Reviewer's report

Title: Association between an 8q24 locus and the risk of colorectal cancer in Japanese.

Version: 1 Date: 7 February 2009

Reviewer: Suminori Kono

Reviewer's report:

The paper described associations of rs6983267 and rs10090154 polymorphisms at 8q24 with colorectal cancer in a Japanese population based on a fairly large case-control studies. The 8q24 loci have drawn considerable attention in recent genome-wide association study on colorectal and other cancers in the United States and Europe. This study found a statistically significant increase in CRC risk associated with the rs6983267 minor allele, but not with rs10090154. The paper would add to literature in the area of the highest importance and interest. But I think that the authors were less scrupulous in preparing the manuscript. Careful consideration is needed with respect to the following points.

Comments 1-7: Minor Essential Revision
1. Careless mistakes are recognized at several places.
   1) Table 1 was missed.
   2) There were grammatical errors, inappropriate words, and less specific description. Examples are: provide=>provided (line 5 on page 5); less specific ranges (page 7 and Table 3); confounder-adjusted => multivariate-adjusted (line 8 on page 8); previous GWASs => those (or observations) from the previous GWASs (line 5 from the bottom on page 8); and the footnotes did not exactly correspond to superscripts in the tables. The authors need to read thoroughly and correct these and others.

2. Line 4 from the bottom on page and the first line on page 8 had duplicate description. Either of them be deleted.

3. Specify for what the odds ratio was obtained in Tables 2-4. It is probably better to change the title of Table 2 like this: Genotype distributions of … and odds ratios of colorectal cancer for the minor alleles.

4. Table 2 showed numbers of cases and controls with unsuccessful genotyping under the sub-header UK. Specify the abbreviation in the footnote, or delete this part in the table and describe these numbers in the text.

5. Table 3 showed the interaction for site of cancer. This is very strange, because controls had no data for this variable. There must have been some mistake in the analysis.

6. Duplicate genotyping was done on a 5% sample of the study subjects (bottom
of page 5). Please specify how this sample was selected; i.e., randomly or consecutively of the first series?

7. Description was not specific at the following places in the second paragraph on page 9.
   1) Was the study of reference 26 in vivo (animal study) or in vitro study?
   2) Regarding the sentence at the next line, did Tomlinson et al show POU5F1 or POU5F1P1 gene expression in primary CRC of humans?
   3) In what sort of materials did Suo et al show the expression of these genes? Were they cultured cancer cells or cancerous tissues of humans?

8. [Discretionary Revisions] In Japanese Americans in the Haiman et al’s study, rs10090154, but not rs6983267, was significantly associated with CRC risk, as stated by the authors. The readers will naturally be interested in possible explanation to the discrepancy in the findings between the two studies of Japanese. Probably it is difficult to provide clear explanation, but some discussion is needed at least referring to the size of odds ratio associated with rs10090154 in the Haiman et al’s study and powers of each study. In this regard, how strong was the LD between the two polymorphism? Cross-tabulation of the genotypes of the two polymorphisms, with numbers of cases and controls and odds ratios presented, would give some thought in discussion.

**Level of interest:** An article of outstanding merit and interest in its field

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

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

**Declaration of competing interests:**

I declare that I have no competing interests.