POSTER

AUTOPHAGY IS IMPAIRED IN GSCS-ENRICHED GLIOBLASTOMA MODELS

G. Trotto[1], M. Calvitto[1], N. Martella[1], D.Gargano[1], M. Cillo[2], E. Sgambati[1], F. Nazio[3], P. Grumati[2|4], S. Di Bartolomeo[1]

[1]Dept. of Biosciences and Territory, University of Molise, Italy; [2]Telethon Institute of Genetics and Medicine (TIGEM), Pozzuoli, Italy; [3]Dept. of Biology, "Tor Vergata" University, Rome, Italy; [4]Dept. of Clinical Medicine and Surgery, Federico II University, Naples, Italy

Glioblastoma (GBM) is the most common and aggressive primary brain tumor in adults, still associated with poor prognosis and limited therapeutic options. A key obstacle to effective treatment is glioma stem cells (GSCs), a subpopulation sustaining tumor initiation, driving progression, and promoting therapy resistance. Autophagy is an essential cellular process responsible for degradation and recycling of intracellular components, maintaining cellular homeostasis. In cancer, autophagy role is complex and context-dependent, as it can either suppress tumor development or support cancer cell survival. In particular, its contribution to GBM biology remains largely unclear and, such as its contribution to stemness. In previous studies, we observed that autophagy competence is required to promote GBM cell differentiation induced by modulating epigenetic regulators. Through proteomic analysis and immunoassays we found that autophagy is defective in GBM models compared to non-tumoral samples. In detail, we found that the autophagy defect is exacerbated in GSCs-enriched cultures. Indeed, we studied autophagy competence in human GBM cells grown either as adherent monolayers, reflecting a more differentiated phenotype, or as 3D spheroids enriched in stem-cells. Our data show that GSCs cells display reduced autophagic competence compared to their differentiated counterparts. This defect is associated with alterations in key players regulating autophagy, along with decreased activation of transcriptional programs required for proper autophagy and lysosomal function. Overall, our findings identify autophagy defect as a distinctive feature of GBM stem-enriched spheroid cultures and suggest its involvement in the maintenance of stemness, ultimately supporting tumor aggressiveness. Targeting autophagy may therefore represent a promising strategy to interfere with GSCs and improve therapeutic outcomes in GBM.

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