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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 an in vitro library of 12-mer covering toxin sequences

Expanding the peptide library with alanine-substituted peptides

Light-directed solid-phase synthesis of custom peptide microarray

1) Binding of antivenom
2) Fluorescence-labeled anti-antivenom

High number of epitopes recognized by SAIMR antivenom

Figure 1. A-C Venn diagrams of peptides classified as bind an antivenom antibodies for each pair of experiments conducted with the same antivenom in two different directions. (A) SAIMR Polyvalent Snake Antivenom, (B) VMS-Africa, and (C) UNB 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 analyses: Type 1 and 2 neurotoxins and dendrotoxins recognized by the SAIMR polyvalent antivenom. The best profiles above each sequence represent the average score of peptides containing a given peptide. The bar 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.

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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.

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

References


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