Department of Bioenergetics, Institute of Physiology (Academy of Sciences of the Czech Republic, Prague) – State of the Art

The research performed at the Department is focused on biotransformation of energy in mammalian organisms with a long-term aim to characterize structure, function and biogenesis of mitochondrial energetic apparatus and its regulation at the level of cell, tissue and organism. Recent and ongoing studies concentrated on oxidative phosphorylation system and its components, namely ATP synthase, cytochrome c oxidase and mitochondrial glycerophosphate dehydrogenase. As elucidation of biological functions of mitochondrial organelles directly depends on application of novel and perspective models, the main emphasis was paid to joint studies combining advanced molecularphysiology approaches and clinical research of inborn metabolic disorders affecting mitochondrial energy provision. Collaboration with the Pediatric Department, 1st Medical faculty, Charles University thus established basis for diagnostics of mitochondrial diseases in the Czech Republic. At the same time it led to elucidation of molecular-genetic basis of several novel diseases as well as of biogenetic processes and function of affected respiratory chain complexes. Among the most important belong identifications of two new disease-causing genes responsible for inborn deficiency of ATP synthase, ATP5E for subunit ε and TMEM70 encoding novel ancillary factor specific for higher eukaryotes, alteration of H+ pumping and assembly of cytochrome c oxidase due to absence of Surf1 factor or identification of mitochondrial glycerophosphate dehydrogenase as novel site of ROS production in mammalian respiratory chain.

Mitochondrial proteom is composed of ~1500 proteins but the function of one third of them is unknown. As mitochondrial involvement is also expected in other types of human diseases, from mono- to polygenic complex diseases, very perspective new line of mitochondrial research became the use of animal genetic models, transgenic or knockout rats produced at the Department of Genetics of Model Diseases at Institute of Physiology, ASCR. This collaboration already enabled studies on the role of mitochondrial genome in type II diabetes and using conplastic model it demonstrated direct involvement of mtDNA haplotypes in predisposition for metabolic dysfunction.

The present studies are thus concentrated on the following problems:

(1) Elucidation of molecular mechanisms of biogenesis and function of respiratory chain components, from assembly of heterooligomeric complexes with the help of specific assembly-biogenetic factors to their interactions with other enzymes and proteins constituting respirasome, ATP synthasome or other supercomplexes.

(2) Identification of new/unknown components of mitochondrial proteome, mitochondria-nuclear interactions and characterization of their patophysiological functions.

(3) Application of new knowledge in diagnostics and future therapeutic strategies in combating mitochondrial diseases.

This program includes external collaborations with pediatric departments of Medical faculties of Charles University, Institute of Clinical and Experimental Medicine (IKEM, Prague), Institute of Molecular genetics, ASCR (Prague) as well as with numerous foreign centers of mitochondrial research. Present research funding includes 3 grants from GAČR (Czech Science Foundation), 2 grants from IGA MHCR (Internal Grant Agency, Ministry of Health of the Czech Republic), 1 grant from Charles University and partial funding by 1 grant from Ministry of Education, Youth and Sports of the Czech Republic.

The staff of the Department includes 2 senior scientists, 6 PostDocs, 4 PhD students, 2 technicians and pre-graduate students. Participation of pre- and postgraduate students is closely associated with their education in the Department and Department members act as lecturers of Bioenergetics at the Faculty of Natural Sciences in Prague and Medical Faculty in Hradec Králové.

Department is well equipped for biochemical, molecular biology and molecular genetic studies, analysis of mitochondrial functions by specific biophysical approaches, use of different florescence probes, mitochondrial phenotyping of animal models, studies on human biopsy samples. Specific equipment includes low and high speed centrifuges, -80 °C deep freezer, liquid nitrogen storage containers, 2 spectrophotometers, fluorescence plate reader, high resolution oxygraph, cytofluorometer, equipment for protein and DNA electrophoretic analysis, two cell culture bio hazard boxes, CO2 thermostats, inverted microscope with epifluorescence and digital camera.