A novel ?-conopeptide, CnIIIC, exerts potent and preferential inhibition of NaV1.2/1.4 channels and blocks neuronal nicotinic acetylcholine receptors

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BACKGROUND AND PURPOSE The ?-conopeptide family is defined by its ability to block voltage-gated sodium channels (VGSCs), a property that can be used for the development of myorelaxants and analgesics. We characterized the pharmacology of a new ?-conopeptide (?-CnIIIC) on a range of preparations and molecular targets to assess its potential as a myorelaxant. EXPERIMENTAL APPROACH ?-CnIIIC was sequenced, synthesized and characterized by its direct block of elicited twitch tension in mouse skeletal muscle and action potentials in mouse sciatic and pike olfactory nerves. ?-CnIIIC was also studied on HEK-293 cells expressing various rodent VGSCs and also on voltage-gated potassium channels and nicotinic acetylcholine receptors (nAChRs) to assess cross-interactions. Nuclear magnetic resonance (NMR) experiments were

carried out for structural data. KEY RESULTS Synthetic ?-CnIIIC decreased twitch tension in mouse hemidiaphragms (IC50= 150 nM), and displayed a higher blocking effect in mouse e