Reviewer's report

Title: Polymorphisms of the insertion / deletion ACE and M235T AGT genes and essential hypertension: surprising new findings and meta-analysis of data

Version: 2 Date: 7 November 2004

Reviewer: Kristina Bengtsson Bostrom

Reviewer's report:

General

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

Discussion:
There is a large proportion (65%) of patients with kidney disease (and renal hypertension?) in the current study. This could influence the interpretation and discussion of the results of the AGT235 polymorphism in relation to other studies. The mechanisms leading to hypertension might be different in patients with kidney disease compared with the mechanisms leading to essential hypertension. Further, could the AGT235 T allele and/or the TT genotype confer a higher mortality in patients with kidney disease compared with younger healthy blood donors and thus be rarer in those patients? This should be discussed.

I don't understand the newly added sentence (third paragraph of discussion) about the recessive inheritance pattern of the AGT235 T allele. The trait hypertension could be recessively inherited but the alleles are randomly picked from the parents.

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

Methods:
The restriction enzyme name should be written in italics.

Figures:
In all figures the p-values (at least those < 0.05) should be inserted. The f(D)/f(T) denominations should be explained in a footnote.
The manuscript should be scrutinized to find inconsistencies in labelling such as using “OR” in stead of “odds ratio” consequently.
The reference numbers in figure 4 (meta-analysis) are still missing.

Discretionary Revisions (which the author can choose to ignore)

Background:
Reference # 4 is available online and it would be helpful for the reader if the link is included in the reference list.
Methods:
The term K/DOQI stage 5 should be explained. The genotyping process is now described in detail. Genotyping of the ACE I/D polymorphism is probably performed by PCR only and not by RFLP analysis as stated in the first sentence in the paragraph under the subheading Genotyping. Have insertion specific analysis been performed to exclude mistyping of DD genotype of ACE I/D polymorphism? (Shanmugan et al 1993).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None