**Equipe d’acceuil** :

Mammalian Mitochondrial Gene Expression and Function in Health and Disease (I. Kühl, Dep. Biologie Cellulaire)

**Titre :**

INVESTIGATE NOVEL PLAYERS IN MAMMALIAN MITOCHONDRIAL GENE EXPRESSION

**Résumé du projet :**

Mitochondrial dysfunction is a major contributor to metabolic and neurodegenerative disorders, cancer and ageing. Mitochondria are indeed essential organelles found in every eukaryotic cell, providing cellular energy via their oxidative phosphorylation system (OXPHOS), which requires a coordinated expression of genes encoded by both, the nuclear and mitochondrial genomes (mtDNA). Mitochondria have like the prokaryotic system no membrane-based compartementalization between the different steps of mtDNA expression. Moreover, transcription and replication of the mtDNA are linked processes and the nuclear-encoded single subunit mammalian RNA polymerase (POLRMT) has an essential function in both. POLRMT function is thus of key importance for OXPHOS biogenesis. A couple of factors are proposed to regulate mtDNA gene expression by interacting with POLRMT to modulate its activity, but the underlying mechanisms are not understood and there is strong evidence that not all POLRMT-in teracting proteins have been found. In a multi-omics study we recently identified a mitochondrial protein of unknown function, potentially interacting with POLRMT functionally or physically. With this M2 project the candidate will investigate the in vivo molecular role of this potential novel player in mammalian mitochondrial gene expression using knockout/ knockdown and knock-in cell lines.

In addition to its high fundamental importance, this project is also undoubtedly relevant at the medical level, given the large number of human pathologies associated with mitochondrial dysfunctions including defects in POLRMT, as recently reported, and the potential of using POLRMT as a target to fight cancer. We are a young dynamic group funded by an ANR JCJC, and looking for a highly-motivated, talented young researcher with the potential to continue on a PhD project.

**Dernières publications en lien avec le projet :**

>Miranda M, Bonekamp N and Kühl I. Starting the engine of the powerhouse: mitochondrial transcription and beyond. Biological Chemistry. 2022 vol. 403, no. 8-9, 2022, pp. 779-805. https://doi.org/10.1515/hsz-2021-0416

>Kühl I\*, Miranda M, Atanassov I, Kuznetsova I, Hinze Y, Mourier A, Filipovska A, Larsson NG\*. Transcriptomic and proteomiclandscape of mitochondrial dysfunction reveals secondary coenzyme Q deficiency in mammals. eLife. 2017 Nov 14;6. pii: e30952.doi:10.7554/eLife.30952