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
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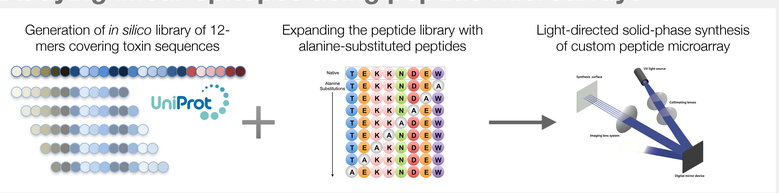
Introduction

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[1]. 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



High number of epitopes recognized by SAIMR antivenom

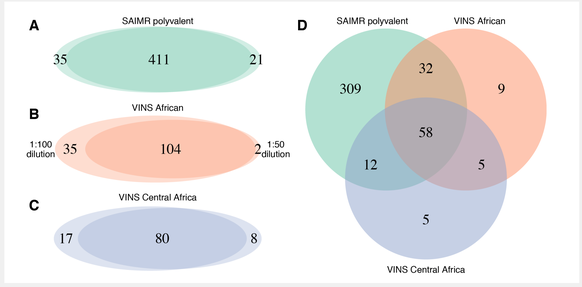


Figure 1. (A-C) Venn diagrams of peptides classified to bind antivenom antibodies for each pair of experiments conducted with the same antivenom in two different dilutions; (A) SAIMR Polyvalent Snake Antivenom, (B) VINS African, and (C) VINS Central Africa. (D) Venn diagram of peptides classified as 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.

Key residues for antivenom toxin recognition

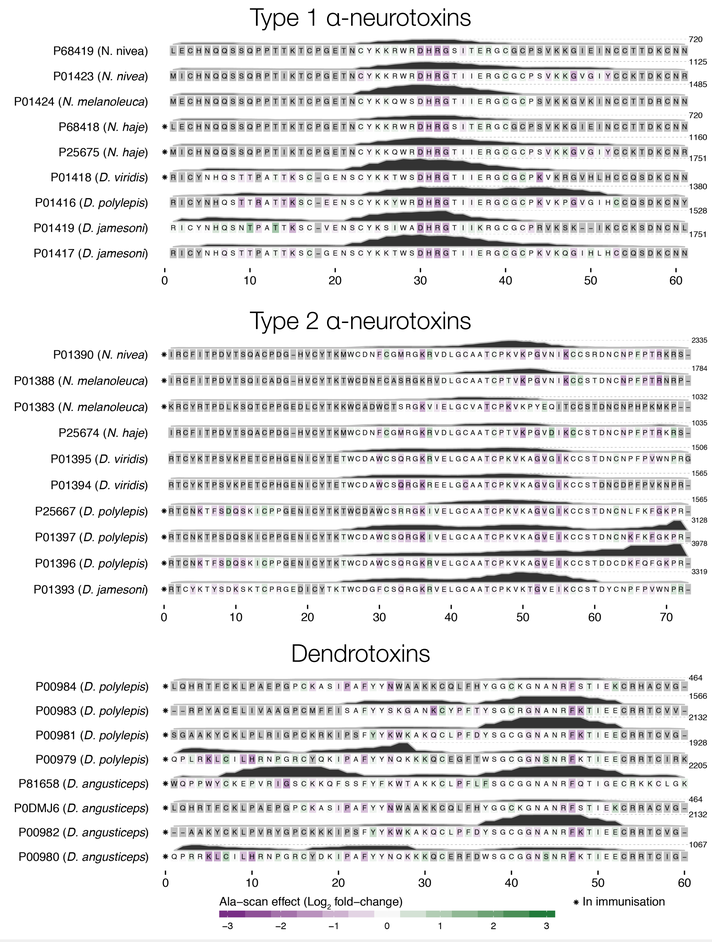


Figure 2. Examples of B-cell epitope analysis: Type 1 and 2 α-neurotoxin and dendrotoxins recognized by the SAIMR polyvalent antivenom. The filled profiles above each sequence represent the average score of peptides containing a given peptide. The tile background represents the average alanine substitution 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.

Antivenoms antibodies bind to functional sites of toxins

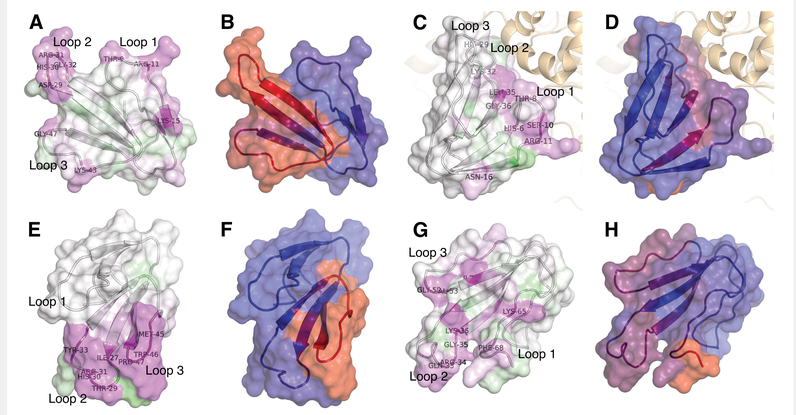


Figure 3. Structural presentation of B-cell epitope analysis: (A-B) Short neurotoxin 1 (P01416) from D. polylepis as an example of a type 1 α-neurotoxin. Structure built upon[1]; (C-D) Fasciculin-2 (P0C1Z0) from D. angusticeps as an example of a fasciculin. The Fasciculin-2 is co-crystallized with the human acetylcholinesterase enzyme. Structure built upon[2]; (E-F) Toxin FS-2 (P01414) from D. polylepis as an example of an L-type calcium channel blocker. Structure built upon[3]; (G-H) α-elapitoxin-Dpp2c (P01397) from D. polylepis as an example of a type 2 α-neurotoxin. Structure built upon[4]. (A,C,E,G) Residues colored according to alanine 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; (B,D,F,H) Residues colored according to residue score, where dark red refers to resides 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[5]

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