Genetic information in eukaryotic cells is divided between the nucleus and cytoplasmic organelles, *i.e.* mitochondria in non-plant organism, mitochondria and chloroplasts in plants. Mitochondria carry the respiratory chain and ensure fundamental function in energy production, redox status, metabolic pathways, programmed cell death, aging and in signaling cascades involving reactive oxygen species.

Mutations in the mitochondrial genome cause severe incurable neurodegenerative diseases in humans. Over 300 pathogenic mutations have been characterized. These fall into three types: 1) missense mutation in protein-coding genes, 2) point mutation in tRNA or rRNA genes that impair mitochondrial protein synthesis and 3) duplications or deletions.

One of the most common mitochondrial diseases is MELAS syndrome. In 80% of the cases, MELAS is due to heteroplasmic m.3243A>G mutation in the MT-TL1 gene encoding the mitochondrial $tRNA^{Leu\ (UUR)}$. The m.3243A>G results in impaired mitochondrial translation and protein synthesis including the mitochondrial electron transport chain complex subunits leading to impaired mitochondrial energy production. The inability of dysfunctional mitochondria to generate sufficient ATP to meet the energy needs of various organs is a major player in the multi-organ dysfunction observed in MEALS syndrome.

The aim of the project is to use the catalytic nucleic acids-based technology to downregulate the level of mutated version of *MT-TL1* gene, encoding the mitochondrial $tRNA^{Leu(UUR)}$, associated with one of the mitochondrial neurological disease - MELAS syndrome. We intend also to explore the potential of designed RNA-based vehicle to deliver the proper unmutated version of tRNA to mitochondria to compensate the effect of the mutated tRNAs.

This strategy according to this particular project can give the very first step to potential therapy of MELAS syndrome, but what is even more important could serve as a general strategy with universal platform for RNA-mediated manipulation of the mitochondrial genetic system.