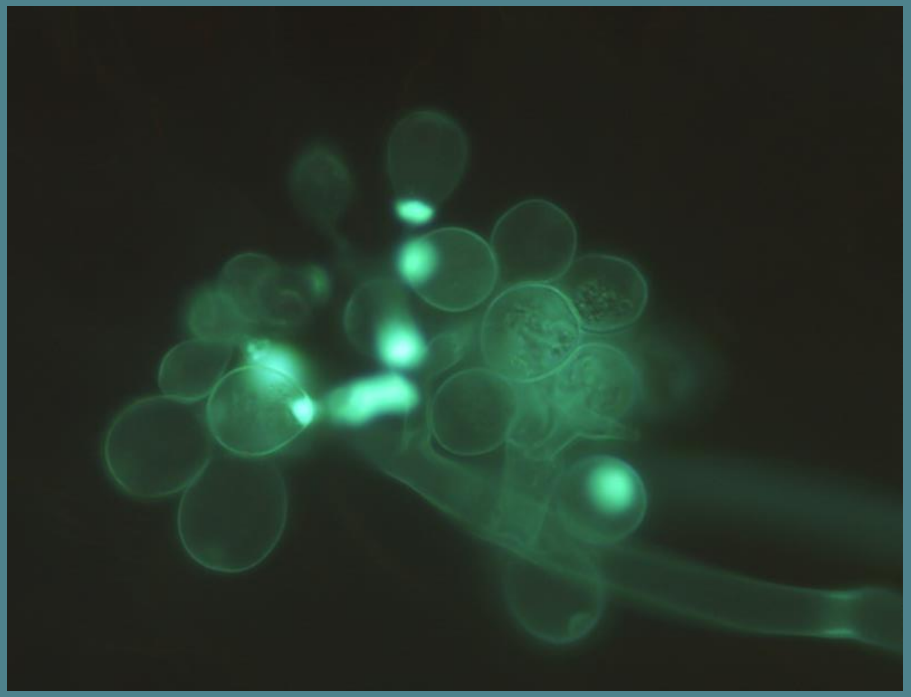
BioISI



Biosystems & Integrative Sciences Institute

Report 2019

Biosystems and Integrative Sciences Institute

Ciências ULisboa

Front page figure: *Plasmopara viticola* sporangiophore visualization by fluorescence microscopy in a *Vitis* vinifera leaf disk 8 days post-infection. Provided by Marisa Maia (PFG 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)

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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 new 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

To achieve its strategic 2018-22 goals BioISI proposes to:

1. Strengthen BioISI research, technology development & innovation by: hiring 10 new PIs in key BioISI areas; expanding current BioISI internal multidisciplinary projects.
2. Reinforce training: create a Junior Studentships Programme dedicated to early career researchers; expand both PhD (BioSys2) and Interdisciplinary Postdoctoral (IPP) programmes.
3. Invest in core-facilities: hire dedicated human resources; upgrade equipment;
4. Stimulate scientific dissemination: organize conferences, seminars, workshops, courses;
5. Foster scientific & technological culture in society: promote multiple outreach events;
6. Encourage collaborations with industry and boost knowledge & technology transfer (KTT): Establish a BioISI-Industry Partnership Programme and hire a dedicated KTT officer.

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/ MG-Carvalho
5) Biological Chemistry (BChem): M Pereira /P Costa

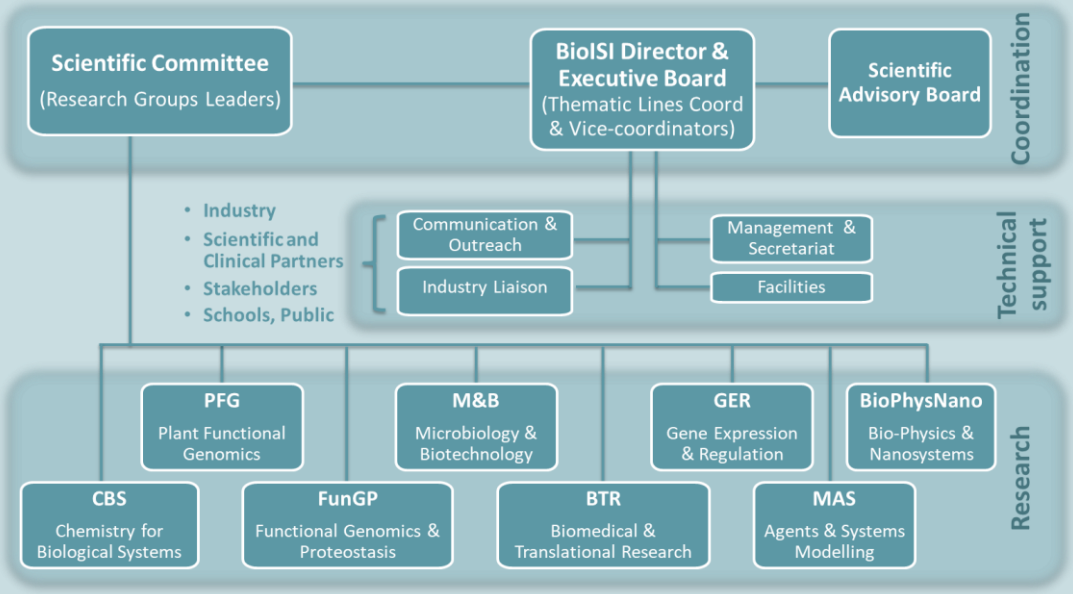
Each TLC is a former centre coordinator with past experience managing internationally funded research, being also a research group leader (RGL). TLCs/VCs promote specific activities and exchange of information to exploit collaborations enhancing multidisciplinary research.

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
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 & Cell Biology)
EMBL – European Molecular Biology Laboratory, Heidelberg (Germany)

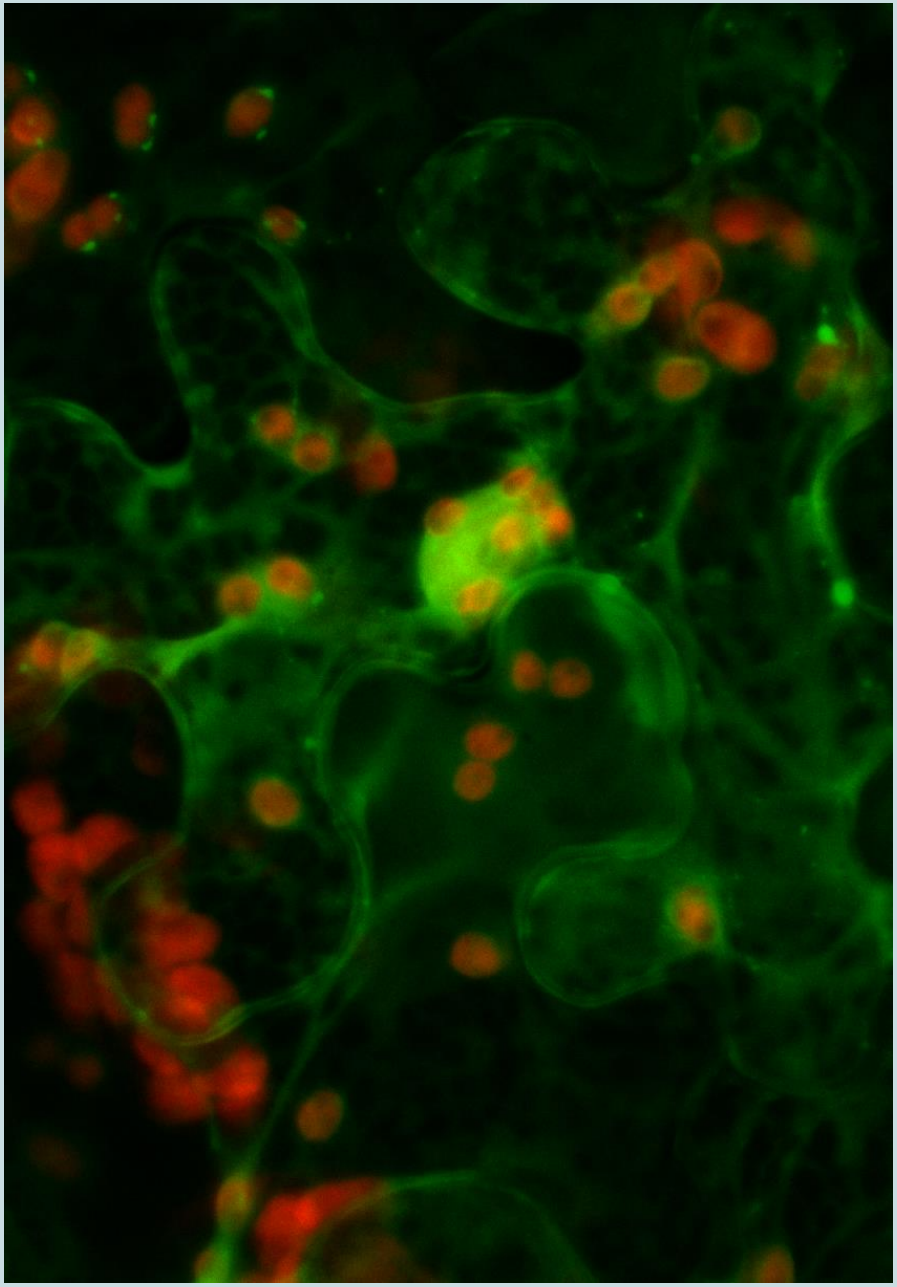
Klaus Palme (Plant Molecular and Cell Biology)
BIOSS Centre for Biological Signalling Studies, University of Freiburg (Germany)

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

Nicotiana benthamiana cells transiently transformed, expressing a chestnut protein fused with GFP. Allene oxide synthase-GFP (green) is visible in traffic from the nucleus through endoplasmic reticulum to the destination, the chloroplast membrane (round red organelles up-left in a neighboring cell). Image acquired in the Leica SP8 confocal microscopy, provided by Susana Serrazina and Teresa Braga (PFG Group, FCUL)

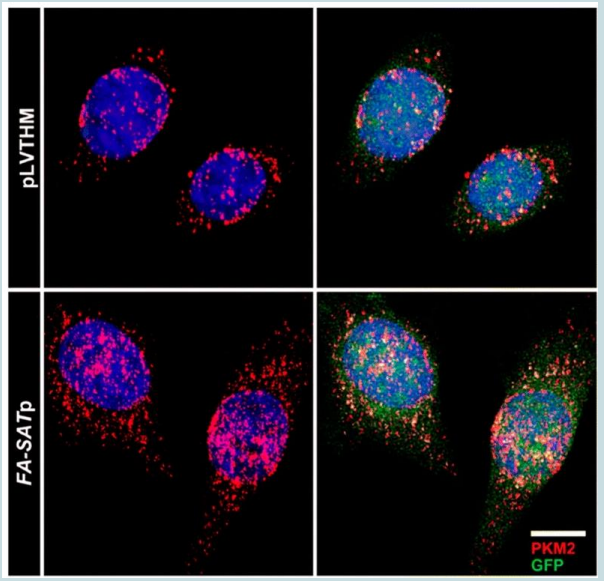
Biomedicine

The BioMed thematic line (TL) seeks to establish new approaches to solve health problems based on a systems-level analysis of causative pathways/ networks including genes, biomolecules as well as well as how they are impacted by the environment and lifestyle.

The focus of BioMed research at BioISI is on mechanisms of disease, personalized medicine and new therapies, 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 three BioISI groups (FunGP, BTR and GER) working closely with researchers from other areas (physicists, bioinformaticians, mathematicians) not only to elucidate the basic mechanisms underlying human disease at the molecular and cellular levels, but also to uncover the genetic and epigenetic determinants of disease.

Out of the six BioISI projects awarded in 2019, one had a major component of Biomedicine, by focusing on mechanisms of the mRNA surveillance mechanism (nonsense-mediated mRNA decay, or NMD) and its functional networks in cancer.



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 is currently establishing a Proteomics & Metabolomics facility. It will also benefit from the establishment of a Genomics facility (Biotechnology TL).

Future plans:

- Understand the regulatory networks underlying traffic disorders, namely Cystic Fibrosis;
- Develop innovative therapeutic strategies, based on tests in patients own cells/tissues towards personalized medicine, namely in Cystic Fibrosis;
- 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.
During 2019 the research activity followed the key actions defined in the strategic program.

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 a new FCT project, "PhysBD", which involves a collaboration with the BChem TL.

Nanostructured magnetic systems

Development of magnetic nanoparticle (MNP) systems for biomedical applications encompassing: synthesis, structural/microstructural and magnetical properties assessment of coated iron oxide nanoparticles; preparation of stable biocompatible ferrofluids, evaluation of specific loss power performance; improvement of organized magnetic nanoparticles aggregates using gels and polymers as hosts for iron oxide particles; 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/fully characterized in 2019 (M.Vitorino, PhD Eng.Physics) becoming totally operational for studies on biological/soft systems; the new equipment allowed to check previous AFM results on the mechanical properties of CFBE cells (collaboration with FunGP). 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, framed by a new BioISI project (collaboration with CBS group); topography and mechanical properties analysis of Bcc bacteria during long term infections (collab with IBB/IST, under FCT grant).

Future plans:

- Establishment of testable theoretical predictions in protein folding physics;
- Study of nanostructured magnetic systems, to develop methodologies with potential application on biomedical devices;
- Development of AFM/FFM methodologies for nanomechanical properties & biological interactions assessment;
- Biomimetic photosynthesis and molecular solar energy storage.

Expertise/facilities of the physics team in optical techniques regularly used in the frame of InterPheno project (PFG/FCT grant); Squid magnetometry and Mossbauer spectroscopy complementarily used for detection/study of spin cross over (SCO) phenomena in Fe complexes (regular collab. with CBS group), and characterization of specific Iron(III) complexes containing phenanthroline derivatives, promising anti-cancer agents (collab. CQE/FCUL).

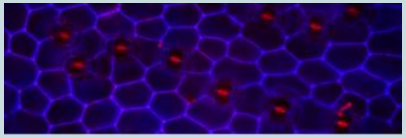
Biotechnology

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 the drought-induced signature in ectomycorrhizal cork oak plants.
- Small RNA profiling of pine embryo development.
- Characterization of lipid signaling pathways involved in sexual plant reproduction.

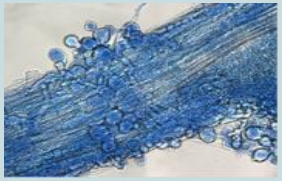


Internal funded projects – *Spectroscopy and Machine Learning: A New Alliance to Vitis Phenomics.*

Crop improvement and security

- Identification of metabolic biomarkers of pathogen infection in vine for plant improvement and agricultural monitoring.
- DNA –based label-free biosensors used for food authenticity purposes.
- Genome-wide transcriptomic analysis of novel regulators of cork formation.

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



Internal funded projects – *"Development of Botrytis cinerea DNA-based detection assays: HRM and Biosensor"*

Microbial pharmacogenomics

Development of a set of yeast genetic tools to screen stress/drug effects.
Phylogenetic, morphological and evolutionary analysis of plant endophytic and parasitic fungi (*Lasiodiplodia & Botryosphaeriales*).

Networking activities of M&B with FunGP group (concerning evaluation of the effects of marine microbial compounds).

Wine biotechnology

- Whole genome sequencing and comparative genomics of non-Saccharomyces yeasts to broaden their application in wine industry.
- Integrative omics-based analysis of the grape microbiome towards the enlightening of its role in wine flavor and metabolic properties.

Networking between PFG, M&B and MAS (development of computational pipelines, complex metabolic traits).

Internal funded projects – *Grape Microbiome and Wine Characteristics: new implications of terroir*

Microbial biotechnology

- Characterization of marine microbes and marine sponges for bioactivity profiles.
- Deciphering *Mycobacterium* phylogeny using genome-wide SNP data.
- Real-time whole genome sequencing for intelligent information system to control infection and personalized antibiotherapy – Project RESISTIR (consortium with Maxdata, Directorate-General of Health & Lx hospitals).
- Analysis of soil and cork plant microbiome upon changes in climatic factors.

Internal funded projects – *Understanding the microbial community effects in a phytochemical-free vineyard"*

BioInformatics

The main scientific goals of the BioInformatics thematic line (BioInf TL) are: to articulate research in **digital biology** at large, to extract **systems-level knowledge** and to **generate models** to describe and predict the behaviour of **complex biological systems**. BioInf TL aggregates research of BioISI concerning **computational modelling** and simulation of biological systems. The scope of computational modelling in BioISI is vertical in terms of systems, from the physical basis of biological systems to social organisation of such systems. Agent based modelling and simulation are basic techniques widely used in the BioInf TL. Virtually all research groups of BioISI develop research related with BioInf TL. They all use numerical and algorithmic models of bio/chemical systems for which computational implementations are fundamental. In particular, we can identify **quantitative biology** and **large-scale integration of biological data**, as well as **knowledge production**, sharing and innovation.

Key Actions:

- Computing & storage common infrastructure set up;
- 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;
- Workshops: Encontro de Jovens Investigadores de Biologia Computacional Estrutural (EJIBCE).

Actions in 2019

Project RESISTIR (ended in 2019) focusing on modelling microbial propagation in hospital settings and project MedPerSyst with a focus on mining data for personalised medicine of neurobehavioural disorders were two of the most relevant activity poles in this TL.

We streamlined the usage of the computing facilities. We continue to use national (INCD) and European (EGI) computational infrastructures when needed.

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;
- To produce multi-agent models and simulations of living and artificial life systems.

Major achievements in flagship projects

Bonnet F, Mills R, Szopek M, Schönwetter-Fuchs S, Halloy J, Bogdan S, Correia L, Mondada F, Schmickl T (2019) Robots mediating interactions between animals for interspecies collective behaviors. Science Robotics, 4(28), eaau7897. doi: 10.1126/scirobotics.aau7897. Main result of EU project ASSISIbf.

Relevant results in RESISTIR project, focused on the development of an intelligent decision support system for personalized prevention and clinical management of infectious diseases on a platform generating epidemiological knowledge in real time. Prediction of outbreaks was shown to be successful approximately 4 days in advance.

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 directely 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.

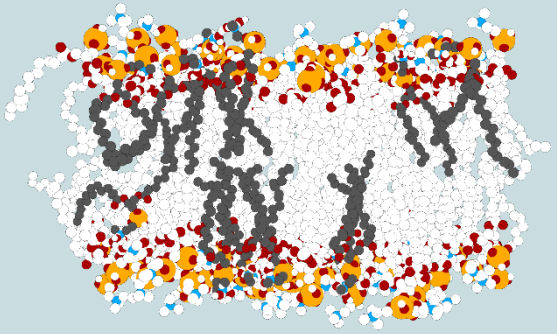
Key Actions and major achievements

BioISI Projects

One awarded BioISI projects involved the Biological Chemistry thematic line. The project "Exploring surfaces of prokaryotic membranes and morphologies of respiratory complexes in membrane mimicking systems" aimed to integrate cellular and molecular perspectives of membrane proteins by a) investigating prokaryotic membranes and b) proteins in reconstituted systems by atomic force microscopy (AFM). Using wild type and mutated strains we were able to connect the presence/function of membrane proteins with cell membrane related features as rugosity and size. Moreover, we were successful in reconstituting membrane proteins in lipid bilayers and exam these structures by AFM. Our positive results show the applicability of this methodology to explore protein structural features in a physiological lipid environment.

Organization of Meetings

Encontro de Jovens Investigadores de Biologia Computacional Estrutural (EJIBCE) 2019, Faculty of Sciences, University of Lisbon, Lisbon, Portugal, December 20th (2019) (http://ejibce.github.io/) - This meeting involved several BioISI thematic lines, namely, BChem, BioPhys, and BioInf.



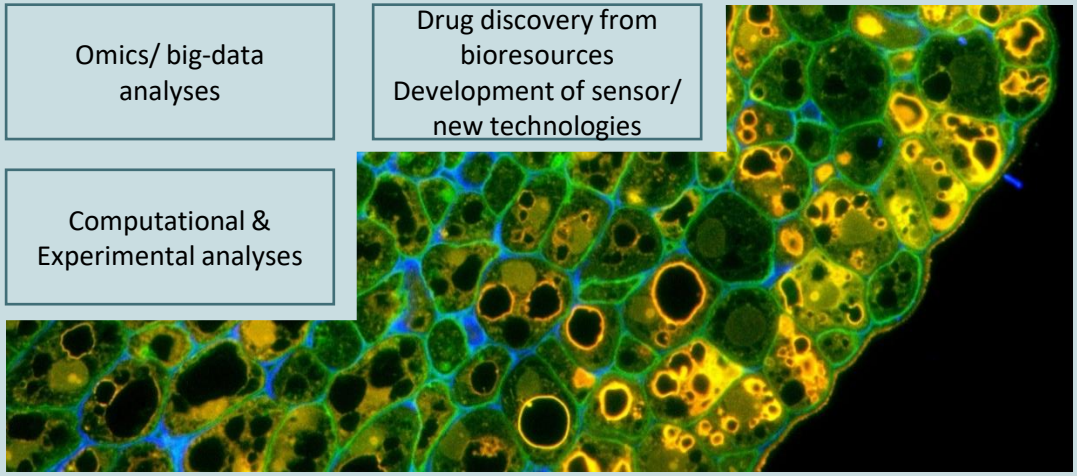
Facilities. Biological Chemistry is involved in the maintenance and development of the computing/bioinformatics facility, enabling BioISI scientists to run calculations and simulations in (bio)chemical systems. Biological Chemistry benefits from the facility of high-throughput screening (BioMed TL) and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

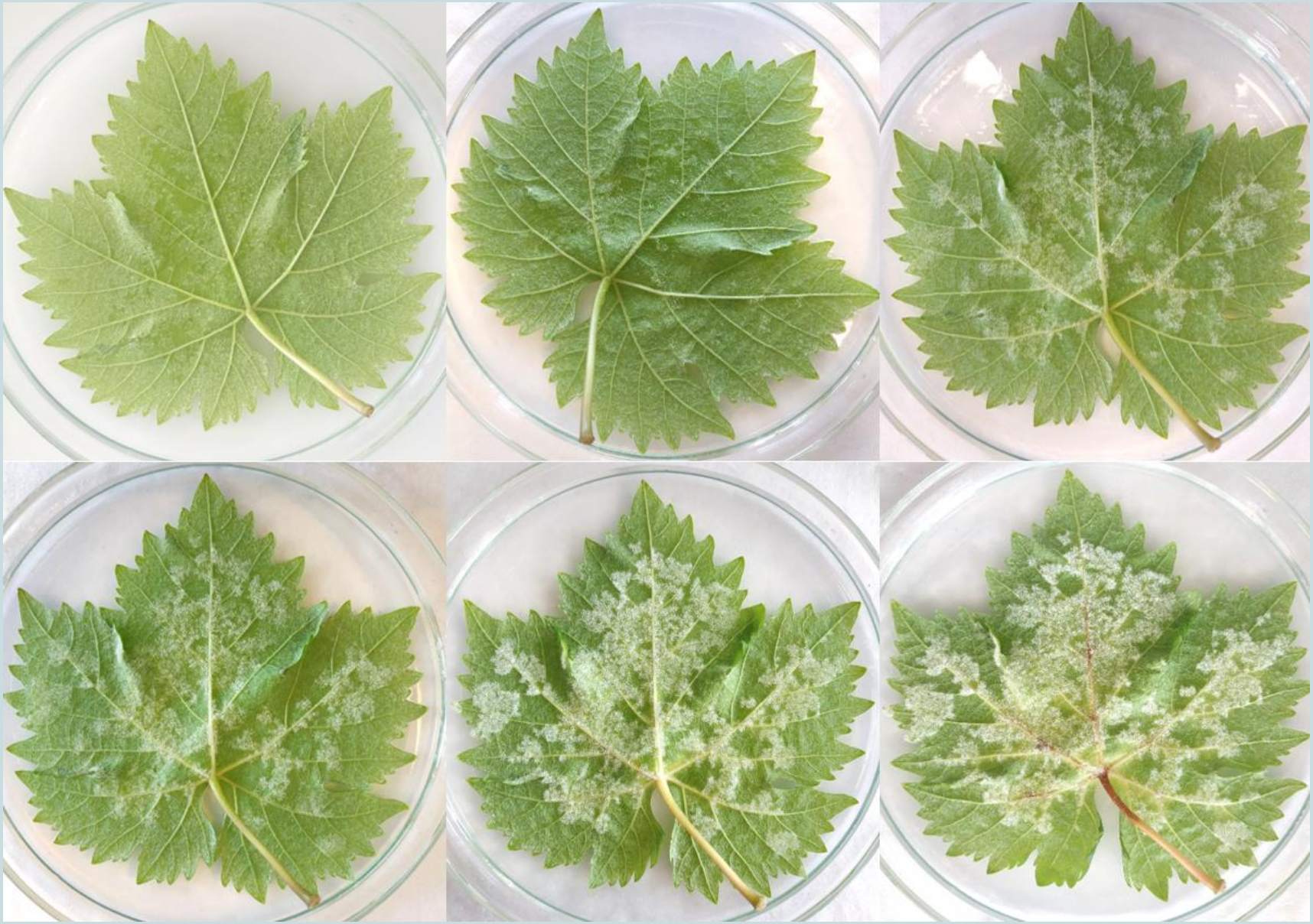
Future Plans. We will keep investing in the identification and purification of bioactive single molecules that are active in the context of CF-therapy. Efforts will be made to finalize the deconvolution and identify the pure active compounds. We shall also continue to investigate membranes proteins from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

We are engaged with the organization of the 7th IIBC - 2020 (Iberian International Biophysical Congress), the 9th EuCheMS Chemistry Congress 2020 and FEBS2021 Congress.

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			





Time-course infection of *Plasmopara viticola* in *Vitis vinifera* cv. Trincadeira leaves. Provided by Marisa Maia (PFG Group, FCUL)

BioISI Projects

For the 4th 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 2019 these included 5 projects:

1. Understanding the microbial community effects in a phytochemical-free vineyard II
PIs: Andreia Figueiredo | Ricardo Dias | Margarida Gama-Carvalho
Thematic Lines involved: Biotechnology | Bioinformatics

2. Exploring surfaces of prokaryotic membranes and morphologies of respiratory complexes in membrane mimicking systems
PIs: Manuela Pereira | Mário Rodrigues
Thematic Lines involved: Biomedicine | Biophysics | Biological Chemistry

3. The involvement of DIS3L2 in nonsense-mediated mRNA decay (NMD) and its functional networks in cancer
PIs: Luísa Romão | Paulo Matos | Peter Jordan
Thematic Lines involved: Biomedicine | Bioinformatics

4. Grape Microbiome and Wine Characteristics: new implications of terroir
PIs: Margarida Baleiras Couto | Ana Margarida Fortes
Thematic Lines involved: Biotechnology | Bioinformatics

5. Development of *Botrytis cinerea* DNA-based detection assays: HRM and Biosensor
PIs: Paula Lopes | Raquel Chaves | Mário Rodrigues
Thematic Lines involved: Biotechnology | Bioinformatics | Biophysics

Understanding the microbial community effects in a phytochemical-free vineyard II

PIs – Andreia Figueiredo | Ricardo Dias | Margarida Gama-Carvalho

Biotechnology & Bioresources | Bioinformatics

Grapevine (*Vitis vinifera* L.) is one of the crops with high economic impact worldwide. In viticulture, the terroir concept was established aiming to define the unique aspects of: 1) a physical place (climate, soil); 2) biological (soil, grape variety and fauna); 3) viticulture and 4) enological techniques, that influence and define the sensory-characteristics of a wine from a particular region. The contribution of native vine microbiota in the winemaking process is well known, however few studies have been conducted relating the microbiota with the terroir effect.

Quinta dos Murças is an organic vineyard from the Portuguese wine producer Esporão, where environmentally friendly agronomic practices were implemented. A metagenomic analysis based on the Oxford Nanopore sequencing technology was conducted in 4 terroirs and on a control vineyard (traditional viticulture practices). Terroir soil parameters (eg water content, pH, organic matter) and the elemental composition (soil and grapevine leaves) were determined.

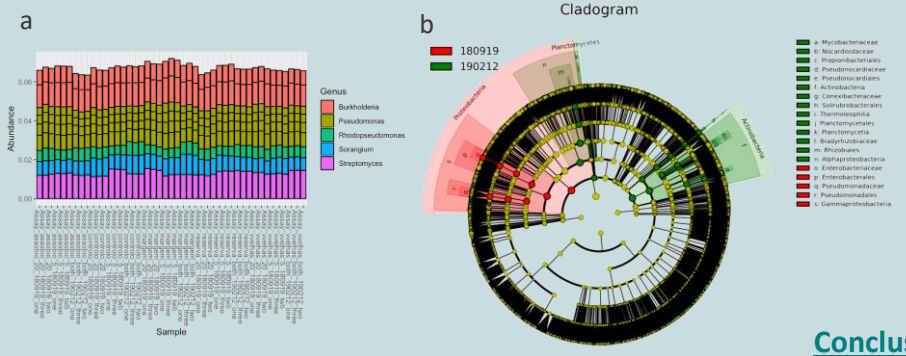


Figure 1 – a) Genus identification b) LEFSE cladogram for sample group discrimination

Results:

- Metagenome sequencing of 45 soil samples:
  - Identification of the following fuctional taxonomical units: 229 Archea, 4152 bacteria, 4346 virus and 11 fungus;
  - Definition of terroir, depth and season specific microbiome;
- Identification of 20 chemical elements through TXRF analysis:
  - 95% classification sucess for the terroirs under analysis;
  - 94% classification sucess for grapevine variety vs terroir.

<u>Conclusion</u>: Soil metagenomic analysis based on long read sequencing allowed terroir discrimination. Elemental composition analysis uncovered a possible grape and wine signature associated to terroir.

Outputs:

Andreia Figueiredo, Mariana Valente, Gonçalo Laureano, Rogério Tenreiro, José Silva, Nuno Oliveira, Margarida Gama Carvalho, Ricardo Dias (2019) Assessing vineyard terroir identity through a metagenomics analysis based on long read nanopore sequencing. Poster presentation at Genome PT Symposia, 10th March, Vairão, Vila do Conde, Portugal

Andreia Figueiredo, Margarida Gama Carvalho, Ricardo Dias (2019) Understanding the microbial community effects in a phytochemical-free vineyard. Oral presentation at Workshop Bioindicadores de Murças, 26th May, Murças, Portugal

Andreia Figueiredo (2019) Coping with sustainability demands for viticulture: breeding programs and soil microbiota as promising approaches for reduction of pesticide and water usage. Oral presenattion at the 15th EEF Lisbon congress, 2nd August, Lisbon, Portugal

Exploring surfaces of prokaryotic membranes and morphologies of respiratory complexes in membrane mimicking systems

PIs - Manuela Pereira | Mário Rodrigues

Biomedicine | Biophysics | Biological Chemistry

Membrane proteins account for 40% of the protein content of the cell. They can act as cellular gate keepers, power suppliers or communication systems. Nevertheless, knowledge of the proteins' morphology in their native environments, i.e. in the membranes, is still scarce. This project aimed to contribute to close this gap by a) investigating prokaryotic membranes and b) proteins in reconstituted systems by atomic force microscopy (AFM), integrating in this way, cellular and molecular perspectives of membrane proteins. Specifically, we investigated membranes of the *Staphylococcus aureus* by AFM. The bacterium were chosen considering their pathogenic behavior and the consequent impact in human health. We targeted both the WT and a KO strain. The knocked-out gene was a membrane respiratory protein, important both for the bioenergetic metabolism of the organism and DNA/RNA synthesis. The same knocked-out gene, was heterologously expressed and purified in order to study the protein membrane interaction by AFM, using a membrane mimicking system constituted by POPC phospholipids.

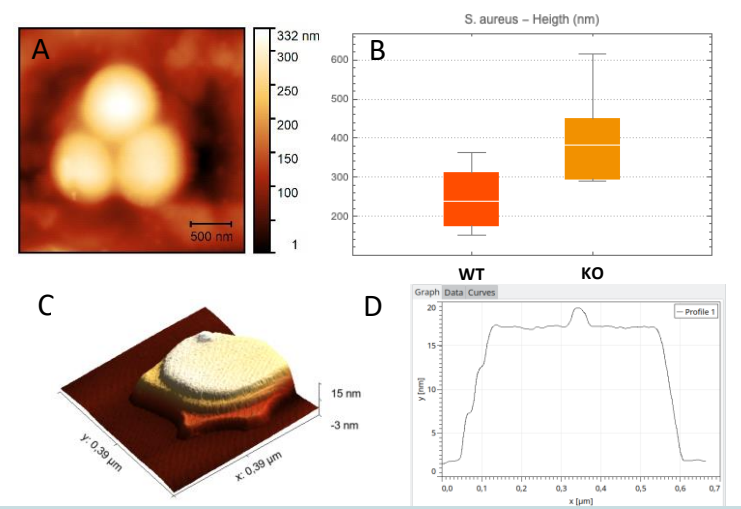


Figure 1 – AFM measurements of S. aureus MW2 cells and POPC bilayers in a mica surface. A) 3 cell cluster of S. aureus MW2 (WT) fixed in a mica surface. B) Height distribution of S. aureus MW2 cells analyzed by AFM (WT – orange; KO - yellow). C) POPC lipid bilayer on top of a mica surface with NDH-2 on top. D) Height profile along a line of panel C (in micrometers).

Results:

- **Successful immobilization and visualization of *S. aureus* cells by AFM**
- **Observation of morphological differences between WT and KO strains**
  KO mutation targeted a central membrane protein in the energetic metabolism of the organism
- **Successful deposition of a** POPC **supported lipid bilayer on top of a mica surface**
  Low reproducibility when membrane proteins were added to the system.

Conclusion:

Morphological diferences between bacterial strains are clearly observed by AFM showcasing the appositeness of the technique.

Membrane mimicking systems in the presence of protein are promising models for further optimization.

Outputs:

The work carried out during this project will be included in a manuscript which is still being prepared. It will also be presented as a poster during 2020.

The involvement of DIS3L2 in nonsense-mediated mRNA decay (NMD) and its functional networks in cancer

PIs – Luísa Romão | Paulo Matos | Peter Jordan

Biomedicine | Bioinformatics

The DIS3-like 3'-5' exoribonuclease 2 (DIS3L2) triggers decay in an exosome-independent manner and preferentially degrades RNA species possessing a non-templated oligo-uridine 3'-end tail. It is capable of inducing decay over a variety of RNAs, including mRNAs, rRNAs, miRNAs and other non-coding RNAs. It has been shown that DIS3L2 is involved in cancer-related cellular processes. Nevertheless, its function in tumorigenesis remains largely unexplored. Recently, we and others showed that DIS3L2-mediated decay together with uridylation also participate in nonsense-mediated mRNA decay (NMD), thus revealing a new NMD branch. NMD is a surveillance pathway that recognizes and degrades mRNAs harboring premature translation-termination codons, protecting the cell from potentially harmful truncated proteins. However, NMD also regulates the level of normal and fully functional mRNAs, arising as a mechanism of gene expression regulation. Here, we have been characterizing, by RNA-seq analyses, how DIS3L2 and uridylation regulate the human transcriptome. Furthermore, we are investigating how this ribonuclease participates in NMD and how its deregulation contributes to tumorigenesis.

