Reviewer’s report

Title: Common variation in EMSY and risk of breast and ovarian cancer: a case-control study using HapMap tagging SNPs

Version: 1 Date: 6 April 2005

Reviewer: Thomas A Sellers

Reviewer’s report:

General
The report by Benusiglio and colleagues explores the association between common variation in the EMSY gene with risk of breast or ovarian cancer. Based on the association of the EMSY gene with BRCA2, it represents a logical candidate gene. Using htSNPs is a reasonable approach given the large sample size and there is careful work to examine the coverage of the SNPs. Analysis seems to suggest that none of the common variants in the EMSY gene are associated with risk of either cancer in this British population. The report is clearly written, the methods are appropriate and well described, and the discussion and conclusions balanced and objective.

My comments are not related to what was done, but what might have been done before concluding that variation in this gene is unrelated to risk.

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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)
1. pg 7. Wavemaker software?
2. The analytic approach used will not allow for adjustment for age or other potentially important covariates when estimating the odds ratios.
3. This reviewer found it difficult to reconcile the statement on pg 5 that there are no coding SNPs in EMSY yet on page 9 it is stated that there are 22 common SNPs available in HapMap. Are all these in non-coding regions?
4. One would presume that data on family history are available. Given that this group has shown that familial cases may be enriched for low-penetrance alleles, an analysis of the familial subset versus controls should be performed.

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Discretionary Revisions (which the author can choose to ignore)
1. Did the authors analyze the association of the htSNPs with the age at onset distribution among the cases? Given the paradigm that genetic influences are manifest in earlier onset, this could be instructive.
2. Consider deleting the non-Caucasians from the study.
3. The source populations have collected data on non-genetic risk factors. Although I’m convinced myself that it would affect the results, it does seem that analyses should be performed to adjust for these in a multivariate model (see #2 below).
What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.