Reviewer’s report

Title: MSH6 and PMS2 Mutation Positive Australian Lynch Syndrome Families: Novel Mutations, Cancer Incidence and Age of Diagnosis of Colorectal Cancer

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Reviewer: anja wagner

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It is nice to read about the experience with MSH6 en PMS2 in Australia. However

Major Compulsory revisions:
I major drawback of this paper is in my opinion the lack of statistical analysis. With 29 MSH6 families it should be possible to give cumulative life time risks at least for colorectal cancer and endometrial cancer. This really limits the value of the observations and makes them impossible to compare to other studies. Since PMS2 mutations are found in only 7 families the additional value of these data are limited and might in my opinion better be presented as an separate kind of case report with pedigrees of the families.

Abstract: 3th sentence only MSH6 may have same risks as MLH1 and MSH2, risk PMS2 is probably lower as also mentions in introduction

The conclusions can not be drawn on this data
Discussion: It is stated that in half of the LS families a mutation is found. Is this based on half of the Amsterdam criteria positive families having a MLH1 or MSH2 mutation? I think Lynch syndrome is redefined as families with a MMR defect and in the majority of these families a mutation is found in one of the known genes. I do not agree that there will probably be more Lynch genes. More likely in my opinion are other kind of "mutations" like TACSTD1.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.