BioISI

Biosystems & Integrative Sciences Institute

Report 2018

Biosystems and Integrative Sciences Institute

Ciências ULisboa

Front page figure: *Dothiorella sempervirentis*. Young conidia developing on conidiogenous cells of the fungus *Dothiorella sempervirentis*. This species was found on twigs and cones of *Cupressus sempervirens* in Northern Iran. Provided by Alan Phillips, M&B Group, FCUL

Contents

BioISI Identification

Name of the Research Unit: Biosystems & Integrative Sciences Institute

Unit Acronym: BioISI

Scientific Director: Margarida Sofia Pereira Duarte Amaral

Scientific Areas: Multidisciplinary/Interdisciplinary Research

Molecular Biology & Biomedical Sciences
Biological sciences
Physics
Chemistry

Keywords Multidisciplinary Research

Molecular Systems Biology
Bioinformatics & computational modelling
Integrative Sciences
Quantitative biology

Management Institution:

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

Participating institutions:

Instituto Nacional de Saúde Dr. Ricardo Jorge (INSARJ)

Universidade do Minho (UM)

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

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

Address: Campo Grande C8 Bdg, room 8.2.42, 1749-016 Lisboa, Portugal | Tel - +351 21 7500857 Fax - +351 21 7500088

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 (BioInfo): L Correia/ MG-Carvalho
5) Biological Chemistry (BioChem): MJ Calhorda (M Pereira in 2019)/P Costa

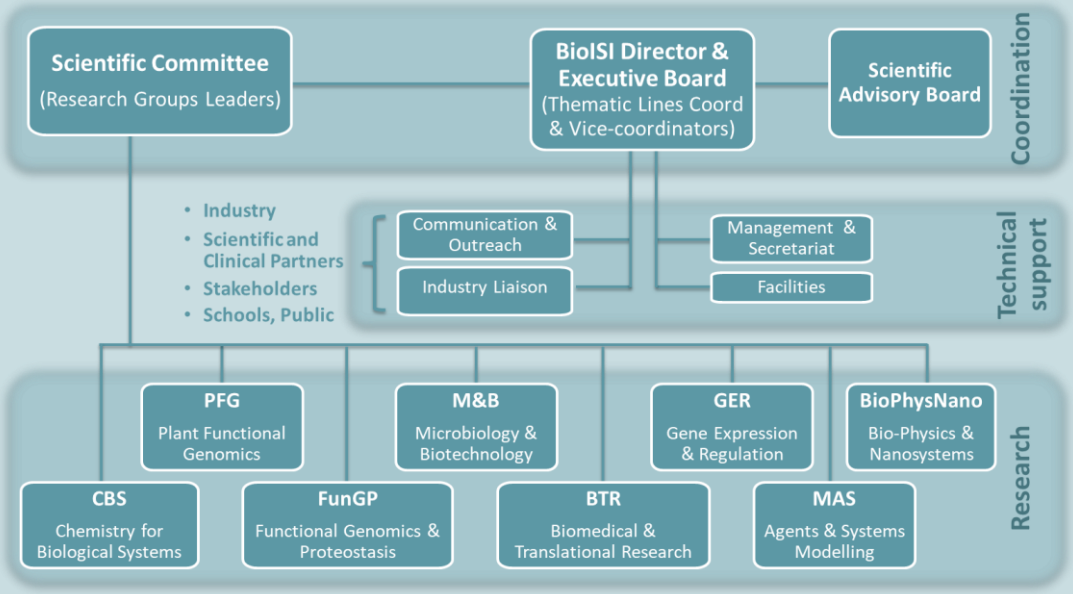
Each TLC is a former centre coordinator with past experience managing internationally funded research, being also a research group leader (RGL). TLCs/VCs promote specific activities and exchange of information to exploit collaborations enhancing multidisciplinary research.

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): MJ Calhorda (M Pereira in 2019)

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)

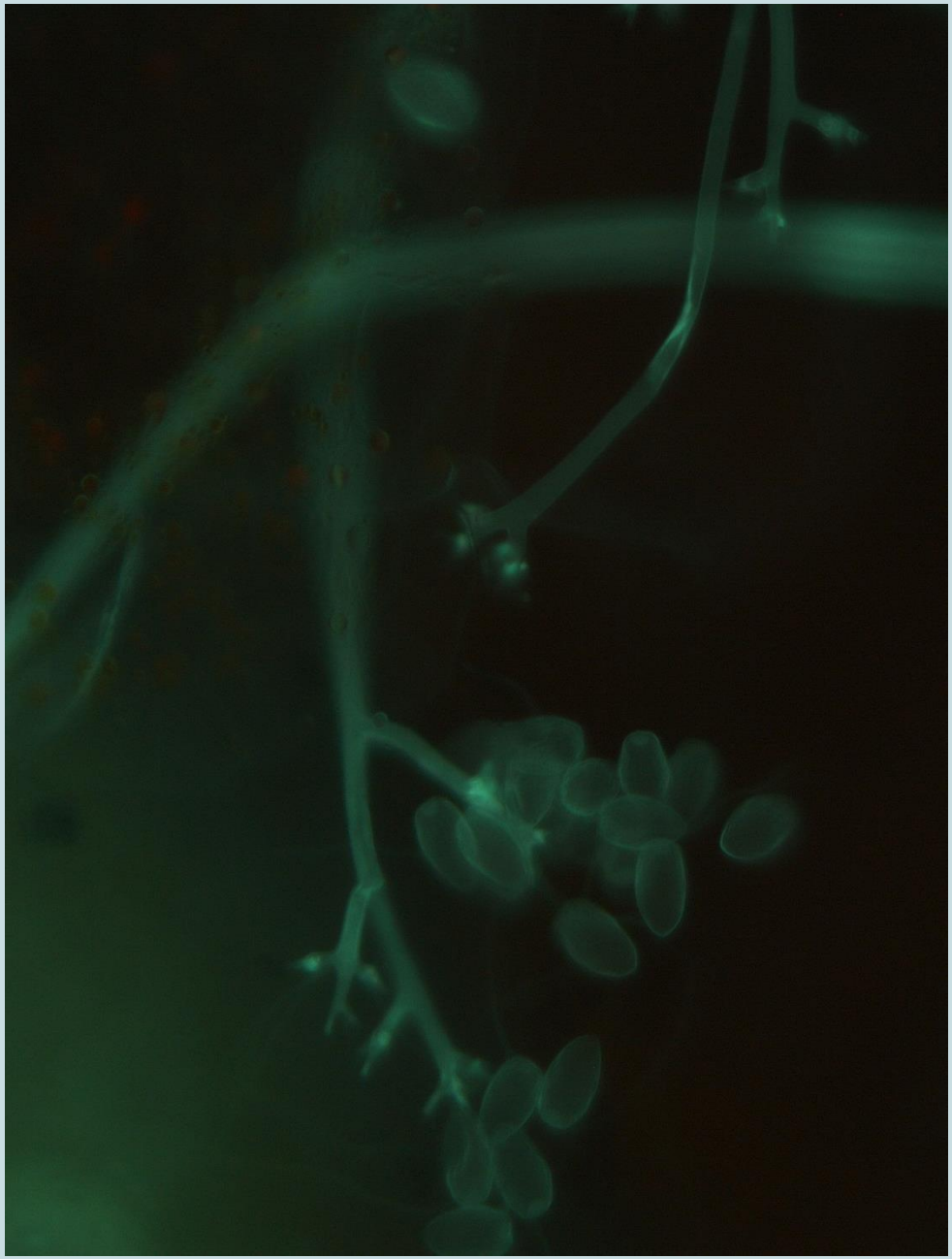
Klaus Palme (Plant Molecular and Cell Biology)
BIOSS Centre for Biological Signalling Studies, University of Freiburg (Germany)

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)

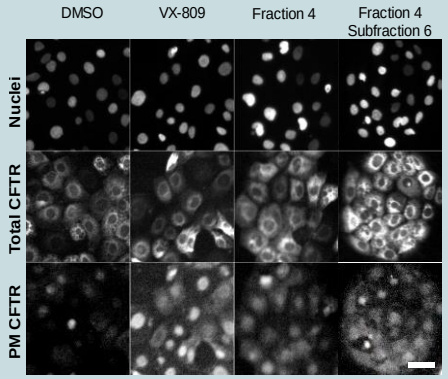
Hans Peter Wessel (Chemistry)
Universidade de Aveiro (Portugal)



BioISI Thematic Lines

Fluorescence microscopy of *P. viticola sporangiophore* in a *Vitis vinifera* leaf disk 8 days post-infection. Image provided by Marisa Maia, PhD student, PFG group, FCUL.

Biomedicine



The Biomedicine thematic line (TL), involves predominantly scientists from three BioISI groups (FunGP, BTR and GER) who work closely with researchers from other areas (physicists, bioinformaticians, mathematicians) to elucidate the basic mechanisms underlying human disease at the molecular and cellular levels but also by uncovering genetic and epigenetic determinants of disease.

Biomedical research at BioISI goes from characterizing Alzheimer-related proteins at atomic level (by innovative atomic force microscopy approaches) to Bioinformatic integrative analyses of large genetic and environmental datasets for improved diagnosis and clinical intervention in autism or even using organoids derived from patients with Cystic Fibrosis to predict their individual responses to drugs and propose clinical trials, in personalized medicine approaches.

Out of the seven BioISI projects awarded in 2017, five involve Biomedicine, in topics which range from mitochondrial disorders caused by protein misfolding to construction of signalling protein networks at the plasma membrane or discovering new potential drugs for CF therapy from natural products derived from Portuguese marine (and other) organisms.

Answering these challenging questions through the use 'omics' and integrative approaches to generate novel mechanistic hypotheses takes a leading place at BioISI. Such aim, however, requires continuous innovation at both the experimental (e.g., new cellular systems for high-throughput microscopy) and computational levels (such as new tools for genomic data mining).

Institutional Cooperation. To stay at the forefront of innovative research, Biomedicine at BioISI keeps strong international collaborations. For example, in 2018 a joint Twinning project with EMBL and Karolinska Institute was submitted to the EU to set up a network for outstanding research and innovation and aimed at reinforcing BioISI's research capacity in Systems Biology. International cooperation contributes to build BioISI's capacities/skills in: 1) cutting-edge technologies (at core-facilities); 2) big data analysis; 3) bioinformatic & computational approaches to integrate multi-level data; and 4) Knowledge and Technology Transfer. 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 molecular mechanisms and regulatory networks underlying traffic disorders and their relationship to cellular epithelial differentiation.
- 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.
- Explain mechanisms of Alzheimer's disease (AD) by in vitro studies of self-assembly and amyloid formation of proteins involved in AD.
- Develop innovative therapeutic strategies, based on tests in patients own cells/tissues towards personalized medicine.

"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 2018 the research activity followed the lines defined in the strategic programme:

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

Synthesis of coated magnetic nanoparticles, study of magnetic properties and specific loss power performance aiming at magnetic hyperthermia applications for cancer therapy; beginning of a new project ("OrMagNa"- FCT grant) in collaboration with FunGP (core group of BioMed TL), focused on the preparation of organized aggregates of magnetic nanoparticles aiming at structures with improved magnetic properties and heating efficiencies.

Development of AFM/FFM methodologies

The recently developed FFM allowed: the measurement of CFBE cells elasticity parameters (in collaboration with FunGP group); the development of a new measurement methodology performed without sample contact; direct probing of the free energy and dissociation constant associated with the binding of single proteins implicated in Alzheimer's disease (in collaboration with Protein Folding and Misfolding Lab). Using AFM, an effective method for mechanical properties assessment allowed the analysis of stress effect on pollen tubes mechanical properties; this approach will be used within a new collaboration FCT project, "StressPI", granted to the PFG group.

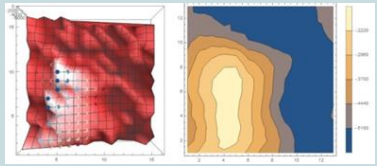


Fig 1 and 2. CFBE cells topography (AFM)

Expertise/facilities of the physics team in optical techniques, Squid magnetometry and Mössbauer spectroscopy were widely used in the development of BioISI internal collaboration projects, leading to another joint FCT funded project of the PFG group ("InterPheno", started in 2018) and to new collaborations with the CBS group.

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/biosensors
- Development of AFM/FFM methodologies to assess nanomechanical properties and biological interactions.
- Biomimetic photosynthesis and molecular solar energy storage

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:

- Field and in vitro selection of plants with abiotic stress tolerance and high nutritional value.
- Omics analysis of grapevine resistance against downy mildew (*Plasmopara viticola*)
- Characterization of the genome sequence of cork oak.
- Reduction of drought induced stress in cork oak by ectomycorrhizal inoculation.
- Transcriptomic analysis of pine embryo development.

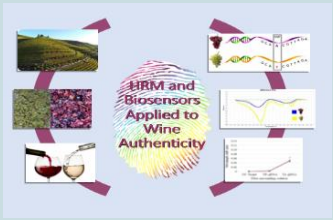
Networking activities of M&B (symbiotic and pathogen interaction), MagNano (phenotypic analysis – membrane and cell wall AFM imaging), and MAS (systems networks).

Internal funded projects – *"GraPoBio – Grape pomace on biological systems"*

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.
- Effects of seed priming with iron and zinc in wheat grain yield.

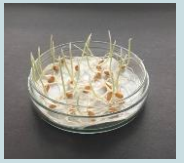
Internal funded projects – *"A cell model to study UV-B effect in Vitis vinifera L."*



CNOIV 2018 Innovation award

Microbial pharmacogenomics:

Development of a set of yeast genetic tools to screen stress/drug effects. Analysis of multiple drug responsive transcription networks – development of a new conceptual platform to interpret stimuli-responsive transcriptional networks (STN), drug resistance and cross-resistance.



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

Internal funded projects – *"Deconvolution of dual CFTR/ANO1 Modulators from Portuguese natural products - A new class of drugs for CF therapy".*

Wine biotechnology:

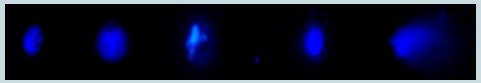
- Whole genome sequencing and comparative genomics of non-Saccharomyces yeasts to broaden their application in wine industry.
- Integrative omics-based analysis of the microbiome of Douro Wine Region towards the enlightening of its adaptive potential to dry and warm conditions due to climate changes.

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

Internal funded project – *"SMART VINE: microbiome effect from soil to bottle"*

Microbial biotechnology:

- 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.
- 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 plant microbiome upon changes in climatic factors.



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. Eight 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:
  - in 2018: Integrative approaches in Neurodegeneration.
  - Bioinformatics & computational modelling for Systems Biology

Actions in 2018

An internal two year post-doc grant in a joint project of BTR and MAS groups, focusing on Autism Spectrum Disorder Genomic Data Analysis – started: April 2016, end: December 2018. It was integrated in an initiative of BioISI to stimulate the thematic lines, and it was very effective in this particular case.

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

A basis of common computing facilities entered production in 2018. We are also using national (INCD) and European (EGI) computational infrastructures. The post-doc of the BioInf TL, Hugo Martiniano (left at the end of December) was instrumental in this infrastructural activity.

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

Network-based approach S2B (double specific-betweenness) can be applied to uncover common molecular mechanisms shared by various diseases, identifying individual proteins (Garcia-Vaquero et al. (2018) Scientific Reports, 8:11555).

First evolutionary algorithm (EA) with non-human animals as fitness providers (Mariano et al (2018) Proc. Alife. MIT Press) resulting from ASSISIbf EU FP7 project focused on the development of cooperation between two animal species (bees & fish) through robots.

Significant results in RESISTIR project, which focuses an intelligent decision support system for personalized prevention and clinical management of infectious diseases on a platform generating epidemiological knowledge in real time.

Biological Chemistry

The Biological Chemistry (BChem) thematic line aims at developing bioactive molecules either 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, in particular, to BioISI flagship projects "Systems approaches to rare diseases: Cystic Fibrosis and neurodegeneration" and "Enabling Technologies for Cutting-edge Research", by combining computational and experimental approaches, addressing health and environmental safety problems, either directly (e.g. new leads), indirectly (studying mechanisms or designing eco-friendly molecules and processes), or by unravelling pathogens bioenergetics. With the involvement of BioISI scientists, predominantly from CBS, M&B, Bio-PhysNano, we hope to contribute to discovering 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

Two awarded BioISI projects involve the Biological Chemistry thematic line. The aim of the project "Portuguese natural products – A new class of drugs for CF therapy" is to purify and validate novel therapeutically-relevant molecules, taken from a natural products library, which show increased traffic of F508del-CFTR and/or the alternative chloride channel ANO1. Combining a range of analytical chemistry techniques (e.g. SPE, HPLC, MS) with high content screening for bioactivity measurements, 13 hit fractions and a preliminary set of 2 hit subfractions were isolated. The "GraPoBio – Grape pomace on biological systems" is attempting to add value to Portuguese grape pomace by analyzing its health promoting activities on intestinal cells. When digested by gastrointestinal enzymes, grape pomace releases bioactive compounds, thus protecting intestinal lining cells from oxidative damage.

Organization of International Meetings

The SPINON WORKSHOP 2018 (Multifunctional Magnetic Materials) was organized in Lisbon (October 2018). This platform brought together renowned scientists and young researchers in the field of molecular magnetism.

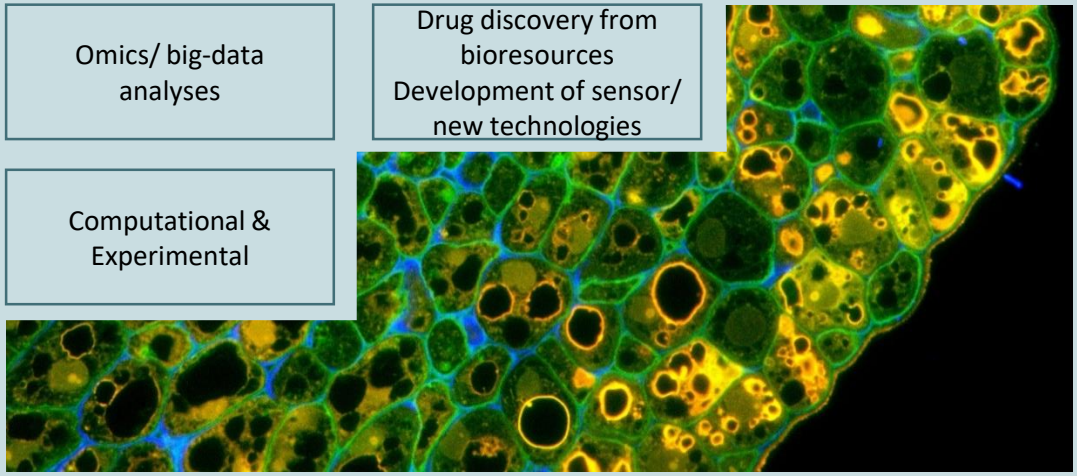
Facilities. Biological Chemistry is involved in the maintenance and development of the computing/bioinformatics facility, enabling BioISI scientists to run calculations and simulations in (bio)chemical systems. Biological Chemistry benefits from the facility of high-throughput screening (BioMed TL) and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

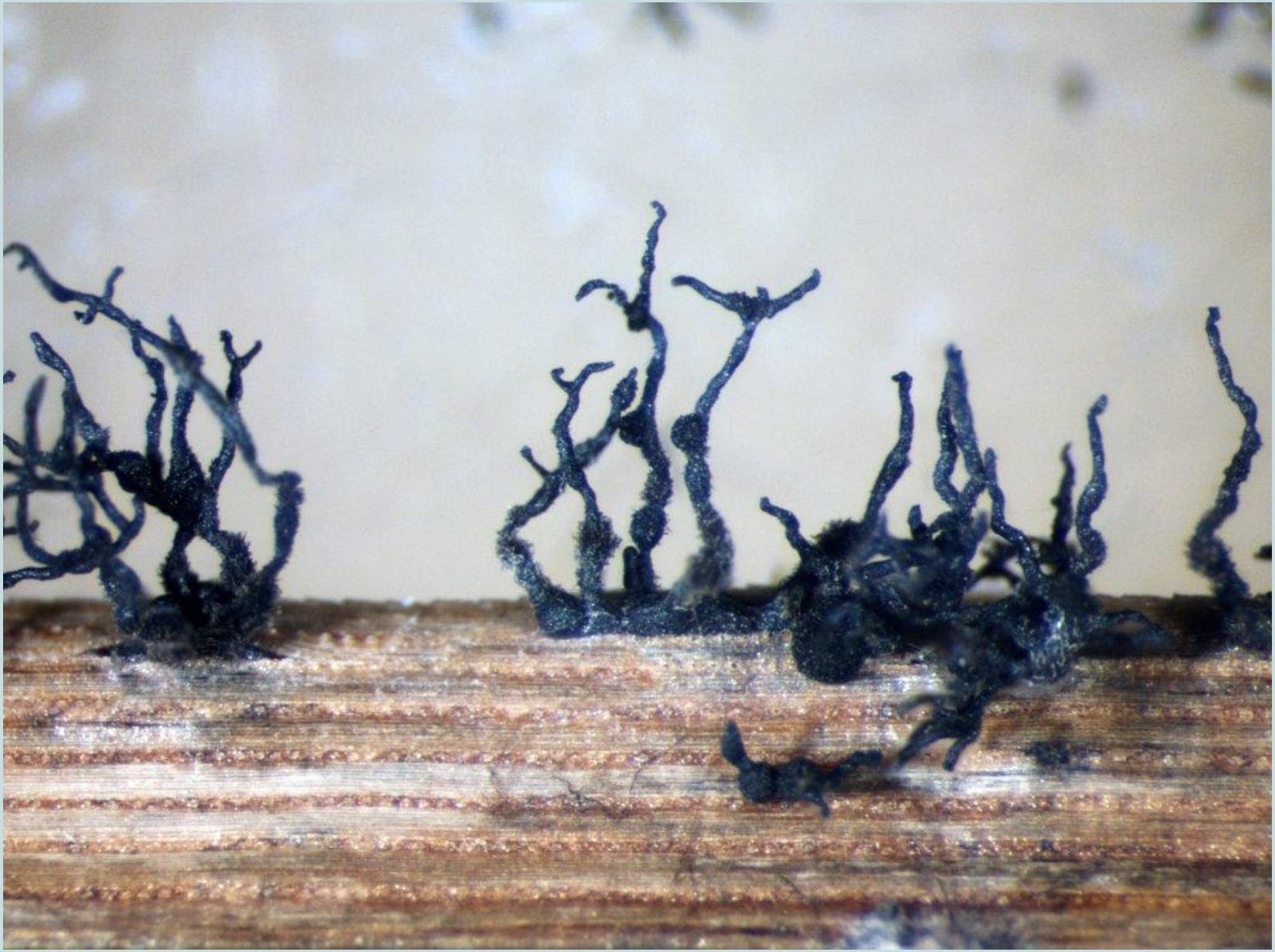
Future Plans. Further work is needed for the identification and purification of bioactive single molecules that are active in the context of CF-therapy. Efforts will be made to finalize the deconvolution and identify the pure active compounds. We shall also continue to investigate membranes proteins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

We shall organize EJIBCE2019 (Meeting of Young Researchers in Computational and Structural Biology) and a conference on the topic of Computational Biophysics is also planned (2020). We are engaged with the organization of 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		
Bioinformatics	Innovative modelling/ computational approaches			





Long, branched necks of the spore-producing structures of the fungus Dothiorella medicaginis growing on the stem of Lucerne (Medicago sativa). Provided by Alan Phillips, M&B Group, FCUL

BioISI Projects

For the third 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 programme by the BioISI SAB early 2018.

In 2018 these included 7 projects:

1. Severe Cystic Fibrosis-causing Mutations: from disease signatures to molecular identifiers
PIs: Carlos Farinha| Margarida Gama-Carvalho
Thematic Lines involved: Biomedicine | Bioinformatics

2. Deconvolution of dual CFTR/ANO1 Modulators from Portuguese natural products - A new class of drugs for CF therapy
PIs: Helena Vieira | Helena Gaspar | Hugo Botelho
Thematic Lines involved: Biomedicine | Biotechnology

3. UnCentre - Unlocking the 14;21 translocated centromere with nanopore sequencing
PIs: Raquel Chaves | Ricardo Dias | Margarida Gama-Carvalho
Thematic Lines involved: Biomedicine | Bioinformatics

4. Single molecule approaches to study S100B protein interactions with Aβ amyloid fibrils
PIs: Mário Rodrigues | Cláudio Gomes
Thematic Lines involved: Biophysics | Biomedicine

5. GraPoBio – Grape pomace on biological systems
PIs: Pedro Falé | Ana Margarida Fortes
Thematic Lines involved: Biomedicine | Biotechnology

6. A cell model to study UV-B effect in *Vitis vinifera L.*
PIs: Paula Lopes | Raquel Chaves
Thematic Lines involved: Biotechnology | Bioinformatics

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

Severe Cystic Fibrosis-Causing Mutations: from disease signatures to molecular identifiers

PIs - Carlos M Farinha | Margarida Gama-Carvalho

Biomedicine | Bioinformatics

Cystic fibrosis (CF) is the most common autosomal recessive disorder in Caucasians affecting 70,000 individuals worldwide. CF is caused by mutations in the CFTR gene that encodes a cAMP-activated anion channel expressed in secretory epithelia. Cellular models are of great value in the elucidation of several molecular mechanisms, especially in cases where access to native tissues and primary cultures is scarce. We used gene editing approaches to create a panel of isogenic cell lines for CF-causing mutations leading to different basic defects. We developed cells with mutations I507del, S341P, M1V and I1234V (complementing those with more common mutations obtained from the Cystic Fibrosis Foundation), all in the 16HBE14o- cell line that has endogenous CFTR expression. These models will be characterized and used as a resource to identify disease signatures using transcriptomic but also proteomic analyses, potentially revealing novel insights into disease mechanisms on a global scale.

