Reviewer's report

Title: No influence of the MDM2 SNP309 on early onset lung cancer in a Caucasian population

Version: 1 Date: 11 October 2007

Reviewer: Gareth Bond

Reviewer's report:

General
In this report, Mittelsrass et al. combined three different populations of Caucasian lung cancer patients diagnosed below the age of 51 in Germany in order to address the question of whether or not the MDM2 SNP309 locus could effect their risk or age of diagnosis. To estimate risk, the authors recruited 1300 healthy population controls, which were matched by sex and age. They applied conditional logistic models with conditioning on the matched variables of age and sex. This analysis yielded no significant changes in risk of lung cancer between the genotypes of the MDM2 SNP309 locus regardless of gender, histological subtypes or smoking status/exposure. The authors went on to compare the average ages of tumor diagnosis between the genotypes and noted no significant differences. The authors concluded that the MDM2 SNP309 locus is not a sufficient risk factor of lung carcinogenesis. The data in this report are for the most part of high quality, thoroughly analyzed, and clearly presented. However, there are a few concerns that should be addressed before a decision on publication can be reached.

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

1. The authors must further compare and contrast the patient populations they are combining for their analysis. For example, what were the similarities and differences in their patient accruals? Furthermore, in the Results section, the authors must show that the trends they are reporting are similar in all three groups, independently. If the trends are not the same or if the groups differ, this must be clearly shown and discussed.

2. Given the literature of the MDM2 SNP309 locus, the analysis and discussion of the average ages of tumor diagnosis is lacking. The authors state that the G-allele was shown in one previous report to associate with an earlier tumor diagnosis in p53 mutation carriers and sporadic soft tissue sarcomas (1). However, in the past 3 years many other reports have further described this phenotype in many other tumor types (2-10). These reports and their conclusions need to be incorporated into their analysis and discussion. For example, three reports demonstrate in four different sporadic tumor types a gender-dependence of this phenotype. Therefore, the authors must minimally show the mean, median
and range of ages for both women and male patients separately. Along these same lines, the frequencies of the different genotypes of MDM2 SNP 309 must be presented for each gender separately as well.

3. The authors state in the first sentence of their discussion that an increased risk of lung cancer for the G allele of MDM2 SNP309 was seen in one Korean population and two Chinese populations. Later they reason that the differences in ethnicity between their populations may provide a partial explanation for the lack of association in their study. I agree with this statement. However, the authors never directly discuss that if ethnicity plays such a role in these differences why does Lind et al. see a significant increased risk in Caucasian lung cancer patients as well (11)? This must be discussed.

References


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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. The authors fail to properly reference Li et al., 2006 in their discussion.
2. In the last paragraph of the Results section, I believe that “we observed a none significantly lower age” should be “we observed a non-significant lower age…”
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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

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