Reviewer's report

Title: Association of Polymorphisms cMyc-N11S and p27-V109G with Breast Cancer Risk and Survival

Version: 1 Date: 31 January 2007

Reviewer: Arto Mannermaa

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General
The manuscript "Association of Polymorphisms cMyc-N11S and p27-V109G with Breast Cancer Risk and Survival" represents an interesting investigation on possible association of cMYC-N11S and p27-V109G polymorphisms with breast cancer and survival. Both cMyc and p27 are well known participants in cell cycle regulation of carcinogenesis. The authors have chosen these polymorphisms on the basis of their probable functional role, even though there are publications of both of these polymorphisms and association with cancer. The data from previous reports do not give clear evidence for or against association with breast cancer and no data for prognostic role of these polymorphisms exists.

The authors find no association between the studied polymorphisms and breast cancer. Authors suggest possible associations between clinical parameters of the tumours and studied polymorphisms, such as between tumour stage and p27-V109G by using p-values without multiple test correction. They propose for larger more comprehensive tagSNP based analysis of these genes to reveal the role of cMYC and p27 in breast cancer risk and prognosis.

This study shows clearly that neither cMYC-N11S nor p27-V109G have no role in breast cancer risk or prognosis. The results and discussion are based on carefully accomplished selection of a reasonably large study material, genotyping and statistical analysis. The major weakness of the manuscript is the amount of polymorphisms used. As the authors themselves suggest, further study with comprehensive amount of SNPs from cMYC and p27 is needed to understand the role of these genes in breast cancer risk and prognosis.

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

1. The text should be revised and shortened to describe just the nonsignificant results of these polymorphisms. There is no point in presenting suggestive associations where no statistical significances exist. Tables 3-5 should be removed

2. The manuscript should be revised to be consistent for multiple testing. There are now results presented without correction but in the discussion it is stated that after adjustment for multiple testing the borderline association results are no longer significant. If the authors choose to not present corrected results, this should be clearly stated in the material and method section.

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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. Although there is no association between the studied polymorphisms and breast cancer, the authors could discuss the strength of linkage disequilibrium around the studied polymorphisms. Based on their results, which domains of the proteins should not contain any potential risk altering variants?

2. Genetic heterogeneity of the material. The authors cite to ref 21 for the suitability of the selected control population to association analysis. As the genetic homogeneity of cases and controls is crucial for the association analysis, the data should be presented also in this manuscript. In reference 21 there was no data about the proportion of Ashkenazi ethnicity in the controls, which is in the manuscript one definition of high genetic breast cancer risk.

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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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests