Reviewer's report

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

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Reviewer: Hiltrud H Brauch

Reviewer's report:

General
The manuscript seeks to establish an association between cMyc-N11S and p27-V109G with breast cancer risk and survival. The authors observed a significant association between p27-V109 TG and breast cancer risk when data were adjusted for age and race in both Whites and all patients (OR 0.71; CI 0.53-0.94) and OR 0.70; CI 0.52-0.93 respectively). For cMyc-N11S they did not find any risk association. When they looked at combined genotypes they observed a similar risk association as with p27-V109 TG alone. Stratification of data according on the patients clinical characteristics showed a significant association between tumor stage and p27-V109G genotypes (p=0.01). The authors suggest further work on the functional relevance and genetic investigations of variations in these and other genes as well as tumor related markers for treatment effects.

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

(1) Is the question posed by the authors new and well defined?
The question is well defined

(2) Are the methods appropriate and well described and are sufficient details provided to replicate the work?
Methods are appropriate

(3) Are the data sound and well controlled?
The data look sound and well controlled

(4) Does the manuscript adhere to the relevant standards for reporting and data deposition?
Tables and Text:
The manuscript tables report data according to current standards. The text in the result section however, is not exactly reflecting these data. This particularly refers to table 2 and 4 which are not adequately described in the results section. Accordingly, significant effects have been overseen or at least not accurately described.
Examples are: The p27-G109 allele MAY be associated…..or “The combined effect of the two polymorphisms ….did NOT show any relationship with risk…… In contrast to this wording table 2 clearly shows a significant p27-109 TG association with breast cancer risk and also the combined analysis with cMycN11S showed an association, which is similar to that of p27-109GT alone.
To focus on the major findings and to avoid confusion for the reader it is critical to clearly distinguish between positive and negative results. What these results may mean is subject to discussion.
Tables 3 and 5 which refer to subgroup analyses and associations with breast cancer survival present null effects only. It will be sufficient to describe these results in the text and to avoid the tables.

Additional remarks:
Introduction: The introduction should be shortened. It is unnecessary to give the details of the results of the quoted literature. Rather present an overview on their meaning and relevance to the work presented in the own manuscript.

Results: page 9 first paragraph. The authors should be careful with their statement on genotype frequencies in non Caucasians because these frequencies and p-values were derived from low numbers. These number should be included.
Are the discussion and conclusions well balanced and adequately supported by the data. The discussion and conclusions are not balanced due to the confusion introduced by the presentation of data in the result section. In order to streamline the discussion it will be important to first decide whether this manuscript will put weight on null results (cMyc-N11S) or significant associations (p27-V109G). This reviewer feels that there is significant data for the latter based on the findings reported in table 2. This refers to an association between p27-V109 TG and breast cancer risk adjusted for age and race (OR 0.7; CI 0.52-0.93, and OR 0.71; CI 0.53-0.94). Of note, the adjusted OR is more reliable than the unadjusted OR which makes this result worthwhile to be reported and discussed. This is not properly appreciated in the current version. Rather, the authors put an unbalanced emphasis on their negative results as it is evident from the order and arrangement as well as contents of paragraphs. Similarly, the findings of a significant association between the p27 polymorphism and tumor stage (p=0.01) needs to be thoroughly addressed and clearly distinguished from all other non significant findings including that of nodal involvement which is not significant (p=0.07). These aspects need to be addressed both in the results and discussion sections of the manuscript. This also refers to the combined protective effect of cMyc AA+ p27 TG/GG which may reflect a carry over effect of the p27 effect.

Furthermore, the discussion is inappropriately rich in aspects referring to functional aspects. The work however, was limited to an association study and does not contain investigations and findings with respect to the functional impact of the SNP under investigation. Recommendations on functional aspects are therefore inappropriate and must be avoided.

(6) Do the title and abstract accurately convey what has been found
As mentioned already there is a discrepancy between results obtained and presentation as well as interpretation. These shortcomings are particularly reflected in the title and abstract. In particular, the title does not reflect to contents of the paper. Authors present their findings mainly as negative results but in the title they provoke the idea of an association between polymorphisms under investigation and breast cancer risk and survival. Based on a thorough revision of the manuscript and focus the authors should settle on a new title.

Abstract: results and conclusions are not in line with standards. The result section is not succinct and does not reflect the main findings of the manuscript. The conclusions are vague and out of proportion with respect to references to functional aspects, tumor-related markers and treatment effects. None of these are subject of this manuscript

(7) Is the writing acceptable
Given the overall shortcomings the writing with respect to emphasis and arrangement of the manuscript is a major obstacle and must be addressed in a new version.

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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)

none

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Discretionary Revisions (which the author can choose to ignore)

none

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

declare that I have no competing interests