## Ion channels in pain pathways: insight from venom peptides

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Millions of years of evolution have fine-tuned the ability of venom-derived peptides to rapidly incapacitate both prey and predators. Voltage-gated sodium channels (NaV) are a particularly attractive pharmacological target for these toxins as they are intimately involved in almost all physiological processes including action potential generation and conduction. Accordingly, venom peptides that interfere with NaV function provide a key defensive and predatory advantage to a range of venomous species including cone snails, scorpions and spiders. Enhanced activation or delayed inactivation of sodium channels by toxins is associated with the extremely rapid onset of tetanic/excitatory paralysis, while delayed activation or pore block leads to flaccid paralysis in envenomed prey animals. In addition to being perfect weapons, sodium channel toxins may also represent perfect cures for channelopathies including pain as they are some of the most subtype-selective pharmacological tools available to date.

We have recently isolated and characterized novel sodium channel toxins, including highly selective NaV1.7 and NaV1.6 modulators. These toxins have provided novel insight into the pathophysiological mechanisms of pain and sodium channel gating and may represent novel lead compounds for the treatment of disease associated with aberrant NaV signalling.