Selective Toxicity of the Anthelmintic Emodepside Revealed by Heterologous Expression of Human KCNMA1 in *Caenorhabditis elegans*

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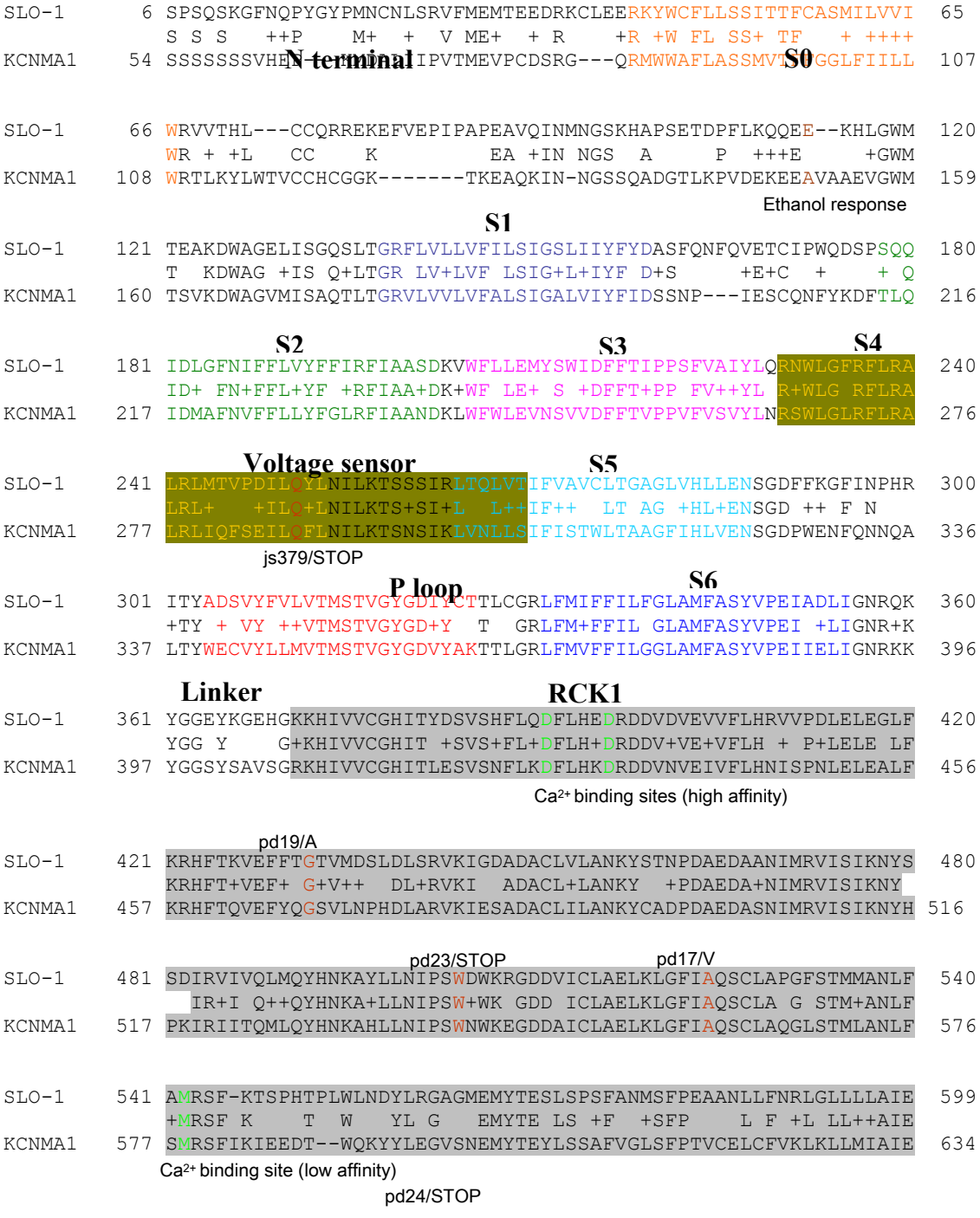
Molecular Pharmacology

