Reviewer’s report

Title: Detection of Large Rearrangements in a Hereditary Pan-Cancer Panel using Next-Generation Sequencing

Version: 0 Date: 25 Jan 2019

Reviewer: Valeria D'Argenio

Reviewer's report:

The manuscript by Mancini-Di Nardo et al., covers an important and actual issue. The possibility to have a unique diagnostic procedure able to simultaneously detect in a set of target genes both point variants and large genomic rearrangements is a challenge in diagnostic setting. However, some issues should be addressed and clarified:

- Please specify the number of patients totally analyzed during the 3.5 years of study-observation time
- The patients carrying LRs were all negative for point mutations? Please specify
- The bioinformatic pipelines used for LRs detection from NGS data has to be described under methods
- All the LRs detected were confirmed? This is not clear and should be specified in order to evaluate the sensitivity of the proposed method
- The pathogenic LRs detected have been evaluated in a clinical context? No data are reported regarding patients familial and personal history

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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

Needs some language corrections before being published

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