Reviewer's report

Title: Identification of a novel CHEK2 variant and assessment of its contribution to the risk of breast cancer in French Canadian women

Version: 1 Date: 1 April 2008

Reviewer: Kathleen Claes

Reviewer's report:

The paper of Novak et al. describes mutation analysis of the CHEK2 gene in 25 probands from French-Canadian breast cancer families and 25 controls. This approach should provide an 80% power to detect an allele with a frequency of 1% or more. The prevalence of 2 recurrent genetic variants was evaluated in breast cancer patients and controls from the same population. As the French Canadian population is known to harbor several founder mutations in breast cancer susceptibility genes, the investigators wanted to find out if founder mutations in CHEK2 could be responsible for breast cancer predisposition in their study population.

Major compulsory revisions
none

Minor essential revisions

pg6: how were the "healthy French Canadian women with unknown BRCA1/2 mutation status" selected? The authors should provide more information how these people were selected. Do the authors have detailed information about the familial anamnesis, etc. Same suggestion for the controls of group 2.

pg 9: the authors used a neonatal set of controls: why can they be used as control group? Can this be considered as a matched control group?

pg9: in the result section the prevalence of the 1100delC mutation described in patients from group 3 and group 1. Based on the numbers tested, I think this should be group 2 instead of group 3???

In the discussion section no further comments are given on this prevalence. E.g. is this in agreement with other Caucasian populations (Europeans: eg correlation with the frequency in the French population, Americans,..)? Wouldn't it be valuable to determine the prevalence of the 1100delC mutation also in group 3?

In the conclusion of the abstract I would also mention the frequency of the 1100delC mutation rather than giving a vague indication that the 1100delC mutation is present in French Canadians.

pg10: the silent variant E84E was observed at similar frequency in cases and controls "suggesting against the possibility that this variant may affect an exonic splicing enhancer". I would suggest to also add data about in silico predictions.
Typing error
pg7: allele specific amplification was pERformed...

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests