Activating Mutation of the Renal Epithelial Chloride Channel ClC-Kb Predisposing to Hypertension

To the Editor:

We write with respect to the article “Activating Mutation of the Renal Epithelial Chloride Channel ClC-Kb Predisposing to Hypertension” by Jeck et al.1 The authors state that this naturally occurring ClC-KbT481S variation is at position 1441 in the gene accession number NM 000085.1 (altering base A to T). We wish to report agreement with the gene frequency for this polymorphism in a South Australian population. However, we note a discrepancy in the gene position assigned to the allelic variant declared in their paper. The correct position is at 1475 in the same gene accession sequence.2

This position was determined when our initial efforts to reproduce the findings of the article failed to find this polymorphism at position 1441 in a cohort of our population. The ClC-Kb genotype was determined with an allele-specific polymerase chain reaction (PCR) used previously.3 This PCR method only extends a sequence if it matches at the 3-prime base (ie, position 1441). This gave PCR product only for the wild type (A) primer, and nothing for the putative 1441(T) mutant. We re-examined the article by Jeck et al and, using the sequence that they published for their primers, found a matching DNA sequence corresponding to a polymorphic site at position 1475 in NM 000085.1.2 A change in our primers to an 18-base sequence, ending at position 1475, succeeded in producing appropriate results for both A and T primers.

We then analyzed the ClC-KbT481S polymorphism in whole genomic DNA samples from a total of 297 control individuals, representing a random selection of people from the South Australian population in the greater Adelaide Metropolitan area who were free of cardiovascular disease. We determined the overall mutant (T) allele frequency to be 14.1% in this population with a prevalence of 25.6% heterozygous and 1.3% homozygous TT individuals. This agrees closely with the data obtained by Jeck et al in 3 Caucasian German population groups (which, when combined, had an average T allele frequency of 12.4%, with 20.4% heterozygous and 2.2% homozygous TT).

We also note a separate but less important error in Table 1 of the article, where the totals (and frequencies) of the A and T alleles are reported by Jeck et al for their Group 3 Southern Bavarian volunteers. These were given as 483 (86.0%) and 79 (14.1%), but should be 547 (87.4%) and 79 (12.6%) respectively, calculated from the data they reported for 313 volunteers.

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