Reviewer's report

Title: Genome-wide association study identifies single-nucleotide polymorphism in KCNB1 associated with left ventricular mass in humans: The HyperGEN Study

Version: 2 Date: 20 September 2008

Reviewer: Nicole L Glazer

Reviewer's report:

A clear and concise paper on a GWAS of LV mass and LV hypertrophy.

Major Compulsory Revisions

1) Discussion, page 9: The authors refer to a "joint P-value", calculated as Pgwas * Prep. This calculation is not appropriate nor is it mentioned anywhere previously in the methods or results. It is also not clear what SNP they are referring to here. This sentence should be removed.

Minor Essential Revisions

1) Background, par 2: The phrase "SNPs with promising significance" is vague and lacks meaning. Do the authors mean statistically significant SNPs (as determined by an a priori threshold) or just top SNPs?

2) Results: There was 1 SNP that had different MAF in the replication sample than in GWAS sample. How different? If it is quite different, it could indicate a genotyping error.

3) Results: The authors only present p-values in the text and in the tables. Inclusion of betas (or ORs) and SEs are appropriate, particularly in the table to allow the reader to see the direction and size of effect in the GWAS and replication populations. The text refers to a figure showing effect sizes, but no such figure was in the manuscript.

Discretionary Revisions

1) Methods: Authors note that they adjust for age, sex, weight, SBP and DM. Was height not available?

2) Inclusion of population attributable risks could be of interest.

3) Were any principal component analyses conducted to determine whether there was any significant population structure beyond self-reported race? If so, please indicate.

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Regarding non-financial competing interests: I am currently working on a genome-wide association study of echo traits in another study. I have also worked with the first author, Donna Arnett, on another project unrelated to this paper.