

# Research Topics

## PhD Programme in Biosciences

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DIPARTIMENTO DI BIOLOGIA  
UNIVERSITÀ DEGLI STUDI DI PADOVA

### Research Topics XL cycle 2024-2025

Below are the descriptions of all projects considered as priorities for the XL cycle. Candidates are encouraged to identify at least one project of interest and mention it in the research statement to be uploaded with their application. For further details regarding the required documents for the application, please refer to the FAQ section available on the PhD Programme's website.

#### Curriculum Biochemistry and Biotechnology

##### Funded by External Public or Private Bodies/Departments

###### **Detectability of molecules deriving from irradiated anoxygenic microorganisms, within the ExoMars mission.**

Contact: Prof. Nicoletta La Rocca, e-mail: [nicoletta.larocca@unipd.it](mailto:nicoletta.larocca@unipd.it)

The proposed project is part of the ESA ExoMars mission, which will be launched in 2028, and aims to provide a solid basis on the effects of a simulated Martian radiative environment (UV and ionizing radiation) on the survival and detectability, through the detection of biomolecules, of different types of microorganisms mixed with a Martian soil simulant. To date, most research on radiation resistance and survival of microorganisms has been conducted on aerobic and spore-forming species. Many non-spore-forming microorganisms have been identified as resistant to radiation, although how they survive radiation appears to be poorly understood. The project aims to expand research to photosynthetic and non-photosynthetic anoxygenic microorganisms and to obtain new data on exposed organisms regarding 1) survival rate; 2) cell/colony morphology; 3) detectability and preservation of irradiated cellular biomolecules (nucleic acids, proteins, pigments, etc.).

###### **From combination treatment halting the progression of poor-prognosis cancers towards possible clinical application.**

Contact: Prof. Ildikò Szabò, e-mail: [ildiko.szabo@unipd.it](mailto:ildiko.szabo@unipd.it)

The fellow will have the opportunity to focus on an exciting and novel aspect of cancer research that links intracellular ion channel function to crucial aspects of cancer development. In addition, the project aims to optimize pharmacological treatments targeting these ion channels against hard-to-treat cancers.

## **Network and quantitative biology: aspects of biochemistry and biotechnologies**

For the topic of this project please refer to any of the projects Funded by the University reported below.

### **Funded by the University**

#### **Investigation of the metabolic coordination in diazotrophic cyanobacteria using genetically-encoded fluorescence probes.**

Contact: Dr. Giorgio Perin, e-mail [giorgio.perin@unipd.it](mailto:giorgio.perin@unipd.it)

Diazotrophic cyanobacteria fix both atmospheric carbon and nitrogen into biomass and the two assimilation pathways must be tightly coordinated to achieve metabolic homeostasis. This project aims to address their functional cooperation, using a model organism that evolved a spatial separation between the two processes in two distinct cell types.

The candidate will implement genetically-encoded fluorescence probes to measure in vivo the concentration of high-turnover and labile metabolites, like ATP, NADH and 2-oxoglutarate, in the two cell types upon exposure to dynamic metabolic inputs (e.g. light and CO<sub>2</sub>).

#### **Organelle interactions in physiology and pathology: mitochondria-lysosome contact sites in neurodegeneration.**

Contact: Prof. Marisa Brini, e-mail: [marisa.brini@unipd.it](mailto:marisa.brini@unipd.it)

Mitochondria and lysosomes are highly dynamic organelles, and their dysfunction has been linked to many neurological disorders. Organelle coupling represents a critical hub for the transfer of information to sustain organelle function. Our research is focused on the understanding of the mutual crosstalk in contact sites remodeling upon manipulation of proteins whose mutations are linked with familial Parkinson disease (i.e., alpha-synuclein, PINK1, Parkin and DJ-1). Genetically-encoded biosensors, for both Ca<sup>2+</sup> and organelle proximity, will be employed to finely dissect the heterogeneity of signalling pathways within the cell.

#### **Engineering Protein Scaffolds for Precision Target Recognition and Delivery in Biomedicine.**

Contact: Prof. Laura Cendron, e-mail: [laura.cendron@unipd.it](mailto:laura.cendron@unipd.it)

The development of biotechnological tools leveraging protein and peptide engineering techniques presents a promising avenue for the precise recognition of target proteins implicated in various pathological conditions, as well as for targeted delivery purposes. This proposed PhD project aims to harness the potential of protein scaffold engineering to design novel platforms capable of recognizing relevant target proteins and concurrently targeting receptors for efficient delivery.

