

Reviewer's report

Title: The association between genetic variants in hMLH1 and hMSH2 and the development of sporadic colorectal cancer in the Danish population

Version: 2 Date: 21 January 2008

Reviewer: Nils Rahner

Reviewer's report:

Christensen et al. report on the allele frequencies of 29 variants in MLH1 and MSH2 in the Danish population and additional 6 variants in other Caucasian populations to reveal whether they are associated with sporadic CRC or whether they are private variants/mutations found only in HNPCC suspected families.

The study design, the genotyping experiences and statistical analyses are well performed. The results of the study are of interest since the frequencies of a large number of variants in MLH1 and MSH2 and their association with sporadic CRC in large Caucasian populations are rare findings in the current literature. A good knowledge of single variants/mutations on well characterized families is important and of clinical and scientific relevance.

Major Compulsory Revisions:

1. The authors state that they searched for mutations in MLH1 and MSH2 in "patients suspected to have HNPCC". There is no further information in the manuscript which criteria they have used and on whether the patient's tumour tissues have been analyzed for microsatellite stability as well as expression of the MMR proteins by immunohistochemistry. To assess the functional relevance of a germline variant/mutation in MLH1 and MSH2 these are essential information that needs to be provided.

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, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.