Reviewer's report

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

Version: 1 Date: 14 November 2006
Reviewer: Elke Holinski-Feder

Reviewer's report:

General
The paper of Jan Willem F. Dierssen deals with the interesting aspect of HLA expression on MSI-H colorectal cancer cells. It bears interesting aspects of tumor formation, the data provided here are essential for microdissection of different tumor pathways.

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

However there is one major concern:
The authors have analysed three different tumor cohorts:
1. MSI-H HNPCC patients
2. right sided MSI-H
3. right sided MSS
This discrimination of tumor cohorts is not clearly visible in the manuscript.

There are three cohorts in the abstract
There are two arrays in the methods section. There is no discrimination in numbers for the sporadic right sided ones concerning MSI-status. Just reading the text, they are all MSI-H, which was confirmed by methylation analysis. What is needed here:

- Confirmation of the HNPCC cohort. Are all tumors caused by germline mutations or is there just a positive family history with an MSI-H tumor. For a study like this, I would ask for proven pathogenic germline mutations.
- The RST-cohort includes two sub-cohorts: Patients with MSI-H tumors and patients with MSS tumors. Have all MSI-H tumors been analysed for hypermethylation of the MLH1 promoter? Did they all have a loss of MLH1 expression? These facts should be stated in the methods section. One can find out in table 1 that the RST-cohort includes 48 MSS tumors and 33 MSI-H tumors, this is not stated in the methods or results section. This missing information abolishes a clear structure of the papers and therefore needs to be added prior to a further review process.

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 nomenclature in the tables should be used uniformly: always MSI-H and not MMR-

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