Crystal structure of *Saccharomyces cerevisiae* Sco1

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Cytochrome *c* oxidase (CcO) is the terminal enzyme in the aerobic respiratory chain, catalyzing electron transfer from cytochrome *c* to molecular oxygen while concomitantly establishing a proton gradient for ATP synthesis. CcO contains four redox active centers, including a Cu_A site. The assembly of the Cu_A center requires the delivery and insertion of two Cu(I) ions facilitated by multiple accessory proteins including Sco1, a membrane-anchored protein with a highly conserved CXXXC motif located within the soluble C-terminal domain. Two different functions have been proposed for Sco1. One possible role is delivery of Cu(I), coordinated by the cysteines of the CXXXC motif, to the Cu_A center. Sco1 has been shown to bind one Cu(I) ion, and overexpression of Sco1 partially restores function to CcO in yeast lacking the copper chaperone Cox17. A reductase role for Sco1 has also been proposed, stemming from its sequence similarity to peroxiredoxins and thioredoxins, and sequence alignments indicate that the CXXXC motif is located at the same position as the conserved residues that catalyze disulfide isomerization in thioredoxins.

Here we report the crystal structures of the *Saccharomyces cerevisiae* Sco1 (ySco1) C-terminal domain in its apo and metallated forms. In agreement with the structures of human Sco1 and *Bacillus subtilis* Sco1, ySco1 possesses a thioredoxin-like fold. There are two additional cysteines in ySco1, separated by 34 residues, which are only conserved among yeast. Interestingly, these cysteines are in close proximity to one another and to the conserved histidine that has been implicated previously in copper binding.