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:** 19 September 2008

**Reviewer:** Sumeet Chugh

**Reviewer's report:**

In this interesting paper, Arnett and colleague report findings from a 2-step association study that seeks to identify genomic determinants of left ventricular hypertrophy. In the first step a GWAS (Affymetrix 100K chip) was conducted by comparisons between 101 vs 101 caucasians with the highest and lowest height-normalized LV mass (ASE equation). A total of 12 SNPs were identified that had q-values<0.8. These were genotyped separately among the Caucasian and African American subgroups of the population. Five SNPs were identified that were significantly associated with increased LV mass, three among Caucasians and two among African Americans.

The identification of a KCNB1 SNP associated with increased LV mass is an important one and potentially implicates a gene that has an established mechanistic role in a pathway that may be involved in development of LVH.

Discretionary Revisions:

1. Were any of the 12 SNPs significantly associated in the combined population (white and African American)?

Minor Essential Revisions:

1. Would clarify the distribution of numbers of patients early in the Study Population section. Would make it easier for readers.

2. Methodology – would describe the approach as a GWAS followed by a validation study (as opposed to “two-step GWAS”. At present this portion of the paper could be written in a more clear manner.

3. Typo “populations” second last line page 8.

4. The Background section mentions 7 significant SNPs in stage 2 but later, in Results there is mention of 5 significant SNPs – would clarify for consistency.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests