INSTITUTO
GULBENKIAN
DE CIÊNCIA

Mission Statements

1. MBT (Tráfico de Membranas) - Adrain, Colin

60% of all current drugs target membrane proteins, illustrating the medical importance of this pathway. However the complex biogenesis and trafficking of many signalling proteins is poorly understood, providing an incentive to understand the secretory pathway better. In eukaryotes, one third of translated proteins are secretory proteins. These fold in the endoplasmic reticulum (ER) and traffic to the plasma membrane, where signalling occurs.

Until recently, it was believed that secretory traffic was accomplished by a default mechanism called 'bulk flow' whereby newly synthesized proteins are packaged into trafficking vesicles at the rate that they are produced.

However, it is now clear that trafficking, especially of membrane proteins, is controlled by additional influences, including trafficking partners, post-translational modifications, or regulation of protein stability.

The group mission is to explores how secretory trafficking coordinates cellular signalling during normal physiology, and its contribution to inflammatory disease and cancer.

Their work currently focuses on three areas being developed, using a combination of mouse genetics, disease models, cell biology and biochemistry:

A. How membrane trafficking regulates signalling controlled by the metalloprotease ADAM17/TACE.
B. Role of quality control in the secretory pathway in vivo in mice, during development and disease.
C. Genetic screens to identify novel trafficking factors

2. EME (Interacções Ácidos Nucleicos - Proteínas) - Athanasiadis, Alekos

Proteins demonstrate an impressive ability not only to recognize and bind to particular pieces of nucleic acids code but also to alter its information content by catalysing reactions that rearrange its sequence or specifically change one nucleotide for another. Organisms have found in such mechanisms the means for creating sequence diversity as it is gloriously exemplified in the diversification of immunoglobulin genes. The recent realization that multi-cellular organisms achieve phenotypic complexity without a parallel increase in number of genes has highlighted the importance of posttranscriptional RNA modifications in creating and fine-tuning a much larger repertoire of proteins originating from a small number of genes.

The EME mission is to study the molecular mechanisms involved in RNA and DNA diversification of sequence as well as understanding the consequences of such processes for molecular evolution dynamics.

Presently their work is focus on the A to I RNA editing process which alters the sequence of thousands of human pre-mRNAs (Athanasiadis et al., 2004), having this way a prominent role in regulating Innate Immune responses to dsRNA.

Their main research projects are:

Molecular basis of the recognition of foreign nucleic acids in innate immunity

Computational modeling of the A to I RNA editing process

3. PSS (Sinalização de Stress em Plantas) - Baena González, Elena

Mounting evidence suggests that in plants, environmental information is partly conveyed through sugar signals. Accordingly, sugars have been linked to stress responses, to the regulation of growth and to specific developmental transitions such as germination and flowering. How the plant nutrient status is integrated with other signals into adequate growth and developmental decisions is poorly understood, but one central component in this process is the SNF1-related Protein Kinase1 (SnRK1). SnRK1 is an evolutionary conserved protein kinase complex that regulates energy homeostasis in plants. In doing so, it promotes tolerance to adverse environmental conditions and influences a large array of growth and developmental processes. Despite the importance of SnRK1 virtually nothing is known about how it operates.

The mission of te group is the dissection of this key pathway as a first step towards understanding how plants cope with adverse conditions and how energy signals influence plant growth and development.

The group is undertaking a multifaceted strategy that combines biochemical approaches, transient cell-based assays, and genetics with mutant screens and proteomics to address:

How is SnRK1 regulated;

How does SnRK1 control gene expression;

How does SnRK1 interact with the ABA pathway, also central to stress responses and development;

What are the cellular processes under SnRK1 control?

4. EVD (Dinâmica evolutiva) - Bank, Claudia

The group investigation revolves around the population genetics of adaptation and speciation, with a particular interest in the prevalence and importance of epistasis and other interaction effects on both the molecular and the population level.

To develop the research they use mathematical modeling, computer simulations, and statistical data analysis (primarily from experimental-evolution approaches). Their main research questions are:

What can empirical fitness landscapes tell us about adaptation to new environments?

How do genetic interactions affect adaptation and speciation?

Can we predict antibiotic resistance using evolutionary theory?

5. PLG (Genómica das Plantas) - Becker, Jörg

The group is investigating the mechanisms controlling sexual reproduction and early embryogenesis. The mission is to study these processes in two plant model species: The angiosperm Arabidopsis thaliana and the bryophyte Physcomitrella patens. Focusing on how (epi)genetic mechanisms act during male gametogenesis and how changes come about and what are their potential consequences after fertilization.

In the long run their project mission is to contribute to a better understanding of sexual reproduction in higher plants - a knowledge gain crucial to overcome fertilization barriers and

enhance crop productivity, with the ultimate goal to increase our capacity to generate sufficient food, animal feed and energy. Curently their main research projects are:

Heterogeneous expression in isomorphic male gametes

Evolution of sexual reproduction in plants

Origins of plant centrioles

6. VDS (Variação: Desenvolvimento e Selecção) - Beldade, Patrícia

Heritable phenotypic variation is the raw material for natural selection, and a universal property of biological systems. Understanding the mechanisms that generate this variation is a key challenge in biological research.

The group is investigating evolutionary developmental biology, focusing on the mechanistic basis of phenotypic variation and adaptation. The group misison is to understand sevreal key questions:

The contribution of novel genes to the formation of evolutionary novelties

Coping with changing environments: genetic and physiological mechanisms of adaptive plasticity

Evolution of caste polyphenism in social insects: patterns of morphological diversification in ants

For the dissection of variation in complex, diversified and ecologically-relevant phenotypes the lab is currently using three complementary systems: wing color patterns in butterflies, body architecture in ants, and pigmentation in flies.

7. CCR (Regulação de Ciclo Celular) - Bettencourt Dias, Mónica

The group is developing it's work in general principles in biology regarding the counting and assembling of complex subcellular structures, and their variations observed during development, in disease and evolution.

In their investigation they use complex cytoskeletal assemblies, such as centrioles and cilia, as study subjects. By using multidisciplinary approaches, the laboratory identified critical molecular regulators of centriole number and cilia motility, circuits that control those players, and mechanisms involved in the evolution of those structures.

Currently they follow three complementary research lines in their output: Basic Mechanisms of Biogenesis, Function and Maintenance, Disease (cancer) and Evolution.

This creates:

i. a broad critical mass;

ii. In-house mastering of assays across all scales (in vitro, ex-vivo, cell and organism, modelling, bioinformatics and clinical samples);

iii. knowledge of the same paradigm from different perspectives (development, disease states and different organisms) which cross-fertilise.

The group mission is to identify rules and paradigms that can be extended to other structures and can be used to synthesize artificial structures that are inherited in cells. Furthermore, they envision to identify novel ways by which cells communicate and regulate each other within an organism, and with this provide novel insights to diagnostics and treatment of human disease. Besides scientific research, Their mission is also one of training scientists and communicating science to lay people.

Main research projects

A. Mechanisms of cilia diversification
B. Spatial control of centriole biogenesis
C. Temporal control of centriole biogenesis
D. Centriole and cilia stability and maintenance
E. Causes and consequences of centriole deregulation in cancer
F. Evolution of microtubule organising centres

8. QOB (Biologia Quantitativa do Organismo) - Carneiro, Jorge

Cells of multicellular organisms cooperate to ensure body development and maintenance throughout life. They do this in a collective distributed manner, without any master or plan.

The Quantitative Organism Biology group mission is to studies the multilevel mechanisms that give rise to properties of the whole organism, in search for general principles of biological organisation and, eventually, the design of artificial systems.

Their main research interests are:

A. The immune system, in which cells collectively ensure body housekeeping and homeostasis, avoid autoimmune diseases, and fight cancer and infections.
B. The morphodynamics of cells and tissues during fertilization and embryonic development of metazoan.

Their approach is twofold: on the one hand, they create mathematical models of specific exemplary systems aiming to uncover basic principles, and on the other hand, they develop the quantitative methods required to assess the properties and predictions of these models.

9. MNB (Neurobiologia Molecular) - Castro, Diogo

MNB mission is to understand how global programmes of gene expression are regulated during vertebrate neurogenesis. Along the neuronal lineage, an intrinsic programme that relies on the activity of transcription factors and the epigenetic landscape coordinates the progression of progenitors throughout distinct cellular stages.

In order to understand the regulatory logic of neurogenesis, they focus our studies on proneural transcription factors (e.g. Mash1/Ascl1) that function as master regulators of neurogenesis by coordinating the various components of the differentiation programme. They investigate how

Ascl1 interacts with the chromatin landscape and other transcriptional networks, in particular the Notch pathway.

In addition, they are also interested in understanding how key transcriptional networks that underlie neural stem cell function are hijacked during tumorigenesis.

They develop their research using a multidisciplinary approach, combining mouse genetics, genomics and stem cell biology techniques.

Groups main research projects:

A. Transcription control of vertebrade neurogenesis by Proneural and Notch pathways
B. Function of the zinc-finger factor ZEB1 in neural stem/progenitor cells
C. Mitotic bookmarking by transcription factors in vertebrate neurogenesis

10. PCG (Genética de Populações e da Conservação) - Chikhi, Lounes

Genetic and genomic data are influenced by the demographic events that have shaped the history of populations. Such events include population collapses, expansions, or admixture processes.

The group mission is to develop new and using/testing existing methods to improve the understanding of these events and of the recent evolutionary history of species. They also, and crucially, want to understand the limits of genetic or genomic data as inferential tools. Where the applications go from human evolution (e.g. the Neolithic transition in Europe) to conservation genetics of wild (e.g. orang-utans, lemurs, dolphins) and domesticated species (e.g. cattle, sheep).

Their work is currently done at the Population and Conservation Genetics (PCG) group involves fieldwork in Madagascar, Guiné-Bissau and Portugal, and the genetic typing of endangered species (lemurs, endemic and invasive rodents, red colobus, bottlenose dolphins) data analysis and simulation. Additionally, they collaborate with the laboratory Evolution & Diversité Biologique, in Toulouse and with colleagues from various institutions, UK (Reading University), France (Institut de Mathématiques de Toulouse), Madagascar (Univ. Mahajanga, Antananarivo, Antsirana), or Malaysia (Danau Girang Field Station).

