Computational dissection of the tumor microenvironment of ovarian cancer metastases through single cell sequencing.
Contact: Dr Enrica Calura, e-mail: enrica.calura@unipd.it

The PhD project is focused on the study of ovarian cancer, which is a highly lethal female malignancy, usually diagnosed at late stages with extensive and frequent chemoresistant metastases. The tumor is a complex ecosystem composed of healthy and malignant cell types, which mediate tumor progression, drug delivery and affect chemoresistance. The PhD candidate will study the ovarian cancer microenvironment through computational analyses of single cell RNA sequencing data, defining the cell components and their context-dependent crosstalk in multiple metastases before and after chemotherapy

Role of tumor-associated macrophages (TAM) in immune evasion in cancer.
Contact: Dr Gaia Codolo, e-mail: gaia.codolo@unipd.it

Tumor-associated macrophages (TAMs) are one of the major immune cells that infiltrate the tumor. In the tumor microenvironment TAMs orchestrate various dynamics that culminate in the inhibition of the antitumor immune response, allowing tumor cells to evade the immune system. In many tumors a high infiltration of TAMs is usually associated with a poor prognosis.
This project is aimed at dissecting the mechanism of immune evasion in tumor models such as colorectal cancer and pancreatic cancer. It will study the molecular pathways and molecules that switch-off the ability of macrophages to counteract tumor growth. Some of these molecules could act as immune-checkpoint; the final goat of this project is to pave the way toward the design of novel approaches for the TAMs-targeted immunotherapy.
Different approaches will be adopted to identify pathways leading, for example, to the impaired antigen presentation process: primary cells isolation and culture from blood and other tissues, organoids/macrophages co-culture, FACS analysis, transcriptome analysis, biochemistry, metabolomics.
Different tumor models will be adopted to understand the mechanisms that regulate the unsuccessful antigen presentation in cancer.

Studying mitochondria-Endoplasmic Reticulum Contact sites during melanogenesis.
Molecular characterization of AIFM3: analysis of the structure-function relationship.
Contact: Dr Marta Giacomello, e-mail: marta.giacomello@unipd.it

The process responsible for melanin synthesis within cells, named melanogenesis, is based on several intracellular steps, some of which still needs elucidation. Our preliminary data suggest that an apoptosis inducing factor like protein is involved in this process. We will study whether and how this protein modulates the production of melanin in normal melanocytes or malignant cells by means of complementary approaches including RNA sequencing, mass spectrometry and high content microscopy.

Shedding light on anti-inflammatory and anti-oxidant origin and function of biomolecules from therapeutic thermal muds of the Euganean District.
Contact: Prof. Nicoletta La Rocca, e-mail: nicoletta.larocca@unipd.it

The application of the Euganean mature thermal muds is a therapy recognized by the Italian health system and particularly recommended for arthro-rheumatic diseases. The mud healing properties are ascribed to heat and electrolytes of thermal waters as well as to bioactive molecules released by a specific microbiota, dominated by cyanobacteria, that grow during the traditional mud maturation process. Focus of the PhD project will be the lipidic molecules released by the microbiota, such as the galactolipids MGDG and DGDG produced by the target species Phormidium ETS 05, that are already the subjects of a European Patent on the Euganean mud efficacy. Main aim of the project will be the quantitative and qualitative characterization of the molecules of lipidic nature directly extracted from the mature muds and released from the entire

microbiota community as well as those produced by isolated strains of the most abundant cyanobacteria. The dose-effect relationship and the effectiveness of these compounds and the molecular pathways involved in their anti-inflammatory and/or antioxidant activities will be assessed by using human cell lines and/or wild-type and transgenic lines of the model organism zebrafish.

Development of photorespiratory bypass in *Physcomitrella patens.*
Contact: Prof. Tomas Morosinotto, e-mail: tomas.morosinotto@unipd.it

Ribulose 1,5-bisphosphate Carboxylase/Oxygenase (RuBisCO) is the most abundant enzyme in the biosphere and is photosynthesis responsible of the CO_2 fixation. RuBisCO low specificity leads its alternative reaction with O_2 with the final production of 2-phosphoglycolate (2-PG). This toxic molecule needs to be recycled by a pathway called Photorespiration. In today's plants Photorespiration is an ineluctable process which, however, dissipates energy and releases CO_2. The resulting decrease in assimilation efficiency and biomass yield by ~30%, represents a prime target to improve agricultural productivity.
In past few years different non-native and synthetical metabolic pathways have been discovered and/or synthetically designed to bypass the photorespiration reactions and more efficiently recycle the products of Rubisco oxygenation.
In the work driving to the introduction of non-native pathways in a large-scale crop, we will employ the bryophyte *Physcomitrella patens* as model organism for the pathway optimization in plants. The high efficiency of genes KO through Homologous-Recombination, the predominance of the haploid phase of the life cycle and the speed in regeneration makes this moss an ideal organism to develop and optimize such a complex metabolic rearrangement before moving the optimized version into crops.

Monitoring the microbiome responsible for CO2 capture and hybrid energy storage through metagenomics and metabolic modelling.
Contact: Dr Laura Treu, e-mail: laura.treu@unipd.it

Life CO2toCH4 aims at developing and demonstrating an innovative, integrated, and sustainable industrial process for simultaneous energy storage and CO2 capture and utilization (CCU). The technology relies on the fact that the Renewable Energy Sources (RES) will be used for water electrolysis, and subsequently the produced H2 will be biologically converted into methane (as a non-fossil biofuel) together with CO2 from exhaust gasses. To maximize the efficiency of methanation, technically advanced systems will be developed by using control architectures based on microbial resource management and computational biology. The currently restricted capacity of the power-to-gas concept will be expanded to use impure CO2 sources by using mixed microbial consortia that are more robust than pure cultures. Microbial monitoring of the archaea population will ensure that the H2 and CO2 will be converted to CH4 and not follow a different metabolic route for acetic acid production (i.e. to avoid homoacetogenesis). To physiologically monitor the microbial activity, metagenomics and, subsequently, genome-scale computational models of microbial populations will be used as a platform for biochemical data integration and interpretation. The process will thus be optimized by routing the fluxes of intermediate metabolic products, evaluating carbon and electron balances and will be coupled with in-depth molecular analysis. Such optimization will be guided by machine learning models combining process monitoring data and model simulations. This project will contribute to the implementation of the European Union policy and legislation on the promotion of the advanced biofuels, circular economy and on sustainable waste management.

Topics "Biological Signals"

The topic of these projects will coincide with one of the topics presented in each Curriculum.