Press Release

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How Complex Cells Developed

A team of researchers provides new insights into the development of mitochondria

Mitochondria are the powerhouse of complex cells. In order to provide cells with energy, they need proteins, which they import from the outside. A team of German and Swiss researchers headed by Prof. Dr. **Bettina Warscheid** from the University of Freiburg and Prof. Dr. **André Schneider** from the University of Bern discovered that the machinery needed for importing proteins has developed differently over billions of years than previously thought. In their study, which they published in the journal *Nature Communications*, the researchers provide new insights into the development of mitochondria – one of the most important events in evolution and the basis for the development of complex eukaryotic cells that make up today's plants, animals, many microorganisms and humans.

Mitochondria are separated from the rest of the cell by two membranes. They have to transport proteins through both of these membranes in order to produce energy. That is why they have two distinct nano “machines” that are responsible for the import of proteins: one in the outer and one in the inner membrane. The research team demonstrated, by using high-resolution mass spectrometry, that these nano machines are differently composed in single-cell parasites than in humans. The parasites – trypanosomes – took an alternative evolutionary route, as the researchers discovered already in a previous study on the import machine in the outer mitochondrial membrane. What they now discovered by decoding its unusual protein composition is that this finding is also true for the import machine in the inner mitochondrial

membrane. The assumption that the import nano machines of all mitochondria have the same composition, regardless of whether they exist in single-cell or higher organisms like humans, is therefore incorrect. This means that the current ideas about how mitochondria have developed need to be reviewed and revised.

The mitochondrion evolved from a simple bacterial cell, which was absorbed roughly two billion years ago by a larger cell and transformed into a cellular compartment, a closed part within a cell where biochemical processes take place. One of the main requirements for the development of mitochondria and, hence, for the evolution of complex cells was the development of an efficient protein import machinery. It was previously assumed that, after its initial development, it had adjusted only slightly to the living conditions of each organism. The new data now shows that, although the nano protein import machines in trypanosomes and humans both consist of roughly 15 different proteins, their components show no similarities, besides three proteins they share in common. This demonstrates that, except for these three basic components, the system in trypanosomes is a new development. This discovery indicates that the first complex cell had only a simple import system that evolved over a lengthy process into a sophisticated import machinery. The efficient import systems consisting of many different modules that exist today therefore developed much later than originally thought, after the first species of complex cells had already developed.

Trypanosomes are not only an important model system for basic research, they are also clinically important as pathogens that cause sleeping sickness, which can be fatal if left untreated. The newly discovered protein-import system is vital for the trypanosomes' survival. Because it is constructed differently than the system found in human mitochondria, it could be suitable for chemotherapy against sleeping sickness. It should be possible to find substances that block the transport system that trypanosomes depend on to survive without affecting the transport system in human mitochondria.

Bettina Warscheid is head of the Department of Biochemistry and Functional Proteomics of the Faculty of Biology at the University of Freiburg. She is also

The University of Freiburg achieves top positions in all university rankings. Its research, teaching, and continuing education have received prestigious awards in nationwide competitions. Over 24,000 students from 100 nations are enrolled in 188 degree programs. Around 5,000 teachers and administrative employees put in their effort every day – and experience that family friendliness, equal opportunity, and environmental protection are more than just empty phrases here.

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a professor at the University of Freiburg's cluster of excellence BIOSS Centre for Biological Signalling Studies.

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A. Harsman, S. Oeljeklaus, C. Wenger, J. L. Huot, B. Warscheid[#] und A. Schneider[#]. The non-canonical mitochondrial inner membrane presequence translocase of trypanosomatids contains two essential rhomboid-like proteins, Nature Communications, 19 December 2016, in press. ([#]These authors contributed equally.)

Caption:

This coloured image produced with a scanning electron microscope shows the single-cell parasite *Trypanosoma brucei* (blue) with a red blood cell. Source: C. Jackson, University of Helsinki

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