Using library selection via display technologies and rational design approaches, this project seeks to engineer protein scaffolds with enhanced specificity and affinity towards target proteins associated with specific diseases, such as cancer biomarkers or pathogens antigens. Integrating biophysical methods, in-vitro assays, and cell culture models, these engineered scaffolds will be validated and further tailored to achieve optimal binding properties with the target molecules.

### **Beyond the collective: microbial investigation through high-resolution single-cell analytics**

Contact: Dr. Laura Treu, e-mail: [laura.treu@unipd.it](mailto:laura.treu@unipd.it)

The diversity and activity of microbial isolates and populations are paramount for understanding the heterogeneity that characterizes them, especially concerning the complexity of anaerobic microbiota. Despite being very informative, meta-omics have some limitations hampering a complete understanding of their collective behavior. Single-cell technologies enable in-depth study of this diversity, utilizing microfluidic techniques for droplet encapsulation of individual cells. This approach offers new perspectives in understanding microbial metabolism and activity dynamics, revealing details at an unprecedented level. Specifically, studies of strains in microbiota at transcriptomic level are still in their infancy; therefore, this Ph.D. project will have a strong methodological component for developing these aspects.

### **Exploring the ATAD3 involvement in cellular metabolic commitment.**

Contact: Prof. Maria Eugenia Soriano, e-mail: [mariaeugenia.soriano@unipd.it](mailto:mariaeugenia.soriano@unipd.it)

Mitochondria function and their interaction with other organelles appear as critical factors in the metabolic commitment of the cell. The ATAD3 protein family is a group of mitochondrial proteins composed of 2 different members, ATAD3A and ATAD3B, the latter expressed only in Hominidae, and its expression is associated with more glycolytic cellular types such as embryonic stem cells, some tumorigenic models, and the germ line. The molecular event by which ATAD3B might regulate cellular metabolism is currently obscure. This project wants to reveal the molecular mechanism of ATAD3B's impact on mitochondrial function and cell metabolism. To this aim, genetic strategies will be developed to generate specific cellular models to investigate metabolic changes, protein interactions, complexomic modifications, and mitochondrial correlated phenotypes.

### **Plant adaptation to changing environmental conditions: key role of mitochondria as stress sensors.**

Contact: Prof. Michela Zottini, e-mail: [michela.zottini@unipd.it](mailto:michela.zottini@unipd.it)

Maintenance of organelle integrity, in terms of functionality, morphology and dynamics, crucial for cellular homeostasis and proper responses to environmental challenges, is provided through anterograde and retrograde signaling. Mitochondrial Unfolded Protein Response (mtUPR) is suggested to be a major retrograde response activated in plants by a variety of different conditions that can lead to the accumulation of misfolded or unfolded proteins. mtUPR is still a poorly understood process and this PhD project aim to characterize it, identifying the molecular components and pathways that act as signals between the organelles and the nucleus, by using an integrated molecular, physiological, and imaging approach.

## Curriculum Cell Biology and Physiology

### Funded by External Public or Private Bodies/Departments

#### **A systematic functional analysis of mitochondrial interorganellar interfaces.**

Contact: Prof. Luca Scorrano, e-mail: luca.scorrano@unipd.it

In the cytoplasm, organelle interactions are specified by membrane contact sites (MCS) that define interfacial microdomains responsible for compartmentalization of signaling cascades and metabolic pathways, ultimately impacting on organellar and cellular function. Our knowledge of MCS is scarce. Even for a central organelle such as mitochondria, we are only starting to unravel the proteome and function of the best studied, mitochondria-endoplasmic reticulum (ER) interface. However, mitochondria can engage in contacts with all other organelles and the occurrence, physical composition, biophysical properties, and function of these MCS are largely unknown. The successful candidate will generate genetically encoded probes FRET or SPLIT-FAST-based probes to measure MCS between mitochondria and lysosomes in mammalian cells.

The candidate will use these probes to unbiasedly identify modulators of these MCS. By combining this approach with iBAQ proteomics on purified interorganellar MCS the candidate will provide a catalogue of functional components of the mitochondria-lysosome MCS.

#### **Targeting mitochondrial dynamics in AML.**

Contact: Prof. Luca Scorrano, e-mail: luca.scorrano@unipd.it

AML, the second most common leukemia in adults, has a 5-year survival rate of 28%. Changes in mitochondrial dynamics i.e., the processes of mitochondrial fusion, fission and cristae remodeling governing organelle shape emerged as key in AML genesis and targeted therapy. AML Leukemia Stem Cells (LSCs) that replenish the proliferating myeloblasts and contribute to AML aggressiveness rely on the mitochondrial fission gene FIS1. However, it is unclear how FIS1 sustains LSCs and if and how we can target it to deplete them. The successful candidate will use a unique Fis1 conditional mouse generated in our laboratory and engineered AML cell lines, metabolomics, RNAseq, proteomics to understand whether FIS1 and mitochondrial fission control myelopoiesis and sustains LSCs in AML by licensing a metabolic switch. The candidate will profile metabolism/mitophagy upon Fis1/Drp1 deletion in myeloid cells and understand molecularly how Fis1/Drp1 deletion induces myeloid differentiation.

