

Cyclic Conotoxin Analogues

KEY FEATURES

- Unlocking the enormous therapeutic potential of conotoxins
- Improved stability, but unchanged specificity and functionality
- The lead compound IMB007, administered orally shows significant *in vivo* efficacy against neuropathic pain.

Platform Applications

Researchers at the Institute for Molecular Bioscience (IMB) at The University of Queensland (UQ) have developed a platform technology that cyclises conotoxin derived from sea snail venom. Conotoxins are small peptides in the order of 20 amino acids that target different receptors and ion channels with exquisite specificity and selectivity. The platform enables conotoxin-derived peptide drugs to be more stable and orally bio-available without compromising specificity or functionality. Potential therapeutic applications include:

- Pain;
- Neuromuscular disorders; and
- Neurological conditions and diseases such as epilepsy, Alzheimer's and Parkinson's Disease.

The Technology

The Cyclised Conotoxin Analogues platform technology has generated a lead compound (IMB007) which is an orally active peptide that has the potential to be a neuropathic pain treatment. IMB007 is a cyclic analogue of α -conotoxin Vc1.1, which itself has analgesic properties. However, Vc1.1 is only effective when delivered by injection,

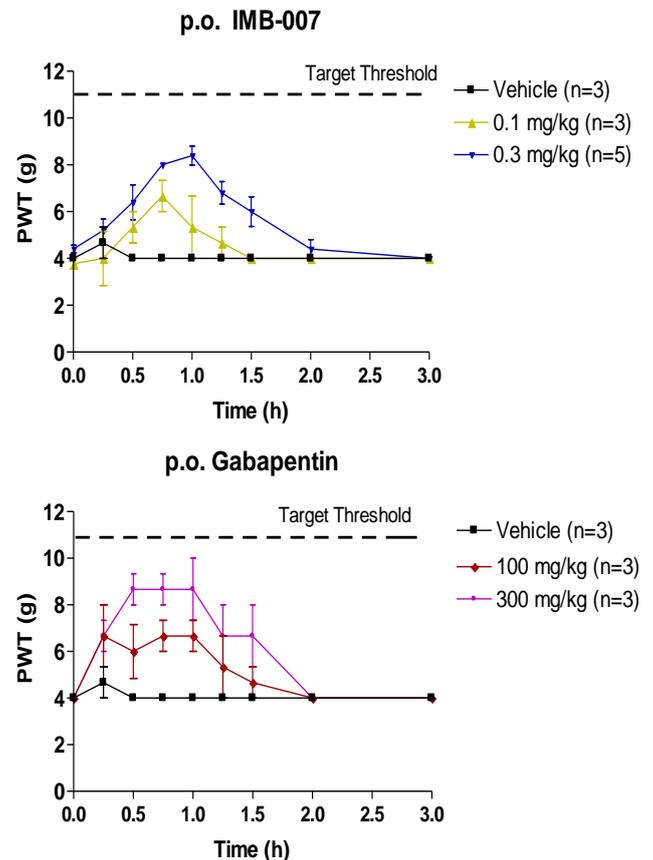


Figure 1. Comparison between IMB007 and gabapentin for *in vivo* efficacy in the rat model of chronic constriction injury neuropathic pain. When both given orally, IMB007 shows comparable efficacy to gabapentin.

which limits its applicability as a drug. Vc1.1 and IMB007 are allosteric activators on the GABA_B receptor (a GPCR). However, IMB007 is even more potent at, and selective for, the GABA_B receptor than Vc1.1. GABA_B receptor activation by IMB007 indirectly blocks N-type calcium channels (IC₅₀ = 7.8 nM) which are a validated pain target. IMB007 shows comparable oral efficacy to gabapentin in a rat neuropathic pain model (Figure 1).

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Problems with Current Therapies

Neuropathic pain affects about 35 million people worldwide, creating a need for effective medications that can be taken conveniently without a high risk of side effects. Drugs currently on the market are associated with side effects that can impact negatively on quality of life, such as drowsiness, dizziness, and lethargy. Furthermore, current drugs have limited efficacy, with only approximately 30-40% of patients reporting improvement.

Intellectual Property

The platform conotoxin cyclisation technology is protected by granted patents in the United States, Europe, Canada and Australia. Patent applications protecting an oral formulation comprising IMB007 are granted in the US, Europe, Japan, and Australia.

Commercialisation Opportunities

UniQuest is seeking investment or licensees to take IMB007 through IND and into clinical trials. We also seek collaborators and R&D funds to generate new lead compounds from the platform technology.

Publication

Clark R J, Jensen J, Nevin ST, Callaghan BP, Adams DJ, Craik DJ (2010), The engineering of an orally active conotoxin for the treatment of neuropathic pain. *Angewandte Chemie International Edition* 49, 6545-6548.



The University of Queensland's
Professor David Craik

RESEARCH LEADER

Professor David Craik is a pre-eminent biological chemist, renowned internationally for his ground-breaking discoveries in the field of circular proteins and their applications in drug design and development. He is the inventor of several patent families and has collaborated with a number of pharma companies.

Prof Craik's research has resulted in almost 500 publications that have received in excess of 14,000 citations. In 2013 he was elected to the Australian Academy of Sciences.

ABOUT UNIQUEST

UniQuest Pty Limited is widely recognised as one of Australia's largest and most successful university commercialisation groups, benchmarking in the top tier of technology transfer worldwide. It has created over 70 companies from its intellectual property portfolio, and since 2000 UniQuest and its start-ups have raised more than \$490 million to take university technologies to market. Combined sales of products using UQ's cervical cancer vaccine technology and MRI machines with UQ's image correction technology inside have been in the order of \$10 billion net sales between 2007-2013.

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