MERCURY - Chemical compounds targeting MERCs: identification of their partners in physiological and pathological conditions

Mitochondria and Endoplasmic Reticulum (ER) Contact sites (MERCs) are points in which the surfaces of the two organelles run in parallel. MERCs gained attention recently due to their fundamental contribution to several cell processes, such as Ca2+ and lipid homeostasis, mitochondrial fission, and apoptosis. To execute and regulate these processes, MERCs must be dynamic and react to the needs and metabolic state of the cell. Interestingly, the organelles stay separated by a narrow cleft, usually 10-50 nm apart. The width of the MERCs gap and its size (i.e. area of a membrane involved in the contacts) are the critical parameters that determine their cellular functions. Despite the literature on MERCs has grown considerably, the precise molecular structure and role of MERCs are poorly defined.
In the proposed project I will investigate the regulation of MERCs plasticity by small molecule compounds. Using a high-content phenotypic screening approach, based on a FRET mitochondria-ER proximity probe, I will identify the compounds affecting MERCs structure. These bioactive hits will be validated through biochemical, confocal and electron microscopy assays. Moreover, I will search for the protein target of the hit molecule using the methodology developed during my PhD. Finally, I will evaluate the capability of the identified hit molecules to act as therapeutic lead compounds for pathological conditions by testing the identified molecules on cells with defective MERCs. Therefore, this project will open new research paths related to both MERCs structure and function.
I will obtain deep knowledge of mitochondrial biology and high content screening, which will complement my current expertise obtained during PhD. Besides, I will develop transferable skills needed to successfully accomplish the proposed project. The project also brings the benefits to the European Research Area, since it builds international collaboration and transfers knowledge between two research areas/teams.

UNIPD Team Leader: Marta Giacomello

MSCA Fellow: Tomas Knedlik

Department: Department of Biology

Coordinator: Università degli Studi di Padova (Italy)

Total EU Contribution: Euro 183.473,28

Call ID: H2020-MSCA-IF-2019

Project Duration in months: 24

Start Date: 01/08/2021

End Date: 31/07/2023

Find out more: **https://cordis.europa.eu/project/id/896745**