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 $a = 170$ Å, $b = 180$ Å, $c = 240$ Å. Three-dimensional structures were determined to 3.0 Å 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.