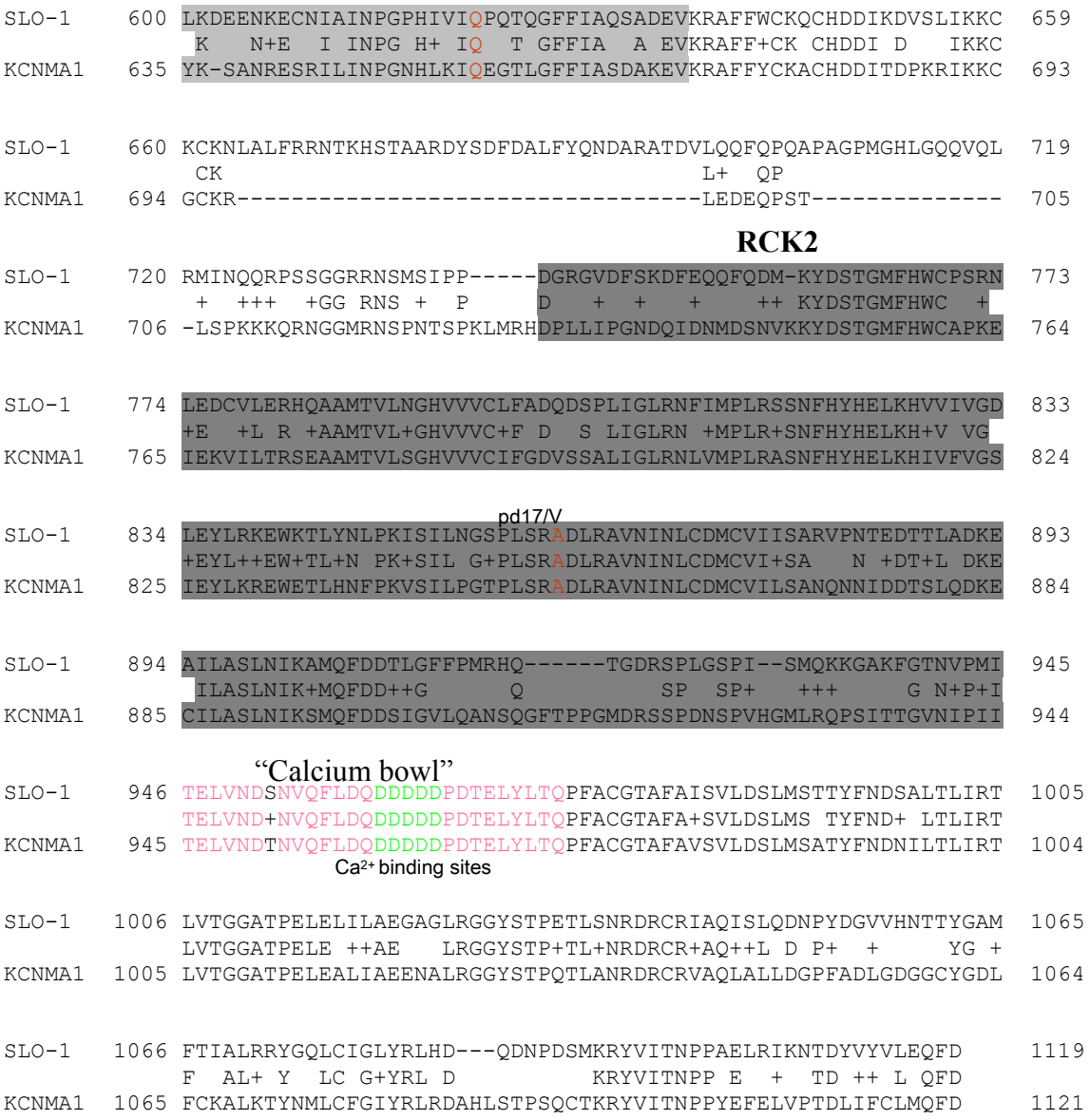
Supplementary Information S3.

Figure S3. Alignment of the amino acid sequences of *C. elegans* SLO-1a and human KCNMA1 (isoform b) using BLAST (NCBI; method compositional matrix adjust).

The alignment shows 55% identity and 69% similarity/positives between the two sequences. Identical amino acids are indicated by their letter symbols and amino acids where side chains have similar physicochemical properties are indicated by "+". Gaps are indicted by "---"symbols and were introduced by the program algorithm (7% gaps) to enable analysis of the most conserved parts of the sequences. The sequences have been annotated with the following features; 'S0' to 'S6' are the transmembrane domains; 'voltage sensor'; 'P loop' is the pore domain; 'RCK1' and 'RCK2' are two domains that regulate the conductance of the potassium channel; 'Linker' is the domain between 'S6' and 'RCK1' and the length of this sequence alters the gating of the channel (Jiang Y, Lee A, Chen J, 2002: Crystal structure and mechanism of a calcium-gated potassium channel. Nature 417, 515-522); 'Calcium bowl' harbours calcium binding sites. The *slo-1* sequence has been annotated with the

location of the mutations which have been described to confer emodepside resistance (*js379, pd17, pd19, pd23, pd24*; Guest M, Bull K, Walker RJ, Amliwala K, O'Connor V, Harder A, Holden-Dye L, Hopper NA. 2007. The calcium-activated potassium channel, SLO-1, is required for the action of the novel cyclo-octadepsipeptide anthelmintic, emodepside, in *Caenorhabditis elegans*. Int J Parasitol 37:1577-88).




RCK2
pd17/V
"Calcium bowl"
Ca²⁺ binding sites