# Master 2 internship project
## Year 2020-2021

**Laboratory/Institute:** Institut pour l'Avancée des Biosciences  
**Director:** P. Hainaut  
**Team:** Tumor molecular pathology and biomarkers  
**Head of the team:** P. Hainaut

**Name and status of the scientist in charge of the project:** N. Reynoird CR-CN HDR: no (soon)  
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## Program of the Master’s degree in Biology:

- ☐ Immunology, Microbiology, Infectious Diseases  
- ☐ Integrative Structural Biology  
- ☑ Physiology, Epigenetics, Differentiation, Cancer  
- ☐ Neurosciences and Neurobiology  
- ☐ Planta International

## Title of the project: MitMeth: Impact of lysine methylation signaling in mitochondrial activity

### Objectives (up to 3 lines):

The objective of this project is to identify lysine methyltransferases regulating mitochondria fitness. Our overarching aim is to unravel how lysine methylation signaling participates in mitochondrial respiratory and metabolic functions, and to link any deregulations of these pathways to human pathologies such as cancer.

### Abstract (up to 10 lines):

Mitochondria play a central role in cell and any deregulation affecting mitochondria might result in drastic disorders and pathologies, such as cancer. Protein lysine methylation is a finely tuned and dynamic post-translational modification regulated by lysine methyltransferases (KMTs). Interestingly, some recent evidences support an implication of KMTs in mitochondria metabolism, either through transcriptional regulation of mitochondrial master genes or through direct methylation of mitochondrial proteins. We have identified a list of potential KMTs localized in mitochondria, and this project aim to characterize new lysine methylation signaling involved in mitochondrial functions and in human cancers. Therefore, this exploratory and innovative project aim to link epigenetic-based signaling together with cell metabolism and cancer. Thanks to high-specificity and reversibility, the characterization of new lysine methylation signaling involved in mitochondria fitness represents an attractive approach to identify novel therapeutic targets for cancers.

### Methods:

First, we will identify a list of KMTs with mitochondrial localization by immunofluorescence. Next, we will monitor changes in cell respiration and metabolites using Seahorse and NMR techniques after shRNA repression of each validated candidate, in order to demonstrate their implication in mitochondria fitness.

### Publications of the team:

- Coordination of stress signals by the lysine methyltransferase SMYD2 promotes pancreatic cancer, N Reynoird, P Mazur et al., *Gene & Dev.*, 2016  
- SMYD3 links lysine methylation of MAP3K2 to Ras-driven cancer, N Reynoird, P Mazur et al., *Nature*, 2014

### Requested domains of expertise (up to 5 keywords):

Mandatory: epigenetics; cell signaling; cancer  
Optional: metabolism