Reviewer’s report

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

Version: 2 Date: 4 January 2008

Reviewer: Gareth Bond

Reviewer’s report:

Review of the revised manuscript entitled “No Influence of the MDM2 SNP309 on early onset lung cancer in a Caucasian population”

Major Compulsory Revision

In this revised manuscript, Mittelstrass et al. have incorporated the comments and concerns of many reviewers including mine. The authors have adequately addressed my concerns. Unfortunately, the resulting data presented in the revised manuscript lead me to question the main argument(s). Specifically, I had asked that the data and subsequent analysis for each study group be shown separately, as the populations were accrued differently. I had also asked that the two genders be analyzed separately, given the gender-specific effects of this locus previously noted in lung cancer (1) as well as in other tumor types. The data presented in Table 4 seem to show that, in the HLC study group, there could be gender-specific effects on lung cancer risk for this locus. First, there are significant differences in the frequencies of the MDM2 SNP309 genotypes between the genders (p=0.0269, Chi-squared test). Second, there is a significant enrichment of the G/Gs in the female cases compared to the controls (21% vs. 10%, p=0.0233, two-sided Fisher exact test). In fact, if you compare G/G vs. T/T there is an OR of 2.29 for G/G to be in the patient population [CI 1.109-4.762, p=0.02244]. These data could suggest that in this population G/G women could be at greater risk for developing lung cancer. These differences are not seen in the LUCY study population. However, they are very similar to the data published by Lind et al. for Caucasians and therefore cannot be ignored. Unfortunately, I have to conclude that, in their present form and presentation, these data bring into question the validity of the main conclusion of this manuscript that the MDM2 SNP309 locus has no influence on the early onset of lung cancer in Caucasians. I, therefore cannot support its publication. More study seems to be required to understand why these populations differ in order to gain a better understanding of the affect of the MDM2 SNP309 locus on lung cancer.


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.