Poster Presentation

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Structural characterisation of the mitochondrial complex IV assembly factor, COA6

Shadi Maghoolpilehrood[1], N. Dinesha G. Cooray[1], David A. Stroud[2], David Aragão[3], Michael T. Ryan[2], Megan J. Maher[1]
[1]*Biochemistry & Genetics, La Trobe University, Melbourne, Australia,* [2]*Biochemistry and Molecular Biology, Monash University, Melbourne, Australia,* [3]*Australian Synchrotron, Melbourne, Australia*
E-mail: smaghoolpilehro@students.latrobe.edu.au

Copper, a redox active metal, is a vital trace element required by all living organisms, where it acts as an active cofactor for a wide range of biological processes, including mitochondrial respiration. However, intracellular free copper must be strictly limited because of its toxic side effects, demanding that living organisms keep intracellular Cu complexed, within a tightly controlled homeostatic system. Intracellular copper trafficking, including that to and within the mitochondria is a crucially important process for eukaryotes, including humans. Copper is an essential cofactor for the enzyme cytochrome c oxidase (CcO), which is the terminal oxidase of the mitochondrial respiratory chain and requires three copper ions for the construction of dinuclear CuA and mononuclear CuB sites, both of which are critical for assembly and activity of the complex.

Recently, it has been suggested that Coa6, a protein located in the intermembrane space of mitochondria, acts in the Cu-delivery pathway to CcO [1]. Interactions between Coa6 and other proteins with roles in mitochondrial copper homeostasis, including subunits of CcO have been characterised in vivo. Our recent work has shown that Coa6 binds Cu(I) with KD ~10-17 M [2], however, the mechanism of how Coa6 might mediate Cu-delivery to CcO is unknown. Studies on a pathogenic mutation of the Coa6 protein, W59C have proposed that the mutation acts to disrupt protein-protein interactions between Coa6 and its proposed protein partners with identified roles in CcO assembly, leading to dysfunctions in Cu incorporation into CcO [3]. This presentation will describe the crystal structures of the wild-type and the W59C mutant Coa6 proteins and implications for its role in CcO assembly and function.

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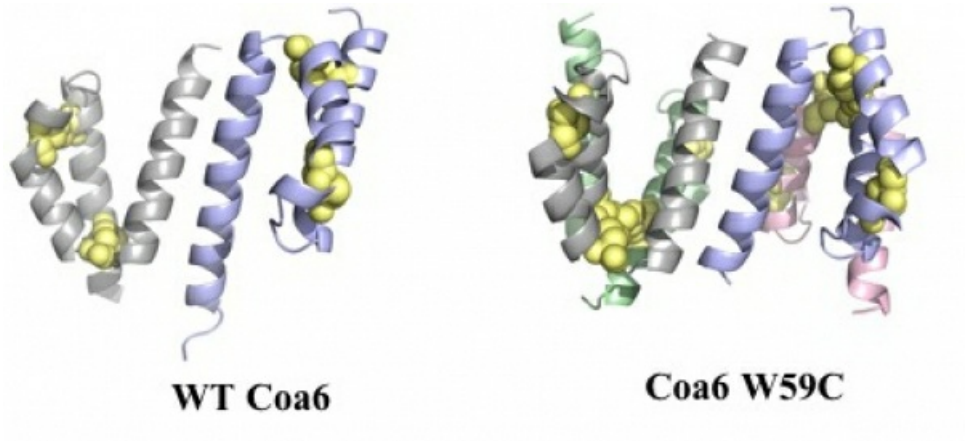

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