Molecular Recognition between Human Mitochondrial Cytochromes: The Cytochrome c1/Cytochrome c Interaction

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The cytochrome bc_1 (Cbc_1) complex is a membrane-bound component of the mitochondrial electron transport chain. The complex, which catalyzes electron transport from ubiquinol to cytochrome *c* (C*c*), comprises three redox centers: cytochrome *b*, the Rieske protein and cytochrome c_1 (Cc_1). Cc_1 is responsible for the reduction of C*c*, which, in turn, results in the transfer of electrons to cytochrome *c* oxidase (C*c* O).The reaction is essential for cellular bioenergetics, insofar asit is coupled with proton translocation leading to ATP formation. Recently, our group has reportedthat plant C*c* shows two binding sites on Cc_1[1]. The first, or so-called *proximal* site, is suitable for electron transfer, whereas the second, or *distal* site, located near the Rieskeprotein,is involved in the channeling of C*c* molecules towards C*c*O[1-3].

Given this, this work aims to determine whether the C*c*-C$c_1$two-binding site model is conserved through out evolution and, specifically, can be found in the interaction between the two corresponding human hemeproteins. First, in close collaboration with the *European Integrating Structure Platform* (*Instruct,* PID1163), several constructions of the soluble N-terminal domain of Cc_1 were designed. Among these, a triple Cc_1 mutant lacking non-heme-coordinated cysteines and containing a bacterial periplasmic signal allowed for the expression of human Cc_1 as a recombinant protein. Physicochemical properties, including redox potential, were then analyzed. Preliminary measurements byisothermal titration calorimetry suggest that the C*c*:Cc_1 stoichiometry of 2:1 is presentin both plants and humans.

[1]Moreno-Beltrán, B *et al.Biochim. Biophys. Acta-Bioenerg.*(2014)1837: 717-729.

[2]Moreno-Beltrán, B*et al.FEBS Lett.* (2015)589: 476-483.

[3]Louro, R.O. & Díaz-Moreno I. (eds). Redox Proteins in Supercomplexes and Signalosomes. *CRC Press* (2015).