Structural changes linked to proton translocation by subunit c of the ATP synthase

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F_1F_O ATP synthases use a transmembrane proton gradient to drive the synthesis of cellular ATP. The structure of the cytosolic F_1 portion of the enzyme and the basic mechanism of ATP hydrolysis by F_1 are now well established, but how proton translocation through the transmembrane F_O portion drives these catalytic changes is less clear. Here we describe the structural changes in the proton-translocating F_O subunit c that are induced by deprotonating the specific aspartic acid involved in proton transport. Conformational changes between the protonated and deprotonated forms of subunit c provide the structural basis for an explicit mechanism to explain coupling of proton translocation by F_O to the rotation of subunits within the core of F_1. Rotation of these subunits within F_1 causes the catalytic conformational changes in the active sites of F_1 that result in ATP synthesis.

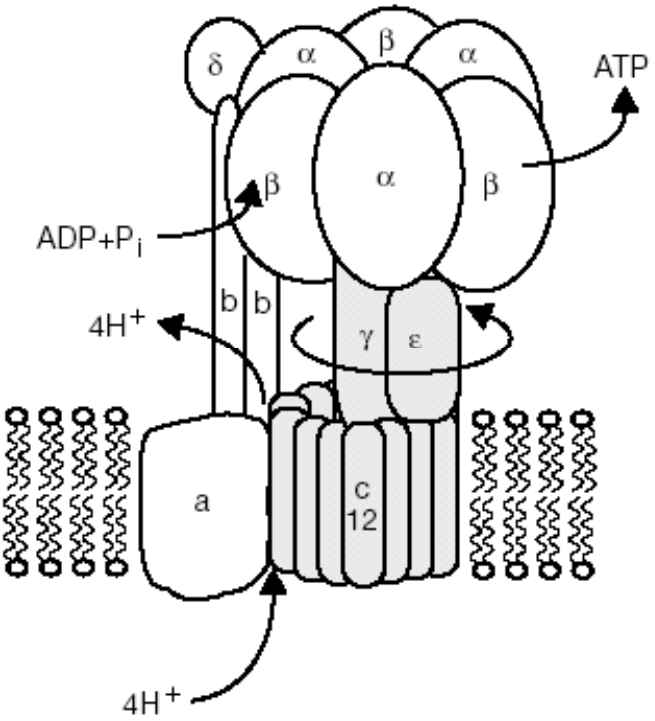

Figure 1 Schematic diagram of F1FO ATP synthase. Subunits shown in white are thought to remain fixed with respect to each other during proton translocation and ATP synthesis. Subunits shown in grey are thought to rotate as a unit with respect to the fixed subunits during catalysis.

Proton translocation and rotation within F_O

Proton translocation through F_O involves residues Asp 61 of subunit c and Arg 210 of subunit a. As Asp 61 is buried in the membrane bilayer, hydrophilic access pathways from both sides of the membrane must exist. One likely pathway connecting the periplasmic membrane surface to Arg 210 and Asp 61 can be found in the model of the ac_{12} oligomer. A set of polar residues entirely within subunit a, including Gln 252, Asn 214, Asn 148, Asp 119, His 245, Glu 219, Ser 144 and Asn 238, form a hydrophilic path between Arg 210 and the membrane surface. During ATP synthesis, the transmembrane H+ electrochemical potential is high at the periplasmic face and low at the cytoplasmic (F_1) face. This gradient would drive protonation of the deprotonated Asp 61 via the pathway through subunit a just described. As this Asp 61 becomes protonated, its C-terminal helix will rotate, clockwise as viewed from F_1 in to adopt its stable protonated conformation. During this rotation, we suggest that subunit a moves with the C-terminal helix of c, linked by hydrogen bonding and steric interactions between residues in subunits a and c, to arrive at the next position between c subunits.