****

**PhD Project Commencing October 2023**

**(Closing date: 5 January 2023)**

**Principal Supervisor:** [**Edmund Kunji**](https://www.mrc-mbu.cam.ac.uk/research-groups/kunji-group)(enquiries to: ek@mrc-mbu.cam.ac.uk)

**Second Supervisor:** [**Judy Hirst**](https://www.mrc-mbu.cam.ac.uk/research-groups/hirst-group)(enquiries to: jh@mrc-mbu.cam.ac.uk)

**Mitochondrial transport proteins involved in the maturation of complex I**

Complex I (NADH:ubiquinone oxidoreductase) is a ~1 MDa multimeric membrane-bound complex that couples the oxidation of NADH to the reduction of ubiquinone and the translocation of four protons. The redox reactions require a flavin mononucleotide and a series of different types of iron-sulphur clusters1. However, the transport processes involved in the import of the components required to produce these co-factors have not been characterised in detail nor have the maturation steps that lead to the incorporation of the co-factors into complex I.

This project will be a collaboration between the groups of Prof. Kunji and Prof. Hirst. The Kunji group studies transport processes in mitochondria, in particular those involving members of the mitochondrial carrier family SLC252,3, whereas the Hirst group focusses on the mechanism and biogenesis of complex I1.

The aim of this project is to characterise the transport steps involved in uptake of flavin species into mitochondria, as well uptake of components required for the synthesis of iron-sulphur clusters. Candidate human transport proteins will be expressed and purified in yeast, and their substrate specificity and mechanistic properties will be analysed using biophysical and biochemical methods and transport assays using robotics. The transport proteins will be knocked-down or knocked-out using genetic techniques in human cell lines and the effect on maturation of complex I will be studied by using functional and structural analyses. The student working on this project will therefore learn a range of different biophysical, biochemical, structural, genetic and cell biological techniques.

**Keywords**

General:

mitochondria, functional assays, transport processes, complex I maturation

More specific:

Mitochondrial carriers, iron-sulphur clusters, FMN

**References**

1. Agip, A.A., Blaza, J.N., Fedor, J.G. & Hirst, J. Mammalian Respiratory Complex I Through the Lens of Cryo-EM. *Annu Rev Biophys* **48**, 165-184 (2019).

2. Ruprecht, J.J. et al. The molecular mechanism of transport by the mitochondrial ADP/ATP carrier. *Cell* **176**, 435–447 (2019).

3. Ruprecht, J.J. & Kunji, E.R.S. Structural Mechanism of Transport of Mitochondrial Carriers. *Annu Rev Biochem* **90**, 535-558 (2021).

**Subject areas**

Biochemistry, Biophysics, Cell Biology, Genetics, Molecular Biology, Structural Biology

**How to apply:** please visit the[MBU's Postgraduate Studies website](https://www.mrc-mbu.cam.ac.uk/postgraduate-studies)