The group main research projects are:

A. Demographic and Genetic Responses to Habitat Fragmentation and Habitat Loss in Large Forest Mammals
B. Conservation, phylogéographie et génetique de lémuriens dans des habitats fragmentés de Madagascar et de l'archipel des Comores

11. IS (Fisiologia Linfócitos) - Demengeot, Jocelyne

The group study the properties of the immune system that guarantee tissue integrity as well as tolerance to commensals and food antigens while maintaining the ability to mount efficient responses to infectious agents and some tumours.

They approach the cellular and molecular bases of immune regulation through the analysis of various mouse models, notably of spontaneous or induced autoimmune and immuno-pathological inflammation.

Their mains research projects are:

A. Targets and off targets of Recombination activating genes
B. Immune regulation for Immunotherapies

12. NOB (Obesidade) - Domingos, Ana

Organisms evolved biological mechanisms that maintain an individual's body weight within a narrow range of variation. For that purpose, different organs such as brain, fat, liver, bone, pancreas, and even the immune system, integrate nutrient-related and hormonal signals to control weight homeostasis.

The lab mission is to increase the knowledge about the function of the nervous system in weight control, aiming at identifying neurons that play a fundamental role in eating behaviour and metabolism.

They rely on newly developed targeted mouse strains that enable the application of state-of-the-art neuro-genetic techniques: using optogenetics to establish the role of molecularly identified populations of neurons, and Translational Ribosome Affinity Purification – TRAP – to identify molecular targets with neuromodulatory activity enriched in those key neurons.

They believe that their experimental approach will pave the way for the identification of novel molecular targets with potential in the treatment of obesity.

13. PRM (Biologia Molecular de Plantas) - Duque, Paula

As sessile organisms, plants have evolved unique strategies to cope with environmental challenges that affect their growth and development. These range from morphological and physiological changes to alterations at the cellular level, but the basis for adaptation or acclimation lies ultimately at the level of the genome.

The Plant Molecular Biology group uses *Arabidopsis thaliana* as a model system to investigate how plants perceive and respond to environmental stress at the molecular level. In particular, the group is focus on the role of RNA alternative splicing in the regulation of gene expression. Another major ongoing project in the lab is uncovering a role for membrane transporters of the Major Facilitator Superfamily (MFS) in plant development and responses to abiotic stress.

Mains research projects:

A. Functional relevance of alternative splicing and SR proteins in plant stress responses
B. Roles of MFS membrance transporters in plant development and stress tolerance

14. EVB (Biologia Evolutiva) - Gordo, Isabel

The group develops research in Evolutionary Biology, with a focus on microbial evolution. They combine both theoretical and empirical work aiming at understanding the major mechanisms that shape variation of bacterial populations in their natural environments.

The present and future projects of the research team are:

A. Adaptation in the gut microbiota ecosystem in health and disease, using Escherichia colias a model organism;

B. Test theoretical models of adaptive evolution against genotypic and phenotypic data obtained in experimentally adapted microbial populations;

C. Study the evolutionary mechanisms underlying the maintenance of antibiotic resistance to commonly used antibiotics and develop novel tools to lower resistance levels;

D. Study the evolution of mutation rates and determine the factors that influence polymorphism for mutation rates in microbial populations.

15. CAI (Co-Evolução Hospedeiro Patogénio) - Howard, Jonathan

The group work is focus on mechanisms of resistance to the ubiquitous intracellular protozoan parasite, *Toxoplasma gondii*, a malaria relative, which infects about 40% of the human race.

They study immunity of mice against *T. gondii* since the primary hosts of the parasite, in which it makes gametes and does meiosis, is cats, so the *T. gondii* life cycle, and its abundance in the environment, is thus driven by an infectious cycle between cat and mouse. Their work stretches from ecological studies on wild mice to cell biological, biochemical and structural studies.

The group currently main research project is:

A . Cell-autonomous resistance of human and mouse cells against Toxoplasma gondii

16. CRI (Padronização e morfogénese) - Mallo, Moises

The group is interested in several aspects of vertebrate embryonic development. The ultimate mission of their research is to understand the molecular mechanisms that translate patterning information into morphogenetic processes during formation of the vertebrate embryo.

Understanding what regulates the behaviour of the axial progenitors responsible for producing the different body elements has become one of the main focuses of their laboratory. More recently, they have also become interested in the role that those processes played in the evolution of the vertebrate body plan.

In general, most of the work uses the mouse as the model system, and the approaches have a main focus on in vivo functional analyses complemented with in vitro differentiation systems based on stem and progenitor cells.

The group main research projects are:

A. The role of Hox genes in the development of the vertebrate axial skeleton

B. Molecular control of vertebrate body axis extension

17. LDL (Desenvolvimento de Linfócitos e Leucemia) - Martins, Vera

Research in the *Lymphocyte development and Leukemogenesis Laboratory* focuses on lymphocyte development, both under steady state, physiological conditions, as well as in leukemia. T lymphocyte development occurs mostly in the thymus from progenitors of bone marrow origin in a process that involves high cellular turnover. We found that thymus turnover is regulated by cell competition. Specifically, the seeding of the thymus by 'young' hematopoietic precursors (with a short dwell time in the thymus) led to the clearance of the 'old' precursors (residing for longer in the thymus).

