

ABSTRACT

Cytochrome bc_1 complex, also known as complex III of the respiratory chain, is a multi-subunit protein complex embedded in the mitochondrial inner membrane and plasma membranes of many aerobic or photosynthetic bacteria. It contains three redox subunits: cytochrome b , cytochrome c_1 and a so-called “Rieske protein” that contains an iron-sulfur cluster. The complex transfers electrons from ubiquinol to cytochrome c and uses the free energy thus released to generate an electro-chemical gradient across the mitochondrial inner membrane that is further utilized in ATP synthesis. The bc_1 complex works through a modified "protonmotive Q-cycle" mechanism, which requires the complex to have two separate quinone-binding sites: a quinone oxidation site (Q_o site) and a quinone reduction site (Q_i site).

Intact bc_1 complex was isolated from chicken heart mitochondria and crystallized in space group $P2_12_12_1$ with cell dimensions of $a = 170 \text{ \AA}$, $b = 180 \text{ \AA}$, $c = 240 \text{ \AA}$. Three-dimensional structures were determined to 3.0 \AA resolution for native bc_1 complex using the Multiple Isomorphous Replacement (MIR) technique. Molecular Replacement (MR) techniques were used to determine the structures of bc_1 complex treated with various inhibitors. Ubiquinone and inhibitor molecules were observed at the two quinone-binding sites in these structures. A comparison of the structures in the presence and absence of the inhibitor stigmatellin reveals two different locations for the extrinsic domain of subunit Rieske protein. This suggests a novel mechanism for electron transfer through domain movement. Significant conformational changes on the protein residues

close to the quinone binding sites were also observed. Based on these observations, a model for the mechanism of bc_1 complex is proposed.