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Structural basis for the interaction of the chaperone Cbp3 with newly synthesized cytochrome during mitochondrial respiratory chain assembly

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Assembly of the mitochondrial respiratory chain requires the coordinated synthesis of mitochondrial and nuclear encoded subunits, redox co-factor acquisition, and correct joining of the subunits to form functional complexes. The conserved Cbp3-Cbp6 chaperone complex binds newly synthesized cytochrome and supports the ordered acquisition of the heme co-factors. Moreover, it functions as a translational activator by interacting with the mitoribosome. Cbp3 consists of two distinct domains: an N-terminal domain present in mitochondrial Cbp3 homologs and a highly conserved C-terminal domain comprising a ubiquinol-cytochrome chaperone region. Here, we solved the crystal structure of this C-terminal domain from a bacterial homolog at 1.4 Å resolution, revealing a unique all-helical fold. This structure allowed mapping of the interaction sites of yeast Cbp3 with Cbp6 and cytochrome b via site-specific photo-cross-linking. We propose that mitochondrial Cbp3 homologs carry an N-terminal extension that positions the conserved C-terminal domain at the ribosomal tunnel exit for an efficient interaction with its substrate, the newly synthesized cytochrome protein.

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