UNIVERSITÀ DEGLI STUDI DI PADOVA

FIAT - Mitochondrial Fission 1 protein Interactions: from discovery to Acute myeloid leukemia pathophysiology and Therapy

---

Mitochondrial morphology is controlled by a set of “mitochondria-shaping” proteins that govern fusion and fission of the organelle. Fission is executed by dynamin-related protein 1 (DRP1) that binds to adaptors on the outer mitochondrial membrane to oligomerize and sever mitochondria. Fission 1 (FIS1) is among the putative mammalian DRP1 adaptors, but it appears dispensable for mitochondrial fission. Conversely, FIS1 seems to participate in the regulation of mitochondrial autophagy (mitophagy), interaction between mitochondria and lysosomes, and apoptosis. Because of these multifunctional roles, FIS1 emerged as an appealing pharmacological target and peptides inhibiting its interaction with DRP1 have been advanced in the experimental treatment of ischemia-reperfusion and of genetic conditions such as Huntington’s disease. More recently, FIS1 was identified as a crucial factor to sustain Leukemia Stem Cells (LSCs) in Acute myeloid leukemia (AML), the second most prevalent and the most fatal leukemia in adult patients. However, our scarce knowledge of the biology of Fis1 is mirrored by the uncertainties on how FIS1 regulates AML LSCs.

To close this gap in knowledge, I will take a chemical biology approach and design innovative genetically encoded sensors for FIS1 functions that I will use to identify potential FIS1 small molecules inhibitors. I will then use these chemical probes to evaluate which cellular function of FIS1 is essential for maintenance of AML LSCs. Overall, this project will unveil how a multipronged mitochondrial protein regulates cell pathophysiology and will deliver novel chemical tools to investigate FIS1 function in the context of AML and potentially to evolve into therapies for this hitherto poorly treatable cancer.

UNIPD Supervisor: Luca Scorrano
MSCA Fellow: Christina Arseni
Department: Biology
Coordinator: Università degli Studi di Padova (Italy)
Total EU Contribution: Euro 193.643,28
Call ID: HORIZON-MSCA-2024-PF-01
Project Duration in months: 24
Find out more: https://cordis.europa.eu/projects/en