Mitobetes: The role of Von Willebrand Domain-containing Protein 8 in mitochondrial physiology

Mitobetes project brings a new research on poorly characterized mitochondrial protein involved in important cellular and physiological processes such diabetes, kidney failure and cancer. It also aims on the role of mitochondria in diabetes, the disease which affects almost 10% of European population. The mitobetes project has a potential to help to find a new mitochondrial protein involved in diabetes, find a mechanism of diabetes development, increase the public knowledge about diabetes and thus helps to decrease EU healthcare costs.
Mitochondria are crucial organelles not only in energy conversion, but also in a plethora of other biological processes. Their function is closely related to their dynamics, controlled by the pro-fusion proteins Mitofusin (Mfn) 1 and 2 and Optic atrophy 1 (Opa1); and by the fission proteins mitochondrial fission factor (Mff) and dynamin related protein 1 (Drp1). Opa1 not only controls mitochondrial fusion, but also shape of the mitochondrial cristae, a crucial parameter in determining mitochondrial function and participation in apoptosis. Opa1 exists in high molecular weight complexes of unknown composition that are dynamically modulated during cristae remodeling.
Recently, the host laboratory completed a proteomic catalogue of proteins associating with Opa1 in intact cristae and leaving the complex only when cristae shape was disrupted. Among the hits associating with Opa1, the host lab discovered Von Willebrand Domain-containing Protein 8 (Vwa8), a mitochondrial protein of unknown function whose higher levels correlate with worse prognosis of Acute Myeloid Leukemia (AML). Here, I propose to understand the function of Vwa8 in mitochondrial network and cristae shape, Opa1 function, apoptosis and bioenergetics. This project will not only characterize the role of a novel protein in involved mitochondrial morphology and function, but also verify if a link between mitochondrial morphology and AML exists.

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