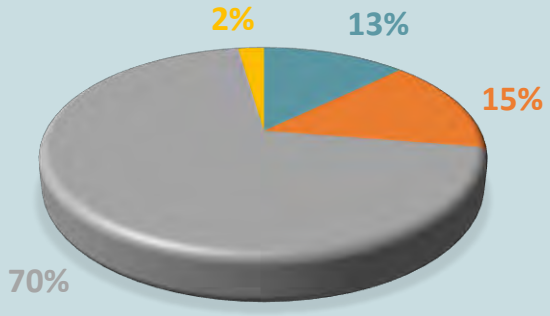
Integrated Members per Group



Project Funding 2015-2020



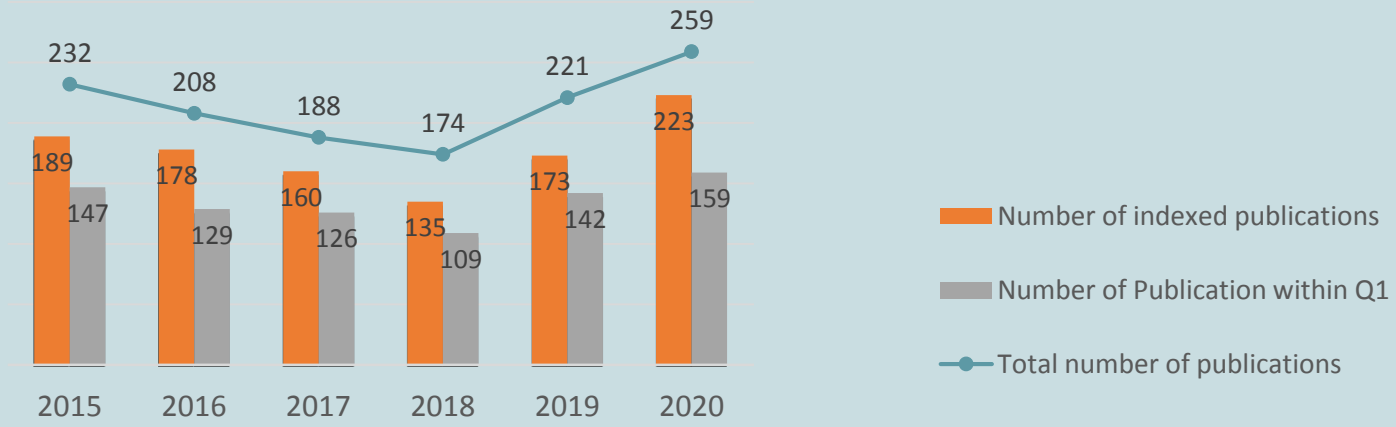
Competitive Funding 2020



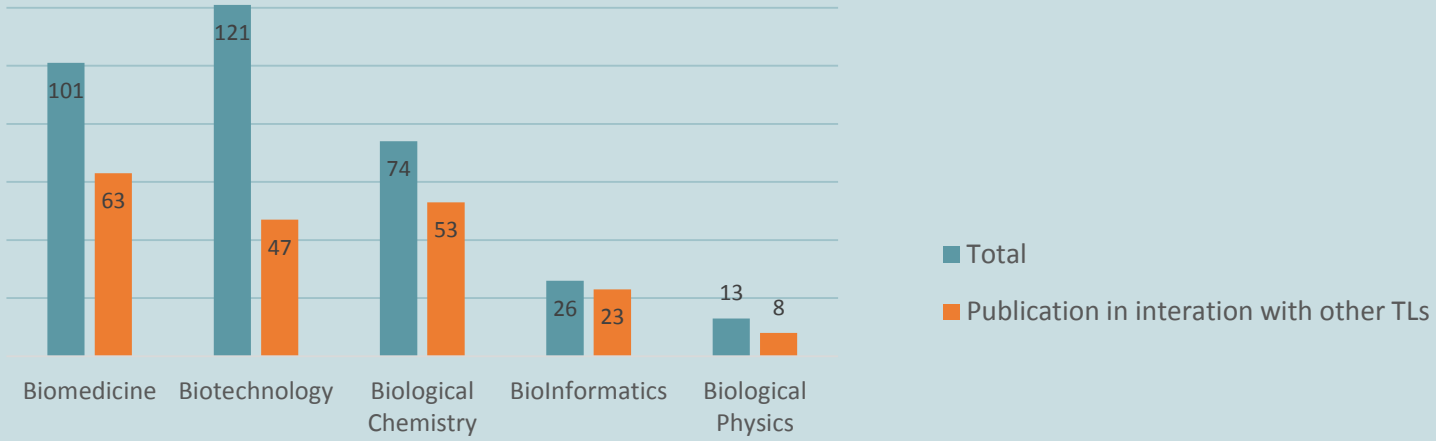
Companies, industry and other private sources
European Commission
Governmental Funding (FCT/OE)
Other funding

BioISI in Numbers

Bibliometrics:

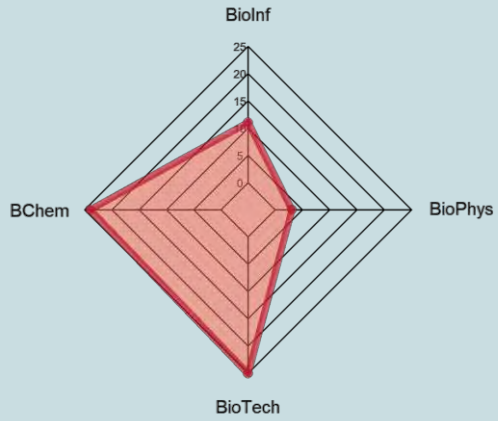


Publications per Thematic Line

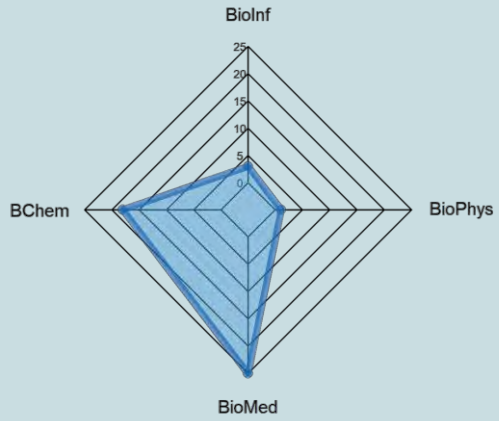


Publications in interactions with other Thematic Lines:

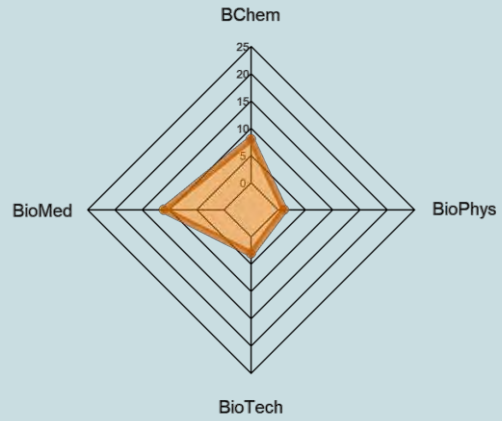
Biomedicine



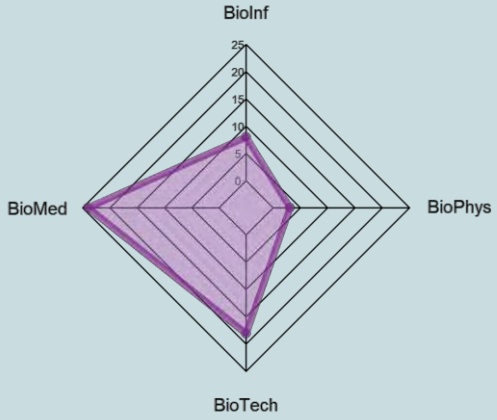
Biotechnology



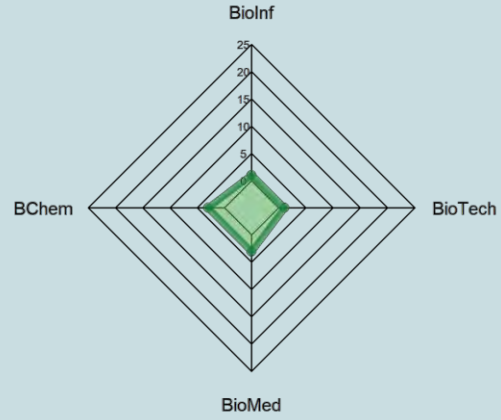
BioInformatics



Biological Chemistry



Biological Physics



BioISI Awards

Prizes:

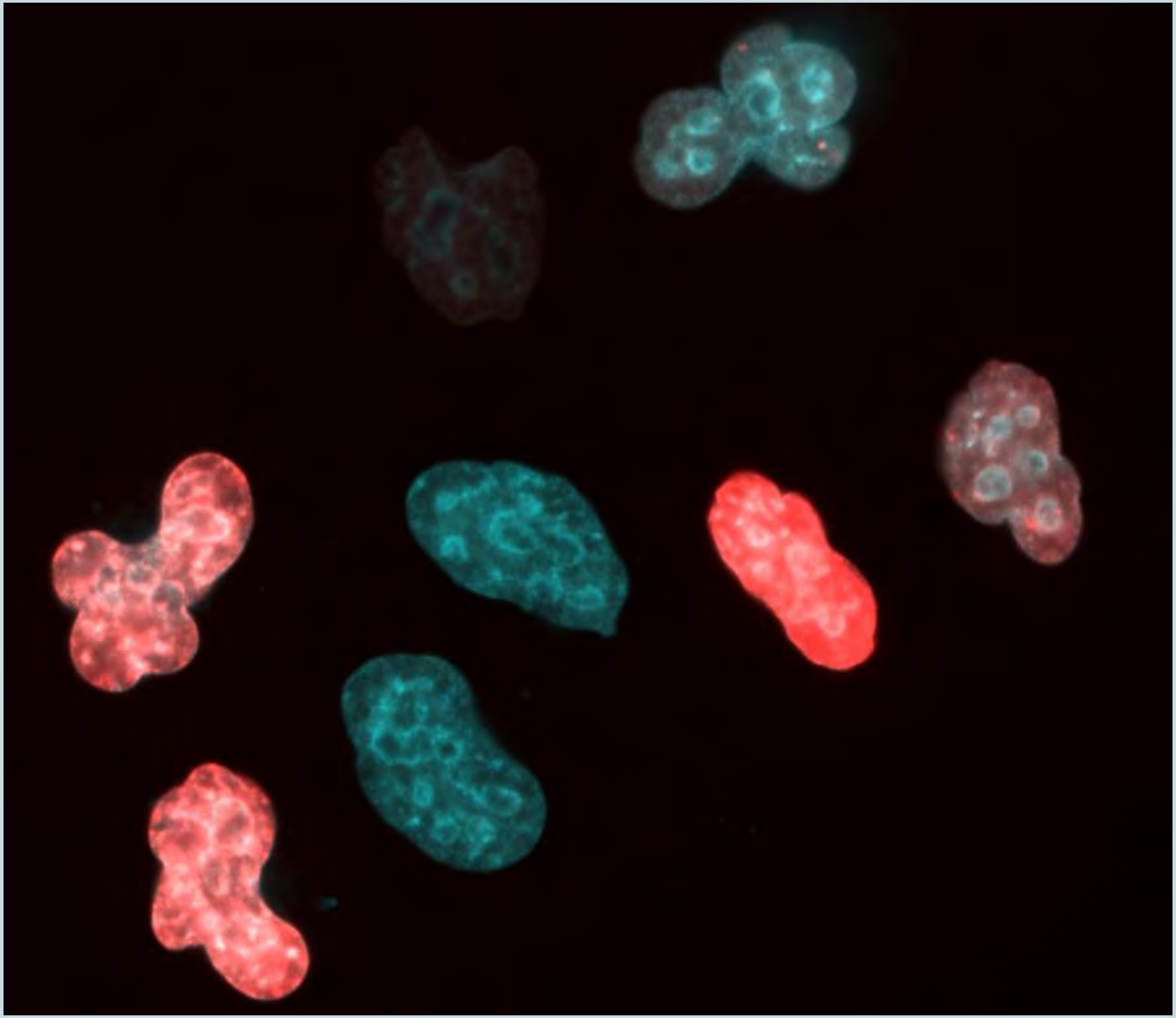
- **Cláudio M Gomes,** **Honourable mention,** 2019 edition of the University of Lisbon Scientific Awards (September 2020) (link)
- **Joana S. Cristóvão,** "The calcium binding S100B protein as a new modulator of amyloid-β peptide aggregation", **Best PhD Thesis in Life Sciences**. FCiências.ID. (link).

