Applications
Therapeutic applications of the Na\textsubscript{v}1.7 inhibitor include:
- Chronic pain;
- Acute pain;
- Chronic cough;
- Cancer; and
- Itch.

The Technology
Researchers at the Institute for Molecular Bioscience (IMB) at The University of Queensland (UQ) have developed a novel peptide-based inhibitor of the voltage-gated sodium channel 1.7 (Na\textsubscript{v}1.7). Na\textsubscript{v}s are integral membrane proteins that allow influx of sodium ions, which is essential for action potential generation and propagation in electrically excitable cells. Mammalian Na\textsubscript{v} channels consist of nine subtypes (Na\textsubscript{v}1.1-1.9) that have distinct expression profiles and subsequent functional roles, with compelling genetic evidence linking Na\textsubscript{v}1.7 to pain.

Loss-of-function mutations of SCN9A, the gene encoding Na\textsubscript{v}1.7, have been identified as the cause of congenital insensitivity to pain, a rare condition characterized by the inability to sense pain in otherwise normal individuals, although anosmia (absence of sense of smell) is reported. Gain-of-function mutations of SCN9A are the cause of two hereditary pain disorders, inherited erythromelalgia and paroxysmal extreme pain disorder. Both disorders are associated with redness, swelling and burning pain and thus, pharmacological inhibition of Na\textsubscript{v}1.7 is a promising therapeutic strategy for the treatment pain.

Developing analgesics with Na\textsubscript{v}1.7 selectivity is essential, as activity at major off-targets, including the skeletal muscle isoform Na\textsubscript{v}1.4, the cardiac isoform Na\textsubscript{v}1.5, and the neuronal isoforms Na\textsubscript{v}1.1, Na\textsubscript{v}1.2 and Na\textsubscript{v}1.6, is likely to cause dose-limiting adverse effects. However, it is difficult to selectively target one Na\textsubscript{v} subtype over the others due to high sequence identity (>50%), particularly in the pore forming segments, where most small molecules, such as local anaesthetics bind. Venom-derived peptides usually bind to the less conserved gate forming segments or voltage sensor domains, and therefore often achieve unparalleled selectivity compared to small molecules.

The UQ peptide termed Pn3a is a potent inhibitor of Na\textsubscript{v}1.7 with an IC\textsubscript{50} of 0.9nM. It is 35 residues in size, and has been extensively characterised in in vitro and in vivo assays. In whole-cell patch-clamp experiments, Pn3a demonstrates 40-fold selectivity over Na\textsubscript{v}1.1, 100-fold selectivity over Na\textsubscript{v}1.2, 1.3, 1.4 and 1.6, and 900-fold selectivity over Na\textsubscript{v}1.5, 1.8, and 1.9.

Proof of Concept
The Pn3a peptide has been evaluated in several rodent pain models, including the Na\textsubscript{v}1.7 spontaneous pain model. When administered by intraperitoneal injection (i.p.) as a single dose, the peptide demonstrated:
- The ability to significantly reduce pain behaviour count in a dose-dependent manner (Figure 1a);
• The ability to significantly reduce pain behaviour count in a time-dependent manner (Figure 1b); and
• No effect on motor coordination (data not shown).

Figure 1. Analgesic effects of Pn3a. (a) Pn3a (i.p.) dose-dependently reversed spontaneous pain behaviours elicited by intraplantar injection of the Na\textsubscript{v}1.7 activator OD1 in mice (over 10 min); n = 3-9 per group. (b) Time course of reversal of OD1-induced spontaneous pain behaviours by Pn3a (3 mg/kg i.p.); n = 6 per group.

Additional data in other rodent pain models is available under a confidentiality agreement.

Intellectual Property
A provisional patent application was filed in June 2016 claiming composition of matter protection over the novel Na\textsubscript{v}1.7 inhibitor and related analogues.

Commercialisation Opportunities
UniQuest is seeking investment or licensee partnerships to further develop this candidate.

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