#### **Characterizing the role of CD300e receptor in obesity: low-grade inflammation, insulin-resistance and immunomodulatory properties.**

Contact: Prof. Marina De Bernard, e-mail: marina.debernard@unipd.it

The project aims at characterizing the role of the immunoreceptor CD300e in the dysmetabolism accompanying obesity. Using a KO animal model for the cd300e gene, the student will be tasked with understanding through which mechanism the receptor, whose expression increases in adipose tissue in obesity, plays a protective role against adipose tissue remodeling (hypertrophy), liver steatosis, and insulin resistance, all conditions that may be present in obesity and that are exacerbated in the animal model that does not express the receptor.

## **Network and quantitative biology: aspects of cell biology and physiology**

For the topic of this project please refer to any of the projects Funded by the University reported below.

### **Funded by the University**

#### **Effects of anthropogenic stress (plastic pollution and noise) on tunicates.**

Contact: Prof. Lorian Ballarin, e-mail: [loriano.ballarin@unipd.it](mailto:loriano.ballarin@unipd.it)

The increasing level of plastic pollution, in the form of micro- and nanoplastics (NPs), as well as underwater noise is a matter of concern for aquatic ecosystems. In particular, the effects of anthropogenic stress on the immune system, development and resilience is poorly studied on sessile invertebrates that, unlike mobile organisms, cannot move apart from the source of pollution. This project aims at studying the effects of NP pollution and underwater noise on ascidians, marine sessile invertebrates belonging to the subphylum Tunicata, considered the sister group of vertebrates. They represent important sentinel organisms for the evaluation of the health status of hard-substrate ecosystems. Animals will be collected in the Lagoon of Venice, in sites with various levels of pollution. In addition, ascidians will be exposed, in the lab, to polyethylene and polypropylene NPs and underwater noise at various concentrations, intensities and frequencies. The effects will be evaluated at behavioral, morphological, physiological and transcriptomic level.

#### **The role of microglia and astroglia in Parkinson's disease-linked synaptic dysfunction.**

Contact: Prof. Elisa Greggio, e-mail: [elisa.greggio@unipd.it](mailto:elisa.greggio@unipd.it)

Several studies support that non-cell autonomous mechanisms lead to dopaminergic neuronal death, a pathological hallmark of Parkinson's disease (PD). Mutations in the LRRK2 gene, encoding a complex GTPase/kinase, either cause or increase the risk of PD. Elevated inflammation and astrogliosis has been observed in the brain of LRRK2 mouse models and postmortem mutant LRRK2 carriers. Despite a well-established role of LRRK2 in synaptic function and inflammation, how aberrant LRRK2 kinase activity increases the inflammatory burden in the nigrostriatal synapse remains to be determined. The candidate will apply biochemical and imaging approaches to cellular models (including primary cultures and iPSCs-derived cells) and mouse models of PD to investigate how LRRK2 contributes to astrocyte and microglia activation and the impact of LRRK2-mediated inflammation on synaptic dysfunction.

#### **Organellar calcium signalling at the core of arbuscular mycorrhizal symbiosis.**

Contact: Prof. Lorella Navazio, e-mail: [lorella.navazio@unipd.it](mailto:lorella.navazio@unipd.it)

Arbuscular mycorrhiza (AM) is the most widespread and ancient plant-microbe symbiosis, involving about 80% of land plants and Glomeromycotina fungi. Changes in intracellular calcium levels mediate the symbiotic signalling pathway leading to the development of arbuscules, sites of plant-fungus nutrient exchange in the plant root inner cortex. The project aims to analyze the contribution of plastids and endoplasmic reticulum in shaping intracellular Ca<sup>2+</sup> signatures activated by symbiotic signals in the model legume *Lotus japonicus*, by using a toolkit of organellar-targeted, genetically encoded Ca<sup>2+</sup> indicators. Moreover, the role of MLO proteins, recently suggested to function as novel Ca<sup>2+</sup>-permeable channels in the plant endomembrane system, will be investigated in the context of the AM symbiosis. Unveiling the cellular and molecular determinants of plant root endosymbioses is essential to improve plant mineral nutrition and to develop sustainable agricultural practices.

### **Glucocerebrosidases in neurons physiology and in neurodegeneration.**

Contact: Dr. Nicoletta Plotegher, e-mail: [nicoletta.plotegher@unipd.it](mailto:nicoletta.plotegher@unipd.it)

Lipid homeostasis is crucial for neuronal function, growth and morphology. Several neurodegenerative diseases were shown to be associated with imbalances in lipid levels or with defects in proteins involved in lipid metabolism. Glucocerebrosidases are enzymes that are key for the homeostasis of glucosylceramide and glucosylcholesterol; defects in these proteins were shown to be associated with different neurodegenerative diseases, such as Hereditary Spastic Paraplegia and Parkinson's disease, and with lysosomal storage disorders, such as Gaucher Disease. This project will involve the study of the molecular mechanisms causing neurodegeneration in diseases associated to glucocerebrosidases dysfunction, with a special focus on the role of intracellular organelles in the neurodegenerative process. To do that, a wide range of biochemical, biophysical and bioimaging techniques will be used, either in vitro, in cell models (such as immortalized cells and primary mice neurons) and/or in animal models. The project implies the possibility of working in collaboration with clinicians to study human-derived samples and models, and to spend some time abroad in the lab of collaborators.

### **Ecophysiology of fish from the Venetian Lagoon.**

Contact: Prof. Gianfranco Santovito, e-mail: [gianfranco.santovito@unipd.it](mailto:gianfranco.santovito@unipd.it)

Marine ecosystems, including lagoons, are facing environmental changes induced by human activities mainly related to industry, agriculture, tourism and urbanization. The Habitat Directive of the European Union lists coastal lagoons (habitat code 1150) among priority habitats because they are in danger of disappearance. The Venetian Lagoon represents an excellent study case due to the severe impact of anthropogenically driven pressures, in particular climate change and chemical pollution. What physiological responses can fish in the Venetian Lagoon bring into play in order to live with this chemical anomaly in their environment? Can the presence of any phenotypic plasticity also protect them from environmental contaminants of emerging concern, such as perfluoroalkyl substances, which are increasingly present in this environment? Are there evolutionarily favoured species within the lagoon fish biodiversity in light of ongoing global changes? The potential impact of pollutants on fish physiology is still largely unknown. Therefore, one of the main goals of this doctoral research is to better understand the physiological responses, both at the transcriptomic and proteomic levels, of fish in the Venice Lagoon against the negative effects of xenobiotic accumulation, with particular reference to cellular stress defences.

### **The function of metabolic signaling in cardiovascular disease.**

Contact: Prof. Massimo Santoro, e-mail: [massimo.santoro@unipd.it](mailto:massimo.santoro@unipd.it)

Vascular cells exhibit unique plasticity in terms of redox biology and metabolism. Our lab has contributed in the past years in decoding some of these cellular and molecular mechanisms (Oberkersch et al., *Developmental Cell* 2022; Facchinello et al., *Nature Metabolism*, 2022; Arslanbaeva et al., *Redox Biology* 2022). By using advanced redox and metabolic platforms, and innovative molecular and genetic approaches in cellular and animal models, we aim to shed light on the role of redox metabolic pathways and antioxidant enzymes in angiogenesis and cardiovascular diseases. The ultimate objective is to open the way for the development of innovative therapeutic strategies and complement the existing ones based on genetic and pharmacological manipulation of redox and metabolic state in cardiovascular processes in health and disease.



### **Mitochondrial quality control in neurodegenerative diseases**

Contact: Elena Ziviani, e-mail: elena.ziviani@unipd.it

Mitochondrial dysfunction and quality control has become a central theme in neurodegenerative diseases. Mitochondrial stress can lead to the release of reactive oxygen species (ROS), which triggers inflammation and cell death. Thus, approaches that boost mitochondrial autophagy (mitophagy) have the potential to clear damaged mitochondria as sources of ROS, and prevents neuroinflammation and neuronal cell death. Mitophagy can be triggered by post-translational modifications (PTM) such as phosphorylation and ubiquitination, and it is associated with the formation of mitochondria-ER contact sites (MERCs). Ubiquitination of mitochondrial proteins in particular is a well-known molecular mechanism that stimulates the so-called ubiquitin mediated mitophagy pathway. To address the effects of ubiquitination and de-ubiquitination and other PTM in mitochondrial physiology and quality control, as well as in the physiology of MERCs, we use primary neurons of human origin, and other cellular models of neurodegenerative diseases. In summary, our research is focused on understanding the molecular mechanisms that regulate macroautophagy and mitophagy in neurodegenerative conditions, and it will explore the potential of enhancing basal mitophagy as therapeutic strategy to treat neurodegenerative diseases.

### **Positions without scholarship**

#### **Treatment of breast carcinoma with specific T lymphocytes activated with nanoparticle materials.**

Contact: Prof Marina de Bernard, e-mail: marina.debernard@unipd.it

Breast cancer is as an excellent example of a solid tumor for which current treatments are indeed effective (with a 20-year survival rate of 80-85%), but equally invasive considering the necessity for surgical intervention in the majority of cases, followed by a treatment regimen that may include radiotherapy, chemotherapy, or hormonal therapy, prolonged over time and with associated side effects. Additionally, the psychological damage for predominantly female patients related to breast removal and/or reduction is evident. Consequently, therapies equally effective as or more effective than current standards of care must involve different approaches. The aim of this project is to develop a minimally or non-invasive treatment for breast cancer based on T lymphocytes isolated from patients with breast cancer and specific for tumor antigens, engineered with biocompatible nanomaterials to enhance their anti-tumor efficacy. The project involves collaboration among three companies and two research institutions, including the University of Padua represented by the Department of Biology and the Department of Pharmaceutical Sciences. The doctoral student will refine the murine model of human breast cancer using nude mice and human breast cancer cell lines and assess the in vivo effectiveness of the system based on engineered lymphocytes. Furthermore, the student will conduct biosafety, biodistribution, and efficacy tests of the system in the murine model.

## **Curriculum Evolution, Ecology and Conservation**

### **Funded by External Public or Private Bodies/Departments**

#### **State, impacts and valorization of small scale fisheries in coastal areas of the Northern Adriatic Sea.**

Contacts: Prof. Carlotta Mazzoldi and Prof. Alberto Barausse,  
e-mail: carlotta.mazzoldi@unipd.it ; alberto.barausse@unipd.it

The Northern Adriatic Sea is a highly productive marine ecosystem and, consequently, is heavily exploited by socio-economically valuable fisheries which cause large impacts on biodiversity. While many research efforts have been made to characterize fishing pressure and mitigate its impacts, knowledge gaps remain about small-scale fisheries that are considered more sustainable than other types of fishing and represent important sources of local jobs and, in some cases, an intangible cultural heritage. This project will combine field work on-board of fishing boats, lab research on species caught by small scale fishing activities, and analyses of fishery records with the goal to characterize the socio-economic state of small scale fisheries in coastal areas of the Northern Adriatic Sea and their environmental impacts. Through collaborative approaches with fishers, the project will also investigate opportunities for impact mitigation and sustainable valorization such as short food supply chains and circular economy to deal with litter caught at sea.

#### **Development of conservation strategies for elasmobranchs in the Mediterranean Sea through sustainable fisheries.**

Contacts: Prof. Carlotta Mazzoldi and Prof. Alberto Barausse,  
e-mail: carlotta.mazzoldi@unipd.it ; alberto.barausse@unipd.it

The conservation status of elasmobranchs is alarming, in particular in the Mediterranean Sea where more than half of the evaluated species are considered under threat. Elasmobranchs are often bycatch of fisheries targeting more valuable species and, due to their large sizes, reducing their accidental catches without compromising the capture of the target species is not an easy task. In the framework of the European LIFE project Prometheus, through collaborations with other research institutes at Mediterranean scale, this project will explore conservation strategies aimed at developing sustainable fisheries with low impact on elasmobranchs. The project will include desk, lab and field work. Areas representing sensitive sites for elasmobranchs (e.g., parturition, nursery or aggregative areas) will be identified and put in relation with protection status and the occurrence of human pressures (e.g., fishery). Fishing gears equipped with tools to reduce elasmobranch bycatch and/or alternative fishing practices will be investigated in these areas.

#### **Network and quantitative biology: aspects of evolution, ecology and conservation**

For the topic of this project please refer to any of the projects Funded by the University reported below.



## **Funded by the University**

### **Assessing the outcomes of marine restoration**

Contacts: Prof.ssa Laura Airoidi  
e-mail: [laura.airoidi@unipd.it](mailto:laura.airoidi@unipd.it) ;

Marine restoration is an emerging field encompassing multiple forms of interventions to repair, enhance, or reinvent damaged native ecosystems. The UN Decade on Ecosystem Restoration and the new EU Restoration Law are encouraging the implementation of marine restoration. However, a lack of common indicators of success still hinders a comprehensive evaluation of the outcomes. The project focuses on assessing the outcomes of real scale restoration projects in the North Adriatic sea (oysters and/or saltmarshes) in terms of their capacity to: i) restore damaged biodiversity and ecosystem processes and services; ii) limit negative impacts on local ecosystems and natural resource use; and iii) be connected with the natural context. Field sampling will be designed to provide comparisons: i) between the restored and reference non-restored sites; and ii) Before and After restoration. We will also iii) assess the broader ecological and functional connectivity of the restoration sites with other landscape elements (natural and anthropogenic). Training in Scientific Diving is a fundamental requirement for this project, as well as English language proficiency. Skills in either oyster ecology or sedimentary benthos is regarded as an advantage, as well as data analysis proficiency with R

### **Leveraging genetic effective population size in historical and prehistoric time to inform models of cultural evolution**

Contacts: Prof. Pagani Luca  
e-mail: [luca.pagani@unipd.it](mailto:luca.pagani@unipd.it) ;

Recent methods enabled the inference of changes in effective population size through time from present day and ancient genomic data with a resolution of up to a generation. Effective population size, in humans, can be used as a valuable proxy for census size and, therefore, genomic data can provide a valuable estimate of census size at a given time for any given human population. Census size is an invaluable and elusive parameter when innovation rate, conformist bias and other parameters that relate to modelling phenomena of cultural evolutions are implied. With this project the candidate will have an opportunity to infer changes in population size through time for human population worldwide, compare the changes with known cultural shifts (e.g. transitions from Initial Upper to Upper Palaeolithic, advent of Agriculture and domestication of plant and animal species in several independent locations, Industrial Revolution in Europe among others) and provide a genetically informed model for these phenomena of cultural evolution through time.

### **Evolutionary consequences of sexual selection under anthropogenic change**

Contacts: Prof. Pilastro Andrea  
e-mail: [andrea.pilastro@unipd.it](mailto:andrea.pilastro@unipd.it) ;

Sexual selection is driven by competition among individuals for reproductive success. Despite being a zero-sum game, it has produced some of the most spectacular examples of reproductive adaptations, from the iconic tail of the peacock to the enormous body size observed in the males of the elephant seals. Sexual selection has also been demonstrated to profoundly influence population dynamics and the response of organisms to environmental change. Whether sexual selection will be aligned with natural selection under environmental change, however, is very difficult to predict, due to the extreme sensitivity of sexual selection dynamics to environmental and population conditions at mating. Human activities are responsible for a myriad of environmental changes that vary in direction and intensity on even small geographic scale. There are however two very general trends that affect most animal populations worldwide: an increase in global temperatures and a progressive defaunation (i.e. a reduction of population densities). The aim of this project is to investigate how climate

warming and population density interact to affect sexual selection dynamics and hence the potential of population to adapt using poeciliid fish as model species.

### **Fitness Consequences of Pre- and Postmating Mate Choice**

Contacts: Prof. Gil Rosenthal  
e-mail: gil.rosenthal@unipd.it ;

Few decisions in life are as important as choosing who to mate with, yet the fitness consequences of mate choice are seldom directly measured. Using two poeciliid fish species as model, the project combines experimental work on the fecundity and viability consequences of mating with preferred and non-preferred partners with genomic and simulation studies of the genetic and phenotypic Consequences of realized versus possible mating outcomes. Work is conducted in the laboratory in Padova and at the CICHAZ field station in central Mexico.

### **Monitoring of biodiversity of the major rivers of the eastern Po Valley by eDNA metabarcoding**

Contacts: Prof. Alessandro Grapputo  
e-mail: alessandro.grapputo@unipd.it ;

Freshwater ecosystems are experiencing biodiversity declines far surpassing those observed in the most impacted terrestrial ecosystems. Consequently, the conservation and management of freshwater resources have become of paramount importance. Our understanding of freshwater biodiversity remains incomplete and challenging to assess using traditional methods. In this project, we intend to investigate the biodiversity of major rivers in the eastern Po Valley using eDNA metabarcoding. We aim to compare this approach, particularly for fish species, with traditional monitoring methods such as electrofishing. To this end, we have already reached out to ichthyologists who typically engage in fish surveys using traditional approaches. The project aims to achieve two objectives: firstly, to evaluate the efficiency and reliability of the eDNA-based approach and develop guidelines for such investigations, and secondly, to lay the groundwork for systematic monitoring of biodiversity in watercourses that are poorly studied. Moreover, eDNA barcoding will enable us to expand biodiversity monitoring to include lesser-known species, particularly invertebrates, as well as to track the presence and spread of invasive species.

### **Positions without scholarship**

#### **Ecological drivers, impacts and mitigation of the Atlantic blue crab, *Callinectes sapidus*, invasion in the coastal areas of the northern Adriatic Sea**

Contacts: Prof. Carlotta Mazzoldi and Prof. Alberto Barausse,  
e-mail: carlotta.mazzoldi@unipd.it ; alberto.barausse@unipd.it

This project will explore the ecological drivers and the impacts of the invasion of the Atlantic blue crab *Callinectes sapidus* in the coastal areas of the northern Adriatic Sea. The Atlantic blue crab recently spread in the area causing alarm in the fishery sector. In this project, the PhD candidate will combine field sampling, fishery record statistical analysis, and experimental approaches to understand the influence of temperature, salinity and bottom characteristics on the occurrence of the different life stages of the blue crab, contributing to building a knowledge base to mitigate this biological invasion. Through collaboration with fishers, the impact of the Atlantic blue crab on the fishing activities will be also evaluated and mitigation measures explored.

