Reviewer’s report

Title: HNPCC versus sporadic microsatellite-unstable colon cancers follow different routes toward loss of HLA class I expression

Version: 1 Date: 6 November 2006

Reviewer: Carmen M Cabrera

Reviewer’s report:

General

In the present report Dierseen et al. studied the molecular mechanisms responsible of the HLA class I loss in colorectal tumors. It is an interesting study in which the authors showed that the colorectal tumors with MSI present two different mechanisms implicated in the HLA class I loss: alterations in the APM components in the sporadic RST, and loss of b2-m in HNPCC tumors.

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

In primary tumors few mutations in the APM components have been described. Therefore, the analysis of the type and number of the mutations that the authors have found is very important. However, in the tables showed in the paper the exact location of the frameshift mutations in the exons is not indicated. The authors must specify the mutations found.

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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)

- The b2-microglobulin protein is a structural component of the HLA class I complex, and not a chaperone; however the b2-m has a role like a “chaperone” in the folding of the HLA class I molecules in the endoplasmic reticulum. The authors should correct the use of the term “chaperone” in the text.

Methods:
- The section “flow cytometric sorting” is barely explained.
- Indicate the abbreviation of LOH (loss of heterozygosity) in the section “LOH and fragment analyses”.
- Indicate in a Table the primers used for the detection of the frameshift mutations in the HLA-A, HLA-B, b2-m, LMP2, LMP7, LMP10, TAP1, TAP2, Calnexin, Calreticulin, ERp57, and Tapasin genes.

Results:
- Table 2, and Table 3a; explain the abbreviations MMR- and MMR+ or exchange by MSI- and MSI+ respectively.
- Table 3a, page 29; correct the term “heterozygousity”.
- Table 2 and Table 3a, indicate in the footnotes the abbreviations of: tpsn, calnx, and crtcln.
- Figures 1 and 2 are not cited in the text.
- Legend of Figure 2: the colour of the normal samples is blue, and green (not blue) for the tumor samples.

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Discretionary Revisions (which the author can choose to ignore)

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 importance in its field
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.