High-throughput epitope profiling of snake venom toxins
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.

Key residues for antivenom toxin recognition

Antivenoms antibodies bind to functional sites of toxins

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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References


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Figure 1. A-C Venn diagrams of peptides classified to bind antivenom antibodies for each pair of experiments conducted with the same antivenin in two different dilutions: (A) SAIMR Polyvalent Snake Antivenom, (B) VNS (Africa) and (C) EUNO Central Africa. D) Venn diagram of peptides classified as binders for each antivenom. Only peptides identified in both experiments with each antivenom, corresponding to the overlap in Venn diagram in part A-C, are included.

Figure 2. Examples of B-cell epitope analysis: Type 1 and 2 neurotoxins and dendrotoxins recognized by the SAIMR polyvalent antivenin. The best profiles above each sequence represent the average score of peptides containing a given peptide. The background represents the average amino substitution effect. When no 12-mer peptide covering a given residue passed the epitope threshold, the residue is colored gray. Dark purple indicates that a residue is of particular importance for antibody recognition.

Figure 3. Structural presentation of B-cell epitope analysis: A-B Short neurotoxin 1 (P01419) from D. polyxena as an example of a type 1 neurotoxin. Structure built upon: (C) D-fasciculin-2 (P00128) from D. angusticeps as an example of a fasciculin. The Fasciculin-2 is co-crystallized with the human acetylcholinesterase enzyme. Structure built upon: (E) F1 toxin FS 2 (P01394) from D. polyxena as an example of an F1-toxin calcium channel blocker. Structure built upon: (F) G2 o-vilorin Opgp2 (P00392) from D. polyxena. The substitution effect in logP fold-change, values indicate that a residue is of particular importance for antibody recognition. Residue numbers refer to original sequence and not alignment. (G,H) Residues colored according to residual score, where dark red refers to residues with high residue score, and blue refers to residues with low residue score.