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.

Studying linear epitopes using peptide microarrays
The high-throughput peptide microarray technology enabled parallel automated identification of linear elements of epitopes in snake neurotoxins. The B-cell epitopes were defined through synthetic peptide microarrays and validated through binding assays. The structural analysis of the antivenom binding patterns indicated the presence of multiple epitopes that were crucial for the antivenom activity. The data were further used to develop a computational model for predicting antivenom epitopes.

Key residues for antivenom toxin recognition
Type 1 α-neurotoxins
- PnA10 (N. naja) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA05 (N. nigerrima) – Synthetic peptide
- PnA05 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide

Type 2 α-neurotoxins
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide
- PnA19 (N. nigerrima) – Synthetic peptide

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