Exploring the Influence of tGLI-1 on Temozolomide Resistance in Glioblastomas: Unraveling Novel Therapeutic Targets

Hannah von Werder [1], Haddie DeHart [2], Richard Carpenter [2]

[1] Indiana University School of Medicine; [2] Department of Biochemistry and Molecular Biology, Medical Sciences Program, Indiana University School of Medicine-Bloomington

Background/Objective:

Temozolomide (TMZ) is a standard chemotherapy treatment for patients with glioblastoma (GBM), but its effectiveness is limited, with only 50% of patients initially responding and developing resistance over time. Glioma stem cells (GSCs) have been implicated in TMZ resistance, particularly the mesenchymal subtype. The truncated form of GLI1, known as tGLI1, is highly expressed in mesenchymal GSCs and has been associated with poor patient outcomes in GBM. However, the role of tGLI1 in TMZ resistance remains unknown.

Methods:

The GBM cell line, U87MG, was utilized for this study. The IC_{50} of TMZ was determined using a cell viability assay. After successful transfection with vector, GLI1, and tGLI1, the cells were treated with the IC_{50} of TMZ to assess changes in cell viability between the groups.

Results:

The IC_{50} of TMZ is 290.1 μM, as averaged between replicate assays. Thus far, the results showed that tGLI1-expressing cells exhibited significantly higher cell viability (average: 39.09%) compared to Vector (average: 26.78%) and GLI1 (average: 27.11%). However, the tGLI1 group displayed higher variability in cell viability results, as evidenced by a larger standard deviation (0.2758) and standard error (0.1592) compared to vector (SD: 0.0325, SE: 0.0188) and GLI1 (SD: 0.1354, SE: 0.0781). The One-Way ANOVA, followed by Tukey's Multiple Comparison Test, results showed no statistically significant differences in cell viability between the groups.

Conclusion/Impact:

The increased cell viability observed in tGLI1-expressing cells suggests a potential association between tGLI1 and TMZ resistance, warranting additional research to fully comprehend its impact on GBM treatment response. Further investigation and replication studies are needed to establish the robustness of these results. This knowledge may contribute to the development of

targeted therapies aimed at inhibiting tGLI1 or its downstream signaling pathways, potentially improving the response to TMZ and patient outcomes.