Reviewer's report

Title: Haplotype analysis suggest common founders in carriers of a recurrent BRCA2 mutation in French Canadian hereditary breast and/ovarian cancer families

Version: 2 Date: 15 August 2005

Reviewer: Bohdan Gorski

Reviewer's report:

The manuscript entitled "Haplotype analysis suggest common founders in carriers of a recurrent BRCA2 mutation in French Canadian hereditary breast and/ovarian cancer families" by Kathleen K Oros et al. presents the evaluation of a common BRCA2 mutation, 3398delAAAAG, as a cancer susceptibility allele in French Canadian population. This is an interesting report of an investigation in a topical area of study. It is a primary goal in clinical cancer genetics to identify the full range of mutant alleles in a population that predispose to breast cancer (or to another cancer) and then to offer a rapid and inexpensive genetic assay to test for these alleles in a single setting. The results will contribute to a growing literature concerning the roles of common BRCA1 and BRCA2 variants in breast cancer predisposition.

Major comments

1. Numbers of tested breast/ovarian cases are very small

2. The 3398delAAAAG mutation is located within Ovarian Cancer Cluster Region (OCCR) of BRCA2 gene. Proportion of breast/ovarian cancers in a group of 3398del5 mutation carriers should be discussed with results on other BRCA2 OCCR mutations previously described in literature.

Minor comments

1. Last sentence in methods section - Why you mentioned that families harbouring the same mutation are not related to one another based on similarity of cancer phenotype?

2. Results and discussion section, line 7 "All mutations carriers of unphased genotypes harboured alleles consist with either haplotype " - Please demonstrate this, include table with haplotype frequency estimations from unphased data.

3. Results and discussion section, line 10 "Due to limited amounts of DNA..." Why is this so important for linkage disequilibrium (LD) estimation? Looking at table 2 one may assume LD, and calculating haplotype frequency.

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