

Deciphering environmental signals in plants through *in vivo* imaging.

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Photosynthetic organisms colonized Earth by adapting to several ecological niches and the investigation of early land plants can give valuable information on this process. The aim of this PhD project is to investigate plant response to environmental changes focusing on the molecular mechanisms which allow sensing environmental conditions to regulate metabolism accordingly. For this purpose, the main task of this PhD project will be the *in vivo* study of plant second messenger and metabolite dynamics through the optimization of specific FRET-based sensors for their measurement.

Central players and biomimetic signals in neuritogenesis, neural development and regenerative medicine.

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Since its discovery, we lead the characterization of the Longin domain, which regulates neuritogenesis together with neuronal L1CAM. We also developed biomimetic, CAM-derived peptides able to boost neuronal differentiation; this helped shedding light on the ability of specific motifs to act as guidance cues and thus involved, when signalling is disrupted by mutation, in severe neurodevelopmental disorders. As part of a local and international network, we also set up a regenerative medicine system combining nanocomposite scaffolds, biomimetic peptides and designed protein domains. The PhD project aims to further define pivotal players and motifs in the regulatory network able to fine tune cell differentiation and tissue regeneration.

Algae metabolic engineering for the sustainable production of Bio-commodities.

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Global demand of biomass is continuously expanding and new sustainable technologies are needed to avoid overexploitation of natural resources, reduce environmental footprints and greenhouse-gas emissions. Algae represent a valuable alternative for the production of several bio-commodities going from biofuels to feed, food and chemicals. Thanks to their efficiency in carbon dioxide (CO₂) fixation, algae large scale cultivation can also contribute to the mitigation of anthropogenic greenhouse gas emissions. Despite this potential, algae large scale cultivation still present several limitations and only a few algae-based products are currently present on the market.

This project will address these issues using genetic engineering to increase biomass yield of algae grown in photobioreactors, engineering the photosynthetic electron transport chain. Complementarily, strains with improved productivity will be isolated using directed evolution applying selective pressure to favour individuals with faster growth.

Molecular bases of algae metabolic regulation and carbon partitioning will also be investigated in cultures with altered content in lipids, proteins or isoprenoids by genetic modifications of different biosynthetic pathways. Successful modifications will then be combined to obtain strains with both increased growth and content in the molecules of interest. The most promising strains generated will also be tested outdoor to assess their potential in industrially relevant conditions.

Role of mitochondrial respiration in photosynthetic organisms.

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Photosynthetic organisms use light energy to support their metabolism and are major contributors of the world primary energy production, supporting most lifeforms on Earth. Photosynthesis drives also the fixation of carbon dioxide into biomass with a fundamental role on carbon cycle and a strong influence on mitigating the accumulation of this greenhouse gas in the atmosphere.

Even if the primary source of energy for photosynthetic organisms is light, mitochondrial respiration supports metabolism in the dark and in non-photosynthetic tissues like roots. Respiration is however active also under illumination when it interacts with photosynthetic reactions through molecular mechanisms that are not yet completely clear.

The present project aims to unveil the biological role of respiration in photosynthetic metabolism by isolating and studying plants where respiratory activity is depleted. These mutant plants are normally non-viable and for this reason they have never been isolated so far. Using a new strategy, involving the model non-vascular plant *Physcomitrella patens*, the respiration-dependent phases of lifecycle can be bypassed allowing for the isolation of lines with strongly reduced respiration. The investigation of mutants with depleted respiratory activity will provide a leap forward in our understanding of role of mitochondria in metabolism of photosynthetic organisms, ultimately offering molecular insights to develop new strategies to improve crops productivity.

Exploring the role of ATAD3B in undifferentiated cells and tumorigenesis.

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ATAD3 is a protein family present up to primates as a single gene, ATAD3A; that then suffered a double in tandem gene duplication that gave rise to ATAD3B and ATAD3C, the latter suggested being a pseudogene. In the last years, our lab has described the role of ATAD3A in the maintenance of mitochondrial ultrastructure and mitoribosomes stability. However, and despite the high similarity between ATAD3A and ATAD3B sequences, almost nothing is known about the function of ATAD3B. Previous studies have described the ATAD3B expression only in undifferentiated and tumoral cells, and a dominant-negative effect on ATAD3A, but the molecular mechanism and pathophysiological relevance is not known. This project aims to understand the role of ATAD3B in mitochondrial pathophysiology, and in particular, how it participates in cell differentiation and tumorigenesis. To this aim, we will use cellular and animal models, where it will be expressed ATAD3B in the presence or absence of ATAD3A to then study mitochondrial function by biochemical approaches, electron, and confocal microscopy. In vivo experiments in zebrafish and mice models are also part of the project.

Integrating chloroplast cation channels into intracellular signaling during stress response in higher plants.

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How plants sense stress signals and adapt to adverse environments are fundamental biological questions of socioeconomic importance, as stress negatively affect plant growth and biomass production. The view is emerging that chloroplasts respond to biotic and abiotic stresses with specific calcium signals. We have recently identified a Ca²⁺-flux mediating ion channel in the chloroplast envelope (Teardo et al, Nature Plants, 2019). The Ph.D. student will aim to integrate this cation channel into intracellular signaling, in order to clarify how calcium transport mediates the response to abiotic stress and generate signals that coordinate a fine-tuned stress response. The student will use innovative and integrative approaches to investigate signaling pathways in the cytosol and within chloroplasts as well as metabolic changes in plants lacking the identified cation channels. The work will likely unravel a currently unknown, yet central aspect of plant response to changing environments. The Ph.D. student will work in a dynamic group and will have the possibility to collaborate with local groups (Prof. Navazio and Dr. Formentin) as well as with internationally recognized experts in the field (Profs. Costa (Milan), Voithknecht (Bonn)).

Intracellular organelles as sensors for abiotic stresses in plants: role of mitochondrial UPR.

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Plant adaptation to stressful environments is a major challenge that agriculture is facing now and will be facing in the coming decades to meet the food and feed needs in the context of the climate changes. Increasing evidences show that chloroplasts and mitochondria act as sensory organelles playing a key role in orchestrating the response of the plant to environmental cues. With this project we are mainly interested in identifying the retrograde molecular components that act as signals between the organelles and the nucleus, focusing on organelle Unfolded Protein Response (orgUPR). orgUPR is, indeed, regarded as a stress response which is activated by a variety of different conditions that can lead to the accumulation of misfolded or unfolded proteins in chloroplasts and mitochondria. By using an integrated molecular, physiological and imaging approach the project aim to characterize this kind of process, identifying the retrograde molecular components that act as signals between the organelles and the nucleus.