Reviewer’s report

Title: Development and Validation of Next Generation Sequencing-Based 35-Gene Hereditary Cancer Panel

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Reviewer: Magdalena Ratajska

Reviewer's report:

The authors describe the study where they developed and validated a targeted NGS-based test for hereditary cancer risk. The test allowed for the simultaneous analysis of 35 genes that when mutated predispose to several hereditary cancers, including breast, ovarian, prostate, uterine, colorectal, pancreatic, stomach and melanoma. The manuscript is nicely written with a detail description of the validation process.

Nevertheless, on the market, there are several commercially available NGS-panels covering selected genes; therefore, in my opinion, the article lacks some novelty. On the other hand, it has to be noted that the presented assay was able to detect more challenging variants, including Complex Indel Variant and larger insertions. My only concern toward the manuscript is authors last comment. I can not agree with the statement that "all the known cancer pathogenic variants are within the coding or splicing regions", as more and more often it is suggested that mutations in specific regulatory sequences might play a role in cancer predisposition, development, progression and prognosis. Besides, it is generally accepted that large genomic rearrangements (LRG) might be responsible for some fraction of hereditary cancers; therefore, it would be useful to include LRG analysis in the presented panel and discuss this aspect further in the submitted manuscript.

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