

Supplemental Material to:

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

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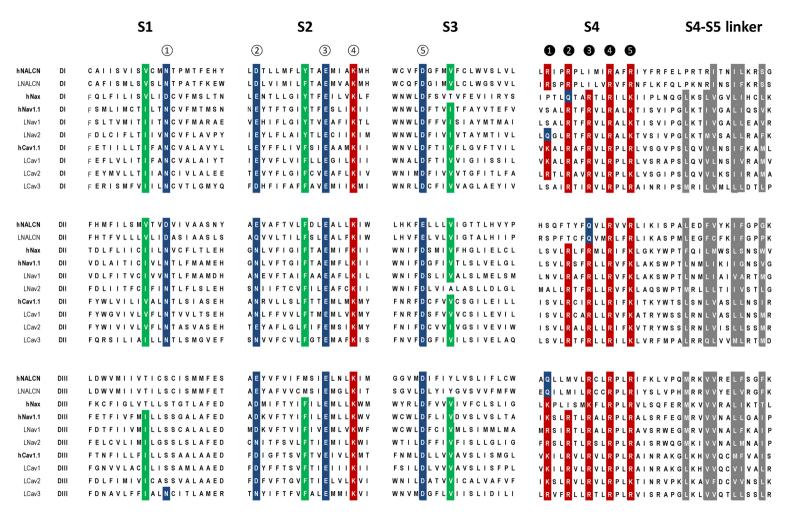


Figure S1. Alignment of the voltage sensor (segments S1-S4) in all four homologous Domains (DI, DII, DIII, DIV) between all six known 4x6TM family members from the snail *Lymnaea stagnalis* (LNALCN, LNa_v1, LNa_v2, LCa_v1, LCa_v2 and LCa_v3) and sample human homologs, hNALCN, hNav1.1 and hCav1.1. Illustrated 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_x 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.