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

BACKGROUND: We conducted a genome-wide association study (GWAS) and validation study for left ventricular (LV) mass in the Family Blood Pressure Program-HyperGEN population. LV mass is a sensitive predictor of cardiovascular mortality and morbidity in all genders, races, and ages. Polymorphisms of candidate genes in diverse pathways have been associated with LV mass. However, subsequent studies have often failed to replicate these associations. Genome-wide association studies have unprecedented power to identify potential genes with modest effects on left LV mass. We describe here a GWAS for LV mass in Caucasians using the Affymetrix GeneChip Human Mapping 100 k Set. Cases (N = 101) and controls (N = 101) were selected from extreme tails of the LV mass index distribution from 906 individuals in the HyperGEN study. Eleven of 12 promising (Q < 0.8) single-nucleotide polymorphisms (SNPs) from the genome-wide study were successfully genotyped using quantitative real time PCR in a validation study.

RESULTS: Despite the relatively small sample, we identified 12 promising SNPs in the GWAS. Eleven SNPs were successfully genotyped in the validation study of 704 Caucasians and 1467 African Americans; 5 SNPs on chromosomes 5, 12, and 20 were significantly (P < or = 0.05) associated with LV mass after correction for
multiple testing. One SNP (rs756529) is intragenic within KCNB1, which is dephosphorylated by calcineurin, a previously reported candidate gene for LV hypertrophy within this population.

**CONCLUSION:** These findings suggest KCNB1 may be involved in the development of LV hypertrophy in humans.

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