Reviewer’s report

Title: Monoallelic Characteristic-Bearing Heterozygous L1053X in BRCA2 Gene among Sudanese women with Breast Cancer

Version: 0 Date: 13 Sep 2016

Reviewer: Valeria D'Argenio

Reviewer's report:

The paper entitled "Novel Stop Codon in BRCA2 Gene in Four Sudanese patients with Breast Cancer" by Alsmawal A. Elimam et al., describes the detection of a novel variant in the BRCA2 gene resulting in a premature stop codon. Even if this result is interesting and is possible to suppose its pathogenic effect, the data shown are too preliminary to strongly assess it and the manuscript is not acceptable in its current form.

In detail, most pathogenic BRCA2 mutations are nonsense variants resulting in a premature stop codon, however, for some of these, the significance in determining an increase of cancer risk is still debate, as for the K3326X cited in the discussion. Therefore, functional assays should be carried out to verify the effects at protein level and adequately discussed.

Discussion is focused on a review of other nonsense variants and lack of comments concerning the main results. The variant should be discussed in the context of patients' personal history of cancer (BC or other cancers) and of their family history. Family members of the variants carriers should be tested to assess the variant segregation within the families. Also limitations and concerns regarding the analytical strategy should be addressed. The authors analyze just one exon of one of BRCA gene; this cannot be considered exhaustive or enough in terms of diagnostic sensitivity, especially when next generation sequencing-based methods are available and currently used to evaluate BRCA status.

The number of patients analyzed is too small. In addition, it will be useful to analyze a large set of control subjects to define the allelic frequency of the variant in the general population. Criteria to define the control group should be clearly described.

In methods section, the features of the patients enrolled in the study should be detailed. Maybe a table could be useful.

English requires some language corrections.

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.

No

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

No

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

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 interests
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.