**Letter Regarding Article by Burke et al, “Role of SCN5A Y1102 Polymorphism in Sudden Cardiac Death in Blacks”**

*To the Editor:*

We would like to comment the article by Burke et al., who reported in a postmortem study a genetic association of the SCN5A Y1102 allele (or Y1103, for the long-splice variant) and patients with sudden cardiac death in the black population (107 noncardiac control samples, 117 with organic heart disease, 40 with cardiac hypertrophy, and 25 with cardiac arrhythmias). Because of the presence of clearly differing allele frequencies, it was concluded that the Y1102 allele might represent a marker for sudden cardiac death in patients with cardiac hypertrophy or arrhythmias, respectively. Previously, another article reported that the SCN5A Y1102 allele might be a risk factor for abnormal repolarization and ventricular arrhythmia occurrence. However, in this study, a gene-dosage effect of the Y1102 allele on the QT interval was not seen in the reported pedigree. The study by Burke et al also touches on the role of the Y1102 allele as an arrhythmia risk factor. Even though the allele distribution was found in the Hardy-Weinberg equilibrium, the power of the case-control study appears to be underpowered. We estimated the needed samples size using the Genetic Power Calculator, assuming 6 heterozygotes in control subjects (n=107; Y1102 allele frequency: 2.8%), 8 in group 3 (n=40; Y1102 allele frequency: 10%), and 7 in group 4 (n=25; Y1102 allele frequency: 14%). For a power of 80% and α=0.05, the needed sample size for group 3 would be 70 and for group 4 52. Therefore, conclusions about potential roles of (ion channel) polymorphisms should be drawn in the setting of powerfully designed studies and confirmatory data. It is likely that future genetic studies resolving current problems of association studies will shed additional light on the modification of arrhythmia susceptibility by natural gene variance.

**Disclosures**

None.

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**Response**

We appreciate Dörte and Schulze-Bahr’s comments about our article. The statistics in our study used standard methods which, although valid, were not specific for calculating significance of differing allele frequencies. Therefore, we agree that confirmation of our findings in a larger group of patients and with family studies is essential in further substantiating our findings, which were initially suggested by Splawski et al. We believe that there are a variety of methods for determining the role of mutations in sudden unexplained death in the absence of morphological substrates. Despite the limitations of autopsy studies, including relatively small numbers of rare events, complete cardiac morphological evaluation offered by autopsies represents, in our opinion, invaluable data for testing hypotheses regarding the link between genetic variations and lethal arrhythmias.

**Disclosures**

None.

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