Reviewer's report

**Title:** P53 genetic polymorphisms, interactions with lifestyle factors and lung cancer risk: a case control study in a Chinese population

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**Reviewer:** Virginie Marcel

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The manuscript of Li et al entitled “p53 genetic polymorphisms, interactions with lifestyle factors and lung cancer risk: a case control study in a Chinese population” reported for the first time an association between a novel p53 SNP, rs2078486, and lung cancer risk in specific Chinese sub-populations (smokers, alcohol drinkers and individuals with high indoor air pollution exposure). In contrast, the most studied p53 SNP at codon 72 is not associated with heterogeneity of lung cancer risk but rather with an overall increase in lung cancer risk.

This study is well conducted, well written and most of the conclusions are supported by the data. Only few points need to be taken into account to improve the manuscript.

**Major points**

1- In the study of the interaction between p53 SNP rs2078486 and lifestyle factors (Table 3), the authors used a dominant model in contrast to p53 SNP rs1042522 for which a recessive model has been used. While it is clear why for p53 SNP rs1042522, the authors should add sentence to explain why they use a dominant model in the case of rs2078486.

2- In the Discussion section, authors claim that “this study is among the first to report an increased lung cancer risk associated with variant genotype of p53 SNP rs2078486 in an Asian population. Moreover, we found synergistic effects of smoking and indoor air pollution exposure with p53 SNP rs2078486 on lung cancer risk” (page 9 lines 2-4). While the second sentence fits with the data, the first one is not supported by the statistics since only a tendency is observed between this p53 SNP and increased lung cancer risk in the overall population (as said by the authors page 8 lines 7-9). This sentence should be re-written accordingly.

3- Authors suggested in the Discussion section that p53 SNP rs2078486 can be a functional SNP that affects p53 function. Can the authors give a hypothesis whether this SNP affects p53 function based on p53 SNP location within p53 gene (impact on p53 expression and/or activity)? When sentences are related to p53 functional SNP, the authors should cite the review of Whibley et al (reference 5), the best one reporting the different impact of p53 SNP on p53 expression and activity.

4- There are few inconstancy between p-value given in the text and Table (i.e.
5- Figure legends are needed to understand that Figure 1 corresponds to p53 SNP rs2078486 and Figure 2 to p53 SNP rs1042522. In addition, significant OR should be highlighted on the 2 figures (use bold letters for example).

Minor points
1- Sentences can be added in the Background section to emphasize the fact that only few publications studied p53 rs2078486 in relation to lung cancer risk (Schildkraut et al, Plos One 2010: SNP rs2078486 and ovarian cancer; Yang et al, Neurosci Lett 2004: SNP rs2078486 and schizophrenia in Chinese population).
2- Population types and number of cases/controls should be given when references are made to other case/control studies in the Background and Discussion sections to allow comparison between statistical power of this study with others.
3- Page 9 line 5: Figure 2 instead of Figure 1?

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

Quality of written English: Acceptable

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

Declaration of competing interests:

NA