Reviewer's report

Title: Rare mutations predisposing to Familial Adenomatous Polyposis in Greek FAP patients.

Version: 1 Date: 1 March 2005

Reviewer: Mef Nilbert

Reviewer's report:

General
This report provides data on 7 mutations in the APC gene from 10 Greek FAP patients. Novel, disease-causing mutations are of clinical value, and should be presented in order to summarize the entire mutation spectrum and to recognize previously identified mutations. Although it is generally debatable whether this needs to be done in the form of an entire research article, the present manuscript specifically adds data on a large intragenic deletion within the APC gene and presents a splice donor mutation resulting in inefficient exon skipping. It thereby emphasizes the need to perform mutation testing with methods that allow detection of large alterations in FAP patients and demonstrates a novel mechanism for the development of attenuated FAP. At the end of the manuscript the authors provide their algorithm for mutation screening in FAP.
The article is well written, the methods used are reliable, and the figures are informative and accurate.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The manuscript lacks details on ethical review or informed consent.

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 estimate that one third of the mutations are caused by large rearrangements is high regarding hMLH1 (an indeed the reference provided refers to BRCA1 and hMSH2). The authors could omit hMLH1 or include “up to one third”.

Discretionary Revisions (which the author can choose to ignore)
The pedigree in figure 2 does not add much data (could be described in the text), but could be kept if the authors wish to do so.

What next?: Accept after minor essential 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