Reviewer’s report

Title: STK39 polymorphisms and blood pressure: an association study in British Caucasians and assessment of cis-acting influences on gene expression

Version: 1 Date: 18 September 2009

Reviewer: Maris Laan

Reviewer’s report:

Reviewer’s comments
Michael S Cunnington, Chris Kay, Peter J Avery, Bongani M Mayosi, Mauro Santibanez Koref and Bernard Keavney “STK39 polymorphisms and blood pressure: an association study in British Caucasians and assessment of cis-acting influences on gene expression” Submitted to BMC Medical Genetics

Major Compulsory Revisions
Introduction
REQUEST:
1. When describing the original study by Wang et al (2009) reporting association with STK39 and blood pressure, please include also the following information:
   – Population history and demographic specificities of the Old Order Amish religious isolate
   – sub-phenotype of the study sample used for GWAS (Amish Family Diabetes Study)
2. Please include a brief comparison of the primary (AFDS) and the replication sample used in the current study

REMARKS: It is noteworthy that in the original study, the significant associations were obtained only in the two samples sets (AFDS, DGI) primarily recruited to address the genetics of T2D.

Usually the replication sample is attempted to choose as similar as possible to the original sample. As the current study sample (large family-based Caucasian cohort ascertained through probands with essential hypertension) differs from the set-up of the Wang et al study, this may be one reason for the non-replication of the association.

Methods, Table 1
REQUEST:
Please provide more detailed clinical characteristics and phenotype description in “Participants” and Table 1.
   – definition of hypertension and normotension in the current study (Methods)
– characteristics of the study sample (Table 1): age, % male/female, cardiovascular medication, alcohol consumption, exercise habits
[all these parameters were used as covariates in association analysis, but the data has not been provided]
– definition of “Clinic SBP, DBP; Day SBP, DBP; Night SBP, DBP” (footnotes of Table 1, 3 or Methods)
[as these are the main phenotypes in this study, referring to a previous study by Palomino-Doza et al (2008) is insufficient, since this is not an open-access article]

Discussion
REQUEST:
Please discuss briefly how the non-replication of the association between SNPs in STK39 and blood pressure in the current study could result from the differences in population history, as well as from the differences in recruitment and phenotype of the subjects in the primary (Wang et al 2009) and in the presented replication study.

Minor Essential Revisions
1. I did not find in the main manuscript text any references to Supplementary Methods and Supplementary Tables.
2. p.11 in “Discussion” the study sample has been referred as “the British Caucasian cohort”, which may be confusing as this is not a traditional population cohort (in Methods: large family-based Caucasian cohort ascertained through probands with essential hypertension)

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