

Supporting Information

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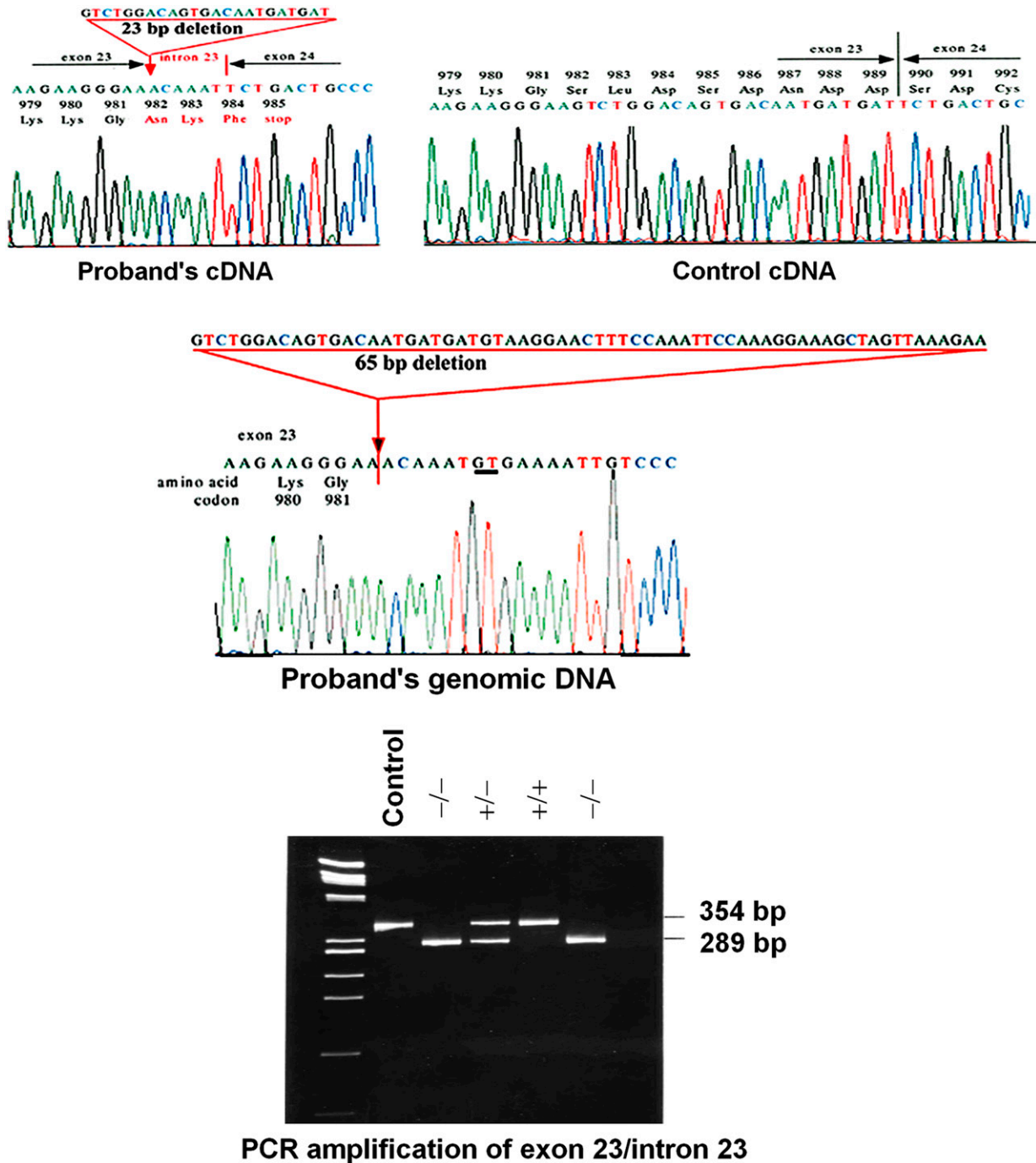


Fig. S1. Mutational analysis of the SLC4A4 gene. The proband's NBCe1A cDNA (top left of figure) shows a deletion of 23 bp at the end of exon 23 and an insertion of 6 bases (ACAAAT) from intron 23, followed by translation of exon 24. The control NBCe1A cDNA is also shown (top right of figure). The proband's genomic DNA (middle of figure) shows a deletion of 65 bp (23 bp from exon 23 and 42 bp from the flanking intron 23). The underlined GT is used as a new splicing donor site, which explains the translation of exon 24 after the 6 inserted bases (ACAAAT) in the proband's cDNA. PCR amplification of the exon 23/intron 23 boundary (bottom of figure) identifies family members with the homozygous mutation (–/–), the heterozygous mutation (+/–), and without the mutation (+/+).

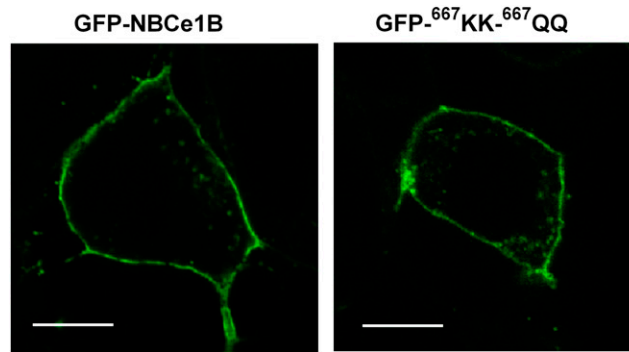


Fig. S2. Confocal images of GFP-tagged wild-type NBCe1B and the ⁶⁶⁷KK-⁶⁶⁷QQ mutant transiently expressed in HEK293 cells. Scale bars, 10 μ m.

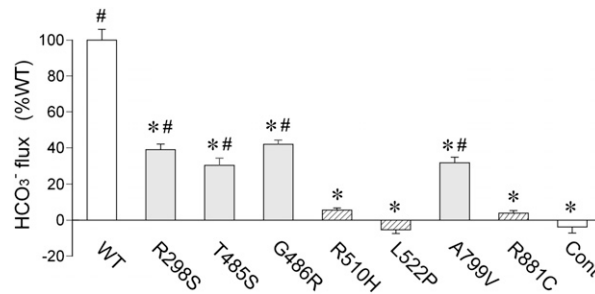


Fig. S3. Summary data for the functional analyses of NBCe1B mutants in HEK293 cells. # $P < 0.01$ vs. wild type (WT). * $P < 0.01$ vs. Control (Cont). Hatched bars indicate the mutations associated with migraine, and gray bars the mutations not associated with migraine. Numbers observed were 24 (WT), 8 (R298S), 8 (T485S), 10 (G486R), 11 (R510H), 11 (L522P), 8 (A799V), 11 (R881C), and 11 (Cont).

Table S1. Clinical phenotypes of NBCe1 mutations

Mutations	Sex	Blood HCO_3^- (mM) ¹	Short stature	Glaucoma	Membrane expression (NBCe1B)	Migraine	Migraine phenotypes
Q29X	F	9.4	Yes	Yes	Yes	No	
R298S	F	8	Yes	Yes	Yes	No	
T485S	M	13	Yes	No	Yes	No	
G486R	F	10	Yes	No	Yes	No	
A779V	F	6.3	Yes	Yes	Yes	No	
R510H	F	5	Yes	Yes	No	Yes	MO
L522P	M	Not reported	Yes	Yes	No	Yes	Hemiplegia ataxia
Δ 2311A	M	13.2	Yes	Yes	No	Yes	MA
R881C	F	10.6	Yes	Yes	No	Yes	MO
Δ 65bp III:3	F	17.3	No	Yes	No	Yes	Hemiplegia
Δ 65bp III:5	F	14.8	No	Yes	No	Yes	Hemiplegia stupor

MO, migraine without aura; MA, migraine with aura.

¹Normal value = 24.