

Automated Patch Clamp Evaluation of Snake Neurotoxins and Recombinant Antivenoms

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Snakebite was reinstated as an official Neglected Tropical Disease (NTD) by the World Health Organization in 2017, as it causes more than 100,000 deaths and around 400,000 amputations every year. Every snake species has a unique venom composition and consists of several dozen different toxins.

The century-old technique to generate conventional antivenoms involves immunization horses with snake venoms, followed by purification of polyclonal antibodies from the horse blood plasma. However, such antivenoms are associated with several drawbacks related to equine-human immunoreactivity and adverse reactions, batch-to-batch variation, and high cost.

In the last decade, advances in antibody engineering have made antibody discovery and development more efficient, and it is now possible to develop recombinant antivenoms based on monoclonal antibodies targeting key venom toxin. One of the most medically relevant groups of snake toxins are the α -neurotoxins, which target nicotinic acetylcholine receptors (nAChRs).

For over two decades, automated patch clamp (APC) systems have been used to advance our understanding of ion channel biophysics, pharmacology, and their roles in physiology and disease.

Here, using QPatch II and Qube 384 APC, we functionally evaluated snake venom α -neurotoxins and toxin-neutralising IgG monoclonal antibodies (mAbs) on the muscle-type $\alpha 1$ -nAChR.

This study demonstrates the potential of a range of IgGs to neutralize α -neurotoxins from several snake species. This is a critically important step towards enabling the design of novel, broadly-neutralizing recombinant antivenoms against snakebite envenoming.

This work highlights the potential and advantages of using high-throughput electrophysiology systems to evaluate the functional activity of protein-based toxins and antibodies.

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