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Press Release

Newly-discovered signal in the cell sets protein pathways to mitochondria

Tübingen researchers investigate the complex makeup of vital cell organelles

Tübingen, 27 June 2016

Mitochondria are often described as the powerhouse in the cells of humans, plants and animals; but they also fulfill a number of other vital functions. These “organs” within the cell have an interesting past: They arose more than a billion years ago as a bacterium, which was adopted into a primeval cell. In the course of evolution, nearly all the genes of the original bacterium have become part of the cell nucleus. One result of this is that most of the protein building-blocks in mitochondria are produced in the cell plasma and put in place via complex importation processes.

In two new studies, researchers at the University of Tübingen’s Interfaculty Institute of Biochemistry headed by Professor Doron Rapaport have shed light on the many questions raised by the construction of mitochondria organelles. Monika Sinzel und Dr. Kai Stefan Dimmer have discovered a new protein which is incorporated into the mitochondrial outer membrane. Interestingly, enzymes in the inner membrane play the deciding role in the protein’s correct positioning. In the second study, Rapaport and another member of his working group, Tobias Jores, worked with colleagues from Frankfurt and Kyoto to discover more about the signal which transports beta-barrel proteins through the cell plasma and into place in the mitochondria. Scientists have been wondering for years what the signal looks like.

Depending on its type, a cell has anything from a mere handful to hundreds of mitochondria. Apart from generating energy, mitochondria play a role in the production of cell building blocks such as amino acids, nucleotides, and iron-sulfur clusters. “Today we know that they are also key players in the cell signalling network. This role gives mitochondria a special significance in processes such as aging and programmed cellular death,” says Rapaport. Defects in the mitochondria can lead to a wide variety of muscular, metabolic, and neurodegenerative diseases. The

organelles also have an effect in conditions such as diabetes, deafness, blindness, cancer, premature aging, dementia, and bacterial infections.

“Importing proteins from the plasma and into the right subsection of the mitochondria is an essential process for cell viability,” Rapaport explains. Scientists already knew about the signals which directed most of the mitochondrial proteins, he adds. “But that was not true of the important group of beta-barrel proteins, which are incorporated into the outer mitochondrial membrane.” Rapaport and Jores uncovered the signal using biochemical experiments, structural analyses, and gene manipulation on yeast cells: One special protein element, the beta-hairpin, guides the beta-barrel proteins safely to the mitochondria.

The Tübingen researchers also identified a receptor on the mitochondrial surface which recognized the beta-hairpin signal. The Kyoto researchers worked out the structural aspects of this molecular interaction. “Our research partners in Frankfurt showed that it was the beta-hairpin signal and no other which determines the path of beta-barrel proteins. They put it onto proteins which were actually meant for the chloroplasts – the cell photosynthesis organs – but the proteins were nevertheless delivered to the mitochondria,” Rapaport says.

Publications:

Monika Sinzel, Tao Tan, Philipp Wendling, Hubert Kalbacher, Cagakan Özbalci, Xenia Chelius, Benedikt Westermann, Britta Brügger, Doron Rapaport & Kai Stefan Dimmer: Mcp3 is a novel mitochondrial outer membrane protein that follows a unique IMP-dependent biogenesis pathway. *EMBO Reports*, DOI 10.15252/embr.201541273.

Jores, T., A. Klinger, L. Groß, S. Kawano, N. Flinner, E. Duchardt-Ferner, J. Wöhnert, H. Kalbacher, T. Endo, E. Schleiff, and D. Rapaport (2016): Characterization of the targeting signal in mitochondrial β-barrel proteins. *Nature Communications*, in press.

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