Reviewer's report

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

Version: 1 Date: 8 November 2006

Reviewer: Fernando Schmitt

Reviewer's report:

Inherited predisposition to breast and ovarian cancer due to mutations in the BRCA genes has been thoroughly described in the medical literature over the last years, being population based studies of major importance in determining the types of screening to be conducted for mutation detection for that purpose this article is biologically and medically relevant.

However in the opinion of this reviewer there are several issues that need further refinement by the authors.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1- The authors state that “only 10-15% of newly diagnosed BC patients are attributable to high penetrance breast cancer predisposing genes” (background, paragraph 3 line 3) however the reference used is from a 1993 JAMA publication. Since then several publications appeared stating that inherited cases correspond only to 5-10% of all breast cancers. My suggestion is that the authors quote a more recent publication.

2- The authors also state in the background (paragraph 4 line 1) that the present study was conducted on a population of 26 PA women, however in the course of the paper the authors referred to not 26 but 31 patients (abstract line 7, materials and methods in the study population, just has an example).

3- I’m puzzled has to why the authors only conducted the mutational analysis in 4 patients since from what I got from the study population the authors had 12 patients diagnosed with breast cancer under the age of 40 and also 8 that had an associated family history of breast cancer (I didn’t get if these 8 patients were from the 12 patients group with breast cancer diagnosed under the age of 40); also there were 3 ovarian cancer patients (I believe it would also be important to state the ages of these patients), 2 of which had also an associated breast cancer history. Since the probability of getting a mutation carrier in an ovarian cancer patient is much higher than in a breast cancer patient I believe that these patients (all three) should be included in the study.

4- How did the authors ruled out the probability of getting PCR fidelity artifacts;

5- The E1373X mutation isn’t apparently a founder mutation, on that I agree but this is where I believe the results are a bit wishful thinking because the authors only conducted the primary study on 4 subjects which might exclude other possible mutations that might be present in the Arab kindred.

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Minor Essential Revisions

As a minor comment the authors should review the references, since there are a few of them that contain some typos (in BMC Cancer after the year is a , and not an ;).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests