Reviewer’s report

Title: Over-Representation of Specific Regions of Chromosome 22 in Cells from Human Glioma Correlate with Resistance to 1,3-bis(2-chloroethyl)-1-nitrosourea

Version: 1 Date: 11 October 2005

Reviewer: Juergen Schlegel

Reviewer’s report:

General

In their manuscript “Over-Representation of Specific Regions of Chromosome 22 in Cells from Human Glioma Correlate with Resistance to BCNU“ Hank and her co-authors used cell lines derived from 3 primary malignant gliomas and the corresponding recurrent tumors. Cells were selected in vitro for resistance against BCNU, a nitrosourea compound in clinical use. The authors demonstrate an association between over-representation of a region of chromosome 22 and the development of BCNU-resistance.

Although the number of cell lines (3 primary and their recurrent tumors) is rather low the manuscript offers interesting new details about the genetic background of acquired therapy resistance in human malignant gliomas. Now, some more work is necessary to confirm these interesting results. The overrepresentation of the chromosome 22 region in BCNU resistant gliomas should be confirmed in an unrelated collection of glial brain tumor samples. The identification of the gene(s) and/or the underlying molecular mechanisms involved in this process could add important novel insight into general chemoresistance in oncology.

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

No

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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)

1. Methods, Page 6, line 3: Were the treatment experiments performed in the presence or absence of FCS?
2. Methods, Page 6, line 4: Were increasing concentration of BCNU used 1 hour each or on subsequent days?
3. Methods, Page 6, line 8: How did the authors evidence the absence of cell death?
4. Methods, Page 6, line 10/11: It is necessary to get a measure of the level of resistance present in the primary tumors and the recurrent tumors. Therefore, the authors should present the data, e.g. time required to select for a resistant cell population, levels of intrinsic resistance.
5. Methods, Page 6, line 11: The authors mention that the cells were re-treated every 8-10 passages. They should also mention the passage numbers in which the experiments were performed.
6. Tab. 1/Tab. 2: The cell lines LX/LXR show different diagnoses between the primary and the recurrent tumor. They also show marked differences in the karyotype of the tumor samples. The authors should comment these differences. Have the diagnoses been made by different pathologists?
7. Fig. 4B: The shift to higher signal numbers of BAC clones C and D is not very convincing, is it
1. Tab. 1: Primary glioblastomas typically occur in older persons, the patients of the present study are rather young. It has been shown, that primary and secondary GBM show different genetic alterations, e.g. alterations of the EGFR and the TP53 genes. Did the authors check for these alterations? The authors should discuss the young age of the patients.
2. Tab. 1: The treatment of the tumors was irradiation and BCNU. The authors should discuss possible effects of the radiotherapy on the development of therapy resistance in the tumor samples.
3. Fig. 5: The distribution of signal numbers of different BAC clones is not instructive. A graphical distribution in comparison to the regional distribution on a chromosomal ideogram would enhance the expressiveness of the Figure.

What next?: Accept after minor essential revisions

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No

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