Colloquia in Cellular Signaling

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "Leseraum".
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Mechanisms of action of analgesic α-conotoxins

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Abstract:

Marine cone snails have developed a distinctive repertoire of small, disulphide bonded peptides (conotoxins) as part of highly evolved venoms used for prey capture and defence. These peptides target a wide range of voltage- and ligand-gated ion channels, transporters and receptors with exquisite selectivity making them an invaluable source of ligands for studying the role and properties of these targets in normal and diseased states. A number of these peptides have shown efficacy in vivo as inhibitors of voltage-gated neuronal calcium (Cav) channels and are in preclinical development for the treatment of chronic and neuropathic pain. In this context, I will discuss the discovery and development of a class of analgesic conotoxins that modulate Cav channels in sensory neurons via a G protein-coupled receptor mechanism. Our recent findings identify GABAB receptor-mediated inhibition of Cav2.2 and Cav2.3 as targets in pain pathways for these and novel 'designer' conotoxins. Activation of GABAB receptors and inhibition of Cav channels by these conotoxins is a novel mechanism for reducing the excitability of sensory neurons involved in chronic visceral and neuropathic pain.