

MITOCHONDRIAL DYNAMICS, INFECTIOUS OR INFLAMMATORY CONDITIONS, AND INTESTINAL REGENERATION IN DROSOPHILA

Mitochondria are cellular organelles vital to cells and essential to many processes in eukaryotic organisms. Their dysfunction is responsible for numerous diseases. As the predominant players in cellular energy production, mitochondria also control the oxidative balance of cells and the biogenesis and homeostasis of major cellular compounds. They regulate cell fate, stress response, cell differentiation, and ultimately cell death. We are studying the impact of mitochondrial dynamics and reactive oxygen species (ROS) on intra- and intercellular signaling and its consequences at the tissue level, particularly in the intestine.

Role of mitochondrial dynamics in the response to inflammatory or infectious stress

Principal investigator; Isabelle Guénal
Keywords: mitophagy, innate immunity, intestinal homeostasis, stem cells, Drosophila

Mitochondria are organized into a dynamic network that can quickly adapt to different cellular needs. The quantity of mitochondria is regulated by molecular mechanisms that enable their fission or fusion, their biogenesis, or conversely their degradation through a specific autophagy process called mitophagy.
We have shown that, in *Drosophila*, apoptosis induced by the tumor suppressor protein Rbf1 depends on mitochondrial reactive oxygen species and mitochondrial fission mediated by the dynamin DRP1 (Clavier *et al.* 2015). More recently, we studied in this context the role of the PINK1 and BNIP3 proteins, two known regulators of mitophagy. In particular, we have shown that the PINK1 kinase can play a pro-apoptotic role independent of its mitophagy function (Fages *et al.* 2023).
To better understand how mitochondria impact cellular stress responses, we have developed an in vivo model using the *Drosophila* intestinal tissue. Several links have been established between mitochondrial dysfunction and inflammatory bowel diseases in the literature. To investigate the involvement of mitochondria in the innate immune response, intestinal function, and homeostasis (cell death, regeneration, and cell differentiation), we characterize responses to various inflammatory or infectious cellular stresses.

The Role of Reactive Oxygen Species in Intestinal Homeostasis
Principal investigator: Sophie Dupré-Crochet
Keywords: H2O2, innate immunity, intestinal homeostasis, Drosophila, signaling

Reactive oxygen species (ROS) are essential for maintaining intestinal homeostasis. However, their overproduction can disrupt this balance and contribute to chronic inflammation. Our research focuses on the generation, function, and regulation of ROS in the intestine, using *Drosophila* melanogaster as a model organism.

Clavier *et al*. (2015) J. Cell Sci. doi: 10.1242/jcs.169896 (hal- 02975515)
Fages *et al.* (2023) BioRkiv. doi: 10.1101/2023.12.10.568976 (hal-04334989)