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## Cancer

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## Original Article

### Identification of survival-related genes of the phosphatidylinositol 3'-kinase signaling pathway in glioblastoma multiforme

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#### KEYWORDS

glioblastoma multiforme • expression profiling • phosphatidylinositol 3-kinase pathway • survival-related genes • molecular signature

#### ABSTRACT

#### BACKGROUND

Knowledge of the molecular mechanisms involved in the biology of glioblastoma multiforme (GBM) is essential for the identification of candidate prognostic markers, new putative therapeutic targets, and early detection strategies predictive of survival.

#### METHODS

The authors performed expression-profiling analyses in a series of primary GBMs by using complementary DNA microarrays. Validation of putative targets was performed in large series of GBMs by immunohistochemistry on tissue microarrays, real-time quantitative reverse transcription-polymerase chain reaction analysis, and Western blot analysis.

#### RESULTS

The expression signature consisted of 159 up-regulated genes and 186 down-regulated genes. Most of these genes were involved in cell adhesion, signal transduction, cell cycle, apoptosis,

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and angiogenesis. Among the genes from the molecular signature, annexin 1 (*ANXA1*) and ubiquitin-specific protease 7 (*USP7*) were evaluated in wider series of GBMs. *ANXA1* analysis carried out in different types of gliomas revealed exclusive overexpression in astrocytomas. Furthermore, survival analysis by using functional clusters of genes related with cancer and glioma biology revealed 7 genes involved in the PI3K-signaling pathway that presented a significant association with clinical outcome. Among these genes, positive expression of BCL2-associated X protein (BAX) was associated significantly with better survival in a larger series of tumors. In addition, activation of the PI3K/Akt pathway was demonstrated in this set of GBMs.

### CONCLUSIONS

The authors concluded that there is a significant role for PI3K pathway survival-related genes in patients with GBM, and putative prognostic markers associated with glioma tumorigenesis were identified. The detailed study of these candidate genes and the molecular pathways regulating PI3K activation reveal that they are promising targets for the clinical management of patients with glioma. Cancer 2008. © 2008 American Cancer Society.

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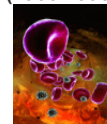
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