COX11 encodes a mitochondrial inner membrane protein that is essential for assembly of the multisubunit enzyme cytochrome c oxidase, which catalyzes the terminal step in the electron transport chain of cellular respiration. Cox11p is involved in the incorporation of copper into the cytochrome oxidase complex, most likely in the formation of the Cusite of the mitochondrially-encoded Cox1p subunit. It is well-conserved, with homologs in bacteria, fungi, plants, and animals.Cox11p is anchored to the mitochondrial inner membrane by a single transmembrane segment. Its C terminus, which includes a copper-binding domain, is exposed to the intermembrane space and forms a homodimer that binds two Cuions. Copper is delivered to Cox11p by Cox17p, which acts as a copper chaperone specific for Cox11p and Sco1p.Cox11p also interacts with mitochondrial ribosomes via its N terminus, although the importance of this is not clear because the N terminus is apparently not essential for function. However, the link between Cox11p function and the mitochondrial translation system appears to be conserved, since both of the two COX11 orthologs in Schizosaccharomyces pombe contain 5' extensions relative to S. cerevisiae COX11 that encode proteins similar to the mitochondrial ribosomal protein Rsm22p. Cox11p may assist in copper incorporation into Cox1p in a co-translational manner. In keeping with this hypothesis, levels of Cox1p are reduced in a cox11 null mutant.The cox11 null mutant exhibits a respiratory defect, failing to grow on nonfermentable carbon sources due to its inability to assemble cytochrome c oxidase. cox11 mutants also display sensitivity to various chemicals including photoactivated psoralens, N-nitrosodiethylamine, 1,2:7,8-diepoxyoctane, and hydrogen peroxide. The Cox11p function in hydrogen peroxide resistance is separable from its function in cytochrome c oxidase assembly, since the null mutant is both respiratory deficient and hydrogen peroxide sensitive, while cox11 point mutations that affect its copper-binding sites block respiratory growth without causing hydrogen peroxide sensitivity. The hydrogen peroxide sensitive phenotype of the null mutant is likely due to accumulation of a transient heme A3-Cox1p intermediate that confers oxidant sensitivity. The intermediate does not form in the presence of wild-type or mutant Cox11p, even though cytochrome c oxidase is not fully assembled in the cox11 point mutant strain.