Snail venom for gut pain?

A peptide derived from the venom of marine cone snails could be a novel candidate for treating abdominal pain associated with IBS.

Characterized by chronic visceral pain that is associated with altered bowel habits, IBS is a common disorder. Changes to sensory mechanisms are believed to be involved in gut pain development, particularly the hypersensitization of sensory neurons (nociceptors). However, limited analgaesic therapies currently exist for IBS.

In previous studies, the investigators showed that inhibiting colonic nociceptors with small peptides was clinically effective in providing gut pain relief. Now, the researchers have focused on the α -conotoxin peptides, sourced from the venom of the marine cone snail. One of these peptides, α -conotoxin

Vc1.1, has been shown to be a potent agonist of the human γ -aminobutyric acid B receptor (GABA_BR). Activation of GABA_BR inhibits downstream voltage-gated calcium channels, and other GABA_BR agonists reduce pain-related responses to colorectal distension in animal models.

In the new study, the researchers first established that Vc1.1 inhibits the neuroexcitability of *in vitro* human dorsal root ganglion neurons at the start of the pain-processing pathway, via a GABA_BR-mediated mechanism. Then, using a preclinical mouse model of IBS, Vc1.1 was found to inhibit colonic nociceptors *in vitro* and *in vivo* and reduce the propagation of colorectal distension-induced pain signals from the colon to the spinal cord. Interestingly, these effects were greater in the mouse model of IBS than in healthy mice, which might

“...limited analgaesic therapies currently exist for IBS...”

be explained by the upregulation of a downstream calcium channel target of Vc1.1 in the colonic neurons of the IBS model mice.

“The inhibitory effect in human neurons, combined with the enhanced antinociceptive action of Vc1.1 in colonic pathways in a mouse model of IBS, suggests it is a novel candidate for the treatment of chronic pain associated with IBS,” reports author Stuart Brierley. “As Vc1.1 has been previously tested in phase I and IIa clinical studies for neuropathic pain, where it was shown to be efficacious and without side effects, this [work] is a promising development in the treatment of chronic visceral pain.” The researchers are now designing modified versions of the Vc1.1 peptide in a bid to improve stability and potency.

Iain Dickson

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