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unveiling the complexity of antigen-antibody interactions of antivenoms

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High-throughput epitope profiling of snake venom toxins – unveiling the complexity of antigen-antibody interactions of antivenoms

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Introduction
Insight into the molecular details of polyclonal antivenom antibody specificity is a prerequisite for accurate prediction of cross-reactivity and can provide a basis for design of novel antivenoms. In this work, a high-throughput approach was applied to characterize linear elements in epitopes in 82 toxins from four African mamba and three neurotoxic cobra snakes obtained from public databases.

Studying linear epitopes using peptide microarrays
Generation of in silico library of 12mers covering toxin sequences
Expanding the peptide library with alanine-substituted peptides
Light-directed solid-phase synthesis of custom peptide microarray

High number of epitopes recognized by SAIMR antivenom

Key residues for antivenom toxin recognition

Antivenoms antibodies bind to functional sites of toxins

Figure 3. Structural presentation of B-cell epitope analysis: (A) Short neurotoxin 1 (P01416) from D. polylepis as an example of a type 1 α-neurotoxins. Structure built upon: (B) D. fasciculin-2 (P01218) from D. defassa as an example of a fasciculin. The Fasciculin-2 is co-crystallized with the human acetylcholinesterase enzyme. Structure built upon: (C) TTX toxin FS-2 (P01416) from D. polylepis as an example of α1 α2 nicotinic calcium channel blocker. Structure built upon: (D) α1(ε)-neurotoxin (P01329) from D. polylepis. For the D. fasciculin-2 a substitution effect in log2 fold-change, where magenta indicates that a residue is of particular importance for antibody recognition. Residue numbers refer to original sequence and not alignment. (E,F,G,H) Residues colored according to residue score, where dark red refers to residues with high residue score, and blue refers to residues with low residue scores.

Conclusions
Custom-designed high density peptide microarray technology enables parallel automated identification of linear elements of epitopes in snake neurotoxins.

Trend: antivenom antibodies recognize and bind to epitopes at the functional sites of toxins.

Perspectives
Determination of linear elements in snake venom toxin epitopes may provide the basis for:
• Explaining the molecular basis of antivenoms para-specificity
• Guiding next-generation antivenoms based on DNA immunization and immunization with synthetic epitope strings

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