Reviewer's report

Title: R337H prevalence in Brazilian hereditary breast cancer

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Reviewer: Edenir Palmero

Reviewer's report:

Major Compulsory Revisions:

- The quality of the written English should be extensively reviewed.

-The title of the manuscript is not appropriate for the work/results presented. A work that studies only 28 families can’t be titled "R337H prevalence in Brazilian hereditary breast cancer." The sample used does not allow such extrapolation.

- In the abstract the authors state that the TP53 R337H mutation is more common in Brazil than in other places. However, in the introduction the authors do not return to mention this fact, thus not justifying the reason for the study of this particular mutation. I suggest briefly detail the history of this mutation in Brazil.

- First paragraph, 5th line: “Two hereditary syndromes are related (…)” should be replaced by “Two hereditary cancer predisposition syndromes (…)”.

- In the second paragraph of the introduction the authors mention that the Li-Fraumeni syndrome is characterized by a broad spectrum of tumors, which is not correct. The classical syndrome as described by Li and Fraumeni has very strict criteria, a small spectrum of tumors (such sarcomas, which were not mentioned by the authors) and a cumulative risk up to 90% for the development of cancer. It is the Li Fraumeni like syndrome that is characterized by a broad tumor spectrum.

- In the last paragraph of the Introduction, the authors mention that they “conducted the study to compare R337H prevalence in healthy controls and breast cancer women from southeast Brazil (Sao Paulo State) that (…) to investigate the surrogate association of R337H and breast cancer in southern region.” To investigate the association between this specific mutation and breast cancer in southern region, authors should study women from this specific region and not from the southeast region. With the small sample group from this study, the authors may conclude about the prevalence of the R337H mutation on women from Ribeirão Preto, São Paulo, located in the Southeast region (and not the prevalence nor the association with breast cancer in the southern region).

- In the last paragraph of the Introduction, 2nd line “(…) and breast cancer women (…)” should be replaced by “(…) and “breast cancer affected women (…)”.

- It is not mentioned in the Methods or results section the status of BRCA1/BRCA2 on these 28 samples. As they fulfill criteria for HBOC, where they previously tested for germline BRCA1/BRCA2 mutations? If yes, which is the status?

- In the Results section, the authors mention that both mutated families do not fulfill Li Fraumeni criteria, according to the NCCN guidelines (v.1.2011). However, authors should use the updated 2013 NCCN criteria, where it is stated that “Individual with breast cancer before or at 35 years of age and BRCA1/BRCA2 negative testing fulfills Li Fraumeni testing criteria”.

- The last paragraph of the Results section should be criteriously reviewed. There are sentences that do not make sense. Example 1: “There was a significant association between R337H mutation presence and breast cancer group.” Example 2: the authors compare the p value obtained in the present study with percentages obtained by other researchers (p=0.001 and 0.003 in comparison to 0.2% and 0.3%, respectively; one-sided exact binomial test).

- Discussion section – first paragraph: The authors compared their results with previous work published by Achatz et al and Assumpcao et al. However the work published by Achatz and collaborators is based on Li Fraumeni/Li Fraumeni like families with other tumors than breast. The comparison between both studies should be done with caution, as they work with different inclusion criteria.

- When the authors mention the LOH published by Achatz et al to justify a role for this mutation on breast cancer development, the authors should have caution, because this aspect of the R337H mutation is currently under debate. In the paper published by Assumpcao and collaborators, 3 breast tumors were analyzed and, founding deletion of the R337H allele in all of them.

- The authors did not mention the weaknesses of the study.

- It was not clear why the authors state, in the last paragraph of the Discussion section and also on abstract and conclusion sections, the presence of other cancer types: “R337H mutation screening should be done in Brazilian women diagnosed with breast cancer at any age, if they have a family history including other cancer types and (...)). It is not clear whether the authors also tested individuals with other tumors than breast cancer. If not, they cannot conclude that the other tumors are related to the R337H mutation.

Discretionary Revisions:

- In the same way the authors did for NCCN criteria for HBOC syndrome, it would be interesting if the authors could include a third table with the NCCN criteria for Li-Fraumeni Syndrome.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.