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**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)

**Structure and mechanism of the human mitochondrial citrate carrier**

The mitochondrial citrate carrier is one of the most important transport proteins in mitochondria. The carrier imports malate, which is fed into the Krebs cycle, and exports citrate, for the synthesis of fatty acids, required for fat storage. Many aspects of its transport mechanism are unresolved, for instance the molecular basis of its broad substrate specificity and proton coupling.

This project will be carried out in the group of Prof. Kunji, which studies transport processes in mitochondria, in particular those involving members of the mitochondrial carrier family SLC251-3.

This aim of this project is to solve the structure of the mitochondrial citrate carrier and to understand the molecular basis of substrate selectivity and proton coupling. The human mitochondrial citrate carrier will be expressed in yeast mitochondria and purified, and its substrate specificity and mechanistic properties will be analysed by using biophysical and biochemical methods and transport assays using robotics. Once transport states have been defined, nanobodies, which are camelid antibodies, and their structures will be solved by x-ray crystallography or single particle analysis of cryo-EM images. Thus, the candidate will be in the position to apply a wide range of different techniques to discover the fundamentals of this important transport protein.

**Keywords**

General:

mitochondria, functional assays, transport processes, complex I maturation

More specific:

Mitochondrial carriers, iron-sulphur clusters, FMN

**References**

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

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

3. Kunji, E.R.S., King, M.S., Ruprecht, J.J. & Thangaratnarajah, C. The SLC25 Carrier Family: Important Transport Proteins in Mitochondrial Physiology and Pathology. *Physiology (Bethesda)* **35**, 302-327 (2020).

**Subject areas**

Biochemistry, Biophysics, Cell Biology, Physiology, Molecular Biology, Structural Biology

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