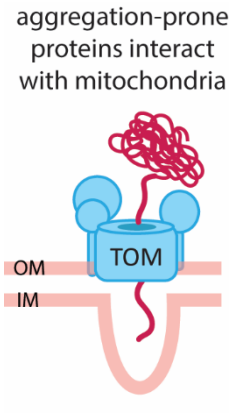

Many neurodegenerative diseases are still incurable and their pathogenesis remains unclear. Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease, has been associated with mitochondrial and protein homeostasis (proteostasis) failure. A common thread in such diseases is protein aggregates accumulation, which is toxic for the cells. Part of those abnormal proteins have been found to associate with mitochondrial membranes. Based on literature data and our results, we hypothesize that certain amount of aggregation-prone proteins can be removed via mitochondrial quality control.

My experiments on model protein revealed a new mechanism that releases proteins stalled during import. I provided evidence that the dissipation of the inner mitochondrial membrane potential activates proteases, leading to cleavage and release of arrested proteins from mitochondrial translocases. OMA1 protease is localized in the inner mitochondrial membrane and is fulfilling many well-described functions. Additionally, after the dissipation of inner membrane potential, it become activated and could cleave stalled proteins. It seems that OMA1 does not perform this function alone, but it is certainly an important element of the degradation mechanism. I have proved that without OMA1 protease or after reducing its amount cells are not degrading incorrect proteins efficiently.

I find these results promising and I would like to verify if the erroneous proteins and their aggregates forming in neurodegenerative diseases may be degraded in OMA1-dependent manner. The main purpose of the project is to find out if mechanisms that clear stalled mitochondrial precursor proteins can also clear disease associated and aggregation prone proteins from mitochondria, thereby enabling efficient import inside the organelle.