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## **MITOCHAN - Regulation of the mitochondrial ATP-dependent potassium channel in health and disease**

ATP-sensitive potassium channels (KATP) are widely distributed ion channels acting as sensors of cellular metabolism. KATP channels are present in the plasma membrane (pmKATP), but they were found to present also in mitochondria (mitoKATP). In the absence of a clear-cut molecular identification of mitoKATP however, even its existence was a matter of debate. The host group has recently identified a mitochondria-localized protein complex that mediates ATP-sensitive potassium currents. They showed that mitoKATP is composed of a pore-forming subunit (MITOK) and an ATP-binding subunit (MITOSUR). In vitro reconstitution of MITOK together with MITOSUR recapitulated the main electrophysiological properties and pharmacological profile of mitoKATP, including activation by diazoxide. Loss of MITOK was able to suppress cardioprotection elicited by diazoxide-induced pharmacological preconditioning in isolated heart. Overall, these data indicate that the novel components forming mitoKATP represent key players in shaping mitochondrial physiology with a potential impact on several pathological processes. However, many questions remain open regarding the biophysical and pharmacological characteristics of this novel channel. Therefore I proposed to exploit my unique expertise in the study of mitochondrial ion channels using the patch clamp technique (only few groups in the world master this method on mitochondria) that allows detection of ion movement in native membranes, in order to compare channel activity in mitochondria from WT and MITOK knock-out animals in various tissues. As a MSCA Seal of Excellence@UNIPD 2021 laureate, I have already started working on MITOCHAN project and obtained the first promising results. Following, I will test the effect of a novel, mitochondria-targeted derivative of a mitoKATP modulator and will set up a state-of the art technique to identify possible protein regulators/interactors of mitoKATP. The project generates important knowledge that could be exploited in the context of ischemia and will have a great impact on my career in terms of scientific output and future direction of my research.