Reviewer’s report

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

Version: 1 Date: 9 January 2007

Reviewer: Michael Wirtenberger

Reviewer’s report:

General

In the present study the authors assessed a putative risk association of two SNPs in cMYC and p27 among 1115 female breast cancer cases and 710 controls. The study revealed a modest, but statistical significant protective effect of the p27-V109G allele in an age adjusted analysis. Furthermore, the same allele showed a statistical significant association with high T stage. The authors have presented a very comprehensive analysis with sound study design and good biological rationale for their analyses.

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

The authors did not perform a power calculation, which is necessary to judge whether the presented study is appropriate to confirm previous results of the cMYC N11S polymorphism in order to exclude a putative beta error. Any follow-up study needs at least a power of 90% to detect the effect described in the previous study (OR = 1.54) to enable a confirmation and exclude a possible beta error.

Based on the power calculation the issue of a possible beta error should be discussed in detail, because this is one of the major reasons why many follow up studies do not confirm previous findings.

The authors state that BRCA status had no influence on their results. The authors should state how many of their cases were BRCA1/2 mutation carriers and possible implications on their null results regarding cMYC. The use of BRCA1/2 mutation negative breast cancer cases excludes all effects derived from these high risk genes.

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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)

I recommend shortening of the manuscript, especially Material and Methods section is too comprehensive.

In the Materials and Methods section, page 5, the following paragraph remains unclear and needs to be rewritten.

“A 25% random sample of individuals in this age category who did not meet the OFBCR definition, 35% of those aged 55-69 at high risk and 8.75% aged 55-69 at low risk were also asked to participate. This multi-step sampling scheme enriches the population for genetically predisposed individuals and is considered the most efficient study design for the identification of genetic factors [22].”

In the Results section, page 9 the authors should substitute the words “may be associated” with “show a statistical significant association with” in line 9 and 12.

Table 3 should be excluded as the non significant results are stated already in the text.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field
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.