Reviewer's report

Title: Transcription factor 7-like 2 (TCF7L2) variant is associated with familial breast cancer risk: a case-control study

Version: 2 Date: 12 October 2006

Reviewer: Hiltrud H Brauch

Reviewer's report:

General

The manuscript seeks to find an association between SNP rs12233372 and familial breast cancer as well as pancreatic cancer risk. The authors genotyped 592 patients with familial breast cancer, 125 patients with pancreatic cancer and 735 controls from Germany. They performed association analyses suggest based on their findings of OR 1.19, 95% CI 1.00-1.42 that this SNP increases the risk of breast cancer. Based on the OR 1.27; 95% CI 0.87-1.85 they suggest that this SNP has a potential effect on the risk to develop pancreatic cancer.

The manuscript contains a number of serious flaws

1) A detailed patient description including known risk associations (Table) is missing. The description should include epidemiological variables and particularly include diabetes type II because the authors state in the introduction that women with diabetes type II have a higher breast cancer risk.

2) Controls are not age matched

3) With the exception of a borderline significance OR 1.19, 95% CI 1.00-1.42, P = 0.04 for an association between the T allelel and breast cancer risk all other results are not significant. Given the fact that 1.0 (no risk) is included in the interval there is a chance for a type 1 error.

4) ORs should be adjusted for diabetes type II

5) The study does not have enough power based on the power calculation on page 6.

6) The group of pancreas patients is to small, no significant results were obtained.

7) Given these shortcomings and lack of significant results the statement of a contribution of TCF7L2 variants to familial breast cancer and possibly to pancreatic cancer in the conclusion is appropriate

8) The discussion on functional aspects cannot help the lack of results

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What next?: Reject because scientifically unsound

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Acceptable

Statistical review: Yes

Declaration of competing interests:

I declare that I have no competing interests