Publication Award:

- **Andreia Figueiredo,** "The interplay between membrane lipids and phospholipase A family members in grapevine re-sistance against Plasmopara vitícola", **Prémio Distinção Viticultura**, Comissão Nacional da Organização Internacional da Vinha e do Vinho (CNOIV) (link).
- **Paula Martins-Lopes,** "Label freeDNA-based optical biosensor as a potential system for wine authenticity", **Prémio Distinção Enologia**, Comissão Nacional da Organização Internacional da Vinha e do Vinho (CNOIV) (link).
- **Margarida Quaresma and Ines Pankonien**, "What Role Does CFTR Play in Development, Differentiation, Regeneration and Cancer?", **Best Review Article Award,** International Journal of Molecular Sciences (link)

Poster or Oral presentation Award:

- **Rafael Nunes,** "Prediction of Hydration Free Energies Involving Halogenated Ligands for Applications in Drug Discovery", **Best Oral Presentation**, 4th International Symposium on Halogen Bonding (ISXB-4) (link).
- **Márcia Faria,** "A expressão de NIS é regulada pelo NF-κB em resposta ao TNF-α em tecido tiroideu", **Honorable Mention for best oral communication**, Portuguese Congress of Endocrinology 2020 – 71st SPEDM Anual Meeting (link)



Overexpression of the transcriptional repressor NKX6-2 (in red) is frequently associated with aberrant nuclear morphologies. In blue, Hoechst staining shows normal nuclei in cells not expressing NKX6-2. Image provided by Federico Herrera (FunGP Group, FCUL).

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Bio-PhysNano

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MAS

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Books

PFG

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Book Chapters

Strategies and Resources for the Identification of microRNAs in Non-model Plants (2020) Costa BV, Chaves I. Plant microRNAs (Part of the Concepts and Strategies in Plant Sciences book series), 45-55. 978-3-030-35771-9

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FunGP

Book Chapters

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BTR

Book Chapters

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GER

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CBS

Book Chapters

Nitrogénio: A âncora no combate à poluição marinha (2020) Silva ER. Os Elementos em Ciências - Uma viagem pela Tabela Periódica, 1, 39. 978-972-9348-21-1

Bio-PhysNano

Book Chapters

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MAS

Book Chapters

Contribution of an Intelligent Virtual Assistant to Healthy Ageing in Adults With Type 2 Diabetes. (2020) Guerreiro MP et al, Exploring the Role of ICTs in Healthy Aging, 194-230. doi: 10.4018/978-1-7998-1937-0.ch012

Theses

PFG

MSc Theses

Mário Jorge Almeida (2020) Establishment and Regulation of gene molecular networks. Supervisor: Manuela Costa (UMinho) , Co-supervisor: Rómulo Sobral (Uminho).

Bruno de Campos Bento (2020) Análise estatística de dados de metabolómica: identificação dos compostos envolvidos na resposta das plantas à simbiose com fungos ectomicorrízicos. Supervisor: Mónica Sebastiana (FCUL)

Margarida Isabel A. Abreu (2020) Caraterização de bolotas de Quercus ilex subsp. rotundifolia ao longo de um gradiente climático no Alentejo. Supervisor: Helena C. Serrano (FCUL) , Co-supervisor: Anabela Bernardes da Silva (FCUL).

Eunice Conceição Lima da Costa (2020) Post-fire restoration of soil microbial communities in a Quercus suber population. Supervisor: Teresa Lino-Neto (UMinho) , Co-supervisor: Paula Baptista (IPBragança).

Rute Amaro (2020) Powdery mildew and grapes: which genes, enzymes and metabolites in resistant and susceptible cultivars. Supervisor: Ana Margarida Fortes (FCUL)

PhD Theses

Alexandra Luísa Ribeiro Dias (2020) Ecologia e Gestão da Pinus nigra em áreas de montanha. Supervisor: José Luís Louzada , Co-supervisor: Maria João Gaspar e Ana Isabel Carvalho.

Andreia Santos Rodrigues (2020) Molecular regulation of Pinus pinaster embryo development: insights from the coding and non-coding transcriptomes. Supervisor: Célia Miguel (FCUL)

Helena Silva (2020) Characterization of flower induction and fertilization of Quercus suber. Supervisor: Manuela Costa (UMinho) , Co-supervisor: Leonor Morais-Cecílio (ISA).

Shweta Singh (2020) Functional analysis of a gene regulatory network involved in flower zygomorphy. Supervisor: Manuela Costa (UMinho) , Co-supervisor: José Pio Beltran (UPV).

João Diogo Calado Martins Mina (2020) Endo- and epiphytic bacteria from olive tree phyllosphere with biocontrol abilities against olive knot. Supervisor: Teresa Lino-Neto (UMinho) , Co-supervisor: Paula Baptista (IPBragança).

Diana Pimentel (2020) Functional Genomics applied to the study of resistance against powdery mildew in grapevine. Supervisor: Ana Margarida Fortes (FCUL) , Co-supervisor: Antonio Granell ((IBMCP, Espanha)).

FunGP

MSc Thesis

Carina Rebelo (2020) Chaperone activity of neuronal S100 proteins. Supervisor: Cláudio Gomes (FCUL)

PhD Theses

Daniel F Cruz (2020) Regulation of the TGF-β1 signaling in cystic fibrosis: the role of LMTK2. Supervisor: Carlos M Farinha (FCUL) , Co-supervisor: Agnieszka Swiatecka-Urban (Univ Pittsburgh).

Vera Ferreira (2020) New Molecular Imaging Tools for Cystic Fibrosis. Supervisor: Filipa Mendes (IST) , Co-supervisor: Carlos M Farinha (FCUL).

Luis Sousa (2020) Role of CFTR in Epithelial Differentiation by Functional Genomics. Supervisor: Margarida Amaral (FCUL) , Co-supervisor: Marc Chanson (University of Geneva (Switzerland)).

M&B

MSc Theses

Ana Duarte (2020) Microbiological control of surfaces in liquid production in the pharmaceutical industry. Co-supervisor: Lélia Chambel (FCUL).

Carolina Almeida (2020) Structural and functional diversity of the diazotrophic community in xeric ecosystems: response to nitrogen availability.. Supervisor: Cristina Cruz (CE3C) , Co-supervisor: Rogério Tenreiro (FCUL).

Francisco Fonseca (2020) Selection of Saccharomyces yeasts for application in alcoholic industry.. Supervisor: Ana Mendes Ferreira (UTAD) , Co-supervisor: Catarina Barbosa (UTAD).

João Lança (2020) Upper respiratory tract microbiota dynamics in healthy adults colonized with Streptococcus pneumoniae: a longitudinal study.. Co-supervisor: Lélia Chambel (FCUL).

Mariana Nascimento (2020) Characterization of the intestinal bacterial microbiota on the recovering Eurasian griffon vulture (Gyps fulvus), Co-supervisor: Ricardo Dias (FCUL).

Mónica Louro (2020) Characterization of biofilms formed by clinical isolates of Clostridium difficile, Co-supervisor: Lélia Chambel (FCUL).

Telma Costa (2020) Development of an immunocytometric approach for surveillance of Erwinia amylovora.. Supervisor: Ana Tenreiro (FCUL) , Co-supervisor: Leonor Cruz (INIAV).

PhD Theses

Allaeddine Mahamedi (2020) Étude de la diversité génétique de la microflore fongique associée au déperíssemente do chêne (Quercus spp.) en Algerie.. Supervisor:, Co-supervisor: Alan Phillips (FCUL).

