Reviewer's report

Title: Association between the Cytotoxic T-Lymphocyte Antigen 4 +49G>A polymorphism and cancer risk: a meta-analysis

Version: 2 Date: 8 August 2010

Reviewer: Keitaro Matsuo

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General comment:
Zheng et al. conducted a meta-analysis to evaluate association between cancer susceptibility and CTLA4 +49 polymorphism based on justification about single SNP selection in terms of functionality. Although aim of the study is clear, there are several concerns, some of them are serious, to be resolved.

Comments:
1. I appreciate to have page number on the manuscript. It's hard to make comments on specific point.

2. Aim of the study should be more clearly stated in the introduction. "To summarize the published data..." looks weak statement as an aim of the study.

3. Method and presentation of results
   a. All the figures resolution is not at the acceptable level of quality. Most of the figures were line drawing type pictures. Although I can figure out all of them, I appreciate to have beautiful ones for review.
   b. Table 1 is incompletely submitted. I can't figure it out.
   c. Lack of confidence interval for Funnel plot for publication bias.

Usually, funnel plot for publication bias accompanies a confidence interval for summary estimate in it. Please add it. Moreover, authors' interpretation of the plot seems a little bit self-centered one. Even if statistical test is not significant, the plot includes more studies reporting positive association with lower precision. Careful interpretation is essential.

d. Lack of keyword in literature search and description of how they decide inclusion or exclusion usually accompanying in meta-analysis.

Even in a meta-analysis of observational study, it is important to warrant replicability by readers or other investigators. Therefore, description about how to identify candidate articles should warrant it. Lack of information about reason for exclusion with reference is helpful. Usually this kind of information is presented with figure about literature search process. The article should refer to guidelines for meta-analysis and take them into consideration in organization of the manuscript.

This paper is submitted in 2010 July, therefore, literature search should be
updated before submission. Simple literature search by this reviewer gave two more studies for it. Moreover, if study is excluded from lack of reporting, authors could contact corresponding authors of the study. Description about contacting is also important to show limitation of comprehensiveness in literature searching.

e. Inclusion of colorectal adenoma is questionable. It is contradicting with authors' criteria for inclusion.

f. It is hard to accept the description like "Yellow-race study."

g. Evaluation and interpretation of heterogeneity testing does not looks acceptable. Basically, this kind of test is highly influenced by number of studies and chance. Authors’ strong adherence to statistical significance is very questionable. How can they deny any source of heterogeneity from lack of power testing?

h. Authors chose a fixed-effect model based upon their interpretation about lack of heterogeneity. Again, it is questionable to choose this model in this study.

i. One of the strong limitation of this study is non-consideration of multiple comparison issue. Strong adherence with p<0.05 dogma with multiple testing may mislead authors' interpretation. It should be discussed. Moreover, there are a lot of limitation in the study, however, it is rarely discussed in the manuscript.

4. English should be checked. There are many grammatical errors throughout the text.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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