Reviewer's report

Title: Association between -T786C NOS3 polymorphism and resistant hypertension: A prospective cohort study

Version: 1 Date: 31 March 2009

Reviewer: jessica caprioli

Reviewer's report:

The authors studied the NOS3 gene in a population of hypertensive patients that were grouped in two subpopulations based upon their responsiveness to therapeutic plan.

Major Compulsory Revisions

The selection criteria are clear, however no indications are given about the various therapeutic regimens that patients received nor, at least, about the first choice drug that was used, an information that might be important in order to correlate the genetic background with the responsiveness to therapy. The studied subpopulations comprise respectively 48 resistant hypertensive patients and 232 responsive patients. (Of note, table 1 includes 254 controlled hypertension subjects. Could you explain this discrepancy?).

The author studied two well known polymorphisms and both ID SNPs code and information on the allelic distribution in a Caucasian control population should be included.

It should be worth to enlarge the group of resistant hypertension patients in order to enhance the statistical power of the study, or at least to provide information about the statistical power of the population studied.

From a strictly statistic point of view, the authors used chi square and Fisher’s exact test to compare the subgroups of patients, however, a correction for multiple tests should also be included, since more than one polymorphism has been studied. It should be relevant to combine the two polymorphisms and to reconstruct the haplotype, if the linkage disequilibrium pattern allows it, as the two polymorphisms are quite near one to the other.

In the logistic regression analysis the authors should also include systolic-diastolic BP as confounding factors.

However, the most important point is that the authors need to analyse at least a second population of hypertensive patients in order to confirm their findings.

Minor Compulsory Revisions

It should be worth to analyse also the allelic distribution of other polymorphic variants that are known to influence the development of hypertension (such as,
for example ACE I/D genotype) and other new genes emerging from WGAS (Whole Genome Association Studies).

Should the influence of the polymorphism of NOS3 be confirmed, the authors need to emphasize the possible clinical implications, such as modifications in management and/or personalization of the approach to patients.

Although the paper does not seem to add much information on the comprehension of the causes of resistant hypertension and it provides only a weak cause-effect relationship between the disease and one polymorphism, it could be reconsidered for publication after major revision.

**Level of interest:** An article of limited interest

**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.