Reviewer's report

Title: Effect Modification of Air pollution on Urinary 8-Hydroxy-2'-Deoxyguanosine by Genotypes -- an Application of the Multiple Testing Procedure to Identify Significant SNP Interactions

Version: 1 Date: 8 June 2010

Reviewer: Ian Yang

Reviewer's report:

Thank you for inviting me to review this interesting paper.

Gene-environment interaction is likely to influence an individual’s response to air pollution, and subsequent development of adverse effects and acute or chronic disease.

This gene-environment study addressed the role of SNPs in oxidative stress genes, in modifying levels of 8OHdG in people exposed to ambient air pollution.

The strengths of the study included a large, well-characterised population; rational selection of candidate genes; robust genotyping and detailed statistical analysis including controlling for a range of confounders and accounting for multiple comparisons.

A number of issues should be addressed:

Major Compulsory Revisions

1. Abstract: It would be useful to include (1) the number of SNPs and genes tested (20 SNPs in 9 genes), and (2) the number of participants in the Abstract Results, to give an idea about the size of the study.

2. Background: In the last paragraph of the Background, it is stated that ‘the selection of certain genes is somewhat arbitrary’. Given this rationale, it would be useful in the Genotypes section of the Methods to provide further detail about the selection of the genes in this study, particularly the criteria of ‘data available to examine effect modification’ (Page 8).

3. Methods: The statistical analysis is given in good detail, particularly about the novel methods implemented. Further details about the level of statistical significance used (a threshold of 0.1 is indicated in the Results for interactions) and the power of the study would be helpful.

4. Results and Tables: (a) For some of the Results presented, it is not clear whether the data are in the Tables and Figures, or not shown e.g. ‘Results show that main effects varied across different day moving averages and 20-, 24-and 18-day moving averages were strongest associated with SO42-, OC and maximal 1-hour O3, respectively, which were used to assess effect modifications’ (Page 11); ‘Similar trends were found in spite of some variations’ (Page 12). The
authors should clarify these.
(b) The data for the SNPs without interactions do not appear to be presented e.g. HFE, HMOX etc. Although no association was found, ideally this paper should provide quantitative data about these.
(c) For the Table 1 Demographics, it would be clearer if the clinical demographics were presented first, then the biomarker measurements. Furthermore, the gender of the subjects should be summarised.

5. Discussion: Whilst provided in excellent detail, the flow of the candidate gene paragraphs could be improved in some areas, particularly the catalase and GC paragraphs.

Minor Essential Revisions

6. HGNC/HUGO gene symbols – for gene names, these are usually given in italics – would suggest amending throughout the manuscript.

Discretionary Revisions

7. Page 5: ‘However, the selection of certain genes is somewhat arbitrary and the use of an array of genes is vulnerable to multiple comparisons, a huge issue in genetic association study.’ – perhaps amend to ‘a major issue in genetic association studies’
8. Page 7: amend spelling of spectrophotometric
9. Abstract – ‘in R modified by out team’ – amend to our team
10. Reference 5: check: Williams GM should be Williams GM?

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

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

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'