Prognostic Value of BIRC2 and BIRC3 Expression in TCGA-Defined Glioblastoma Variant Categories

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Introduction

Eight distinct BIRC proteins belong to the inhibitor of apoptosis protein (IAP) family. BIRC5 (survivin) is currently the subject of vaccine-based immunotherapy and small molecule inhibitor studies for treatment of glioblastoma and other cancers. Survivin and other BIRC family members play a role in the resistance of tumor cells to apoptotic signals and may be associated with chemoresistance. Recently, BIRC3 specifically has been identified as a marker for resistance of glioblastoma to therapy.

Methods

Data from The Cancer Genome Atlas (TCGA) were analyzed with respect to the expression of BIRC family proteins based on glioblastoma type, including mesenchymal, classical, neural and proneural variants. Overall survival and gene expression levels of the various BIRCs were assessed within each of the various glioblastoma variant categories.

Conclusions

High BIRC3 and BIRC2 expression are negatively associated with survival in proneural and mesenchymal glioblastoma respectively. Certain members of the IAP family may provide useful prognostic information to complement that given by the current TCGA classification scheme for glioblastoma.

Results

BIRC3 expression was higher in mesenchymal glioblastoma than in the other forms. High BIRC3 expression was associated with shorter overall survival in glioblastoma patients as a whole (p=0.02). High BIRC3 expression was distinctly associated with poor survival in patients with the proneural variant (p=0.009). No statistically significant difference in survival was seen with regard to BIRC3 expression in the classical, mesenchymal or neural variants. Glioblastoma patients with high BIRC2 expression had no significant survival difference compared to those with low expression. However, patients with the mesenchymal variant and high BIRC2 expression had significantly shorter survival than patients with low expression (p=0.001). BIRC2 and BIRC3 expression were significantly associated with one another (R=0.64) for the mesenchymal variant, but not the others.

Learning Objectives

Understand prognostic implications of high expression of IAPs in glioblastoma and as possible therapeutic targets

References

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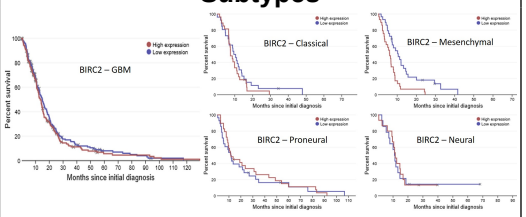
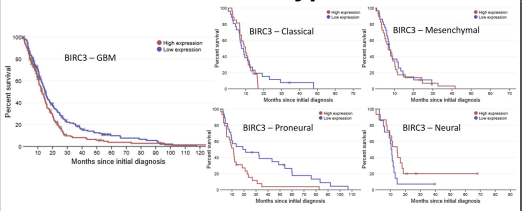
Survival and BIRC2 Expression in GBM Subtypes



High BIRC2 expression in GBM showed a significant survival disadvantage in only the Mesenchymal subtype (p=.0012). No significant difference was seen in GBM (non-categorized) p=0.552, Classical (p=0.378), Proneural (p=0.718), Neural (p=0.846).

Survival and BIRC3 Gene Expression in GBM Subtypes



High expression of BIRC3 gene in all GBM showed a significant survival disadvantage (p=.021) and specifically in Proneural subtypes (p=.00934). There was no significant survival change in Mesenchymal (P=.666), Classical (p=.593), and Neural (p=.103).