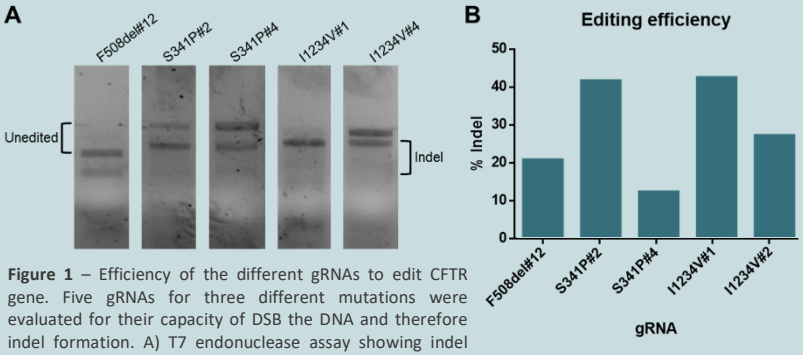


Figure 1 – Efficiency of the different gRNAs to edit CFTR gene. Five gRNAs for three different mutations were evaluated for their capacity of DSB the DNA and therefore indel formation. A) T7 endonuclease assay showing indel formation in pools of edited cells. B) Editing efficiency evaluated by TIDE web tool.

Results:

- Development of cell lines each homozygous for a different CF-causing mutation.
  - 16HBE cells homozygous for I507del, S341P, M1V and I1234V
  - BCi cells homozygous for F508del
- Cell line characterization, transcriptome and proteome analysis in progress

Conclusion:

A panel of 8 novel cell lines for study (5 produced and 3 obtained from CFF)

Outputs:

Mention K, Cavusoglu-Doran K, Sanz D.J, Santos L, Rojas E, Farinha C.M, Scallan M, Harrison P.T (2018) Gene Editing for Cystic Fibrosis: Correcting the disease at the source. Poster presented at the UK Cystic Fibrosis Conference, Birmingham (UK). 10-11 Sep.

Santos L, Sanz D.J, Cavusoglu-Doran K, Mention K, Farinha C.M, Harrison P.T (2018) Development Of Gene Edited Cell Models To Study Cystic Fibrosis. Poster presented at the 15th ECFS Basic Science Conference, (Greece). 21-24 Mar. Abs no.52, p.132.

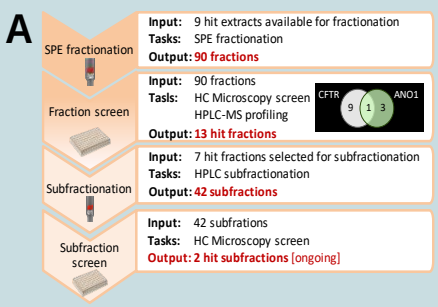
Deconvolution of dual CFTR/ANO1 Modulators from Portuguese natural products - A new class of drugs for CF therapy

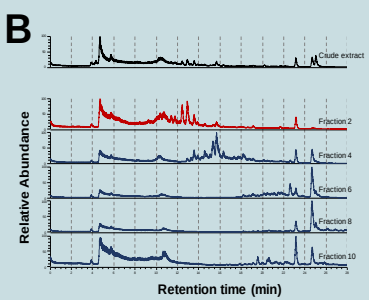
PIs - Helena Gaspar | Hugo M. Botelho | Helena M. Vieira

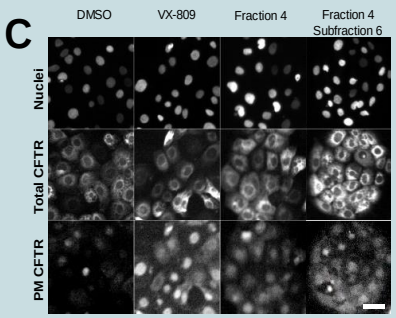
Biomedicine | Biotechnology | Biological Chemistry

Cystic Fibrosis (CF) is the most common life-shortening rare disease affecting ~85,000 individuals worldwide. It is caused by mutations in the gene encoding CFTR, an epithelial chloride/bicarbonate channel. About 85% of CF cases are due to F508del, a mutation preventing CFTR traffic to the plasma membrane (PM). Three drugs are currently approved for CF but most eligible patients only enjoy modest lung function improvement. We have previously screened a diverse natural products library and selected 9 hit extracts which increased the traffic of F508del-CFTR and/or the alternative chloride channel ANO1. In this project, we sought to purify and validate novel therapeutically-relevant molecules regarding traffic enhancement in these model systems by combining chromatography, spectroscopy, mass spectrometry and high content screening.

Results:







Summary of results

(A) By performing cycles of bio-guided fractionation, the 9 hit extracts generated 13 hit fractions, which enhance the traffic of F508del-CFTR and/or ANO1. Sub-fractionating has so far revealed 2 active subfractions.

(B) Monitoring the fractionation of one of the hit extracts using HPLC-MS. The total ionic current (y-axis) reports on the differential distribution of compounds across fractions. The active fraction is shown in red.

(C) CFBE cells expressing the F508del-CFTR traffic reporter and treated with an active fraction or subfraction of another hit extract. The amount of immunodetected plasma membrane (PM) F508del-CFTR is much higher than the negative control and comparable to the one observed with the pharmaceutical drug VX-809. Scale bar: 50 µm.

Outputs:

Calado R et al (2018) How to Succeed in Marketing Marine Natural Products for Pharmaceutical, Cosmetics & Nutraceutical Markets in: Rampelotto P., Trincone A. (eds) Grand Challenges in Marine Biotechnology. Grand Challenges in Biology and Biotechnology. Springer, Cham, Switzerland

Botelho, HM (2018) Innovating the search for novel Cystic Fibrosis therapies using high content microscopy screening". Invited oral presentation at SPAOM2018, Granada (Spain). 24-26 Oct.

Conclusion:

The 9 hit extracts produced 13 hit fractions and a preliminary set of 2 hit subfractions, all of which increase the traffic of F508del-CFTR and/or ANO1. Further work is required to obtain pure molecules.

UnCentre - Unlocking the 14;21 translocated centromere with nanopore sequencing

PIs – Raquel Chaves | Ricardo Dias | Margarida Gama-Carvalho

Biomedicine | Bioinformatics

Satellite DNA (satDNA), found predominantly in heterochromatic regions, is known to play a critical role in centromere structure/function, heterochromatin maintenance and gene expression regulation. Like other repeats, the sequence of centromeric satDNA arrays remains poorly characterized and is a major knowledge gap in the current Human Genome Assembly. Ultra-long reads generated by nanopore-based sequencing hold the potential to provide the understanding of satDNAs. In this project, we have characterized the centromeres of human chr 14 and 21 and der(14;21) and explored novel sequencing methods for its sequence level characterization, which will be of critical value both to the understanding of basic chromosome biology and related biomedical disease contexts, and as a platform for the development of novel genetic diagnostic tools

Table 1 – Summary statistics for sequencing assays

Metric	HEK cells	GM03417 Fibroblasts	
		Run I	Run II
Total Gbp/flow cell	4.8	10.5	3.3
Total reads (millions)	1.1	1.3	0.3
Mean read length (bp)	4381	7781	9980
Number of reads > 800bp	675742 (60%)	1165743 (86%)	304681 (92%)
Mean read length >800bp (bp)	6841	8959	10782
Longest read	292 kbp	155 kbp	256 kbp
# of long reads (>10kbp)	88815 (8%)	304280 (23%)	97502 (30%)
# of ultra long reads (>100kbp)	3793	196	250
Estimated human genome coverage	1.6x	3.5x	1x

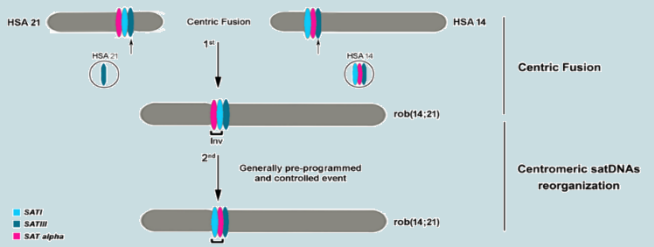


Fig.1 - Representation of the proposed two-step translocation mechanisms for human rob(14;21) derivation.

Results:

- Identification of Sat sequences at the 14 and 21 centromeres
- Demonstration of the presence of an inverted organization of centromeric satDNAs in the translocated chromosome;
- First long-read sequencing for the characterization of centromeric arrays (Table 1)

Conclusion:

A new two-step model for the 14;21 Rob translocation (Fig. 1)

Outputs:

2 manuscripts in preparation

- Ricardo Dias (2018) Onsite real time production of biological knowledge: Will nanopore bio-cyberphysical molecular sensing be a game changer? Workshop in "Innovation in Genomic Technologies"

- SUMMER INNOVATION CAMPUS Sep 2018, UTAD, Vila Real. BioISI Genomics – Bringing knowledge to you: anyTime anyWhere. Organization: Ricardo Dias and Margarida Gama-Carvalho

Single molecule approaches to study S100 protein interactions with Aβ amyloid fibrils

PIs – Mário S. Rodrigues | Cláudio M. Gomes

Biomedicine | Biophysics

S100B is among the most abundant proteins in the brain with important roles in the inflammatory response. During neurodegeneration, as caused by amyloid-beta (Aβ) deposition in Alzheimer's Disease this protein acts as an alarmin, being overexpressed mainly by astrocytes and secreted at high extracellular concentrations. The co-localization of S100B and amyloid beta in AD plaques is well known. AFM, besides allowing high-resolution imaging of protein structures, can characterize dynamic protein-protein and protein-membrane interactions. In this project we have proposed to use AFM in single molecule Dynamic Force Spectroscopy measurements to measure binding interactions between several S100 proteins. Of most interest was the interaction between S100A9 and pre-formed S100A9 oligomers to determine interaction parameters.

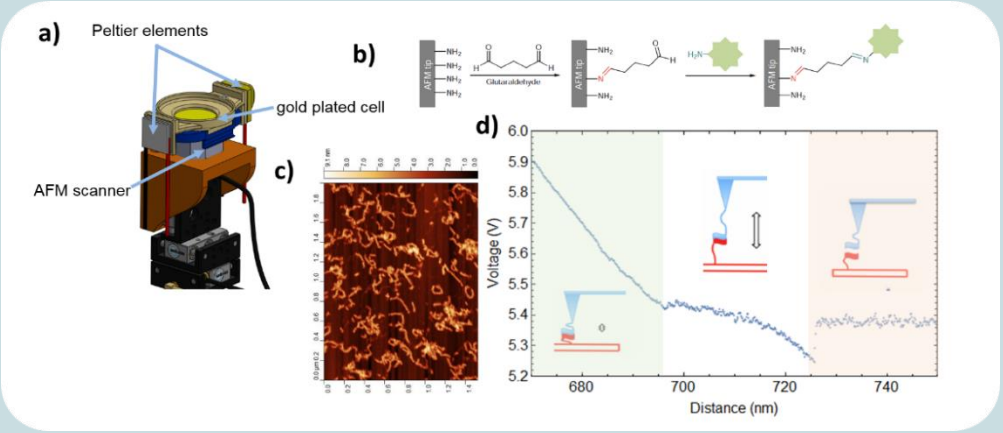


Figure 1: a) Newly developed AFM liquid cell; b) AFM tip functionalization; c) S100 polymers (AFM liquid imaging); d) Force recreation curves

Outputs:

Posters communications (4) in meetings; Prototype (1) – liquid AFM cell; Manuscript (1) in preparation

Results:

- Protein purification and biochemistry
- AFM liquid cell development
- Functionalization of AFM tips
- Force-mapping of protein-protein interactions

Conclusion:

We have now a robust and reliable strategy to functionalize the AFM tips with S100 molecules. This opens up the door to the study of a multitude of S100:protein interactions. We have characterized the S100A9 interaction with its fibril structures.

GraPoBio – Grape pomace on biological systems

PIs – Pedro Falé | Ana Margarida Fortes

Biomedicine | Biotechnology | Biological Chemistry

This project aimed at adding value to Portuguese grape pomace as dietary supplement by analyzing its health promoting activities on intestinal mainly using Caco-2 monolayers as an accepted model of intestinal lining. Two grape cultivars (Trincadeira and Syrah) at three stages of development were used. The composition and general bioactivities (antioxidant, acetylcholinesterase (AChE) inhibition, cytotoxicity) of grape pomace digested by gastrointestinal enzymes were analysed, as well as cytoprotective capacity against hydrogen peroxide injury in Caco-2 cells, metabolomic (FTIR) and proteomic profiles (2D-electrophoresis) of cells treated with the most promising digested grape pomace. Changes in lipids, glycogen, increased metabolization of MTT, and cell cytoprotection suggested induction of a higher metabolic rate and better redox maintenance in pomace-treated cells. This project fulfilled the core aims of its proposal, achieving preliminary data for proposals and publications.

Results:

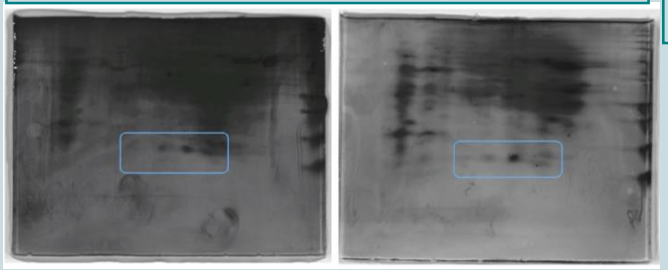
GASTROINTESTINAL DIGESTION

POLYPHENOL RELEASE:
Catechin
Epicathechin
Malvidin glucoside derivatives

Trincadeira at stage 38
↑polyphenols
↑*in vitro* activities
- free radical extinction,
- lipid protection,
- AChE inhibition,
- cytoprotection against oxidative injury

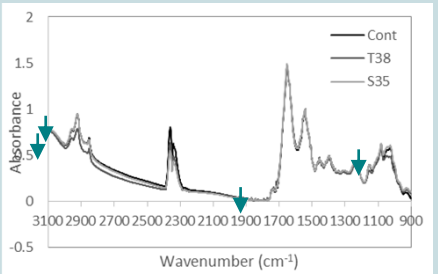
Bioactivity in Caco-2 cells

Changes in protein profile by 2D electrophoresis



T38 Cont

Changes in metabolomic profile by FTIR spectroscopy



Conclusion:

Trincadeira pomace at harvest-ripe stage releases bioactive compounds by gastrointestinal digestion that can protect intestinal cells from oxidative damage, modulating metabolism and redox homeostasis.

Outputs:

-Scientific papers (2, in preparation).
- Preliminary data for grant proposals (2, submitted), and for a recently approved FCT project.
- International training and career development (2 ERASMUS+ internships)

A cell model to study UV-B effect in *Vitis vinifera L.*

PIs - Paula Martins-Lopes| Ana Margarida Fortes | Raquel Chaves

Biotechnology | Bioinformatics

Vitis vinifera L. is one of the most economically important crops in Portugal, and although it is well adapted to the actual climate, it is expected that the changes foreseen can alter both the distribution of grapevine in the country and the physical-chemical parameters of the berries used to produce wines. The large genetic variability found within the Portuguese grapevine germplasm constitutes an opportunity for wine-markers to overcome some of the problems foreseen. The prediction of the possible impact of an amino acid substitution on the structure and function of the anthocyanidin 3-O-glucosyltransferase 2 protein (UFOG) is the basis of a selection process for varietal choice. The light effect on the establishment of embryogenic cultures plant regeneration in *V. vinifera L*. Portuguese grapevine varieties was also explored. Other experimental procedures are undertaken for the establishment of a cell model using CRISPR-Cas9 technology for two transcription factors, VvMYBA6.1 and VvMYBA7, silenced in the red grapevine Sousão variety.

Variant	Wine varieties presenting the variant
p.(Pro74Ala)	Tinta Barroca, Merlot, Touriga Nacional and Touriga Brasileira
p.(Gly161Ala)	Tinta Francisca, Tinta Amarela, Cõdega do Larinho, Alicante Bouschet, Touriga Franca, Tinta Barroca, Merlot, Touriga Nacional, Sousão and Cabernet Sauvignon
p.(Asn174Tyr)	Rufete, Tinta Roriz and Malvasia Fina
p.(Ser180Tyr)	Tinto Cão, Donzelinho Tinto, Tinta Francisca, Tinta Amarela, Cõdega do Larinho, Alicante Bouschet and Touriga Franca
p.(Ala361Gly)	Tinto Cão, Donzelinho Tinto, Tinta Francisca, Tinta Amarela , Cõdega do Larinho, Alicante Bouschet and Touriga Franca
p.(Gly363Trp)	Rufete
p.(Val385Ala)	Moscatel Galego, Gouveio, Tinta Barroca, Merlot, Touriga Nacional and Touriga Brasileira
p.(Lys399Glu)	Donzelinho Tinto, Pinot Noir, Chardonnay, Moscatel Galego, Gouveio, Touriga Nacional and Touriga Brasileira
p.(Phe443Tyr)	Tinta Roriz

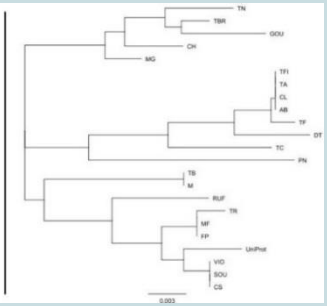


Figure 1. UFOG variants predicted as deleterious using the PROVEAN software (score <-2,5); tree generated based on the Geneious algorithm, using Geneious R9 software.

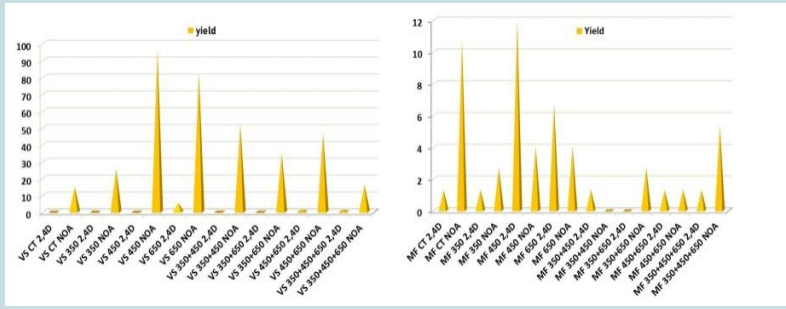


Figure 2. Viosinho a Malvasia fina behavior through UV–light exposure**.**

Conclusions:

The UFGT amino acid sequences aligned revealed thirty-four amino acid changes, of which 9 were considered to be deleterious. In this group, 5 a.a. changes have never been reported being some of them specific to the Portuguese varieties and one of French origin. Up till now, VS was more receptive to light treatments, considering primary *calli* proliferation; however, no somatic embryos were produced. Nevertheless, new experiments are underway for further investigation.

Outputs:

BSc final degree report: Paula Figueira (2018): SNP effect on the UFOG *Vitis vinifera L.* protein: an *in silico* approach.

Poster presentations: L. Pereira, AM Fortes, F Leal, JRA Fernandes, Martins-Lopes P. Light effect on the establishment of embryogenic cultures of *Vitis vinifera L.* Portuguese grapevine varieties. International Congress on Grapevine and Wine Sciences; **P. Figueira, L. Pereira, R. Chaves, P. Martins-Lopes.** SNP effect on the UFOG *Vitis vinifera L.* protein: an *in silico* approach. Workshop: Innovation in Genomic Technologies.

Understanding the microbial community effects in a phytochemical-free vineyard

PIs - Andreia Figueiredo| Ricardo Dias| Margarida Gama Carvalho

Biotechnology | Bioinformatics

Grapevine (*Vitis vinifera L.*) is one of the crops with high economic impact worldwide. In the viticulture, the terroir concept was established aiming to the unique aspects of a place (physical, biological, viticulture and 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. We have characterized the terroir associated microbiota in Quinta dos Murças, the Douro organic vineyard from Esporão, one of the most well-known Portuguese wine companies. We have used the novel real time direct DNA sequencing technology, Nanopore, and identified several microbial communities within each terroir and defined terroir-specific biomarkers. Differences in the soil bacterial communities of different terroirs analysed correlate with soil characteristics which may lead to specific vineyard regionalization.

Results:

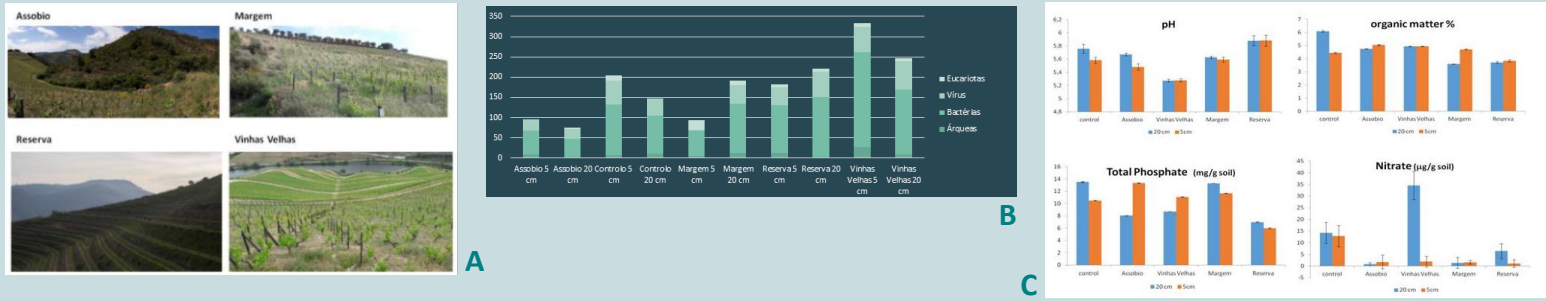


Figure 1: A- Quinta dos Murças terroirs under analysis (Assobio, Margem, Reserva, Vinhas Velhas) Photo Credit by Esporão; B- Microbiome profile at 5 and 20 cm depth of Assobio, Margem, Reserva, Vinhas Velhas and Control (vineyard with phytochemical application) soil samples - unique taxa identified at each terroir and depth; C- soil parameters analysed.

Conclusion: Microbial community structures are significantly different between the terroirs analysed. Differences in the soil bacterial communities influence soil characteristics that may to specific vineyard regionalization.

Outputs (oral communications)

1-Figueiredo A, Dias R, Carvalho MG, Valente M, Laureano G, Tenreiro R, Silva J, Oliveira N (2018) Exploring the microbiota in a organic vineyard. Ciência 2018 – Science and Technology in Portugal Summit, 2rd-4th July, Lisbon –Portugal

2-Figueiredo A (2018) Post 'OMICS. Contribution for a sustainable viticulture. Academia das Ciências de Lisboa, 5th April, Lisboa, Portugal

3-Figueiredo A, Dias R, Carvalho MG, Valente M, Laureano G, Gouveia C, Cruz C, Tenreiro R, Silva J, Oliveira N (2018) What lies beneath: learning more about soil microbiota to support new guidelines for sustainable organic wine production. Seminário Internacional Alimentação Saúde e Ambiente: Sustentabilidade e Desafios. 10th-12th October, Lisbon

BioISI Research Units (Groups)

Expression of transcription factor in the root apical meristem of *Arabidopsis thaliana,* Image provided by Andreia Matos, PFG

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
- Plant responses to pollutants and their use as remediation tools
- Genetic variability and plant cytogenomics

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.
- Publication of the draft genome sequence of cork oak and ectomycorrhizal diversity studies.
- 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.
- Analysis of plant microbiome and physiological indicators upon abiotic toxicity stress.
- Characterization of novel proteins involved in angiosperm (Arabidopsis) morphogenesis and sexual reproduction.

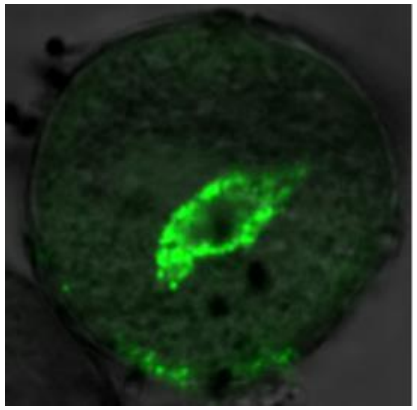


Figure 1. Tobacco pollen grain expressing GFP-bound nuclear protein.

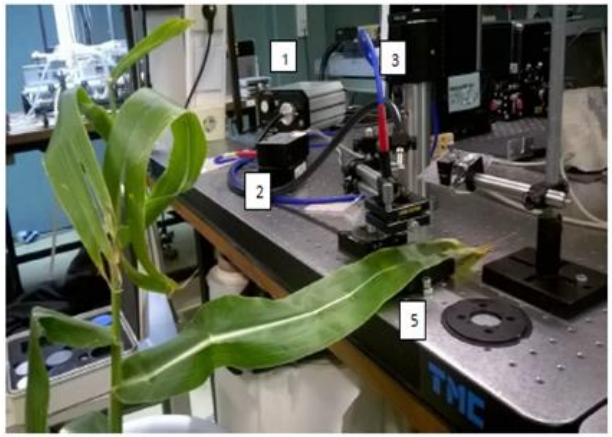


Figure 2: Phenotyping analysis of maize plants grown under abiotic stress.

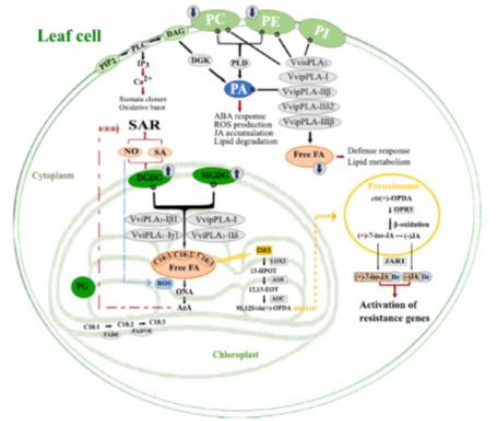


Figure 3: Lipid and fatty acid modulation in *Vitis vinifera* (in response to pathogen attack)

Figure 4: Arabidopsis seedlings.

