Reviewer’s report

Title: Implementation of massive sequencing in the genetic diagnosis of hereditary cancer syndromes: diagnostic performance in the Hereditary Cancer Programme of the Valencia Community (FamCan-NGS)

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Reviewer: Evgeny Imyanitov

Reviewer's report:

This study is interesting, although it provides somewhat expected results: of course, NGS-based multigene testing is likely to reveal some germ-line mutations in patients, who qualify clinical criteria of hereditary cancer but were tested negative by a single-gene approach. However, the presented numbers are interesting and important.

Discordance between single-gene testing and NGS, which was observed in selected patients, needs to be clarified in great detail. In fact, I suggest to retrieve DNA samples, which were tested false-negative by conventional methods, check the laboratory procedures, and perform HRM analysis. It is critical to recognize, whether this discordance is caused by a human error, or, alternatively, by the failure of pre-screening methods to visualize the mutation.

Monoallelic mutations in MUTYH should not be considered in the overall statistics as they are unlikely to cause hereditary cancer syndrome in the tested individuals.

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Quality of written English
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