

Clinical Cancer Research



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Imaging, Diagnosis, Prognosis

Novel Glioblastoma Markers with Diagnostic and Prognostic Value Identified through Transcriptome Analysis

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Purpose: Current methods of classification of astrocytoma based on histopathologic methods are often subjective and less accurate. Although patients with glioblastoma have grave prognosis,

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significant variability in patient outcome is observed. Therefore, the aim of this study was to identify glioblastoma diagnostic and prognostic markers through microarray analysis.

Experimental Design: We carried out transcriptome analysis of 25 diffusely infiltrating astrocytoma samples [WHO grade II—diffuse astrocytoma, grade III—anaplastic astrocytoma, and grade IV—glioblastoma (GBM)] using cDNA microarrays containing 18,981 genes. Several of the markers identified were also validated by real-time reverse transcription quantitative PCR and immunohistochemical analysis on an independent set of tumor samples ($n = 100$). Survival analysis was carried out for two markers on another independent set of retrospective cases ($n = 51$).

Results: We identified several differentially regulated grade-specific genes. Independent validation by real-time reverse transcription quantitative PCR analysis found growth arrest and DNA-damage-inducible α (GADD45 α) and follistatin-like 1 (FSTL1) to be up-regulated in most GBMs (both primary and secondary), whereas superoxide dismutase 2 and adipocyte enhancer binding protein 1 were up-regulated in the majority of primary GBM. Further, identification of the grade-specific expression of GADD45 α and FSTL1 by immunohistochemical staining reinforced our findings. Analysis of retrospective GBM cases with known survival data revealed that cytoplasmic overexpression of GADD45 α conferred better survival while the coexpression of FSTL1 with p53 was associated with poor survival.

Conclusions: Our study reveals that GADD45 α and FSTL1 are GBM-specific whereas superoxide dismutase 2 and adipocyte enhancer binding protein 1 are primary GBM-specific diagnostic markers. Whereas GADD45 α overexpression confers a favorable prognosis, FSTL1 overexpression is a hallmark of poor prognosis in GBM patients.

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