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: 24 October 2006

Reviewer: Jörg Epplen

Reviewer's report:

General

Accept possibly after substantial revision.

We agree with the suggestion of reviewer Mannermaa: The authors should investigate (at least in a subset of) families whether the T allele of rs12255372 segregates with the phenotype (BC). In case material of family members were not available, the authors should state this fact in the manuscript.

Due to the small sample size of the PC group and the unmatched controls (mean age 64 years vs 49 years, sex?) no valid conclusions can be drawn from this analysis. Therefore we suggest to omit this part entirely from the manuscript.

The discussion and conclusion sections should be voiced cautiously and carefully. In view of the borderline significance levels confirmation of this result in an independent cohort is obligatory. Otherwise involvement of TCF7L2 in BC remains quite speculative.

The suggestion of reviewer Brauch to consider diabetes type II data may theoretically be reasonable. Yet in practice, this is asking really a lot. First, it cannot be expected that such data are readily available for a cancer cohort. Second, diabetes type II status alone is probably not sufficient since insulin levels would be the more reasonable parameter.

After all a major shortcoming of this MS remains: Not the respective haploblock has been subject of the study but rather exclusively a single polymorphism.

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

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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)

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Discretionary Revisions (which the author can choose to ignore)