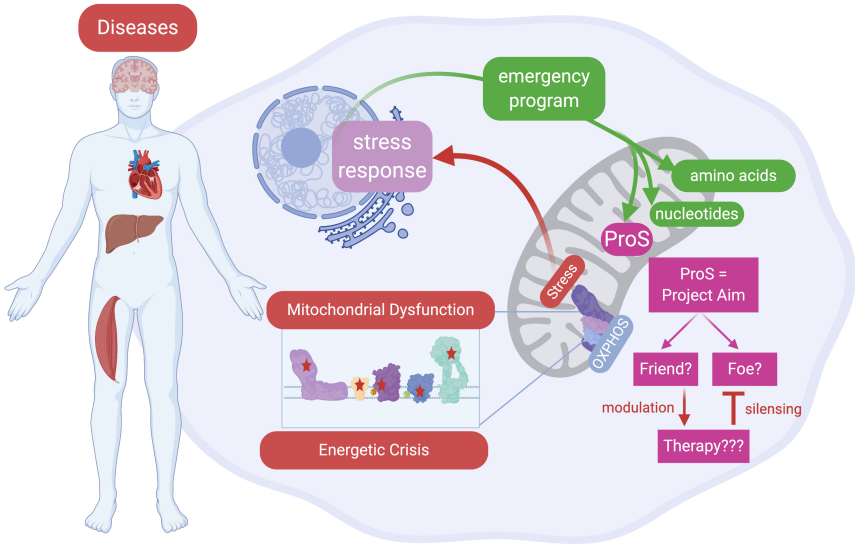
Can the silencing of the "metabolic emergency plan" help to combat diseases caused by the energy crisis in our body?



Mitochondria are critical power plants of our cells. Defects in mitochondrial function impair the energy balance of organisms and result in severe, often fatal, genetic disorders that primarily affect organs with high energy demand, such as the heart, brain, liver, and muscle. Furthermore, so-called mitochondrial dysfunction underlies many other diseases, including diabetes, obesity, Parkinsonism, or dramatic consequences of heart attack and brain stroke, that typically associate with progressing age.

Failing mitochondria send signals about an energetic crisis to the rest of the cell. In feedback, the cell reprograms its function to the "emergency plan" to help organisms cope with an energy deficit. This plan consists of different metabolism changes, for example, increased production of some amino acids and nucleotides, and intensified consumption of other types of amino acids. Intriguingly, cancer cells use a similar program to reproduce extensively. When short-termed, this "emergency program" seems to be beneficial and helps to survive. However, recent studies suggest that if this "emergency plan" runs too long or is too intensive, the cells with damaged mitochondria start to suffer even more, leading to the fatal end.

In my future research, I want to silent a part of this emergency plan, the excessive production of amino acid proline (ProS pathway) inside the mitochondria, and see whether it will help the cells with mitochondrial dysfunction survive longer and stay healthier. Strikingly, we still do not know if the boosted synthesis of proline is a friend or foe of damaged mitochondria. To follow my plan, I will silence the major players of the ProS pathway from suffering mitochondria using genetic modification or drugs, and I will check how it affects different physiological functions of the cells. Furthermore, I will determine if the ProS pathway alone is used by cells to send stress signals and alter the way how our cells behave and get energy. Finally, I will explore the yet uncharted consequences of mitochondrial failure on the synthesis of proline-rich collagens and changes in an extracellular niche that may contribute to tissue fibrosis or aging.

My research will allow us to understand what is the mean of the ProS pathway for challenged mitochondria. Together with my research team, we will investigate if it is possible to help people suffering from mitochondrial dysfunction by silencing or modifying the proline synthesis inside the mitochondria. My studies can be used in the future to design new therapies to combat diseases caused by defective mitochondria.