Mitochondria are best known for being the eukaryotic cell “powerhouses”. They participate in many cellular processes, i.e. ATP production, calcium homoeostasis, reactive oxygen species generation, execution of apoptosis and steroid hormone biosynthesis. The metabolite exchange between mitochondria and cytoplasm is supported by VDAC (voltage dependent anion-selective channel), a protein regarded as crucial for mitochondrial functioning. In human mitochondria, as in the case of other vertebrates, there are three isoforms of VDAC (VDAC1- VDAC3) able to form functional channels have been identified. They are expressed in different tissues and organs at different levels and their dysfunctions contribute to numerous pathological conditions. VDAC1 is the most abundant protein and the best known, VDAC2 protein has similar activity that VDAC1 while VDAC3 is the least known protein and seems to be mandatory for sperm motility. This is why VDAC3 can be a candidate to participate in the molecular mechanisms of fertilization and etiology of male infertility. It is therefore very important to investigate whether mutations in the VDAC3 gene may cause impaired physiological function of the VDAC3 channel in spermatozoa resulting in a decrease in sperm motility - commonly observed symptom in infertile patients.

In this project we are going to perform studies addressing functional impact of VDAC3 mutations in patients with markedly reduced sperm motility. Namely, the following investigations will be estimated: (1) identification of mutation of the VDAC3 gene in spermatozoa with low motility, (2) *in vitro* functional analysis of the mutated VDAC3 proteins reconstituted in planar lipid membrane, and (3) *in vivo* functional analysis of the mutated VDAC3 proteins in the outer mitochondrial membrane. These investigations will combine biophysical, physiological, molecular and cell biology approaches. The obtained results will provide a deeper insight into mechanisms responsible for the etiology of infertility in patients with low sperm motility. They might also contribute to development of new markers of male infertility and male contraceptives.