List of supervisors and project titles currently accepting students:

Mónica Bettencourt-Dias and Joana Bugalhão: Regulation of centriole biogenesis by the actin network

Title: Regulation of centriole biogenesis by the actin network
Supervisors: Mónica Bettencourt-Dias and Joana Bugalhão
IGC group: Cell Cycle Regulation Lab
E-mail contact: jbugalhao@igc.gulbenkian.pt
Abstract: Centrosomes are composed of two centrioles surrounded by pericentriolar material and play critical roles in cell cycle progression. Centriole duplication is regulated in space by the pre-existing centriole and in time by the cell cycle. However, in certain acentriolar cells, centrioles can also form de novo. Recent studies highlighted novel relationships between centrosomes and the actin cytoskeleton. For instance, centrosomes can nucleate actin filaments and the number of centrosomal microtubules is regulated by the actin-network architecture. Also, a proteomic study from our lab aiming to detect proteins interacting with regulators of centriole biogenesis led to the identification of proteins with actin-related functions and actin-microtubule cross-linkers. The aim of this project is to understand the role of the actin cytoskeleton in canonical/de novo centriole biogenesis using different approaches, including molecular biology techniques, co-immunoprecipitation assays, immunoblotting, fluorescence microscopy and live cell imaging. Altogether, these approaches are expected to contribute to a better understanding of centrosomal regulation.

Lounès Chikhi, Olivier Mazet and Beatriz Mourato: Comparative demography of endangered species using genomic data

Title: Comparative demography of endangered species using genomic data
Supervisors: Lounès Chikhi, Olivier Mazet and Beatriz Mourato
IGC group: Population and Conservation Genetics (Collaboration with "Institut de Mathématiques de Toulouse", Toulouse, France)
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Abstract: Genomic data have become increasingly available for many taxa including endangered species. In addition, the computational methods used to reconstruct the recent evolutionary history of species from genomic data have become increasingly sophisticated. However, despite the increasing amount of data, most studies focus on one species making it difficult to determine whether the history reconstructed informs us only on that particular species or provides a general information on past changes in habitat or on the influence of human populations on endangered species. Comparative studies are crucially needed but difficult to carry out. In our group we are studying how models of population structure influence the inference of the demographic history of species. In this

project the student will analyse in close collaboration with the supervisors the properties of genomic data from species living in the same habitats. We will compare the results of computer simulations and real data from endangered species from the same or neighboring regions for which genomic data are available. We are thus looking for a candidate who would like to explore with us the properties of past changes in connectivity on genomic data from co-distributed endangered species. The candidate will perform coalescent simulations under varying scenarios (using scripts that have been already developed in the team, she/he will also be able to develop her/his own depending on her/his interests). Simulations will be compared to real data sets from endangered species. More specific details of the project will be discussed with the candidates, as this is an ongoing project.

Lounès Chikhi and Rémi Tournebize: Testing the confounding impact of sampling schemes and spatial structure on signals of population size change and admixture

Title: Testing the confounding impact of sampling schemes and spatial structure on signals of population size change and admixture
Supervisors: Lounès Chikhi and Rémi Tournebize
IGC group: Population and Conservation Genetics
E-mail contact: chikhi@igc.gulbenkian.pt (rtournebize@igc.gulbenkian.pt)
Abstract: A major interest in population genetics is to reconstruct the demographic history of species using genetic data. Yet, although species evolve in space and time, a large amount of research largely oversees the importance of space. Consequently, several methods used to reconstruct that history assume that population structure, including spatial structure, can be neglected. In other words, individuals are analysed as if they were sampled from large populations (often representing continents) wherein individuals reproduce freely without considering spatial distances. By ignoring spatial structure (i.e. the heterogeneous geographic distribution of allele frequencies across a species distribution), these methods can produce results that are interpreted in terms of population size change, admixture or selection when spatial structure might be a contributing factor. Our team is interested in the use of alternative models of species demography that integrate population structure. Previous research suggests that spatial structure can generate signatures that are interpreted as admixture by several commonly used tests or statistics such as the ABBA-BABA test. Still several studies have identified admixture events in lemurs or humans on the basis of this test. In this project the student will carry out spatial simulations in close collaboration with the two supervisors to study the properties of this and other statistics in models with and without admixture. We are thus looking for a candidate who would like to explore with us the properties of spatial processes with applications in endangered species or in the human species. The candidate will perform coalescent simulations under varying scenarios (using scripts that have been already developed in the team, she/he will also be able to develop her/his own depending on her/his interests). Simulations will be compared to real data sets from endangered species or from humans. More specific details of the project will be discussed with the candidates, as this is an ongoing project.