Jane Collins (2020) Streamlining the legal, policy and governance aspects as well as the innovation management and entrepreneurship of the marine biodiscovery pipeline, Co-supervisor: Helena Vieira (FCUL).

Pedro Jorge Dias Teixeira (2020) New microbial inocula for bioaugmentation: novel product design and valorization.. Supervisor: Sandra Chaves (FCUL) , Co-supervisor: Rogério Tenreiro (FCUL).

GER

MSc Thesis

Sofia Conceição (2020) Double Specific Betweenness Variants For Cross Disease Network Analysis. Supervisor: Francisco Pinto (FCUL)

PhD Thesis

Rafael Fernandes (2020) uORF-mediated translational regulation of PERK: implications for cell homeostasis and human disease. Supervisor: L Romão (INSA/FCUL) , Co-supervisor: M Bourbon (INSA/FCUL).

CBS

MSc Theses

Ana Margarida Marques Lopes (2020) Recuperação de compostos bioativos da alga Fucus vesiculosus por ultrafiltração/diafiltração e avaliação da ação biológica em doenças cardiovasculares.. Supervisor: Rita Pacheco (ISEL) , Co-supervisor: Luís Miguel Minhalma (ISEL).

Diogo Miguel Nunes da Silva (2020) Antioxidant properties and enzymatic activity towards acetylcholinesterase in the macroalga Fucus Vesiculosus and its variation with sex, growth stage and seasonality. Supervisor: Maria Luisa Serralheiro (FCUL) , Co-supervisor: Ricardo Melo (FCUL).

Maria Constança Batista da Cunha e Lorena (2020) Influence of Guava Leaf Decoctions on Cholesterol Permeation through the Intestinal Barrier and Cholesterol Biosynthesis. Supervisor: Maria Luisa Seralheiro (FCUL) , Co-supervisor: Asma Ressaissi (FCUL).

PhD Theses

Jiawei Wang (2020) Porous Materials as Metal Catalysts Supports. Supervisor: Luísa Margarida Dias Ribeiro de Sousa Martins (IST) , Co-supervisor: Marta S. Saraiva (FCUL).

Mohamed Soliman (2020) Design and green synthesis of new nanomaterials and their application in catalysis. Supervisor: Elisabete Clara Bastos do Amaral Alegria (ISEL) , Co-supervisor: Marta S. Saraiva (FCUL).

Bio-PhysNano

MSc Theses

João Freitas (2020) MICROFABRICATION OF A CANTILEVER PROBE. Supervisor: M. Rodrigues (FCUL) , Co-supervisor: João Mouro (INESC-MN).

Ana Sofia Fernandes da Fonseca (2020) Characterization of magnetic nanoparticles for hyperthermia. Supervisor: M.M. Cruz (FCUL)

PhD Thesis

MIguel Vargas Vitorino (2020) Development of a Force Feeback Microscope. Supervisor: M. Rodrigues (FCUL)

MAS

MSc Theses

Rafael Rosado Torres (2020) Experiências de Realidade Aumentada Móvel para o Jardim Botânico Tropical. Supervisor: Maria Beatriz Carmo (FCUL) , Co-supervisor: Ana Paula Cláudio (FCUL).

Ricardo Jorge Veríssimo Santos (2020) Humanos virtuais para treino de competncias na área da saúde. Supervisor: Ana Paula Cláudio (FCUL) , Co-supervisor: Maria Beatriz Carmo (FCUL).

Joao Maria Santos Machado Anastácio (2020) VASelfCare: Aplicação de apoio ao autocuidado da diabetes tipo 2 para pessoas mais velhas. Supervisor: João Balsa da Silva (FCUL) , Co-supervisor: Ana Paula Cláudio (FCUL).

Maria Francisca Sirgado da Luz Canais (2020) Exploratory Psychometric Validation and Efficacy Assessment Study of an Agoraphobia Treatment based on Virtual Reality Serious Games and Biofeedback. Supervisor: Hugo Ferreira (FCUL) , Co-supervisor: Ana Paula Cláudio (FCUL).

Rita das Neves Alves Maçorano (2020) Exploratory Psychometric Validation and Efficacy Assessment Study of Social Phobia Treatment based on Augmented and Virtual Reality Serious Games and Biofeedback. Supervisor: Hugo Ferreira (FCUL) , Co-supervisor: Maria Beatriz Carmo (FCUL).

Rafael Nuno Fragoso Afonso (2020) VisuaLeague III: Visual Analytics of Multiple Games. Supervisor: Ana Paula Afonso (FCUL) , Co-supervisor: Maria Beatriz Carmo (FCUL).

PhD Theses

Nuno Henriques (2020) SensAI+Expanse Prediction of Emotional Valence Changes on Humans in Context by an Artificial Agent Towards Empathy . Supervisor: Helder Manuel Ferreira Coelho (BioISI/FCUL) , Co-supervisor: Leonel Garcia Marques (FLUL).

António Manuel Rodrigues Manso (2020) Populações Baseadas em Multisets para Algoritmos Evolutivos. Supervisor: L Correia (FCUL)

Projects

PFG

2018 Functional studies of plant membrane trafficking and secretion - the phosphoinositide pathway in the responses to abiotic stress, FCT. BioISI Budget: 187 361.80€ (Total Amount of the project: 187 361.80€). BioISI PI: Rui Malhó

2018 GRAPINFECTOMICS - Reprogramação do transcritoma e do metaboloma em uvas *Vitis vinifera* cv. Aragonês e uvas *Vitis rupestris* após infecção com *Erysiphe necato*, FCT. BioISI Budget: 1 510 76.66€ (Total Amount of the project: 239 123.6€). BioISI PI: Ana Margarida Fortes

2018 MitiVineDrought - Uma abordagem integrada com vista à validação de estratégias de mitigação de secura em videira diminuindo o recurso a água: combinação de análises ómicas, moleculares, bioquímicas e fisiológicas, FCT. BioISI Budget: 28 398€ (Total Amount of the project: 225 875.35€). BioISI PI: Ana Margarida Fortes

2018 BerryPlastid - Biosíntese de compostos secundários no bago de uva: estudo do papel do plastídeo, FCT. BioISI Budget: 26 750€ (Total Amount of the project: 239 303.56€). BioISI PI: Ana Margarida Fortes

2018 Development of molecular markers for resistance to pine wilt disease in *Pinus pinaster*, FCT. BioISI Budget: 185 538.60€ (Total Amount of the project: 239 613.60€). BioISI PI: Célia Miguel

2018 Fostering High-Throughput Plant Phenotyping by an Interdisciplinary Approach (INTERPHENO), FCTBioISI Budget: 166 661.30€ (Total Amount of the project: 236 953.97€). BioISI PI: Jorge Marques da Silva

2018 FlowerCAST- Characterization of genetic and and environmental determinants involved in reproductive development of *Castanea sativa*, FCT. BioISI Budget: 239 964.42€ (Total Amount of the project: 239 964.42€). BioISI PI: Manuela Costa

2018 Grapevine immunity: the innovative role of subtilisin-like proteases, FCT. BioISI Budget: 230 767.31€ (Total Amount of the project: 235 767.31€). BioISI PI: Andreia Figueiredo

2018 ResisTing - Markers of resistance in Grapevine: correlating metabolome changes with mildew resistance , FCT. BioISI Budget: 50 000€ (Total Amount of the project: 239 309.87€). BioISI PI: Andreia Figueiredo

2017 Characterization of grapevine subtilisin-like proteases and their role in pathogen recognition and immune priming, FCT. BioISI Budget: 50 000€ (Total Amount of the project: 50 000€). BioISI PI: Andreia Figueiredo

2018 Influence of endosphere microbiome to control diseases in cork oak (*Quercus suber* L.), FCT. BioISI Budget: 210 133.12€ (Total Amount of the project: 210 133.12€). BioISI PI: Teresa Lino-Neto

2018 Exploiting plant induced resistance by beneficial fungi as a new sustainable approach to olive crop protection, FCT. BioISI Budget: 239 877.67€ (Total Amount of the project: 239 877.67€). BioISI PI: Teresa Lino-Neto

2018 GOJIBERRIES, PDR2020. BioISI Budget: 73 000€ (Total Amount of the project: 388 094.08€). BioISI PI: Anabela Bernardes da Silva

2017 OPTIMAL (Optimização, Maçãs, Alcobaça), PDR2020. BioISI Budget: 60 000€ (Total Amount of the project: 391 852€). BioISI PI: Anabela Bernardes da Silva

2017 MACFERTIQUAL, novos métodos de diagnóstico nutricional em macieiras 'Gala' visando a sustentabilidade e a qualidade, PDR2020. BioISI Budget: 11 000€ (Total Amount of the project: 365 798€). BioISI PI: Anabela Bernardes da Silva

2020 "vWISE" Vine and Wine Innovation through Scientific Exchange H2020-MSCA-RISE, H2020. BioISI Budget: 29 200€ (Total Amount of the project: 693 500€). BioISI PI: Ana Margarida Fortes

2019 HeatDroughtPheno - Wheat Phenotyping for a Warmer and Drier Climate., H2020. BioISI Budget: (Total Amount of the project: n.d. (access to facility, travel and accomodation expenses)). BioISI PI: Pedro Correia

2019 Pheno-ARL - Exploring the Diversity of Rice Landraces in West Africa: Getting Insights Into Salinity and Drought Stress Tolerance., H2020. BioISI Budget: (Total Amount of the project: n.d. (access to facility, travell and accomodation expenses)). BioISI PI: Jorge Marques da Silva

2019 EM LISBOA E VALE DO TEJO, NOVAS CASTAS PARA NOVOS VINHOS - Em demanda dos segredos da evolução natural da videira portuguesa, BioISI Budget: 42000 (Total Amount of the project: €200,000.00). BioISI PI: Paulo Lopes

2018 Development of molecular markers for resistance to pine wilt disease in Pinus pinaster, BioISI Budget: 185538,6 (Total Amount of the project: €239,613.60). BioISI PI: Célia Miguel

2020 Cdots Biosensing COVID19, BioISI Budget: 30000 (Total Amount of the project: €30,000.00). BioISI PI: Paula Martins-Lopes

2020 Pinheiro bravo: Conservação e melhoramento de recursos genéticos florestais, BioISI Budget: 6465 (Total Amount of the project: €147,014.77). BioISI PI: Célia Miguel

2020 Exploring new sources of coffee resistance to leaf rust (Hemileia vastatrix), BioISI Budget: 15000 (Total Amount of the project: €239,900.80).

2020 Phenotype to genotype assessment of cashew genetic resources for sustainable production in Guinea-Bissau (West Africa), BioISI Budget: 57652,5 (Total Amount of the project: €249,006.87). BioISI PI: Filipa Monteiro

FunGP

2018 CFMOLIM – Novas sondas de imagiologia molecular para Fibrose Quística, FCT. BioISI Budget: 30 000€ (Total Amount of the project: 233 315.10€). BioISI PI: Carlos M. Farinha

2018 Mechanisms of Protein Dysfunction in mitochondrial disease, FCT. BioISI Budget: 219 260.80€ (Total Amount of the project: 219 260.80€). BioISI PI: Bárbara J. Henriques

2018 Malaria drug resistance: treatment alternatives and optimization – a project strengthening a national reference centre for anti-malarial clinical trials and capacity building in Angola, Aga Khan Dev Network/FCT. Total Amount of the project: 286 587€. BioISI PI: José P. Gil

2019 A phase 2 and 3 clinical trial program to assess safety, efficacy and transmission blocking properties of the new anti-malarial KAF156 combined with a new formulation of lumefantrine in children and adults with uncomplicated Plasmodium sp. malaria in West and Central Africa, EDCTP 2 (European & Developing Countries Clinical Trials Partnership), RIA - 2017-Treatment Innovations). Total Amount of the project: 260 000€. BioISI PI: José P. Gil

2018 iDrugCF - Identification of New Drugs for Cystic Fibrosis, FCT. BioISI Budget: 160 000€ (Total Amount of the project: 240 000€). BioISI PI: Margarida D. Amaral

2018 Personalised Therapies for all: Restoring airway function in CF using Alternative Chloride Channels, CF Trust Strategic Research Centre Award. BioISI Budget: 224 000€ (Total Amount of the project: 843 491€). BioISI PI: Margarida D. Amaral

2019 Identification of novel cftr traffic correctors among fda-approved drugs, gilead - gilead sciences, lda. BioISI Budget: 116 258€ (Total Amount of the project: 116 258€). BioISI PI: Miquéias Lopes-Pacheco

2019 Identification of portuguese patients with cystic fibrosis by complete cftr gene mutation genotyping and rectal biopsy analyses, VertexBioISI Budget: 50 863€ (Total Amount of the project: 50 863€). BioISI PI: Margarida D. Amaral

2019 PTSense: – Novel Compounds as Potential Drugs for CFTR PTC Mutations, Cystic Fibrosis Foundation. BioISI PI: Margarida D. Amaral

2018 HIT-CF – Personalised Treatment For Cystic Fibrosis Patients With Ultra-rare CFTR Mutations (and beyond), European UnionBioISI Budget: 257 000€ (Total Amount of the project: 8 753 615€). BioISI PI: Margarida D. Amaral

2017 Isogenic models to study CF disease signatures: HITI gene edit to fix them, CFFBioISI Budget: 60 304€ (Total Amount of the project: 60 304€). BioISI PI: Carlos M. Farinha

