Reviewer’s report

Title: A novel duplication polymorphism in the FANCA promoter and its association with breast and ovarian cancer.

Version: 1 Date: 27 November 2004

Reviewer: Christopher Mathew

Reviewer’s report:

General

This manuscript describes the detection of a novel 13 bp duplication polymorphism upstream of the initiation codon of the FANCA gene, and tests this for association with breast cancer and ovarian cancer. No association of the duplication was found with breast cancer, but there was a marginally significant decrease in its frequency in ovarian cancer. No attempt was made to replicate the reduction in frequency in a second set of ovarian cancer samples, or to investigate whether the duplication altered the expression of the FANCA gene. The number of controls is substantially lower than the numbers of cases in the disease groups.

Given the enormous number of type 1 errors in the literature for association studies with such marginal significance, the authors should attempt to replicate the finding in a further set of British ovarian cancer cases, and should increase the number of controls.

The interest in the novel duplication would be greatly enhanced if the authors were able to demonstrate that it altered the expression of the FANCA gene. For example, constructs of the 2 alleles could be transfected into human cells and expression analysed from a reporter gene. Also, quantitative PCR of FANCA mRNA could be performed in cell lines from individuals who were homozygous for the presence or absence of the duplication.

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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)

There is some text missing in the first sentence of the Discussion.

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Reject because scientifically unsound

Level of interest: Too insignificant to warrant publication in any journal
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I have no competing interests.