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Albracht, S.P.J.; de Jong, A.M.P.; Kotlyar, A.B.

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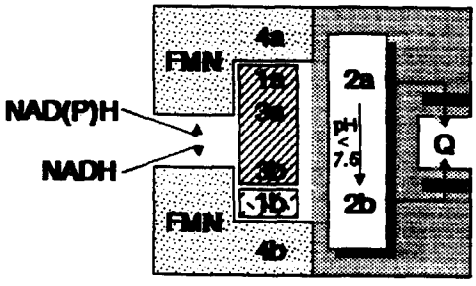
L01 FROM COMPLEX I TO HYDROGENASE AND BACK

S.P.J. Albracht[a], A.M.Ph. de Jong[a] and A.B. Kotlyar[b]
[a]E.C. Slater Institute, BioCentrum Amsterdam, Plantage Muidergracht 12, NL-1018 TV Amsterdam, The Netherlands and [b]Laser Laboratory for Fast Reactions in Biology, Department of Biochemistry, George S. Wise Faculty of Life Sciences, Ramat Aviv, 69978, Tel Aviv, Israel

Since the discovery of iron-sulphur clusters in mitochondrial Complex I by Beinert and Sands in 1960 [1] quite some research groups have been studying this most complicated enzyme. At present at least four different Fe-S clusters have been detected with EPR, but their precise function in the energy-linked electron transfer catalyzed by the enzyme is not really understood. The analysis of Weidner et al. [2] of the operon encoding Complex I in *Escherichia coli* indicates that only 14 of the 41 polypeptides of the bovine-mitochondrial enzyme [3] are essential for coupled electron transfer. Five polypeptides show conservative Cys patterns that might accommodate Fe-S clusters. Four of these are quite likely inherited from hydrogenases [see e.g. 4]. The remaining polypeptide, the TYKY subunit [3], contains a Cys pattern typical for two classical cubane clusters. With this information a monomeric model, rather than a dimeric one [5] can be constructed, explaining most physico-chemical and kinetic properties of the enzyme (see figure). All Fe-S clusters of Complex I are fully reduced within 5 ms, when SMP are mixed with NADH. Within 40 ms the g_z line of the EPR signal of the clusters 2, but not the g_{xy} line, disappears in coupled particles. This effect is sensitive to uncouplers. It is also reversed upon anaerobiosis. It is concluded that we have detected an 'energized' form of Complex I in which the protein structure around the clusters 2 has changed. It is proposed here that the TYKY subunit holds the Fe-S clusters 2 and renders the enzyme the ability to perform coupled electron transfer.



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