Charles University in Prague, Faculty of Science
Department of Parasitology

Ph.D. study program: Parasitology

Abstract of the Ph.D. Thesis

Reductive Evolution of Mitochondria - Related Organelles in Anaerobic Protist

Petr Rada

Supervisor: Prof. RNDr. Jan Tachezy,Ph.D.
Advisor: Doc. RNDr. Ivan Hrdý, Ph.D.

Prague, 2011

ABSTRACT

Trichomonas vaginalis and *Giardia intestinalis* are parasitic protists of the Excavata group. Both contain anaerobic forms of mitochondria called hydrogenosomes (*Trichomonas*) and mitosomes (*Giardia*). Hydrogenosomes produce hydrogen and ATP by substarte level phosphorylation and mitosomes represent the highly-reduced form of mitochondria that do not participate in cellular energy metabolism and ATP generation. Both types of organelles lost the majority of mitochondrial pathways and their genomes during the mitochondrion to hydrogenosome transition. Consequently, hydrogenosomes and mitosomes facilitate translocation of nuclearly encoded proteins into the matrix of the organelle as well as exchange of metabolites and ions across their membranes. Little is known about the membrane machineries required for the biogenesis of the organelle and metabolite exchange and the limited knowledge of mitosomal proteomes has been mostly gained from genomic analysis and localization studies of a few representative mitosomal proteins.

We performed (i) extensive study of the hydrogenosomal membrane proteome to characterize the core components of the organelle biogenesis and membrane transport and (ii) we performed extensive proteomic analysis of the *Giardia* mitosome to contribute to the understanding of evolutionary origin and function of this novel organelle. In the *Trichomonas* hydrogenosome, we identified and characterized (i) core components required for the protein import machinery, (ii) several novel C-tail anchored proteins and a pathway for their assembly into the outer membrane of the hydrogenosome, (iii) five homologues of the ADP/ATP carrier and (iv) multiple isoforms of the β-barrel proteins Hmp35/36. We confirmed previous suggestion that mitosomal proteomes were dramatically reduced. In the *Giardia* mitosome, we identified (i) a minimal protein import machinery,

(ii) a complete machinery required for iron sulphur cluster assembly, (iii) a novel diflavin protein with NADPH reductase activity and (iv) a VAP (Vesicle Associated Protein) homologue which likely interacts with a cell compartments and cytoskeletal structures.

The minimal proteome of the *Giardia* mitosome and the reduced proteome of the *Trichomonas* hydrogenosome reflect a loss of typical mitochondrial functions as a response to living strategy of anaerobic protist under oxygen limited conditions. Our findings contributed to new insights into the reductive evolution of mitochondria related organelles present in anaerobic protists and extend our previous knowledge on their biogenesis and metabolism.