The *Lymphocyte development and Leukemogenesis Laboratory* focuses on the identification of the cellular and molecular mechanisms governing lymphocyte differentiation, normal thymus turnover, thymus autonomy and on the changes associated with the malignant transformation of lymphocyte precursors.

18. III (Imunidade Inata e Inflamação) - Moita, Luis

The laboratory works on two different topics: innate immunity and inflammation.

Their focus on innate immunity is centered on the study of antigen cross-presentation mechanisms and the immunobiology of dendritic cells. They usw a series of systematic genetic approaches to identify the molecular machinery involved in antigen cross-presentation. In addition, they want to explore antigen cross-presentation as an early immune-regulatory checkpoint in the control of CD8+ T cell priming by dendritic cells, to find drugs that inhibit negative regulators of this process, as they are likely to improve the generation of effective T cells responses against tumors and are good candidates for novel adjuvant therapies for cancer treatment.

The second theme of the laboratory relates to inflammation. Severe sepsis remains a poorly understood systemic inflammatory condition with high mortality rates and limited therapeutic options outside of infection control and organ support measures. The central goal of their research program in this field is to identify and characterize novel cytoprotective mechanisms, with a focus on DNA damage response dependent protection activated by anthracyclines as a window into stress-induced genetic programs leading to tissue protection.

19. IBBG (Integrative Behavioral Biology Group)- Oliveira, Rui

ANB group main research interest is the integrative study of social behaviour, which combines the study of proximate causes (gene modules, hormones, neural circuits, cognitive processes) and ultimate effects (evolutionary consequences).

Particularly, the group aim to understand how brain and behaviour can be shaped by the social environment and how the cognitive, neural and genetic mechanisms underlying plasticity in the expression of social behaviour have evolved.

Current research questions centre on four topics:

A. Evolution of social cognition and of its neuromolecular mechanisms – we aim to understand if social cognition is an organismal performance trait that impacts Darwinian fitness and may itself be subject to selection;

B. Genomic and epigenomic mechanisms of social behaviour – we seek to understand how the same genome can produce different social phenotypes in response to key social cues in the environment;

C. Neuroendocrinology of social behaviour – we aim to understand the role of hormones and neuropeptides (oxytocin/vasotocin) as neuromodulators involved in the plasticity of social behaviour;

D. Fish cognition and welfare – since our model organisms are fish we aim to use our knowledge in this field to improve fish husbandry and handling procedures towards better research and animal welfare.

20. CHR (Dinâmica dos Cromossomas) - Oliveira, Raquel

The group studies how chromosome architecture contributes to faithful genome segregation. The laboratory adopts a multidisciplinary approach, combining Drosophila genetics, acute protein inactivation, 4D-live cell imaging and biophysical/mathematical modelling to evaluate how dynamic mitotic chromosomes are assembled and how their morphology influences the mechanical aspects of chromosome movement and cell cycle checkpoint signalling.

In parallel they aim to dissect how different cells respond to compromised chromosome cohesion and condensation, both at the cellular and organism level. By studying the contribution of chromosome structure in the mechanics of nuclear division they want to to identify novel routes to aneuploidy that underlie several human conditions, including developmental diseases, cancer and infertility.

21. IIM (Infecção & Imunidade) - Parkhouse, Michael

The theme of the group is the reciprocal adaptation between an infectious organism and its host. The necessity to recognise and destroy invading pathogens has played a crucial role in the evolution of the immune system of both vertebrates and invertebrates. At the same time, pathogens, in particular, viruses have evolved strategies to manipulate the immune system. An efficient immune system must select the immune effector mechanism most appropriate to the biology of the pathogen. Thus the study of how pathogens control immune responses will offer novel approaches for the manipulation of the immune responses in health and disease, with novel vaccines and strategies to downregulate the immune system (e.g. inflammation) being the most obvious possibilities.

Therefore, the group mission is identifying and characterising virus host evasion genes directed towards subversion of cell biology and innate immunity. In order to do it, they have selected two viruses with very different lifestyles (HCMV and ASFV)

the main research projects are:

A. The potential and application of virus host evasion genes that modify apoptosis and cytokine responses

B. Control of human, bovine and porcine cysticercosis through vaccination and improved diagnostics

22. GDO (Genética de Doenças) - Penha Gonçalves, Carlos

The group previous research in genetics of inflammatory responses to malaria infection drove them to the question: how infection/inflammation impacts on cellular metabolism and organ physiology?
One line of their research is focused on how placental inflammation caused by malaria leads to placental dysfunction. This research will impact the understanding of the involvement of foetal factors in vaso-inflammatory placental disorders and may unveil pharmacological targets to promote fetal viability and fetal protection mechanisms valuable in abortion and stillbirth prevention.

The malaria research group is also looking at the dialogue of brain microvessel endothelial cells with infected erythrocytes and immune cells in the context of the requirement of interferon in the development of cerebral malaria. This

A third line of research concerns the role of liver cells in metabolic imbalances including diabetes, non-alcoholic fatty liver disease and liver fibrosis. Translation of this research profits from analysis of human population collections and is geared to scrutinize cellular and molecular targets of liver disease treatments.

23. DIN (Sistemas Adaptativos Complexos e Biologia Computacional) - Rocha, Luís

The group research is focused in the informational properties of natural and artificial systems, which enable them to adapt and evolve. Their mission is to investigate both, understanding how information is fundamental for controlling the behaviour and evolutionary capabilities of complex systems, as well as abstracting principles from natural systems to produce adaptive information technology. This theoretical and applied research agenda is organized in three main threads:

i. Complex networks & systems
ii. Computational & Systems Biology
iii. Computational Intelligence.

The group mains research projects are:

A. Biomedical Literature Mining
B. Collective Dynamics in Complex Biochemical Networks
C. Computational Models of RNA Editing
D. Artificial Models of T-Cell Cross-Regulation
E. Stochastic Models of Topology Constraints on Complex Networks

24. INF (Inflamação) - Soares, Miguel

Immunity evolved in multicellular organisms to limit the negative impact exerted through their interaction with microbes. Innate and adaptive components of the immune system can sense and target pathogenic microorganisms for containment, destruction or expulsion as the means to preserve host homeostasis and fitness. Resistance to infection refers to these immune functions. In addition, multicellular organisms evolved another defense strategy that preserves homeostasis and fitness without exerting a direct negative impact on microorganisms. This defense strategy, referred to as disease tolerance, relies on evolutionarily conserved stress and

damage responses that limit the extent of metabolic dysfunction and damage imposed to host parenchyma tissues by pathogenic microorganisms or by immune-driven resistance mechanisms. The major aim of the INF laboratory is to identify and characterize these stress and damage responses conferring tissue damage control and establishing disease tolerance to infections. The central hypothesis tested is that there is a functional interplay between immune-driven resistance mechanisms and stress and damage responses acting in parenchyma tissues, which limits the pathogenic effects of infection. Understanding the mechanisms governing this functional interplay should be transformative in our understanding of host microbial interactions, with direct impact on the treatment of infectious diseases.

The group mains research projects aim to identify and characterize:

A. Organismal metabolic responses establishing disease tolerance to infection.
B. The involvement of the autonomic nervous system in the establishment of disease tolerance to infection.
C. How components of the transcriptional stress and damage control network contribute to the establishment of disease tolerance to infection.
D. How components of the transcriptional stress and damage control network controle the pathogenesis of immune-mediated inflammatory diseases.
E. How core effector genes of the transcriptional stress and damage control network contribute to the establishment of disease tolerance to infection.
F. How core effector genes of the transcriptional stress and damage control network control the pathogenesis of immune-mediated inflammatory diseases.
G. How cellular component of the innate and adaptive immune system contribute to the establishment of disease tolerance to infection.
H. How α-gal immunity can be manipulated towards the development of vaccines against pathogens expressing α-gal.
I. How α-gal immunity impacts on host microbial symbiotic interactions

25. EVO (Evolução e Desenvolvimento) - Sucena, Élio

The *Evolution and Development* lab mission is to explore the interface between the fields of evolution and developmental biology with the ultimate purpose of contributing to the understanding of the rules by which this interplay shapes organisms across evolutionary time.

In particular, research carried out in the lab focuses on evolutionary novelties, that is, new traits (either morphological, physiological or behavioural) that may participate in the emergence of adaptive radiations into novel niches.

They approach this concept experimentally at different levels of biological organization and through both the comparative method and experimental evolution. Specifically, looking into novelty at:

i. The genetic level, studying gene expression evolution upon gene duplication;
ii. The cellular level, approaching immune cell function diversity and hematopoiesis in *Drosophila*;
iii. The organismal level, by studying the evolution of the immune response in arthropods using *Drosophila melanogaster* as a reference model.

The group main research projects are:

A. Evolution of gene regulation and function
B. Immune cell function diversity in Drosophila
C. Dissecting the developmental genetic basis of morphological novelty
D. Evolution of immune response in Drosophila melanogaster

26. HMI (Interacções Hospedeiro – Microorganismo) - Teixeira, Luis

HMI research group mission is to understand how hosts interact with microorganisms at the functional and evolutionary levels. The group approaches this subject from the classical pathogen versus host immunity perspective and also by analysing the interaction of the host with commensals and mutualists. We address this general problem studying Drosophila melanogaster interaction with viruses, intracellular bacteria (Wolbachia), and gut microbiota, with an emphasis on symbiotic associations. We are studying them with the perception that a particular microorganism is not solely interacting with the host but also with all its other symbionts. A reductionist approach to these complex relationships is possible in Drosophila because of its powerful genetics and relatively simple symbiotic community.

27. PND (Princípios Físicos de Divisão Nuclear) - Telley, Ivo

This multidisciplinary team is interestedsystem, they study the earliest stages of Drosophila development, from the oocyte to fertilization to preblastoderm cleavages. The group is developing three research tracks: They focus on minimal chemical and physical cues that determine oocyte polarity. They study the chemo-mechanical mechanisms leading to pronuclear fusion in the fertilized egg, and how the syncytial embryo defines the inter-nuclear distance during syncytial divisions. The scientific methods they adopt are reconstitution approaches in egg explants, physical and chemical manipulation combined with time-lapse light microscopy and image processing while taking advantage of Drosophila genetics.

