Reviewer's report

Title: Mutation analysis of the AATF gene in breast cancer families

Version: 1 Date: 12 October 2009

Reviewer: Nazneen Rahman

Reviewer's report:

Please number your comments and divide them into

- Major Compulsory Revisions

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

I wasn't clear if the 121 patients included the 17 with mutations in other genes. If so, they should be excluded and the number included in this study should be 104. If they do not it should be made clearer in the text.

- Minor Essential Revisions

The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

I feel that the introduction should include at least a short portion on the low penetrance breast cancer susceptibility alleles identified through GWAS.

In the abstract the results / conclusions could be more straight-forward. This would help the reader. It would be preferable if in the abstract it states that they identified one non-synonymous missense variant and six intronic variants, none of which were predicted to be pathogenic. There was no significant difference between cases and controls and there was no evidence of an association with breast cancer.

- Discretionary Revisions

These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

The final sentence in the discussion, hypothesising that the absence of deleterious mutations could suggest that pathogenic mutations are poorly tolerated is best removed. AATF is a small gene and many genes of this size screened by CSGE in 120 individuals would give a similar profile.

The authors should add that this was a small study and cannot exclude the
possibility that very rare mutations might predispose to breast cancer, but AATF cannot be making a sizeable contribution to breast cancer predisposition.

Please note that both the comments entered here and answers to the questions below constitute the report, bearing your name, that will be forwarded to the authors and published on the site if the article is accepted.

What next?
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Based on your assessment of the validity of the manuscript, what do you advise should be the next step?

- Accept without revision
- Accept after discretionary revisions (which the authors can choose to ignore)
- Accept after minor essential revisions (which the authors can be trusted to make)
- Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
- Reject because scientifically unsound
- Reject because too small an advance to publish (note that BMC Cancer will publish all sound studies including sound negative studies)

My assessment:

- Accept after minor essential revisions (which the authors can be trusted to make)

Level of interest
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BMC Cancer has a policy of publishing all scientifically sound research whatever its level of interest. However if you choose one of the first three categories below, we may ask the authors if they would like the manuscript considered instead for the more selective journal BMC Medicine.

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- An article of importance in its field
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Level of interest
- An article of limited interest

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Acceptable

Statistical review
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Is it essential that this manuscript be seen by an expert statistician?
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