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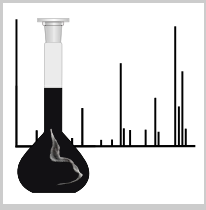

Highlights of Analytical Sciences in Switzerland

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Parasite Reveals Mitochondrial Inheritance Machinery

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Mitochondria are double membrane bounded organelles that together with the nucleus define the eukaryotic cell. Their main function is energy production by oxidative phosphorylation. Mitochondria derive from bacteria, which during evolution have gradually been converted into organelles. The bacterial descent of mitochondria is reflected by their genome which encodes a small number of essential proteins. Every eukaryote therefore needs mechanisms that during cell division correctly distribute mitochondria and their genomes to the daughter cells. In a typical eukaryotic cell this distribution process is however difficult to study because it contains many dozens of mitochondria each of which carries multiple mitochondrial genomes.

The unicellular flagellar parasite *Trypanosoma brucei*, best known for causing African sleeping sickness, provides a way out: unlike other eukaryotes it has a single mitochondrion with a single unit genome, which can easily be observed with a microscope. This genome is physically linked, across the two membranes, to the base of the flagellum. Prior to cell division a new flagellum is produced which subsequently is segregated to the daughter cell. Due to its linkage to the flagellum this leads to simultaneous segregation of the replicated mitochondrial genome.

Using a combination of organellar proteomics, biochemistry, and molecular genetics we have discovered a protein, termed TAC40, that mediates this linkage. Removing TAC40 by genetic tricks interrupts the linkage causing a failure of segregation which results in unviable daughter cells that lack mitochondrial DNA. Thus, TAC40 is a key component required for mitochondrial inheritance in trypanosomes. But there is more: A bioinformatic analysis shows that TAC40 defines a novel trypanosome-specific subclass of the mitochondrial porin protein family that is conserved in all eukaryotes. Mitochondrial porins are beta-barrel structured membrane proteins that have been implicated in many different functions including mitochondrial inheritance.

In summary, the discovery of the mitochondrial outer membrane protein TAC40 in the tropical parasite *Trypanosoma brucei* has revealed that mitochondrial genome inheritance is likely the main and ancestral function of this group of mitochondrial porins.

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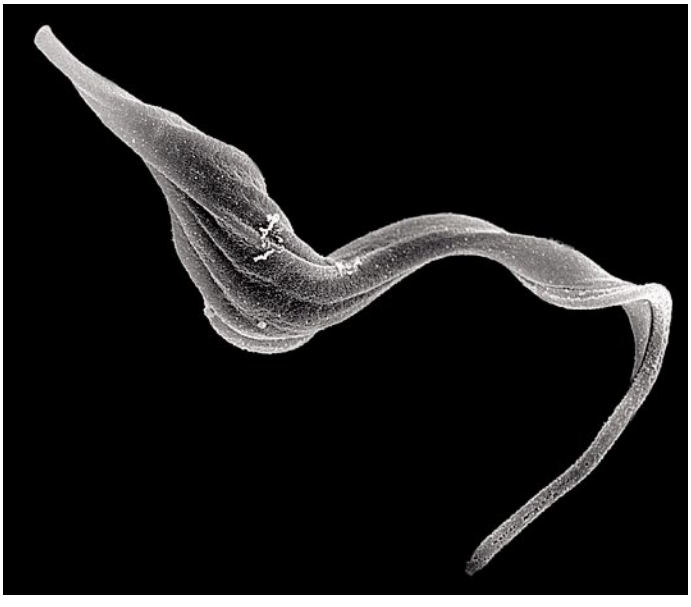
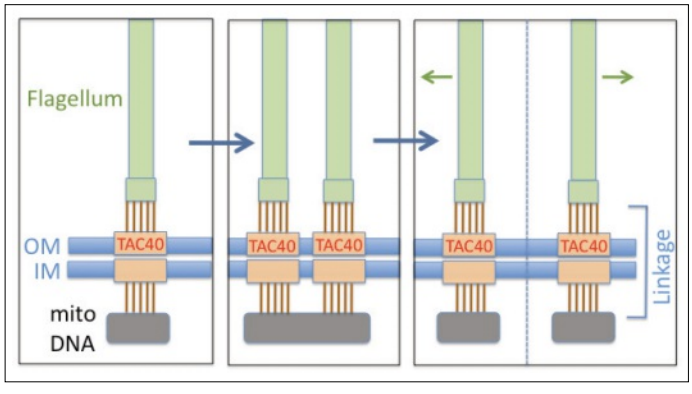
Reference

F. Schnarwiler, M. Niemann, N. Doiron, A. Harsman, S. Käser, J. Mani, A. Chanfon, C. E. Dewar, S. Oeljeklaus, C. B. Jackson, M. Pusnik, O. Schmidt, C. Meisinger, S. Hiller, B. Warscheid, A. C. Schnaufer, T. Ochsenreiter, A. Schneider, *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 7624.



Scanning electron micrograph of the bloodstream form of the parasitic protozoa *Trypanosoma brucei*. The single flagellum is laterally attached to the cell body and extends the cell on the right side. The length of the cell is approximately 30 μm (image courtesy of Christopher P. Jackson).



Schematic diagram of the mitochondrial DNA-flagellum linkage and position of the TAC40 protein (red) in *T. brucei*. The three pictures show different stages of the cell cycle. In the left panel the cell has a single mitochondrial genome and a single flagellum. In the middle panel the mitochondrial DNA has been replicated but not segregated yet. It is linked to both the old and the newly produced flagella. The right panel shows how the replicated mitochondrial DNA and the flagella co-segregate (green arrows). The broken line indicates the position where the mitochondrion will be divided. OM, mitochondrial outer membrane; IM, mitochondrial inner membrane.

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