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Development of peptidic anti-dendrotoxins

Saioa Oscoz¹, Andreas H. Laustsen², Mads H. Clausen³, and Brian Lohse²

¹Department of Systems Biology, Technical University of Denmark

²Department of Drug Design and Pharmacology, University of Copenhagen

³Department of Chemistry, Technical University of Denmark

Brief description of research area:

The black mamba (*Dendroaspis polylepis*) is one of the most feared and dangerous snakes in the world, and its bite has a very high mortality and morbidity rate. Dendrotoxins, the most abundant and some of the most toxic components present in black mamba venom, target potassium channels in neuronal tissue, leading to hyper-excitability in victims and prey. Blockage of the potassium channels can lead to respiratory paralysis and eventually death. Early administration of appropriate antivenom is the only effective snakebite therapy to date. However, current antivenoms are still being produced by the very laborious and expensive traditional animal immunization techniques, leading to severe side effects in human recipients due to their heterologous nature. In contrast, novel approaches based on synthetic or recombinant antivenoms may offer an alternative solution, saving cost, limiting side effects, and providing more effective neutralization of snake venom.

What we know:

Peptide-based antitoxins against Dendrotoxin B were previously discovered through phage display selection. The peptidic hits were able to cross-react with toxins from different snake species in ELISA-based assays. Competition assays and ITC experiments were also performed, but so far strong binding has not been detected.

What we need

Currently, we are working on measuring the affinity of the peptidic antitoxins in order to rank how well these bind to the dendrotoxins. This will enable us to select the promising toxin binder, which we intend to test in two-electrode voltage clamp experiments to determine if toxin binding translates to toxin inhibition. Hopefully, these experiments will help guide future optimization of our peptidic antitoxins. However, we are in need of a more effective method for determine affinity.