UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

DOTTORATO DI RICERCA IN Tecnologie Convergenti per i Sistemi Biomolecolari – XLII CICLO

Research Topic ID: XLII – 1.2

Project Tutor: Renata Tisi

Project Supervisor/s: Michela Ceriani

Project Title: UNRAVELING THE SECRET OF RALGPS2 T-DARK: A NEW POTENTIAL TARGET IN GLIOBLASTOMA

Scientific background & Objectives

Glioblastoma (GB) is the most aggressive and the common primary tumor of the central nervous system with a median lifespan of 15 months from diagnosis. GB is classified as rare cancer and is particularly challenging due to its heterogeneous microenvironment; no resolutive treatment exists. Communication between cells plays a key role in GB drug resistance: GB cells form tunneling nanotubes (TNTs) which are involved in tumor progression and recurrence. TNTs are actin-based highly-dynamic membrane protrusions that enable cells to directly communicate and play a central role in cancer progression and malignancy. One of the proteins involved in TNTs formation is RalGPS2 a Ras-independent Guanine Nucleotide Exchange Factor for RalA GTPase. RalGPS2 is classified as a Tdark gene due to the minimal knowledge of its biological function. The goal of this project is to analyze the role of RalGPS2 in GB and the formation of TNTs in the GB microenvironment.

Project's Networks, Sustainability & Mobility

a) the coherence of the suggested project with competences/tools of the hosting lab
b) intradepartmental or external collaborations
c) at least one pertinent research article published by the proposer/s
d) 1 (or more) putative foreign institutions for achieving the required ordinary mobility (6 months)

a) RalGPS2 has been cloned in 2002 by Michela Ceriani. Actually there are only 7 articles on PubMed on RalGPS2 and Michela Ceriani is an author of 5 of them. Therefore, our laboratory is the leading experts in the study of this Tdark. Furthermore, in our laboratory we studied tunneling nanotubes on different cells model (breast, bladder, Kidney), included Glioblastoma cells.

b) For this project we have many collaborators: - Prof. Serena Pellegatta of the Fondazione IRCCS Istituto Neurologico Carlo Besta, who work and will provide cell lines obtained from patients; - prof. Elena Sacco (BtBs-Unimib) for metabolism studies, prof. Marzia Lecchi (BtBs-Unimib) for electrophysiology studies.

c) Relevant Literature by the Proponent:
-Formicola B, D'Aloia A, Dal Magro R, Stucchi S, Rigolio R, **Ceriani M. (last author**), Re F. (2019) Differential Exchange of Multifunctional Liposomes Between Glioblastoma Cells and Healthy Astrocytes via Tunneling Nanotubes Frontiers in Bioengineering and Biotechnology, 2019, 7, pp 403 doi: 10.3389/fbioe.2019.00403 M103454200
- D'Aloia A, Arrigoni E, Costa B, Berruti G, Martegani E, Sacco E, **Ceriani M. (**2021) RalGPS2 interacts with AKT and PDK1 promoting tunneling nanotubes formation in bladder cancer and kidney cells microenvironment. Cancers, 13(24), pp 6330 doi: 10.3390/cancers13246330

- D'Aloia A., Pastori V., Blasa S., Campioni G., Peri F., Sacco E., **Ceriani M. (last author)**, Lecchi M., Costa B. (2024) A new advanced cellular model of functional cholinergic-like neurons developed by reprogramming the human SH-SY5Y neuroblastoma cell line. Cell Death Discovery, 10(1), pp 24 doi: 10.1038/s41420-023-01790-7

d) FOREIGN INSTITUTIONS:
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