Applications
Potential therapeutic applications of the oxytocin analogues include:
- Gastrointestinal pain
- Women’s health
- Anxiety disorders

The Technology
Researchers at the Institute for Molecular Bioscience (IMB) at The University of Queensland (UQ) have developed novel analogues of oxytocin with improved stability and selectivity.

Oxytocin (OT) is an endogenous nine amino acid peptide hormone with a variety of physiological actions. OT and OT-analogues are used clinically to induce labour, treat post-partum haemorrhage and to elicit lactation. However, the lack of selectivity of OT for the OT receptor versus the closely related vasopressin receptors and the low stability have prevented its use in more widespread clinical indications.

The IMB team have investigated OT to improve its properties. Through engineered of the disulphide bond and modifications to the C-terminal, OT analogues have been generated which demonstrate a three-fold longer half-life in human serum. Importantly the OT analogues are also significantly more selective (1000-fold higher affinity) for the oxytocin receptor.

KEY FEATURES
- Significantly increased selectivity for the oxytocin receptor
- Improved metabolic and thermal stability
- Potential for oral dosing in the treatment of gastrointestinal pain

Figure 1. Evaluation of an OT analogue in a chronic visceral hypersensitivity (CVH) mouse model.

a) Colonic dorsal root ganglion (DRG) neurons from healthy mice lack OT receptor expression (below level of qRT-PCR detection), whereas expression of OT receptors is highly upregulated in colonic DRG neurons from CVH mice. b) Ex vivo luminal application of the OT analogue SeCtt 12 had no effect at any dose on colonic nociceptor mechanosensitivity in healthy mice (P>0.05). c) In CVH mice ex vivo luminal application of SeCtt 12 causes a dose-dependent reduction in mechanosensitivity, fully reversing the mechanical hypersensitivity of CVH mice (*** P<0.001, one-way ANOVA, Bonferroni post-hoc test).
human OT receptor relative to three closely related human vasopressin receptors, whilst maintaining comparable agonist potency at the OT receptor as OT.

In an extension of the work, the team have recently identified that the OT receptor is significantly upregulated in a mouse model of chronic abdominal pain (Figure 1a). Furthermore, administration of OT analogues to the mice ex vivo reduces colonic pain signalling to baseline levels (Figure 1b,c). These data suggest that the OT analogues may have therapeutic application in the treatment of gastrointestinal pain.

Intellectual Property
The OT analogues are the subject of national phase patent applications undergoing prosecution in the USA and Australia. The claims are directed to composition of matter of the novel OT analogues.

Commercialisation Opportunities
UniQuest is seeking licensing, investment or collaborative partners to further develop the OT analogue technology.

Publications