Reviewer's report

Title: The genetic basis of colonic adenomatous polyposis syndromes

Version: 0 Date: 06 Jun 2016

Reviewer: Desiree DuSart

Reviewer's report:

A review of the current understanding of the genetics of FAP is essential to inform changes to clinical services; this manuscript is therefore important to facilitate this process. However, the review needs to be comprehensive and clearly written. Routine genetic testing for FAP currently involves the APC and MYH genes only. The new genes reported to be associated with FAP is still regarded as research and not part of clinical practice. A comprehensive review, presenting all the data from gene panel testing publications to support the clinical sub-typing of classical FAP and the genes associated with these phenotypes is required to present the evidence to support the change. This would also include presentation of frequencies or percentages of patients identified.

The discussion about the different ways the APC gene is associated with FAP pathogenesis is confusing. The author has omitted key words like mosaicim or germline when discussing the impact of greater sequencing depth generated by new technologies. A flow-chart presentation or diagram of this information may be a clearer way to present this.

To present the case for modifier genes or alleles, discussion of key publications presenting evidence of an example or examples of modifiers rather than making general statements would better support that the search for modifier genes/alleles should continue.

In summary, this review needs to present more detailed information and less summary statements to provide evidence to change clinical practice.

Level of interest
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An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited
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