Unraveling the secret of RalGPS2 Tdark: a new potential target in glioblastoma

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Abstract:

Glioblastoma (GBM) is the most aggressive form of glioma and the common primary tumor of the central nervous system accounting for approximately 50% of gliomas with a median lifespan of 15 months from diagnosis. GBM is classified as rare cancer (annual incidence 1/33.330 individuals) and is particularly challenging among brain tumors due to its heterogeneous microenvironment representing a strategic network for treatment escape and recurrence after surgical resection. Currently, no resolutive treatment exists for recurrent GBM. In this scenario, communication between cells plays a key role in GBM drug resistance: more specifically, GBM cells form tunneling nanotubes (TNTs) which are probably involved in tumor progression and recurrence. TNTs are actin-based highly-dynamic membrane protrusions that enable cells to directly communicate with each other over long distances 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 (GEF) for RalA GTPase, whose knock-down in G523NS patient-derived GBM cell line affects cell proliferation. 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.