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Molecular diagnostic system for gliomas based on gene expression profiling

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Background: As the histological diagnosis of glioma is often difficult, the patients outcome will fail to match the predicted biological behavior.Therefore, it is clinically important to identify the molecular prognosis predictors for gliomas.

Purpose: Our aim was to identify prognostic gene signature forgliomas based on gene expression profiling.

Materials and Methods: We selected 3456 genes expressed in gliomas, including 3012 genes found in a gliomal expressed sequence tag collection. The expression levels of these genes in 152 gliomas (100 glioblastomas, 21 anaplastic astrocytomas, 19 diffuse astrocytomas, and 12 anaplastic oligodendrogliomas) were measured using adaptor-tagged competitive polymerase chain reaction, a high-throughput reverse transcription–polymerase chain reaction technique. We applied unsupervised and supervised principal component analyses to elucidate the prognostic molecular features of the gliomas. The prognostic gene scores(PGS) were determined by expression levels of 58 prognostic genes identified by Cox regression analysis.The prognosis predictability of the PGSwas tested in independent sample sets.

Results: The grobalgene expression data matrix was significantly correlated with the histological grades, oligo-astro histology, and prognosis. Using 110 gliomas, we identified PGS based on the expression profile of 58 genes, resulting in a scheme that reliably classified the glioblastomas into two distinct prognostic subgroups. The prognosis predictability of PGS was then tested with another 42 cases. Multivariate Cox analysis of the glioblastoma patients using other clinical prognostic factors, including age and the extent of surgical resection, indicated that the PGS was a strong and independent prognostic parameter.

The clinical utility of the PGS was demonstrated in another 55 cases of anaplastic glioma.

Conclusion: The gene expression profiling identified clinically informative prognostic molecular features in astrocytic and oligodendroglial tumors that were more reliable than the traditional histological classification scheme.