High-throughput epitope profiling of snake venom toxins
unveiling the complexity of antigen-antibody interactions of antivenoms

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Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Citation (APA):
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 epitopes in venoms 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 epitopes in snake neurotoxins.

Trend: antivenom antibodies recognize and bind to epitopes at the functional sites of toxins.

Perspectives
Determination of linear epitopes 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

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) VNS-African, and (C) UNI-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 antivenom. The best profile above each sequence represents the average score of peptides containing a given peptide. The tie 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.

Figure 3: Structural presentation of B-cell epitope analysis: A-B Short neurotoxin 1 (P01415) from D. polylepis as an example of a type 1 neurotoxin. Structure built upon: (C) 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: (D) F1 toxin FS 2 (P01396) from D. polylepis as an example of an F1 toxin. The FS 2 is a calcium channel blocker. Structure built upon: (A) α-neurotoxin (P01391) from D. polylepis. The α-neurotoxin represents the antigenic effect in log-I fold-change, where magenta indicates that a residue is of particular importance for antibody recognition. Residues colored according to residue score, where dark red refers to residues with high residue score, and blue refers to residues with low residue scores.

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Acknowledgement
We would like to thank Morten Nielsen for scientific discussion and the Novo Nordisk Foundation for financial support (grant number NNF13OC0005613)