Effects of underwater anthropogenic noise on sessile aquatic invertebrates.
Contact: Prof. Loriano Ballarin, e-mail: loriano.ballarin@unipd.it

Many studies have shown that noise can affect several animal physiological processes, in particular immune responses. Indeed, the increasing level of underwater noise due to anthropogenic activities (mainly maritime traffic) is a matter of concern for aquatic ecosystems. In particular, the effects of underwater noise on immune system, development and resilience is much less studied and data are available mostly for aquatic vertebrates (fish and whales). Almost nothing is known on the effects of underwater noise on sessile invertebrates that, unlike mobile organisms, cannot change their position and move apart from the source of noise. Ascidians are marine sessile invertebrates belonging to the subphylum Tunicata, considered the sister group of vertebrates. Previous research have shown that they possess mechanoreceptors resembling vertebrate hair cells. This project aims at studying the effects of underwater noise on sessile ascidians that will be collected in the field, in the Lagoon of Venice, in both "silent" and noisy sites. In addition, ascidians reared in the lab will be exposed to underwater noise of various intensities and frequencies. Noise effects will be evaluated at behavioral, morphological, physiological and transcriptomic level.

Mitochondria-lysosomes interplay in neurodegeneration with brain iron accumulation.
Contact: Prof. Marco Bisaglia, e-mail: marco.bisaglia@unipd.it

Neurodegeneration with brain iron accumulation (NBIA) encompasses a group of rare genetic neurological disorders characterized by iron accumulation in the basal ganglia. Mutations in the C19orf12 gene have been recently identified in a specific NBIA subtype termed mitochondrial membrane protein-associated neurodegeneration (MPAN), clinically characterized by dystonia, weakness, optic atrophy, and neuropsychiatric changes. While the physiological role of the C19orf12 protein is still unknown, a variety of phenotypes have been associated with C19orf12 deficiency, such as mitochondria defects, alterations in lipid metabolism and autophagosome formation, although contrasting results have been reported.
This Ph.D. project aims to characterize in vivo the primary function of the C19orf12 protein in specifically designed *Drosophila* models and, possibly, in iPSCs from patients, through the use of complementary biochemical assay and state-of-the-art imaging techniques. More specifically, the interplay between lysosomes and mitochondria will be carefully evaluated as well as the participation of mitochondria in the iron-associated toxicity.

The reprogramming of mevalonate pathway in pathological systems and its contribution to mitochondrial dysfunction and redox imbalance.
Contact: Dott. Alessandro Carrer, e-mail: alessandro.carrer@unipd.it

The mevalonate pathway (MVP) leads to the de novo synthesis of sterols and isoprenoids (also, terpenoids) that significantly contribute to multiple cellular functions. In fact, the MVP is often deregulated in neurodegenerative diseases and tumors. The role of MVP intermediates in redox homeostasis remains however unclear. The candidate will apply biochemical approaches to cellular models of disease in order to document the specific role of metabolites downstream of mevalonate in disease-associated mitochondrial dysfunction and redox dishomeostasis. The candidate will also interrogate their impact for pathogenesis.

An evolutionary insight to chordate inflammation: Searching for the origin of mast cells in tunicates and their role in acute inflammation.
Contact: Prof.ssa Francesca Cima, e-mail: francesca.cima@unipd.it

Due to their phylogenetic position, the defense system of tunicates has awakened for a long time a remarkable interest in the attempt of correlating it to the immune system of vertebrates in an evolutionary scenario. The research will address to the comprehension of the content and role of polyfunctional immunocytes in a very stimulant evolutionistic context searching the origin of vertebrate mast-cells and their functional heterogeneity, immunosurveillance mechanisms, cross-talking and signalling with other circulating immunocytes. It will concern the following points by means of various techniques on research models mainly represented by ascidian species, for which the genome and transcriptome databases are publicly available, i.e., 1) morpho-functional characterization, 2) role of immunosurveillance, 3) presence of chemical mediators and receptors shared with vertebrate mast-cells, 4) effects and mechanisms of action of the mast-cell mediators.

Host-microbiota interactions in colorectal cancer onset and disease progression.
Contact: Dott.ssa Gaia Codolo, e-mail: gaia.codolo@unipd.it

The gut microbiota plays a central role in health, and alterations in the gut microbiota have a pivotal role in the homeostasis of intestinal epithelial cells and disease progression, such as that of colorectal cancer (CRC). Yet, the mechanisms behind host-microbiota interactions in CRC, especially at the intestinal epithelial cell level, are not fully understood. Dissecting the role of host-microbiota interactions in disease onset and progression is pivotal, and requires representative models mimicking the gastrointestinal ecosystem, including the intestinal epithelium, the gut microbiota, and immune cells. Tumor-associated macrophages (TAMs) are the most abundant immune cell population in the tumor microenvironment (TME) of CRC, which orchestrates various dynamics in the TME.
Intestinal organoids are emerging as a powerful tool to study CRC host-microbiota interactions and the interactions between the tumor epithelium and immune cells.
This project is aimed at deciphering the crosstalk between microbiota, intestinal epithelium, and macrophages both in vitro and in vivo. To better resemble the interaction occurring in the TME, we will adopt a physiologically relevant model already established in our laboratory, in which intestinal organoids (derived from normal tissue or tumor tissue) will be co-cultured with macrophages; this model will be implemented with microbiota or specific metabolites produced by microbiota known to modulate intestinal barrier functions and integrity, and in modulating immune response. Data obtained in vitro will be validated in vivo adopting a well-established mouse model of colorectal cancer.

Lipid homeostasis in neurons physiology and in neurodegeneration.
Contact: Dott.ssa Nicoletta Plotegher, e-mail: 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. Lipids can impact neurons by affecting both signalling pathways and membrane properties. The project will involve the study of the role of neuronal lipids and of enzymes involved in lipid catabolism in the physiology of neuronal cells. Moreover, we will investigate the lipid contribution to neuronal damage in neurodegenerative diseases such as Hereditary Spastic Paraplegia and Parkinson's disease, and in lysosomal storage disorders, by exploiting pharmacological and genetic disease models. To do that, a wide range of biochemical, biophysical and bioimaging techniques, in vitro, in cell models (such as immortalized cells and primary mice neurons) and in animal models, i.e. zebrafish, will be used. 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.