Reviewer's report

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

Version: 0 Date: 12 Nov 2018

Reviewer: Andrzej Semczuk

Reviewer's report:

In their manuscript, the authors performed a statistical analysis of patients with EC searching for the potentially pathogenic germline variants. In total, "nine genes were identified as having the potential to distinguish EC participants from non-cancer controls".

Similar data were also presented in the TCGA. Finally, the authors stated that "only four genes had variants unique to the EMCA cohort",

although "larger sample sizes or alternative approaches will be needed to capture statistically significant associations"

Limited corrections:

1. Type 2 EC are treated by different methods, including also radiotherapy in selected cases.
2. In my opinion, the methodology should be described in the main text not as a supplementary material.
3. Most of the cases were early-staged tumors, are the same variants present in advanced-stage ECs?
4. Please check the main text, especially results, trying no to repeat the informations, for example page 6.
5. From Table S1, leiomyosarcoma is not endometrial cancer, please verify data!!!!!
6. From Table S1, surgery as a treatment - all patients were operated on or not /36 were staged 3 or 4/?
7. Did the patients with family history different in variants from others?
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

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.

I recommend additional statistical review

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

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interest.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.