Reviewer's report

Title: TGFB and TGFBR1 polymorphisms and breast cancer risk in the Nurses' Health Study

Version: 1 Date: 15 June 2007

Reviewer: Victor Moreno

Reviewer's report:

General

This large nested case-control study that shows a negative association between TGFB L10P polymorphism and breast cancer. For the -509 SNP, a marginally significant inverse association is found for main effects that might be the result of the interaction with estrogen receptor status.

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

This study includes the cases and matched controls identified prospectively within a cohort and this should be resistant to biases. However, the authors give no detail about the studied population. They use a reference from 1998 when this cohort only had 156 women with breast cancer. A table with characteristics of the cohort and the selected cases and controls would be helpful, or a more recent reference for these data that agrees with the 1267 cases and 1758 controls.

Reference 33 states that 2 controls per case were selected, but in this analysis the ratio control:case is 1.4. Some explanation about that and missing data should be given so that any reader can assess that selection bias cannot be a relevant issue in this study.

The interaction with estrogen receptor status is only reported as conditional OR and CI, but we don't know the number of cases for each status and the number of missing data. This is important to give more or less relevance to this finding.

The authors report unconditional logistic regression estimates. This usually is more powerful when some matched set have missing values, but could lead to biased estimates towards the null hypothesis. The adjustment for matching criteria can avoid this, but the authors should also perform the conditional logistic regression analysis and state that the results are similar, if this is the case, or report the conditional estimates if the unconditional show bias.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests, though I am coauthor with D. Cox in a paper published in 2004.