

<i>C. elegans</i>	L-type	EGL-19
<i>L. stagnalis</i>	L-type	
<i>H. sapiens</i>	L-type	CACNA1C
<i>H. sapiens</i>	L-type	CACNA1S
<i>C. elegans</i>	P/Q-type	UNC-2
<i>L. stagnalis</i>	P/Q-type	
<i>H. sapiens</i>	P/Q-type	CACNA1A

PWIYFVTLVIL**GSFFVNLVLGVLSGEFS**
 PWIYFISLIII**GSFFVNLVLGVLSGEFS**
 PWIYFVTLIII**GSFFVNLVLGVLSGEFS**
 PWIYFVTLILL**GSFFILNLVLGVLSGEFT**
 NWAYFIPLIVL**GSFFMLNLVLGVLSGEFA**
 NFLYFIPLIIL**GSFFMLNLVLGVLSGEFA**
 NWLYFIPLIII**GSFFMLNLVLGVLSGEFA**

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<i>H. sapiens</i>	L-type	CACNA1C
<i>H. sapiens</i>	L-type	CACNA1S
<i>C. elegans</i>	P/Q-type	UNC-2
<i>L. stagnalis</i>	P/Q-type	
<i>H. sapiens</i>	P/Q-type	CACNA1A

VKILRVLRVLRPLRAINRA
VKILRVLRVLRPLRAINRA
VKILRVLRVLRPLRAINRA
VKILRVLRVLRPLRAINRA
IKSLRVLRVLRPLKTIKRI****
IKSLRVLRVLRPLKTINRV****
IKSLRVLRVLRPLKTIKRL****

Fig. S1. Sequence similarity between α_1 subunits from *Caenorhabditis elegans*, *Lymnaea stagnalis* and *Homo sapiens*. The accession numbers are: *C. elegans*, EGL-19 NP_741442.1; *L. stagnalis* L-type α_1 subunit, AAO83839.1; *H. sapiens* CACNA1C, NP_000710.5; *H. sapiens* CACNA1S, NP_000060.2; *C. elegans* UNC-2, NP_741734.1; *L. stagnalis* P/Q-type α_1 subunit, AAO83841.1; *H. sapiens* CACNA1A, NP_000059.3. (A) The GX_9GX_3G motif in the S6 segment of the first domain (IS6) is conserved in all high voltage-activated α_1 subunits (L- and P/Q/R/N-types). The location of mutation in *egl-19(n2368)* is boxed in black: the glycine is replaced with an arginine. (B) The voltage sensor S4 segment of the third domain (IIIS4) is well conserved in all high-voltage-activated α_1 subunits (L- and P/Q/R/N-types). Charged residues (lysine or arginine) are highlighted in bold. The location of mutation in *egl-19(ad695)* is boxed in black; the alanine, conserved in all L-type α_1 subunits, is replaced with a valine.