Luca Cirino and Mónica Bettencourt-Dias: Studying life at microscopic scale: variant mitoses 1 in non-model organisms

Title: Studying life at microscopic scale: variant mitoses 1 in non-model organisms
Supervisors: Luca Cirino and Mónica Bettencourt-Dias
IGC group: Cell Cycle Regulation Lab
E-mail contact: lcirino@igc.gulbenkian.pt
Abstract: Our current knowledge of mitosis and meiosis, two peculiar eukaryotic processes, is mainly based on a limited number of model organisms, mostly composed of complex multicellular eukaryotes. In contrast, very little is known regarding cellular division processes and the relative cytoskeletal components involved in protists, the predominant constituents of Eukarya. Exploring

mitotic processes that fall outside canonical models could provide valuable insight into the evolution of the cellular division and the cytoskeleton. In light of this, the present project aims at investigating cellular division configurations in several non-model organisms, with a particular focus on the cytoskeletal architectural rearrangements at the onset of the mitotic process. Great efforts will be dedicated to develop efficient culture protocols and determine life cycle environmental triggers for organisms seldom housed in laboratories. Electron and fluorescence microscopy will be then employed to characterize the early remodeling signs exhibited by the cytoskeleton before mitotic division in these largely unknown organisms.

Paula Duque and María Niño-González: Characterization of the transport properties of a plant MFS protein through heterologous expression in yeast and Xenopus oocytes

Title: Characterization of the transport properties of a plant MFS protein through heterologous expression in yeast and Xenopus oocytes
Supervisor: Paula Duque; **Co-supervisor:** María Niño-González
IGC Group: Plant Molecular Biology lab
E-mail contact: duquep@igc.gulbenkian.pt

Paula Duque and Dóra Szakonyi: SR protein splicing factors and plant adaptation to stress

Title: SR protein splicing factors and plant adaptation to stress
Supervisor: Paula Duque; **Co-supervisor:** Dóra Szakonyi
IGC Group: Plant Molecular Biology lab
E-mail contact: duquep@igc.gulbenkian.pt
Abstract: Land plants are constantly subjected to a changing environment and have therefore developed mechanisms to survive and reproduce under adverse conditions. External stresses activate molecular pathways leading to key adaptive changes in plant growth and development. Alternative splicing, a posttranscriptional regulation mechanism allowing the production of multiple transcripts from the same gene, is being implicated in plant stress tolerance. Recent studies in our lab demonstrate a role for SR proteins, which are highly conserved RNA-binding factors playing major roles in alternative splicing, in stress signaling via the abscisic acid hormonal pathway. This project will make use of the model flowering plant Arabidopsis thaliana and genetic, molecular biology and biochemistry approaches to elucidate the role and mode of action of specific SR proteins in the response to environmental stress.

Giulia Ghedini: Does coevolution decrease invasion risk in competitive communities?

Title: Does coevolution decrease invasion risk in competitive communities?
Supervisor: Giulia Ghedini
IGC Group: Functional Ecology
E-mail contact: gghedini@igc.gulbenkian.pt
Abstract: The diversity of species in nature has long fascinated biologists. Decades of studies on competition have shown how so many species can coexist despite often competing for similar resources. The evolutionary consequences of competition are however little explored. Competition can lead to metabolic adaptations that facilitate coexistence and that increase the efficiency with which a community uses resources. Since greater efficiency means that less resources are available for an invading species, communities of competitors that have coevolved for longer periods of time should be less susceptible to invasion. However, empirical tests are lacking. This project will leverage the diversity of phytoplankton to study how competitor diversity and coevolution time affect invasion risk. We will combine experimental evolution of phytoplankton communities with measurements of resource uptake and expenditure to quantify changes in efficiency over time. We will then test the

structural (species composition) and functional (resource use) stability of these coevolved communities to invading species. Given the increasing frequency of disturbances and changes in biodiversity across ecosystems worldwide, experimental tests such as this are critical to identify which communities are more stable and less susceptible to invasions.

Giulia Ghedini: Metabolic responses to chemical cues

Title: Metabolic responses to chemical cues
Supervisor: Giulia Ghedini
IGC Group: Functional Ecology
E-mail contact: gghedini@igc.gulbenkian.pt
Preferred start date: November 2022 (flexible)
Abstract: All organisms compete for resources. Competition does not only act through direct resource competition – organisms often compete indirectly by releasing chemical cues. Chemical communication is well known to mediate competition in plants, but little is known about chemical cues in the ocean. This project builds on our preliminary data to explore how chemical cues affect the physiology and metabolism of marine phytoplankton. These unicellular algae are responsible for over half of global oxygen production. Therefore, it is essential to understanding the consequences of chemical communication on the diversity and productivity of phytoplankton communities. The work will involve a combination of physiological assays to phenotype growth and metabolism, competition experiments and assays to characterize the profile of chemical cues.

Isabel Gordo: Theoretical models of evolution in the Gut Microbiome

Title: Theoretical models of evolution in the Gut Microbiome
Supervisors: Isabel Gordo
IGC Group: Evolutionary Biology
E-mail contact: igordo@igc.gulbenkian.pt
Abstract: The mammalian gut is home to thousands of species and its diversity is a biomarker for health. This project aims to use mice as a model system to understand how dynamic is the gut microbiome and how newly colonisers of the gut evolve. We are interested in assessing conditions, such as microbe-microbe competition and/or diet supplementation capable of lowering the ability of antibiotic resistant bacteria to persist in the gut. (See Cardoso, Durao, Amicone and Gordo 2020, Nature Ecology & Evolution).

Jaakko Lehtimäki and Caren Norden: Role of filopodia in multipolar neuronal navigation

Title: Role of filopodia in multipolar neuronal navigation
Supervisors: Jaakko Lehtimäki and Caren Norden
IGC Group: Cell Biology of Tissue Morphogenesis
E-mail contact: jlehtimaki@igc.gulbenkian.pt
Preferred date of start: Possible to start from 01/03/2023 onwards
Abstract: The orchestration of neurons into functional layers, is the key event in brain development. As neurons are often born away from where they later function, they need to migrate to their correct positions. To date, we have a general understanding on radial and tangential migration modes where neurons with defined polarity use extracellular matrix and other neuronal processes as tracks. However, much less is known about how neurons moving in a multipolar fashion and frequently change their direction and extend long, seemingly randomly oriented filopodia, find their correct location and how they interpret what type of environmental signals. This is important as multipolar neurons play a prominent role in the formation of different parts of the central nervous system (CNS).

Our overarching objective is thus to understand the cell- and tissue-derived factors neurons undergoing multipolar migration use to navigate.

To investigate this, we study multipolar neurons, named horizontal cells (HC), in the developing zebrafish retina. The transparent vertebrate retina is the most accessible part of the CNS that undergoes fascinating transformation from a pseudostratified epithelium into ordered and layered assembly of five retinal cell types. In zebrafish, the whole process is complete within 72 hours post fertilization. Differentiating HCs engage into multipolar migration extending multiple filopodial protrusions to travel through the developing retina. They take very heterogeneous paths to reach their final destination and migrate in an ECM-free environment. These findings suggest that cell/tissue-derived guidance cues could be guiding the HC migration. To support this, we are analysing a recently generated transcriptomics dataset providing a list of candidate genes expressed in HCs or in other retinal neurons that could act as a secreted or contact-mediated guidance molecules for the HCs.

During this project, you will investigate if filopodia, generally known to act as a "a sensory organs" for the cell, are used by HCs to a) probe for the surrounding guidance cues and / or b) find the path of least resistance through other cells inhabiting the developing retina, to reach their final location. Your toolbox will include state-of-the -art techniques for in vivo imaging of HCs' filopodia e.g., light-sheet-, super-resolution-, and expansion microscopy. You have the chance to generate knockout embryos to analyse if or how HCs lacking filopodia navigate and potentially extend these observations by comparing HCs in vivo vs. in vitro cultures. Unveiling the role of filopodia in multipolar neuronal migration, will provide important insights into the in vivo mechanisms of similar migratory patterns observed also in other developing brain areas.

