Author's response to reviews

Title: A novel BRCA-1 mutation in Arab kindred from east Jerusalem with breast and ovarian cancer

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To the Editor,

We attach the revised manuscript entitled: "A novel BRCA-1 mutation in Arab kindred from east Jerusalem with breast and ovarian cancer" according to the reviewers comments.

We thank the reviewers for the important comment and relate to them point by point.

Reviewer: Orland Diez

The BRCA2 was screened by 40 fragments. The wrong number in the paper of 27, was corrected.

We added a sentence to the discussion which relates to the history of male BC in the family and a relevant reference. ("A history of male BC, which was recorded in the family, is a typical feature of BRCA2, although BRCA1 carrier status was associated with male BC as well (ref 12)")

We referenced the previous reported mutations in Arab patients (no. 8), we now added a citation which was missing in the text.

Reviewer: Fernando Schmitt

1. We agree with the number suggested by the reviewer of the frequency of mutation carriers among breast cancer cases and a more recent publication was added. (Peto et al, J Natl Cancer Inst, 1999)
2. The study included 31 individual as stated in the paper, we corrected the number in the background.
3. We chose those with the highest probability for carrying a mutation. Indeed, another woman with OC and a history of breast in the family is also a candidate for BRCA mutation analyses. Among the 12 patients diagnosed with BC below age 40, 3 women, with the most suggestive combination of age at onset and a
family history of BC were chosen for screening. Additional 2 women of that age group had a family history of BC in one second degree family members. A third individual had 2 cases of BC in the family and is also an important candidate for full screening of BRCA1/2 genes. Therefore in the study population additional 2 women would be of high priority for screening. We revised the paragraph of "study population" trying to emphasize the fact that other women are probable BRCA1/2 carriers. After finding the E1373X mutation we decided to first assess the role of that particular mutation in the Palestinian population. We intend to continue this project by ascertaining more individuals and provide genetic analyses for them.

4. All E1373X mutation analyses included positive and negative controls confirmed by sequencing. We added a picture of the gel of PCR products to better clarify the methods.

5. Analyzing 30 affected individual for the E1373X mutation does not completely rule out a founder mutation, however if it would have been found in a larger affected population the role of it in the population would be low. Still, we did relate to the fact that other private mutations, and in lower probability a founder mutation may be found in a larger study. As we mentioned before, this is an on going project into gene-environment interactions in the Palestinian population and we hope to continue for the benefit of preventive screening and treatment in that population.

The references were corrected according to BMC Cancer format.

Regards,

Luna Kadouri