Reviewer's report

Title: Low Frequency of Defective Mismatch Repair in a Population-based Series of Upper Urothelial Carcinoma

Version: 1 Date: 14 December 2004

Reviewer: heikki J jarvinen

Reviewer's report:

General A registry based study of 216 cases with upper urothelial cancer with the aim to explore the frequency of underlying DNA mismatch repair gene defects pointing to hereditary nonpolyposis colorectal cancer syndrome. The authors analysed MSI and MMR proteins by immunohistochemistry from the tumour samples. MSI-high phenotype was identified in 4% of cases and loss of MMR protein expression in 5%.

The finding is important and interesting indicating that a portion of urothelial cancer cases should be examined for possible familial cancer susceptibility.

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

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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)

There are some minor linguistic mistakes needing correction (e.g. p. 12, 2nd paragraph, 2nd line: too (instead of to))

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Discretionary Revisions (which the author can choose to ignore)

There was no attempt to identify the MMR gene mutations because the study was retrospective and registry-based. However, since the authors have now identified several families with probable HNPCC susceptibility, it would be interesting to know whether mutation search has been planned on the basis of these results. Furthermore, the discussion could perhaps include a phrase or two about the possibilities for cancer prevention following the verification of the HNPCC diagnosis in a family (such as predictive genetic testing and preventive surveillance of the colon and possibly even other tumour sites).

What next?: Accept after discretionary 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.