PROJECT

PhD curriculum: Cellular and Molecular Neuroscience

Title of the project:
Iron homeostasis, oxidative stress and mitochondrial function in physiopathological conditions: an analysis in primary brain cultures and iPSC-derived neurons

Despite the crucial role played by iron in the CNS, many aspects of its cellular homeostasis are still unclear. Moreover, the cellular pathways involved in iron control have not been considered in view of their elaborate interplay and of the complexity of morphological and functional cell interactions within the SNC. This is particularly important considering that any intra or intercellular alteration of the iron homeostasis can cause or contribute to neurotoxic processes. In fact, iron dysregulation, with the ensuing increase in oxidative stress, can affect both neuronal and glial cells, ultimately leading to neurodegeneration.

The project will focus on the characterization of the mechanisms and pathways responsible for iron handling in primary brain cultures (neurons, astrocytes and microglia) with particular attention to the role of mitochondria on the induction of oxidative stress. In parallel, the effects of oxidative insults will be evaluated also in the more physiological model of organotypic slices obtained from rat brain. These studies, performed in physiological conditions, will be extended to a model of Friedreich’s ataxia, a neurodegenerative disease caused by a decreased expression of frataxin, a mitochondrial protein involved in iron handling. In view of the lack of appropriate animal models, iPSC-derived neurons from Friedreich’s ataxia patients will be used.

The experimental studies will mainly employ fluorescence videomicroscopy techniques (including Total Internal Reflection microscopy and high-throughput microscopy), complemented by biochemical and molecular biology approaches.

Selected related publications: