Reviewer's report

Title: BACH1 Ser919Pro variant and breast cancer risk

Version: 1 Date: 24 October 2005

Reviewer: Chen-Yang Y Shen

Reviewer's report:

General

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

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

The present study was carried to examine whether genetic polymorphism of the gene encoding BRCA1-associated C-terminal helicase (BACH1) is associated with increased breast cancer risk. A relatively large group of study subjects was recruited to genotype seven single-nucleotide polymorphisms (SNPs), some causing amino acid changes though functional significance of such changes being unknown. The results show no significant associations, even though study subjects were further stratified into subgroups with different clinical or pathological profiles.

Given functional and physical interactions between BACH1 and BRCA1, the hypothesis of the present is reasonable. The sample size of this study is adequate to address study questions. The information generated by this study is suitable to be published. The major concerns of this study are (1) Given the “low-penetrance” nature of SNPs, it might be not surprising to found no significant association; it is not unusual that the effect associated with low-penetrance alleles is modified by risk factors, and the joint effect of SNPs and risk factors would determine cancer risk significantly. Thus, the failure to consider the effect reproductive risk factors of this study is the major limitation, which should be addressed. (2) Single SNP may be unable to capture genetic effect of the whole gene, and haplotype analysis is suggested to overcome this limitation.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: Yes