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Imaging, Diagnosis, Prognosis

Gene Expression-Based Molecular Diagnostic System for Malignant Gliomas Is Superior to Histological Diagnosis

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Purpose: Current morphology-based glioma classification methods do not adequately reflect the complex biology of gliomas, thus limiting their prognostic ability. In this study, we focused on anaplastic oligodendroglioma and glioblastoma, which typically follow distinct clinical courses. Our goal was to construct a clinically useful molecular diagnostic system based on gene expression profiling.

Experimental Design: The expression of 3,456 genes in 32 patients, 12 and 20 of whom had prognostically distinct anaplastic oligodendroglioma and glioblastoma, respectively, was measured by PCR array. Next to unsupervised methods, we did supervised analysis using a weighted voting algorithm to construct a diagnostic system discriminating anaplastic oligodendroglioma from glioblastoma. The diagnostic accuracy of this system was evaluated by leave-one-out cross-validation. The clinical utility was tested on a microarray-based data set of 50 malignant gliomas

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from a previous study.

Results: Unsupervised analysis showed divergent global gene expression patterns between the two tumor classes. A supervised binary classification model showed 100% (95% confidence interval, 89.4-100%) diagnostic accuracy by leave-one-out cross-validation using 168 diagnostic genes. Applied to a gene expression data set from a previous study, our model correlated better with outcome than histologic diagnosis, and also displayed 96.6% (28 of 29) consistency with the molecular classification scheme used for these histologically controversial gliomas in the original article. Furthermore, we observed that histologically diagnosed glioblastoma samples that shared anaplastic oligodendroglioma molecular characteristics tended to be associated with longer survival.

Conclusions: Our molecular diagnostic system showed reproducible clinical utility and prognostic ability superior to traditional histopathologic diagnosis for malignant glioma.

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