We are seeking highly motivated, organized applicant to conduct this cutting-edge research project on cell-tissue interplay in neuronal migration. Background in developmental and cell biology as well as experience in in vivo / in vitro imaging, is considered a plus as is experience with model organisms. However, motivation and curiosity are the main selection criteria.

Raquel Oliveira: Modifiers of sister chromatid cohesion loss

Title: Modifiers of sister chromatid cohesion loss
Supervisor: Raquel Oliveira
IGC Group: Chromosome Dynamics
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Abstract: Sister chromatid cohesion is essential for faithful mitosis, as premature cohesion loss leads to random chromosome segregation and aneuploidy, resulting in abnormal development. To identify specific conditions capable of restoring defects associated with cohesion loss, we screened for genes whose depletion modulates *Drosophila* wing development when sister chromatid cohesion is impaired (a first report on the results of this screen can be found here: https://www.cell.com/current-biology/pdfExtended/S0960-9822(18)30853-4. This project aims to validate other hits arising from this screen with regard to their ability to modulate defects associated with sister chromatid loss.

Rui Oliveira: Identification of genes and brain gene networks associated with rapid evolution of sociality in zebrafish
Title: Identification of genes and brain gene networks associated with rapid evolution of sociality in zebrafish
Supervisor: Rui Oliveira
IGC Group: Integrative Behavioral Biology Lab
E-mail: roliveira@igc.gulbenkian.pt

Funding Available. Details for application available soon.
Abstract: An artificial selection experiment for sociality on zebrafish has been ongoing for six generations. To measure the brain transcriptomic response to the artificial selection for sociality, we will use spatial transcriptomics across the brain social decision-making network (a collection of nuclei responsible for the processing of social information) to compare gene multi-layered networks between the selected lines. Gene networks will be extracted using WGCNA (weighted gene co-expression network analysis) and co-expression modules, co-splicing networks and network topology will be compared between the divergent lines for each brain region. Thus, we will be able to assess the relative contribution of convergence in differentially expressed genes and similarity in network connections for the rapid evolution of a social trait.
Preference will be given to candidates with a background in Bioinformatics, Biology, or related areas.

Rui Oliveira: Identification of genes and brain gene networks associated with rapid evolution of sociality in zebrafish

Title: Oxytocin regulation of brain transcriptional networks in response to social behavior in zebrafish
Supervisor: Rui Oliveira
IGC Group: Integrative Behavioral Biology Lab
E-mail: roliveira@igc.gulbenkian.pt
Funding Available. Details for application available soon.
Abstract: In this project, we will test the occurrence of genetic toolkits for social behaviour by comparing their genetic architecture across species that independently evolved the different social phenotypic traits. For this purpose, social phenotypes will be mapped on the phylogeny of Lake Tanganyika cichlids to identify evolutionary transitions between them. Repeated evolution of social phenotypes will be determined and used for studying convergent phenotypes using complementary DNA sequence and functional genomics approaches.
As a trustable reconstruction of the cichlid species tree, we will use a genome-wide phylogenetic hypothesis based on the recent genome sequencing of all Lake Tanganyika cichlids.
Preference will be given to candidates with a background in Bioinformatics, Biology, or related areas.

Miguel P. Soares: Metabolic reprograming in infectious diseases

Title: Metabolic reprograming in infectious diseases
Supervisor: Miguel P. Soares
IGC Group: Inflammation
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Abstract: Immunity evolved in multicellular organisms to limit the fitness costs imposed by the continuous interactions with microbes. Innate and adaptive components of the immune system emerged early through evolution, to sense and target pathogenic microorganisms for containment, destruction or expulsion. Resistance to infection refers to these cardinal features of immunity.

Plants and animals share yet another evolutionary conserved defense strategy that does not exert a direct negative impact on microorganisms, referred as disease tolerance. Our body of work has contributed to uncover some of the core mechanisms establishing disease tolerance to systemic infections in mammals. These were found to act at a cellular and organismal level to limit the extent of metabolic dysfunction and damage, caused by pathogenic microorganisms and immune-driven resistance mechanisms.

The overarching objective of our research program is to identify and characterize stress and damage responses driving metabolic adaptation and underlying the establishment of disease tolerance to viral, bacterial or protozoan infections. The central hypothesis is that reprograming of organismal metabolism in response to infection relies on a functional interplay between immune-driven resistance mechanisms and stress and damage responses operating in parenchymal tissues. Pathogenic microorganisms sense and react to this host metabolic response, modulating virulence

and transmissibility, an emerging area of research we are actively pursuing. Unveiling general principles governing disease tolerance, as proposed herein, should be transformative towards our understanding of host-microbe interactions, with a major impact on the development of therapeutic approaches against everlasting human infectious diseases of global proportions.

Élio Sucena: Haematopoiesis in *Drosophila*: mechanistic control of haemocyte proportions during larval development

Title: Haematopoiesis in *Drosophila*: mechanistic control of haemocyte proportions during larval development
Supervisor: Élio Sucena
IGC Group: Evolution and Development
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Élio Sucena: Chasing the genetic bases of resistance and tolerance in *Drosophila melanogaster*

Title: Chasing the genetic bases of resistance and tolerance in *Drosophila melanogaster*
Supervisor: Élio Sucena
IGC Group: Evolution and Development
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Silvia Vale-Costa and Maria João Amorim: MSc Project LipidFLU: Understanding the role of phosphoinositide metabolism in the formation of influenza A virus liquid inclusions

Title: Understanding the role of phosphoinositide metabolism in the formation of influenza A virus liquid inclusions
Supervisors: Silvia Vale-Costa and Maria João Amorim
IGC Group: Cell Biology of Viral Infection
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Abstract: Viruses exploit the cellular architecture and pathways to establish biomolecular condensates for spatiotemporal control of viral reactions and escaping host immune recognition [1]. The influenza A virus (IAV) forms condensates designated viral inclusions, that have been linked to assembly of its genome [2–11]. The IAV genome consists of 8 distinct RNA segments arranged into viral ribonucleoproteins (vRNP), in which the RNA binds the viral RNA-dependent RNA polymerase complex and multiple units of nucleoprotein (NP) [12,13]. Upon nuclear synthesis, progeny vRNPs are exported to the cytosol and assembled into an 8-vRNP complex [12,13], via a poorly characterized process. Evidence supports that genome assembly depends on RNA-RNA interactions between vRNPs and is a selective process as infectious virions contain genomes with precisely 8 different vRNPs [14].

We have recently proposed an appealing model to explain IAV genome assembly [15], which involves the formation of liquid viral inclusions by the process of demixing from the cytosol akin to liquid-liquid phase separation [9]. These condensates form upon expression of a single vRNP type and enlarge as infection progresses, allowing the concentration of vRNPs and facilitating RNA-RNA interactions [9]. By displaying liquid properties (contain no delimiting membrane, are highly dynamic, and internally rearrange) these viral condensates constitute a confined space wherein IAV genome assembly may be efficiently orchestrated [9]. To abrogate the formation or modulate the material properties of viral inclusions, it is required in-depth understanding of the underlying molecular drivers governing their biogenesis and of the mechanisms regulating their material properties.

We have recently identified that some phosphoinositides (PI) and their regulating factors as critical for viral replication and for the development of liquid viral inclusions. However, it is currently unclear the molecular details of how these candidates contribute to their biogenesis. Depletion of these factors leads to reduction in viral production and an increase in the size of liquid viral inclusions. This project proposes to understand how these PI and associated factors regulate IAV infection, namely to understand if:

1. Which PIs and associated factors interacts with the recycling endosome (or a viral factor) to regulate size of viral inclusions
2. How specific PIs and associated factors regulator of the material properties of viral inclusions
3. How specific PIs and associated factors affect the assembly of viral genome at viral inclusions

To tackle these questions, the student will perform viral infections, live cell imaging, immunofluorescence, real-time RTqPCR, western blotting and pull-down assays.

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Karina Xavier: Quorum Sensing in Microbiota Gut Communities

Title: Quorum Sensing in Microbiota Gut Communities

Supervisor: Karina Xavier:

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Karina Xavier and JingTao Lilue: Bioinformatics approached to analyze Microbiota communities in response to dietary perturbation

Title: Bioinformatics approached to analyze Microbiota communities in response to dietary perturbation

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