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Structural principles of venom insulins: can these be applied to the development of new therapies for diabetes?

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Certain fish-hunting cone snails produce venoms that contain insulins. These venom insulins facilitate the capture of prey by the rapid induction of hypoglycemic shock. We have studied one such insulin, Conus geographus G1 (Con-Ins G1), the smallest known insulin in nature. In particular, Con-Ins G1 lacks the C-terminal segment of the canonical B chain that in human insulin mediates both receptor engagement and hormone storage. Here, we present crystal structures both of the venom insulin itself and of its complex with the primary binding site components of human insulin receptor (the latter being a surrogate of fish insulin receptor). Taken together, these structures suggest principles that may be applicable to the design of novel, ultra-rapid-acting therapeutic insulins.

Primary author: Dr LAWRENCE, Michael (Walter and Eliza Hall Inst of Med Res)

Presenter: Dr LAWRENCE, Michael (Walter and Eliza Hall Inst of Med Res)

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