## **Curriculum Genetics, Genomics and Bioinformatics**

### **Funded by External Public or Private Bodies/Departments**

#### **Gene editing to correct inherited cardiac diseases.**

Contact: Prof. Milena Bellin, e-mail: milena.bellin@unipd.it

Inherited cardiac diseases are caused by specific genetic variants with subsequent discrete disease mechanisms. Gene editing approaches designed to correct precise gene mutations offer exciting options to repair genetic diseases, including those of the heart. This project will develop and test gene editing tools to correct gene mutations causing channelopathies and cardiomyopathies in three-dimensional cardiac microtissues from patient-specific human induced pluripotent stem cells (hiPSCs). We offer an international environment and cutting-edge technology.

#### **Generation and characterization of allelic series of hiPSC to classify variants of unknown significance in arrhythmogenic cardiomyopathy.**

Contact: Prof. Milena Bellin, e-mail: milena.bellin@unipd.it

Arrhythmogenic cardiomyopathy (ACM) is a genetic disease that predisposes to malignant ventricular arrhythmias and sudden cardiac death, mainly in young adults and athletes. However, classification of genetic variants as malignant or benign is not always trivial. The aim of this project is to develop human induced pluripotent stem cell (hiPSC)-based tools to assist the classification of variants of unknown significance (VUS) in ACM. Gene editing will be used to generate allelic series of hiPSCs containing at distinct VUS in plakophilin2 (PKP2), the main ACM-causative gene. The allelic hiPSC series will be used to derive cardiomyocytes and build three-dimensional multicellular cardiac microtissues that will be characterised with regards to ACM-related phenotypes. This project will assist ACM patient stratification by determining the contribution of variants of unknown significance. We offer an international environment and cutting-edge technology.

#### **CircRNAs involved in mechanisms of malignant transformation and relapse in T-ALL.**

Contact: Prof. Stefania Bortoluzzi, e-mail: stefania.bortoluzzi@unipd.it

This PhD position is linked to an AIRC research project started in 2024 that aims to characterize the circRNAome dysregulation in T-cell Acute lymphoblastic Leukemia-ALL at diagnosis, defining circRNAs associated to distinct clinical, biological and genetic features of patients, to disclose circRNAome variation during T-ALL progression wiring circRNAs to chemoresistance networks, and to obtain an extensive functional characterization, at biological and mechanistic levels, of circRNA roles in malignant transformation and disease progression in T-ALL, disclosing new therapeutic targets. The PhD student will be involved in all the bioinformatics activities of the project and will collaborate with researchers operating in experimental and clinical studies, at national and international level.

#### **Generation and characterization of 3D in vitro models for arrhythmogenic cardiomyopathy.**

Contact: Dr. Martina Calore, e-mail: martina.calore@unipd.it

Arrhythmogenic cardiomyopathy is a genetic cardiac disorder characterized by fibro-fatty replacement of the myocardium which results in fatal arrhythmias, especially in the young. Currently, there is no effective treatment for the disease. In this PhD project, we aim to generate and characterize novel 3D in vitro models based on induced-pluripotent stem cells

generated from affected patients. These models will be used as a platform to test FDA-approved compounds as well as RNA-based therapies for the disease.

**Optimization of biogas production through an innovative method for microbiological surveillance of full-scale plants.**

Contact: Prof. Stefano Campanaro, e-mail: [stefano.campanaro@unipd.it](mailto:stefano.campanaro@unipd.it)

In biogas production (anaerobic digestion, AD), organic matter is decomposed under anaerobic conditions by a complex microbial community to form biogas and a nutrient-rich biofertilizer. The quantity and composition of biogas, as well as the efficiency and stability of the process, depend on various parameters, both direct, such as substrate characteristics and temperature, and indirect, such as volatile fatty acid concentration and methane content in biogas. Among these parameters, the composition of the microbiome is one of the main process indicators but is rarely considered. The overall goal of the project is to develop a rapid method for monitoring the microbiome in industrial biogas plants that allows for the prediction of any imbalances and proactive intervention to restore optimal conditions.