Group Members

GL: Rui Malhó

PI's:


Ana Margarida Fortes


Rui Tavares


Andreia Figueiredo


Célia Miguel


Sónia Gomes


Manuela Costa


Manuela Matos


Susana Serrazina


Anabela Silva


Ana Milhinhos


Rómulo Sobral


Leonor Pereira


Mónica Sebasteana


Jorge Silva


Paula Lopes


Ana Rita Matos


Fernanda Leal


Rita Teixeira


Teresa Lino-Neto


Eduardo Lima-Brito


Maria João Gaspar


Ana Carvalho


Fernando Vaz Dias

PhD & MSc Students: Vanessa Azevedo, Catarina Gouveia, Diana Pimentel, Flávio Soares, Teresa Braga, Rita Catarino, 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, Cláudia Fernandes, Elisabete Santos, João Alves, Francisca reis, Daniela Costa, Helena Silva, Teresa Gomes, João Mina, Shweta Singh

Selected Publications

1. The interplay between membrane lipids and phospholipase A family members in grapevine resistance against *Plasmopara viticola*. Laureano et al. Scientific Reports 8: 14538. DOI:10.1038/s41598-018-32559-z.

2. Successive Domain Rearrangements Underlie the Evolution of a Regulatory Module Controlled by a Small Interfering Peptide. Raimundo et al. Mol Biol & Evol 35. 10.1093/molbev/msy178.

3. The draft genome sequence of cork oak. Ramos et al. Sci. Data 5:180069 doi: 10.1038/sdata.2018.69

Key Funded Projects

Development of molecular markers for resistance to pine wilt disease in *Pinus pinaster*. LISBOA-01-0145-FEDER-028379, 185.500€. Coordination.

Functional studies of plant membrane trafficking and secretion – the phosphoinositide pathway in the responses to abiotic stress. LISBOA-01-0145-FEDER-028170, 188.00€. Coordination.

Grapevine immunity: the innovative role of subtilisin-like proteases. PTDC/BIA-BQM/28539/2017. 236.000€. 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 CF-related ion channels: CFTR, anoctamins.
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 and in mitochondrial rare diseases.
8. Pharmacology of drug resistance and pharmacogenetics, having *Plasmodium falciparum* (malaria) as the main model

Major Achievements:

- Impact of HGF treatment on the functional rescue of F508del-CFTR and on epithelial differentiation effects of
- Interactome regulating F508del-CFTR exit from the endoplasmic reticulum – kinesin family member C1 (KIFC1) as a key interactor
- Characterization of the impact of rare CF-causing mutations (including nonsense and missense variants)
- New role for cytokine S100B as a novel chaperone inhibiting amyloid aggregation in Alzheimer's Disease
- Data concerning the efficacy and safety for Artesunate-Pyroniridine (AP), a new 2nd generation Artemisin Combination Therapy (ACT) for European Medicines Agency approval

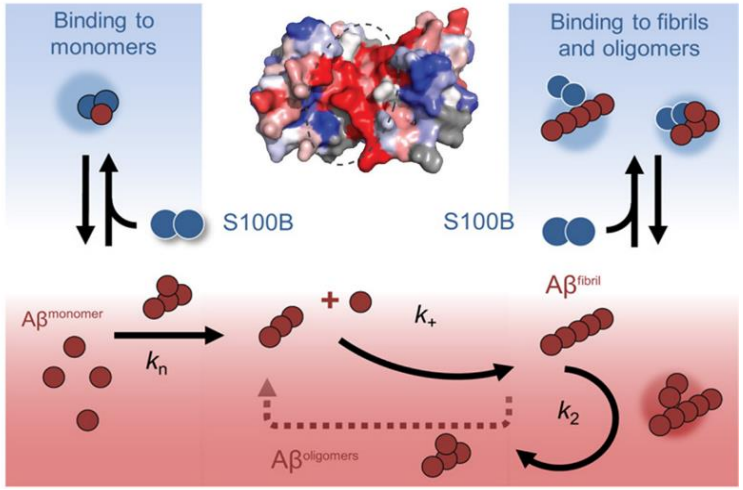


Figure 1: Mechanism of inhibition of A?42 aggregation by S100B and structural mapping of A?42 binding into S100B (red)

Selected Publications

1. Canato S, Santos JD, Carvalho AS, Aloria K, Amaral MD, Matthiesen R, Falcão AO, Farinha CM (2018) Proteomic interaction profiling reveals KIFC1 as a factor involved in early targeting of F508del-CFTR to degradation. Cell Mol Life Sci. 75(24):4495-4509. doi: 10.1007/s00018-018-2896-7. IF 6.721
2. Cristovão, JS, Morris, VK, Cardoso, I, Leal, SS, Martinez, J, Botelho, HM, Gobl, C, David, R, Kierdorf, K, Alemi, M, Madl, T, Fritz, G, Reif, B, and Gomes, C M (2018) The neuronal S100B protein is a calcium-tuned suppressor of amyloid-beta aggregation. Science Advances 4, eaaq1702. doi: 10.1126/sciadv.aaq1702 IF 11.511
3. Inoue J, Silva M, Fofana B, Sanogo K, Mårtensson A, Sagara I, Björkman A, Veiga MI, Ferreira PE, Djimde A, Gil JP (2018) Plasmodium falciparum Plasmepsin 2 Duplications, West Africa. Emerg Infect Dis. doi: 10.3201/eid2408.180370. IF 7.422
4. Lérias JR*, Pinto MC*, Botelho HM, Awatade NT, Quaresma M, Wanitchakool P, Schreiber R, Pepperkok P, Kunzelmann K, Amaral MD (2018) A Novel Microscopy-Based Assay Identifies Extended Synaptotagmin-1 (ESYT1) as a Regulator of Anoctamin 1 Traffic. BBA- Mol Cell Res 1865: 421-431. (*1st co-authorship) IF 4.521

Group Members

GL: Margarida D. Amaral

PI's:


Bárbara Henriques


Carlos Farinha


José Pedro Gil


Cláudio M. Gomes


Paulo Matos

Post Docs: Patrícia Barros | Luka Clarke | Miquéias Lopes-Pacheco | Susana Igreja | Ines Pankonien | Hugo Botelho

PhD Students: Ana Margarida Matos (BioSYS) | Márcia Faria (BioSYS) | Sara Canato (BioSYS) | João Santos (BioSYS) | Daniel Cruz (BioSYS) | Lúcia Santos (BioSYS) | Sofia Ramalho (BioSYS) | Luís Sousa (BioSYS) | Margarida Quaresma (BioSYS) | Madalena Pinto (BioSYS) | Filipa Simões (BioSYS) | Tiago Pedreira (BioSYS) | Joana Cristovão | Mariana Romão (BioSYS) | Romina Coelho (BioSYS) | Leyre Pernaute (BioSYS)

MSc Students: André Gomes |Carina Rebelo | Maria Joana Ribeiro| Guilherme Moreira | Ana Rita Pradal

BI Researchers: Ricardo Vieira | Violeta Railean | Joana Ferreira | Rodrigo David | Tânia Lucas

Technicians: Sofia Correia

Key Funded Projects

Sodium-iodide symporter posttranslational interactome: identification of novel targets to enhance iodide-related cancer therapy. FCT (PTDC/BIA-MOL/31787/2017). P. Matos (Co-PI) – funding BioISI: 100 K€.
CFMOLIM – Novel molecular imaging probes for Cystic Fibrosis. FCT (PTDC/BTM-TEC/29256/2017). C.M. Farinha (Co-PI) – funding BioISI: 30 K€.
Mechanisms of protein dysfunction in mitochondrial diseases. FCT (PTDC/BIA-BQM/29963/2017). B. Henriques (PI) – funding BioISI: 219 K€.
(FCT/02/SAICT/2017/28800) "iDrugCF - Identification of New Drugs for Cystic Fibrosis". Budget: 240K€; 3 yrs. PI: MD Amaral.
2018 CF Trust Strategic Research Centre Award (Ref. SRC 013) "Personalised Therapies for all: Restoring airway function in CF using Alternative Chloride Channels ". Total budget: 750K£. FCUL Budget: 224K€; 4 yrs. PI: M Gray, Newcastle (UK). PI for the FCUL group: 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) and co-involvement in outreach events like Young Creators'18, Science Days and 2018 International Microorganism Day.

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

Figure 1*: Circinotrichum*. Microscope image of the fungus *Circinotrichum*. This fungus grows in the compact layer of leaves fallen from trees where it re-cycles the nutrients locked in the leaves and returns them to the soil. It forms these structures, just 0.1 mm tall, that push apart the leaves to create a space in which it lives and that allows water to flow through and spread its spores. Image provided by Alan Phillips.

Figure 2

Figure 2*: Dothiorella medicaginis*. Long, branched necks of the spore-producing structures of the fungus *Dothiorella medicaginis* growing on the stem of Lucerne (*Medicago sativa*). Image provided by Alan Phillips.

Group Members

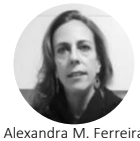
GL: Rogério Tenreiro

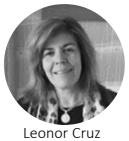
PI's:


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. Dias C, Pais J, Nunes R, Almeida AF, Serra P, Xavier N, Vila-Viçosa D, Machuqueiro M, Viana A, Martins A, Santos M, Pelerito A, Dias R, Tenreiro R, Oliveira M, Contino M, Colabufo N, Almeida R, Sanchez-Blazquez M, Marquês L, Rauter A (2018). The first sugar-based bactericides targeting phosphatidylethanolamine-enriched membranes. Nature Communications 9: 4857. DOI: 10.1038/s41467-018-06488-4.

2. Phillips AJL, Hyde KD, Alves A, Liu J-K (2018). Families in Botryosphaeriales: a phylogenetic, morphological and evolutionary perspective. Fungal Diversity (online 23.11.2018). DOI: 10.1007/s13225-018-0416-6 [Q1 | IF: 14.078]

3. Seixas I, Barbosa C, Mendes-Faia A, Güldener U, Tenreiro R, Mendes- Ferreira A, Mira NP (2018). Genome sequence of the non-conventional wine yeast Hanseniaspora guilliermondii UTAD222 unveils relevant traits of this species and of the Hanseniaspora genus in the context of wine fermentation. DNA Research, dsy 039. DOI: 10.1093/dnares/dsy039. [Q1 | IF: 5.360]

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 for improved diagnosis and intervention using systems Medicine frameworks.

Major Achievements:

- In collaboration with the Clinical Genome Resource (ClinGen), we defined guidelines for FH variant classification and are awaiting approval for publication. Our ClinGen group effort to increase variant submission to ClinVar was published in Human Mutation (Iacocca et al., 2018). The guidelines for Clinical Genetic Testing for Familial Hypercholesterolemia were published with the collaboration of a BTR member (Sturrm et al 2018).
- We found that DFNB1 status is significantly associated to higher oral performance scores, with DFNB1individuals performing, on average, 6% better than the individuals without DFNB1-associated deafness.
- We functionally characterized novel variants causing FH, increasing the number of variants with a likely pathogenic or pathogenic classification. A new project to establish novel biomarkers to distinguish monogenic from polygenic dyslipidaemia was initiated.
- We implemented a molecular diagnostic assay for human leptospirosis, a worldwide zoonotic infection disease, to identify the Leptospira species at the earliest onset of infection in a clinical setting, in less than 2 hours (Esteves LM et al, 2018).
- Molecular genetic alterations responsible for congenital ocular anomalies with neurologic impairment were identified in an individual with a de novo balanced chromosome translocation t(11;18) (David D et al., 2018).
- We developed novel systems biology algorithms to identify disease genes based on machine learning and functional similarities (Asif et al., 2018).
- As part of the Psychiatric Genomics Consortium and the International Stroke Genetics Consortium (METASTROKE), we contributed to a study showing that several neuropsychiatric disorders and some cognitive measures share common risk variants, while neurological diseases are more distinct. The study was conducted in a dataset with over 700,000 participants, and has implications for etiology and nosology of these diseases (Antilla V et al, 2018).
- The Autism Spectrum Disorder in the European Union (ASDEU) study determined autism prevalence in 13 regions of Europe, estimated the burden of the disease and examined risk factors and biomarkers for autism. The final report was published (http://asdeu.eu/findings/).

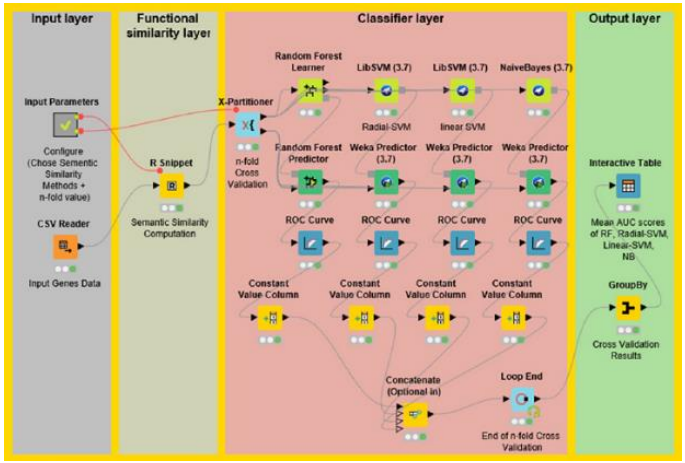


Figure 1: Architecture of automated workflow to predict disease genes

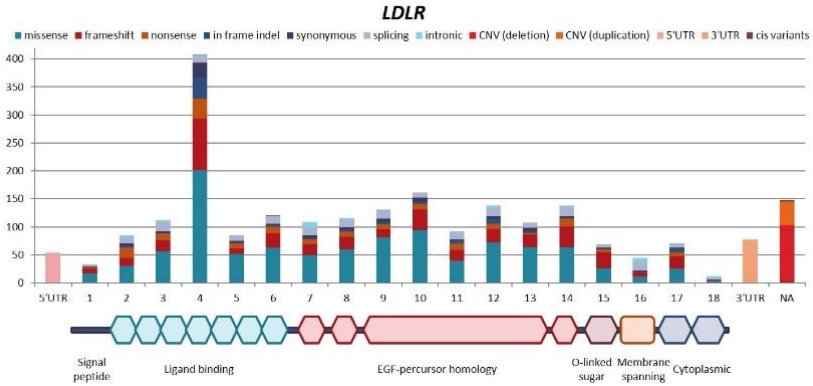


Figure 2: LDLR variants submitted to ClinVar worldwide found in FH patients. Submission increase substantially due to ClinGen VCEP FH group efforts (Iaccoca & Chora et al, 2018)

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 | Inês Conceição | Tiago Matos |Renato Pires | Hugo Martiniano | Sonija Luzi | Maria Luis Cardoso

PhD Students: Ana Margarida Medeiros|Ana Rita Marques (BioSYS) Cibelle (BioSYS) | Haula Haider | Joana Chora | João Pedro Santos (BioSYS) | Muhammad Asif (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

Selected Publications

1. Brainstorm consortium Analysis of shared heritability in common disorders of the brain. Science. 2018 Jun 22;360(6395)
2. Sturm AC, et al; Convened by the Familial Hypercholesterolemia Foundation. Clinical Genetic Testing for Familial Hypercholesterolemia: JACC Scientific Expert Panel. J Am Coll Cardiol. 2018 Aug 7;72(6):662-680.
3. Iacocca MA*, Chora JR*, et al, on behalf of the ClinGen FH Variant Curation Expert Panel. ClinVar database of global familial hypercholesterolemia-associated DNA variants. Hum Mutat 2018;39:1631–1640. DOI:10.1002/humu.23634. *both authors contributed equally to this work.

Key Funded Projects

Synaptic networks and personalized medicine approaches to understand neurobehavioral disease across the lifespan (MEDPERSYST). Funded by Portugal 2020, Programa de Atividades Conjuntas, Operação POCI-01-0145-FEDER-016428. Total funding 2.487.042,85€, BioISI funding 469.678,33€ (collaborator Astrid Vicente).

Dyslipidaemia stratification : new screening tools for a cost effective approach 2018-2021 Funded by Science and Technology Foundation (FCT), Total Budget 239 511,12€. Co-PI Mafalda Bourbon.

GER Group

Gene Expression and Regulation

http://bioisi.pt/ger/

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

Major Achievements:

- Regulation of developmental processes by alternative polyadenilation: using zebrafish as a model, we have shown that APA sites can be used to fine-tune fgf8a expression, modulating Fgf signalling and downstream processes during embryonic development1.
- Understanding disease mechanisms through biological network analysis: we have developed a novel computational method to identify candidate genes associated with two diseases with common phenotypes2.
- Modeling the phosphoinositide pathways: a new model for all phosphoinositides species in the plasma membrane of mammalian cells replicates the steady-state of the pathway and most known dynamic phenomena and highlights novel strategies to achieve therapeutically desirable decreases in PI(4,5)P2 levels while avoiding undesirable alterations in other phosphoinositide pools3.
- Mechanisms of gene expression: we have revealed an unexpected role for DIS3L2 in the degradation of human nonsense-mediated mRNA decay targets, involving a mechanism that is dependent on mRNA uridylation by terminal uridylyl transferases (submitted).
- Generation of Comparative maps in mammalian species: we generated a comparative map between two subspecies of *Genetta* and the domestic cat (doi: 10.1159/000491868).
- Regulation of alternative splicing decisions by cell signaling: we have shown that the presence of M1 macrophages is able to induce alternative splicing changes in colorectal cells in cellular co-culture models.
- Gene expression pathways in neurodegeneration: we have characterized common gene expression changes in three Drosophila LOF models for TBPH, Caz and Smn through RNA-seq, in conjunction with the profiling of their nuclear and cytoplasmic mRNA targets, revealing novel insights into critical shared pathways for SMA and ALS.

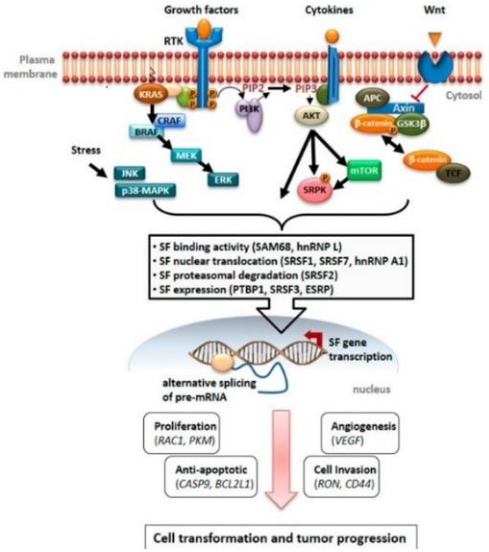


Figure 1: Schematic representation of key connections between cancer cell signaling and alternative splicing (Gonçalves et al, doi:10.3390/genes9010009)

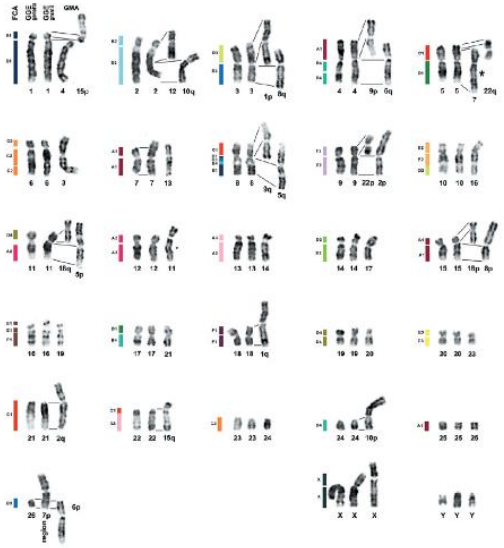


Figure 2: Comparative cytogenetic map of two Geneta geneta subspecies and the domestic cat (Adega et al, doi: 10.1159/000491868)

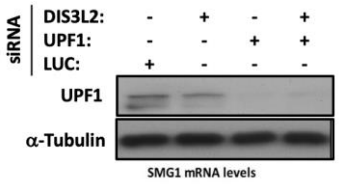


Figure 3: effects of DIS3L2 and UPF1 knowck-down on SMG1 mRNA levels reveals a non-additive role for the two proteins (Costa et al, submitted).

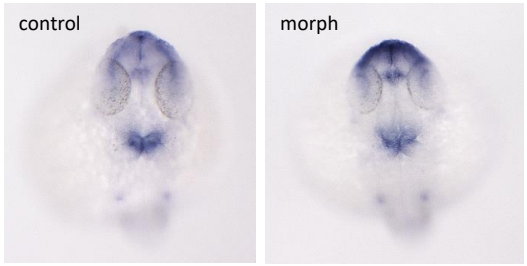


Figure 4: *in situ* hybridization for fgf8a in 24hpf zebrafish embryos revealing increased expression in response to morpholino-induced APA site switch[1].

Selected Publications

1. Fernandes et al (2018) Fine-tuning of fgf8a expression through alternative polyadenylation has a selective impact on Fgf-associated developmental processes. BBA Gene Reg Mech, 1861, 783.
2. Garcia-Vaquero et al (2018) Searching the overlap between network modules with specific betweeness (S2B) and its application to cross-disease analysis. Sci Rep, 8, 11555.
3. Olivença et al (2018) A Mathematical Model of the Phosphoinositide Pathway. Sci Rep, 8, 3904.

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 | Marcelo Pereira | Mark Gibson | Daniela Ferreira

PhD Students: Ana Escudeiro | Andreia Henriques | Cláudia Loureiro | Daniel Olivença | Guillem Santamaria (BioSYS) | Gonçalo Nogueira (BioSYS) | Hugo Santos | Joana Pereira | Joana Silva | Mariana Pinhão | Marina Garcia-Vaquero (BioSYS) | Marta Correia (BioSYS) | Nuno Domingues (BioSYS) | Paulo Costa | Rafael Fernandes | Tânia Marques (BioSYS)

Other researchers: Bruna Pereira | Cláudia Estima | Inês Martins | Joao Paulo Silva | Miguel Pereira | Patrícia Dias | Mariana Lopes

Key Funded Projects

- miRiAD - Exploring the role of microRNAs in T cell function and anti-HIV defense PTDC/BIA-CEL/29257/2017, Oct 2018-Sep 2021 Budget: 240K€
- New signaling pathways involved in the retention of epithelial chloride transporters PTDC/BIA-CEL/28408/2017, Oct 2018-Sep 2021 Budget: 240K€
- Microenvironmental effects on alternative splicing in malignant progression of colorectal tumor cells PTDC/BIA-MOL/28386/2017, Oct 2018-Sep 2021 Budget: 240K€
- PulmaGENE – Portugal2020; Co-promotion Projects: STAB VIDA and BioISI/UTAD. Jan 2019-Dec 2021 Budget: 680.902,52€ global/332.000 € local
- 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:

- Understanding spin crossover in Fe(III) compounds and development of new Co(II) photocatalysts for methane production;
- Calculation (QM) of the mechanism of the cyclisation reaction of triazo molecules catalysed by the {Mo132} molecular metal oxide in aqueous solution
- MD simulations: estimation of the binding free energy of a sickle cell hemoglobin dimer, understanding of the molecular details of pHLIP peptide pH-dependent membrane insertion, and comprehensive description of halogen bonds in protein-ligand systems.
- Isolation of new bioactive products from marine seaweeds and study of the antiproliferative activity of cork wastewater compounds. The antitumor effects of food components were associated to changes in apoptotic cell proteins.
- Elucidation of the structure of the respiratory alternative complex III, enabling to enlighten the energy transduction mechanism.
- New patents concerning biofouling control and chemical immobilization were achieved (WO2018055102/ EP3298895 A1 and WO201805516/ EP3299083)

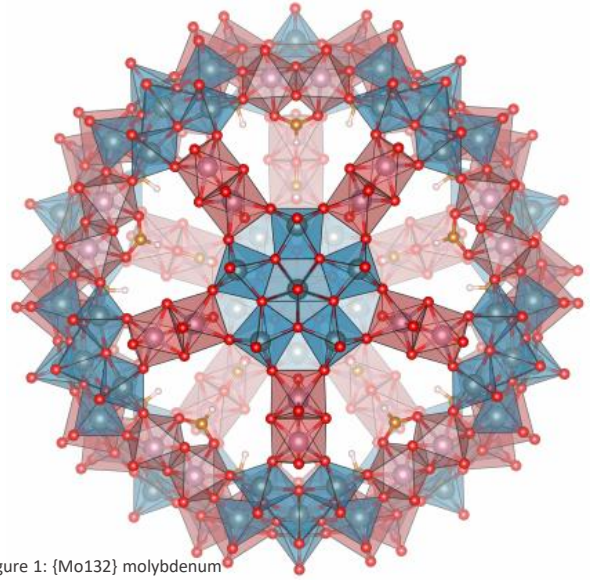


Figure 1: {Mo132} molybdenum Keplerate structure is able to act as a catalyst for the Huisgen reaction

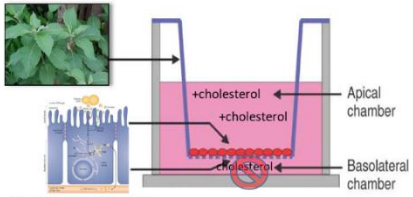


Figure 2: A caco-2 cell monolayer model, simulating intestinal lining, was used to probe the inhibition of cholesterol permeation by bioactive compounds from herbal infusions.