The group's main research projects are:

Physical principles of nuclear positioning in the Drosophila syncytial embryo

Reconstitution of insect fertilization to study Wolbachia transmission

Reconstitution of cell polarity and axis determination in a cell-free system

28. BAS (Sinalização em bactérias) - Xavier, Karina

The group use laboratory biochemical and genetic approaches to study the molecular mechanisms underlying quorum sensing, with an emphasis on systems promoting bacterial inter-species communication. Their research includes an integrated study involving elucidation of the chemical molecules that are used as signals, the network components involved in detecting the signals and processing information inside individual cells, and finally

characterization of the behaviour of the bacterial community in multi-species bacterial consortia.

Their mission to understand how bacteria use inter-species cell-cell communication to coordinate population-wide behaviours in consortia and in microbial-host interactions.

The main research projects are:

A. Interspecies Signaling in Bacterial Communities
B. Inter-species cell-cell signalling in bacteria
C. Identification and characterization of quorum sensing systems involved in bacterial inter-species communication
D. Quorum Sensing in Escherichia coli

29. Biologia celular da infeção viral - Amorim, Maria João

Influenza A virus is one of the major causes of acute contagious respiratory disease in humans, leading to seasonal epidemics and sporadic deadly pandemics. Despite tight surveillance of circulating strains worldwide, and the implementation of yearly vaccination schemes, the pathogen is responsible for high mortality, morbidity and economic damage. Development of novel ways to control infection is therefore necessary. My lab is interested in understanding the interactions between influenza A virus and the infected host at different levels. By identifying the host machinery necessary to sustain viral infection we seek to understand the viral lifecycle and unravel key aspects of the biology of the cell. By studying the host response to the viral challenge, we seek to unravel host innate immune responses and ways to control viral infection.

Research Projects

A. Host factors involved in influenza A virus assembly
B. Influenza A virus regulation of host immunity
C. The interaction between influenza A virus and the mitochondria

30. Modelação matemática de processos biológicos - Gjini, Erida

Our research lies in mathematical biology with special focus on infectious disease dynamics and control. Adopting mechanistic approaches, our aim is to develop a deeper quantitative understanding of how system behavior emerges from the interaction of its components, and how processes at one biological scale affect patterns we observe at another. At the evolution-ecology-epidemiology interface, we link processes at the individual to the population level. Data-driven mathematical models are applied to a variety of topics, including microbial ecology, within-host interactions in health and disease, vaccination effects in host-pathogen systems and antibiotic resistance dynamics. We are particularly interested in studying and quantifying the role of host immune defences in controlling bacterial infections and in mitigating the ascent of drug-resistant microorganisms during treatment. We combine mathematical analysis with computer simulations, and we are also broadly interested in population dynamics, stochastic processes, and parameter inference problems arising across different areas of biology. The insights from our mathematical models can have practical

implications for biomedical settings and public health policy. We currently collaborate with several research groups in Portugal (IMM, U. Lisbon) and abroad, including in France (U. Tours) and the USA (U. Tennessee, U. Michigan).

FACILITIES AND SERVICES AVAILABLE AT IGC

CORE FACILITIES

1. The Animal House Facility

The mission of the Animal House Facility is to facilitate research based on animal models, ensuring compliance with European and national animal care principles, guidelines and regulations. This is achieved by providing wellness care for animals and training in laboratory animal sciences for the staff of the vivarium and researchers. Another aspect is to ensure to the researchers technological services associated to the use of the animals (management of animal colonies, rederivations for the experimental areas of imported animals, cryopreservation of embryos, axenization service and gnotobiology).

1.1 Mouse Facility

The Mouse Facility consists of five independent units: One Production facility; One Experimental facility; One Experimental facility; One Quarantine and One Germ-free facility, which is open to the international community.

The mission of this facility is to ensure the breeding and housing of more than 100 different mouse strains that are available to the scientific staff for research purposes. As services, the IGC Animal Facility may provide: Research opportunities for external investigators/institutions; Rederivation of mouse lines into Specific Pathogen Free conditions; In vitro fertilization and Cryopreservation of mouse germplasm.

EMMA - European Mouse Mutant Archive

The specific mission of the IGC Unit within EMMA is the transfer to germ-free conditions of targeted mouse lines with immunological defects. These lines are then made available, upon request from interested scientists in Europe. In order to facilitate the analysis of such animals, notably avoiding costly special transportation at the risk of losing the "germ-free" condition, the IGC decided to open its laboratories and facilities to external scientists engaged in these studies.

1.2 Fish Facility

The mission of this facility is the investigation of vertebrate development, physiology and disease mechanisms. As a service, this facility can provide housing, adult zebrafish production, egg production and importation of new lines.

1.3 Fly Facility

The mission of the Fly facility is to host species that are powerful model systems to investigate most questions in Biology. Several Groups at the IGC use this Facility, working in cell cycle, early development, actin dynamics, evolution and neuroscience.

The Fly Facility is composed of several walk-in chambers, a preparation room and a procedure lab. In addition, a quarantine is set outside the Facility.

