Reviewer's report

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

Version: Date: 2 16 October 2006
Reviewer: Arto Mannermaa

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General
This is a straightforward study assessing the possible role of transcription factor 7-like 2 (TCF7L2) gene in familial breast cancer risk. For this, one polymorphism, rs12255372, was analyzed at TCF7L2 gene. The main result is the finding of both significant allelic association between TCF7L2 and familial breast cancer and a significant allele-dose dependent association. Also, a non-significant association was found using pancreatic cancer material.
The result is very interesting and possibly valuable since TCF7L2 has been recently shown to be associated with type 2 diabetes and it is known that diabetes and breast cancer may share some common etiological factors. If true, and succesfully repeated, the results of this paper would give an indication about these factors.
The material for the study is well documented. The sample size of this study is big enough to draw the presented conditional conclusions.
The methods of the study are also well documented and valid.
The study is overall very well constructed and written. I have only a few suggestions which I feel may be beneficial to the manuscript.

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

Methods section: Page 5, There is a typing error in the title of statistical analysis

Discussion: Page 6, the second paragraph. It is stated that this study supports the findings of Grant et al (2006). The main topic of Grant et al is association of TCF7L2 with type 2 diabetes, which is not studied here. The citing should be either removed or specified more accurately to the possible common etiological factors of cancer and diabetes that could be found from the enteroendocrine role of TCF7L2 protein

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)
Familial breast cancer material is used. To further evaluate the role of TCF7L2 polymorphism as a cancer risk factor, authors should genotype some of their families to find out whether TCF7L2 variant is inherited together with breast cancer risk.
The authors should consider leaving the pancreatic cancer material out of this manuscript and publish it as another manuscript with a larger material. The results presented with pancreatic cancer are not significant and no power estimations have been offered.

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests