Researchers describe structure of the largest protein complex in the respiratory chain

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Mitochondria produce ATP, the energy currency of the body. The driver for this process is an electrochemical membrane potential, which is created by a series of proton pumps. These complex, macromolecular machines are collectively known as the respiratory chain. The structure of the largest protein complex in the respiratory chain, that of mitochondrial complex I, has been elucidated by scientists from the Frankfurt "Macromolecular Complexes" cluster of excellence, working together with the University of Freiburg, by X-ray diffraction analysis.

"Mitochondrial complex I plays a critical role in the production of cellular energy and has also been associated with the onset of diseases, such as Parkinson's disease", explains Volker Zickermann, an assistant professor at the Institute for Biochemistry II at the Goethe University. In order for the respiratory chain to function, there must be consistently sufficient amounts of oxygen available in all the cells in our bodies. The energy released during biological oxidation is used to transport protons from one side of the inner mitochondrial membrane to the other. The resulting proton gradient is the actual "battery" for ATP synthesis.

Complex I switches between two forms

What surprised the researchers: Previous studies suggested that redox reactions and proton transport in complex I occurred spatially isolated from one another. The Frankfurt scientists in Zickermann's working group and the working groups led by Prof. Harald Schwalbe and Prof.

Ulrich Brandt have now been able to deduce how the two processes are connected to one another from the detailed analysis of the structure. They have therefore made an important contribution towards the understanding of an elementary process in energy metabolism.

Pathophysiologically significant properties of complex I

It has long been known that complex I can switch reversibly between an active and inactive form. This has been interpreted as a protective mechanism against the formation of dangerous free oxygen radicals. The structure now clearly indicates how these two forms are differentiated from one another and transformed into one another. "The research results thus also give important information about the molecular basis of a pathophysiologically significant property of complex I that may be significant for the extent of tissue damage after a myocardial infarction," explains Zickermann.

More information: Zickermann V, Wirth C, Nasiri H, Siegmund K, Schwalbe H, Hunte C, Brandt U (2015) "Mechanistic insight from the crystal structure of mitochondrial complex I." *Science* 347:44-49. DOI: 10.1126/science.1259859

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