In this issue of the Journal, Yamada et al present their article “Assessment of the Genetic Component of Hypertension.”1 The manuscript describes the results of genotyping and association testing for 150 polymorphisms in 128 genes in a Japanese case-control study of hypertension. The ethnic homogeneity of the sample and large sample size were strengths of this study. The authors identified four single-nucleotide polymorphisms individually associated with hypertension, three of which continued to be associated when combined in a multivariate model. The combination of carrying a minor allele at ITGA2, a minor allele at GCK, and two common alleles for PTGIS resulted in a reduced odds of hypertension with an odds ratio estimate of 0.47. The authors suggest that assessment of this combination of alleles may contribute to personalized prevention, but they report a prevalence of 1.1% in hypertensive subjects and 2.0% in control subjects. All of the combined genotypes presented in Table 4 of their article had estimated odds ratios of <1.

The combination of alleles that would produce an increased risk of hypertension is the common allele homozygotes across all three single-nucleotide polymorphisms compared with carriers of any minor allele. This combined common allele multilocus genotype is present in 38.6% of hypertensive subjects and 33.2% in control subjects and the crude odds ratio estimate is 1.27 (95% confidence interval 1.14, 1.44). The investigators have chosen to focus their reporting of results on a rare protective genotype combination, the identification of which in the individual would not necessitate preventive action. Instead, the potential for an assessment of the genetic component of hypertension arises from the observation that combinations of common alleles confer an increased risk of hypertension. Further replication and validation of the finding is needed5; results from other ethnic groups may shed light on the genetic heterogeneity of hypertension and the generalizability of the finding. Assessment of whether these polymorphisms, or ones in linkage disequilibrium with them, are driving the association is also needed. Nonetheless, the authors have added an intriguing new result to the frustratingly inconsistent field of hypertension genetics.4

References