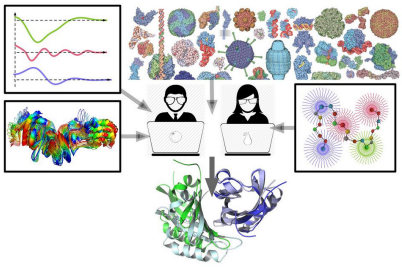

Contribution ID: **17** Type: **Poster**

Structural studies of the interaction between ACAD9 and ECSIT using small-angle scattering methods

The mitochondrial respiratory complex I is the largest of the large mitochondrial respiratory complexes, being roughly 1 MDa in size. Consequently, its assembly process is extremely complicated, requiring multiple assembly factors. Two such factors, acyl-CoA dehydrogenase 9 (ACAD9) and the evolutionarily conserved signalling intermediate in the Toll pathway (ECSIT) appear to act in a complex during complex I assembly. Although pending structural studies and a variety of assays on the ACAD9-ECSIT binding interaction exist, the exact location and stoichiometry of the binding and the associated conformational changes remain unclear. To this end, we attempted to investigate the ACAD9-ECSIT binding interaction using small-angle X-ray and neutron scattering, with the use of isotopic labelling to visualise multiple parts of the binding interface. Initial results showed large changes in the conformation of ECSIT upon binding to ACAD9. Such studies shed further light upon complex I assembly and oxidative phosphorylation in the cell, with valuable implications in neurodegenerative disease.

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