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Medulloblastoma outcome is adversely associated with overexpression of EEF1D, RPL30, and RPS20 on the long arm of chromosome 8

Massimiliano De Bortoli , Robert C Castellino , Xin-Yan Lu , Jeffrey Deyo , Lisa Marie Sturla , Adekunle M Adesina , Laszlo Perlaky , Scott L Pomeroy , Ching C Lau , Tsz-Kwong Man , Pulivarthi H. Rao  and John YH Kim 

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Abstract (provisional)

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Background

Medulloblastoma is the most common malignant brain tumor of childhood. Improvements in clinical outcome require a better understanding of the genetic alterations to identify clinically significant biological factors and to stratify patients accordingly. In the present study, we applied cytogenetic characterization to guide the identification of biologically significant genes from gene expression microarray profiles of medulloblastoma.

Methods

We analyzed 71 primary medulloblastomas for chromosomal copy number aberrations (CNAs) using comparative genomic hybridization (CGH). Among 64 tumors that we previously analyzed by gene expression microarrays, 27 were included in our CGH series. We analyzed clinical outcome with respect to CNAs and microarray results. We filtered microarray data using specific CNAs to detect differentially expressed candidate genes associated with

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survival.

Results

The most frequent lesions detected in our series involved chromosome 17; loss of 16q, 10q, or 8p; and gain of 7q or 2p. Recurrent amplifications at 2p23-p24, 2q14, 7q34 or 12p13 were also observed. Gain of 8q is associated with worse overall survival ($p=0.0141$), which is not entirely attributable to MYC amplification or overexpression. By applying CGH results to gene expression analysis of medulloblastoma, we identified three 8q-mapped genes that are associated with overall survival in the larger group of 64 patients ($p < 0.05$): eukaryotic translation elongation factor 1D (EEF1D), ribosomal protein L30 (RPL30), and ribosomal protein S20 (RPS20).

Conclusions

The complementary use of CGH and expression profiles can facilitate the identification of clinically significant candidate genes involved in medulloblastoma growth. We demonstrate that gain of 8q and expression levels of three 8q-mapped candidate genes (EEF1D, RPL30, RPS20) are associated with adverse outcome in medulloblastoma.

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