

Discovery of stable, selective venom peptides for cancer research

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Initial research on venoms in cancer research started in the early 1950's., this field only really gained traction in the early 1980's but has still failed to deliver a clinical cancer therapeutic compound. However there have been some successes in tumour imaging in surgery utilising venoms. Tumour paint (Tozuleristide) is a labelled venom peptide discovered in the venom of the death stalker scorpion (*Leiurus quinquestriatus*) that binds specifically to glioma cells. Given intra-venously the labelled peptide crosses the blood brain barrier and the surgeon is able to illuminate the patient's brain to visualise the fluorescing tumour cells and avoid the non-fluorescent healthy brain tissue¹. Further work is investigating fusion proteins to deliver toxic payloads specifically to the targeted tumours. This presentation will give an overview of our current work on the next generation of venom peptides for cancer therapeutics. This includes phenotypic screening for cancer specific cytotoxins in breast, pancreatic and colon cancer, as well as target-based screening for receptor tyrosine kinase ligands etc. In order to carry out such screens we used two dimensionally fractionated venom libraries, prepared from whole venoms and standardised in 384-well plates. We also recently published the first kinome scale profiling of venom effects in cancer cells² and are following this up with specific work targeting the Epidermal Growth Factor Receptor. Venom peptides are also ideally suited to tackle difficult drug targets such as protein-protein interactions and evidence for this will also be presented here for the first time.

1. Patil CG, Walker DG & Miller DM et al. Phase 1 Safety, Pharmacokinetics, and Fluorescence Imaging Study of Tozuleristide (BLZ-100) in Adults With Newly Diagnosed or Recurrent Gliomas. *Neurosurgery*. 2019 Oct 1;85(4):E641-E649.
2. McCullough D, Atofanei C, Knight E, Trim SA, Trim CM. Kinome scale profiling of venom effects on cancer cells reveals potential new venom activities. *Toxicon*. 2020 Oct 15;185:129-146.