ABSTRACT

Inborn errors of metabolism represent a heterogeneous group of rare conditions, most having an incidence of less than 1 in 100,000 births. Because of their low prevalence, they are on the margin of attention of general research and even more so of large pharmaceutical companies. Study of rare diseases is the only way to design therapeutic options in order to improve quality of life of affected patients.

Present Thesis particularly focuses on disturbances in mitochondrial energy metabolism. The main goals were the characterization of mitochondrial biogenesis within foetal development, as well as in childhood and adulthood. Another aim was to define clinical, biochemical and molecular aspects of mitochondrial optic neuropathies in childhood and adulthood.

This work supported the earlier observations that gestational week 22 is the edge of viability, which has to be taken into account in upcoming discussions about guidelines on resuscitation of preterm neonates. Secondly, over last four years, we managed to examine and describe large cohort of patients with optic neuropathies based on a mitochondrial dysfunction. We have managed to characterize the biochemical and molecular-genetic background in more than 200 patients, and both selected cases (LHON/MELAS overlap syndrome) and cohort studies (MELAS, DOA, LHON plus) were published, bringing novel phenotype and genotype findings. Finally, the main contribution of this Thesis was the application of our results and experience in clinical practice. In 2013, we succeeded in creating a National Center for Patients with Mitochondrial Optic Neuropathies in order to bring the best care to patients with rare mitochondrial optic diseases, to improve diagnostic tools and to harmonize (pre-)clinical research.

Key words: mitochondrion, biogenesis, development, mitochondrial optic neuropathies, Leber Hereditary Optic Neuropathy (LHON)