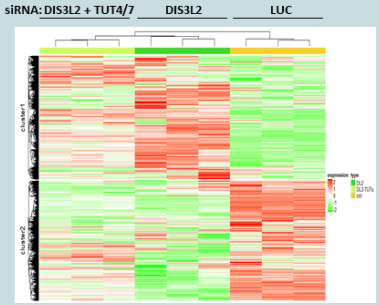


Figure 1 – Heatmap showing differences in gene expression levels across indicated conditions (TUT = Terminal Uridylyl Transferase). Red and green color indicate greater or lower counts for each gene than the row mean respectively.

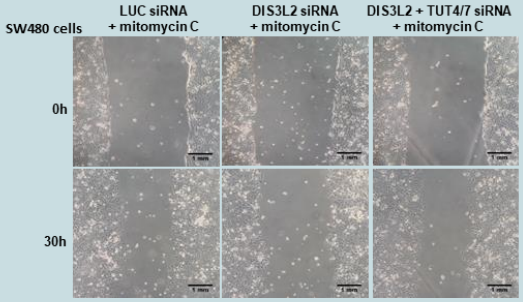


Figure 2 – Wound healing assay to evaluate the cell migration capacity under the indicated conditions. Images at 0h and 30h after scratching for the three considered conditions.

Results:

- DIS3L2 regulates the levels of transcripts encoding proteins associated with the cell cycle regulation, autophagy and membrane trafficking processes;
- DIS3L2 regulates transcripts with shorter 3'UTRs and higher GC content than the remaining transcriptome;
- DIS3L2 depletion reduces the proliferative rate of SW480 colorectal cancer cell line, while there is no effect in the NCM460 control colonocytes;
- DIS3L2 depletion tends to reduce the mobility of colorectal cancer cells.

Conclusion: DIS3L2 activity contributes to proliferation and migratory behavior of transformed colorectal cells.

Outputs:

da Costa PJ, Menezes J, Saramago M, García-Moreno JF, Santos HA, Gama-Carvalho M, Arraiano CM, Viegas SC, Romão L. A role for DIS3L2 over natural nonsense-mediated mRNA decay targets in human cells. Biochem Biophys Res Commun. 2019 Oct 22;518(4):664-671. doi: 10.1016/j.bbrc.2019.08.105.

da Costa PJ, Menezes J, Saramago M, García-Moreno JF, Santos HA, Gama-Carvalho M, Arraiano CM, Viegas SC, Romão L. Experimental supporting data on DIS3L2 over nonsense-mediated mRNA decay targets in human cells. Data Brief. 2019 Dec 6;28:104943. doi: 10.1016/j.dib.2019.104943

García-Moreno JF, da Costa PJ, Menezes J, Saramago M, Viegas, SC Arraiano CM, Romão L. The function of DIS3L2 in the mechanism of nonsense-mediated mRNA decay. 24th Annual Meeting of the RNA Society, Krakow, Poland, 11-16 June 2019

García-Moreno JF, da Costa PJ, Menezes J, Pereira M, Gama-Carvalho M, Matos P, Romão L. Functional networks of DIS3L2 in cancer and NMD. RNA Meeting: ptRNA, Porto, 24-25 January 2019

Grape Microbiome and Wine Characteristics: new implications of *terroir*

PIs – Margarida Baleiras Couto | Ana Margarida Fortes

Biotechnology | Bioinformatics

Wines made from identical grape cultivars but grown in different regions are appreciated for their distinctive features. The influence of *terroir* in determining wine sensory properties, and in particular, the role of grape microbiota on regional characteristics is a growing research field. A molecular approach using the long-read capability of the Oxford Nanopore sequencing was followed in this project providing microbial fingerprinting with resolution up to strain-level. Grape and wine metabolite analysis was performed giving insights on how grape-associated microbiota might influence chemical and sensory properties of wines. This study focused on the putative relation between grape microbiome and metabolic profiles of Syrah grape variety cultivated in two closely located vineyards in the wine Demarcated Region of Lisbon.

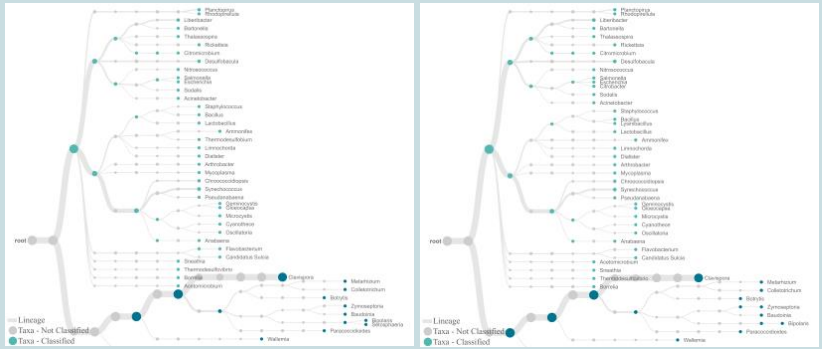


Figure 1 – Preliminary result of the taxonomy tree from grape metagenome at sites S1 and S2 at genus level. To each taxonomic placement an abundance score was assigned (over 0.1 % of total reads).

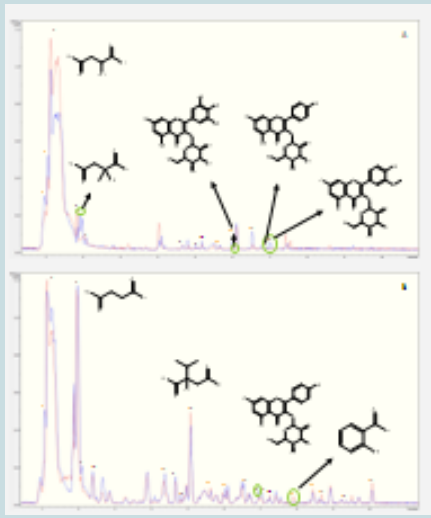


Figure 2 – Comparison between S1 (blue) and S2 (red) of metabolic profiles of Syrah variety obtained from grapes (A) and from wine (B). Compounds are identified by numbers.

Results:

- Preliminary assessment of the sequencing data of whole grapes allowed the detection of more than 40 genera;
- Differences in the metabolic profiles were detected between the two vineyards with some distinct compounds.

<u>Conclusion:</u> The genus *Clavispora* accounted for most of the reads in both vineyards. Some specific *taxa* could be distinguished between sites. The correlation between microbial diversity and wine metabolites at the vineyard level will provide new insights on the definition of local *terroir*.

Outputs:

• <u>Baleiras-Couto, M.M.</u>, Guedes, Rita, Nascimento, M., Monteiro, Filipa, Dias, R, Duarte, F.L., Serralheiro, M.L., Fortes, A.M. (2019) Microbiome and Metabolic Profiles from two Syrah Vineyards in Portugal. Poster presented at the 35th International Specialised Symposium on Yeasts (ISSY35), Antalya, Turkey. 21 – 25 October. Proceedings Book, p.127.

• Two papers in preparation.

Development of *Botrytis cinerea* DNA-based detection assays: HRM and Biosensor

PIs – Paula Lopes | Raquel Chaves | Mário Rodrigues

Biotechnology | Bioinformatics | Biophysics

Fungal infections are a major concern in worldwide viticulture. The early and accurate detection of fungal infections may decrease phytochemicals´ application which are detrimental to human health and environment. *Botrytis cinerea* Pers. is one of the most dramatic grape diseases, causing severe reductions in both quality and quantity of grapes and wine. DNA-based techniques such as conventional PCR and dot blot hybridization have been proposed for pathogen identification, but these methods are complex, expensive and time-consuming. Therefore, there is an urgent need for development of different technological approaches that can tackle this problem. In this project, the proposed teams develop a nanoparticle DNA-based biosensor suitable to differentiate between two of the tested pathogens (*B cinerea* versus *Erysiphe necator*) using DNA extracted from infected grapes based on ITS region. Simultaneously, a High Resolution Melting (HRM) assay was designed, based on the same rDNA-ITS region used in the biosensor platform, allowing the differentiation of the two pathotypes (*B. cinerea* versus *E. necator*). These results allowed the development of two distinct and alternative platforms that are suitable for *B.cinerea* detection and that can be further applied to field samples.

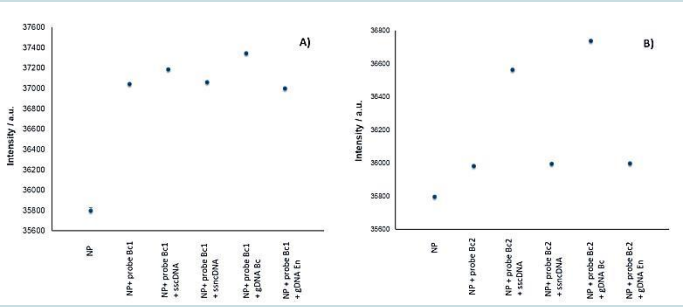


Figure 1 - Nanoparticle DNA-based biosensor detection of Botrytis cinerea using:
(A) Probe Bc1;
(B) Probe Bc2.

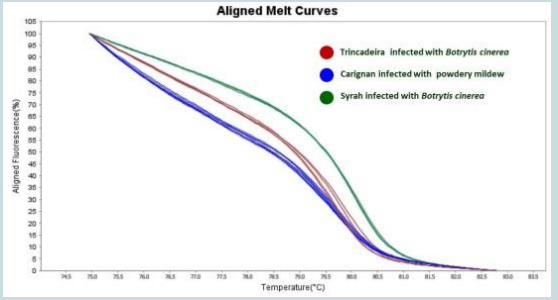
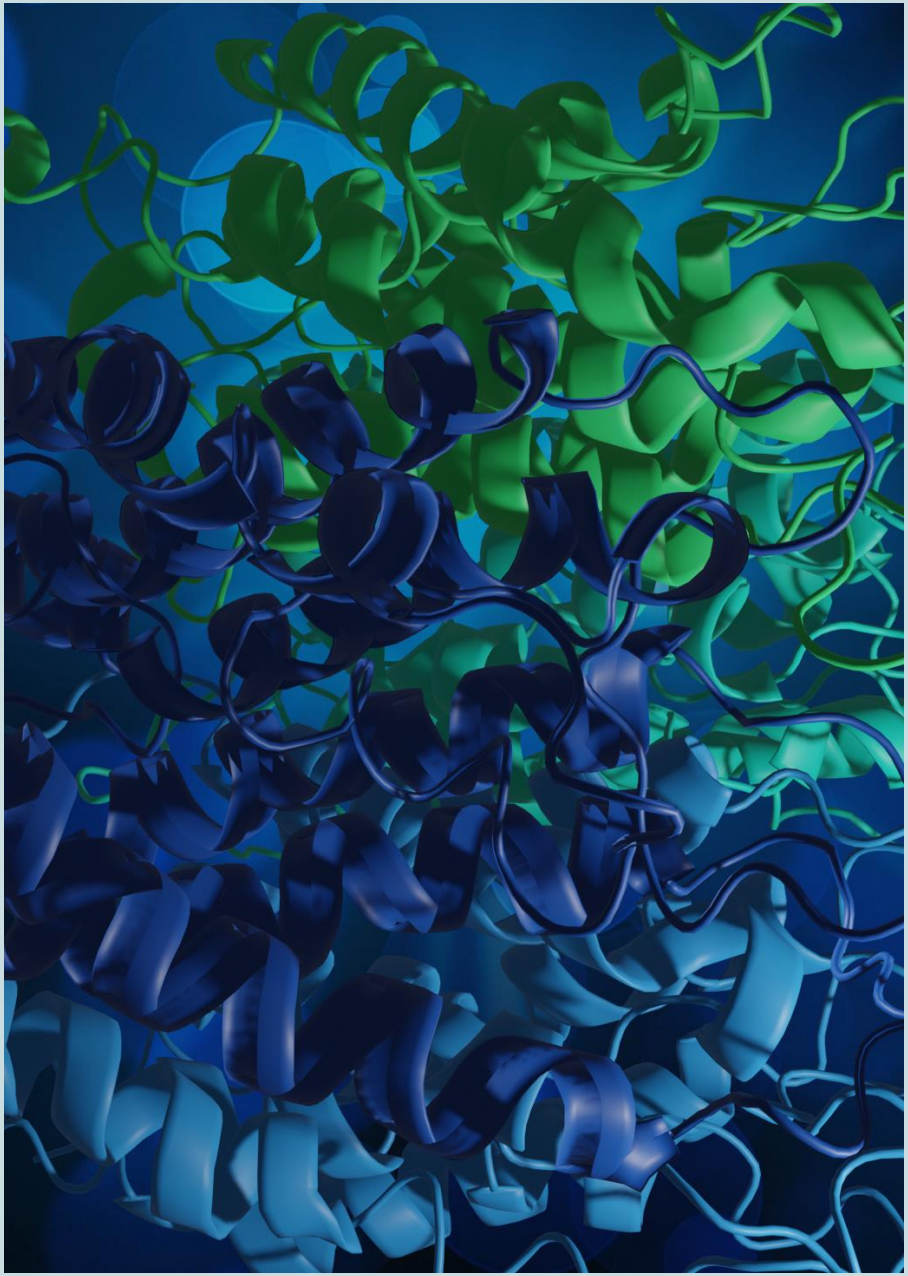


Figure 2 - HRM profiles obtained using rDNA-ITS sequences in different grapevine varieties, with differential susceptibility:
- Trincadeira (susceptible to B. cinerea);
- Carignan (tolerant to B. cinerea and susceptible to E. necator), and
- Syrah (moderately tolerant to B. cinerea).

Results:

- The Nanoparticle DNA-based biosensor system used in genomic DNA extracted from grapes infected with *B. cinerea* and *Erysiphe necator* allowed the detection of *B. cinerea,* revealing the specificity of the used probes (Figure 1).
- The HRM profiles obtained allowed a complete distinction of the tested pathotypes (*B. cinerea vs E. necator*) and allowed to understand that the grapevine variety Syrah presented apart from the *B. cinerea* other pathogens (Figure 2).

Conclusion: Both DNA-based detection assays have been successfully applied in the detection and differentiation of *B. cinerea* in *Vitis vinifera* L..



BioISI Research Units (Groups)

Aquaporin shades of blue - Artistic tri-dimensional representation of the Aquaporin protein structure. Image provided by Bruno Victor (CBS 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 signalling and secretory pathways regulating growth and morphogenesis;
- Omics analysis of plant (and fruit) development and responses to biotic interaction (parasitic and symbiotic) and abiotic stresses;
- Food authenticity and traceability;
- Genetic variability and plant cytogenomics;
- Genome editing of relevant crops and cultivars for better traits and increased resilience.

Major Achievements:

- Omics and phenotyping analysis in *Vitis vinifera* upon biotic and abiotic stresses to characterize mechanisms involved in plant resistance and adaptative responses;
- DNA-based label-free biosensors used for food authenticity purposes;
- Transcriptome analysis highlights regulation of seed development by small non-coding RNAs (sRNAs) in conifers;
- Field and *in vitro* selection of plants with abiotic stress tolerance and high nutritional value aiming crop improvement using cytogenomic, gene expression and cyto-genotoxic approaches;
- Climatic impacts on the bacterial community profiles of cork oak soils;
- Characterization of novel proteins involved in angiosperm (Arabidopsis) morphogenesis and sexual reproduction.

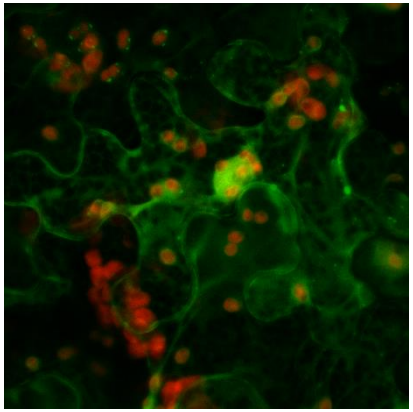


Figure 1. Tobacco cells expressing GFP-bound chestnut endomembrane protein.

Figure 3: Lipid and fatty acid modulation in *Vitis vinifera* (in response to pathogen attack)

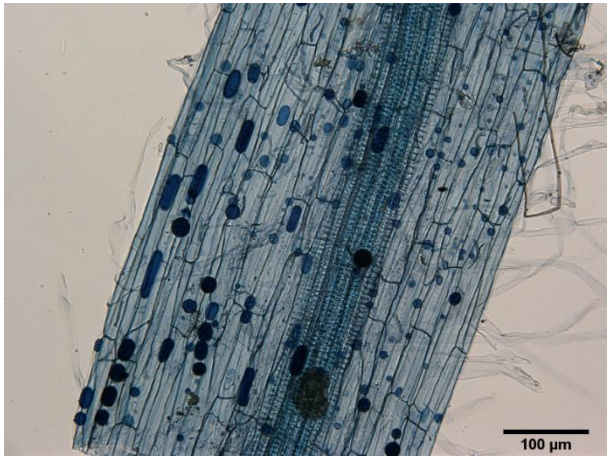


Figure 2: Tomato root inoculated with symbiotic fungus (*Rhizophagus irregularis*).

Figure 4: Arabidopsis seedlings.

