Reviewer’s report

Title: Novel BRCA2 pathogenic variant c.5219T>G p.(Leu1740Ter) in a consanguineous Senegalese family with hereditary breast cancer

Version: 1 Date: 13 Mar 2019

Reviewer: Sara Gutiérrez-Enríquez

Reviewer's report:

Minor essential editions:

ABSTRACT

-LINES 41-42: Please change the sentence "Pathogenic variants associated with hereditary breast cancer have been reported for BRCA1/2 in patients from multiple ethnicities"

For

"Pathogenic variants associated with hereditary breast cancer have been reported for BRCA1 and BRCA2 (BRCA1/2) genes in patients from multiple ethnicities"

METHODS

BRCA1 and BRCA2 screening

-LINES 102-103: Please change the sentence "In the proband BRCA1 and BRCA2 exons were amplified……"

For

"In the proband from the consanguineous family as well as in the remaining 14 index cases with familial breast cancer, BRCA1 and BRCA2 exons were amplified…."

-LINE 107: the numbers of supplementary tables are incorrect. Their right numbers are supplementary tables 1 and 2

-LINE 114: Please clarify who are the control populations. Suggestion: "For the control populations (healthy and sporadic breast cancer groups) and healthy relatives of the proband……"

-LINE 124: Please clarify who are the control populations. Suggestion: "but not in any participant from the two control groups (healthy and sporadic breast cancer groups)."
-LINES 130-131: Please change the sentence "Any pathogenic variant was detected for the remaining 8 families (data not reported)".

For

"No pathogenic variant was detected for the remaining 8 families (data not shown).

DISCUSSION

-LINES 142-143: Please change the sentence "All these characteristics have been described in the studied index case."

For

"The phenotype of the breast cancer diagnosed in the studied index case matched with this epidemiology".

-LINES 156-159: Please change the sentence "Any pathogenic variant at this position has not yet been reported in SSA populations. Meanwhile other pathogenic variants surrounding this position of the BRCA2 gene have been reported in the ClinVar database."

For

"Although other pathogenic variants surrounding this position of the BRCA2 gene have been reported in the ClinVar database, no pathogenic variant at this position has been yet reported in SSA populations (Table 3)."

-LINEs 159-160: Delete the sentence "These pathogenic variants lead to stop codons or frameshift at amino acid 1740 or 1741 of BRCA2 protein (Table 3)." It is redundant.

-LINES 190-192: Please change the sentence "In this family it is unclear whether there was family member with Fanconi anemia like symptoms or early death, or not. Meanwhile it has been reported that Fanconi Anemia (FA) is caused by biallelic FANC1/BRCA2 pathogenic variants [51]."

For

"It has been reported that Fanconi Anemia (FA) is caused by biallelic FANCD1/BRCA2 pathogenic variants [51]. In this family it is unclear whether there was family member with Fanconi anemia like symptoms or early death, or not."

Moreover, please notice that the alias name for denoting BRCA2 gene as Fanconi Anemia gene is FANCD1
CONCLUSIONS

-LINE 196: Please change the word "new" for the word "novel".

-LINE 198: Please delete "between and 198 within populations". They are unneeded in the conclusions

-LINES 199-200: The sentence "BRCA1/2 genetic testing should then be implemented in each country as a mean of prevention for women at risk" needs to be reworded.

Suggestion: The benefits of clinical genetic testing of BRCA1/2 in prevention and personalised treatment is unquestionable and it should be implemented adapted to each population's intrinsic genetic characteristics.

ADDITIONAL FILE

-LINES 404-405: The numbers of supplementary tables are wrong. Their correct numbers are supplementary tables 1 and 2. Please revise them along all manuscript.

-SUPPLEMENTARY MATERIAL: NDIAYE R BRCA2 SUPPLEMENTARY MATERIAL.DOC

The numbers of supplementary tables are wrong. Their correct numbers are supplementary tables 1 and 2. Please revise them along all manuscript.

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.

Not relevant to this manuscript

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