Reviewer's report

Title: Absence of association between SERPINE2 genetic polymorphisms and COPD in Han Chinese; a case-control cohort study

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Reviewer: Noor Kalsheker

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The study explores the role of five proposed causal SNPs in SERPINE2 in COPD in a Han Chinese population. Three of the causal SNPs show complete linkage disequilibrium but these same SNPs were used in a previously published study by another group that showed an association with COPD. The authors then examined haplotypes of these SNPs. No associations were found with COPD either with individual SNPs or with haplotypes. This is consistent with one previous report for Caucasian populations where no associations were found either with SNPs or haplotypes but in conflict with two reported positive association studies.

In general the study has been well designed and clearly presented. The data are worth reporting but there are some major concerns about the study which should be addressed.

1) The size of the study is modest with 327 COPD and 349 non-diseased smoking controls and could potentially miss weak effects e.g. odds ratios of 1 to 1.5 and some comment needs to be made about this since many genetic factors associated with identified to date tend to be in this range.

2) It is a little disappointing that the authors did not consider studying other SNPs within the SERPINE2 gene with minor allele frequencies of >5% as this would have provided further information about the gene in COPD. There are over 20 SNPs in SERPINE2 with minor allele frequencies >5%. It would be worth knowing in particular whether SNP rs 6734100 is associated with COPD as this was the most significant result obtained by Zhu et al (Amer Rev Respir Crit Care Med 2007). A comment needs to be made to reflect this. It would be unusual, for example, also to study 3 SNPs that are in complete linkage disequilibrium, though the authors chose them as they have been reported previously.

3) The comment about multiple testing is relevant, though the use of a Bonferroni correction may be too stringent and there is some debate over this in the literature. A comment should be included to reflect this.

4) There are a number of better statistical packages available for data analysis though SPSS and PHASE is sufficient for the analyses undertaken. It would have posed some problems potentially if many SNPs were being investigated for example.

5) Some discussion about the quality control of the genotyping is warranted. Although DNA sequencing was used and this is the gold standard for genotyping,
the inclusion of known positive and negative controls in the assays used would have provided additional checks for the accuracy of genotyping.

**Level of interest:** An article of importance in its field

**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.