Venom-inspired design of novel drug leads for diabetes

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The venoms of predatory marine cone snails are a rich source of biomedical tools, drug leads, and diagnostic agents. It has long been known that cone snail toxins (conotoxins) target the prey's nervous, sensory or locomotor system with high potency and efficacy[1]. Additionally, we recently showed that a subset of fish-hunting cone snails evolved specialized insulins to rapidly induce dangerously low blood sugar (hypoglycemic shock) in prey[2]. Unlike human insulin and its therapeutic analogs which form dimers and hexamers, we have shown that venom insulins are monomeric thereby acting more rapidly[3]. Inspired by this discovery, we designed a human-venom insulin hybrid that combines the fast-acting nature of venom insulins with the high potency and low immunogenicity of the human hormone[4]. This compound is currently in preclinical studies.
Remarkably, different species of fish-hunting cone snails have evolved divergent strategies to activate the insulin receptor in prey; each of these insulins represents a new opportunity for diabetes drug design[5-7]. In this seminar, I will give an overview of the discovery of specialized venom insulins, their structure-function studies and their potential as drug leads for diabetes.

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