

A mutant of the *BmK* antitumor-analgesic peptide exhibits reduced inhibition to hNav1.4 and hNav1.5 channels while retaining analgesic activity

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Supplementary

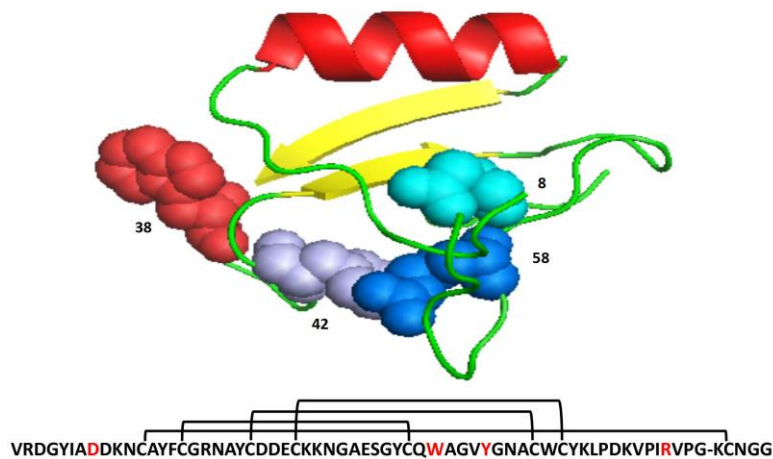
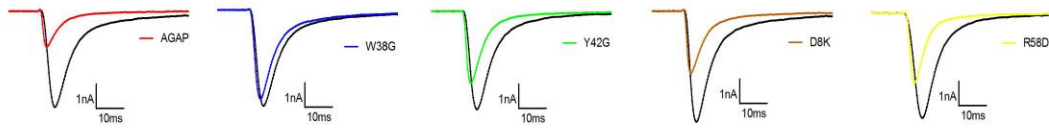


Figure S1. Homology modeling structure of AGAP.

Based on the sequence analysis and homology modeling, AGAP has been classified as an α -type long-chain scorpion toxin, it constitutes two surfaces opposite to each other, named Face A and Face B. Three domains are closely associated with its biological activities, including the N-terminal domain (the first three N-terminal residues), the core domain (the loop preceding the α -helix and the other loop between the β 2- and β 3-sheets) and the NC domain (8-12 residues turn and 56-64 residues in C-terminal region). Trp³⁸ and Tyr⁴² are located in core domain, Asp⁸ and Arg⁵⁸ are located in NC domain. The amino acid sequence of AGAP are showed and the disulfide bonds formed between cysteine pairs are marked by solid lines.

A hNa_v1.4



B hNa_v1.5

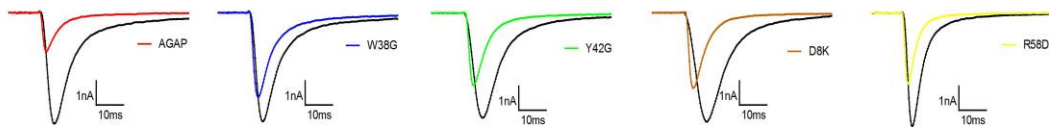


Figure S2. Effects of AGAP and its mutants on the Na⁺ peak current of hNa_v1.4 and hNa_v1.5.

The Na⁺ currents were obtained by plotting current peak amplitudes with a function of test potentials ranging from -80 mV to +80 mV for 50 ms from the holding potential of -80 mV in increments of 10 mV. The current traces were evoked by -20 mV for 50 ms from a holding potential of -80 mV in the absence and presence of 100nM AGAP and its mutants. Averaged current traces were obtained from hNa_v1.4-CHO (A) and hNa_v1.5-CHO (B) (n = 5).

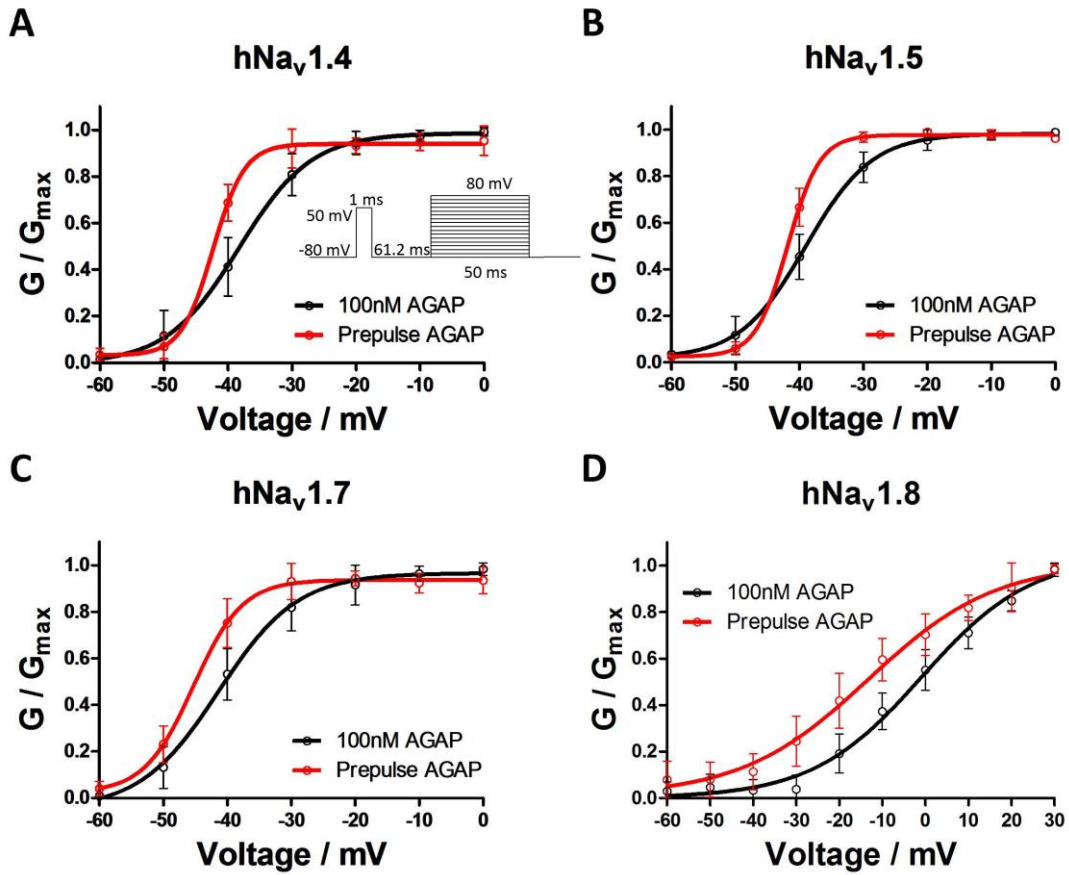


Figure S3. Effects of AGAP on activation of hNav_v1.4, hNav_v1.5, hNav_v1.7 and hNav_v1.8 without a prepulse or with a prepulse

Normalized conductance-voltage relationships of hNav_v1.4 (A), hNav_v1.5 (B), hNav_v1.7 (C) and hNav_v1.8(D) in the presence of 100 nM AGAP without a prepulse or with a +50 mV, 1 ms prepulse that preceded the test pulse by 61.2 ms. Each point represents mean \pm SEM (n = 5).