Reviewer's report

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

Version: 1 Date: 29 April 2009

Reviewer: Albert Tenesa

Reviewer's report:

Dear Dr Matsuo,

please, see below my review of your manuscript.

All the best,
Albert

Matsuo et al. describe a replication study of the association of the 8q24 locus with colorectal cancer in the Japanese population. They report an association with rs698326 of similar size to the one reported by us last year in a Japanese population (Tenesa, Nat Genet. 40:631-636) and show not significant interaction with any of the variables they tested.

I think the paper is interesting but lacks attention to detail which makes the review process very difficult. For example, Table 1 seems missing or, in page 8, there is rs4693267 which one doesn’t know where it came from.

They also miss the publication mentioned above, which reported another SNP within the same LD block to be associated with CRC in a Japanese population.

The first sentence within the second paragraph (Background) seems wrong and does not make sense. For example, MYC is ~340kb from the region, so I am not sure whether the 600Kb the authors mention is just a typo/mistake for 60kb which is the size of the LD block where rs698326 is.

Also, they genotyped rs10090154 because it was associated with a Japanese population in Hawaii. They cite Haiman et al. but as far as I know this association was with prostate cancer and not with colorectal cancer. To my best knowledge only one LD block has been associated with CRC within the 8q24 locus.

In the second line of page 8, the authors state that potential confounders showed no clear difference between cases and controls. Then, what is the rationale to include them in the model? And equally, what is the rationale for testing for an interaction of the SNP with variables with no significant main effects?

I also do not like the recessive/dominant models analysis the authors do since they don’t help to distinguish alternative hypotheses. I think the authors should either test an allelic model (i.e. a model that assumes a proportional and equal increase in risk with each allele and 1 degree of freedom) or a genotypic model (with no assumptions and 2 df). These models are nested and can easily be compared and appropriate effect estimates for the different genotypes given.
Level of interest: An article of limited interest

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’