**Targeting fibro-adipogenic precursors in cardiac fibrosis as a new therapeutic option**

Contact: Prof. Alessandra Rampazzo, e-mail: [alessandra.rampazzo@unipd.it](mailto:alessandra.rampazzo@unipd.it)

Fibrosis is defined as a pathological remodeling of the extracellular matrix that can result from various causes, ranging from acute tissue injury to inherited molecular defects. In the heart, injury of myocardium activates stromal cells towards a fibrogenic program, which ultimately leads to the replacement of contractile tissue with a fibrous scar; these scars can cause severe heart failure, often with life-threatening consequences.

This project aims to study the key cellular and molecular mechanisms that regulate cardiac fibrosis, as well as to identify small molecules potentially capable of blocking the proliferation/pathological differentiation of fibrogenic progenitors. To achieve this, we will couple relevant animal models and human induced pluripotent stem cell (iPSC)-derived cardiac models.

**Network and quantitative biology: aspects of genetics, genomics and bioinformatics**

For the topic of this project please refer to any of the projects Funded by the University reported below.

**Funded by the University**

**Long non-coding RNAs: the new layer of regulation of gene expression and mitochondrial function during aging.**

Contact: Prof. Stefano Cagnin, e-mail [stefano.cagnin@unipd.it](mailto:stefano.cagnin@unipd.it)

Average life expectancy and the proportion of elderly individuals in the human population continue to increase. The molecular mechanisms underlying age-related decline associated with altered regulation of gene expression and organelle function remain largely unresolved. In the field of gene expression regulation, the study of long noncoding RNAs (lncRNAs) is becoming increasingly important for their ability to epigenetically regulate cellular functions. Starting from a transcriptomic approach, we aim to identify and functionally characterize some lncRNAs involved in energy modulation of skeletal muscle cells during aging.

**Identification of RNA targets in *D. melanogaster* by TRIBE reveals insights into hnRNPs mediated post-transcriptional regulation.**

Contact: Prof. Gabriella Mazzotta, e-mail [gabriella.mazzotta@unipd.it](mailto:gabriella.mazzotta@unipd.it)

Heterogeneous nuclear ribonucleoproteins (hnRNPs) are RNA binding proteins involved in many post-transcriptional processes and their disrupted regulation correlates with various disorders, including neurodegeneration. *Drosophila* has greatly contributed to understanding basic mechanisms associated to many diseases. This project exploits TRIBE (Targets of RNA-binding proteins Identified By Editing), to identify hnRNPs targets in fly selected neuronal subtypes, pivotal for their functional understanding. It combines genetics and molecular methodologies with sophisticated transcriptomic analyses

**Looking for new molecular mechanisms underlying neoplastic transformation processes in endocrine tumors.**

Contact: Prof. Gianluca Occhi, e-mail [gianluca.occhi@unipd.it](mailto:gianluca.occhi@unipd.it)

This is a basic/translational project aimed at addressing important scientific and clinical issues related to the etiology and pathogenesis of endocrine tumors (i.e., Non-medullary Thyroid Cancer, Primary Bilateral Macronodular Adrenal Hyperplasia, Multiple Endocrine Neoplasia). Specifically, the main objective is to investigate the genetic components and molecular mechanisms that characterize these tumors through the integrative analysis of -omics data, combined with functional studies using appropriate cell models (i.e., cell lines and primary cultures).

**Machine Learning Approaches for Advancing Microscopy Image Segmentation: Reconstructing Shapes of Irregular and Partially Overlapping Cells.**

Contact: Prof. Gabriele Sales, e-mail [gabriele.sales@unipd.it](mailto:gabriele.sales@unipd.it)

The aim of this project is to develop novel machine learning algorithms for the precise segmentation of irregular and partially overlapping cells captured in microscopy images. We will specifically focus on deep learning methods that have recently shown the best performances in delineating cell boundaries, even in complex scenarios. By integrating denoising approaches to reduce measurement artefacts with structured embeddings that constrain different objects in single dimensions, we aim to improve segmentation performance and reduce the manual effort associated with this task

**Zebrafish-based modelling and treatment of POLG-related mitochondrial disorders**

Contact: Prof. Natascia Tiso, e-mail [natascia.tiso@unipd.it](mailto:natascia.tiso@unipd.it)

The mitochondrial (mt) DNA polymerase gamma (Pol gamma), composed of a catalytic component (POLG) and two accessory subunits (POLG2), is an enzyme involved in mtDNA replication and maintenance. Mutations in POLG or POLG2 underlie POLG mt disorders, characterized by multi-organ dysfunction and a poor prognosis. Recently, our team succeeded in producing zebrafish *polg* and *polg2* KO lines, faithfully modeling human POLG disorders, and suitable for testing therapeutic drugs. We now aim to: a) generate KI lines; b) test additional molecules; c) elucidate drug mechanisms on Pol gamma and mt activity.