Reviewer’s report

Title: The association between the angiotensin-converting enzyme-2 gene and blood pressure in a cohort study of adolescents

Version: 1 Date: 7 February 2013

Reviewer: Barry Palmer

Reviewer’s report:

The manuscript describes a study of 555 adolescents recruited as part of the Nicotine Dependence in Teens (NDIT) cohort study from schools in Montreal. Participants with 3 blood pressure measurements taken longitudinally over 5 years of follow-up were included in this study and genotyped for 4 tag SNPs in the ACE2 gene, which has been implicated in BP regulation. Association between SBP, DBP and change in BP over time and SNP genotyped was tested. Three of the SNPs were found to be significantly associated with BP or change in BP in at least one of the gender/ethnic groups examined.

Major Compulsory Revisions

1. What was the justification separating participants of French Canadian and European descent in the ethnic stratification? Is there evidence from other studies of significant genetic heterogeneity between these groups? If not, the loss of statistical power is undesirable.

2. Page 9/para 2/line 1
The statement is made: Over half (53%) the participants were male (Table 1). However this doesn’t agree with the data in Table 1. Am I missing something?

3. Page 10/Para 2
Can the authors offer any explanation for the large difference in allele frequencies for rs2074192 between males and females in the French Canadian and Other ethnicity groups? Given all four SNPs were in Hardy-Weinberg Equilibrium in females this seems an unusual finding.

4. Page 12/para 1/ line 1
While none of the SNPs were associated with either SBP or DBP in females (data not shown)...
This statement appears to contradict with Para 1 Page 11.
Was this referring to data after adjustment for height and whether or not the participant was overweight or obese? If so this needs to be made clear.

• Discretionary Revisions
Given the source of the participants was the NDIT cohort was any analysis made of nicotine exposure and its relationship to BP and ACE2 genotype?
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