Reviewer’s report

Title: ADAR2 editing activity in newly diagnosed versus relapsed pediatric high-grade astrocytomas

Version: 2 Date: 9 August 2012

Reviewer: Gerrit Gielen

Reviewer’s report:

The authors describe four cases of pediatric high-grade astrocytomas and their local recurrences concerning the difference in RNA editing profiles by ADAR2 activity. They mainly want to emphasize a possible contribution of the rescue of ADAR2-mediated RNA editing in one peculiar case of a relapsing glioblastoma multiforme with a more favourable outcome of this patient in comparison to three cases without ADAR2 recovery and with bad outcome.

The manuscript is well-written, logically structured in content and data presentation is clearly arranged at the very most, but there are some issues I want to mention:

Major compulsory revisions

1. Analysis of Ki67: In which manner were the immunohistochemically analyzed Ki67 proliferation indices on the paraffin-embedded tissues evaluated shown in Table 1? Did you use any computational evaluation or manually counting the number of positive stained cell nuclei per high power-field? Or is it based on the investigator’s experience? Please comment on that. – To test the Ki67 expression levels (shown in figure 2B), also three independent RT-PCRs were performed? If not, why not? If yes, please add error bars to the graph. [Maybe it would be better to separate figure 2B into 2B (gel electrophoresis) and 2C (graph of mRNA expression levels).]

2. Because of its age at diagnosis, the child in case 4 underwent significantly different treatment with pre-surgical chemotherapy and a later onset of irradiation. The impact of these treatment differences should be discussed in reference to the more favourable outcome of this patient.

3. Figure 2A shows no evaluation of statistical significances. While it is clear for GluR-B, GluR-6, GluR-5 and Kv1.1 from figure 1, it is not shown for Gabra-3 and BLCAP. Please add p-values or the asterisks, respectively.

4. Why do you focus on transcripts that translate into brain membrane receptors and ion channels, respectively? Could you briefly comment on that? Please introduce and explain also Gabra-3 and BLCAP in the “Background” text.

Minor essential revisions

1. Typographical errors:

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1. Typographical errors:
a. Material and Methods, Patients and samples collection: lane 4:
immunohistochemistry instead of immunohystochemistry.
b. Materials and Methods, Editing analysis: lane 2: Carlsbad instead of Carlsband.
2. Abbreviation: The abbreviation RMN in table 1 should be explained in the text below.

Discretionary revisions:
1. Maybe it would be helpful to introduce the term “recoding” in the “Background” part.
2. To highlight the techniques of editing analyses a typical sequence chromatogram with nucleotides that undergo editing and thereby create a double peak could be included.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

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