Reviewer's report

Title: TOPBP1 missense variant Arg309Cys and breast cancer in a German hospital-based case-control study

Version: 1 Date: 22 October 2010

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Blaut et al. have assessed the breast cancer risk of TOPBP1 missense variant Arg309Cys in a series of about 1000 German breast cancer cases and controls. Previously, the variant was proposed to confer an elevated familial breasts cancer risk in a study from Finland. In the German breast cancer patient series, no evidence for increased breast cancer risk for the TOPBP1 Arg309Cys variant was observed in the main analysis or in the subgroup analyses stratified by family history or bilateral disease. Any putative, nonsignificant effect was in the opposite direction to the risks reported in the previous study, and the age of diagnosis was higher for the carriers than for non-carriers, refuting the previous findings.

The study is well performed with appropriate quality control and well defined and extensive sample series. The manuscript is clear and well written and the conclusions justified.

Minor Essential Revisions

For comparison of the studies, it would be informative to indicate the number of cases and controls included in the previous (Finnish) study.

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.