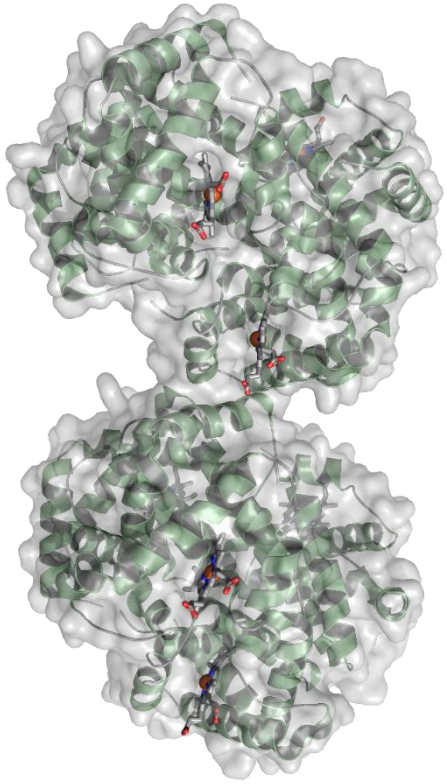


Figure 3: Sickle cell hemoglobin dimer was studied by molecular dynamics simulations

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. Joana S. Sousa, Filipa Calisto, Julian D. Langer, Deryck J. Mills, Patrícia N. Refojo, Miguel Teixeira, Werner Kühlbrandt, Janet Vonck, Manuela M. Pereira (2018) Structural basis for energy transduction by respiratory alternative complex III. NATURE COMMUNICATIONS, 9, 1728. 10.1038/s41467-018-04141-8
2. Rafael Nunes, Diogo Vila-Viçosa, Miguel Machuqueiro, Paulo J. Costa (2018) Biomolecular simulations of halogen bonds with a GROMOS force field. Journal of Chemical Theory and Computation , 14, 5383-5392. 10.1021/acs.jctc.8b00278
3. A. I. Vicente, L. P. Ferreira, M. D. Carvalho, V. H. N. Rodrigues, M. M. Dîrtu, Y. Garcia, M. J. Calhorda, P. N. Martinho (2018) Selecting the spin crossover profile with controlled crystallisation of mononuclear Fe(III) polymorphs. Dalton Transactions, 47, 7013-7019. 10.1039/C8DT00227D

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-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:

- FFM developments: measurement of the capillary condensation time of a water nanobridge, [M V Vitorino et al, Scient. Reports 8, 1348, 2018]; development of a new methodology for mechanical properties assessment of soft cells, in liquid environment, without contact - preliminary results on CFBE cells - in collaboration with FunGP group.
- Magnetic nanoparticles for biomedical applications: study of magnetic particles in nanoweb systems [N Sarier et al, IOP Conf. Series: Mat. Sc. & and Eng, 460 (2018) 012025, 2018]; detailed magnetic hyperthermia assessment of surface modified magnetic nanoparticles.
- Protein physics: simulation results show that hydrophobic confinement provided by the chaperonin cage assists the folding of knotted proteins by facilitating the unfolding of topologically trapped states and by enhancing the knotting frequency.
- Atomic/electronic structure: energy and radiative/non-radiative transition probabilities calculations in systems with internal holes [Y. Ito et al, Phys. Rev. A 97, 042501, 2018]; first report of a correlation between the nuclear magnetic shielding of the oxygen atom and the tetrahedral order parameter in liquid water [N Galamba et al, J. Chem. Phys. 148, 044510, 2018]

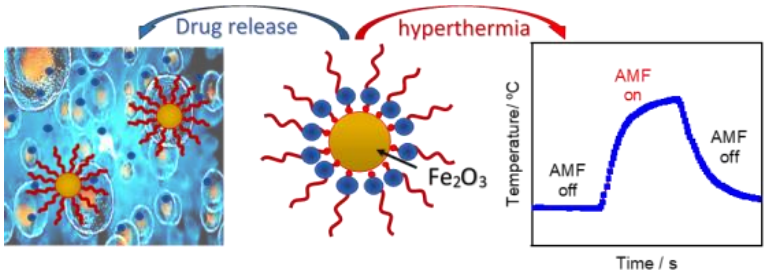


Fig 1. Magnetic nanoparticles: applications in cancer therapy

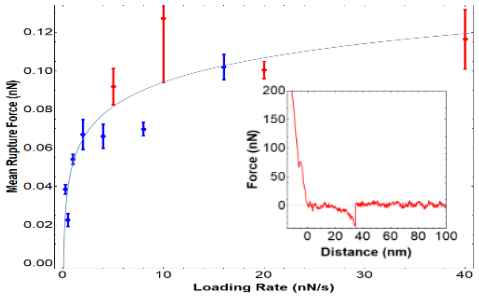


Fig 3. Protein-protein interactions: AFM force spectroscopy measurements

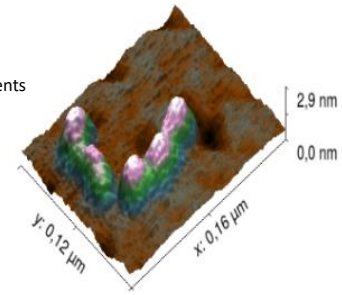


Fig 3. AFM imaging of protein structures (S100A9)

Selected Publications

1. M. Moskvin, M. Babic, Salette. Reis, M. M. Cruz, L. P. Ferreira, M. D. Carvalho, S. A. Costa Lima, D. Horák (2018) Biological evaluation of surface-modified magnetic nanoparticles as a platform for colon cancer cell, Colloids and Surfaces B: Biointerfaces, 161, 35 10.1016/j.colsurfb.2017.10.034
2. Ana I. Vicente, Liliana P. Ferreira, Maria José Calhorda and Paulo N. Martinho (2018) Selecting the spin crossover profile with controlled crystallization of mononuclear Fe(III) polymorphs, Dalton Transactions, 47,7013, 10.1039/c8dt00227d
3. Benedito J. Costa Cabral (2018) Born-Oppenheimer molecular dynamics, hydrogen bond interactions and magnetic properties of liquid hydrogen cyanide, Journal of Molecular Liquids, 272, 778, 10.1016/j.molliq.2018.09.092 10.1016/j.molliq.2018.09.092

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 (funded by BioISI)

Other integrated members: Margarida Pires | António Casaca | M. Estrela M. Jorge | Tânia Ramos (Oct 2018)

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

Master Students: João Especial (concluded Dec 2108)| Elsa Teixeira (concluded Nov 2018) | Gabriel Frederico Martins (concluded Nov 2018) | (Daniela Pires (ongoing)

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

Key Funded Projects

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

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

Theoretical design of molecular machines with applications in organic photovoltaics and solar thermal storage, FCT project grant, 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:

- Development of 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
- Data mining and knowledge discovery

Major Achievements:

- ASSISIbf FP7-FET project concluded with Excellent final grade
- ASSISIbf exhibited at ARS electronica 2018 (Austria), with 105k visitors to festival
- A novel semi-supervised learning method that allows Genetic Programming to correctly learn from noisy data sets with erroneous labels, ignoring the outliers
- A novel regression method based on a GP-evolved combination of hyper-features
- Integrated vision of dimensionality reduction in data mining data sets across three types of problems: classification, association and segmentation
- N. Magessi (2018). O Risco e a sua Perceção: Factos e Razões. PhD thesis, Universidade de Lisboa. Supervision: L. Antunes

Figure 1:
ASSISIbf demonstrator: Interspecies consensus (1 bit) between bees and fish

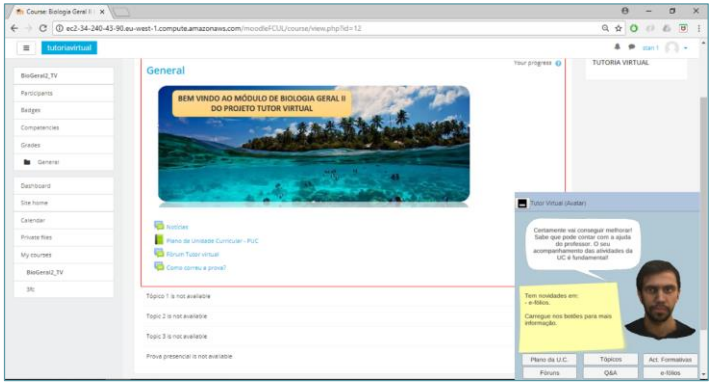


Figure 2:
An anthropomorphic virtual tutor (avatar) implemented in the Moodle environment of the Universidade Aberta (provides e-learning teaching). This virtual tutor provides synchronous support to the student and creates an empathic relationship that potentiates his/her positive academic results. The speech and facial expression of the tutor are coherent with the student's current attendance and grades in the course unit.

Group Members

GL: Luís Correia

PI's:


Ana Paula Cláudio


Hélder Coelho


Luís Antunes


Beatriz Carmo


Luís Cavique


Paulo Trigo


Sara Silva


Paulo Urbano


Graça Gaspar

Post Docs: Rob Mills| Pedro Mariano| Hugo Martiniano (jointly with BTR)

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

Key Funded Projects

VASelfCare- Assistente virtual para facilitar o autocuidado de pessoas mais velhas com diabetes tipo 2. Start: Jan 2018, duration 18 months. Proj. nr. 024250, 02/SAICT/2016, co-funded by: FCT, Lisboa 2020, Alentejo 2020, Portugal 2020. Total amount for BioISI: 58 k€. 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

Selected Publications

1. Silva, S., Vanneschi, L., Cabral, A.I.R., Vasconcelos, M.J. A semi-supervised Genetic Programming method for dealing with noisy labels and hidden overfitting. Swarm and evolutionary computation, 39, pp. 323-338, 2018

2. Cavique, L., Mendes, A.B., Martiniano, H.F.M.C., Correia,L. A biobjective feature selection algorithm for large omics datasets. Expert Systems, 35(4):e12301, 2018

3. Carvalho, A., Neto, J.P., Santos, C. Ordinal sums of impartial games. Discrete Applied Mathematics, vol.243, pp.39-45, 2018

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.

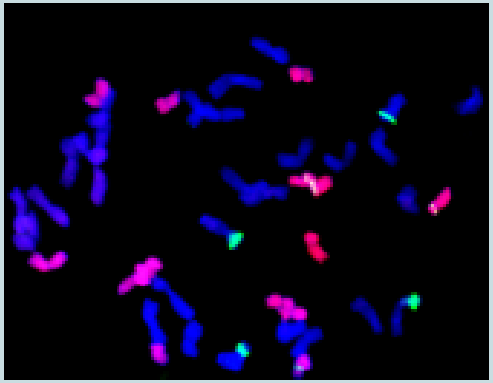
Main Goals:

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



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 techniques.

Major Projects:

- High-throughput screening of genes and compounds regulating the secretory traffic of the CFTR and ANO1 proteins.
- Screening of novel drug leads for cystic fibrosis from Portuguese natural products.
- 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 patterns, 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.

Publications:

- Oncotarget. 9: 28586-28598 - The histone deacetylase inhibitor panobinostat is a a promising therapeutic agent for treatment of canine diffuse large B-cell lymphoma (Dias et al.)
- Biochim Biophys Acta Mol Cell Res. 865(2): 421-431 - A novel microscopy-based assay identifies extended synaptotagmin-1 (ESYT1) as a positive regulator of anoctamin 1 traffic (Lérias, Pinto et al.)
- J Cyst Fibros. S1569-1993(18)30643-X - R560S: A class II CFTR mutation that is not rescued by current modulators (Awatade et al.)

Technicians: Luís Marques | Telmo Nunes | Aires Duarte

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 Infrastruture 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;

Technician: Mariana Nascimento

Dissemination & Training:

1. Host for BioISI Research Seminars dedicated to Nanopore based Sequencing Technologies;
2. Engagement in international training programs (EU - Innovative Training Networks; Erasmus exchange programs);
3. Participation in “Young Creators 2018” promoted by the Lisbon City Council – April 2-6, Lisbon, Portugal
4. Participation in the “Workshop in Innovation in Genomic Technologies" – June 29th, UTAD, Vila Real, Portugal.
5. Participation in the SUMMER INNOVATION CAMPUS with the Stand “BioISI Genomics – Bringing knowledge to you: anyTime anywhere” and LifeDemo in the Summer Innovation Market – September 26th and 27th, UTAD, Vila Real.
6. Participation in several Masters and PhD programs at FCUL.

Goals for 2019:

1. Consolidation of the facility infrastructure, equipment and human resources;
2. Establishment of external partnerships and protocols for service exchange with institutional facilities offering supplementary services and technologies;
3. External dissemination targeting potential industry partners;
4. Creation of an external facility website and intranet system for service and data management;

Major Projects:

- MicroYard - Understanding the microbial community effects in a phytochemical-free vineyard by the characterization and identification of Portuguese vine microbial terroirs using native long reads metagenomics (in collaboration with Esporão S.A.).
- CMRoot - Identification of microbial paths of transmission from soil-to-root. Characterization of soil and root microbiome of centennial vineyards at Cyprus (Cyprus University of Technology).
- MetaOcean – Determination of the Whole Metagenome from oceanic sample recovered from Antarctica (in collaboration with MARE-FCUL).
- UnCenter - Provide novel insights into the structure and transcriptional activity of centromeric satDNA by developing methods for Nanopore-based targeted sequencing of ultra-long reads from native DNA, captured, laser microdissected and sorted chromosomes (in collaboration with UTAD and University of Cambridge).
- MTTPlus - Metataxonomics based on NL1-NL4 locus and 16S rRNA operon by long read multi-targeted sequencing (in collaboration with BioTask, Biotecnologia Lda).

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.

Proteomics

The recently created Proteomics facility:

Will deliver information on proteins molecular weight and identification through mass spectrometry determination and data-based analysis

Will allow BioISI to be in the top knowledge of cell proteome changes in health and diseases

Will allow the identification of cell-drug targets

Computing

In terms of computing and data storage facilities, BioISI has currently installed 408 cores, 1144 GB RAM, and 88 TB storage in equipment concentrated essentially in 4 groups: GER, PBS, M&B, and FunGP.

We have been following an approach of exploiting common facilities available nationwide and at European level, INCD and EGI, respectively. The former is currently operational with an availability for BioISI of 200 virtual CPUs, 870 GB RAM and 5 TB storage.

Infrastructures

Plant House

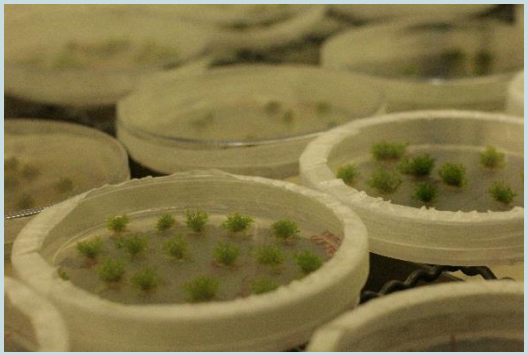
The Plant House Facility has specialized plant growth chambers and provides support to research groups.

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.

BioSys-PhD

BioISI Post-Doc Programme

BioISI has the ideal training environment for post-docs to further develop as scientists. BioISI post-docs find a supportive and mentoring faculty, have access to facilities, and are part of a lively scientific community. BioISI Post-Doc programme included four 2yr fellowships to enrol into activities related with BioISI Thematic Lines:

Hugo Martiniano - Development of computational pipelines combining machine learning/data mining and systems biology methods for multilevel data analysis, Supervisors: Luís Correia, Astrid Vicente

Ana Carapeto - Exploring protein-protein interactions with Atomic Force Microscopy

Jules Morand – The physical basis of Dialysis Related Amyloidosis, Supervisors: Patrícia Faísca, Mário Rodrigues

BioISI Post-DOC

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 25 research seminars and several workshops such as:

-Workshop on Integrative Approaches in Neurodegeneration, 21-23 June 2018, Lisboa

-HTM2018 | Hands-On Workshop On Fluorescence And High-Throughput Microscopy, 9-13 July 2018, Lisboa

-Epithelial Systems: Physiology and Pathophysiology Workshop, 23 – 27 July 2018, Lisboa

BioSYS 1- Enrolled Students

- **Ana Margarida Matos** - siRNA screen for modulators of CFTR surface retention, Supervisor - Paulo Matos (FCUL), Co-supervisor - Rainer Pepperkok (EMBL) *
- **Cibelle Costa** - System Biology Approach for Cardiovascular Medicine, Supervisor - Mafalda Bourbon (FCUL), Co-supervisor - Marília Antunes (FCUL)
- **Cláudia Loureiro** - Regulation of epithelial chloride transport by phospho-tyrosine-initiated protein networks, Supervisor - Peter Jordan (FCUL), Co-supervisor - Luka Clarke (FCUL)
- **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) *
- **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 - Rainer Schreiber (Univ Regensburg), Co-supervisor - Margarida Amaral (FCUL) *
- **Muhammad Asif** - System medicine approach to improve diagnosis and prognosis in Autism Spectrum Disorders (ASD), based on extensive genomic, biochemical and clinical data, Supervisor - Astride Vicente (FCUL), Co-supervisor - Francisco Couto (FCUL)
- **Nikhil Awatade** - CFTR2Drugs - Using a Systems Approach to Identify the Mechanism of Action of Correctors, Supervisor - Margarida Amaral (FCUL), Co-supervisor - Rainer Pepperkok (EMBL) *
- **Paulo Costa** - Functional networks in which the DIS3 and DIS3L1 exosome subunits participate and their relevance in colorectal cancer, Supervisor - Luísa Romão (FCUL), Co-supervisor - Margarida Gama-Carvalho (FCUL)
- **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 ER quality control: Dissecting protein networks to identify drug targets for Cystic Fibrosis, Supervisor - Carlos Farinha (FCUL), Co-supervisor - André Falcão (FCUL)

*International / mixed scholarships

BioSYS 2- Enrolled Students

- **Ana Marques** - Neuropsychiatric disease clustering in families with Autism Spectrum Disorder (ASD): genetic, epigenetic and environmental issues., Supervisor - Astride 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)
- **Andreia Henriques** - Regulation of glucose uptake in mammalian cells by protein phosphorylation networks, Supervisor - Peter Jordan, Co-supr - Luka Clarke (FCUL)
- **Joana Silva** - Analysis of the translatome by ribosome profiling in colorectal cancer, Supervisor - Luísa Romão (FCUL), Co-supervisor - Augusto Luchessi (Univ. de Campinas) *
- **João Santos** - Nucleotide signalling in the regulation of CFTR trafficking and function, Supervisor - Carlos Farinha (FCUL), Co-supervisor - Manuela Zaccolo (Univ. de Oxford) *
- **Luís Sousa** - Role of CFTR in epithelial differentiation by functional genomics, Supervisor - Margarida Amaral (FCUL), Co-supervisor - Marc Chanson (Univ Geneva) *
- **Niccolò Rossi** - IdentifIcation and characterization of the cause of lipid metabolism disruption in patients with severe and unexplained familial dyslipidaemia, Supervisor - Mafalda Bourbon (FCUL), Co-supervisor - Cesar Martin (Univ País Vasco) *
- **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** - The aggregation mechanism of β2-microglobulin in amyloid disease investigated through molecular simulations, Supervisor - Patrícia Faísca (FCUL), Co-supervisor - Eugene Shakhnovich (Univ Harvard) *
- **Rute Teixeira** - The role of sorting nexins and binding phosphoinositides in metabolite (ex)changes in tip growing cells., Supervisor - Rui Malhó (FCUL), Co-supervisor - Patrick Moreau (Univ Bordeaux) *
- **Samina Kausar** - An integrated systems approach to identify receptor and ion-channel binding networks in the Human brain, Supervisor - André Falcão (FCUL), Co-supervisor - Rita Mendes (Fac Farmácia - ULisboa)

BioSYS 3- Enrolled Students

- **DanielCruz** - LMTK2 signalling in cystic fibrosis: an interactomics approach, Supervisor - Carlos Farinha (FCUL), Co-supervisor - Agnieszka Swiatecka-Urban (UPitt) *
- **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 - Astride 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)

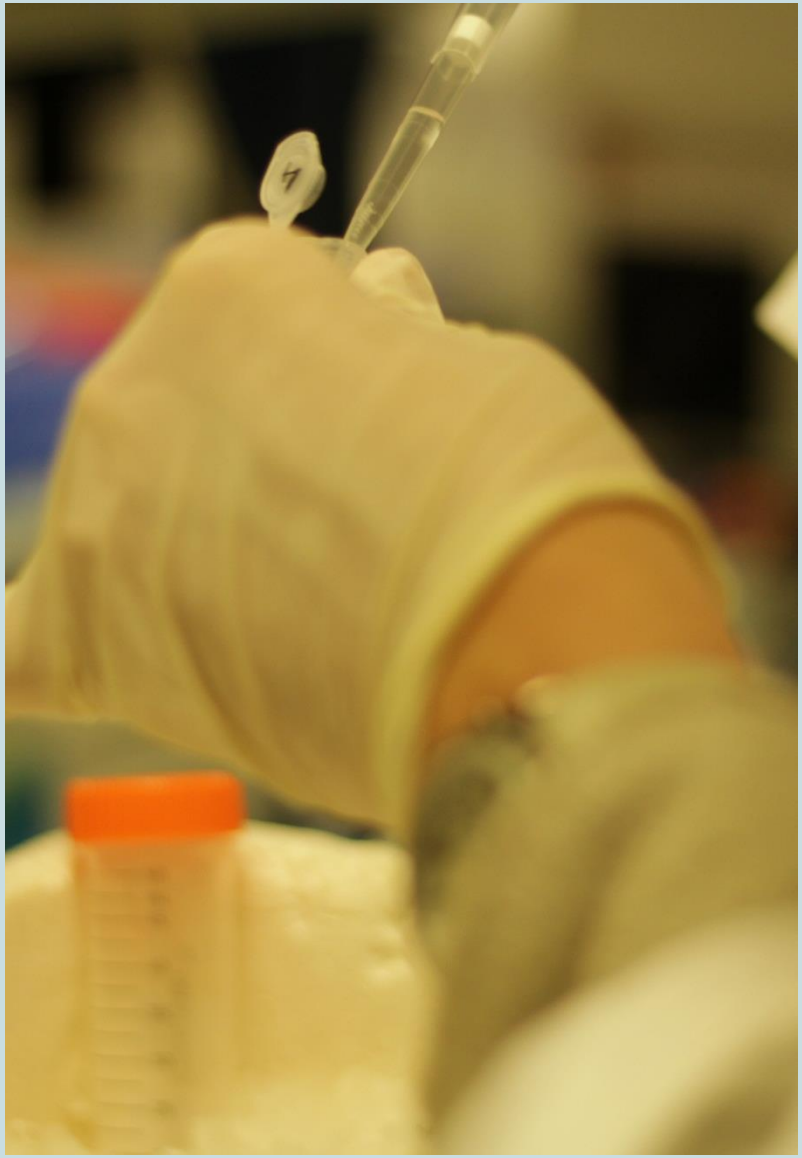
BioSYS 4- Enrolled Students

- **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 Moura 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 M Farinha (FCUL), Co-supervisor - Patrick T Harrison *
- **Mariana Pinhão** - What are the determinants of human genetic individuality?, Supervisor - Francisco Couto (FCUL), Co-supervisor - Margarida Gama-Carvalho (FCUL)
- **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/FCUL
- **Leyre Pernaute Lau** – Resistance to antimalarials - a pharmacogenomics approach for both parasite and human host, Supervisor - Jose 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, INSARJ and 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/FCUL and André Falcão, DI/FCUL
- **Tânia Marques** - An integrative approach to tissue-specific effects of microRNA regulatory networks, Supervisor - Margarida Gama-Carvalho, BioISI, Co-supervisor - Nham Tran, UTS
- **Tiago Pedreira** - Cystic Fibrosis Therapies through Non-CFTR Anion Channels/Transporters, Supervisor - Margarida Amaral, BioISI, Co-supervisor - Karl Kunzelmann, Uregensburg, Germany
- **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 Post-Doc programme

Ana Carapeto

Mário Rodrigues | Cláudio Gomes | Carlos Farinha

Biophysics

Atomic force microscopy (AFM) is used to detect interactions of a ligand attached to the measuring tip with proteins present in cells, fixed to the surface. This setup is employed to the characterization of two distinct biological systems: a) CFTR interactions, in which we move from antibodypeptide antigen to antibody-CFTR domain and ultimately to specific interactions between CFTR and other proteins; b) S100 amyloid interactions.

Additionally, AFM allows to obtain mechanical properties of cells and, in that context, we have studied the elasticity of human bronchial epithelial cells in interaction with drugs.

Major Achievements:

- Development of AFM tips functionalization protocol
- Study of mechanical properties in human bronchial epithelial cells
- High-resolution imaging of proteins

BioISI Projects involved:

Measuring protein interactions – insights into Cystic Fibrosis Atomic Force Microscopy approaches to study protein

selfassemblies and interactions

Single molecule approaches to study S100B protein interactions

with Aβ amyloid fibrils

Hugo Martiniano

Luís Correia | Astrid Vicente

Bioinformatics & Modelling | Biomedicine

Development and application of combined data mining/machine learning and systems biology approaches to multilevel data (demographic, life style, clinical, physiological, genetic) from cohorts of Autism Spectrum Disorder (ASD) patients, with the objective of understanding the biological processes underlying this pathology, predicting the effects of molecular perturbations and ultimately developing improved diagnostic tools and more efficient and personalized therapeutic targets.

Major Achievements:

- Development of an analysis pipeline for large-scale exome sequencing data
- Development of machine learning models for ASD gene risk prediction.

BioISI Projects involved:

MedPersyst

Jules Morand

Patricia Faísca | Mário Rodrigues

Biophysics

By using discrete molecular dynamics (DMD) simulations, we study folding transition and early aggregation stage of protein be-ta-2-microglobulin (b2m), associated with dialysis related amyloi-dosis. On the folding pathway towards the native conformation, the protein populates intermediate states, which may trigger the amyloid cascade. The population is modulated either by intrinsic or external factors.

In vivo, b2m aggregates in a confined collagen environment. To mimic this effect we modified the DMD code, introducing a box with reflective walls, and study its effect on the folding transi-tion.

