Reviewer's report

Title: Systematic characterization of germline variants from the DiscovEHR study Endometrial Carcinoma population

Version: 1 Date: 05 Mar 2019

Reviewer: Mari Kylleso Halle

Reviewer's report:

General comments:

The authors have made a clear, appropriate and comprehensive response to the review and the suggested changes have been incorporated appropriately into the manuscript. However, the text, and especially the results part, should be revised once more in order to detect typos and to clarify.

I appreciate that you have incorporated a more detailed description of the several patient/non-patient cohorts, although preferably percentages and p-values should be included instead of just patient numbers (Supplementary Table S1, S2). The differences in BMI between the cohorts are described in the results. Still, the potential bias that obesity may introduce is not evaluated. As far as I can see, the detected germ line variants in the DiscovEHR EMCA cohort could just as likely be associated with obesity. In my opinion, this should be mentioned in the discussion.

Minor comments:

1. Page 9, Line 18: Please rephrase the sentence: The OHRM cohort has an obese BMI which is consistent with the association between obesity and cancer'. My suggestion: 'The average BMI of the OHRM cohort is XX, which is classified as obese and consistent with the association between obesity and cancer.'

2. Page 9, Line 24 'similar distributions grade two samples'. There appears to be a typo here. To clarify, I suggest the following change: 'similar distributions of grade 2 samples'.

3. Page 9, Line 33: the sentence seems to be incomplete. Consider adding 'are performed': 'Downstream analysis of all grades and stages are performed together unless otherwise noted'.

4. Page 11, Line53: Please remove 'the'; it appears to be a typo.

5. Page 16, Line29: Please remove 'this work'; it is written twice and appears to be a typo.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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

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I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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