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SUPPLEMENTAL FILES

Supplemental Figure 1. Helical wheel representation of amino acids in transmembrane segment DIVS6. Twenty amino acids from the wildtype and mutant sequence are represented by the output from the helical wheel projection program www.rzlab.ucr.edu/script/wheel/wheel/cgi) (Zidovetzki et al., 2003). The strength and direction of the hydrophobic moment is indicated in the center of the wheel and represented by the black arrows.

Supplemental Figure 2. Behavior of *Scn8a*$^{9J/+}$ heterozygous mice and wildtype littermated controls in the open field test. The distance traveled was lower for heterozygous mutant mice in the novel environment but not in the familiar environment. Total distance traveled did not differ between heterozygous mutant and wildtype mice.

Supplemental Figure 3. Alignment of DIVS6 from Nav1.6 with two bacterial sodium channels. Amino acid sequence of transmembrane segment DIVS6 from mouse $Na_v1.6$ is aligned with the mammalian channels rat $Na_v1.2$, mouse $Na_v1.4$, human $Na_v1.5$, and the bacterial sodium channels NavAb (*Acrobacter butzleri* RM4018) and NavMs (*Magnetococcus marinus MC-1)*. Dots represent sequence identity. Except for $Na_v1.6$, the Clustal alignments are taken from (Payandeh et al., 2011; Zhang et al., 2012; Bagneris et al., 2015)

Supplemental Figure 4. $Na_v1.6\Delta1750$ is not detectable at the axon initial segment (AIS) of cortical neurons at 20 months of age. Layer II/III of the visual cortex from 20 month old mice were immunostained using anti-Ankyrin G (red) and anti-$Na_V1.6$ (green). AnkG-Nav1.6 colocalized to the distal AIS in wild-type mice (top right), while AnkG-$Na_V1.6$ co-localization was absent in ΔI/ ΔI mice (bottom right). Eight micron optical sections are shown as sum intensity z-stack of 23 slices. Scale bar, 10 microns.

Supplemental Video. Movement disorder in *Scn8a*$^{9J/9J}$ mice is more severe than in the hypomorphic *Scn8a*^{medJmedJ} mice. The *Scn8a*$^{9J/9J}$ mouse (black) at 6 months of age is active and mobile. The hypomorphic *Scn8a*^{medJmedJ} mouse (agouti) of the same age is immobile and cannot support his weight.