Reviewer's report

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

Version: 2 Date: 20 July 2006
Reviewer: Katleen De Preter

Reviewer's report:

General

The authors have performed CGH on 72 medulloblastoma tumors. They identified several recurrent genomic alterations, among which 8q gain was associated with worse overall survival. 27 tumors were also analyses with expression arrays. These data were used in order to identify the genes that are differentially expressed in samples with vs. without 8q gain. Five of the genes that are upregulated in 8q gained samples are located on 8q. Survival analysis in 64 patients for which expression array data were available showed that 3 of the 5 genes, i.e. EEF1D, RPL30 and RPS20 were associated with survival.

The authors use a nice approach (integrating genomics and transcriptomics) in order to identify genes that might be implicated in medulloblastoma. However, most survival data are generated on small sample sizes.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) Page 11: The authors performed (or show) survival analysis on a small subset of cytogenetic changes that have been identified. Please provide also the p-values for OS and EFS log-rank test for all other cytogenetic changes, e.g. in Table 2.

2) Page 15: I don’t understand why you can not perform multivariate analysis on all CNAs in order to find the CNA with highest prognostic significance.

3) Table 4: The header of column 5 is not clear enough: mention that this is the ratio with CNA/without CNA. Do the values in column 6 represent the expression ratio of samples with versus without CNA, or not? If so: how can you explain the high value for MYC, but not significant and is the statistical comparison of 2 samples with CNA compared to 10 samples without CNA reliable? If not: what does these data tell us?

4) Page 13: Have you used a statistically based algorithm in order to identify the genes that are differentially expressed in the 2 subgroups, e.g. SAM?

5) Comment on the fact that the small expression changes that you notice for the three genes in CNA samples compared to non-CNA samples might only be due to dosage effect (more copies of the genes give slightly higher expression) and are possibly not involved in medulloblastoma oncogenesis.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

6) Page 8: Why do you compare the qRT-PCR results with the U133Plus2.0 data, and not with the HuGeneFL microarray data?

7) Page 17: Please give more explanation about the possible role of the genes with ribosomal function in cancer.

8) Table 1 will be more clear when you put significant p-values in Italics or Bold.
What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests