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Identification of Gene Markers Associated With Aggressive Meningioma by Filtering Across Multiple Sets of Gene Expression Arrays.

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Abstract

Meningiomas are common intracranial tumors, but relatively little is known about the genetic events responsible for their clinical diversity. Although recent genomic studies have provided clues, the genes identified often differ among publications. We used microarray expression profiling to identify genes that are differentially expressed, with at least a 4-fold change, between grade I and grade III meningiomas. We filtered this initial set of potential biomarkers through a second cohort of meningiomas and then verified the remaining genes by quantitative polymerase chain reaction followed by examination using a third microarray expression cohort. Using this approach, we identified 9 overexpressed (TPX2, RRM2, TOP2A, PI3, BIRC5, CDC2, NUSAP1, DLG7, SOX11) and 2 underexpressed (TIMP3, KCNMA1) genes in grade III versus grade I meningiomas. As a further validation step, we analyzed these genes in a fourth cohort and found that patients with grade II meningiomas with high topoisomerase 2- α protein expressions (>5% labeling index) had shorter times to death than patients with low expressions. We believe that this multistep multicohort approach provides a robust method for reducing false-positives while generating a list of reproducible candidate genes that are associated with clinically aggressive meningiomas and are suitable for analysis for their potential prognostic value.

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