Genomic Association Analysis Identifies Multiple Loci Influencing Antihypertensive Response to an Angiotensin II Receptor Blocker

To the Editor:

The interesting article by Turner et al 1 concerns the pharmacogenomics of the angiotensin receptor blocker Candesartan and the validation of the associated single-nucleotide polymorphisms by their opposite direction associations with blood pressure response to hydrochlorothiazide.

We are also performing a pharmacogenomic study of the angiotensin receptor blocker Losartan 2 and hydrochlorothiazide in a slightly larger sample of white-only, essential hypertensives, carefully recruited and followed up by the Italian Network for Pharmacogenomics of Hypertension over several years. All patients have been genotyped within the HYPERGENES project. 3 The major differences between our and Turner’s study are as follows: (1) the genotyping array: missing genotypes were obtained by imputing (imputation quality ≥ 87%); (2) we used Losartan 50 mg instead of Candesartan 16 to 32 mg, hydrochlorothiazide dose being the same (results in the Table). The major limitation of both studies is the small sample size, leading to low statistical power. Also, if the bulk of our data are still under analysis, we have not been able to reproduce Turner’s specific findings.

The present negative report is not at all against the importance of pharmacogenomics. It only poses a warning on the technical and methodological issues and indicates the absolute need of large consortia that share results to produce solid results.

Sources of Funding

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Table. Data From the INPH. Genotyping Array: Illumina 1M

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<thead>
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<th>Markers Information</th>
<th>ARB-Italy</th>
<th>HCTZ-Italy</th>
<th>Frequency</th>
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</table>

INPH indicates Italian Network for Pharmacogenomics of Hypertension; ARB, angiotensin receptor blocker; HCTZ, hydrochlorothiazide; SNP, single-nucleotide polymorphism; Chr, Chromosome; r² values, which indicate imputation quality, are missing for nonimputed SNPs.

Data analysis as in reference 1. The first 10 principal components, age, and sex considered as covariates. To exclude any carry-over effect, only hypertensives that had been untreated for hypertension were recruited.
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