2019 DysMut2– Characterization of Dysfunctional Mechanisms in Class II Mutations, CFF. BioISI Budget: 97 350€ (Total Amount of the project: 97 350€). BioISI PI: Carlos M. Farinha

2018 Mechanistic and optogenetic control of astroglia for neural repair, FCT. Total Amount of the project: 239 000€). BioISI PI: Federico Herrera

2020 Identification of novel F508del-CFTR traffic correctors among FDA-approved drugs, Gilead Sciences - Research Scholars Program in Cystic FibrosisBioISI Budget: 107000 (Total Amount of the project: €107,000.00). BioISI PI: Miqueias Lopes-Pacheco

M&B

2016 POINT-PAC 2016, LISBOA-01-0145-FEDER-016405: Precision Oncology by Innovative Therapies and Technologies. FCUL and 9 National Institutions, 2016-2020 Total Budget: 1.9 M€; Total Funding: 763 K€; FCUL Funding: 75 k€. M&B BioISI Team: H Vieira (FCUL/BioISI). [Red/Blue M&B]

2017 BIOINVENT: Generic bio-inventory of soil microbial diversity and functioning in permanent grassland ecosystems across management and climate gradients. University of Hohenheim (Proponent), FCUL, Univ Açores, Swedish University of Agricultural Sciences, Agroscope Switzerland. 2017-2020. Total Funding: 1.68 M€.FCUL PI: C Cruz. M&B-BioISI team: R Tenreiro (FCUL/BioISI). [Grey/Green M&B]

2017 Euphresco 2016-A-180 - Development, validation and verification of a diagnostic tool for detection and identification of Ralstonia solanacearum and Clavibacter michiganensis subsp. sepedonicus directly on plant tissue. INIAV and 8 EU institutions. 2017-2020. Total funding: 80 k€. INIAV funding: 21 k€. M&B BioISI team: L Cruz (INIAV/BioISI). [Green M&B]

2017 Sistema Satelital de Monitoreo Ambiental en Tiempo Real para el estudio del cambio climático basado en un biosensor bacteriano altamente sensible. Proponent: Universidad Catolica Valparaiso, Vicerrectoria de Investigacion y Estudios Avanzados, Chile. 2017-2020. Total Funding: 500 k€. PI: J. Olivares. BioISI amount: 50 k€. BioISI partner: R Dias (FCUL/BioISI). [Grey M&B]

2017 EUROXANT - Integrating science on Xanthomonadaceae for integrated plant disease management in Europe.Cost Action 16107. EU H2020. INIAV and 18 EU institutions. 2017-2022. Total Funding: 68 M€. INIAV funding: 200 k€. M&B BioISI team: L Cruz (INIAV/BioISI). [Green M&B]

2019 VECTRACK: Earth observation service for preventive control of insect disease vectors. EU H2020. IRIDION (Proponent, Spain), AVIAGIS (Belgium), IRTACRESA (Spain), INSA (Portugal) 2019-2022. Total Funding 1.391 M€; INSA Funding: 268 k€. M&B BioISI team: L Zé-Zé (INSA/BioISI) [Red M&B]

2019 PlantEd: Plant genome editing – a technology with transformative potential. COST Action CA18111. 2019-2023. Leader: Swedish University of Agricultiral Sciences (SLU) with experts from 36 EU countries. Funding: undisclosed. M&B BioISI team: M Baleiras-Couto (INIAV/BioISI) [Green M&B]

2019 EUROMICROpH: Understanding and exploiting the impacts of low pH on micro-organisms. COST Action CA18113. 2019-2023. EU Framework Programme . M&B BioISI team: A. Mendes-Ferreira. [Yellow M&B]

2020 BLUE CC, ID 61-BLUECC, BLUE CO-FUND2019, H2020 . Commercial exploitation of marine collagen and chitin from marine sources. 2020-2023. Total Budget: 2,1M€. total Funding: 1,9 M€; FCUL Funding: 99,9 K€. M&B/FCUL/BioISI team: H Vieira (FCUL/BioISI). [Red/Blue M&B]

2016 Phleboviruses in Portugal: vectors, pathogenesis and co-infections. FCT. PTDC/DTP-SAP/0859/2014. Proponent: INSA. 2016-2020. Total funding: 164 k€. PI: F Amaro (INSA). M&B-BioISI Team: L Zé-Zé (INSA/BioISI). [Red M&B]

2018 COLOSSUS - Control of tuberculosis at the wildlifelivestock interface using innovative nature-based solutions. 2018-2021. POCI-01-0145-FEDER-29783. Proponent institution: INIAV. Partners: FCiências.ID, ICETA. Total funding: 239 k€. PI: MV Cunha (INIAV/CE3C). M&B-BioISI Team: A Tenreiro (FCUL/BioISI), R Tenreiro (FCUL/BioISI). [Red/Green M&B]

2018 Fire4Cast - Fitting immunocytometry and RNAtechnologies for epidemiological modeling of fire blight. 2018-2021. PTDC/ASP-PLA/28305/2017. Proponent institution: INIAV. Partners: FCiências.ID, COHTN. Total funding: 240 k€. PI: L Cruz (INIAV/BioISI). M&B Team: J Cruz (INIAV/BioISI), A Tenreiro (FCUL/BioISI), R Tenreiro (FCUL/BioISI). [Green M&B]

2018 LisbonCrop - Producing functional food crops in buildings using microbial hydroponics in combination with light-emitting diode (LEDS). 2018-2021. PORLisboa/029187/2017. Proponent: FCiências.ID. Total funding: 177 k€. PI: C. Cruz (FCUL/CE3C). M&B-BioISI Team: R Tenreiro (FCUL/BioISI), A Tenreiro (FCUL/BioISI), R Dias (FCUL/BioISI), A Reis (FCUL/BioISI), L Chambel (FCUL/BioISI). [Yellow/Green M&B]

2018 R3Forest - Using exotic biomass for post-fire recovery: Reuse, Regenerate and Reforest. 2018-2021. PCIF/GVB/0202/2017. Proponent: FCiências.ID. Partner: Raiz. Total funding: 200 k€. PI: C Máguas (FCUL/CE3C). M&B-BioISI Team: R Tenreiro (FCUL/BioISI). [Gray/Green M&B]

2018 WYG - Advancing wine yeast genomics: exploring the evolutionary dimensions of domestication and the emergence of virulence. 2018-2021. PTDC/BIA-MIC/30785/2017. Proponent: NOVA.ID.FCT. Partners: INIAV, UM. Total funding: 232 k€. PI: JP Sampaio (FCT/UNL). M&B-BioISI Team: F Duarte (INIAV/BioISI), M Baleiras-Couto (INIAV/BioISI). [Yellow/Red M&B]

2018 FRESAN – Strengthening Resilience and Food and Nutrition Security in Angola (FRESAN) 11º FED – Programa Indicativo Nacional (PIN 2014-2020) para Angola. FED/2017/389-710. 2018-2022. Proponent Institution: Instituto Camões. Total funding: 48.5 M€. M&B Team: L. Cruz. [Green M&B].

2019 A tripartide set of yeast tools for drug screening. 2019-2020. IPL/IDI&CA2019/ESTeSL (funded by Instituto Politécnico de Lisboa). Host institution: BioISI. Total funding: 5k€. PI: L Fernandes (ESTeSL-IPL/BioISI). [Red M&B] Collaboration with L Kuras (I2BC, France) [Red M&B]

2019 Regis – Conservation of Forest Genetic Resources in Madeira. 2019-2023. Proponent Institution: Instituto das Florestas de da Conservação da Natureza da Madeira (IP – RAM). Partners: IFCN, INIAV, LQA: Total funding: 298 k€. PI: D. Ornelas (IFCN): M&B Team: L Cruz. [Green M&B].

2020 MarCODE: Development and application of biochemical tools for marine commercial product tracking. Project PO MAR 2020. 2020-2023. Proponent: FCUL (PI: B Duarte |MARE). Partners: DocaPesca, IPMA. Total funding: 1.257 M€. M&B-BioISI funding: 335 k€. M&B-BioISI Team: A Tenreiro (FCUL/BioISI), R Tenreiro (FCUL/BioISI) and R Dias (FCUL/BioISI). [Blue/Gold M&B]

2016 INNOVINE&WINE – Vineyard and Wine Innovation Platform. NORTE-01-0145-FEDER-000038. Activity 3.2 – Managing fermentation practices towards the production of targeted high quality wines with regional character. FEDER) através do NORTE 2020. 2016-2020. Partners: UTAD, CQ-VR, CITAB. Total funding: 5.29 M€. UTAD/BioISI funding: 123 k€. UTAD/BioISI team: A Mendes-Ferreira. [Yellow/White M&B]

2016 RESISTIR - Intelligent information system to control infection and personalized antibiotherapy. POCI and POR Lisboa. P2020 project nº 3379. Proponent Company: MAXDATA Software SA. Partner: FCUL. 2016-2020. Total funding: 1.05 M€. M&B-BioISI funding: 449 k€. FCUL PI: R. Dias (FCUL/BioISI). [Red/Gold M&B]

2017 CRASSOREAB - Rehabilitation of Portuguese oyster (Crassostrea angulata) production using autochthonous microalgae. Project 16-02-01-FMP-0050 | MAR 2020. 2017-2020. Total Funding: 353 k€, Proponent: FCUL (PI: A Amorim). Subcontracted: IPMA, Neptune Pearl Lda. M&B-BioISI team: A Tenreiro (FCUL/BioISI) and R Tenreiro (FCUL/BioISI). [Blue M&B]

2018 Grapevine conservation and breeding improvement. 2018-2021. PO PDR2020-784-042738. Total funding: 385 k€. PI: Eiras-Dias (INIAV). M&B-BioISI Team: M Baleiras-Couto (INIAV/BioISI). [Green/Yellow M&B]

2018 GO-BioChestnut-IPM. Implementing effective strategies to combat chestnut and almond diseases. PDR2020-101-030950. 2018-2021. Proponent: CNCFS. Partners: CNCFS, ARBOREA, ARATM, REFCAST, UTAD, IPVC, AFVDN, INIAV, LCN, PRORURIS, FRP, COAMENDOA, CAAF, SOC, CAPB, ARB, IPB. Total funding: 442 k€. PI: A Bento (CNCFS). M&B Team: J Henriques (INIAV/BioISI). [Green M&B]

2019 Support of Wine Sector in Centro Region: 2nd phase. CENTRO 2020 - CENTRO-04-3928-FEDER-000028. 2019-2022. Total funding: undisclosed. Leader: Comissão Vitivinicola da Região de Lisboa (CVR Lisboa). M&B-BioISI Team: F Duarte (INIAV/BioISI), M Baleiras-Couto (INIAV/BioISI). [Green/Yellow M&B]

2019 ABCyeasts: A portfolio of antagonist yeasts for biocontrol of phytopathogenic agents in a sustainable winemaking. Project 39793 - FEDER through N2020. 2019-2022. Promotor: Proenol Indústria Biotecnológica SA. Co-Promotors: UTAD and ADVID (Associação para o Desenvolvimento da Viticultura Duriense). Partner: Sogrape Vinhos SA. Total funding: 1.007 M€. UTAD/BioISI funding: 453 K€. M&B-BioISI Team: A Mendes-Ferreira (UTAD/BioISI), A Mendes-Faia (UTAD/BioISI), A Tenreiro (FCUL/BioISI) and R Tenreiro (FCUL/BioISI) . [Yellow/White M&B]

2020 Predikt - Predicting Infectious Disease Outbreaks and Patients at Risk. Portugal 2020. 2020-2021. Promotor: MaxData. Funding: undisclosed. M&B Team: R Dias. [Gold M&B].

2020 BLUEBIO VALUE Ideation Program – an innovation and entrepreneurship program for students and researchers, promoting and developing marine related science and technology based ideas for solving major ocean and circular bioeconomy challenges (2020). Partners: Fundação Oceano Azul & Fundação Calouste Gulbenkian. Total Funding: 250 K€. FCUL/BioISI funding: 50 K€. M&B/FCUL/BioISI team: H Vieira (FCUL/BioISI). [Red/Blue M&B]

2020 COV2AIR - Correlation assessment between SARS-CoV-2 virus and interior air quality parameters to implement mitigation strategies. Portugal 2020. 2020-2021. Promotor: SGS Portugal. Partners: Lusíadas Saude & FCUL. Total Funding: 362k€. M&B Team: R Dias. [Red/Gold M&B]

BTR

2017 Synaptic networks and Personalized Medicine Approaches to Understand Neurobehavioural Diseases Across the Lifespan (MEDPERSYST), PROGRAMAS DE ATIVIDADES CONJUNTAS (PAC), Portugal 2020, BioISI Budget: 469 678,33€ (Total Amount of the project: 2 487 042,85€). BioISI PI: Astrid M Vicente, Margarida Gama Carvalho, Luis Correia, Patricia Faísca, Hugo Martiniano

GER

2018 New signaling pathways involved in the retention of epithelial choride transporters, FCT. BioISI Budget: 238 681.73€ (Total Amount of the project: 238 681.73€). BioISI PI: Peter Jordan

2018 miRiAD - Exploring the role of microRNAs in T cell function and anti-HIV defense, FCT. BioISI Budget: 198 723.58€ (Total Amount of the project: 239 673.59€). BioISI PI: Margarida Gama-Carvalho

2018 Microenvironmental effects on alternative splicing in malignant progression of colorectal tumor cells, FCT. BioISI Budget: 239 411.11€ (Total Amount of the project: 239 411.11€). BioISI PI: Vânia Gonçalves

2018 PulmaGene - Análise genética ao sangue para guiar a terapia de pacientes com carcinoma do pulmão de não pequenas células (CPNPC), Portugal2020. Total Amount of the project: 680 902.52€. BioISI PI: Raquel Chaves

2017 Blood test for clinical therapy guidance of non-small cell lung cancer patients, EU project.Total Amount of the project: 1M€. BioISI PI: Margarida Gama-Carvalho

2018 Mecanismos celulares e moleculares de toxicidade dos nanomateriais ingeridos, FCT, (Total Amount of the project: 239 563€). BioISI PI: Peter Jordan

2018 Caracterização pós-traducional do interactoma do simportador de sódio e iodo: identificação de novos alvos para potenciação da terapêutica com iodo radioactivo, FCT. BioISI Budget: 120 000€ (Total Amount of the project: 240 000€). BioISI PI: Paulo Matos

Dates refer to the start of the project

CBS

2018 Uncovering blind spots in halogen bonding applications, FCT. BioISI Budget: 239 399.61€ (Total Amount of the project: 239 399.61€). BioISI PI: Paulo J. Costa

2018 Metabolic odyssey of Staphylococcus aureus, FCT. BioISI Budget: 0 (Total Amount of the project: 233 254.12€). BioISI PI: Manuela Pereira

2018 Discovering structure and functional determinants in alternative complex IIII, FCT. BioISI Budget: 0 (Total Amount of the project: 203 654.32€). BioISI PI: Manuela Pereira

2018 Targeting multi-resistant tuberculosis with new potent isoniazid derivatives: an integrat-ed medicinal chemistry approach, FCT. BioISI Budget: 20 000€ (Total Amount of the project: 226 020.98€). BioISI PI: Miguel Machuqueiro

2018 Deal with PAINS: strategies to identify membrane modulators, FCT. BioISI Budget: 235 111.50€ (Total Amount of the project: 235 111.50€). BioISI PI: Bruno Victor

2018 In Silico nanobiosolutions: computational design of bioactive Metal complexes and polyoxometalates for medical applications, FCT. BioISI Budget: 238 761.11€ (Total Amount of the project: 238 761.11€). BioISI PI: Adria Gil-Mestres

2018 Radon - A gas-phase ion chemistry perspective, FCT. BioISI Budget: 12 500€. BioISI PI: Nuno A. G. Bandeira

2018 Novas estratégias ecológicas anti-incrustantes baseadas em metabolitos bioactivos de cianobactérias, Programa Operacional Competitividade e Internacionalização e Programa Operacional Regional de Lisboa (FEDER) and Fundação para a Ciência e a Tecnologia (OE). BioISI Budget: 37 400€ (Total Amount of the project: 240 867.08€). BioISI PI: Elisabete Silva

2018 Molecules for Health: cholsterol absorption, and expression of its transporter proteins, interactions with drugs, FCT. Total Amount of the project: 232 723.40€). BioISI PI: Luísa Serralheiro

2018 Molecules for Health: cholsterol absorption, and expression of its transporter proteins, interactions with drugs, FCT. Total Amount of the project: 232 723.40€). BioISI PI: Luísa Serralheiro

2018 Creating Opportunities from Seaweed Sulfated polysaccharides for Application in Therapeutics, FCT. Total Amount of the project: 239 898.16€). BioISI PI: Helena Gaspar

2018 POINT4PAC – Precision Oncology by innovative therapies and technologies, FCT. (Total Amount of the project: 2 405 032.23€). BioISI PI: Helena Gaspar

2018 New Organometallic Materials with Thermally Activated Delayed Fluorescence for Applications in High Efficiency OLEDs, FCT. BioISI Budget: 15 000€ (Total Amount of the project: 238 723.75€). BioISI PI: Maria José Calhorda

2019 Seaweeds as source of active ingredients for health: Fractioning by membrane technology and *in silico* model development, IPL. BioISI Budget: 5 000€ (Total Amount of the project: 5 000€). BioISI PI: Rita Pachecox

2019 SMARTMEM ESR2, Procter and Gamble Company. BioISI Budget: 5 000€ (Total Amount of the project: 5 000€). BioISI PI: Nuno A. G. Bandeira

2018 Molecules for Health: choleterol absorption, and expression of its transporter proteins, interactions with drugs, FCT BioISI Budget: 232723 (Total Amount of the project: 232723). BioISI PI: Maria Luisa Serralheiro

2018 Novel eco-friendly Antifouling Strategies based on Cyanobacterial bioactive Metabolites, Programa Operacional Competitividade e Internacionalização e Programa Operacional Regional de Lisboa (FEDER) and Fundação para a Ciência e a Tecnologia (OE)BioISI Budget: 35 575.00 € (Total Amount of the project: 240 867.08 €). BioISI PI: Elisabete R. Silva

2020 Multidisciplinary approach to study post-translational modifications in metabolic enzymes, BioISIBioISI Budget: 10 000.00 € (Total Amount of the project: 10 000.00 €). BioISI PI: Bruno L Victor and Bárbara Henriques

BioPhysNano

2018 Organized Magnetic Nanopaticles, FCT. BioISI Budget: 215 145€ (Total Amount of the project: 232 887.57€). BioISI PI: Margarida Cruz

2018 Development of sustainable materials for application in flexible electronic and energy harvesting devices, FCT. BioISI Budget: 20 612.50€ (Total Amount of the project: 232 481.10€). BioISI PI: Margarida Cruz

2018 Theoretical design of molecular machines with applications in organic photovoltaics and solar thermal storage, FCT. BioISI PI: Benedito Cabral

2018 The Physical Basis of Disease: The case of dialysis related amyloidosis, FCT. BioISI Budget: 195 144.75€ (Total Amount of the project: 195 144.75€). BioISI PI: Patrícia Faísca

MAS

2019 Modelação do fluxo de estudantes no sistema de ensino Português (ModEst), FCT. BioISI Budget: 247 000€ (Total Amount of the project: 247 000€). BioISI PI: Luís Correia

2019 Visual word recognition and Orthographic processing: Experiments and contributions from cognitive psychology, neurosciences, and computational modeling (VOrtEx), FCT. BioISI Budget: 19 500€ (Total Amount of the project: 19 500€). BioISI PI: Luís Correia

2016 Personalizing cancer therapy through integrated modeling and decision, FCT. BioISI Budget: 17 600€ (Total Amount of the project: 200 000€). BioISI PI: Sara Silva

Patent

CBS

WIPO PCT, WO2020128674 - Xanthonic Compounds and their use as antifouling agentes, by Correia-da-Silva M, Pinto MMM, Vasconcelos V, Almeida JR, Silva ER, Sousa E (link).