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,
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 (GADD45α) 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 GADD45α and FSTL1 by immunohistochemical staining reinforced our findings. Analysis of retrospective GBM cases with known survival data revealed that cytoplasmic overexpression of GADD45α conferred better survival while the coexpression of FSTL1 with p53 was associated with poor survival.

**Conclusions:** Our study reveals that GADD45α and FSTL1 are GBM-specific whereas superoxide dismutase 2 and adipocyte enhancer binding protein 1 are primary GBM-specific diagnostic markers. Whereas GADD45α overexpression confers a favorable prognosis, FSTL1 overexpression is a hallmark of poor prognosis in GBM patients.