



## **Supplemental Material to:**

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**A uniquely adaptable pore is consistent with NALCN being  
an ion sensor**

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**Figure S1.** Alignment of the voltage sensor (segments S1-S4) in all four homologous Domains (DI, DII, DIII, DIV) between all six known 4x6TM family members from the snail *Lymnaea stagnalis* (LNALCN, LNav1, LNav2, LCa<sub>v</sub>1, LCa<sub>v</sub>2 and LCa<sub>v</sub>3) and sample human homologs, hNALCN, hNav1.1 and hCav1.1. Illustrated are basic residues (in red color), acidic residues (in blue color), and “portal gate” residues (in green color). A conserved amphipathic S4-S5 linker (gray colored residues) couples S4 voltage-sensor movements to gating of voltage-gated channels. NALCN has fewer charged residues in S4 segments (white on black numbers) like specialized, non-conductive Na<sub>x</sub> channel. All 4x6TM channels have conserved counter-charges (black on white numbers) in S2 and S3 segments which are required for the mobility of the voltage-sensor. NALCN also appears to have a conserved S4-S5 linker.