Lesson’s from nature: Drug discovery from venomous marine snails

Holford’s interdisciplinary research combines chemistry and biology to discover, characterize, and deliver novel peptides from venomous marine snails (cones snails, terebrids, and turrids) as tools for manipulating cell signaling in the nervous system.

The peptidic toxins found in the venom of Toxoglossate (“poisoned-tongued”) marine snails (cone snails, terebrids, and turrids), have been identified as effective biochemical tools for studying the structure-activity relationships of ion channels in the nervous system. The first marine snail drug, ziconotide (Prialt®), used to alleviate chronic pain in HIV and cancer patients, is a major breakthrough that caused a paradigm shift in analgesic drug development.

The pharmacological and biological diversity of toxoglossate peptide toxins present a vibrant and largely unexplored repository for investigating ion channels and receptors. To date the majority of snail toxins characterized are from cone snails, conotoxins, however, more recent efforts have identified the peptide toxins of terebrids and turrids as equally viable for investigating the mechanics of the neuronal circuit. Holford’s research applies inventive tools from chemistry and biology to:

1. Identify disulfide rich peptide toxins from a venom source,
2. Develop high-throughput methods for characterizing structure-function peptide interactions, and
3. Produce novel peptide targets for therapeutic development.

Holford’s presentation will highlight a dissociative peptide-drug delivery system applicable for investigating neuronal disorders such as pain. Despite ziconotide (Prialt®) being a breakthrough drug, widespread application of ziconotide is limited due to its size (25 amino acids), and lack of efficacy when delivered via common routes, an intrathecal delivery is required as ziconotide does not cross the blood brain barrier (BBB). The Holford lab has developed an alternative to intrathecal application of ziconotide by encapsulating it in a viral capsid nanocontainer for delivery across the BBB.