RESEARCH TOPICS

Our research topics concern the study of the response of cells to various stresses, such as the deregulation of oncosuppressor activity or signaling pathways involved in inflammation or viral or bacterial infection. Mitochondria play a key role in the response of cells to these stresses by controlling a number of processes such as apoptosis, ferroptosis, mitophagy, or mitochondrial UPR. The projects of the laboratory are focused on the study of the **integration of cellular stress at the mitochondrial level**. Three types of mitochondrial regulators are at the center of our projects: proteins of the Bcl-2 family known as regulators of apoptosis, ATF transcription factors involved in UPR responses and sideroflexins, mitochondrial membrane transporters still poorly characterized. For this, we use mammalian cell models and Drosophila.

In Drosophila, we are also developing **models that mimic human pathological mechanisms**.

"Sideroflexins, mitochondria and cell fate" axis:

Beyond its crucial involvement in energetic metabolism, the mitochondria have many other functions. They integrate cellular stresses and can decide if a cell must die or subsist. Mitochondrial dysfunctions or altered mitochondrial dynamics are observed in several diseases (neurodegenerative, cancers, mitochondrial diseases). Our projects focus on the molecular mechanisms whereby mitochondria influence cell fate. We are currently investigating the role of sideroflexins that are mitochondrial proteins of unknown functions.

"Mitochondrial stress and apoptosis" axis:
Rbf1, the homolog of the RB protein in *Drosophila*, can exert pro- or anti-apoptotic activities depending on the proliferative status of the cell. We are currently studying the way by which, during Rbf1-induced apoptosis, Debcl (proapoptotic *Drosophila* Bcl-2 family member), induces mitochondrial fragmentation by binding the pro-fission protein Drp1, which triggers the production of mitochondrial reactive oxygen species (ROS), thereby activating the JNK (c-Jun N-terminal kinases) pathway and cell death.

"Mitochondria and ER stress resolution" axis:
Among various possible stresses, oxidation and protein aggregation are prominent. We study cell death and compensatory mechanisms associated with the formation of mitochondrial or endoplasmic reticulum stresses in *Drosophila*.

"Human pathological mechanisms in *Drosophila*" axis
We also develop *Drosophila* models that mimic human pathological mechanisms. In particular, we are studying the activities of the HLA-B27 antigen, the main genetic predisposing factor for ankylosing spondylitis, and looking for factors enabling *Mycobacterium abcessus* to resist the immune response. More recently, we have begun to study the protective effects of bacterial culture supernatants and lysates on intestinal physiology and immune response in the context of post-infection inflammation and dysbiosis.