Reviewer’s report

Title: Case-only study of interactions between metabolic enzymes and smoking in colorectal cancer

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Reviewer: José M. M Ladero

General

In this work the authors have studied the possible relation between some enzymatic polymorphisms related to activation/inactivation of environmental carcinogens and the risk of colorectal cancer, using as a dichotomous criterion the smoking habit of patients. The sample size seems somehow small, as experts in this field have suggested that series smaller than 4 digits should offer non-conclusive results, but as a preliminary study that uses an original focusing I consider that it may be suitable for publication after some amendments.

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

1. Although this is a case-only study, it would be interesting that the authors include some data on the distribution of the studied polymorphisms in the general Han population. The percentage of null GSTM1 genotypes is quite high (58.8%) and, according to the Hardy-Weinberg equilibrium, the supposed allele frequency of the CYP2E1 T allele seems also unexpectedly elevated, indeed for an Oriental population.
2. It should be easier and more informative to express tobacco use as pack-years, reflecting the life-dose of tobacco more than the heaviness or the duration of the smoking habit. Moreover, in this way, the authors could express the tobacco exposure as an unique parameter.
3. The dichotomous division in ethanol drinkers/non-drinkers is too rigid. It seems more adequate to use the daily dose of ethanol, thus classifying patients as non/moderate drinkers (i.e., less than 50 g ethanol a day) or heavy drinkers.
4. The patients were survivors of the studied cohort diagnosed with colorectal cancer. It should be noted that some dead individuals could have died of colorectal cancer, perhaps introducing a bias, as these subjects could have suffered from more aggressive forms of the disease.
5. In page 10, first paragraph, the authors state that SULT1A1 and CYP1B1 pathways “may not be of importance in the metabolic activation of these carcinogens in vivo”. Is this the statement that the authors want to express?

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

The feet for table 2 contains a mistake, as it is quite difficult to smoke alcohol... In some countries it may be inhaled after boiling any spirit, but I think that this is not the case in China.

Not being a native English speaker, I can only recommend a language revision before publishing

Discretionary Revisions (which the author can choose to ignore)

Data on dietary habits could have improved the accuracy of the conclusions. At least the authors should include a comment on this subject. Was the diet in the studied period and in this specific region of China very homogeneous? There were major differences in the intake of meat or in the cooking methods of foods?
What next?: Accept after minor essential revisions

Level of interest: An article of limited interest

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

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