TITLE: ATCO, A MITOCHONDRIAL PROTEIN COMPLEX OF ATP9 AND COX6, IS A PRECURSOR OF THE ATP SYNTHASE ASSEMBLY

AUTHORS: FRANCO, L. V. R. [1,2], SU, C. H. [2], BURNETT, J. [2], TEIXEIRA, L.S. [2], BARROS, M. H. [1], TZAGOLOFF, A. [2]

INSTITUTIONS: 1. Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, SP, Brasil; 2. Department of Biological Sciences, Columbia University, New York, NY, United States of America

ABSTRACT

The principle source of ATP used by eukaryotic cells for their energy needs is supplied by the mitochondrial respiratory chain that consists of four electron transport complexes and the ATP synthase (OXPHOS complexes). Three of the OXPHOS complexes (*bc*1 complex, cytochrome oxidase and the ATP synthase) are genetic hybrids derived from mitochondrial and nuclear genes. An important emerging area of mitochondrial research strives to decipher the mechanisms by which the respiratory complexes of mitochondria are assembled and how expression of the compartmentally separated genes are coordinately regulated to achieve an optimal stoichiometry of the electron transport complexes vis-à-vis each other and the ATP synthase. Mitochondrial ATP synthase is a hetero-oligomeric protein complex that conserves energy released during the oxidation of different nutrients in the form of ATP. Yeast ATP synthase is made up of three main assembly modules, one of which is a ring consisting of 10 copies of the Atp9 subunit. Our research group has previously identified the presence in yeast mitochondria of high molecular weight complexes, named Atco, consisting of Atp9 encoded from mitochondrial DNA and Cox6, a subunit of cytochrome oxidase encoded from the nuclear DNA. Pulse-chase experiments of isolated mitochondria show that newly translated Atp9 is exclusively present in Atco and is incorporated into ATP synthase, showing that Atco is a precursor of ATP synthase ring module. Furthermore, crosslinking Atp9 with cysteine substitutions at residues 3-4 Å apart on neighboring subunits of the ring indicate that the interaction of Atp9 in Atco is similar to that of the ATP synthase ring. We propose that the role of Atco is to provide an adequate stoichiometry of ATP synthase and cytochrome oxidase during the biogenesis of the two complexes.

Keywords: mitochondrial biogenesis, ATP synthase, cytochrome oxidase, *Saccharomyces cerevisiae*, respiratory chain

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