Project area: Cellular and Molecular Neuroscience

Supervisor: Federico Herrera, Cell Structure and Dynamics Laboratory, ITQB NOVA

Duration: 8-12 months

Number of students: 1-2

Title: The role of post-translational modifications and protein interactions in STAT3 behavior

Project Summary/abstract:

STAT3 is a transcription factor involved in immunity, development, cancer and neurodegeneration. It is activated by various kinds of extracellular signals, including cytokines from the IL-6 family. STAT3 forms dimers spontaneously in the cytosol. When cytokines bind to their receptors in the cell membrane, they trigger a cascade of protein phosphorylations, leading to the phosphorylation of STAT3 dimers at Y705 and their translocation to the nucleus. Once there, it binds to specific response elements in the DNA and starts the transcription of target genes. However, several additional post-translational modifications can regulate its behavior, and the binding to alternative protein partners can translocate STAT3 to the mitochondria, where its role is unclear. We are studying the signalling pathways that lead to key post-translational modifications of STAT3 and the protein partnerships that determine its intracellular localization. Current advances in microscopy tools allow the visualization and study of protein-protein interactions in living cells. One of these tools is the bimolecular fluorescence complementation (BiFC) assay. In BiFC assays, two proteins of interest are fused to two non-fluorescent halves of a reporter. When the proteins of interest interact, the halves come back together and reconstitute fluorescence. Fluorescence is therefore proportional to the amount of protein dimers, and can be easily measured by conventional methods, such as microscopy or flow cytometry. The students will work with STAT3 BiFC systems and learn a diverse array of cellular and molecular biology methods including cloning, site-directed mutagenesis, culture and transfection of mammalian cells, immunocytochemistry or western blotting (protein analyses), among others.