Reviewer's report

Title: Resequencing PNMT in European hypertensive and normotensive individuals: no common susceptibility variants for hypertension and purifying selection on intron 1.

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Reviewer: David E Comings

Reviewer's report:

General
This is a well-executed study of the hypothesis that genetic variants at the PNMT gene, that codes for phenylethanomamine-N-methyltransferase and is responsible for the conversion of norepinephrine to epinephrine, might play a role in human essential hypertension. To examine this out they recruited 25 Estonians and 25 Czechs with essential hypertension, and 25 Estonian and 25 Czech controls. The PNMT gene, including the 5¹ and 3¹ regions were sequenced in these individuals. In silico prediction of transcription factor-binding sites for intron 1 was also carried out.

They found that the human PNMT gene was characterized by a minimum of variation in both the hypertensives and controls and that none of the SNPs varied in frequency either between ethnic groups or normals versus hypertensives. This low diversity was felt to be consistent with conservation of the PNMT sequence.

Other Comments:
On page 10 the authors state that using Fisher¹s exact test none of the polymorphisms observed showed either allelic or genotypic differentiation among Estonians and Czechs controls or hypertensives. However, in Table 2 the allele and genotype frequencies for the different SNPs in Estonians versus Czechs and normotensives versus hypertensives are given. The data for the 5¹UTR GA frequency for the A/G SNP was: Estonian normotensives = .40, Estonian hypertensives = .68, Czech normotensives = .44, Czech hypertensives = .68. Since there were 25 subjects in each group this gives an n of 10 vs 17 for the Estonian normotensives vs hypertensives, and 11 versus 17 for the Czech normotensives vs hypertensives. For normotensive vs hypertensive the totals are 21 vs 34. This gives a Fisher Exact chi square of 6.828, p = .0045. Thus, either this table is wrong or the conclusion of the paper that there were no significant differences between the normotensive vs hypertensive subjects is wrong. This clearly needs clarification.

Minor comments. There were a few minor corrections.
P 4 line 7: ³has reported² should be ³has been reported²
P 10 line 7: ³in contrast, upstream² should be ³in contrast, the upstream²

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

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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