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The Diverged Trypanosome MICOS Complex as a Hub for Mitochondrial Cristae Shaping and Protein Import

RNDr. Thesis

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Annotation

This work deals with MICOS, which stands for mitochondrial contact site and cristae organization system. Until now this multiprotein complex has been analyzed experimentally only in yeast and mammals, who belong to the supergroup Opisthokonta. Our study was done on the parasitic protist *T. brucei*, a member of the another supergroup called Excavata, which is very diverged from opisthokonts.Thus, it is the very first study done outside of Opisthokonta. This could be very useful in the future for a comparative analysis approach. Our results show that the MICOS complex in *T. brucei* is composed of 9 subunits, most of which are essential for normal growth. It is required for the maintenance of discoidal cristae that typify excavates such as kinetoplastids and euglenids and mediating the mitochondrial outer and inner membranes contacts. In addition, we discovered that the mitochondrial contact site and cristae organization system may participate in the intermembrane space protein import and help in the oxydative phosphorylation complex formation. It seems that this interesting complex is involved in even more cellular processes.

Declaration in Czech

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České Budějovice 3.1. 2019

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Jiří Heller

Declaration of corresponding author

I hereby declare that Jiří Heller contributed to the article. He helped with generation of *T. brucei* transgenic cell lines in the following way: preparation of RNAi and *in situ* tagging constructs and helped with cell line generation and verification;did mitochondria isolation and was responsible for sub-fractionation by carbonate extration; Northern blotting.

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Doc. Mgr. Hassan Hashimi, Ph.D.

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Current Biology

Article

The Diverged Trypanosome MICOS Complex as a Hub for Mitochondrial Cristae Shaping and Protein Import

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Summary

The mitochondrial contact site and cristae organization system (MICOS) is a multiprotein complex responsible for cristae formation. Even though cristae are found in all mitochondria capable of oxidative phosphorylation, only Mic10 and Mic60 appear to be conserved throughout eukaryotes. The remaining 4 or 5 known MICOS subunits are specific to supergroup Opisthokonta, which includes yeasts and mammals that are the only organisms in which this complex has been analyzed experimentally. We have isolated the MICOS from *Trypanosoma brucei*, a member from supergroup Excavata that is profoundly diverged from opisthokonts. We show that it is required for the maintenance of the unique discoidal cristae that typify excavates, such as euglenids and kinetoplastids, the latter of which include trypanosomes. The trypanosome MICOS consists of 9 subunits, most of which are essential for normal growth. Unlike in opisthokonts, it contains two distinct Mic10 orthologs and an unconventional putative Mic60 that lacks a mitofilin domain. Interestingly, one of the essential trypanosomatid-specific MICOS subunits called TbMic20 is a thioredoxin-like protein that appears to be involved in import of intermembrane space proteins, including respiratory chain complex assembly factors. This result points to trypanosome MICOS coordinating cristae shaping and population of its membrane with proteins involved in respiration, the latter via the catalytic activity of TbMic20. Thus, trypanosome MICOS allows us to define which of its features are conserved in all eukaryotes and decipher those that represent line-age-specific adaptations.