1.4 Frog Facility

The mission of the Frog facility is to kept and maintain frog species under ideal conditions for production of oocytes and eggs and for the performance of technical procedures, with the main target of keeping the colony free from potential cross contamination.

The Xenopus Facility has a 9 tank capacity of individual circulating fresh water system and associated preparation area able to house up to 90 Xenopus laevis, available to research at the Institute.

1.5 Plant Facility

The mission of the Plant Facility is to ensure the growth and maintenance of Arabidopsis thaliana plants, the model organism used by the plant research groups hosted by the Institute.

The facility consists of a custom-built greenhouse with lighting control and temperature regulation and three custom-made fully controlled growth chambers with short day, long day and continuous light settings, as well as a walk-in plant growth room and three small reach-in chambers that allow the performance of cell-based assays and more precise phenotypical analyses

2. Imaging & Cytometry Facilities

This Facility is organised into three areas that provide dedicated and focused services on their technical areas and collaborate with the “Equipment Unit”:

3. Flow Cytometry Facility

The aim of this facility is to provide high-quality technical and scientific services and assistance in multiparameter cell sorting and flow cytometry analysis to all researchers at the IGC as well as outside groups or companies. Experienced laboratory staff operate cell sorters, while analyzers are operated by researchers. Training can be provided for all analytical instruments.

4. Advanced Microscopy

This facility provides services on technical support and development on high-end optical microscopy equipment/techniques, and regular training on microscopy and bio-image analysis. The facility is an international reference laboratory for confocal and multi-photon microscopy, super-resolution, light-sheet and optical tomography.

5. Electron Microscopy Facility

The aim of this facility is to provide centralized, high quality electron microscopy infrastructure to support scientific investigation; offer electron microscopy services, mentorship and skill training; collaborate with researchers within our institute, our country and the scientific community to foster knowledge of technical developments in electron microscopy.

6. Genomics Unit

The aim of this unit is to use state-of-the-art equipment to provide a wide range of key genomic applications to its internal and external customers. The services the facility offers range from experimental design over complete sample processing to expert advice on data analysis.

The Genomics Facility provides services on whole genome sequencing, long-read sequencing, transcriptomics, single-cell analysis, metagenomics, genotyping and quality control of nucleid acids.

7. Transgenics Unit

The goal of the Transgenics Unit (TU) is to help research groups at the IGC by generating genetically modified animals required for their research activities. Currently, this service includes the introduction of a wide spectrum of genetic modifications into the mouse and Drosophila genomes.

This unit works together with the researchers throughout the different stages of the project to make sure that they produce genetically modified animals that best meet the specific requirements of their research activities. Also, the goal is to discuss with the researchers the different alternatives and help them to select the best strategy for their specific experimental approach. In addition, this unit advises on the design of the transgenic and targeting constructs, supply basic reagents that facilitate their production and provide guidance on the production of stable transformants and screening strategies that simplify future work with the mutant strains.

8. Antibodies Services

The Antibody Service provides a centralized resource for the production, purification and labeling of monoclonal antibodies. It also maintains a collection of hybridomas, purified and

coupled antibodies for IGC investigators. This service offers specific procedures on the quality of hybridomas like thawing, expanding, freezing, mycoplasma testing and cleaning and quantification of Ig production.

9. Histopathology Unit

The Histopathology Unit offers knowledge and expertise through a full range of services encompassing microtomy, vibrotomy and cryotomy as well as pathology assessment to IGC scientists investigating animal models of human disease. HU also provide users with histochemical stains upon request, support in research immunohistochemistry (IHC) testing, training for both cryo and vibratome sectioning techniques and guidance in general histology practices. Furthermore, the Unit offers services such as slide brightfield scanning, image analysis; and stereology.

10. Bioinformatics Unit

The unit's mission is to promote the use of computational methods in biological research, through training and development of resources and materials; to provide direct user support in biological data analysis using computational methods; to conduct research and development in bioinformatics, in particular in data-flows, data warehousing and data analyses, supporting the associated laboratory and to develop and maintain an infra-structure for high performance bio-computing.

The Bioinformatics Unit at IGC offers a broad range of services, like consulting services in bioinformatics and computational biology during initial stages of study design and grant proposals support for ongoing studies requiring external expertise in bioinformatics. Also, the unit provides assistance in the analysis of a broad range of biological data, from phylogenetic analysis to studies using high-throughput sequencing technologies such as ChIP-seq, RNA-Seq and genome re-sequencing. In addition, the aim of the Unit is to promote the use of computational methods in biological research, through training and development of resources and materials, such as the development of web application to manage flow cytometry experiments, the deployment of OMERO software and the administration of BC Gene provided by the Genomics Unit.

Another goal is related to the custom-built tools and workflows like the building of scripts to facilitate the biologist's analyses, the integration of multiple tools in a pipeline with an easier way to use visual interface and the installation of local instances of complex, computationally heavy tools.

SERVICE UNITS

1. Biosafety Unit

The Biosafety Unit aims to ensure that all reasonably practicable efforts are made to safeguard the institute's workers, visitors and contractors and also promote the security of the environment surrounding the IGC campus. In order to achieve these goals, the IGC, through the Biosafety Unit is committed to make available the adequate resources to support all relevant statutes, regulations and codes of practice and will take the appropriate steps to ensure: suitable and sufficient assessment of the risks to Health and Safety for all tasks performed by this

organization; information, instructions and the necessary training of all workers concerning health and safety; the minimization of risks for health and safety in relation to the use, handling, storage and transportation all chemical and biological substances used in the institute; that all equipment handled at the institute is safe and without risks to health and the maintenance of a safe workplace and safe means of access to it as well as safe egress from it.

The ultimate goal of the biosafety unit is to create a safety awareness culture where safety in so entrenched in everyone that the natural conduct is to support safety practices.

Informatics Technical Infrastructure

The Informatics Technical Infrastructure (ITI) is responsible for managing and maintaining the IT of the IGC. Some of the services provided by the ITI includes E-Mail, VPN, printing, hosting of servers and services for researchers, administrative and collaborative Intranet services, central data storage, database and web site maintenance, surveillance and access control, consulting, training and support.
This services rely heavily on Open Source and strive to support equally all of the Windows, Mac and Linux platforms.

Technico-scientific Support

The Technico-scientific Support service is a technical platform aiming to support equipment acquisition, distribution and rational usage. Also, to support scientists form the institute on the prototyping of hardware apparatus for innovative experimental approaches. This service works in close collaboration with core facilities for keeping with the high service standards and equipment uptime, by providing tools for better manage resources and by fostering best practices on financial models.

The services offered by the Technico-scientific support service include: Equipment repair and maintenance; General equipment acquisition; Building of scientific hardware apparatus; Development of a facilities managing software (booking, requests and quality control); Maintenance of scientific equipment database; Assist to the usage of all equipment not located in a core facility; Remote monitoring for close to 200 critical parameters in the institute ranging from -80s temperatures to equipment hardware status.

Research Funding Affairs Unit

The Research Funding Affairs Unit is responsible for the implementation of a pre-award grant administration service. Its main goal is to increase the IGC's capacity to attract research funds and to improve direct fund-raising by research teams, and their scientific projects, for competitive calls launched by national, international, public and private grant programs. This unit reports directly to the IGC Managing Deputy-Director, understands the different grant financial policies and requirements and works in collaboration with researchers, The IGC Directors and the IGC three Deputy-Directors and the Project Management Unit.

The services offered to researchers involve: Identifying in a timely manner, calls for proposals that might interest the IGC, evaluating the conditions and preferences for grant applications (eligibility, deadlines, how to apply and prepare full proposals, filling-in forms and web-pages, knowing how it works, what are the specific targets, what is behind each call, etc.) &

disseminating these opportunities by several means: newsletter, online calendar, internal grants informative database, emails, meetings, etc.; Supporting grant proposal development & submission, namely: arranging administrative forms, host documents & signatures, assisting with the scientific proposal's writing and budget design, etc.; Post-award negotiation with funding agencies of contracts and agreements. The unit also organizes and lectures several informative sessions and workshops for grant application training of in-house and external researchers at all career stages. The Research Funding Affairs' responsibilities cease with contract signature and after passing all grant information to the project management unit as well as to the researchers. In addition, this unit also monitors the impact of the services offered through the quantification of several criteria.

Scientific Events Management

The Scientific Events Management & Welcome sub-unit is responsible for: Meetings, conferences and simposia organisation of logistics for the IGC; Travel arrangements for IGC visitors; Seminars Visitor logistics; Welcome issues: admin support for new incoming researchers on all issues related to settling down in Portugal and at the IGC. The IGC is part of the Euraxess - a EU network that supports researcher mobility; SSV refund processes; Meeting rooms bookings.

Project Management

The Project Management sub-unit is responsible for:

Cost control, financial report submission, audit preparations, call preparation, etc.

This sub-unit is divided in three groups: International Projects (grants, prizes public or private); National Projects (FCT and Others) and Internal Projects

Procurement Unit

The unit mission is to identify common needs for products and services and to accomplish better conditions for all parts involved in the process: research groups, support teams and suppliers. It starts with the user request, follows with the goods deliver directly at the lab and ends upon the invoice reception.

The main tasks of the Office area (administrative tasks) rely on: Create official Purchase Orders according to the Fundação Calouste Gulbenkian guidelines - Validate the necessary data for new suppliers; Manage the purchasing workflow using the LabOrders platform integrated with our ERP (SAP); Manage the non-conformity invoices workflow. Prices, quantity, purchasing terms and other differences that require interactions with the internal users, supplier and the Direction; Quarterly update of open Purchase Orders in order to get invoices on time thus maximizing project execution; Manage importation procedures and customs clearance; Negotiate the annual contracts, such as cleaning, gardening, security, maintenance and other predictable costs; Cooperate with other institutions to improve purchasing conditions for all by sharing a product catalog with 3 million SKUS and 50 suppliers.

The main tasks of the Warehouse area include: Receive incoming products from suppliers and carry out the internal distribution to the final users at the labs; Stock, pick up and distribute the products from the "supplier's warehouse" at IGC; Express shipments.

Dra Mónica Bettencourt Dias

Director Instituto Gulbenkian de Ciência