MS03-2-4 Mitochondrial COA7 is a heme-binding protein with disulfide reductase activity, which acts in the early stages of complex IV assembly
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Abstract
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Cytochrome c oxidase (complex IV) catalyses the transfer of electrons from cytochrome c in the intermembrane space, to molecular oxygen in the matrix. Assembly of complex IV requires the participation of a host of cysteine-rich proteins of the mitochondrial intermembrane space, which take part in a tightly choreographed series of intermolecular interactions for complex IV assembly. In addition, complex IV requires the incorporation of three copper ions, heme a and heme a3cofactors for the assembly and activity of the complex. Crucially, disruptions in this pathway lead to defects in complex IV assembly and inhibition of oxidative phosphorylation and, in humans, manifests in mitochondrial disease [1].
Despite the importance of complex IV assembly in health and mitochondrial disease, we have only a limited understanding of the molecular basis of its biogenesis, due to a lack of knowledge about structures and precise functions of the individual assembly factors. Cytochrome c oxidase assembly factor 7 (COA7) is a metazoan-specific assembly factor, the absence or mutation of which in humans accompanies complex IV assembly defects and neurological conditions. COA7 binds heme with micromolar affinity, even though the protein structure does not resemble previously characterized heme-binding proteins. The heme-bound COA7 can redox cycle between oxidation states Fe(II) and Fe(III) and shows disulfide reductase activity toward copper metallochaperones SCO1 and SCO2 [2]. This presentation will describe the role of COA7 in the early stages of complex IV assembly using structural and functional approaches and importantly, explain the disulfide reductase activity of the heme bound COA7.

References
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