TET2 Expression Correlates with IDH1 Mutation and Favorable Clinical Features in Low-Grade Glioma: Insights from a TCGA Cohort

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Background
Diffuse low-grade gliomas (LGGs) exhibit marked molecular heterogeneity, with mutations in IDH1 representing a defining alteration associated with extensive epigenetic remodeling. TET2 encodes a dioxygenase that mediates active DNA demethylation and participates in regulation of the epigenetic landscape. Despite the central role of epigenetic dysregulation in LGG, the clinical significance of TET2 expression in this tumor type remains incompletely understood.
Methods
Transcriptomic, mutational, and clinical data from the LGG cohort of The Cancer Genome Atlas were analyzed using datasets accessed through cBioPortal. Associations between TET2 mRNA expression and molecular features were assessed, and survival outcomes were evaluated using Kaplan–Meier analysis.
Results
Elevated TET2 expression was observed in LGG relative to reference normal brain datasets. Higher TET2 expression was associated with improved overall survival ($p = 0.041$) and progression-free survival ($p = 0.023$). Subgroup analysis demonstrated a survival association within astrocytomas (overall survival $p = 0.048$), whereas no significant relationship was observed among oligodendrogliomas. Notably, tumors with high TET2 expression exhibited a significantly greater prevalence of IDH1 mutation ($p = 0.005$). Genomic alterations affecting TET2 were uncommon (1.2%, 6/514) and consisted exclusively of missense variants.
Conclusions
TET2 expression is enriched in IDH1-mutant LGG and is associated with favorable clinical outcomes. These findings suggest that TET2 expression may reflect the epigenetic context of IDH1-driven gliomagenesis rather than functioning as an independent prognostic determinant. Further investigation incorporating multivariable modeling and functional studies will be required to define the mechanistic relationship between TET2 activity and the epigenetic architecture of IDH-mutant gliomas.