

ABSTRACT NO:04

RESEARCH ARTICLE

Integrative Cross-Population Multi-Database Analysis Reveals an Association Between GORASP2 and Autophagy in Glioblastoma

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Abstract

Objective: Glioblastoma (GBM), IDH-wildtype WHO Grade IV, is the most aggressive primary brain tumour. Although temozolomide (TMZ) remains standard-of-care, ~50% develop resistance driven by cytoprotective autophagy. GORASP2, an autophagy regulator linked to hyperactivated mTOR signaling in GBM, remains largely unexplored. This study characterized the molecular significance of GORASP2 across independent Western and Eastern cohorts using an integrative multi-database approach.

Methods: This in silico study used GEPIA2 (TCGA, n=163; GTEx, n=207) and CGGA cohorts (mRNAseq_693, n=672; mRNAseq_325, n=329) for expression/prognosis; cBioPortal (n=592, 611) for genomic alterations; and UALCAN/CPTAC (normal, n=10; tumour, n=99) for protein expression. Co-expression, immune infiltration, single-cell, and pathway analyses used GEPIA2/CGGA, TIMER3.0, TISCH2, and STRING/GO, with significance via ANOVA, t-tests, log-rank tests, and Pearson correlation ($p < 0.05$).

Results: GORASP2 mRNA and protein were overexpressed in GBM versus normal brain ($p < 0.05$), elevated further in mTOR-altered tumours ($p = 0.0109$). Expression rose with WHO grade in mRNAseq_325 ($p = 0.00018$) but not mRNAseq_693 ($p = 0.52$), with no difference between primary and recurrent GBM. GORASP2 was non-prognostic for survival, but showed strong correlation with Golgi-trafficking (RAB1A, RAB2A, GOLPH3) and autophagy-initiation genes (BECN1, UVRAG, STX17), and moderate-to-strong correlation with mTOR genes (MTOR, RPTOR, RICTOR); late autophagy markers (MAP1LC3B, LAMP2, SQSTM1) strengthened only in recurrent GBM. Immune profiling showed positive correlation with cytotoxic T-cells, negative with macrophages. GORASP2 was minimal in T-lymphocytes but enriched in malignant cells, found highest cell line expression of GBM in T98G/DK-MG and moderate in U-87MG/U-251MG (nTPM ~58–90). GO enrichment highlighted Golgi vesicle transport and autophagosome assembly; STRING placed GORASP2 within a 29-gene network.

Conclusion: Integrative cross-population multi-database analysis reveals an association between GORASP2 and autophagy-related pathways in glioblastoma. Although GORASP2 does not independently prognostic biomarker. GORASP2's consistent association with Golgi-trafficking, autophagy, and mTOR signaling supports its prioritization for in vitro validation and evaluation as a therapeutic target in TMZ-resistant glioblastoma.

Keywords: GORASP2, Glioblastoma, Cytoprotective Autophagy

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