

**Supplemental Data**

**MOLECULAR DETERMINANTS OF GEM INHIBITION OF P/Q-TYPE  $Ca^{2+}$  CHANNELS**

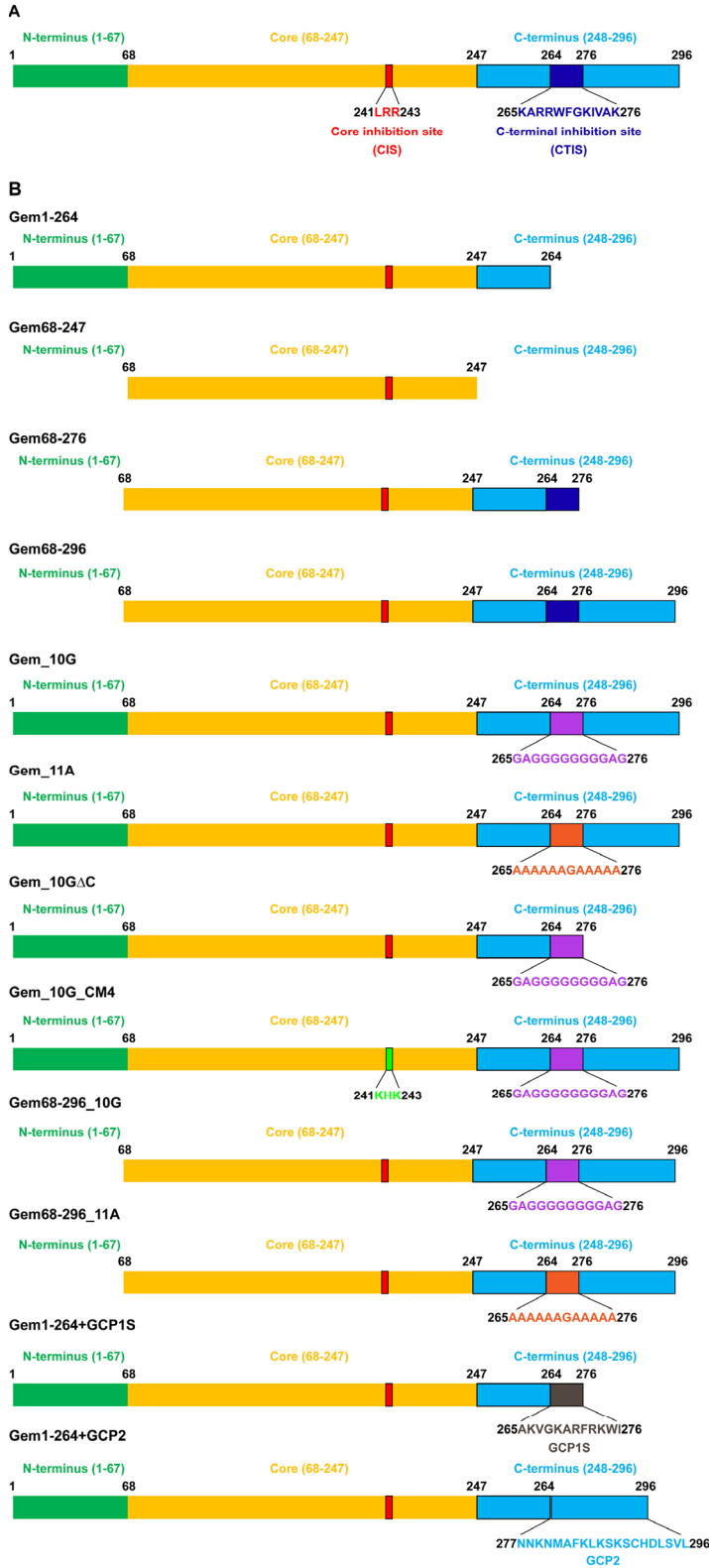
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\*Running title: *Role of two sites in Gem in  $Ca^{2+}$  channel inhibition*

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# Supplemental Fig. 1



**C**

Construct	CTIS intact?	CTIS functional?	CIS intact?	CTIS functional?	Inhibition of P/Q channels?
Gem_WT	√	√	√	√	√
Gem1-264	X	X	√	X	X
Gem68-247	X	X	√	X	X
Gem68-276	√	√	√	X	√
Gem68-296	√	√	√	√	√
Gem_10G	X	X	√	√	√
Gem_11A	X	X	√	√	√
Gem_10GΔG	X	X	√	X	X
Gem_10G_CM4	X	X	X	X	X
Gem68-296_10G	X	X	√	√	√
Gem68-296_11A	X	X	√	√	√
Gem1-264+GCP1S	X	X	√	X	√
Gem1-264+GCP2	X	X	√	X	X

**Supplemental Fig. 1.** Summary of the functional effect of selected Gem constructs and the presumed functional state of their C-terminal inhibitory site (CTIS) and core inhibitory site (CIS). (A) Schematic domain organization of WT Gem, marking the location of CTIS and CIS. (B) Schematic of the indicated Gem mutants. (C) Summary of the effect of the indicated Gem constructs on P/Q-type Ca<sup>2+</sup> channel currents and the proposed structural status and functional state of the two Gem inhibitory sites. The last 20 amino acids in the C-terminus form a C-terminal regulatory element that is necessary for the proper function of CIS.