Reviewer's report

Title: The frequent BRCA1 mutation 1135insA has multiple origins: a haplotype study in diverse ethnic groups

Version: 1 Date: 29 September 2005

Reviewer: Heli Nevanlinna

Reviewer's report:

Rudkin et al. have studied a four marker haplotype around the recurrent BRCA1 mutation 1135insA in three Dutch families, two families of Italian descent and one French Canadian family, and compared the haplotype to the one previously described in Norwegian families with the same mutation. Two distinct haplotypes were seen in the Dutch or Italian/French families studied. The authors conclude that the mutation has occurred independently in different populations and may represent a hot spot, and that it should be included in targeted BRCA1 mutation testing panels in any population.

Minor Essential Revisions

1) Page 4-5, clinical description
The families with the 1135insA mutation studied in this report are not very thoroughly described. Information of only some carriers or cancer cases per family is not sufficient to make conclusions about penetrance of the mutation. If such confirmatory estimation was to be made based on the new families studied, complete family and cancer information would be needed. However, if complete information is not available, this could be rephrased for instance so that the available information is consistent with the reported high penetrance of the mutation. The TNM stage for one breast cancer patient only is not very informative.

2) Page 5, haplotype analysis
The families sampled to this study are quite few and do not exclude the possibility that also the Norwegian haplotype may have migrated to and be present in other populations or different parts of the world as well. The data merely suggests that the 1135insA mutation has occurred independently in other populations as well.

3) Page 7, conclusions
Are the authors aware of clinical BRCA1/BRCA2 testing with targeted mutation screening panels? Could some discussion be included of the relevance of such panels in different populations vs. screening of the whole genes?

4) Page 7, conclusions
I suggest using "possible hot spot for mutations"

5) Title: would "different populations" be better than "diverse ethnic groups"? Norwegian, Dutch, Italian and French families were studied.

What next?: Accept after minor essential revisions
Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: No
Declaration of competing interests:
I declare that I have no competing interests