DESCRIPTION FOR THE GENERAL PUBLIC

Because human cells die in the absence of sufficient oxygen supply, myocardial infarction and stroke are responsible for the death of millions of persons worldwide due to ischaemia/reperfusion injury. It has been recently shown that mitochondria play an important role in cell death and survival processes. The mitochondrial damage during hypoxia is one of the important mechanisms resulting in cellular death. On the other hand, better understanding of mitochondrial role during pathological processes could lead to the discovery of natural protecting mechanisms. Activation of potassium ion transport in the inner mitochondrial membrane is thought to be beneficial under stress conditions. Potassium transporting proteins (potassium channels) were discovered in the inner mitochondrial membrane. Many studies suggest that their activation significantly protects tissues (heart, brain and others) against damage during ischeamia. However, due to the lack of specific and non-toxic mitochondrial potassium channel modulators, the clinical application of these strategies has been limited. Therefore, there is a great need to find specific molecules targeting mitochondria of living cells for therapeutic gain.

Flavonoids belong to a vast group compounds that are widely distributed in all foods of plant origin, exhibiting a large variety of biological properties. Interest in health benefits of flavonoids has increased due to their potent antioxidant and free-radical scavenging activities. Flavonoids have been shown to reveal the anticancer, antiarrhythmic, hypotensive and anti-estrogenic actions as well as other beneficial actions. The biological activity, bioavailability and low toxicity set broad prospects of the usage of some of these substances as a potential therapeutics for a number of human diseases. Some flavonoids have also been shown to be cardioprotective. Although the antioxidant effect of flavonoids has been long thought to be a crucial factor accounting for cellular cardioprotection, mitochondrial pathways (including mitochondrial ion channels) are presently emerging potential targets for a specific pharmacological action of some flavonoids in the anti-ischemic strategies.

However, the detailed research describing a direct interaction of cytoprotective flavonoids with mitochondrial potassium channels is lacking. Therefore, the scientific aim of the proposed project is the description of the regulation of the mitochondrial potassium channels by flavonoids and its functional consequences. We expect that the electrophysiological studies with an unique mitoplast patch-clamp technique and biochemical studies will lead to the understanding of the interaction mechanisms between flavonoids and the mitochondria, defining the specific partner of this interaction, i.e., mitochondrial potassium channel protein. We also suspect that the flavonoid-affected mitochondrial potassium channel activity may contribute to signalling pathway induction leading to cytoprotection.

We also expect that our studies describing the regulation of mitochondrial potassium channels by the natural substances of plant origin will bring us closer to a better understanding of flavonoid-induced cytoprotective mechanisms. Additionally, the discovery of specific and non-toxic mitochondrial potassium channel activators could contribute to the development of new therapeutic strategies, leading to protecting effects against oxidative damage. This could also leads us to a better understanding how to improve the treatment of ischemic or neurodegenerative disorders.