Structure-function of conotoxin-membrane protein interactions – lessons for therapeutic peptide development

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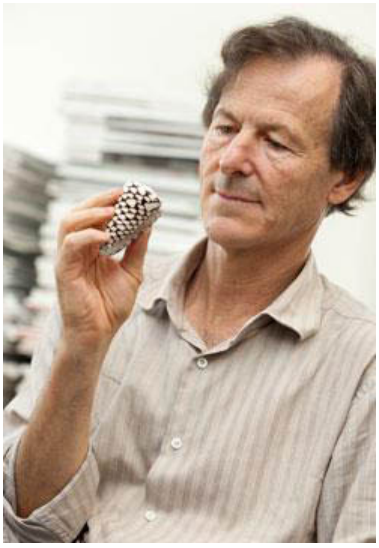
Cone snails inject highly sophisticated venoms comprising many thousands of peptides known as conotoxins into their prey through a hollow barbed harpoon. Remarkably, conotoxins have separately evolved for prey capture or defence, with defensive peptides likely facilitating the shift in prey preference from worms to molluscs and fish. Conotoxins allosterically modulate > 15 different membrane proteins, including ion channels, GPCRs and transporters, with several entering clinical trials for the treatment of severe pain. In this presentation, the structure-function of potential analgesic conotoxins targeting voltage gated calcium channels and the noradrenaline transporter highlight the strengths and weaknesses of developing peptide-based therapeutics.

Biosketch. Prof. Richard J. LEWIS started his PhD studies at the University of Queensland with the late Bob Endean researching polyether sodium channel activator toxins known as ciguatoxins, which are responsible for ciguatera fish poisoning. He then spent 10 years researching the problem at the Queensland Department of Primary Industries before moving back to The University of Queensland in 1995 to initiate research into the discovery and phamacology of conotoxins, small venom peptides produced by cone snails. This research led to the development of Xen2174 as a new class of non-competitive norepinephrine transporter inhibitors for the treatment of severe pain at Xenome Ltd, a company he co-founded. Professor Lewis' current research interests include the elucidation of the evolution and pharmacology of conopeptides, especially the discovery of novel classes of peptides peptides that may be useful for the treatment of pain. Presently he is Professor of Molecular Pharmacology, and was inaugural Director of the *IMB Centre for Pain Research* in the Institute for Molecular Bioscience (IMB), at The University of Queensland, Australia.



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