Reviewer’s report

Title: BACH1 Ser919Pro variant and breast cancer risk

Version: 1 Date: 11 October 2005

Reviewer: Mieke Schutte

Reviewer’s report:

General
This paper describes a mutation analysis of the complete coding sequence of BACH1 in a series of 43 non-BRCA1/BRCA2 families with breast cancer. Seven BACH1 variants were identified, four of which were in exonic sequences and one was only 7 bp from a splice site. Two of the exonic variants predicted an amino acid change. The frequent Ser919Pro variant was also screened in a cohort of 888 unselected breast cancer patients and 736 healthy women, and the rare Val193Ile variant was also screened in another 336 familial breast cancer patients and in 167 healthy women. The prevalence of neither BACH1 variant differed among breast cancer cases versus controls.

BACH1 is a reasonable breast cancer susceptibility candidate because of its interaction with the high-risk BRCA1 breast cancer susceptibility gene. Yet, others have already done a similar analyses and also with disappointing results, as referenced by the authors. The negative data in this paper are of limited interest to researchers in the field, as it may aid them in deciding not to screen BACH1 in their patient cohorts.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. It is still possible that BACH1 is a susceptibility gene in other countries and it would therefore be appropriate to restrict the title and conclusions of the paper to Finnish breast cancer families.
2. The methods and results in the abstract are incomplete. Seven variants were identified in 43 breast cancer families and two variants were screened in larger, but different sample cohorts.
3. Sample cohorts. It is unclear whether blood and/or tumor samples have been analyzed for the breast cancer patients and families. Also, the cohorts that were screened for the Val193Ile variant are not described.

Discretionary Revisions (which the author can choose to ignore)

1. Results and Discussion. The remark that silent alterations have no effect on protein structure is dangerous, as such variants may affect splicing. The same applies for the 2097+7 G>A variant that is located relatively close to the splice site. Instead of speculating on the functional effects, it would be appropriate to analyze these variants with a splice-prediction algorithm.
2. Table 1: the 1935+22delT variant was apparently always homozygous. Should one consider this variant as "the Finnish wild-type", in other words is this variant also exclusively found in healthy controls?
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.