The structure of the respiratory membrane protein complex quinol:fumarate reductase (QFR) from Wolinella succinogenes has been determined by X-ray crystallography at 2.2 Å resolution [Lancaster et al., Nature 402, 377-385 (1999)]. Based on the structure of the three protein subunits A, B, and C and the arrangement of the six prosthetic groups (a covalently-bound FAD, three iron-sulfur clusters, and two haem b groups) a pathway of electron transfer from the quinol-oxidising dihaem cytochrome b in the membrane to the site of fumarate reduction in the hydrophilic subunit A has been proposed. Based on crystallographic analysis of three different crystal forms of the enzyme, indicating interdomain movement at the site of fumarate reduction, and the results from site-directed mutagenesis, we have derived a mechanism of fumarate reduction and succinate oxidation [Lancaster et al., Eur. J. Biochem. 268, 1820-1827 (2001)], which should be generally relevant throughout the superfamily of succinate:quinone oxidoreductases. The structure of the membrane-integral dihaem cytochrome b reveals that, firstly, all transmembrane helical segments are tilted with respect to the membrane normal, secondly, the dihaem binding motif is very different from those of the cytochrome bc1 complex and of the formate dehydrogenase/nitrate reductase/hydrogenase group, and thirdly, the g-hydroxyl group has an important role in stabilising a kink in transmembrane helix IV. By combining the results from site-directed mutagenesis, functional and electrochemical characterisation, and X-ray crystallography, a residue was identified which was found to be essential for menaquinol oxidation. [Lancaster et al., Proc. Natl. Acad. Sci. U.S.A. 97, 13051-13056 (2000)]. The distal location of this residue in the structure indicates that the oxidation of menaquinol to the reduction of dihaem-containing succinate:quinone oxidoreductases could in principle be associated with the generation of a transmembrane electrochemical potential. However, it is suggested [Lancaster, Biochim. Biophys. Acta Special Issue on Membrane Protein Structure, submitted] that in W. succinogenes QFR, this electrogenic effect is counterbalanced by the transfer of two electrons via the membrane-bound haem groups. According to this 'E-pathway hypothesis', the net reaction catalysed by W. succinogenes QFR does not contribute directly to the generation of a transmembrane electrochemical potential.

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