Reviewer's report

**Title:** Genotype-phenotype correlations among BRCA1 c.4034delA (4153delA) and c.5266dupC (5382insC) mutations carriers from Latvia

**Version:** 1  **Date:** 11 April 2011

**Reviewer:** Miguel M de la Hoya

**Reviewer's report:**

Major compulsory revisions

1) I miss population prevalence of c.5266dupC and c.4034delA BRCA1 mutations in Latvia. Is the data already known? The authors should address this issue in the text. This will provide a better estimation of risk for c.5266dupC and c.4034delA carriers.

2) I am not convinced by the survival analysis. In particular:
   - age at diagnosis is relevant for survival analysis. I expect an early age at onset in carriers.
   - ER/PR/erb2 status is relevant for survival analysis. I expect an excess of triple negative/basal-like cases among carriers. In addition, is there any difference between c.5266dupC and c.4034delA carriers?
   - Most probably, mutations carriers have a distinctive clinical management, such as risk-reduction surgery or intensive surveillance programs.

The authors should clarify these points.

Minor essential revisions

The manuscript needs revision by a native English speaker.

- Page 4, line 10. Reference 4 does not seem appropriate.
- Apparently, the study population is comprised of unselected breast and ovarian cancer cases, but the patients and methods first paragraph (page 5 at the end, page 6 top) is confusing. It should be rewritten.
- Page 7. The following sentence seems rather confusing to me:

- Page 13. I doubt the claim that several authors have suggested that other genes may explain BRCA1 genotype/phenotype correlations?. Other genes may explain variable penetrance of BRCA1 mutations but not that two specific mutations such as c.4034delA and c.5266dupC confer different risk (unless modifier risk genes are linked to BRCA1). The authors should clarify this point.

Discretionary revisions

- The manuscript will improve clarity if Figures 2 and 3 use the same code for c.4034delA, c.5266dupC and control curves.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

'I declare that I have no competing interests'