





RaIGPS2 Tdark: a new potential target in Glioblastoma

<u>**D'Aloia A.1**</u>, Sacco E.^{1, 2, 3,4}, Tisi R.^{1,2}, Lecchi M. ^{1,2,4}, Costa B ^{1,2}, Re F.^{1,2,5}, Pellegatta S.⁶ and Ceriani M. ^{1,2}

E-mail: alessia.daloia@unimib.it

¹ Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy

² Milan Center for Neuroscience (NeuroMI), University of Milano-Bicocca, Piazza dell'Ateneo Nuovo 1,20126 Milano, Italy

³ ISBE.IT, SYSBIO Centre of Systems Biology, Piazza della Scienza 2, 20126 Milan, Italy ⁴ Inter-University Center for the Promotion of the 3Rs Principles in Teaching & Research ⁵ BioNanoMedicine Center NANOMIB, School of Medicine and Surgery, University of Milano-Bicocca, 20854 Monza, Italy.

⁶ Laboratory of Immunotherapy of Brain Tumors, Unit of Neuro-Oncology Fondazione IRCCS Istituto Neurologico Carlo Besta.

Keywords: RalGPS2, Glioblastoma, senescence, tunneling nanotubes, proliferation

Abstract:

Glioblastoma is a very rare brain tumor, with an annual incidence of around 1/33.330, but is the most common and aggressive brain tumor, associated with poor prognosis and survival, representing a challenging medical issue for neurooncologists. The current standard care for Glioblastoma (GB) is based on radiotherapy and a concomitant treatment with temozolomide (TMZ) chemotherapy after surgical resection of the primary tumor mass. Unfortunately, GB shows a high grade of recurrence, which is the reason for the median lifespan from the time of diagnosis to death of approximately 15 months. Since there are no curative treatments for GB and the prognosis is poor, finding novel molecules to control tumor progression represents an important research topic. This project aimed to investigate the potential role of the Tdark RalGSP2, a Ras-independent Guanine Nucleotide Exchange Factor (GEF) for RalA GTPase, in GB pathogenesis and/or progression. In fact, RalGPS2 seems to be involved in the regulation of cell proliferation and motility in GB cells. The results deriving from the proposed research will be useful to better understand unknown aspects of this rare disease and to identify new targets for future drug design.