We also investigate the role of the disulphide bond in native state's stability. This bond, between residues 25 and 80, is bro-ken at low pH, suggesting the aggregation prone intermediate states.

Major Achievements

- Learn the DMD simulation code
- Learn replica-exchange molecular dynamics simulations
- Learn the weighted histogram analysis method to compute free energy profiles and surfaces
- Conduct several simulations for the different scenarios

BioISI Projects involved: Condensed matter physics, bioinformatics and modelling and biomedicine

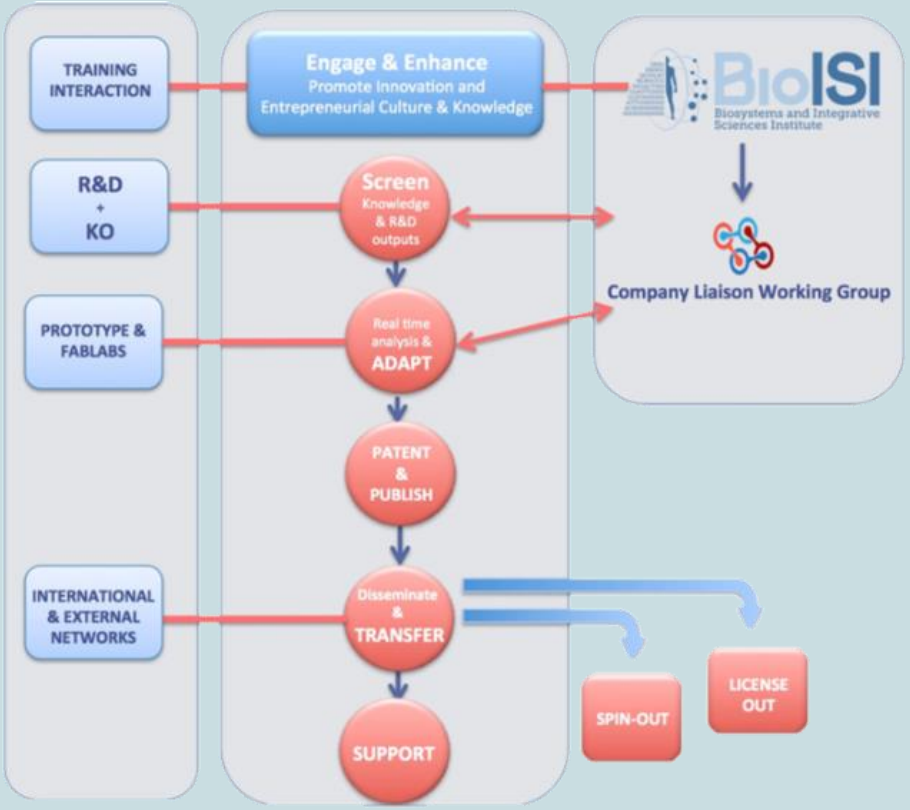
BioISI - KTT
Knowledge & Technology Transfer

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.



Communication and Outreach Workgroup

The main aim of the Communication and Outreach Workgroup is the promotion of BioISI's aims, vision and research activities to all stakeholders, making them aware of the value of our work and achievements for society and human well-being, while contributing towards an increased scientific education and the dissemination of scientific knowledge.

Major 2018 Achievements

- Launch of BioISI Newsletter and BioISI Institutional video

- Strong presence in the media: 14 interviews + 4 opinion articles; 58 minutes on TV

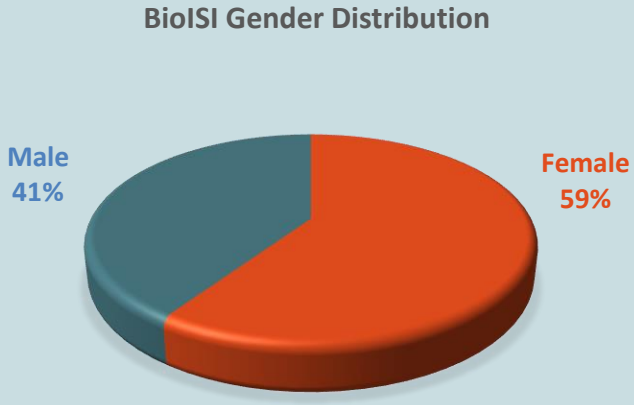
- Organization of the 4th edition of the event "Wine with Science"

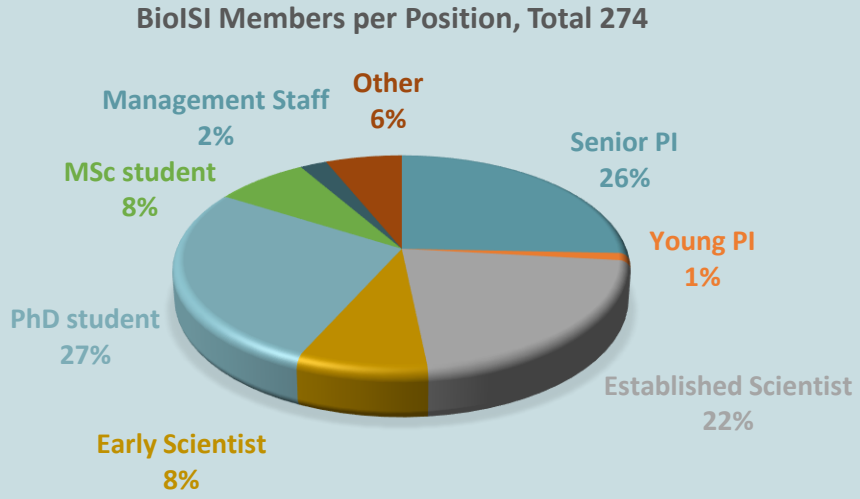
- Participation in Outreach events: European Researcher´s Night and JobShop Ciências

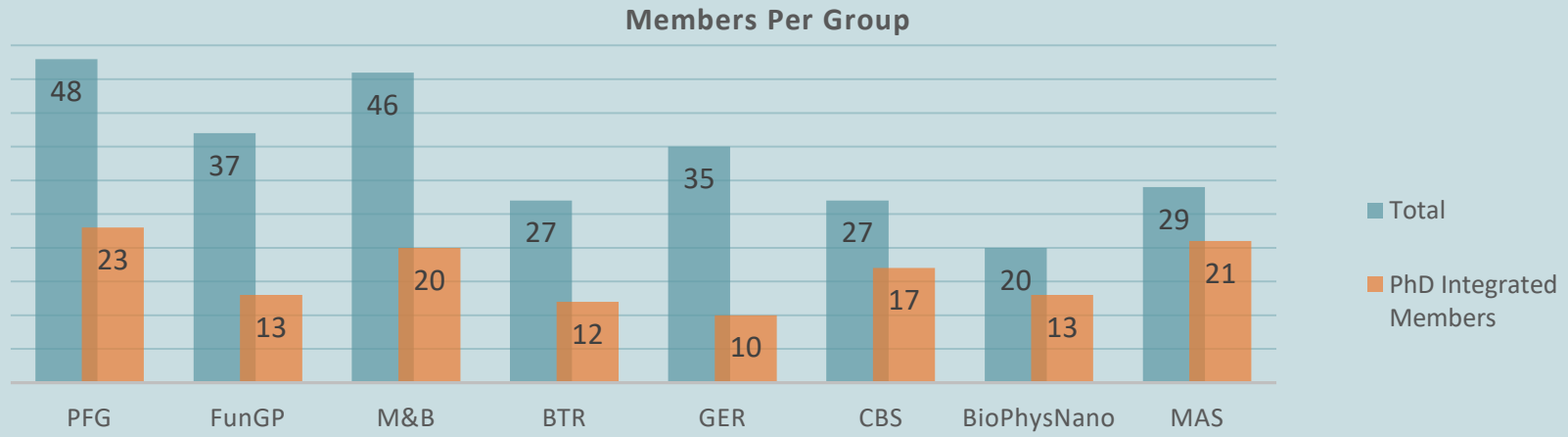
Coordinator: Margarida Gama-Carvalho
Team: Andreia Reis and Filipa Tomé

BioISI in Numbers

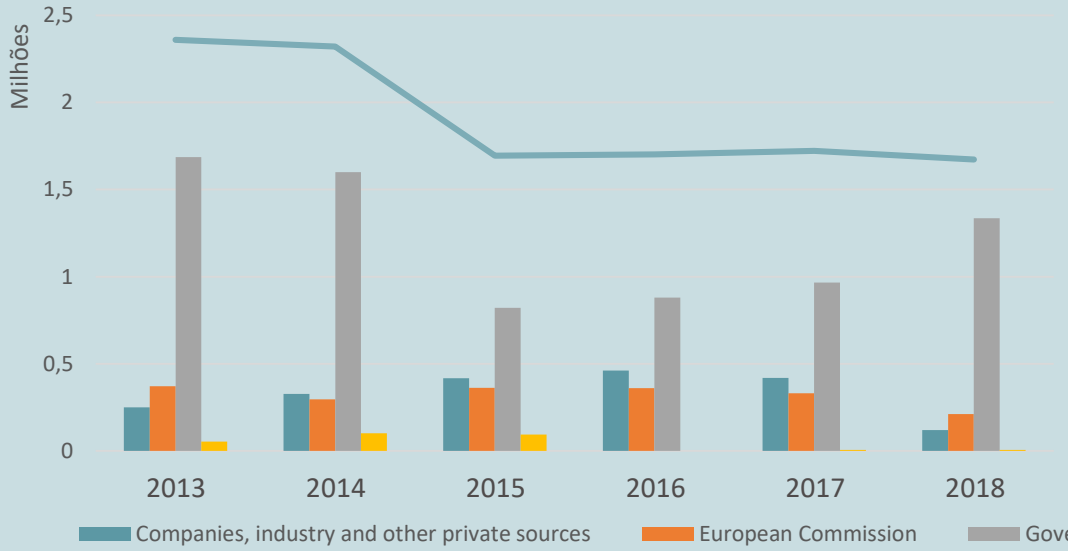
Members:

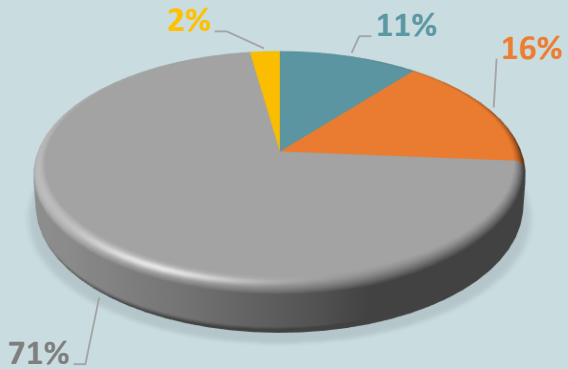




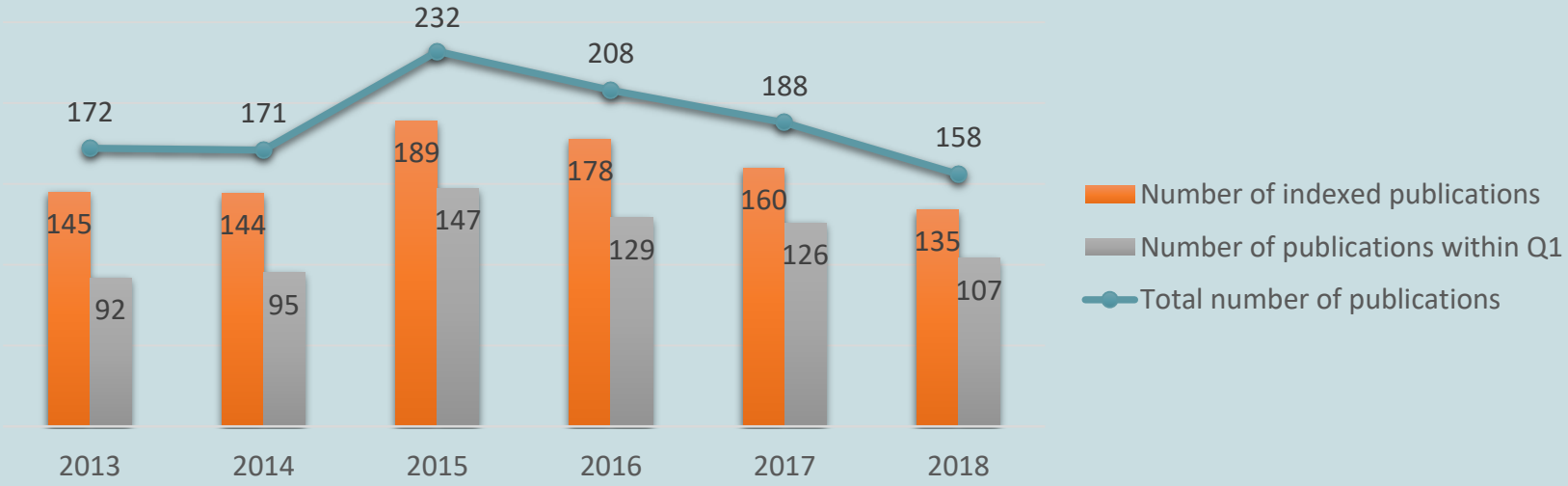


Project Funding 2013-2018





Bibliometrics



Publications

PFG

Dias JNR, Aguiar SI, Pereira DM, André AS, Gano L, Correia JDG, Carrapiço B, Rütgen B, Malhó R, Peleteiro C, Goncalves J, Rodrigues CMP, Gil S, Tavares L, Aires-da-Silva F. (2018) The histone deacetylase inhibitor panobinostat is a a promising therapeutic agent for treatment of canine diffuse large B-cell lymphoma. ONCOTARGET, 9(47), 28586-28598. 10.18632/oncotarget.25580

Sebastiana M, da Silva AB, Matos AR, Alcântara A, Silvestre S, Malhó R (2018) Ectomycorrhizal inoculation with Pisolithus tinctorius reduces stress induced by drought in cork oak. MYCORRHIZA, 28(3), 247-258. 10.1007/s00572-018-0823-2

Laureano G, Figueiredo J, Cavaco AR, Duarte B, Caçador I, Malhó R, Sousa Silva M, Matos AR, Figueiredo A. (2018) The interplay between membrane lipids and phospholipase A family members in grapevine resistance against Plasmopara viticola. SCIENTIFIC REPORTS, 8(1), 14538. 10.1038/s41598-018-32559-z

Malhó R (2018) Expand, colonize and consolidate. Nature Plants, 4(11), 861–862. 10.1038/s41477-018-0297-4

Barrias S., Fernandes J.R., Eiras-Dias J.E., Brazão J., Martins-Lopes P (2019) Label free DNA-based Optical Biosensor as a potential system for Wine Authenticity. FOOD CHEMISTRY, 270, 299-304. 10.1016/j.foodchem.2018.07.058

Gomes S., Breia R., Carvalho T., Carnide V., Martins-Lopes P. (2018) Microsatellite High-Resolution Melting (SSR-HRM) to Track Olive Genotypes: From Field to Olive Oil. Journal of Food Science, 83(10), 2415-2423. 10.1111/1750-3841.14333

Garcia-Oliveira A.L., Benito C., Guedes-Pinto H., Martins-Lopes P. (2018) Molecular cloning of TaMATE2 homoeologues potentially related to aluminium tolerance in bread wheat (Triticum aestivum L.). Plant Biology, 20(5), 817-824. 10.1111/plb.12864

Gomes S., Castro C., Barrias S., Pereira L., Jorge P., Fernandes J.R., Martins-Lopes P. (2018) Alternative SNP detection platforms, HRM and biosensors, for varietal identification in Vitis vinifera L. using F3H and LDOX genes. SCIENTIFIC REPORTS, 8(1), 5850. 10.1038/s41598-018-24158-9

Pereira L., Gomes, S., Barrias S., Fernandes, J.R., Martins-Lopes, P. (2018) Applying high-resolution melting (HRM) technology to olive oil and wine authenticity. FOOD RESEARCH INTERNATIONAL, 103, 170-181. 10.1016/j.foodres.2017.10.026

Castro C, Carvalho A, Pavia I, Leal F, Moutinho-Pereira J, Lima-Brito J (2018) Nucleolar activity and physical location of ribosomal DNA loci in Vitis vinifera L. by silver staining and sequential FISH. SCIENTIA HORTICULTURAE, 232, 57-62. 10.1016/j.scienta.2017.12.064

Dias A, Gaspar MJ, Carvalho A, Pires J, Brito JL, Silva ME, Louzada JL (2018) Within and between-tree variation of wood density components in Pinus nigra at six sites in Portugal. Annals of Forest Science, 75, 58. 10.1007/s13595-018-0734-6

Carvalho A, Leal F, Matos M, Lima-Brito J (2018) Effects of heat stress in the leaf mitotic cell cycle and chromosomes of four wine-producing grapevine varieties. PROTOPLASMA, 255(6), 1725-1740. 10.1007/s00709-018-1267-4

Reis S, Pavia I, Carvalho A, Moutinho-Pereira J, Correia C, Lima-Brito J (2018) Fungal penetration associated with recognition, signaling and defence-related genes and peroxidase activity during the resistance response of coffee to Colletotrichum kahawae. PROTOPLASMA, 105, 119-127. 10.1016/j.pmpp.2017.12.005

Coutinho J, Carvalho A, Martín A, Lima-Brito J (2018) Molecular characterization of Fagaceae species using inter-primer binding site (iPBS) markers. Molecular Biology Reports, 45, 133-142. 10.1007/s11033-018-4146-3

Teixeira, R.T., Fortes, A.M., Bai, H., Pinheiro, C., Pereira, H. (2018) Transcriptional profiling of cork oak phellogenic cells isolated by laser microdissection. PLANTA, 247(2), 317-338. 10.1007/s00425-017-2786-5

Meireles B, Usié A, Barbosa P, Fortes AM, Folgado A, Chaves I, Carrasquinho I, Costa RL, Gonçalves S, Teixeira RT, Ramos AM, Nóbrega F. (2018) Characterization of the cork formation and production transcriptome in Quercus cerris × suber hybrids. Physiology and Molecular Biology of Plants, 24(4), 535-549. 10.1007/s12298-018-0526-3

Ramos AM, Usié A, Barbosa P, Barros PM, Capote T, Chaves I, Simões F, Abreu I, Carrasquinho I, Faro C, Guimarães JB, Mendonça D, Nóbrega F, Rodrigues L, Saibo NJM, Varela MC, Egas C, Matos J, Miguel CM, Oliveira MM, Ricardo CP, Gonçalves S. (2018) The draft genome sequence of cork oak. Scientific Data, 5, 180069. 10.1038/sdata.2018.69

Martins M, Silva A, Costa MH, Miguel C, Costa PM. (2018) Co-exposure to environmental carcinogens in vivo induces neoplasia-related hallmarks in low-genotoxicity events, even after removal of insult. SCIENTIFIC REPORTS, 8(1), 3649. 10.1038/s41598-018-21975-w

Rodrigues AS, De Vega JJ, Miguel CM. (2018) Comprehensive assembly and analysis of the transcriptome of maritime pine developing embryos. BMC PLANT BIOLOGY, 18(1), 379. 10.1186/s12870-018-1564-2

Adessi, A., Cruz de Carvalho, R., De Phillippis, R., Branquinho, C., Marques da Silva, J. (2018) Microbial extracellular polymeric substances improve water retention in dryland biological soil crusts. Soil Biology and Biochemistry, 116, 67-69. 10.1016/j.soilbio.2017.10.002

D. Wetzel-Gastal F. Feitor S. van HartenM. SebastianaL. M. R. SousaL. A. Cardoso (2018) A genomic study on mammary gland acclimatization to tropical environment in the Holstein cattle. Tropical Animal Health and Production, 50(1), 187-195. 10.1007/s11250-017-1420-7

Félix LM, Vidal AM, Serafim C, Valentim AM, Antunes LM, Monteiro SM, Matos M, Coimbra AM. (2018) Ketamine induction of p53-dependent apoptosis and oxidative stress in zebrafish (Danio rerio) embryos. CHEMOSPHERE, 201, 730-739. 10.1016/j.chemosphere.2018.03.049

Félix LM, Luzio A, Themudo M, Antunes L, Matos M, Coimbra AM, Valentim AM. (2018) MS-222 short exposure induces developmental and behavioural alterations in zebrafish embryos. Reproductive Toxicology, 81, 122-131. 10.1016/j.reprotox.2018.07.086

Santos, E, Benito, C, Silva-Navas, J, Gallego, FJ, Figueiras, AM, Pinto-Carnide, O, Matos, M (2018) Characterization, genetic diversity, phylogenetic relationships, and expression of the aluminum tolerance MATE1 gene in Secale species. BIOLOGIA PLANTARUM, 62(1), 109-120. 10.1007/s10535-017-0749-0

Vidigal P, Duarte B, Cavaco AR, Caçador I, Figueiredo A, Matos AR, Viegas W, Monteiro F. (2018) Preliminary diversity assessment of an undervalued tropical bean (Lablab purpureus (L.) Sweet) through fatty acid profiling. PLANT PHYSIOLOGY AND BIOCHEMISTRY, 132, 508-514. 51410.1016/j.plaphy.2018.10.001

Diniz, I., Azinheira, H., Figueiredo, A., Guichuru, E., Oliveira, H., Guerra-Guimarães, L., Silva, M.C. (2019) Fungal penetration associated with recognition, signaling and defence-related genes and peroxidase activity during the resistance response of coffee to Colletotrichum kahawae. Physiological and Molecular Plant Pathology, 105, 119-127. 10.1016/j.pmpp.2017.12.005

Figueiredo J, Sousa Silva M, Figueiredo A. (2018) Subtilisin-like proteases in plant defence: the past, the present and beyond. Molecular Plant Pathology, 19(4), 1017-1028. 10.1111/mpp.12567

Reis F, Valdiviesso T, Varela C, Tavares RM, Baptista P, Lino-Neto T (2018) Ectomycorrhizal fungal diversity and community structure associated with cork oak in different landscapes. MYCORRHIZA, 28(4), 357-368. 10.1007/s00572-018-0832-1

Gomes T, Pereira JA, Benhadi J, Lino-Neto T, Baptista P. (2018) Endophytic and epiphytic phyllosphere fungal communities are shaped by different environmental factors in a Mediterranean ecosystem. MICROBIAL ECOLOGY, 76(3), 668-679. 10.1007/s00248-018-1161-9

Raimundo, J., Sobral, R., Laranjeira, S. Costa, M.M.R. (2018) Successive domain rearrangements underlie the evolution of a Regulatory module controlled by a small interfering peptide. Molecular Biology and Evolution, 35(12), 2873-2885. 10.1093/molbev/msy178

Castro PH, Santos MA, Freitas S, Cana-Quijada P, Lourenço T, Rodrigues MAA, Fonseca F, Albert JR, Azevedo JE, Tavares RM, Castillo AGG, Bejarano ER, Azevedo H. (2018) Arabidopsis thaliana SPF1 and SPF2 are nuclear-located ULP2-like SUMO proteases that act downstream of SIZ1 in plant development. JOURNAL OF EXPERIMENTAL BOTANY, 69(19), 4633-4649. 10.1093/jxb/ery265

Coito, J.L., Silva, H.G., Ramos, M.J.N., Montez, M., Cunha, J.M.M., Amâncio, S.,Costa, M.M.R., Rocheta, R. 2018. (2018) Vitis Flower Sex Specification Acts Downstream and Independently of the ABCDE Model Genes. FRONTIERS IN PLANT SCIENCE, 9, 1029. 10.3389/fpls.2018.01029

Carvalho M, Matos M, Castro I, Monteiro E, Rosa E, Lino-Neto T, Carnide V. (2019) Screening of worldwide cowpea collection to drought tolerant at a germination stage. Scientia Horticulturae, 247, 107-115. 10.1016/j.scienta.2018.11.082

Albertini, A., Santos, S.A.P., Martins, F., Pereira, J.A., Lino-Neto, T., Petacchi, R., Baptista, P. (2018) Detection of Bactrocera oleae (Diptera: Tephritidae) DNA in the gut of the soil species Pseudoophonus rufipes (Coleoptera: Carabidae). Spanish Journal of Agricultural Research, 16 (3), e1007. 10.5424/sjar/2018163-12860

Santos E, Barros A, Lino-Neto T, Barros A, Marques G. (2018) Phytochemicals properties and antioxidant activities of some accessions of Phaseolus vulgaris L. Free Radical Biology and Medicine. Medicine, 120(1), s156-7. 10.1016/j.freeradbiomed.2018.04.516

FunGP

Sara Canato, João D. Santos, Ana S. Carvalho, Kerman Aloria, Margarida D. Amaral, Rune Matthiesen, André O Falcao, Carlos M. Farinha (2018) Proteomic interaction profiling reveals KIFC1 as a factor involved in early targeting of F508del-CFTR to degradation. Cellular and Molecular Life Sciences, 75: 4495-4509.

Ferreira VFC, Oliveira BL, Santos JD, Correia JDG, Farinha CM, Mendes F (2018) Targeting of the cystic fibrosis transmembrane conductance regulator (CFTR) protein with a technetium-99m imaging probe. ChemMedChem, 13, 1469-1478. 10.1002/cmdc.201800187

Liu J, Bihler H, Farinha CM, Awatade NT, Romão AM, Mercadante D, Cheng Y, Musisi I, Jantarajit W, Wang Y, Cai Z, Amaral MD, Mense M, Sheppard DN (2018) Partial rescue of F508del-CFTR channel gating with modest improvement of protein processing, but not stability by a dual-acting small molecule. British Journal of Pharmacology, 175, 1017-1038. 10.1111/bph.14141

Farinha CM, Matos P (2018) Rab GTPases regulate the trafficking of channels and transporters - a focus on cystic fibrosis. Small GTPases, 9, 136-144. 10.1080/21541248.2017.1317700

Farinha CM, Miller E, McCarty N (2018) Protein and lipid interactions – modulating CFTR trafficking and rescue. Journal of Cystic Fibrosis, 17, S9-S13. 10.1016/j.jcf.2017.08.014

Nikhil T Awatade, Sofia Ramalho, Iris AL Silva, Verónica Felício, Hugo M Botelho, Eyleen de Poel, Annelotte Vonk, Jeffrey M Beekman, Carlos M Farinha, Margarida D Amaral (2018) R560S: a class II CFTR mutation that is not rescued by current modulators. Journal of Cystic Fibrosis, e-pub ahead of print. 10.1016/j.jcf.2018.07.001

Matos AM, Matos P (2018) Combination therapy in Phe508del CFTR: how many will be enough?. Journal of Lung Health and Diseases, 2, 43359.

