Author’s response to reviews

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

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Author’s response to reviews:

11 September, 2019

Dr. Arwa Tawfiq
Editor, BMC Medical Genomics
BioMed Central
The Campus, 4 Crinan Street
London N1 9XW
Dear Dr. Tawfiq,

Thank you for editorial review of our manuscript, entitled “Detection of Large Rearrangements in a Hereditary Pan-Cancer Panel using Next-Generation Sequencing,” submitted for consideration as a research article in BMC Medical Genomics. We were pleased to receive your message stating that the manuscript is potentially acceptable for publication in BMC Medical Genomics, with the essential revisions you listed. We have made those revisions and provide a point-by-point response here.

We look forward to hearing from you soon.

Sincerely,

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Editor Comments:

1. Ethics approval

Please note that ethics approval should:
- Be Independent from the investigators or sponsors
- Be Local - From the same institute, region or country in which the study took place
- Cover all countries – for studies performed in multiple countries, appropriate ethical committee approval must be included for each country.

We require a clear, unambiguous statement of ethics committee approval:

- Specific project approval, not simply general guideline adherence
- The full name and affiliation of each ethics committee
- Not simply “the local IRB approved the study”
- Reference numbers if applicable

Please confirm whether your study was submitted to and approved by a local ethics committee and include a statement to this effect in the ‘Ethics approval and consent to participate’ section of your declarations. Please also ensure that the full name of the ethics committee is included in this statement.

If the need for ethics approval was waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this, including the name of the IRB or a reference to the relevant legislation.

Response: We have added the following statement to the “Ethics approval and consent to participate” section under the Declarations heading on page 16: “The analysis described in this manuscript was performed using de-identified data obtained during the course of routine healthcare operations. Only aggregate data are presented in the manuscript. Therefore, this analysis did not meet the U.S. Health and Human Services definition of research on human subjects (HHS 46.102) and did not require Institutional Review Board approval.”

2. Form of consent to participate
While you have stated that “All individuals provided consent for clinical testing” in the Methods section of your manuscript this is insufficient.

In the section 'Ethics Approval and Consent to Participate', please state whether the informed consent that obtained was written or verbal.

If consent was verbal, please state the reason and whether the ethics committee approved this procedure. If the need for consent was waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this, including the name of the IRB or a reference to the relevant legislation.

Response: We have clarified that patients provided written informed consent for clinical testing, both in the “Ethics approval and consent to participate” statement and in the Methods section. Regarding IRB approval, please see the response to Comment 1. We have added the necessary statement to the “Ethics approval and consent to participate” section under the Declarations heading on page 16.

3. Role of funding body

Please provide more details regarding the specific role of the funding body in your study. If the funding body only provided the financial means to allow the authors to carry out the study, please state “The funding body played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript” and include this statement in the Funding section of your manuscript.

However, if the funding body took part in the design of the study and collection, analysis, and interpretation of data, and the writing of the manuscript, this must be stated in the Competing Interests section of your manuscript.

Response: We have added the following statement to the “Competing interests” section under the Declarations heading on page 17: “Myriad Genetic Laboratories, Inc. oversaw the design of the study, the collection, analysis, and interpretation of data, and the writing of the manuscript.”

4. Availability of data and materials
While we respect and admire the authors’ wishes to protect patient confidentiality, we also strongly encourage the sharing of data. Please consider whether you would be willing to make a de-identified dataset available to future inquiring researchers. If you would agree to this, please update your Availability of data and materials statement to read as: “The datasets used and/or analysed during the current study are de-identified and available from the corresponding author on reasonable request.”

Response: All data used for this analysis were collected in the course of clinical testing. In order to comply with patient privacy regulations, the manuscript presents only aggregate data. Raw data contains potentially identifiable, patient-level information that is not appropriate to make available publicly.

5. Remove attachments

Please remove the additional files entitled ‘diNardo Editor Response 2019-07-30’ and ‘DiNardo revised REDLINE 2019-05-28’ from your manuscript and from the file inventory.

Response: We have removed these two files from the inventory.

6. Authors’ contributions

Please clarify whether all of the authors of this manuscript have read and approved the final manuscript in the Authors’ contributions section of your manuscript. If so, please include the statement “All authors read and approved the final manuscript.” in the Authors’ contributions section of your manuscript.

Response: We have added the following statement to the “Authors’ contributions” section under the Declarations heading on page 17: “All authors read and approved the final manuscript.”

7. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Should you wish to
respond to these revision requests, please put your responses to the reviewers'/editors’ comments in the Response to Reviewers box in Editorial Manager. Please do not upload a separate letter.

Will do.

Response: We have uploaded the final, clean version as instructed.