INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 03 de febrero de 2023
12:30 h. Instituto Cajal (CSIC) Madrid

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Mitochondrial transfer: Dynamics beyond the cellular edges

Abstract

The acquisition of mitochondria through intercellular connections or via endocytosis is a biological concept recently shown to promote tumor growth in glioblastoma, the most common and aggressive brain tumor. However, the molecular mechanisms behind those processes are yet to be characterized. Here, we have used a series of genetic and pharmacological approaches to uncover how exogenous organelle importation rewires the native mitochondrial content and function in glioblastoma cells. Capitalizing on connexin-43 (Cx43) as a key modulator of mitochondrial acquisition, we show a differential impact for this protein on the acquisition of isolated or transferred mitochondria from co-cultured fibroblast and primary astrocytes. The importation of exogenous organelles remodels the content, protein composition and native configuration, as well as the functionality of the endogenous mitochondrial network in glioblastoma. In sum, we provide evidences for a functional remodelling of the native mitochondrial network in glioblastoma cells, paving the way to correct alterations in the respiratory metabolism aimed to halt glioblastoma development.

Affiliation and short bio

My work aims to characterize molecular determinants of mitochondrial physiology, particularly in the nervous system. Supervised by Prof. Juan Pedro Bolaños (Univ. Salamanca, USAL), we described how γ-glutamylcysteine acts as a mitochondrial antioxidant in neuroprotective gene therapy, worthy of several awards. A research stage (EMBO STF, Univ. Geneva) expanded our results on the mitochondrial antioxidant capacity at the crossroads with mitochondrial dynamics and autophagy. Staying in the laboratory of Prof. Luca Scorrano (Univ. Padua, Italy) for my postdoc, I contributed to seminal works on mitochondrial dynamics and ultrastructure at setting respiratory bioenergetics, tissue homeostasis and autophagy sorting of mitochondria, among others. We described how cristae engage ATPase oligomerization and activity to prevent mitochondrial dysfunction. We also linked ultrastructure and ATPase at setting transition pore occurrence and mitochondrial redox status. Back to USAL with a Juan de la Cierva-Incorporación and Marie Curie-IF fellowships, I contributed to further works in neural metabolic and redox communication. My current interests as a Ramón y Cajal fellow at the Cajal Institute (CSIC, Madrid) focus on exogenous mitochondrial acquisition and intercellular transfer, to uncover how mitochondrial content and functional reprogramming drive physio(patho)logy.

Related publications with the topic:

1 - Quintana-Cabrera R *et al*. 2021. *Opa1 relies on cristae preservation and ATP synthase to curta*il *reactive oxygen species accumulation in mitochondria*. **Redox Biology**. 2021.

2 - Quintana-Cabrera R *et al*. 2018. *The cristae modulator Optic atrophy 1 requires mitochondrial ATP synthase oligomers to safeguard mitochondrial function*. **Nature Communications**, 2018

3 - Varanita T *et al*. *The OPA1-dependent mitochondrial cristae remodeling pathway controls atrophic, apoptotic, and ischemic tissue damage*. **Cell Metabolism**. 2015.

4 - Cogliati S; *et al*. *Mitochondrial cristae shape determines respiratory chain supercomplexes assembly and respiratory efficiency.* **Cell***.* 2013*.*

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