Reviewer's report

Title: Five recurrent BRCA1/2 mutations are responsible for cancer predisposition in the majority of Slovenian breast cancer families

Version: 1 Date: 26 May 2008

Reviewer: Arto Mannermaa

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The manuscript Mateja Krajc, Erik Teugels, Janez Zgajnar, Guido Goelen, Nikola Besic, Srdjan Novakovic, Marko Hocevar and Jacques De Grève BMC Medical Genetics Five recurrent BRCA1/2 mutations are responsible for cancer predisposition in the majority of Slovenian breast cancer families represents an interesting investigation on the frequency and importance of BRCA1/2 mutations in Slovenian breast cancer families. BRCA1/2 are at the moment the most important cancer susceptibility genes for inherited breast cancer / breast and ovarian cancer. More than 3700 mutations have been found in various populations around the world. There are no specific mutational hotspots in the genes, but some population specific founder mutations still exist. The importance of this manuscript lies behind the fact that identification of possible population specific (founder) mutations could help in genetic counselling of the cancer families and/or promote more cost-efficient laboratory diagnostics.

The paper is concisely and clearly written and data sufficiently presented. I have some comments that need to be replied by the authors. In general, the manuscript requires minor revision before being accepted.

Comments:

Major Compulsory Revisions:

The critical point of the manuscript is the fuzzy description of patient material. The number of probands with two or more first-degree relatives, individual patients without family history and bilateral breast cancer patients with other cancer types should be included in the section Methods, Patients and families. Are all 145 families of high risk with two or more breast and/or ovarian cancer cases among first-degree relatives?

The authors should consider to exclude the subject of patients' and their relatives' interest to genetic counselling from the aims of the study. This was poorly described in both methods and results section.

Minor comments:

Methods:

- Describe how many families were fully screened and how many partially screened by PTT and recurrent mutation screening... One can not deduce this now.
- How was MLPA test for BRCA1 performed? Describe especially the data analysis.

Results:
- After identification of the sequence variants from BRCA genes, were any control material tested to reveal the frequencies of the mutations at the population? This is especially important in the case of novel missense mutations with possible reduced penetrance.

Figure 1.

Figure 1 is poorly drawn, please redraw. Breast /Breast and ovarian cancer families are now impossible to identify.

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

**Quality of written English:** Acceptable

**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