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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\textsuperscript{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

1. Venn diagram 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 Antivenom, and (C) UNAM 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 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 Antivenom, and (C) UNAM 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.

High number of epitopes recognized by SAIMR antivenom

Figure 2. Examples of B-cell epitope analysis: Type 1 and 2 neuratoxins and dendrotoxins recognized by the SAIMR polyvalent antivenom. The list profiles above each sequence represent the average score of peptides containing a given peptide. The background represents the average amino acid 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.

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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