Matos AM, Gomes-Duarte A, Faria M, Barros P, Jordan P, Amaral MD, Matos P (2018) Prolonged Co-Treatment with HGF Sustains Epithelial Integrity and Improves Pharmacological Rescue of Phe508del-CFTR. SCIENTIFIC REPORTS, 8, 13026. 10.1038/s41598-018-31514-2

Joana S. Cristóvão, Vanessa K. Morris, Isabel Cardoso, Sónia S. Leal, Javier Martínez, Hugo M. Botelho, Christoph Göbl, Rodrigo David, Katrin Kierdorf, Mobina Alemi, Tobias Madl, Günter Fritz, Bernd Reif, Cláudio M. Gomes (2018) The neuronal S100B protein is a calcium-tuned suppressor of amyloid-β aggregation. Science Advances, Jun 29;4(6):eaaq1702. 10.1126/sciadv.aaq1702. eCollection 2018 Jun

Simone Hagmeyer, Joana S Cristóvão, John J Mulvihill, Tobias Maria Boeckers, Cláudio M. Gomes, Andreas Martin Grabrucker (2018) Zinc binding to S100B affords regulation of trace metal homeostasis and excitotoxicity in the brain. Frontiers in Molecular Neuroscience, 10, 456. 10.3389/fnmol.2017.00456. eCollection 2017.

Santos G, Barateiro A, Gomes CM, Brites D, Fernandes A (2018) Impaired oligodendrogenesis and myelination by elevated S100B levels during neurodevelopment. Neuropharmacology, 129, 69-83. 10.1016/j.neuropharm.2017.11.002

Ribeiro, J.V.; Lucas, T.G.; Bross, P.; Gomes, C.M.; Henriques, B.J. (2018) Structural and functional effects of clinical missense mutations on glutaryl-CoA dehydrogenase. Free Radical Biology and Medicine, 120, S144-S144 P327. 10.1016/j.freeradbiomed.2018.04.474

Ferreira, J.F., Gomes, C.M., Henriques B.J. (2018) Implication of post-translational modifications on ETF, a structural and functional approach. Free Radical Biology and Medicine, 120, S144-S144 P328. 10.1016/j.freeradbiomed.2018.04.475

Kum CK, Thorburn D, Ghilagaber G, Björkman B, Gil JP. (2018) Effects of some Biological Covariates on the Probability of First Recurrence of Malaria following Treatment with Artemisinin Combination Therapy. Int. J. Stats. Med. Res, 7, 43109. 10.6000/1929-6029.2018.07.01.1

Sagara I, Beavogui AHA, Zongo I, Soulama I, Borghini-Fuhrer I, Fofana B, Diakite H, Togo AH, Koumare S, Keita M, Camara D, Somé AF, Coulibaly AS, Traore OB, Dama S, Goita S, Djimde M, Bamadio A, Dara N., Maiga H, Sidibe B, Dao F, Coulibaly M, Alhousseini ML, Niangaly H, Sangare B, Diarra M, Coumare, S, Moïse J T, Kabore MJT, Ouattara SM, Barry A, Kargougou D, Diarra A, Henry N, Soré H, Bougouma EC, Thera I, Compaore YD, Sutherland CJ, Sylla, MM Nikiema F, Diallo MS, Dicko A, Picot S, Borrmann S, Duparc S, Miller RM, Doumbo OK, Shin J, Gil JP, Bjorkman A, Ouedraogo JB, Sirima SB, Djimdé AA (The West African Network for Clinical Trials of Antimalarial Drugs (WANECAM). (2018) Pyronaridine–artesunate or dihydroartemisinin–piperaquine versus current rst-line therapies for repeated treatment of uncomplicated malaria: a randomised, multicentre, open-label, longitudinal, controlled, phase 3b/4 trial. The Lancet, 391, 1378-1390. 10.1016/S0140-6736(18)30291-5

Inoue J, Silva M, Sagara I, Mårtensson A, Björkman A, Veiga MI, Ferreira E, Djimde A, Gil JP. (2018) Plasmodium falciparum plasmepsin 2 (pfpm2) duplications are present in West Africa. Emerging Infectious Diseases, 24, e-pub ahead of print. 10.3201/eid2408.180370

Uliyakina I, Da Paula AC, Afonso S, Lobo MJ, Felício V, Botelho HM, Farinha CM, Amaral MD (2018) Full Rescue of F508del-CFTR Processing and Function by CFTR Modulators can be Achieved by Removal of Two Unique Regulatory Regions. bioRxiv.

Nagy B Jr, Bene Z, Fejes Z, Heltshe SL, Reid D, Ronan NJ, McCarthy Y, Smith D, Nagy A, Joseloff E, Balla G, Kappelmayer J, Macek M Jr, Bell SC, Plant BJ, Amaral MD, Balogh I (2018) Human epididymis protein 4 (HE4) levels inversely correlate with lung function improvement (delta FEV1) in cystic fibrosis patients receiving ivacaftor treatment. Journal of Cystic Fibrosis.

Marcão A, Barreto C, Pereira L, Vaz L, Cavaco J, Casimiro A, Felix M, Silva T, Barbosa T, Freitas AC, Nunes S, Felicio V, Lopes L, Amaral M, Vilarinho L (2018) Cystic Fibrosis newborn screening: PAP value in populations with stringent rules for genetic studies. International Journal of Neonatal Screening. 4:22

Amaral MD, Boj SF, Shaw J, Leipziger J, Beekman JM (2018) Cystic fibrosis: Beyond the airways. Report on the meeting of the basic science working group in Loutraki, Greece. Journal of Cystic Fibrosis.

Clancy JP, Cotton CU, Donaldson SH, Solomon GM, VanDevanter DR, Boyle MP, Gentzsch M, Nick JA, Illek B, Wallenburg JC, Sorscher EJ, Amaral MD, Beekman JM, Naren AP, Bridges RJ, Thomas PJ, Cutting G, Rowe S, Durmowicz AG, Mense M, Boeck KD, Skach W, Penland C, Joseloff E, Bihler H, Mahoney J, Borowitz D, Tuggle KL (2018) CFTR modulator theratyping: Current status, gaps and future directions. ACS CHEMICAL BIOLOGY.

Lérias JR*, Pinto MC*, Botelho HM, Awatade NT, Quaresma M, Wanitchakool P, Schreiber R, Pepperkok P, Kunzelmann K, Amaral MD (2018) A Novel Microscopy-Based Assay Identifies Extended Synaptotagmin-1 (ESYT1) as a Regulator of Anoctamin 1 Traffic. BBA- Mol Cell Res 1865: 421-431

JLérias J, Pinto M, Benedetto R, Schreiber R, Amaral M, Aurelic M, Kunzelmann K (2018) Compartmentalized crosstalk of CFTR and TMEM16A (ANO1) through EPAC1 and ADCY1. Cellular Signalling.

Clarke LA, Awatade NT, Felicio VM, Silva IAL, Calucho M, Pereira L, Azevedo P, Cavaco J, Barreto C, Bertuzzo CM, Gartner S, Beekman J, Amaral MD (2018) The effect of PTC mutations on CFTR mRNA abundance in human nasal epithelium and intestinal organoids: a basis for read-through therapies in Cystic Fibrosis. Hum Mutat.

Patel W, Moore PJ, Sassano MF, Lopes-Pacheco M, Aleksandrov AA, Amaral MD, Tarran R, Gray MA (2018) Increases in cytosolic Ca2+ induce dynamin- and calcineurin-dependent internalisation of CFTR. Cell Mol Life Sci.

M&B

Alves M, Pereira A, Vicente C, Matos P, Henriques J, Lopes H, Nascimento F, Mota M, Correia A, Henriques I. (2018) The role of bacteria in Pine Wilt Disease: insights from microbiome analysis. FEMS Microbiology Ecology, 94(7). 10.1093/femsec/fiy077

Barbosa C, Lage P, Esteves M, Chambel L, Mendes-Faia A, Mendes-Ferreira A (2018) Molecular and phenotypic characterization of Metschnikowia pulcherrima strains from Douro wine region. Fermentation, 4(1), 8. 10.3390/fermentation4010008

Ariyawansa HA, Phillips AJL, Chuang W-Y, Tsai I (2018) Tzeananiaceae, a new pleosporalean family associated with Ophiocordyceps macroacicularis fruiting bodies in Taiwan. MycoKeys, 37, 1–17. 10.3897/mycokeys.37.27265

Cruz J, Tenreiro R, Cruz L (2018) Inference of the phylogenetic diversity and population structure of Xanthomonas campestris affecting Brassicaceae using a MLST-based approach. Plant Pathology, 67(4), 948- 956. 10.1111/ppa.12791

Dias C, Pais J, Nunes R, Almeida AF, Serra P, Xavier N, Vila-Viçosa D, Machuqueiro M, Viana A, Martins A, Santos M, Pelerito A, Dias R, Tenreiro R, Oliveira M, Contino M, Colabufo N, Almeida R, Sanchez-Blazquez M, Marquês L, Rauter A (2018) The first sugar-based bactericides targeting phosphatidylethanolamine-enriched membranes. Nature Communications, 9, 4857. 10.1038/s41467-018-06488-4

Doilom M, Hyde KD, Phookamsak R, Dai DQ, Tang LZ, Hongsanan S, Chomnunti P, Boonmee S, Dayarathne MC, Li WJ, Thambugala KM, Perera RH, Daranagama DA, Norphanphoun C, Konta S, Dong W, Ertz D, Phillips AJL, McKenzie EHC, Vinit K, Ariyawansa HA, Jones EBG, Mortimer PE, Xu JC, Promputtha I (2018) Mycosphere Notes 225–274: types and other specimens of some genera of Ascomycota.. Mycosphere, 9, 647–754. 10.5943/mycosphere/9/4/3

Fernandes C, Sousa R, Tavares F, Cruz L (2018) First report of Xanthomonas arboricola causing bacterial blight on pecan trees in Portugal. Plant Disease, 12, 2632. 10.1094/PDIS-03-18-0467-PDN

Lopes A, Linaldeddu BT, Phillips AJL, Alves A (2018) Mating type gene analyses in the genus Diplodia: From cryptic sex to cryptic species. Fungal Biology, 122, 629-638. 10.1016/j.funbio.2018.03.012

Loreti S, Cunty A, Pucci N, Chabirand A, Stefani E, Cruz L, et al. (2018) Performance of diagnostic tests for the detection and identification of Pseudomonas syringae pv. actinidiae (Psa) from woody samples. European Journal of Plant Pathology, 152 (3), 657-676. 10.1007/s10658-018-1509-5

Osório HC, Zé-Zé L, Neto M, Silva S, Marques F, Silva AS, Alves MJ (2018) Detection of the invasive mosquito species Aedes (Stegomya) albopictus (Diptera: Culicidae) in Portugal. INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH, 15(4), 820. 10.3390/ijerph15040820.

Sassetti M, Zé-Zé L, Franco J, Cunha JD, Gomes A, Tomé A, Alves MJ. (2018) First case of confirmed congenital Zika syndrome in continental Africa. Transactions of The Royal Society of Tropical Medicine and Hygiene, 112(10), 458-462. 10.1093/trstmh/try074

Seixas I, Barbosa C, Mendes-Faia A, Güldener U, Tenreiro R, Mendes- Ferreira A, Mira NP (2018) Genome sequence of the non-conventional wine yeast Hanseniaspora guilliermondii UTAD222 unveils relevant traits of this species and of the Hanseniaspora genus in the context of wine fermentation. DNA Research, 0(0), 43482. 10.1093/dnares/dsy039

Silva R, Gomes V, Mendes-Faia A, Melo-Pinto P (2018) Using Support Vector Regression and Hyperspectral Imaging for the Prediction of Oenological Parameters on Different Vintages and Varieties of Wine Grape Berries. Remote Sensing, 10, 312. 10.3390/rs10020312

Tavares M, Guldener U, Esteves M, Mendes-Faia A, Mendes-Ferreira A, Mira NP (2018) Genome sequence of the wine yeast Saccharomycodes ludwigii UTAD17. Microbiology Resource Announcements, 7(18), e01195-18. 10.1128/MRA.01195-18

Tibpomma S, Hyde KD, McKenzie EHC, Bhat DJ, Phillips AJL, Wanasinghe DN, Samarakoon MC, Jayawardena RS, Dissanayake AJ, Tennakoon DS, Doilom M, Phookamsak R, Tang AMC, Xu J, Mortimer PE, Promputtha I, Maharachchikumbura1 SSN, Khan S, Karunarathna SC (2018) Fungal diversity notes 840–928: micro-fungi associated with Pandanaceae. Fungal Diversity, 93, 1-160. 10.1007/s13225-018-0408-6

Yansambou MS, Ferreira AC, Bada-Alambedji R, Botelho A (2018) Seroprevalence of contagious bovine pleuropneumonia in Niamey region. Journal of Veterinary Medicine and Research, 5(8), 1151. 10.1007/s11250-014-0738-7

Wareth G, Abdeen A, Ali H, Bardenstein S, Ferreira AC et al. (2019) Brucellosis in the Mediterranean countries: REview of history, prevalence, dfistribution, current situation and attempts for surveillance and control. OIE Scientific and Technical Review.

Cruz L, Cruz J, Sousa R (2018) Studies on differential susceptibility of 'Rocha' pear clones and Portuguese varieties of pear and apple to fire blight - tools for the sustainability of fruit chain production. Revista Ciencias Agrarias de Portugal. 10.19084/RCA18028.

Ferreira AC, Simões S (2018) Controlo laboratorial da brucelose em ruminantes e suídeos. Vida Rural, ano 66, nº 1835, 28-30.

Jiang N, Phillips AJL, Zhang ZX, Tian CM (2018) Morphological and molecular identification of two novel species of Melanops in China. Mycosphere, 9, 1187–1196. 10.5943/mycosphere/9/6/8

Marcuello C, Chambel L, Rodrigues MS, Ferreira LP, Cruz MM (2018) Magnetotactic Bacteria: Magnetism Beyond Magnetosomes. IEEE Transactions on NanoBioscience, 17(4), 555-559. 10.1109/TNB.2018.2878085

Mullett, M. S.; Adamson, K.; Bragança, H; Bulgakov, T. S.; Georgieva, M.; Henriques, J.; Jürisoo, L.; Laas, M.; Drenkhan, R. (2018) New country and regional records of the pine needle blight pathogens Lecanosticta acicola, Dothistroma septosporum and Dothistroma pini. Forest Pathology, 48, e12440. 10.1111/efp.12440"

Phillips AJL, Hyde KD, Alves A, Liu J-K (2018) Families in Botryosphaeriales: a phylogenetic, morphological and evolutionary perspective. Fungal Diversity. 10.1007/s13225-018-0416-6

Pereira L, Gomes S, Barrias S, Gomes EP, Baleiras-Couto M, Fernandes JR, Martins-Lopes P (2018) From the field to the bottle - An integrated strategy for wine authenticity. Beverages, 4 (4), 71. 10.3390/beverages4040071

Santana J, Gramacho K, Ferreira K, Rezende R, Mangabeira P, Dias R, Couto F, Pirovani C (2018) Witches' broom resistant genotype CCN51 shows greater diversity of symbiont bacteria in its phylloplane than susceptible genotype catongo. BMC MICROBIOLOGY, 18(1), 194. 10.1186/s12866-018-1339-9

Cruz, L. (2018) Dossier Técnico: Declínio amarelo das Asteráceas: Um novo risco para a horticultura Portuguesa. Vida Rural, 1835, 34-35.

BTR

Argyropoulou Z, Liu L, Ozoemena L, Branco CC, Senra R, Reis-Rego Â, Mota-Vieira L. (2018) A novel PLEC nonsense homozygous mutation (c.7159G > T; p.Glu2387*) causes epidermolysis bullosa simplex with muscular dystrophy and diffuse alopecia: a case report. BMC Dermatology, 18, 1. doi: 10.1186/s12895-018-0069-x

David D, Anand D, Araújo C, Gloss B, Fino J, Dinger M, Lindahl P, Pöyhönen M, Hannele L, Lavinha J (2018) Identification of OAF and PVRL1 as candidate genes for an ocular anomaly characterized by Peters anomaly type 2 and ectopia lentis. Experimental Eye Research, 168, 161-170. 10.1016/j.exer.2017.12.012

Ventura C, Sousa-Uva A, Lavinha J, Silva MJ (2018) Conventional and novel "omics"-based approaches to the study of carbon nanotubes pulmonary toxicity. Environmental and Molecular Mutagenesis, 59, 334-362. 10.1002/em.22177

Fletcher-Watson S, Larsen K, Salomone E; Members of the COST ESSEA Working Groups. Astrid M Vicente (2018) What do parents of children with autism expect from participation in research? A community survey about early autism studies. Autism, 43112. doi: 10.1177/1362361317728436

Esteves LM, Bulhões SM, Branco CC, Carreira T, Vieira ML, Gomes-Solecki M, Mota-Vieira L. (2018) Diagnosis of Human Leptospirosis in a Clinical Setting: Real-Time PCR High Resolution Melting Analysis for Detection of Leptospira at the Onset of Disease. SCIENTIFIC REPORTS, 8, 9213. doi: 10.1038/s41598-018-27555-2

Dias Pereira B, Nunes da Silva T, Bernardo AT, César R, Vara Luiz H, Pacak K, Mota-Vieira L. (2018) A Clinical Roadmap to Investigate the Genetic Basis of Pediatric Pheochromocytoma: Which Genes Should Physicians Think About?. International Journal of Endocrinology, 2018, 8470642. doi: 10.1155/2018/8470642

Vaz SO, Dâmaso C, Liu L, Ozoemena L, Mota-Vieira L. (2018) Severe phenotype of junctional epidermolysis bullosa generalised intermediate type caused by homozygous COL17A1:c.505C>T (p.Arg169*) mutation. European Journal of Dermatology, 28, 412-413. doi: 10.1684/ejd.2018.3279

Brainstorm Consortium, et all. (2018) Analysis of shared heritability in common disorders of the brain.. Science, 360, 43113. 10.1126/science.aap8757.

Sturm AC, Knowles JW, Gidding SS, Ahmad ZS, Ahmed CD, Ballantyne CM, Baum SJ, Bourbon M, Carrié A, Cuchel M, de Ferranti SD, Defesche JC, Freiberger T, Hershberger RE, Hovingh GK, Karayan L, Kastelein JJP, Kindt I, Lane SR, Leigh SE, Linton MF, Mata P, Neal WA, Nordestgaard BG, Santos RD, Harada-Shiba M, Sijbrands EJ, Stitziel NO, Yamashita S, Wilemon KA, Ledbetter DH, Rader DJ; Convened by the Familial Hypercholesterolemia Foundation. (2018) Clinical Genetic Testing for Familial Hypercholesterolemia: JACC Scientific Expert Panel. Journal of the american College of Cardiology, 72(6), 662-680. 10.1016/j.jacc.2018.05.044.

Futema M, Bourbon M, Williams M., Humphries SE (2018) Clinical utility of the polygenic LDL-C SNP score in familial hypercholesterolemia. Atherosclerosis, 277, 457-463. 10.1016/j.atherosclerosis.2018.06.006.

Alves AC, Benito-Vicente A, Medeiros AM, Reeves k, Martin C, Bourbon M. (2018) Further evidence of novel APOB mutations as a cause of familial hypercholesterolaemia. Atherosclerosis, 277, 448-456. 10.1016/j.atherosclerosis.2018.06.819.

EAS Familial Hypercholesterolaemia Studies Collaboration, Vallejo-Vaza AJ , De Marcoa M, Stevensa CAT, Akramb A, FreibergercF, Hovingh GE, Kasteleine JP, Mata P,. Raalg FJ, Santos RD, Soran H, Watts G, Abifadel M, Aguilar-Salinas CA, Al-khnifsawi M, AlKindi FA, Alnouri F, Alonso R, Al-Rasadi K, Al-Sarraf A, Ashavaid TF, Binder CJ, Bogsrud MP, Bourbon M, Bruckert E, Chlebus K, Corral P, Descamps O, Durst R, Ezhov M, Frasai Z, Genest J, Grosel U, Harada-Shiba M, Kayikciogluan M, Lalicao K,. Lamaq CSQ, Latkovskis G, Laufs U, Liberopoulos E, Lin J, Maher V, Majano N, A. Marais D, März W, Mirrakhimov E,. Miserez AR, Mitchenko O, Nawawi HM, Nordestgaard BG, Paragh G, Petrulioniene Z, Pojskic B, Postadzhiyan A, Reda A, Reiner Z, Sadoh WE, Sahebkar A, Shehab A,Shek AB, Stoll M, Su T-C, Subramaniam T, Susekov AV, Symeonides P, Tilney M, Tomlinson B, Truong T-H, Tselepis AD, Tybjærg-Hansen A, Vázquez-Cárdenas A, Viigima M, Vohnout B, Widén E, Yamashita S, Banach M, Gaita D, Jiangcu L, Nilsson L, Santosc LE, Schunkert H, Tokgözoğlu L, Car J, Catapano AL,. Ray KK, On behalf of the EAS Familial. Hypercholesterolaemia Studies Collaboration (FHSC) Investigators. (2018) Overview of the current status of familial hypercholesterolaemia care in over 60 countries - The EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). Atherosclerosis, 277, 234-255. 10.1016/j.atherosclerosis.2018.08.051

Iacocca MA, Chora JR, Carrié A, Freiberger T, Leigh SE, Defesche JC, Kurtz CL, DiStefano MT, Santos R, Humphries SE, Mata P, Jannes C, Hooper AJ, Wilemon KA, Benlian P, O'Connor R, Garcia J, Wand H, Tichy L, Sijbrands EJ, Hegele RA, Bourbon M and Knowles JW on behalf of the ClinGen FH Variant Curation Expert Panel (2018) ClinVar database of global familial hypercholesterolemia-associated DNA variants. Human Mutation, 39, 1631-1640. 10.1002/humu.23634

Chora JR, Medeiros AM, Alves AC, Bourbon M. (2018) Analysis of publicly available LDLR, APOB, and PCSK9 variants associated with familial hypercholesterolemia: application of ACMG guidelines and implications for familial hypercholesterolemia diagnosis. Genetics in Medicine, 20(6), 591-598. 10.1038/gim.2017.151. Epub 2017 Oct 2

Cardoso MC, Raposo MI, Ormonde M, Monteiro R, Sampaio A, Cosme P, Mota-Vieira L. (2018) Prenatal sonographic diagnosis of isolated fetal ascites in cri-du-chat (5p-) syndrome: A case report.. Journal of Clinical Ultrasound, 0(0). doi.org/10.1002/jcu.22679

GER

Kotelevets L, Walker F, Mamadou G, Lehy T, Jordan P, Chastre E (2018) The Rac1 splice form Rac1b favors mouse colonic mucosa regeneration and contributes to intestinal cancer progression. Oncogene, in press. 10.1038/s41388-018-0389-7

Matos AM, Gomes-Duarte A, Faria M, Barros P, Jordan P, Amaral MD, Matos P. (2018) Prolonged co-treatment with HGF sustains epithelial integrity and improves pharmacological rescue of Phe508del-CFTR. SCIENTIFIC REPORTS, 8, 13026. 10.1038/s41598-018-31514-2

Garcia-Vaquero ML, Gama-Carvalho M, Rivas JL, Pinto FR (2018) Searching the overlap between network modules with specific betweeness (S2B) and its application to cross-disease analysis. SCIENTIFIC REPORTS, 8, 11555. doi: 10.1038/s41598-018-29990-7

Olivença DV, Uliyakina I, Fonseca LL, Amaral MD, Voit EO, Pinto FR (2018) A Mathematical Model of the Phosphoinositide Pathway. SCIENTIFIC REPORTS, 8, 3904. doi: 10.1038/s41598-018-22226-8

Fernandes SF, Fior R, Pinto F, Gama-Carvalho M, Saúde L (2018) Fine-tuning of fgf8a expression through alternative polyadenylation has a selective impact on Fgf-associated developmental processes. Biochimica et Biophysica Acta - Gene Regulatory Mechanisms, 1861, 783. doi: 10.1016/j.bbagrm.2018.07.012

Mason D, Zhang X, Marques TM, Rose B, Khoury S, Hill M, Deutsch F, Lyons JG, Gama-Carvalho M, Tran N (2018) Human papillomavirus 16 E6 modulates the expression of miR-496 in oropharyngeal cancer. Virology, 521, 149. doi: 10.1016/j.virol.2018.05.022

Adega F, Matoso Silva R, Kjöllerström HJ, Vercammen P, · Raudsepp T, · Collares-Pereira MJ, · Fernandes C, do Mar Oom M, · Chaves R (2018) Comparative Chromosome Painting in Genets (Carnivora, Viverridae, Genetta), the Only Known Feliforms with a Highly Rearranged Karyotype. Cytogenetic and Genome Research. 10.1159/000491868

Gomes-Duarte A, Lacerda R, Menezes J, Romão L (2018) eIF3: a factor for human health and disease. RNA Biology, 15, 26-34. 10.1080/15476286.2017.1391437

Inês Teles Siefers Alves, Manuel Condinho, Sónia Custódio, Bruna F. Pereira, Rafael Fernandes, Vânia Gonçalves, Paulo J. da Costa, Rafaela Lacerda, Ana Rita Marques, Patrícia Martins-Dias, Gonçalo R. Nogueira, Ana Rita Neves, Patrícia Pinho, Raquel Rodrigues, Eva Rolo, Joana Silva, André Travessa, Rosário Pinto Leite, Ana Sousa, Luísa Romão (2018) Genetics of personalized medicine: cancer and rare diseases. Cellular Oncology, 41, 335-341. 10.1007/s13402-018-0379-3

CBS

Ivânia R. Cabrita, Pedro R. Florindo, Paulo J. Costa, M. Conceição Oliveira, Ana C. Fernandes (2018) Hydrophosphonylation of Aldehydes Catalyzed by Cyclopentadienyl Ruthenium(II) Complexes. Molecular Catalysis, 450, 77-86. 10.1016/j.mcat.2018.03.001

Rita Gonçalves-Pereira, Margarida P. Pereira, Sofia G. Serra, Anne Loesche, René Csuk, Samuel Silvestre, Paulo J. Costa, M. Conceição Oliveira, Nuno M. Xavier (2018) Novel Furanosyl Nucleoside Analogs Embodying Triazole or Theobromine Units as Potential Lead Molecules for Alzheimer's Disease. European Journal of Organic Chemistry, 2667-2681. 10.1002/ejoc.201800245

Frantisek Hartl, Maarten J. Bakker, Vanessa F. Santos, Paulo J. Costa, Maria José Calhorda (2018) Accurate Description of Low-Lying Excited States in a Series of Photoreactive Clusters [Os3(CO)10(α-diimine)] by DFT Calculations. Inorganic Chemistry, 57, 11704-11716. 10.1021/acs.inorgchem.8b01847

Rafael Nunes, Diogo Vila-Viçosa, Miguel Machuqueiro, Paulo J. Costa (2018) Biomolecular simulations of halogen bonds with a GROMOS force field. Journal of Chemical Theory and Computation, 14, 5383-5392. 10.1021/acs.jctc.8b00278

Filipe M. Sousa, Juliana G. Pereira, Bruno C. Marreiros, Manuela M. Pereira (2018) Taxonomic distribution, structure/function relationship and metabolic context of the two families of sulfide dehydrogenases: SQR and FCSD. Biochimica et Biophysica Acta - Bioenergetics, 1859, 742-753. 10.1016/j.bbabio.2018.04.004

Joana S. Sousa, Filipa Calisto, Julian D. Langer, Deryck J. Mills, Patrícia N. Refojo, Miguel Teixeira, Werner Kühlbrandt, Janet Vonck, Manuela M. Pereira (2018) Structural basis for energy transduction by respiratory alternative complex III. NATURE COMMUNICATIONS, 9, 1728. 10.1038/s41467-018-04141-8

Oscar Gutiérrez-Sanz , Enrico Forbrig, Ana P. Batista, Manuela M. Pereira, Johannes Salewski, Maria A. Mroginski, Robert Götz, Antonio L. De Lacey, Jacek Kozuch, Ingo Zebger (2018) Catalytic Activity and Proton Translocation of Reconstituted Respiratory Complex I Monitored by Surface-Enhanced Infrared Absorption Spectroscopy. Langmuir, 34, 5703-5711. 10.1021/acs.langmuir.7b04057

Strahinja Stevanović , Andrej Perdih, Milan Senćanski, Sanja Glišić, Margarida Duarte, Ana M. Tomás, Filipa V. Sena, Filipe M. Sousa, Manuela M. Pereira, Tom Solmajer (2018) In Silico Discovery of a Substituted 6-Methoxy-quinalidine with Leishmanicidal Activity in Leishmania infantum. Molecules, 23, 772. 10.3390/molecules23040772

Filipa V.Sena, Filipe M.Sousa, A. Sofia F.Oliveira, Cláudio M.Soares, Teresa Catarino, Manuela M.Pereira (2018) Regulation of the mechanism of Type-II NADH: Quinone oxidoreductase from S. aureus. Redox Biology, 16, 209-214. 10.1016/j.redox.2018.02.004

Filipe, H.A.L., Sousa, C., Marquês, J.T., Vila-Viçosa, D., Flor, A. G., Viana, A.S., Santos, M.S.C.S., Machuqueiro, M., de Almeida, R.F.M. (2018) Differential targeting of membrane lipid domains by caffeic acid and its ester derivatives. Free Radical Biology and Medicine, 115, 232-245. 10.1016/j.freeradbiomed.2017.12.002

Marques, S. C. R., Mestre, A.S., Machuqueiro, M., Gotvajn, A. Z., Marinsek, M., Carvalho, A. P. (2018) Apple tree branches derived activated carbons for the removal of beta-blocker atenolol. Chemical Engineering Journal, 345, 669-678. 10.1016/j.cej.2018.01.076

Reis, P. B. P. S., Vila-Vicosa, D., Campos, S. R. R., Baptista, A. M., Machuqueiro, M. (2018) The role of counterions in constant-pH MD simulations of PAMAM dendrimers. ACS Omega, 3, 2001-2009. 10.1021/acsomega.7b01708

Brito, E., Gomes, E., Falé, P.L., Borges, C., Pacheco, R., Teixeira, V., Machuqueiro, M., Ascensão, L., Serralheiro, M.L.M. (2018) Bioactivities of decoctions from Plectranthus species related to their traditional use on the treatment of digestive problems and alcohol intoxication. Journal of Ethnopharmacology, 220, 147-154. 10.1016/j.jep.2018.04.006

Vila-Vicosa, D., Silva, T. F. D., Slaybaugh, G., Reshetnyak, Y. K., Andreev, O. A., Machuqueiro, M. (2018) Membrane-induced pKa shifts in wt-pHLIP and its L16H variant. Journal of Chemical Theory and Computation, 14, 3289-3297. 10.1021/acs.jctc.8b00102

Gaspar, H., Bronze, S., Oliveira, C., Victor, B. L., Machuqueiro, M., Pacheco, R., Caldeira, M. J., Santos, S. (2018) Proactive response to tackle the threat of emerging drugs: synthesis and toxicity evaluation of new cathinones. Forensic Science International, 290, 146-156. 10.1016/j.forsciint.2018.07.001

Bandeira, N. A. G.; Bo, C., (2018) Regioselective Catalysis by the {Mo132} nanocapsule: A computational inspection. European Journal of Inorganic Chemistry, 2018, 2512-2517. 10.1002/ejic.201800155

Fianchini, M.; Bandeira, N. A. G. (2018) Are homoleptic complexes of ethylene with group 12 metals isolable in solution? A DFT study. Journal of Molecular Modeling, 24, 161:1-4. 10.1007/s00894-018-3683-y

Trojanowska, A.; Bandeira, N. A. G.; Nogalska, A.; Marturano, V.; Giamberini, M.; Cerruti, P.; Ambrogi, V.; Tylkowski, B. (2018) Squeezing release mechanism of encapsulated compounds from photo-sensitive microcapsules. Applied Surface Science. 10.1016/j.apsusc.2018.03.061

Trojanowska, A.; Marturano, V.; Bandeira, N. A. G.; Giamberini, M.; Tylkowski, B. (2018) Smart microcapsules for precise delivery systems. Functional Materials Letters, 11, 1850041. 10.1142/s1793604718500418

Vieira, B. J. C.; da Gama, V.; Santos, I. C.; Pereira, L.; Bandeira, N. A. G.; Waerenborgh, J. C. (2018) Magnetic and structural correlations in [Fe(nsal2trien)] salts: The role of cation-anion interactions in the spin crossover phenomenon. CrystEngComm, 20, 2465-2475. 10.1039/C8CE00275D

F. F. Martins, A. Joseph, H. P. Diogo, M. E. Minas da Piedade, L. P. Ferreira, M. D. Carvalho, S. Barroso, M. J. Romão, M. J. Calhorda, P. N. Martinho (2018) Irreversible magnetic behaviour caused by the thermosalient phenomenon in an iron(III) spin crossover complex. European Journal of Inorganic Chemistry, 2018, 2976-2983. 10.1002/ejic.201800605

I. Vicente, L. P. Ferreira, M. D. Carvalho, V. H. N. Rodrigues, M. M. Dîrtu, Y. Garcia, M. J. Calhorda, P. N. Martinho (2018) Selecting the spin crossover profile with controlled crystallisation of mononuclear Fe(III) polymorphs. Dalton Transactions, 47, 7013-7019. 10.1039/C8DT00227D

M. S. Saraiva, C. D. Nunes, V. Félix, A. P. C. Ribeiro, C. Nieto de Castro, M. J. Calhorda (2018) Molybdenum (II) complexes with α-diimines: catalytic activity in organic and ionic liquid solvents. European Journal of Inorganic Chemistry, 3922-3932. doi.org/10.1002/ejic.201800700

E. R. Silva, O. Ferreira, P. A. Ramalho, N. F. Azevedo, A. Igartua, J. C. Bordado, M. J. Calhorda (2019) Eco-friendly non-biocide-release coatings for marine biofouling prevention. Science of the Total Environment, 650, 2499-2511. 10.1016/j.scitotenv.2018.10.010

M. V. Loureiro, A. De Schrijver, J. C. Bordado, E. Silva, A. C. Marques (2018) Hybrid custom-tailored sol-gel derived microscaffold for biocides immobilization. Microporous and Mesoporous Materials, 261, 252-258. 10.1016/j.micromeso.2017.10.056

E. R. Silva, O. Ferreira, P. Rijo, J. C. Bordado, M. J. Calhorda (2018) Antifouling Eco-Filters for water Bio-Decontamination. Proceedings, 2, 181. 10.3390/ecws-2-04950

S. Pinteus, M. F. L. Lemos, C. Alves, A. Neugebauer, J. Silva, O. P.Thomas, L. M. Botana, H. Gaspar and R. Pedrosa (2018) Marine invasive macroalgae: Turning a real threat into a major opportunity - the biotechnological potential of Sargassum muticum and Asparagopsis armata. Algal Research, 24, 217-234. doi.org/10.1016/j.algal.2018.06.018

C. Alves, J. Silva, S. Pinteus, H. Gaspar, M. C. Alpoim, L. M. Botana and R. Pedrosa (2018) From marine origin to therapeutic: The antitumourpotential of marine algae-derived compounds. Frontiers in Pharmacology, 9, 1--14. 10.3389/fphar.2018.00777

Elsa Brito, André Silva, Pedro Luis Vieira Falé, Rita Pacheco, António Serralheiro, Parvez I Haris, Lia Ascensao, Maria Luísa Serralheiro. (2018) Serum Albumin Modulates the Bioactivity of Rosmarinic Acid. Journal of Medicinal Food, 21. 10.1089/jmf.2017.0086

Luís Gomes, Carlos Borges, M Luísa Serralheiro, Miguel Minhalma, Rita Pacheco. (2018) Cork processing wastewaters componentes fractioned by ultrafiltration membranes- Studies of antioxidant and antitumoral activity. Journal of Chemical Technology and Biotechnology, 93, 861-870. 10.1002/jctb.5441

F Mejri, S Selmi, A Martins, H Benkhoud, T Baati, H Chaabane, L Njim, ML Serralheiro, AP Rauter, K Hosni (2018) Broad bean (Vicia faba L.) pods: a rich source of bioactive ingredients with antimicrobial, antioxidant, enzyme inhibitory, anti-diabetic and health-promoting properties. Food & Function, 9, 2051-2069. 10.1039/c8fo00055g

Neusa Figueiredo, Maria Luísa Serralheiro, João Canário, Aida Duarte, Holger Hintelmann, Cristina Carvalho (2018) Evidence of mercury methylation and demethylation by the estuarine microbial communities obtained in stable Hg isotope studies. International Journal of Environmental Research and Public Health, 15, 2141. 10.3390/ijerph15102141

BioPhysNano

Rouzine IM, Rozhnova G (2018) Antigenic evolution of viruses in host populations. PLoS Pathog 14(9): e1007291. 10.1371/journal.ppat.1007291

A. N. Pogorily, A. F. Kravets, V. V. Nevdacha, D. Y. Podyalovskiy, S. M. Ryabchenko, V. M. Kalita, M. M. Kulik, A. F. Lozenko, A. Ya. Vovk, M. Godinho, L. Maurel, J. A. Pardo, C. Magen, and V. Korenivski, Magnetic anisotropy of epitaxial Co2Fe-Ge Heusler alloy films on MgO (100) substrates, AIP Advances 7, 055831 (2017). 10.1063/1.4978209

M. Moskvin, M. Babic, Salette. Reis, M. M. Cruz, L. P. Ferreira, M. D. Carvalho, S. A. Costa Lima, D. Horák (2018) Biological evaluation of surface-modified magnetic nanoparticles as a platform for colon cancer cell theranostics. Colloids and Surfaces B: Biointerfaces, 161, 35-41. 10.1016/j.colsurfb.2017.10.034

C. Marcuello, L. Chambel, M. S. Rodrigues, L. P. Ferreira, M.M. Cruz (2018) Magnetotactic bacteria: magnetism beyond magnetosomes. IEEE Transactions on NanoBioscience, 17. 10.1109/TNB.2018.2878085

M V Vitorino, Arthur Vieira, Carolina A. Marques e Mario S. Rodrigues (2018) Direct measurement of the nucleation time of a water nanobridge. Scientific Reports, 8 (13848). 10.1038/s41598-018-32021-0

Ana I. Vicente, Liliana P. Ferreira, Maria de Deus Carvalho, Vítor H. N. Rodrigues, Marinela M. Dîrtu, Yann Garcia, Maria José Calhorda and Paulo N. Martinho (2018) Selecting the spin crossover profile with controlled crystallization of mononuclear Fe(III) polymorphs. Dalton Transactions, 47, 7013-7019. 10.1039/c8dt00227d

M. Guerra, J. M. Sampaio, F. Parente, P. Indelicato, P. Hönicke, M. Müller, B. Beckhoff, J. P. Marques, and J. P. Santos (2018) Theoretical and experimental determination of K- and L-shell X-ray relaxation parameters in Ni. Physical Review A, 97, 42501. 10.1103/PhysRevA.97.042501

Y. Ito, T. Tochio, M. Yamashita, S. Fukushima, A. M. Vlaicu, Ł. Syrocki, K. Słabkowska, E. Węder, M. Polasik, and K. Sawicka, P. Indelicato, J. P. Marques, M. C. Martins, F. Parente, J. P. Santos (2018) Structure of high-resolution Kβ1,3 x-ray emission spectra for the elements from Ca to Ge. Physical Review A, 97, 52505. 10.1103/PhysRevA.97.052505

Y. Ménesguen, M.-C. Lépy, J. M. Sampaio, J. P. Marques, F. Parente, M. Guerra, P. Indelicato, J. P. Santos, P. Hönicke, and B. Beckhoff (2018) A combined experimental and theoretical approach to determine X-ray atomic fundamental quantities of Tin. X-Ray Spectrometry, 43111. 10.1002/xrs.2948

Y. Ménesguen, Marie-Christine Lepy, J. M. Sampaio, J. P. Marques, F. Parente, M. Guerra, P. Indelicato, J. P. Santos (2018) Experimental and theoretical determination of the L-fluorescence yields of bismuth. Metrologia, 55, 621. 10.1088/1681-7575/aad1d6

J. P. Marques, M. C. Martins, J. P. Santos, A. M. Costa, P. Indelicato, and F. Parente (2018) Theoretical determination of K X-ray transition energy and probability values for highly charged (He- through B-like) Nd, Sm, Gd, Dy, Er, and Yb ions. Radiation Physics and Chemistry. 10.1016/j.radphyschem.2018.02.003

Benedito J. Costa Cabral (2018) Born-Oppenheimer molecular dynamics, hydrogen bond interactions and magnetic properties of liquid hydrogen cyanide. Journal of Molecular Liquids, 272, 778-786. 10.1016/j.molliq.2018.09.092

Nuno Galamba, Benedito J. Costa Cabral (2018) Magnetic properties and core electron binding energies of liquid water. Journal of Chemical Physics, 148, 44510. 10.1063/1.5011037

MAS

Pedro Mariano, Ziad Salem, Rob Mills, Stefan Schönwetter-Fuchs-Schistek, Luís Correia, Thomas Schmickl (2018) Evolving robot controllers for a bio-hybrid system. 155-162. 10.1162/isal_a_00036

Antonio J Tallón-Ballesteros, Luís Correia, Bing Xue (2018) Featuring the Attributes in Supervised Machine Learning. Hybrid Artificial Intelligent Systems, 350-362. 10.1007/978-3-319-92639-1_29

Ana Cristina Bicharra Garcia, William Silva, Luís Correia (2018) The PredNews forecasting model. 69:1-69:6. 10.1145/3209281.3209295

Luís Cavique, Armando B Mendes, Hugo FMC Martiniano, Luís Correia (2018) A biobjective feature selection algorithm for large omics datasets. Expert Systems, 35(4), e12301. 10.1111/exsy.12301

L. Correia, S. Silva, A. Garcia (2018) Detecting Influence in Wisdom of the Crowds. 17--24.

Ana Marisa Salgueiro, Catarina Biló Alves, Joao Balsa (2018) Querying an Ontology Using Natural Language. 164-169. 10.1007/978-3-319-99722-3_17

Carvalho, A., Neto, J.P., Santos, C., (2018) Ordinal sums of impartial games. AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY, 243, 39-45. 10.1016/j.dam.2017.12.020

Cavique L., N.C. Marques, A. Gonçalves (2018) A data reduction approach using hypergraphs to visualize communities and brokers in social networks. Social Network Analysis and Mining.

Tiago Gonçalves, Pedro Vieira, Ana Paula Afonso, Maria Beatriz Carmo, Tiago Moucho (2018) Analysing Player Performance with Animated Maps. 103-109.

Marcos A F, Cláudio A P, Martinho C, Barros D, Carvalho E, Carmo MB, Seixas S. Virtual Tutoring (2018) Virtual Tutoring. 56-61.

L. Cruz-Filipe, G.Gaspar, I. Nunes, and P. Schneider-Kamp (2018) Active integrity constraints for general-purpose knowledge bases. Annals of Mathematics and Artificial Intelligence, 213-246. 10.1007/s10472-018-9577-y

Graçaliz Dimuro, Luis Antunes (editors) (2018) Multi-Agent Based Simulation XVIII: International Workshop, MABS 2017, São Paulo, Brazil, May 8-12, 2017, Revised Selected Papers. LNCS 10798

Fernando De la Prieta, Zita Vale, Luis Antunes, Tiago Pinto, Andrew T Campbell, Vicente Julián, Antonio JR Neves, María N Moreno (editors) (2018) Trends in Cyber-Physical Multi-Agent Systems. The PAAMS Collection-15th International Conference, PAAMS 2017.

Passos, D., Coelho, H., Sarti, F. M. (2018) Measuring Bank´s Antifragile via Fuzzy Logic.

Passos, D., Coelho, H., Sarti, F. M. (2018) Interbank Networks and the Benefits of Using Multilayer Structures.

Books

PFG

Resimprove – Contribuição para a melhoria da eficiência, racionalização e expansão da atividade de resinagem (2018) Maria Emilía Silva; Maria João Gaspar; Jani Pires; Marco Ribeiro; Carlos Loureiro; João Paulo Coutinho; Elisabete Santos; Ana Carvalho; José Lima Brito; António Salgueiro; José Luís Lousada. Coordenação: Maria Emilía Silva, Carlos Loureiro, 1, 1-40. ISSN: 978-989-704-264-5

FunGP

Book Chapters

Preparation of Amyloidogenic Aggregates from EF-Hand β-Parvalbumin and S100 Proteins (2018) Martínez,J., Cristóvão, J.S., Sánchez, R., Gasset, M., Gomes, C.M.. Amyloid proteins. Methods in Molecular Biology, 1779, 167-179. 978-1-4939-7815-1

Thermal Shift and Stability Assays of Disease-Related Misfolded Proteins Using Differential Scanning Fluorimetry (2019) Lucas, T.G., Gomes, C.M., Henriques, B.J. Protein Misfolding Diseases. Methods in Molecular Biology, 1873, 255-264. 978-1-4939-8819-8

Biophysical and Spectroscopic Methods for Monitoring Protein Misfolding and Amyloid Aggregation (2019) Cristóvão J.S., Henriques B.J., Gomes C.M. Protein Misfolding Diseases. Methods in Molecular Biology, 1873, 3-18. 978-1-4939-8819-8

M&B

Agenda Temática de Investigação e Inovação Mar 2030 (2019) Santos A M, Peliz A. Noronha A, Falcão A, Pascoal A, Guedes Soares C, Vieira H, Antunes J, Gato L, Menezes Pinheiro L, Mateus M, Cunha M, Pires P, Pousão P, Bettencourt R, Calado R, Ribeiro S, Rebelo T, Silva T. Fundação para a Ciência e Tecnologia.

Book Chapters

How to Succeed in Marketing Marine Natural Products for Pharmaceutical, Cosmetics & Nutraceutical Markets (2018) Calado R, Leal MC, Gaspar H, Santos S, Marques A, Nunes ML, Vieira H. ELSEVIER Series "Grand Challenges in Marine Biotechnology", pages 317-403. 978-3-319-69074-2

BTR

Book Chapters

Quantitative Proteomic Analysis of Skeletal Muscle Detergent-Resistant Membranes in a Smith-Lemli-Opitz Syndrome Mouse (2018) Maria Luís Cardoso, Rui Vitorino, Henrique Reguengo, Susana Casal, Rui Fernandes, Isabel Duarte, Sofia Lamas, Renato Alves, Francisco Amado and Franklim Marques. Cholesterol – Good, Bad, and the Heart, 125-143.

GER

Targeted Therapy of Colorectal Cancer Subtypes (2018) Jordan P. Advances in Experimental Medicine and Biology, 80. in press

Book Chapter

Colorectal Cancer Subtypes- the current portrait (2018) Jordan P. Advances in Experimental Medicine and Biology, 5. in press

Targeting colon cancers with mutated BRAF and microsatellite instability (2018) JordanP, Matos P. Advances in Experimental Medicine and Biology, 10. in press

CBS

Book Chapters

The halogen bond: Nature and Applications (2018) Paulo J. Costa. Chemical Synergies: From the Lab to In Silico Modelling, Chapter 3, 81-102. 978-3-11-048206-5

Advances in the Computational Modeling of Halogen Bonds in Biochemical Systems (2018) Paulo J. Costa, Rafael Nunes. Frontiers in Computational Chemistry, 4, 144-183. 978-1-68108-442-8

Modeling of Azobenzene-Based Compounds (2018) Several/ Bandeira, Nuno A.G.; Tylkowski, Bartosz (Ed.s),Marturano, V.; Ambrogi, V.; Bandeira, N. A. G.; Tylkowski, B. ; Giamberini, M. ; Cerruti, P.. Chemical Synergies: From the Lab to In Silico Modelling, Chap. 5, 310. 978-3-11-048206-5

MAS

Electricity Markets with Increasing Levels of Renewable Generation: Structure, Operation, Agent-based Simulation, and Emerging Designs (2018) Lopes, F., Coelho, H. (Eds.). Electricity Markets with Increasing Levels of Renewable Generation: Structure, Operation, Agent-based Simulation and Emerging Designs, 327. 978-3-319-74263-2

Thesis

PFG

MsC Thesis

João Tiago Roque Alves (2018) Effectiveness of Ascorbic Acid and Zinc as drought antagonists in bread wheat plants monitored by different DNA markers. Supervisor: JE Lima-Brito (UTAD), Co-supervisor: Ana Carvalho (UTAD).

Elisabete Cristina Jesus dos Santos (2018) Aluminum tolerance in Secale species: genetic diversity, molecular mechanisms and gene characterization. Supervisor: Manuela Matos (UTAD), Co-supervisor: Cesar Benito (UCM).

Ana Inês Bento Fonseca e Silva (2018) Polimorfismo no gene hOGG1 (Ser326Cys): estudo do efeito do exercício físico no dano e na capacidade de reparação do DNA em humanos. Supervisor: Manuela Matos (UTAD), Co-supervisor: Jorge Frederico Pinto Soares (UTAD).

Gonçalo Laureano (2018) Fatty acids and lipid signaling in grapevine resistance to Plasmopara viticola. Supervisor: Andreia Figueiredo (FCUL), Co-supervisor: Ana Rita Matos (FCUL).

João Silva (2018) Engineering low-noise gene expression systems for single-molecule experiments. Supervisor: Zach Hensel (ITQB), Co-supervisor: Andreia Figueiredo (FCUL).

PhD Thesis

Francisca Rodrigues dos Reis (2018) Effect of mycorrhization on Quercus suber L. tolerance to drought. Supervisor: Teresa Lino-Neto (UMinho), Co-supervisor: Rui Tavares (UMinho).

Teresa Maria da Cruz Gomes (2018) Role of olive tree phyllosphere microrganisms in the biological control of olive leaf spot and olive knot. Supervisor: Paula Baptista (IPBragança), Co-supervisor: Teresa Lino-Neto (UMinho).

Márcia Raquel Gomes Carvalho (2018) Genetic diversity and molecular responses to drought stress in Vigna unguiculata L. Walp. Supervisor: Valdemar Carnide (UTAD), Co-supervisor: Teresa Lino-Neto (UMinho).

Ana Maria Cunha (2018) Functional characterization of AtDRIFs in Arabidopsis thaliana. Supervisor: Manuela Costa (UMinho), Co-supervisor: Sara Laranjeira (UMinho).

FunGP

MsC Thesis

Maria Joana Ribeiro (2018) Biochemical Studies on clinical variants of Glutaryl-CoA Dehydrogenase, a mitochondrial enzyme involved in the rare disease Glutaric Aciduria type-I. Supervisor: Bárbara J. Henriques (FCUL/BioISI), Co-supervisor: Cláudio M. Gomes (FCUL/BioISI).

Guilherme Gil Moreira (2018) Biochemistry of Tau aggregation and interactions in Alzheimer´s disease. Supervisor: Cláudio M. Gomes (FCUL/BioISI)

Raquel Centeio (2018) Diagnosis, Prognosis and Personalized Treatment of Cystic Fibrosis. Supervisor: Margarida D. Amaral (FCUL/BioISI), Co-supervisor: Karl Kunzelmann (Regensburg university).

Filipe Saúde (2018) Role of PKD1 and PKD2 on Ion Currents in Renal Epithelial Cells. Supervisor: Karl Kunzelmann (Regensburg university), Co-supervisor: Margarida D. Amaral (FCUL/BioISI).

PhD Thesis

Sara Canato (2018) The Endoplasmic Reticulum Quality Control: Dissecting Protein Networks in Cystic Fibrosis. Supervisor: Carlos M Farinha (FCUL), Co-supervisor: André Falcão (FCUL).

Ana Margarida Matos (2018) Search for new modulators of Phe508del-CFTR retention at the plasma membrane of epithelial cells. Supervisor: Paulo Matos (FCUL), Co-supervisor: Rainer Pepperkok (EMBL).

Verónica Felício (2018) Characterization of RNA dysfunctional mechanisms associated with the genetic disease Cystic Fibrosis. Supervisor: Margarida D. Amaral (FCUL/BioISI).

Nikhil T Awatade (2018) Using a Systems Approach to Identify the Mechanism of Action of Correctors. Supervisor: Margarida D. Amaral (FCUL/BioISI), Co-supervisor: Rainer Pepperkok (EMBL).

Joana Lérias (2018) Anoctamins - A Novel Family of Ion Channels With Extended Functions and Significance in Disease. Supervisor: Karl Kunzelmann (Regensburg university), Co-supervisor: Margarida D. Amaral (FCUL/BioISI).

M&B

MsC Thesis

Ana Marta Lourenço (2018). Deep-sea bacteria: a quest for sulfur and manganese oxidizers. MSc thesis UL (Master in Microbiology). Supervisor: R Tenreiro (FCUL/BioISI).

Ana Raquel Nogueira (2018). Building novel bioaugmention consortia for degradation of polycyclic aromatic hydrocarbons: from selection to metabolic and genetic characterization of adaptive evolved microbial strains. MSc thesis FCUL (Master in Applied Microbiology). Supervisor: R Tenreiro (FCUL/BioISI).

Gabriela Simões (2018). Construction of screening plataforms to evaluate bioactivity of Portuguese marine natural products. MSc thesis FCUL (Master in Molecular Biology and Genetics). Supervisor: H Vieira (FCUL/BioISI).

Miguel Ângelo Guerreiro (2018). Craft beer: from fermentation monitoring and optimization to microbiological quality control programme. MSc thesis UL (Master in Microbiology). Supervisor: R Tenreiro (FCUL/BioISI).

Rodolfo Ferreira (2018). Relation between biofilm formation and phytohormone production in plant growth promoting rhizobacteria. MSc thesis FCUL (Master in Applied Microbiology). Co-Supervisor: R Tenreiro (FCUL/BioISI).

PhD Thesis

Joana Costa Cardoso Cruz (2018). New Insights on Black Rot of Crucifers: disclosing novel virulence genes by in vivo host/pathogen transcriptomics and functional genetics. PhD thesis UL. Supervisors: L Cruz (INIAV/BioISI) and R Tenreiro (FCUL/BioISI).

João Pedro Pais (2018). Development of new antibiotics against Bacillus anthracis. PhD thesis UL. Co-supervisor: R Dias (FCUL/BioISI).

Susana Marques (2018). Carbon materials for removal of compounds with therapeutic activity in the aqueous phase and/or inactivation of pathogenic bacteria. PhD thesis UL. Co-supervisor: R Dias (FCUL/BioISI).

BTR

MsC Thesis

João Santos (2018) Investigating the Oligodendrocyte Progenitor Cells and their Progeny heterogeneity in the mammalian central nervous system- ERASMUS student. Supervisor: Gonçalo-Castelo-Branco (Kaolinska Institute), Co-supervisor: Helena Caria (FCUL/ESS-IPS).

PhD Thesis

Haúla Haider (2018) Frequência e características dos acufenos associados à Presbiacúsia. Supervisor: João Paço; (FCM-UNL;), Co-supervisor: Nuno Trigueiros e Helena Caria (FCUL/ESS-IPS). (FM-UP e FCUL/ESS-IPS).

Muhammad Asif (2018) A systems medicine approach to study Autism Spectrum Disorder based on genomic and clinical data. Supervisor: Astrid Moura Vicente (Instituto Nacional de Saúde Doutor Ricardo Jorge), Co-supervisor: Francisco Couto (Faculdade de Ciências).

Cibelle Mariano (2018) Biochemical and molecular characterisation of the dyslipidaemia in Portugal. Supervisor: Mafalda Bourbon (Instituto Nacional de Saúde Doutor Ricardo Jorge), Co-supervisor: Marilia Antunes (Faculdade de Ciências).

GER

MsC Thesis

Bárbara Raquel Cruz Martins (2018) Molecular characterization of cancer critical genes in feline mammary carcinomas and in the FkMTp cell line. Supervisor: Raquel Chaves (BioISI), Co-supervisor: Fernando Ferreira (Faculdade de Medicina Veterinária da Universidade de Lisboa).

Ana Rita Rodrigues Neves (2018) Identification and characterization of Internal Ribosome Entry Sites (IRES) in cancer pathways. Supervisor: L Romão (INSA), Co-supervisor: M Candeias (INSA).

Bruna Filipa Francisco Pereira (2018) Study on the regulation of the expression of alternative protein isoforms involved in carcinogenesis. Supervisor: L Romão (INSA), Co-supervisor: M Candeias (INSA).

João Paulo de Sá e Silva (2018) O papel da LARP4 no Sistema Nervoso Central: relação com a Atrofia Muscular Espinal. Supervisor: M Gama-Carvalho (FCUL), Co-supervisor: Ana Sebastião (IMM/FML).

Lúcia de Mendonça Heitor (2018) Development of a new pharmacogenomics system for lung cancer based in next generation sequencing. Supervisor: M Gama-Carvalho (FCUL)

PhD Thesis

Daniela Perneta Ferreira (2018) Molecular and Functional Characterization of a Satellite Non-Coding RNA– FA-SAT – a Key Player of Cycling Cells. Supervisor: Raquel Chaves (BioISI), Co-supervisor: Filomena Adega and Elsa Logarinho (BioISI and I3S).

Daniel Vigário Olivença (2018) A mathematical model of the phosphoinositide pathway in human pulmonary epithelial cells. Supervisor: Francisco Rodrigues Pinto (BioISI), Co-supervisor: Eberhard Voit (Georgia Tech).

Paulo Jorge Gomes Pereira da Costa (2018) The human mRNA decay machinery: an unexpected role for DIS3L2 over nonsense-mediated decay targets. Supervisor: L Romão (INSA), Co-supervisor: M Gama-Carvalho (FCUL).

Sara Maria Ferreira Fernandes (2018) Post-transcriptional regulation in the developing embryo. Supervisor: Maria Leonor Tavares Saúde (IMM/FML), Co-supervisor: M Gama-Carvalho (FCUL).

CBS

MsC Thesis

Andreia Fortuna (2018) Síntese e design racional de novos análogos de nucleósidos e de nucleótidos como potenciais inibidores de cinases com interesse terapêutico. Supervisor: Nuno Xavier (FCUL), Co-supervisor: Paulo J. Costa (FCUL).

Bárbara Oliveira (2018) New sensors based on chiral and achiral coordination polymers. Supervisor: Ana Vicente (FCUL), Co-supervisor: Paulo Martinho (FCUL).

Janaína Almeida (2018) Activation and Conversion of Small Molecules by Coordination Compounds. Supervisor: Paulo Martinho (FCUL), Co-supervisor: Sara Realista (FCUL).

Frederico Martins (2018) Magnetic Properties of First-row Transition Metal Compounds with Different Nuclearities. Supervisor: Paulo Martinho (FCUL), Co-supervisor: (FCUL).

César Reis (2018) Magnetic and Electrochemical Properties of new Mn(III) and Mn(IV) compounds. Supervisor: Paulo Martinho (FCUL), Co-supervisor: Liliana Ferreira (FCUL).

Monica Antunes (2018) Desenvolvimento de Novas Metodologias Analíticas para a Identificação de Novas Substâncias Psicoativas em Matrizes Biológicas. Supervisor: H. Gaspar (FCUL), Co-supervisor: Mario Barrosos (INMLCF).

Margarida Sequeira (2018) Identificação e Quantificação de Novas Substâncias Psicoativas em material apreendido em Portugal. Supervisor: H. Gaspar (FCUL), Co-supervisor: Maria João Caldeira (PJ).

Daniela Silva (2018) Otimização do fracionamento do efluente da cortiça recorrendo à tecnologia de membranas e quantificação do seu potencial anticancerígeno e antioxidante. - Supervisor : R. Pacheco (ISEL/BioISI), Co-Supervisor Miguel Minhalma (ISEL)

Laura Guedes (2018) Estudos de bioatividade de decocções de Centaurium erythraea.- Supervisor : M. Luisa Serralheiro (FCUL /BioISI), Co-Supervisor : Conceição Oliveira (IST)

PhD Thesis

Sara Realista (2018) Sequestration and reduction of CO2 using multifunctional metal-organic materials. Supervisor: Paulo Martinho (FCUL) , Co-supervisor: Maria José Calhorda and Ana Margarida Martins (FCUL and IST).

Asma Reissaissi (2018) Effect of Opuntia ficus-indicas's cladodes on cholesterol absorption, regulation of intracellular cholesterol metabolism and prevention from Alzheimer disease : in vitro studies. Supervisor : Nebil Attia (UC/FCB) Co-Supervisor : M. Luisa Serralheiro (FCUL /BioISI)

BioPhysNano

MSc Thesis

César Augusto Pifre Reis (2018) Magnetic and Electrochemical Properties in new Mn(III) and Mn(IV) compounds. Supervisor: Paulo Martinho (FCUL - BioISI), Co-supervisor: Liliana P. Ferreira (FCTUC - BioISI).

Gabriel Frederico Martins (2018) Photoactive molecular systems for solar thermal energy storage:application of density functional theory to the determination of thermodynamic parameters of azobenzene. Supervisor: Benedito Cabral (FCUL-BioISI)

João Nuno Especual (2018) Effects of confinement in the folding of knotted proteins. Supervisor: Patrícia Faísca (FCUL-BioISI)

MAS

MsC Thesis

Luana Brasil Dias (2018) Por que gostamos de música? - Um entendimento interdisciplinar para a Hipótese das Expectativas. Supervisor: Luís Correia (FCUL), Co-supervisor: Paulo Ventura, António Lopes (FPUL, FLUL).

David Sousa (2018) A Memória como Condição para o Sucesso da Cooperação. Supervisor: Luís Correia (FCUL), Co-supervisor: Leonel Garcia Marques (FPUL).

Inês Correia Viegas (2018) Identifying the sequence complexity of miRNAS and their functional impact in small-RNA-seq data. Supervisor: Andreia Amaral Fonseca (FMV-UL), Co-supervisor: Maria Beatriz Carmo (FCUL).

Catarina Cesteiro Alves (2018) Tutor Virtual para o ensino a distância (e-learning). Supervisor: Ana Paula Cláudio (FCUL), Co-supervisor: Maria Beatriz Carmo (FCUL).

Susana dos Santos Buinhas (2018) Assistente virtual para facilitaro autocuidado de pessoas mais velhas com diabetes tipo 2. Supervisor: Ana Paula Cláudio (FCUL), Co-supervisor: Maria Beatriz Carmo (FCUL).

Ricardo Costa (2018) Virtual Tutor: Information Retrieval in Moodle and Parametrization via a Backoffice Application. Supervisor: Ana Paula Cláudio (FCUL), Co-supervisor: Maria Beatriz Carmo (FCUL).

Miguel Melo (2018) Realidade Aumentada móvel combinada com mapas. Supervisor: Maria Beatriz Carmo (FCUL), Co-supervisor: Ana Paula Afonso (FCUL).

Tiago Moucho (2018) Visualeague II - Animated Maps for Performance Analysis in Games. Supervisor: Ana Paula Afonso (FCUL), Co-supervisor: Maria Beatriz Carmo (FCUL).

Alexander Fernandes (2018) Soluções para Alinhamento em Realidade Aumentada. Supervisor: Maria Beatriz Carmo (FCUL), Co-supervisor: Ana Paula Cláudio (FCUL).

N. Magessi (2018). O Risco e a sua Perceção: Factos e Razões. PhD thesis, Universidade de Lisboa. Supervision: L. Antunes

Projects

PFG

2018 Functional studies of plant membrane trafficking and secretion - the phosphoinositide pathway in the responses to abiotic stress, FCT. BioISI Budget: 187361.8€ (Total Amount of the project: 187361.8€). 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 & Raquel Chaves

2016 Plataforma de Inovação da Vinha e do Vinho – INNOVINE & WINE, União Europeia – FEDER. BioISI Budget: 0€. (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: 0€ (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: 151.076,66€ (Total Amount of the project: 239.123,6€). BioISI PI: Ana M 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 M 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 M Fortes

2018 Development of molecular markers for resistance to pine wilt disease in Pinus pinaster, FCT. BioISI Budget: 185.538,6€ (Total Amount of the project: 239.613,6€). BioISI PI: Célia Miguel

2018 Fostering High-Throughput Plant Phenotyping by an Interdisciplinary Approach (INTERPHENO), FCT. BioISI Budget: 166.661,3€ (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

FunGP

2018 CFMOLIM - Novas sondas de imagiologia molecular para Fibrose Quística, FCT. BioISI Budget: 30.000€ (Total Amount of the project: 233.315,1€). 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: 219.260,8€ (Total Amount of the project: 219.260,8€). 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. BioISI Budget: 0€ (Total Amount of the project: 286.587€). BioISI PI: José P Gil

2018 Identification of novel F508del-CFTR traffic correctors among FDA-approved drugs., Gilead Sciences. BioISI Budget: 113.978€ (Total Amount of the project: 113.978€). BioISI PI: M Lopes-Pacheco, mentored by MDAmaral

2018 iDrugCF - Identification of New Drugs for Cystic Fibrosis, FCT. BioISI Budget: 160.000€ (Total Amount of the project: 240.000€). BioISI PI: MD Amaral

2018 Personalised Therapies for all: Restoring airway function in CF using Alternative Chloride Channels, CF Trust Strategic Research Centre AwardBioISI Budget: 224.000€ (Total Amount of the project: 843.491€). BioISI PI: 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.

2016 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL16I0) "Characterization of Orphan CFTR mutations". Budget: 108K$; 2 yrs. PI: MD Amaral

2016 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL15XX1) "RNA LIFE – Novel RNA Regulators as Potential Drug Targets for Cystic Fibrosis". Budget: 324K$; 2 yrs. PI: MD Amaral.

2016 FCT/POCTI (PTDC/BIM-MEC/2131/2014) "DIFFTARGET-Novel Factors of CFTR Traffic Related to Epithelial Cell Differentiation: Potential Therapeutic Targets for Cystic Fibrosis". Budget: 200.000€; 3 yrs. PI: MD Amaral.

2016 FCT/POCTI (PTDC/QEQ-SUP/4283/2014) "FARMTRANSANION-Anion transmembrane transport promoted by drug-like molecules: building a library of anion carriers inspired in Ataluren (PTC124)". Budget: 200.000€; 3 yrs. PI: V Félix.

FCT/POCTI (PTDC/EEI-ESS/4923/2014) "MIMED - Mining the Molecular Metric Space for Drug Design". Budget: 127.000€; 3 yrs. PI: A Falcão

2015 ERARE15-pp-010/JTC 2015 "INSTINCT - Induced Pluripotent Stem Cells for Identification of Novel Drug Combinations Targeting Cystic Fibrosis Lung and Liver Disease". Budget (FFCUL): 124K; 3 yrs. Principal Investigator (U Martin, Univ. Hannover, Germany). FCUL PI: MD Amaral.

2014 CF Trust Strategic Research Centre Award (Ref. SRC 003) "INOVCF-Innovative non-CFTR Approaches for Cystic Fibrosis Therapies". Total budget: 750K£. FCUL Budget: 178.4K€; 4 yrs. PI: M Gray, Newcastle (UK). PI for the FCUL group: MD Amaral.

M&B

2016-2019 POINT-PAC 2016, LISBOA-01-0145-FEDER-016405: Precision Oncology by Innovative Therapies and Technologies. FCUL and 9 National Institutions. Total Budget: 1.9 M€; Total Funding: 763 K€; FCUL Funding: 75 k€. M&B BioISI Team: H Vieira (FCUL/BioISI).

2016-2019 VINOVERT: Wines, competitiveness, environmental and health policies of the entreprises of SUDOE area - Support for methodologies implementation. INTERREG project SOE1/P2/F0246. Funding: 10 k€. M&B-BioISI team: F Duarte (INIAV/BioISI).

2017-2020 BIOINVENT: Generic bio-inventory of soil microbial diversity and functioning in permanent grassland ecosystems across management and climate gradients. University of Hohenheim (Proponent), FCUL, Univ Açores, Swedish University of Agricultural Sciences, Agroscope Switzerland. Total Funding: 1,68 M€.FCUL PI: C Cruz. M&B-BioISI team: R Tenreiro (FCUL/BioISI).

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

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

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

2015-2019 SMARTWINE - Smarter wine fermentations: integrating Omics-tools for development of novel mixed-starter cultures for tailor-made wine production. FCT, COMPETE, FEEI. PTDC/AGR-TEC/3315/2014. Total funding: 196 k€. BioISI/UTAD: 103 k€. PI: A. Mendes-Faia (UTAD/BioISI).

2016-2019 BIOCLUB - Designing biofertilizers by mimicking plants' recruitment of rhizospheric partners. FCT. PTDC/AGR-PRO/1852/2014. Proponent: FCiências.ID (CE3C). Total funding: 199 k€. PI: C. Cruz (FCUL/CE3C). M&B Team: R Tenreiro (FCUL/BioISI), A Tenreiro (FCUL/BioISI), S Chaves (SGS/BioISI) .

2016-2019 HOSTSTREP II - Specific evaluation of the host and pathogen-host interactions agent in Streptococcus. FCT. PTDC/CVT-EPI/6685/2014. Proponent: FCT-UNL. Total funding: 199 k€. PI: I Sanches/JP Sampaio (FCT/UNL). M&B Team: R Tenreiro (FCUL/BioISI), L Chambel (FCUL/BioISI).

2016-2019 Molecular and Mechanical Forces in Biology measured with Force Feedback Microscopy. FCT. PTDC/FIS-NAN/6101/2014. Proponent: FFCUL (BioISI). Total funding: 197 k€. PI: M Rodrigues (BioISI-MagNano). M&B Team: L Fernandes (IPL/BioISI).

2016-2019 NEMATRANSFER - Can the Pine Wilt Disease cycle be broken? Decoding transfer mechanisms of the pinewood nematode Bursaphelenchus xylophilus between its insect-vector Monochamus galloprovincialis and the host tree Pinus pinaster. FCT. PTDC /AGR FOR/4391/2014. Total funding: 199 k€. PI: L Bonifácio (INIAV). M&B-BioISI team: J Henriques (INIAV/M&B-BioISI).

2016-2019 Phleboviruses in Portugal: vectors, pathogenesis and co-infections. FCT. PTDC/DTP-SAP/0859/2014. Proponent: INSA. Total funding: 164 k€. PI: F Amaro (INSA). M&B Team: L Zé-Zé (INSA/BioISI).

2018 Yeast as a model to assess drugs - the case of Cystic Fibrosis. IPL/IDI&CA2018/ESTeSL (funded by Instituto Politécnico de Lisboa). Host institution: BioISI. Total funding: 5 k€. PI: L Fernandes (EST-IPL/BioISI).

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

2018-2021 Fire4Cast - Fitting immunocytometry and RNAtechnologies for epidemiological modeling of fire blight. 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/BioISI), R Tenreiro (FCUL/BioISI).

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

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

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

2016-2018 LEVEalliance II - towards a portfolium of adaptively evolved yeasts for the production of lower ethanol content wines. Associated company: Proenol. Funding 2018: 10 k€. M&B-BioISI team: AC Rocha, A Tenreiro, R Tenreiro

INNOVINE&WINE – Vineyard and Wine Innovation Platform. NORTE-01-0145-FEDER-000038. Activity 3.2 – Managing fermentation practices towards the production of targeted high quality wines with regional character. FEDER) através do NORTE 2020. Partners: UTAD, CQ-VR, CITAB. 2016-2019. Total funding: 5.29 M€. UTAD/BioISI funding: 123 k€. UTAD/BioISI team: A Mendes-Ferreira.

2016-2019 INTERACT– Integrated Research in Environment, Agro-Chain and Technology. NORTE-01-0145-FEDER-000017, in its line of research entitled VitalityWINE. ERDF, NORTE 2020. Partners: UTAD, CQ-VR, CITAB. Total funding: 4.12 M€. UTAD/BioISI funding: 124 k€. UTAD/BioISI team: A Mendes-Faia, A Mendes-Ferreira, C Barbosa .

2016 RESISTIR - Intelligent information system to control infection and personalized antibiotherapy. POCI and POR Lisboa. P2020 project nº 3379. Proponent Company: MAXDATA Software SA. Partner: FCUL. 2016-2019. Total funding: 1.05 M€. M&B-BioISI funding: 449 k€. FCUL PI: R. Dias (FCUL/BioISI).

2016-2019 Strategic Project for Support of Wine Sector in Centro Region: Evaluation of agronomic and enologic behaviour of recommended and autochthonous vine varieties with potential interest for CVR LIsboa region. PO CENTRO-04-3928-FEDER-000001. Total funding: 183 k€. PI: Eiras-Dias (INIAV). M&B Team: F Duarte (INIAV/BioISI), M Baleiras-Couto (INIAV/BioISI).

2017-2018 Vale I&D - Development of starter cultures through the isolation and selection of autochthonous yeasts to improve expression of organoleptic and sensory characteristics specific for each wine region. Total funding: 21 k€. UTAD/BioISI team: A Mendes-Ferreira.

2017-2019. NewID - New approaches for taxonomic identification and profiling of poli-clonal samples based in Next Generation Sequencing. Associated company: SGS Molecular. Total funding: undisclosed. M&B-BioISI team: R Dias

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

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

GER

2018-2021 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

2018-2021 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.

2018-2021 New signaling pathways involved in the retention of epithelial chloride transporters FCT. BioISI Budget: 239.411,11€ (Total Amount of the project: 239.411,11€). BioISI PI: Vânia Gonçalves

2018-2021 PulmaGENE Portugal2020 Proponent Company: STAB VIDA and BioISI/UTAD. BioISI Budget: 332.000 € (Total Amount of the project: 680.902,52€). BioISI PI: Raquel Chaves

2017-2020 LungCARD. H2020-MSCA-RISE EU Project. Proponent Company: STAB VIDA. Budget: 144K€ (Total Amount of the project: 1M€) BioISI PI: Margarida Gama-Carvalho.

2016-2019 Nonsense-mediated mRNA decay in genetic diseases and cancer: key players, mechanisms, and a novel approach for suppression therapy FCT. BioISI Budget: 200K€. BioISI PI: Luisa Romão

2015-2018 FlySMALS: Common RNA-dependent pathways for motorneuron degeneration in SMA and ALS. EU JPND BioISI Budget: 139K€€ (Total Amount of the project: 796K€) 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: 233254.12€). BioISI PI: M. 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: M. 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: M. Machuqueiro

2016 Multifunctional Luminescent Spin Labile Hybrid Materials, FCT. BioISI Budget: 27.500€ (Total Amount of the project: 191.879€). BioISI PI: Paulo Martinho

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: M. Machuqueiro

2018 Deal with PAINS: strategies to identify membrane modulators, FCT. BioISI Budget: 235.111,5€ (Total Amount of the project: 235.111,5€). 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€ (Total Amount of the project:). 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: M. J. Calhorda

2016 Overcoming environmental problems associated with antifouling agents: synthesis of Nature-inspired non-toxic biocides and immobilization in polymeric coatings, FCT-COMPETEBioISI 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. BioISI Budget: 0€ (Total Amount of the project: 232.723,4€). BioISI PI: L. Serralheiro

2018 Creating Opportunities from Seaweed Sulfated polysaccharides for Application in Therapeutics, FCT. BioISI Budget: 0€ (Total Amount of the project: 239.898,16€). BioISI PI: H. Gaspar

2017 POINT4PAC – Precision Oncology by innovative therapies and technologies, FCT. BioISI Budget: 0€ (Total Amount of the project: 2.405.032,23€). BioISI PI: H. Gaspar

2016 Red2Discovery - The red macroalgae Sphaerococcus coronopifolius and Asparagopsis armata as targets for the discovery of new drugs of marine origin, FCT. BioISI Budget: 0€ (Total Amount of the project: 174.110 €). BioISI PI: H. 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: M. J. Calhorda

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: 150.000€ (Total Amount of the project: 200.000€). BioISI PI: Mário Rodrigues

2018 Development of sustainable materials for application in flexible electronic and energy harvesting devices, FCT. BioISI Budget: 20.612,5€ (Total Amount of the project: 232.481,1€). 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

2018 VASelfCare – Assistente virtual para facilitar o autocuidado de pessoas mais velhas com diabetes tipo2, FCT. BioISI Budget: 58,261.74€ (Total amout 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, FCTBioISI Budget: 60.967€ (Total Amount of the project: 199.706,00€). BioISI PI: Ana Paula Cláudio

Dates refer to the start of the project