Reviewer’s report

Title: Association of RASSF1A and CASP8 promoter methylation in neuroblastoma

Version: 1 Date: 14 July 2006

Reviewer: Reinhard Dammann

Reviewer’s report:

General

In the manuscript “Association of RASSF1A and CASP8 promoter methylation in neuroblastoma” Lazcoz et al. have analyzed the hypermethylation of the CpG island promoters of RASSF1A, Nore1A, Blu and CASP8 in neuroblastoma. Expression of these genes was analyzed in cell lines by RT-PCR.

The manuscript does not add substantial new findings to the known literature. Hypermethylation of RASSF1A, Blu and CASP8 in neuroblastoma was reported by several papers. The correlation of RASSF1A and CASP8 methylation was already reported in 2001. The inactivation of Nore1A in neuroblastoma is interesting, however the frequency is rather low.

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

It would be interesting to include more findings on the correlation between methylation status and clinico- or histopathological data. It would be interesting to analyze the methylation of the four genes in the 21 blood controls.

The expression data of Nore1 are not convincing. What means low expression? It would be helpful to perform real-time RTPCR or to reactivate promoters by DNA methyltransferase inhibitors.

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

The conclusion that “RASSF1A methylation might be an alternative mechanism to alter the Ras signaling pathway in neuroblastoma” is clearly an over-interpretation of their data: the authors have not analyzed Ras mutations in their samples.

The writing is not acceptable. The abstract is poorly written and the number of analyzed cases is missing. The discussion is weak. The quality of written English is not suitable for publication.

Discretionary Revisions (which the author can choose to ignore)

The layout of figures could be improved. It would be helpful to label the controls in figures.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.