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, Rute Amaro, Inês Diniz, Ana Rita Santos, Rui Nascimento, Ana Alves, Sara Barrias, Francisca Reis, Daniela Costa, Helena Silva, Teresa Gomes, João Mina, Shweta Singh, Dario Marchese, Ana Alhinho, Marlene Santos

Selected Publications

1. A role for Diacylglycerol Kinase 4 in signaling crosstalk during Arabidopsis pollen tube growth. Vaz Dias *et al. New Phytologist* 222: 1434-1446. doi.org/10.1111/nph.15674.
2. Label free DNA-based Optical Biosensor as a potential system for Wine Authenticity. Barrias *et al. Food Chemistry*, 270: 299-304. DOI: 10.1016/j.foodchem.2018.07.058
3. Small RNA profiling in Pinus pinaster reveals the transcriptome of developing seeds and highlights differences between zygotic and somatic embryos. *Rodrigues et al. Scientific Reports* 9, 11327. doi: 10.1038/s41598-019-47789-y

Key Funded Projects

Fostering High-Throughput Plant Phenotyping by an Interdisciplinary Approach (INTERPHENO)". PTDC/ASP-PLA/28726/2017, 166.661€. Coordination.
Characterization of genetic and environmental determinants involved in reproductive development of *Castanea sativa*. POCI-01-0145-FEDER-027980, 239.964€. Coordination.
Transcriptome and metabolome reprogramming in *Vitis vinifera* cv. Aragonês and *Vitis rupestris* berries upon infection with *Erysiphe necator*. PTDC/ASP-HOR/28485/2017. 239.123€. Coordination.

FunGP Group

Functional Genomics and Proteostasis

http://bioisi.pt/fungp/

Biomedicine: translating genes and genomics into personalized & systems medicine; relating protein structural changes to disease states; elucidating mechanisms of disease; development of innovative therapeutic strategies & drug discovery; performing pharmaco-genetics & pharmaco-resistance tests.

1. Translational science and personalized medicine in Cystic Fibrosis.
2. Molecular and cellular mechanisms of secretory traffic of CFTR and CF-related ion channels (anoctamins, SLC26A9).
3. Signalling/ signal transduction pathways in human disease.
4. Systems approaches to tackle mechanisms of disease: Cystic Fibrosis, cancer and neurodegeneration.
5. Drug development for CF, cancer and neurodegeneration.
6. Protein structure and (mis)folding in the context of complex biomedical problems;
7. Identification of disease mechanisms in Alzheimer's Disease (AD) and in mitochondrial rare diseases.
8. Pharmacology of drug resistance and pharmacogenetics, having *Plasmodium falciparum* (malaria) as the main model

Major Achievements:

- Characterization of the interactome regulating the ER exit of CFTR bearing the most common disease-causing mutation
- Application of network biology approaches to identify novel regulators of CFTR trafficking (with GER)
- Identification of the protease Calpain 1 as new a druggable target with potential therapeutic application in Cystic Fibrosis
- Development of new tools for the visualization and study of the JAK/STAT3/GFAP pathway
- Elucidation of functional relationships between S100 inflammatory mediators and AD pathophysiology.
- Molecular diagnosis, prognosis, structural analysis and clinical correlations in a rare mitochondrial disease.

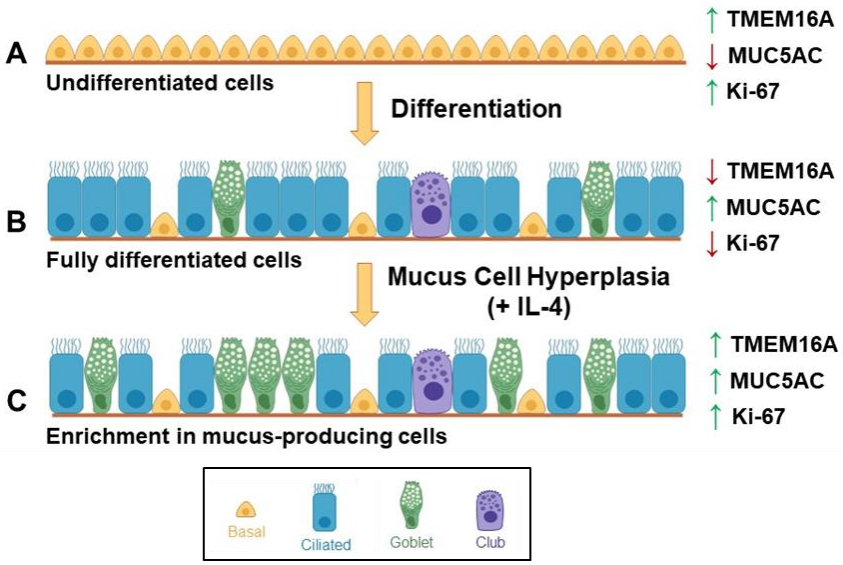


Figure 1: Scheme of the relationship between TMEM16A, MUC5AC and proliferation (Ki-67) during differentiation and mucus cell hyperplasia of respiratory cells.

Selected Publications

1. Simões FB, Quaresma MC, Clarke LA, Silva IAL, Pankonien I, Railean V, Kmit A, Amaral MD (2019) TMEM16A Chloride Channel Does not Drive Mucus Production. *Life Sci Alliance*. 2 (6). doi: 10.26508/lsa.201900462.

2. Santos JD, Canato S, Carvalho AS, Botelho HM, Aloria K, Amaral MD, Matthiesen R, Falcao AO, Farinha CM. (2019) Folding Status Is Determinant over Traffic-Competence in Defining CFTR Interactors in the Endoplasmic Reticulum. *Cells* **8**: 353. doi: 10.3390/cells8040353

3. Matos AM, Pinto FR, Barros P, Amaral MD, Pepperkok R, Matos P (2019) Inhibition of calpain 1 restores plasma membrane stability to pharmacologically rescued Phe508del-CFTR variant. *J Biol Chem* **294**: 13396-13410. doi:10.1074/jbc.RA119.008738.

4. Letra-Vilela R*, Cardoso B*, Silva-Almeida C, Rocha AM, Murtinheira F, Branco-Santos J, Rodriguez C, Martin V, Santa-Marta M, Herrera F (2019) Can asymmetric post-translational modifications regulate the behavior of STAT3 homodimers? *FASEB Bioadvances*. In press. [*equal contributions]

5. Henriques BJ, Lucas TG, Martins E, Gaspar A, Bandeira A, Nogueira C, Brandão O, Rocha H, Vilarinho L, Gomes CM (2019) Molecular and Clinical Investigations on Portuguese Patients with Multiple acyl-CoA Dehydrogenase Deficiency. *Curr Mol Med* **19**: 487-493. doi: 10.2174/1566524019666190507114748.

6. Protein Misfolding Diseases - Methods and Protocols' from the Methods in Molecular Biology series. Vol. 1873. Gomes, CM (Ed.)

Group Members

GL: Margarida D. Amaral

PI's:

Bárbara Henriques | Carlos Farinha | Cláudio Gomes | Federico Herrera | José-Pedro Gil | Miquéias Lopes-Pacheco | Paulo Matos

Post Docs: Ana Margarida Matos | Andrea Gutierrez | Arthur Kmit | Hugo Botelho | Ines Pankonien | Iris Silva | Luka Clarke | Mafalda Bacalhau | Mickael Diallo | Patrícia Barros | Susana Igreja

PhD Students: Beatriz Cardoso | Catarina Pereira (BioSYS) | Daniel Cruz (BioSYS) | Fernanda Murtinheira | Filipa Simões (BioSYS) | Inês Leitão | Joana Cristovão | João Santos (BioSYS) |Leyre Pernaute (BioSYS) | | Juan Fernandez-Moreno (BioSYS) | Lúcia Santos (BioSYS) | Luís Sousa (BioSYS) | Madalena Pinto (BioSYS) | Márcia Faria (BioSYS) | Margarida Quaresma (BioSYS) | Mariana Romão (BioSYS) | Ricardo Vilela | Romina Coelho (BioSYS) | Sofia Ramalho (BioSYS) | Tiago Pedreira (BioSYS) | Violeta Railean

MSc Students: Ana Rita Prada | André Gomes | Carina Rebelo | Catarina Narciso | Guilherme Moreira |João Ferreira | Maria Joana Ribeiro | Maria Carolina Silva | Ricardo Marques| Ricardo Quiteres

BI Researchers: Guilherme Moreira | Joana Ferreira | Maria Joana Ribeiro | Rodrigo David | Tânia Lucas

Technicians: Sofia Correia

Key Funded Projects

iDrugCF-Identification of New Drugs for Cystic Fibrosis. FCT (PTDC/MED-QUI/2017/28800). Budget: 240K€. MD Amaral (PI).
Novel signalling pathways regulating membrane retention of epithelial chloride transporters. FCT (PTDC/BIA-CEL/28408/2017). Budget: 239K€. Co-PI (CM Farinha).
NISomics - Characterization of the sodium iodine symporter Post-translational interactome. FCT (PTDC/BIA-MOL/31787/2017). Budget: 240K€. P Matos (co-PI)
Mechanistic and optogenetic control of astroglia for neural repair. FCT (PTDC/MED-NEU/31417/2017). Budget: 239K€. F Herrera (PI).
Mechanisms of protein dysfunction in mitochondrial diseases. FCT/PTDC/BIA-BQM/29963/2017). Budget: 219K€. B. Henriques (PI).
Gilead Sciences (Research Scholars Program in Cystic Fibrosis) Identification of novel F508del-CFTR traffic correctors among FDA-approved drugs. Budget: 130K$; 2 yrs. PI: M Lopes-Pacheco (Mentored by MD Amaral).
2017 European Union (H2020-SC1-2017-755021). HIT-CF – Personalised Treatment For Cystic Fibrosis Patients With Ultra-rare CFTR Mutations (and beyond). Total budget: 6.7M€ / FCID: 257K€; 5 yrs. Coordinator: Kors van der Ent, University Medical Centre Utrecht, Utrecht (Netherlands). Coordination FCUL Group: MD Amaral.

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).

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 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.
- Integrative omics-based analysis of the microbiome of Douro Wine Region towards the enlightening of its adaptive potential to dry and warm conditions due to climate changes.
- Validation of flow cytometry methodology for viability monitoring of beer yeasts.
- Detection of long-range size magnetic crystalline structures other than magnetosomes in magnetotactic bacteria.

Grey and Green M&B

- Major contributions in the field of Ascomycete systematics, with introduction of new families, genera and species and reappraisal of families in Botryosphaeriales.
- Unveiling the evolutionary history of fungal families and genera through dating divergence time in relation to major evolution events of angiosperms on a geological timescale.
- Identification of symbiotic microbial diversity associated to phylloplane of different Nicotiana tabacum genotypes
- Characterization of root microbiome of centennial vineyards from Cyprus.
- In-depth characterization of the global microbiome associated with Pine Wilt Disease, including the nematode, the insect vector and the host tree.
- New country, state and regional records of the needle blight pathogens affecting different pine species
- Novel microbial consortia (combining natural and adaptive evolved strains) for bioaugmentation.
- Optimization of real-time PCR assays for expression analysis of terpene synthase genes in thyme varieties with different aromatic content
- Identification of two new bacterial plant diseases affecting cultivated plants in Portugal
- Isolation of pathogenic and endophytic bacteria associated to forest trees in Portugal
- Identification of turf-grass diseases through Green Project phytopathology service.

Gold and Red M&B

- Implementation of an unique dedicated computational infrastructure for processing genomic data in real-time (BioISI Genomics) under the coordination of R Dias.
- Intelligent Decision Support Systems for personalized prevention and clinical management of infectious diseases.
- Identification of biotechnological potential on genomic nonfunctionalized orthologs elements from microbial origin
- Development of the first comprehensive worldwide database on Microbial Genomic Dak-Matter
- Development of new approaches for geotraceability based on whole genome sequencing information.
- Validation of yeast STN genetic tools with drugs able to modify the ethiology of cystic fibrosis.
- Detection of Aedes albopictus mosquito (dengue vector) in the North of Portugal (Penafiel) and South of Portugal (Algarve) within the vector surveillance network- REVIVE.
- Re-emergence of Zika virus in Africa by proving the circulation of Asian lineage Zika virus in Angola and linkage to the increase of microcephaly cases.
- Identification of bioactives from environmental fungi and bacteria with the potential to treat cystic fibrosis

Blue M&B

- Participation of a group member and co-coordination of writing for National Agenda for Research and Innovation in Ocean 2030, upon request by Fundação para a Ciência e Tecnologia.
- Characterization of marine microbes and marine sponges for bioactivity profiles for several applications in health, cosmetics and food and evaluation of sea host- associated microbiomes.
- Nomination of a group member as an international expert at Blue Economy and Science for the United Nations, Ocean Affairs Department, to participate in the writing team of the 2nd World Ocean Assessment.
- Positioning of a group member as an international expert at Blue Economy and Science contributing for BioBased and Bioeconomy networks in EU (BBI-JU and ERA-NET MARINE BIOTECH) as well as a national (BLUEBIO ALLIANCE) and EU Commission reference for marine biotech.
- Reinforcement of group collaborations, at national (CIIMAR, MARE, IPL and CESAM) and international (EU, Baltic and Mediterranean) levels, with approved projects and new projects for future grant applications.
- Full genome reconstruction of deep sea vent prokaryote with relevant biotechnological potential.
- Isolation and characterization of a collection of ca. 170 isolates from deep-sea sediments with potential sulfur and/or manganese oxidizing activity

Figure 1*:* Morphology of *Capnodium sp.* pycnidia on the host. Image provided by Alan Phillips.

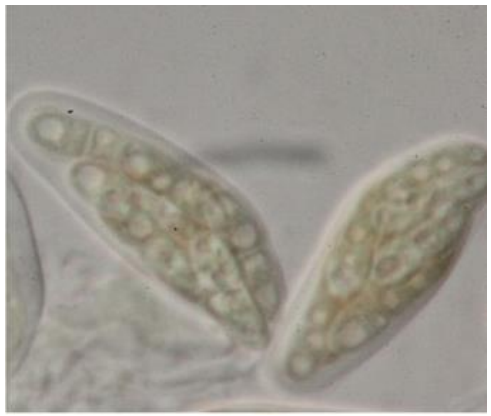


Figure 2*: haetothyrina guttulate a*sci at maturity Image provided by Alan Phillips.

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Group Members

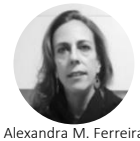
GL: Rogério Tenreiro

PI's:


Alan Phillips


Arlete Faia


Líbia Zé-Zé


Alexandra M. Ferreira


Leonor Cruz


Ricardo Dias


Ana Tenreiro


Helena Vieira


Lélia Chambel


Lisete Fernandes


Filomena Duarte


Margarida B. Couto


António Pagarete

Established Scientists: Ana Reis |Catarina Barbosa | Joana Henriques | João Baptista Ferreira | Mário Santos | 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

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

MSc Students: Ana Lourenço | Francisco Fonseca | Gabriela Simões | Miguel Guerreiro

Early Scientists: Ana Rocha | Inês Santos | João Melo | Marcos Esteves

CLO: Filipa Silva

Selected Publications

1. Jayawardena RS, Hyde KD, McKenzie EHC, Jeewon R, Phillips AJL, Perera RH, de Silva NI, Maharachchikumburua SSN, Samarakoon MC, Ekanayake AH, Tennakoon DS, Dissanayake AJ, Norphanphoun C, Lin C, Manawasinghe IS, Tian Q, Brahmanage R, Chomnunti P, Hongsanan S, Jayasiri SC, Halleen F, Bhunjun CS, Karunarathna A, Wang Y (2019) One stop shop III: taxonomic update with molecular phylogeny for important phytopathogenic genera: 51–75 (2019). Fungal Diversity, 98(1), 77-160. doi: 10.1007/s13225-019-00433-6

2. Esteves M, Barbosa C, Vasconcelos I, Tavares MJ, Mendes-Faia A, Mira NP, Mendes-Ferreira A (2019) Characterizing the Potential of the Non-Conventional Yeast Saccharomycodes ludwigii UTAD17 in Winemaking. Microorganisms, 7(11), 478. doi: 10.3390/microorganisms7110478.

3. Duarte FL, Egipto R, Baleiras-Couto MM (2019) Mixed Fermentation with Metschnikowia pulcherrima Using Different Grape Varieties. Fermentation, 5(3), 59. doi: 10.3390/fermentation5030059

Key Funded Projects

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. 2016-2019. Total funding: 1.05 M€. M&B-BioISI funding: 449 k€. FCUL PI: R. Dias (FCUL).

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: A Tenreiro (FCUL), R Tenreiro (FCUL

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 Team: R Tenreiro (FCUL), A Tenreiro (FCUL), R Dias (FCUL), A Reis (FCUL), L Chambel (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:

- We progressed in the development of systems medicine approaches to understand the biological pathways underlying the very complex phenotype of autism spectrum Disorder. Namely, we established a proof of concept that genotype-phenotype correlations can be defined in ASD, and that biological processes can predict multidimensional clinical phenotypes, highlighting machine learning approaches using multidimensional measures in the construction of more homogeneous clinical profiles (Asif et al, epub 2019)
- As part of the Coordination Group of the 1+Million Genomes Initiative in Europe, we participated in the construction of the roadmap for sharing genomic and health data for at least 1 million individuals in Europe by 2022 and implementation in healthcare systems.
- 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)
- The Paediatric European Familial Hypercholesterolaemia (FH) Registry published the characteristics of diagnosis and treatment of children with FH. The characteristics of Portuguese children are similar to other European countries, but an effort must be made to increase early diagnosis and implementation of appropriated treatment. We further progressed with the characterization of the FH phenotype and identification of novel genes (Mariano et al in press; Ramaswami U et al, epub 2019; Alves et al, 2019)
- The effects of a specific drug (Evinacumab) in homozygous FH patients with a spectrum of LDLR activity were defined by functional analysis in lymphocytes (Banerjee et al, 2019)
- The work “Translational Medicine in Familial hypercholesterolaemia: from genotype to phenotype” received a Distinction in BIAL award in Clinical Medicine (Honorable Mention). The work will be published in a book format by BIAL Foundation.
- We further developed our work on the genotype-phenotype correlations in rare diseases (Cardoso MC et al, 2019, Mariana M, 2019).
- In collaboration with the European School for Interdisciplinary Tinnitus Research, among other partners, we developed the Portuguese version for Tinnitus evaluation considering European criteria. We also concluded a study on Sex and Gender Differences in Tinnitus in the Portuguese population and explored the role of inflammatory processes in Tinnitus and hearing loss (Haider H et al, 2019; Aguiar L et al, 2019).

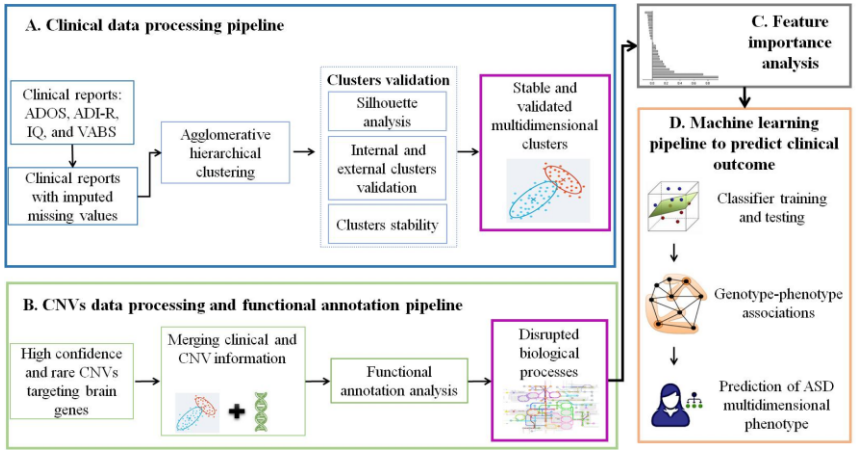


Figure 1: Integrative systems medicine approach to identify complex genotype-phenotype associations in Autism Spectrum Disorder

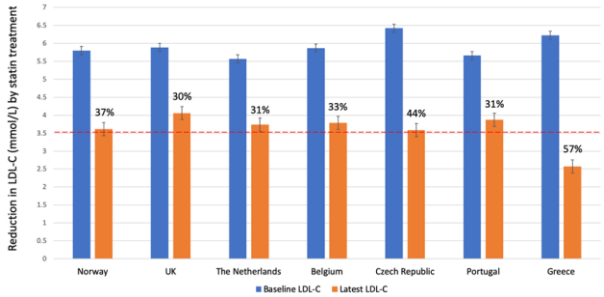


Figure 2: Baseline and treated LDL-C in children who went on receiving statins. The percentage on top of latest LDL-C bars represent the reduction in LDL-C by treatment in each cohort. The target LDL-C level of 3.5 mmol/L is shown by a dashed red line

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) Cibelle Mariano (BioSYS) | Haula Haider | 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: Ana Leonie | Micaela Santos

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

Selected Publications

1. Asif M, Martiniano HFMC, Marques AR, Santos JX, Vilela J, Rasga C, Oliveira G, Couto FM, Vicente AM. Identification of biological mechanisms underlying a multidimensional ASD phenotype using machine learning. Translational Psychiatry, 10, 43 (2020) epub 2019,.
2. Ramaswami U, Futema M, Bogsrud MP, Holven KB, van Lennep JR, Wiegman A, Descamps OS8, Vrablik M, Freiberger T, Dieplinger H, Greber-Platzer S, Gabriele Hanauer-Mader G, Bourbon M , Drogari E, Humphries SE. Comparison of the characteristics at diagnosis and treatment of children with Heterozygous Familial Hypercholesterolaemia (FH) from eight European countries. Atherosclerosis 2019, Accepted for publication
3. Mariana M Chaves MM, Castro R, Mota-Vieira L, Carneiro V. A rare case of a primary retroperitoneal mucinous cystic tumour with borderline malignancy and literature review. BMJ Case Rep, 12 (9):e230708.
4. Haúla F. Haider, Sara F. Ribeiro, Catarina Martins, Diogo Ribeiro, Nuno Trigueiros, Agnieszka J. Szczepek, Helena Caria, Derek J. Hoare, João Paço & Luís-Miguel Borrego (2019) Tinnitus, hearing loss and inflammatory processes in an older Portuguese population, International Journal of Audiology
5. Nicolau M, Vargas S, Silva M, Coelho A, Ferreira E, Mendonça J, Vieira L, Kjöllerström P, Maia R, Silva R, Dias A, Ferreira T, Morais A, Soares IM, Lavinha J, Faustino P. Genetic modulators of fetal hemoglobin expression and ischemic stroke occurrence in African descendant children with sickle cell anemia. Ann Hematol. 2019 Dec;98(12):2673-2681.

Key Funded Projects

1. Gene-environment interactions in Autism Spectrum Disorder (ASD). Funded by Fundação para a Ciência e Tecnologia, PTDC/MED-OUT/28937/2017 . 2019-2022 Total Budget 239 340€ PI Astrid Vicente.
2. FH in Iberoamerica 2018-2021Funded by FASTA University Mar del Plata, Argentina Total funding 40 320€ Principal Investigator

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 namely in human health and disease.

Major Achievements:

• **Non-coding genome:** Satellite non-coding RNA, specifically FA-SAT ncRNA, was found to be associated with cancer and its regulation cannot be explained solely by DNA methylation1. Other satellite DNA (1.713 from cattle) was established to be associated with centromeric activity in bovidae genomes.

• **RNA processing, translation & decay:** The DIS3L2-mediated decay together with uridylation participate in nonsense-mediated mRNA decay (NMD). This pathway constitutes a new NMD branch2.

• **Network biology:** Development of a method to integrate sets of co-immunoprecipitated proteins and identify candidates specifically bridging bait proteins. This strategy led to the discovery of novel modulators of CFTR trafficking and membrane stability3.

• **Signaling Pathways:** Tyrosine phosphorylation of two epithelial choride transporter proteins was identified to modulate their retention at the plasma membrane.

• **miRNAs in disease:** Identification of the miR-34a/SIRT1:AMPK pathway as an inducer of mitochondrial dynamics dysfunction in skeletal muscle and in the pathogenesis of non-alcoholic fatty liver disease.

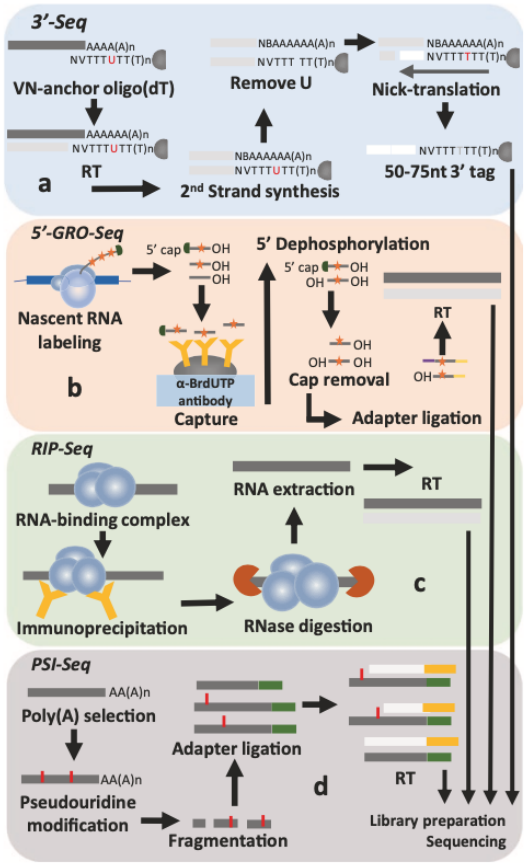


Figure 1: RNA-seq derived methods for global analysis of mRNA processing.

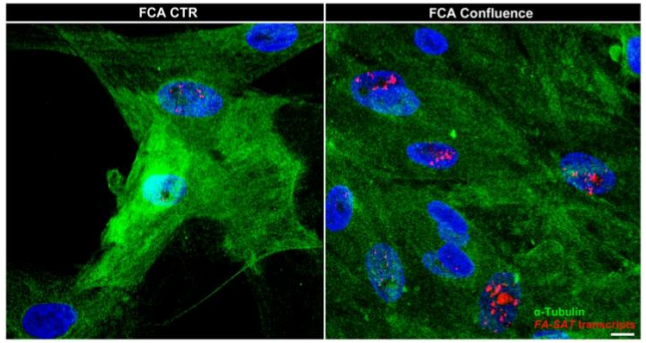


Figure 2: FA-SAT ncRNA (detected through RNA-FISH) accumulation naturally triggered in confluence stress.

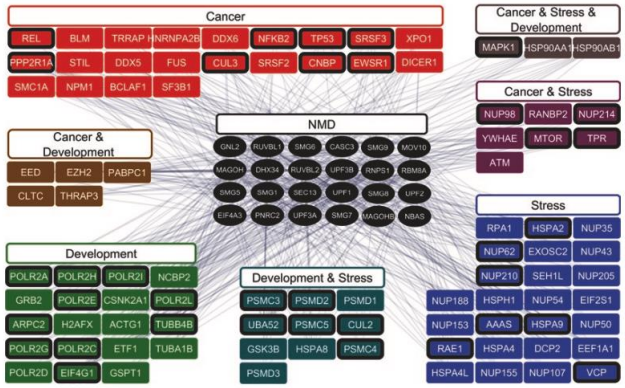


Figure 3: Protein interaction network linking NMD factors and related biological processes.

Group Members

GL: Margarida Gama-Carvalho

PI's:


Francisco R. Pinto


Luísa Romão


Peter Jordan


Raquel Chaves

Post Docs: Maria Filomena Adega | Vânia Gonçalves | Juliane Menezes | Rafaela Santos | Mark Gibson | Daniela Ferreira | Cláudia Loureiro | Ana Margarida Matos | Cláudia Bessa | Sandra Louzada | Ana Escudeiro

PhD Students: Andreia Henriques | Guillem Aguilar | Gonçalo Nogueira | Joana Pereira | Joana Silva | Mariana Pinhão | Marina Garcia-Vaquero | Marta Correia | Juan García-Moreno | Rafael Fernandes | Tânia Marques | Mariana Lopes

Other researchers: Bruna Pereira | Cláudia Estima | Inês Martins | Joao Paulo Silva | Miguel Pereira | Patrícia Dias | Sofia Conceição | Fábio Resende | Daniel Eleutério| Diogo Lucas | Juliana Miranda | Catarina Cunha | Albano Pinto

Selected Publications

1. Ferreira et al (2019) FA-SAT ncRNA interacts with PKM2 protein: depletion of this complex induces a switch from cell proliferation to apoptosis. Cell Mol Life Sci., 77, 1371.
2. da Costa et al (2019) A role for DIS3L2 over natural nonsense-mediated mRNA decay targets in human cells. Biochem Biophys Res Commun, 518, 664.
3. Loureiro et al (2019) Network Biology Identifies Novel Regulators of CFTR Trafficking and Membrane Stability. Front Pharmacol, 10, 619.

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€
- New signaling pathways involved in the retention of epithelial choride transporters PTDC/BIA-CEL/28408/2017, October 2018-September 2021 Budget: 240K€
- LungCARD. EU project 734790 Call H2020-MSCA-RISE-2016. Proponent: STAB VIDA. Jan 2017-Dec 2020 Budget: 1M€ global/144K€ local

CBS Group

Chemistry for Biological Systems

http://bioisi.pt/cbs/

CBS research embraces vast complementary topics: a) molecules and materials from synthesis: catalysts, magnetic systems for spintronics, and green systems for artificial photosynthesis or antifouling; b) drug leads or bioactive compounds from marine organisms, algae, food components, industrial waste, and medicinal herbs; c) *in silico* solutions for materials and catalysis (reaction mechanisms, magnetism, and photochemistry); d) simulation methods to study 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:

- The molecular basis for the catalysis of the hydrogen evolution reaction using group 6 oxy-sulfides was demonstrated;
- Reduced diet cholesterol permeation by phenolic compounds was shown;
- Twelve new psychoactive substances were identified. These were essential for the resolution of 8 judicial cases;
- A comprehensive analysis of the composition of the respiratory chains of different taxonomic clades was delivered;
- New computational methods and parameters allowed the calculation of solvation energies of halogenated molecules with impact in medicinal chemistry;
- Methodological development of constant pH Molecular Dynamics coupled with enhanced sampling techniques was developed;
- New patent concerning biocides immobilization in polymeric matrices was achieved (PT108096).

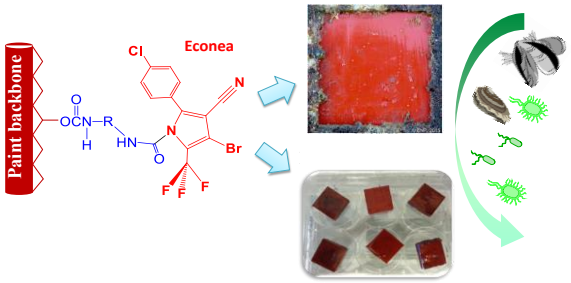


Figure 1: Blueprint of shipping endorsed by non-biocide release antifouling paints.

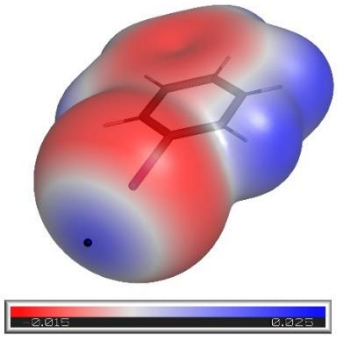


Figure 2: Electrostatic potential mapped on the electronic density of iodobenzene. A positive region on the halogen, shown as a black dot and termed sigma-hole, is responsible for halogen bonding.

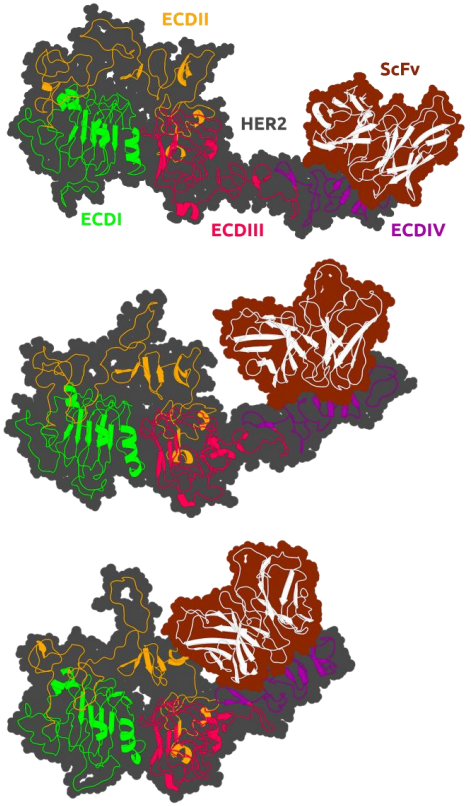


Figure 3: ScFv:HER2 system in different conformation states obtained from MD simulations.

Group Members

GL: Maria José Calhorda

PI's:


Manuela M. Pereira


Paulo Costa


Mª Luísa Serralheiro


Miguel Machuqueiro


Helena Gaspar


Paulo Martinho


Nuno Bandeira


Elisabete Silva


Rita Pacheco


Nuno Galamba

Post Docs: Marta Saraiva| Diogo Vila-Viçosa| Sara Realista| Pedro Magalhães | Celso Almeida | Ana Vicente | Pedro L. V. Falé

PhD Students: Rafael Nunes| Tomás Silva| Pedro Reis| Olga Ferreira | Ana Rita Neves | Joana Hipólito | Mohamed Soliman | Jiawei Wang | Rebeca Esperança André | Ana Rita Ferraz| Joana Matos

MsC Students: Andreia Fortuna | Bárbara Oliveira | Janaína Almeida | Frederico Martins | Diogo Reis | César Reis | Mónica Antunes | Margarida Sequeira | Daniela Silva | Laura Guedes

Other researchers: Adrià Gil-Mestres

Selected Publications

1. J. McAllister, N. A. G. Bandeira, J. C. McGlynn, A. Y. Ganin, Y.-F. Song, C. Bo, H. N. Miras, 'Tuning and mechanistic insights of metal chalcogenide molecular catalysts for the hydrogen-evolution reaction', Nature Commun., 10, 370 (2019) [10.1038/s41467-018-08208-4]
2. E.R. Silva, O. Ferreira, P.A. Ramalho, N.F. Azevedo, R. Bayón, A. Igartua, J.C. Bordado, M.J. Calhorda, 'Eco-friendly non-biocide-release coatings for marine biofouling prevention', Sci. Total Environ., 650, 2499–2511 (2019) [10.1016/j.scitotenv.2018.10.010]
3. D. Vila-Viçosa, P. B. P. S. Reis, A. M. Baptista, C. Oostenbrink, M. Machuqueiro, 'A pH Replica Exchange scheme in the Stochastic Titration constant-pH MD method', J. Chem. Theory Comput., 15, 3108-3116 (2019) [10.1021/acs.jctc.9b00030]

Key Funded Projects

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

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

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

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

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:

- AFM/FFM: mechanical properties of human bronchial epithelial cells stably transduced with either wt-CFTR or F508del-CFTR, were analysed using a conventional AFM and a custom-made FFM. In both cases wild type cells have shown significantly higher Young's modulus than the CFBE cells expressing mutant CFTR, a difference which can be interpreted as a signature of a more disorganized actin cytoskeleton, related to the F508del mutation; detailed AFM studies on topography and mechanical properties of Bcc bacteria provided the first insigts into adaptative evolution of these bacteria,during long-term infection [Hassan A.A. et al., Scientific Reports 9(1),16118,2019].
- Magnetic nanoparticles for biomedical applications: using green chemistry iron oxide nanoparticles and biocompatible water based ferrofluids with very high stability and good thermal efficiency were produced, giving promising results for subsequent organization aiming at improved magnetic anisotropy features [OrMagna, FCT grant].
- Protein physics: to get further information on the early stage of the β2m aggregation mechanism, molecular simulations were used to perform an in depth comparative analysis of the dimerization phase of the D76N mutant and the DN6 variant. The results from the extensive simulations carried out allowed to obtain first theoretical insights into the tetramerization interface of the mutant [Rui J S Loureiro et al. Biomolecules 9,366,2019].
- Atomic/electronic structure: based on the calculation of electron binding energies for two conformers of a prototypical photo-switch molecular system (azobenzene) a mechanism for the dark cis-trans isomerization in different environments (azobenzenes in interaction with gold nanoparticles) was proposed and supports some experimental findings [Martins G F et al., J Phys Chem A, 123,2091,2019]; in collaboration with experimental research groups from LNHB (Saclay) and Kyoto University, a new theoretical approach for the X-ray energies of Gadolinium was proposed [Y. Ménesguen et al., J. Quant Spectr & Rad Transf,236,106585,2019].

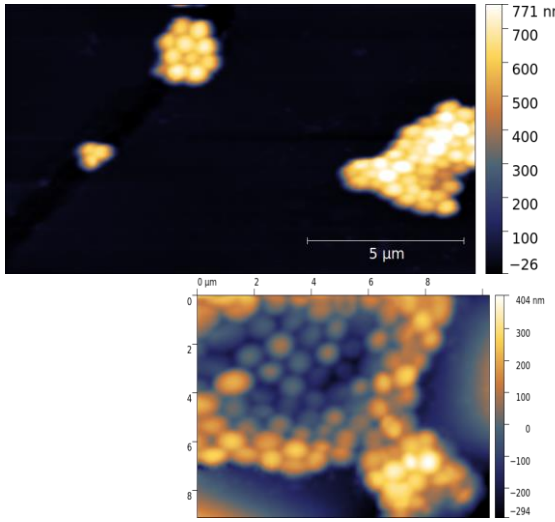


Fig.1. S. aureus MW2 WT cluster in a mica surface.

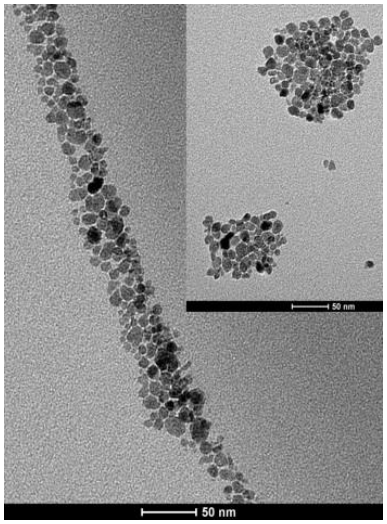


Fig.3. TEM images of magnetite organized NPs prepared by the co-precipitatio method.

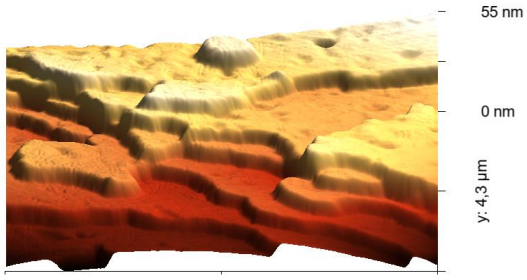


Fig 2. POPC lipid bilayer on top of mica surface (AFM)

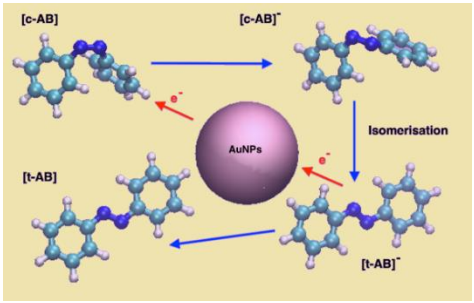


Fig.4 . Possible pathway for dark *cis–trans* isomerization of azobenzene in interaction with gold nanoparticles.

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

Other integrated members: Margarida Pires | António Casaca | M. Estrela M. Jorge | Tânia Ramos | Abdollah Hajalilou (Jan 2019)

PhD Students: Miguel Vitorino (DAEPHYS) | Rodrigo Antunes (DAEPHYS) | João P Santos (BioSYS, with BTR) | Rui J Loureiro (BioSYS)

Master Students: João Freitas | Daniela Pires (ongoing)

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

Selected Publications

1. RJ Loureiro , Diogo V Viçosa, Miguel Machuqueiro, Eugene Shakhnovich, Patricia FN Faísca, "The early phase of the β2m aggregation mechanism: An integrative computational study based on the D76N mutant and ΔN6 variant", Biomolecules 9, 366 (2019).
2. A. Hassan, Miguel V. Vitorino, Tiago Robalo, Mário S. Rodrigues, Isabel sá-Correia,"Variation of Burkholderia cenocepacia cell wall morphology and mechanical properties during cystic fibrosis lung infection, assessed by atomic force microscopy", Scientific Reports 9, 16118 (2019).
3. Fernando Vaz Dias, Susana Serrazina, Miguel Vitorino, Dario Marchese, Ingo Heilmann, Margarida Godinho, Mario Rodrigues and Rui Malhó, "A role for diacylglycerol kinase 4 in signalling crosstalk during Arabidopsis pollen tube growth", New Phytologist, 222, 1434 (2019).

Key Funded Projects

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

Organized Magnetic Nanoparticles, FCT project grant, start date: 01/09/2018 – 3 years; BioISI total amount – 215.145€; Total amount of the project - 232.888€; 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; BioISI total amount - 232.675€; Total amount of the project: 232.675€; PI: B.J. Cabral

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:

- A new formalism for dealing with answers to continuous queries over data streams, based on the notions of hypothetical and supported answers, and a two-phase algorithm, based on a variant of SLD-resolution, that computes those answers
- Coelho, H. Possible Ways Out for Intelligence: Yes, the future will be more complex and uncertain, Keynote Speech, 1st Interdisciplinary Summer School on Artificial Intelligence (ISSAI2019), Vila Nova de Cerveira, Junho 5-7, 2019
- An interactive virtual assistant to support self-management of type 2 diabetes in elder patients

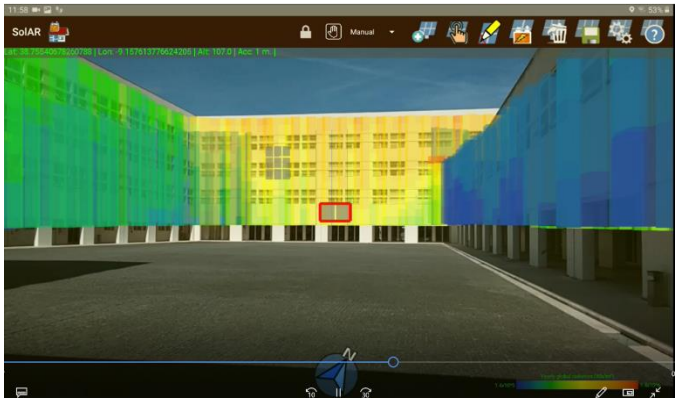


Figure 1: Augmented reality app to support the installation of solar panels on buildings' façades

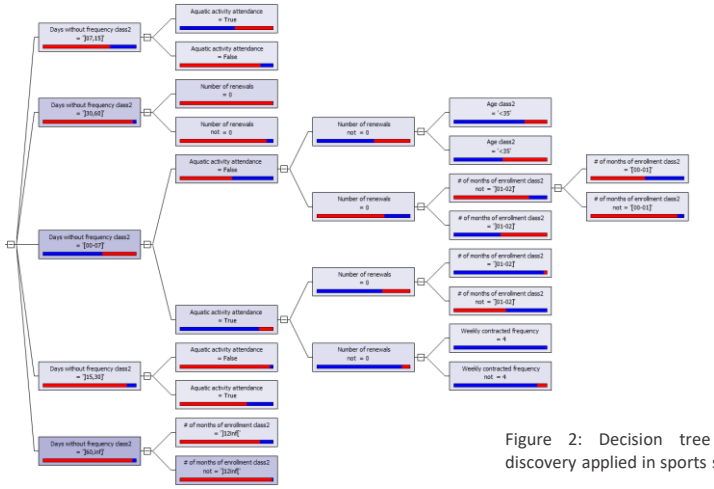


Figure 2: Decision tree of actionable knowledge discovery applied in sports services

Selected Publications

1. Bonnet, F, et al. "Robots mediating interactions between animals for interspecies collective behaviors." Science Robotics 4.28 (2019): eaau7897
2. Pereira-Guerreiro, M., Brito-Félix, I., Cavaco, A., Cláudio, A. P., Mendes, A., Balsa, J., Carmo, M.B., Pimenta, N., & Henriques, A. (2019). Development of a complex intervention to improve adherence to antidiabetic medication in older people using an anthropomorphic virtual assistant software. Frontiers in pharmacology, 10, 680
3. A. Mendes, I. Costa e Silva, A. Henriques, A. P. Cláudio, J. Balsa, M. B. Carmo, S. Buinhas, A. Cavaco, N. Pimenta, I. Félix & M. Pereira-Guerreiro (2019) Involving undergraduate nursing students in a multidisciplinary research project: strategy for implementation, first results and future perspectives, Annals of Medicine, 51:sup1, 205-205

Group Members

GL: Luís Correia

PI's:


Ana Paula Cláudio


Hélder Coelho


Luís Antunes


Beatriz Carmo


Luís Cavique


Paulo Trigo


Paulo Urbano


Graça Gaspar

Post Docs: Paulo P. Matos

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

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.

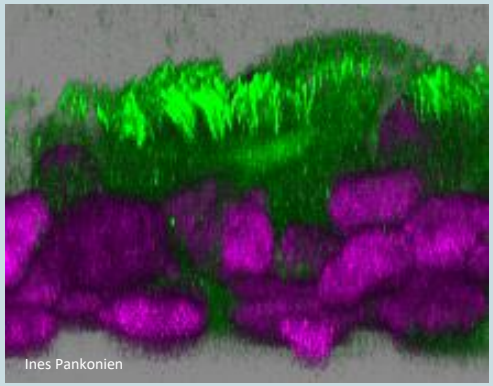
Main Goals:

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.

(BioISI/FCUL) Microscopy Facility

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

Coordinator: Rui Malhó; Co-coordinator: Hugo Botelho


Ines Pankonien

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 for Bioimage. BioISI Microscopy Facility functions as a service provider and technical support hub on stereo, widefield fluorescence, confocal and electron microscopy as well as high-throughput microscopy. It also supports its users in image analysis and quantification.

Major Projects

- High-throughput screening of genes and compounds regulating the secretory traffic of the CFTR and ANO1 proteins.
- Screening of genes affecting cell proliferation and differentiation in cystic fibrosis.
- Live cell imaging of the forskolin-induced swelling of intestinal organoids: identification of drug-responsive individuals to inform therapeutic intervention in cystic fibrosis.
- 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.

Main Publications:

- Life Science Alliance. 2 (6) - TMEM16A chloride channel does not drive mucus production (Simões et al)
- Cells. 8(4). E353 - Folding status is determinant over traffic-competence in defining CFTR Interactors in the endoplasmic reticulum (Santos & Canato et al)
- Front Pharmacol. 10:619 - Network biology identifies novel regulators of CFTR trafficking and membrane stability (Loureiro & Santos et al)
- Cell Mol Life Sci. 76(5):977-994 - Increases in cytosolic Ca^{2+} induce dynamin- and calcineurin-dependent internalisation of CFTR (Patel et al)
- New Phytologist. 222: 1434-1446 - A role for diacylglycerol kinase 4 in signaling crosstalk during Arabidopsis pollen tube growth (Dias et al)

Technicians: Luís Marques | Telmo Nunes | Aires Duarte

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.

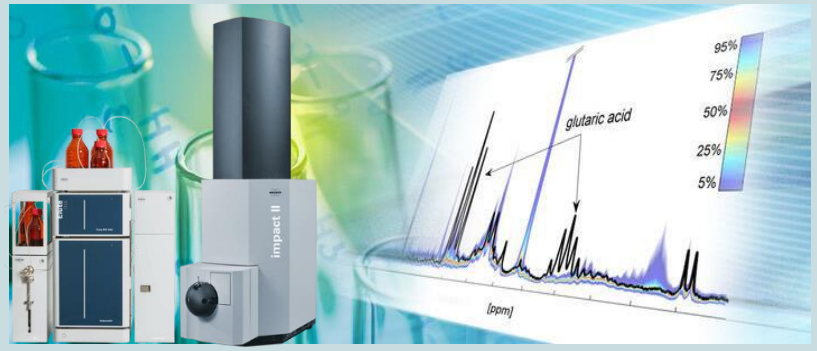
Activities & Achievements:

1. Consolidation of the facility infrastructure, equipment and human resources;
2. Consolidation of protocols and workflows for a set of basic services (ISIGen Services) focusing on genome, metagenome and transcriptome analysis;
3. Implementation of a unique dedicated computational Infrastructure for processing genomic data in real-time;
4. Internal dissemination of advantages of nanopore sensing technologies and available services;
5. Establishment of an appropriate financial and management infrastructure for external service provision;
6. Active participation in the main national & international funding programs;
7. Generation of the first whole human genome sequencing datasets from native DNA in Portugal;
8. Establishment of best tools to generate a detailed structural map of human centromeric regions.
9. Affiliation with Observer status at the GenomePT – National Infrastructure for Genome Sequencing and Analysis;

Technicians: Mariana Nascimento & Marcelo Pereira

(BioISI/FCUL) 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, in the filed of 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, in the field of the environmental chemistry.
- Quantification of several compounds, in waters.
- Screening and identification of several compounds throughout the fermentation process of wine samples (wine metabolomics).
- Screening of several compounds, in the field of forensic chemistry.
- Screening of compounds that are central in metabolism (NAD and its charged forms).
- Attempt to detect DNA primers and individual nucleotides.

Submitted publications:

- Bioactivities of iridoids and flavonoids present in decoctions from aerial parts of *Verbascum betonicifolium* (Fadel et al.) Rev Bras Pharmacogn, submitted (2020)
- Microbiome and metabolic profiles from two syrah vineyards in Portugal. Baleiras-Couto, M.M., Guedes, Rita, Maia, M., Monteiro, Filipa, Dias, R., Duarte, F.L., Serralheiro, M.L., Fortes, A.M. Presented in ISSY35. Antalaya, 21-25 Out 2019.

Technician: Rita Guedes

Physics

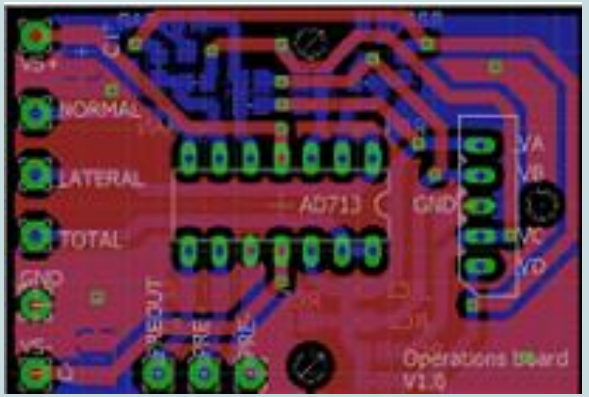
The Atomic Force Microscopy and Related Techniques Laboratory (AFM-RT Laboratory) serves both scientists and students.

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

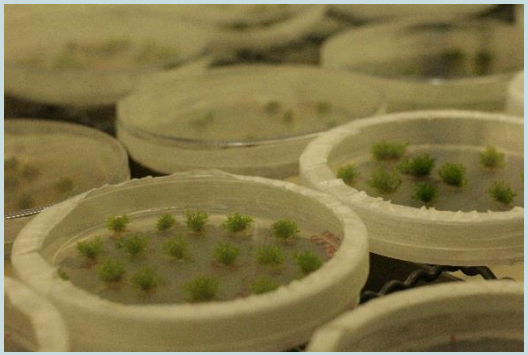
The Plant House Facility has specialized plant growth chambers and provides support to research groups.

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 contributes to advanced training, as it hosts the multidisciplinary BioSys PhD programme and participates in two more PhD programmes. In 2016 BioISI launched a post-doc programme, besides its continuous mentoring of young PIs to establish themselves independently. 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.

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.

BioISI Workshops/ Seminars

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 17 Senior Research Seminars and others, and several workshops such as:

- Workshop on Integrative Approaches in Protein Folding & Aggregation, 11-12 June 2019, Lisboa

- Epithelial Systems: Physiology and Pathophysiology Workshop, 22-26 July 2019, Lisboa

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 | 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 | 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 | 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 | 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 | 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 | 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 | 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 | 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 | http://hdl.handle.net/10451/34856

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 | 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 | 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 | 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 | 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) *
- **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 | 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 | 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 | http://hdl.handle.net/10451/42764

*International / mixed scholarships

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

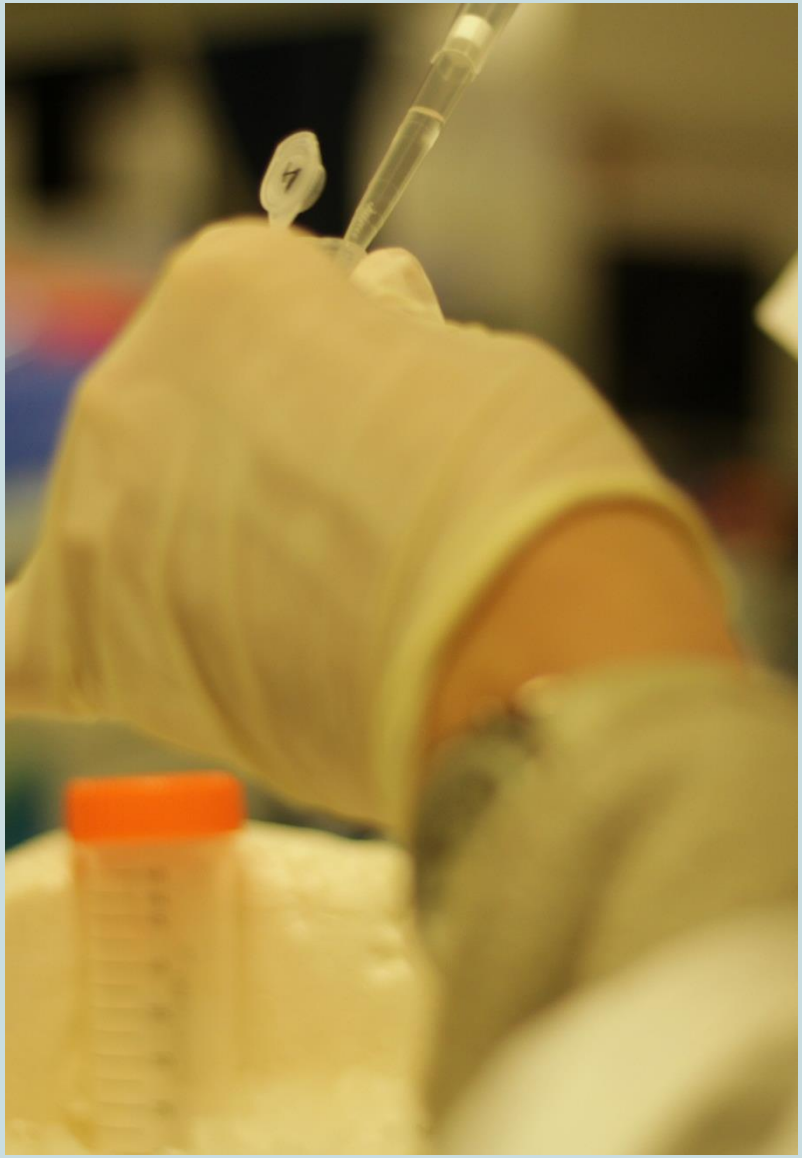
BioSYS 4 - Enrolled Students

- **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)



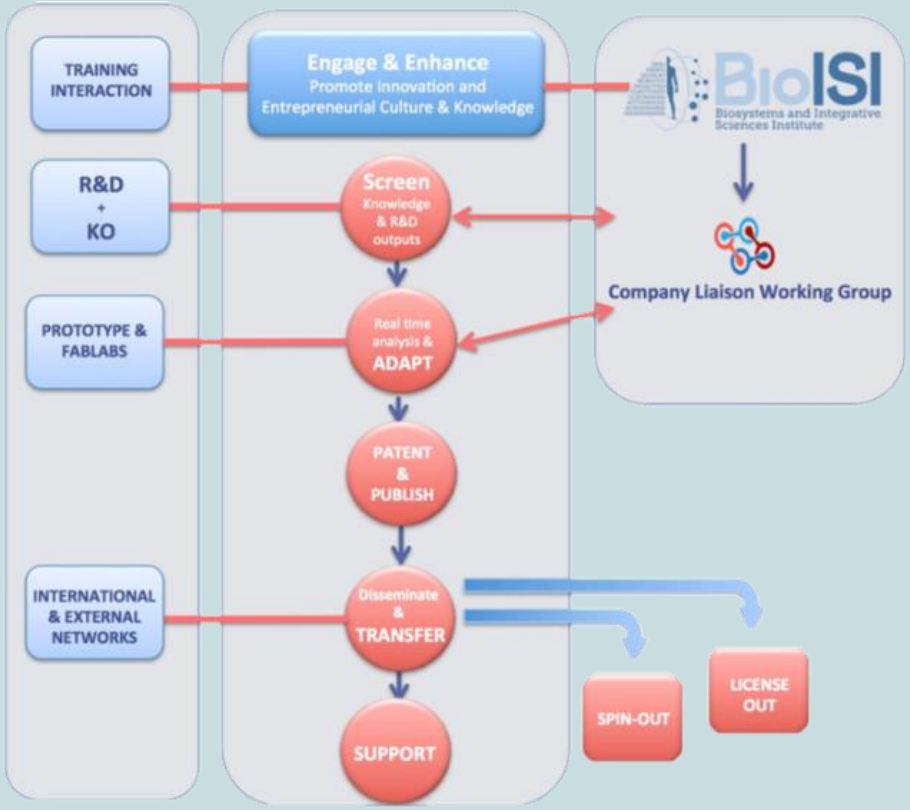
BioISI - KTT
Knowledge & Technology Transfer

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:

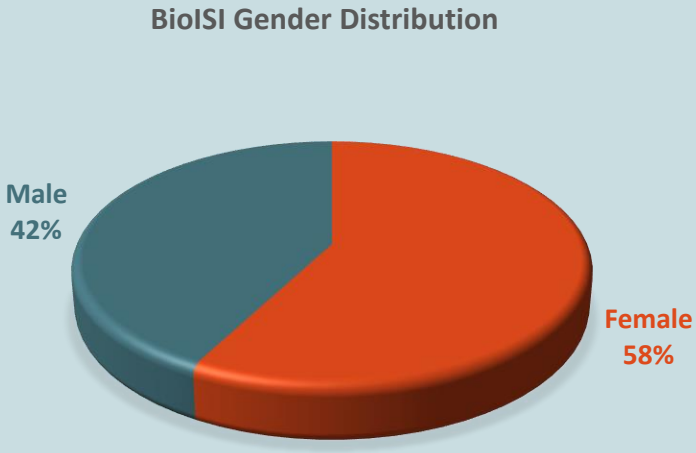
- internal and external awareness activities for the current KTT thematic realities, opportunities and challenges
- promote other activities, like service providing, contract R&D, project collaborations, Fablabs, etc, that can lead to economic valorisation of the knowledge outputs generated by the centre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

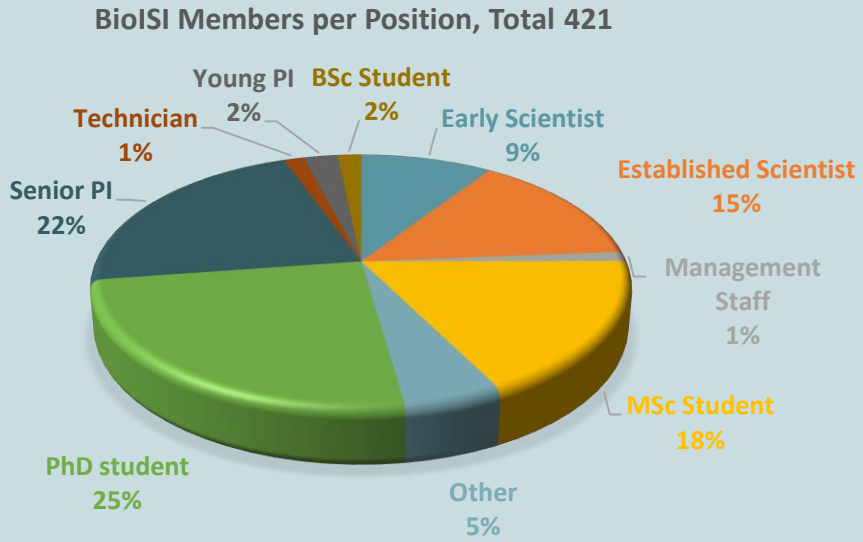
The management of KTT within BioISI will be under the responsibility of each PI who will communicate on commercially valuable results to the UL-INOVAR, after which they will work closely with CL-WG and external IP experts to identify and develop all necessary steps for IP protection and commercial exploitation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

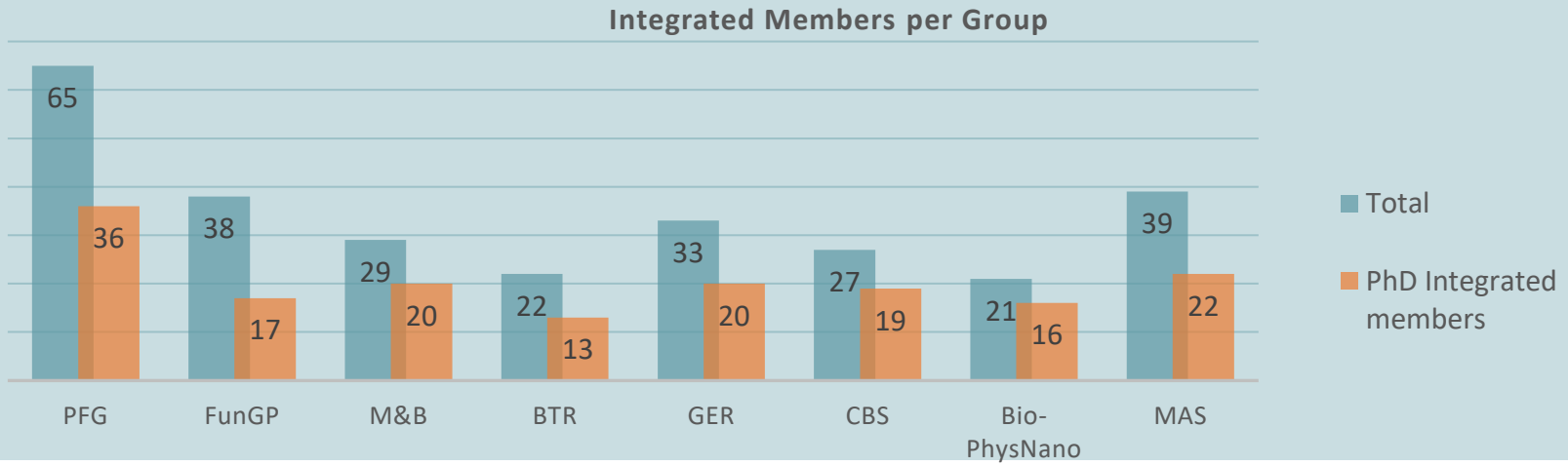


BioISI in Numbers

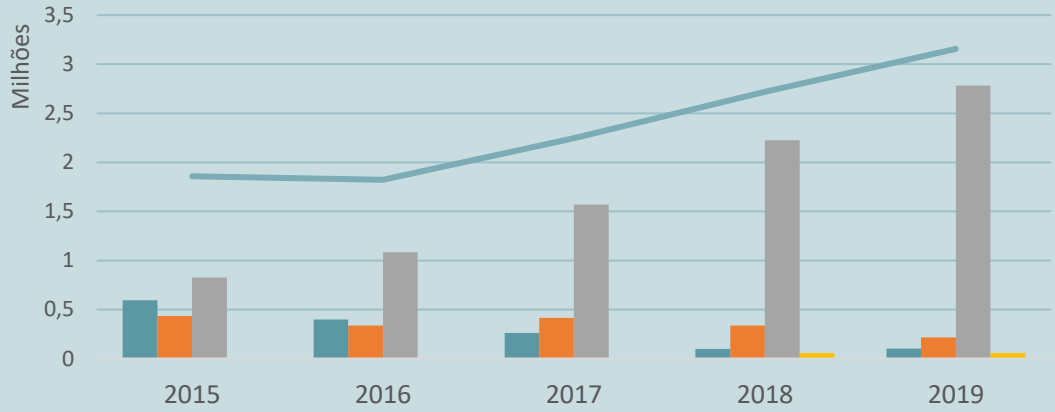
Members:



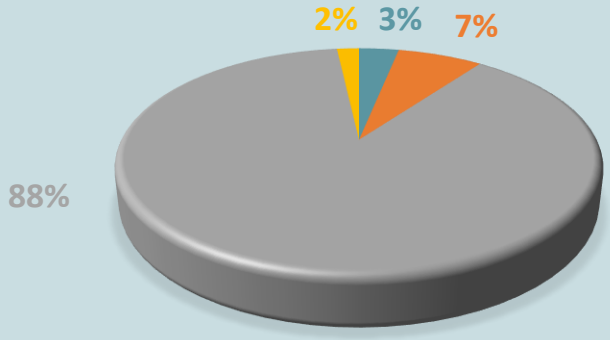




Project Funding 2015-2019



Competitive Funding 2019



Companies, industry and other private sources | European Commission | Governmental Funding (FCT/OE) | Others | Total Geral

BioISI in Numbers

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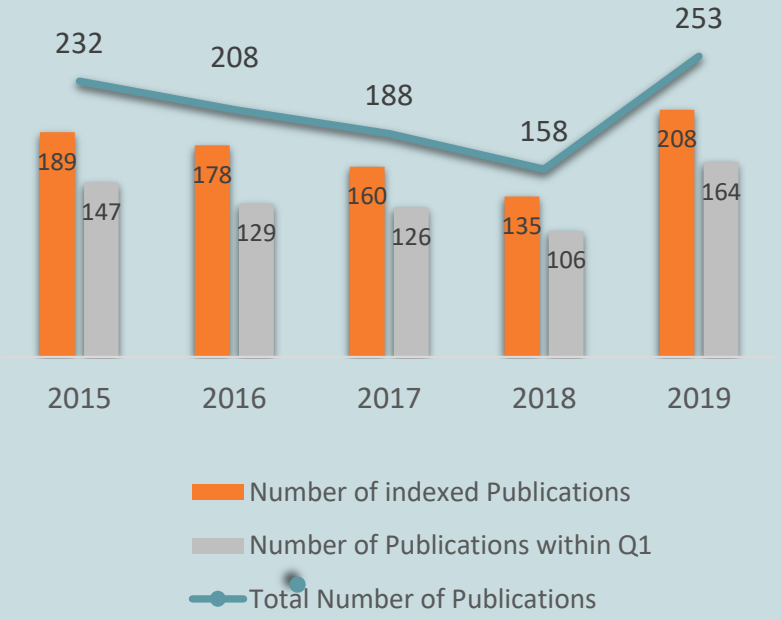
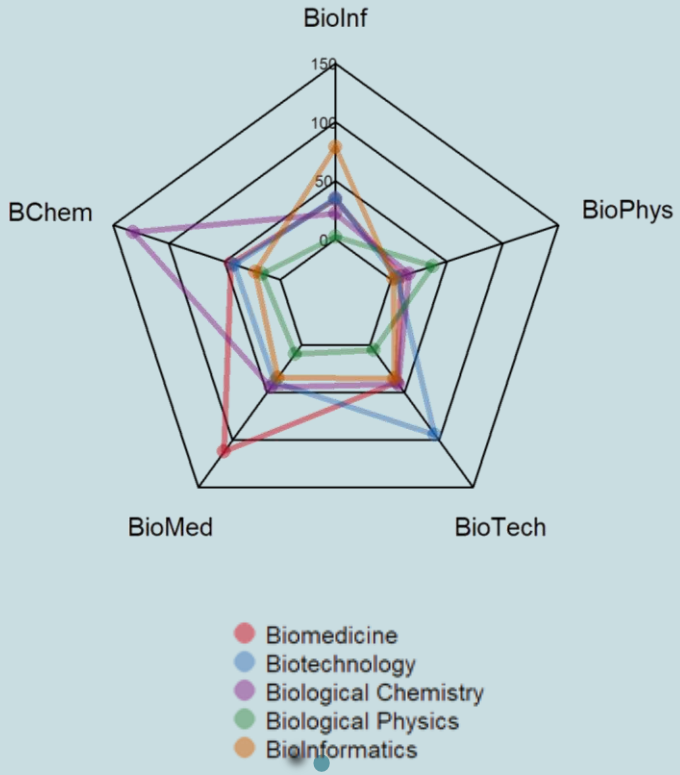


Publications per Thematic Lines in interaction with the others



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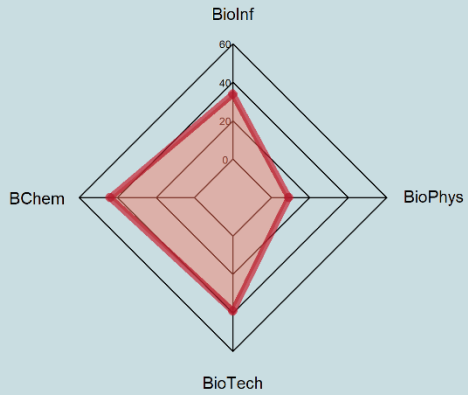

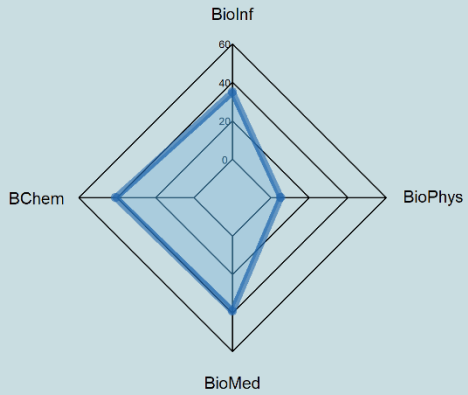

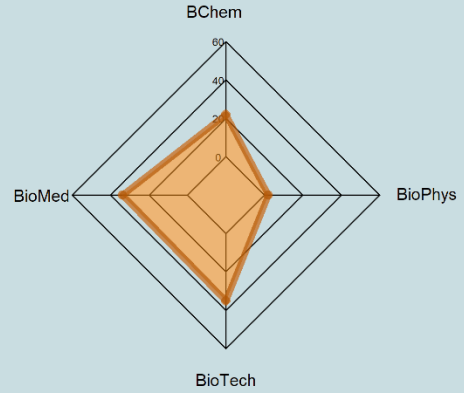

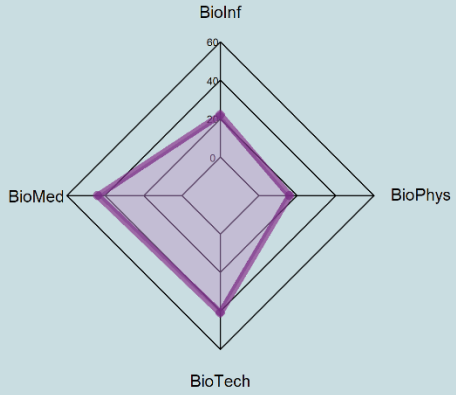

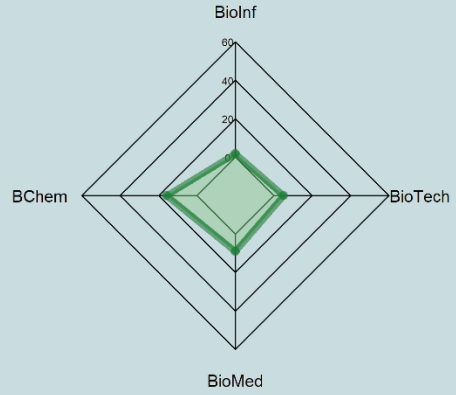

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GER

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Book Chapters

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Thesis

PFG

MSc Thesis

Filipe Nogueira Azevedo (2019) Detection and quantification of *Colletotrichum acutatumin* infected olive and olive oil samples. Supervisor: Paula Martins-Lopes (UTAD), Co-supervisor: Sónia Gomes (UTAD).

Catarina Augusto (2019) The aroma of Portuguese wine grapes: impact of infection with *Botrytis cinerea*. Supervisor: Ana Margarida Fortes (FCUL), Co-supervisor: Ana Cristina Figueiredo (FCUL).

Mário Jorge Barbosa de Almeida (2019) Establishment and evolution of gene regulatory networks. Supervisor: Manuela Costa (UMinho), Co-supervisor: Rómulo Sobral (UMinho).

Sara Filipa Pinto Coelho (2019) Study of ancestral genes in *Marchantia polymorpha*. Supervisor: Manuela Costa (UMinho).

Cíntia da Silva Macedo (2019) Expression profiling of rust resistance-related genes in coffee and development of a virus induced gene silencing (VIGS)-based tool for functional analysis. Supervisor: Dora Batista (ISA/FCUL), Co-supervisor: Célia Miguel (FCUL).

Paulo Jorge Oliveira Sampaio (2019) Composição e bioatividade de óleos essenciais de *Thymus vulgaris*, *Thymus citriodorus* e *Thymus fragrantissimus*. Supervisor: Fernanda Leal (UTAD), Co-supervisor: Amélia -Dias (UTAD).

Paulina Ziółkowska (2019) Study of *Vitis vinifera* subtilisin-like proteases in host-pathogen interaction: production, purification and subcellular localization of subtilase VviSBT1.11. Supervisor: Rita Santos (Łódź University of Technology International Faculty of Engineering), Co-supervisor: Andreia Figueiredo (FCUL).

Rafał Skrzypek (2019) Identification and expression analysis of cell death serine proteases associated to grapevine response to *Plasmopara viticola*. Supervisor: Andreia Figueiredo (Łódź University of Technology International Faculty of Engineering), Co-supervisor: Rita Santos (FCUL).

PhD Thesis

Helena Sofia Gomes da Silva (2019) Characterization of flower induction and fertilization of *Quercus suber*. Supervisor: Manuela Costa (UMinho), Co-supervisor: Leonor Morais (ISA).

FunGP

MSc Thesis

André Gomes (2019) Epithelial Differentiation: From Organoids to Cells in Cystic Fibrosis Patients. Supervisor: Margarida D. Amaral (FCUL), Co-supervisor: Iris Silva (FCUL).

Ana R. Prada (2019) Studies on the role of calprotectin as a mediator of iron-induced inflammation with implications in Parkinson's disease. Supervisor: Raffaella Gozzelino (CEDOC), Co-supervisor: Cláudio M. Gomes (FCUL/BioISI).

Paulo Sousa (2019) Development and Validation of a Machine Learning Models for Molecules with Therapeutic Potential. Supervisor: André Falcão (FCUL/LASIGE), Co-supervisor: Carlos M. Farinha (FCUL/BioISI).

Ricardo Marques (2019) Optical Neurostimulation Spine Endoprosthesis. Supervisor: Jorge Martins (IST), Co-supervisor: Federico Herrera (FCUL).

Beatriz Cardoso (2019) Asymmetric post-translational modifications regulate the intracellular distribution of unstimulated STAT3 dimers. Supervisor: Federico Herrera (FCUL).

Ricardo Quiteres (2019) Developing new molecular tools to study and visualize the in-termediate filament GFAP in living cells. Supervisor: Federico Herrera (FCUL), Co-supervisor: Zach Hensel (ITQB).

PhD Thesis

Joana M. Cristovão (2019) The calcium binding S100B protein as a new modulator of amyloid-β peptide aggregation. Supervisor: Cláudio M. Gomes (FCUL).

Tânia G. Lucas (2019) Protein misfolding and cellular responses in metabolic disorders. Supervisor: Cláudio M. Gomes (FCUL).

João F. Santos (2019) Regulation of CFTR trafficking and membrane anchoring: new insights into cAMP signalling. Supervisor: Carlos M. Farinha (FCUL), Co-supervisor: Manuela Zaccolo (Univ Oxford).

M&B

MSc Thesis

Diogo Rafael Santos Pereira (2019) Palm leaf fungi in Portugal: ecological, morphological and phylogenetic approaches. Supervisor: Alan John Lander Phillips (FCUL) , Co-supervisor: Rogério Paulo de Andrade Tenreiro (FCUL).

GER

MSc Thesis

Mariana Lopes (2019) Unlocking Robertsonian translocated chromosomes in its repetitive DNA content to tackle genomic and mechanistic issues. Supervisor: Raquel Chaves (UTAD), Co-supervisor: Margarida Gama-Carvalho (FCUL).

Catarina Pinheiro (2019) Systemic factors and tumour progression. Supervisor: Sérgio Dias (IMM), Co-supervisor: Raquel Chaves (UTAD).

Manuel Carvalho (2019) Study of human Argonaute 1 cap-independent translation. Supervisor: Luísa Romão (INSA).

Miguel Pereira (2019) Caracterização de pequenos RNAs não-codificantes na resposta ao HIV. Supervisor: Margarida Gama-Carvalho (FCUL).

PhD Thesis

Ana Escudeiro (2019) What is the impact of the cattle chromosome polymorfism Rb t(1;29) in Bovini genome biodiversity and functionality? Supervisor: Raquel Chaves (UTAD), Co-supervisor: Filomena Adega and JS Heslop-Harrison (UTAD and University of Leicester, UK).

Joana Silva (2019) Analysis of translation of 5' untranslated regions in cancer. Supervisor: Luísa Romão (INSA), Co-supervisor: Augusto Luchessi (Universidade de Campinas).

Cláudia Loureiro (2019) Regulation of epithelial chloride transport by phosphotyrosine-initiated protein networks. Supervisor: Peter Jordan (INSA), Co-supervisor: Luka Clarke (FCUL).

Andreia Henriques (2019) Regulation of glucose uptake in mammalian cells by protein phosphoylation networks. Supervisor: Peter Jordan (INSA), Co-supervisor: Luka Clarke (FCUL).

CBS

MSc Thesis

Stephanie Daniela Mendonça Almada (2019) Antimicrobial cyclam derivative agents for water bio-decontamination. Supervisor: Luís Alves (IST), Co-supervisor: ER Silva (FCUL).

Beatriz Teixeira Lopes (2019) Estudo do Metabolismo de Catinonas Psicoativas, Mestrado em Química. Supervisor: Helena Gaspar (FCUL), Co-supervisor: Alexandra Antunes (IST).

Maria Estevão Fidalgo von Cüpper (2019) Screening for New Psychoactive Substances (NPS) without reference standards on High Resolution Mass Spectrometers (HR-MS). Supervisor: Helena Gaspar (FCUL), Co-supervisor: Kristian Linnet (Section of Forensic Chemistry at the Department of Forensic Medicine, University of Copenhagen, Denmark).

Sara Margarida Duarte Júlio (2019) Síntese e Quantificação de Novas Substâncias Psicoativas. Supervisor: Helena Gaspar (FCUL), Co-supervisor: Maria Miguéns Pereira (FCTUC).

MAS

MSc Thesis

Catarina Barreira Cavique Santos (2019) Promoção da educação em osteoartrose combinando a narrativa de um paciente virtual e um quiz. Supervisor: Ana Paula Boler Cláudio (FCUL), Co-supervisor: Maria Beatriz Duarte Pereira do Carmo (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 A cell model to study UV-B effect in *Vitis vinifera* L, FCT. BioISI Budget: 10 000€ (Total Amount of the project: 10 000€). BioISI PI: Paula Martins-Lopes and Raquel Chaves

2016 Plataforma de Inovação da Vinha e do Vinho – INNOVINE & WINE, União Europeia – FEDER. BioISI Budget: (Total Amount of the project: 4 499 887.05€). BioISI PI: JE Lima-Brito and Ana Carvalho

2016 INTERACT – Integrative Research in Environment, Agro-Chains and Technology, União Europeia – FEDER. BioISI Budget: (Total Amount of the project: 4 127 773 .50€). BioISI PI: JE Lima-Brito and Ana Carvalho

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

2019 Development of Botrytiscinerea DNA-based detection assays: HRM and Biosensor. , FCT. BioISI Budget: 8 000€ (Total Amount of the project: 8 000€). BioISI PI: Paula Martins-Lopes and Raquel Chaves

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

2018 A cell model to study UV-B effect in *Vitis vinifera* L, FCT. BioISI Budget: 10 000€ (Total Amount of the project: 10 000€). BioISI PI: Paula Martins-Lopes and Raquel Chaves

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 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

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 PRODYSMITO - Mecanismo de disfunção proteica em doença mitocondriais, FCT. BioISI Budget: 219 261€ (Total Amount of the project: 219 261€). BioISI PI: Bárbara J. Henriques

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

2016 MODUL-AD - The calcium binding S100B protein as a modulator of amyloid β aggregation and potential therapeutic target in Alzheimer's disease., FCT. BioISI Budget: 199 972€ (Total Amount of the project: 199 972€). BioISI PI: Cláudio M. Gomes

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

2016 MitoPTM - Regulation of mitochondrial beta oxidation by nonenzymatic posttranslational modifications in health and disease, FCT. BioISI Budget: 182 810€ (Total Amount of the project: 182 810€). BioISI PI: Bárbara J. Henriques

M&B

2017 BIOCLUB - Designing biofertilizers by mimicking plants' recruitment of rhizospheric partners., FCT. BioISI Budget: 0,00 € (Total Amount of the project: 199 000€). BioISI PI: Rogério Tenreiro

2015 SMARTWINE - Smarter wine fermentations: integrating Omics-tools for development of novel mixed-starter cultures for tailor-made wine production, FCT, COMPETE, FEEI. BioISI Budget: 103 000€ (Total Amount of the project: 196 000€). BioISI PI: Arlete Mendes Faia

2016 I&D INNOVINE&WINE - Vineyard and Wine Innovation Platform, NORTE-01-0145-FEDER-000038. BioISI Budget: 123 340€ (Total Amount of the project: 5 293 984,76€). BioISI PI: Alexandra Mendes Ferreira

2017 Euroxanth: Integrating science on Xanthomonadaceae for integrated plant disease management in Europe, EU framework programme H2020. BioISI Budget: 200 000€ (Total Amount of the project: 68 000 000€). BioISI PI: Leonor Cruz

2017 Development, validation and verification of a diagnostic tool for detection and identification of *Ralstonia solanacearum* and *Clavibacter michiganensis* subsp. sepedonicus directly on plant tissue, Euphresco network/ INIAV. BioISI Budget: 20 589€ (Total Amount of the project: 79 929€). BioISI PI: Leonor Cruz

2016 HOSTSTREP II - Unveiling host specificity and host pathogen interactions of Streptococcus, FCT. BioISI Budget: 20 000€ (Total Amount of the project: 199 782€). BioISI PI: Rogério Tenreiro, Lélia Chambel

2016 INTERACT– Integrated Research in Environment, Agro-Chain and Technology., NORTE-01-0145-FEDER-000017. BioISI Budget: 124 000€ (Total Amount of the project: 4 120 000€). BioISI PI: A Mendes-Faia

2017 Sistema Satelital de Monitoreo Ambiental en Tiempo Real para el estudio del cambio climático basado en un biosensor bacteriano altamente sensible, Vicerrectoria De Investigacion Y Estudios Avanzados – Chile. BioISI Budget: 50 000€ (Total Amount of the project: 500 000€). BioISI PI: Ricardo Dias

2017 NewID - New approaches for taxonomic identification and profiling of poli-clonal samples based in Next Generation Sequencing, SGS Molecular. BioISI PI: Ricardo Dias

2016 Precision Oncology by Innovative Therapies and Technologies., POINT-PAC 2016, LISBOA-01-0145-FEDER-016405. BioISI Budget: 75 000€ (Total Amount of the project: 763 000€). BioISI PI: Helena Vieira

2017 BIOINVENT: Generic bio-inventory of soil microbial diversity and functioning in permanent grassland ecosystems across management and climate gradients., EU-Biodiversa. BioISI Budget: 0,00 € (Total Amount of the project: 1 680 000€). BioISI PI: Rogério Tenreiro

2016 RESISTIR - Intelligent information system to control infection and personalized antibiotherapy., POCI and POR Lisboa. BioISI Budget: 449 000€ (Total Amount of the project: 1 059 675€). BioISI PI: Ricardo Dias

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

2016 Avaliação Molecular do proto-oncogene HER2 e das Topoisomerases no carcinoma mamário felino – Desenvolvimento de novas estratégias para melhorar a Imunoterapia, FCT. Total Amount of the project: 174 760€. BioISI PI: Raquel Chaves

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

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

2015 Halogen bonds in (bio)chemical systems: a theoretical approach for 'real world' applications, FCT. BioISI Budget: 50 000€ (Total Amount of the project: 50 000€). 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

2015 CpHMD-L simulations of pHLIP peptides: design of new tumor-targeted drug delivery systems, FCT. BioISI Budget: 185 088€ (Total Amount of the project: 185 088€). BioISI PI: Miguel Machuqueiro

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

2017 Studies on metal-catalyzed C-H functionalization, FCT. BioISI Budget: 15 600€ (Total Amount of the project: 15 600€). BioISI PI: Maria José Calhorda

2017 Overcoming environmental problems associated with antifouling agents: synthesis of Nature-inspired non-toxic biocides and immobilization in polymeric coatings, FCT-COMPETE. BioISI Budget: 52 352€ (Total Amount of the project: 161 852€). BioISI PI: Elisabete Silva

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 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

2016 Red2Discovery - The red macroalgae *Sphaerococcus coronopifolius* and *Asparagopsis armata* as targets for the discovery of new drugs of marine origin, FCT. (Total Amount of the project: 174 110€). 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 Pacheco

2016 Multifunctional Luminescent Spin Labile Hybrid Materials, FCT. BioISI Budget: 191 879€ (Total Amount of the project: 191 879€). BioISI PI: Paulo N. Martinho

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

BioPhysNano

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

2016 Mechanical and molecular interactions in Biology measured with Force Feedback Microscopy, FCT. BioISI Budget: 197 000€ (Total Amount of the project: 197 000€). BioISI PI: Mário Rodrigues and Lisete Fernandes

2016 Multifunctional Luminescent Spin Labile Hybrid Materials, FCT. BioISI Budget: 27 500€ (Total Amount of the project: 191 879€). BioISI PI: Paulo Martinho

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

2018 VASelfCare – Assistente virtual para facilitar o autocuidado de pessoas mais velhas com diabetes tipo2, FCT, LIsboa2020, Alentejo2020,PT2020. BioISI Budget: 58 261.74€ (Total Amount of the project: 139 361.69€). BioISI PI: Ana Paula Cláudio

2016 VIRTUAL TUTORING – the virtual tutor as learning mediating artifact in online university education, FCT. BioISI Budget: 60 967€ (Total Amount of the project: 199 706€). BioISI PI: Ana Paula Cláudio

2014 Putting Genetic Programming on the map of Machine Learning for data mining, FCT. BioISI Budget: 50 000€ (Total Amount of the project: 50 000€). BioISI PI: Sara Silva

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

2018 Improving Bio-Inspired Deep Learning for Radiomics, FCT. BioISI Budget: 26 100€ (Total Amount of the project: 240 000€). BioISI PI: Sara Silva

2013 Animal and robot Societies Self-organise and Integrate by Social Interaction (ASSISIbf), EC. BioISI Budget: 516 000€ (Total Amount of the project: 6 000 000€). BioISI PI: Luís Correia

Dates refer to the start of the project