ERMITO - Molecular Anatomy and Pathophysiology of the endoplasmic reticulum-mitochondria interface

Organelles are not randomly organized in the cytoplasm of the cell, but often are orderly arranged in mutual relationships that depend on physical, protein bounds. Understanding the molecular nature of the tethers that regulate relative position and juxtaposition of the organelles is one of the main quests of cell biology, given their functional importance. For example, the juxtaposition between mitochondria and endoplasmic reticulum (ER) has been suggested by us and others to crucially impact on Ca2+ signalling and apoptosis. We recently identified the first structural ER-mitochondrial tether in mitofusin 2 (Mfn2), a pro-fusion mitochondria-shaping protein. A fraction of Mfn2 is also located on the ER regulating its morphology, and acting in trans to tether it to mitochondria. The tethering function of Mfn2 impacts on the transmission of Ca2+ signals between the two organelles and is regulated by the oncosuppressor trichoplein/mitostatin. Mfn2 is likely only one of the tethers, as others exist in yeast. Furthermore, the dynamicity of the ER-mitochondria contact is known, but remains poorly understood. Therefore, a clear picture of the anatomy and pathophsyiology of ER-mitochondrial connection is far from being reached.Here we hypothesize that ER-mitochondrial contacts are crucial specialized hubs of cellular signalling whose architecture is modulated by cellular cues, impacting on integrated signalling cascades and ultimately affecting cellular function. To address this hypothesis we wish to setup a research project that aims at (i) increasing our knowledge on the molecular nature of tethers and modulators of ER-mitochondrial tethers in mammalian cells; (ii) clarifying how mitochondrial and ER function are controlled by the tethering; (iii) addressing how juxtaposition influences complex cellular responses including autophagy and cell death; (iv) elucidating the role of tethering in vivo by generating animal models with defined ER-mitochondrial distance.

ERC Grantee: Luca Scorrano

Department: Biology

Coordinator: Università degli Studi di Padova

Total EU Contribution: Euro 1.499.995

Call ID: ERC-2011-StG

Project Duration in months: 60

Start Date: 01/01/2012

End Date: 01/01/2017

Find out more: https://cordis.europa.eu/project/id/282280