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Abstracts

S2 ATP SYNTHASE/ATPase

Lectures

2L.1 Structural basis of ion binding modes in the F_O rotor of H^+ and Na^+ translocating ATP synthases

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A membrane-embedded rotor ring of hairpin-like c-subunits plays a central role in ion translocation during adenosine triphosphate (ATP) synthesis by proton- or sodium motive force-dependent F_1F_O-ATP synthases. The careful design of c-ring rotors in different species defines both rotor size and ion binding specificity, two important parameters in cell bioenergetics. It appears that the structure of these rotor rings represents a finely-tuned adaptation of the enzyme to the environment of the corresponding organism. To our knowledge today, the stoichiometry of rotor rings is constant within a species but variable (from 10 to 15 hairpins are known) among different species. In the Na^+-binding c_{11} ring of *Ilyobacter tartaricus* and the H^+-binding c_{15} ring from *Spirulina platensis*, the translocated ions are bound within the groove of two adjacent c-subunits in a coordination network including a conserved glutamate (or aspartate). Both structures suggest that the precise coordination chemistry keeps the ion (H^+ and Na^+) in an ion locked conformation during the passage through the lipid/c-ring interface. The notion is supported by combined structural, biochemical and also *in silico* generated data of the proton binding site. Exchange of the ion, including subtle conformational adaptations of the ion binding glutamate, would exclusively occur in a more hydrophilic environment, such as it presumably is the case at the rotor–stator interaction site, the a-subunit/c-ring interface. Furthermore, it now becomes structurally evident that a new type of ion coordination needs to be considered in the operation mode of some of the F_O motors.

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2L.2 ATP hydrolysis in ATP synthases can be differently coupled to proton transport and modulated by ADP and phosphate: A structure based model of the mechanism

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In the ATP synthases of *Escherichia coli* ADP and phosphate exert an apparent regulatory role on the efficiency of proton transport coupled to the hydrolysis of ATP. Both molecules induce clearly biphasic effects on hydrolysis and proton transfer. At intermediate concentrations (about 0.5–1 μM and higher) ADP inhibits hydrolysis and proton transfer; a quantitative analysis of the fluxes however proves that the coupling efficiency remains constant in this concentration range. On the other hand at nanomolar concentrations of ADP (a level obtainable only using an enzymatic ATP regenerating system) the efficiency of proton transport drops progressively, while the rate of hydrolysis remains high. Phosphate, at concentrations 0.1 mM, inhibits hydrolysis only if ADP is present at sufficiently high concentrations, keeping the coupling efficiency constant. At lower ADP levels phosphate is, however, necessary for an efficiently coupled catalytic cycle. We present a model for a catalytic cycle of ATP hydrolysis uncoupled from the transport of protons. The model is based on the available structures of bovine and yeast F_1 and on the known binding affinities for ADP and P_i of the catalytic sites in their different functional states. The binding site related to the inhibitory effects of P_i (in association with ADP) is identified as the $\alpha_{HC}\beta_{HC}$ site, the pre-release site for the hydrolysis products. We suggest, moreover, that the high affinity site, associated with the operation of an efficient proton transport, could coincide with a conformational state intermediate between the $\alpha_{TP}\beta_{TP}$ and the $\alpha_{DP}\beta_{DP}$ (similar to the transition state of the hydrolysis/synthesis reaction) that does not strongly bind the ligands and can exchange them rather freely with the external medium. The emptying of this site can lead to an unproductive hydrolysis cycle that occurs without a net rotation of the central stalk and, consequently, does not translocate protons.

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2L.3 Ion transport by the sodium pump

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The first crystal structure of the Na^+,K^+-ATPase revealed the potassium-bound form of the pig kidney enzyme at 3.5 Å resolution. This large membrane protein complex consists of an alpha subunit similar to the Ca^{2+}-ATPase, a heavily glycosylated beta subunit and a small regulatory gamma subunit (also known as FXYD2). The electrogenic transport performed by the Na^+,K^+-ATPase causes extrusion of three sodium ions and uptake of two potassium ions per ATP split. The gradients thus formed are of fundamental importance in

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