Discovery and optimization of peptide-based anti-cobratoxins

Sola, M.; Laustsen, Andreas Hougaard; Johannesen, J.; Lynagh, T.; Clausen, Mads Hartvig; Lohse, B.

Publication date: 2015

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

Link back to DTU Orbit

Citation (APA):
Discovery and optimization of peptide-based anti-cobratoxins

M. Sola¹, A. H. Laustsen², J. Johannesen², T. Lynagh², S. A. Pless², M. Clausen,³ B. Lohse²

¹ Department of Systems Biology, Technical University of Denmark
² Department of Drug Design and Pharmacology, University of Copenhagen
³ Department of Chemistry, Technical University of Denmark

Fully synthetic antitoxins - The antivenoms of the future

More than 5.5 million people per year are victims of snake envenomation, resulting in 125,000 deaths and 400,000 amputations worldwide [1][2]. Antivenoms are still produced by animal immunization procedures, and they are associated with a high risk of severe adverse reactions. Alternatively, synthetic peptides may open the possibility for new therapies with better efficacy and safety. Here, we report the discovery and optimization of a synthetic peptide directed against α-cobratoxin (α-CTX), the most toxic component of Monocled cobra (Naja kaouthia) [3].

**Discovery of Peptide 1 - Binder and inhibitor of α-cobratoxin**

1. Cobratoxins target and inhibit the nicotinic acetylcholine receptors (nAChRs), thus efficient anti-cobratoxins must block this interaction.

2. Peptide P1 was identified by phage display selection.

3. Peptide P1 binds to α-CTX and inhibits its interaction with nAChRs

4. According to docking studies Peptide 1 binds to the same α-CTX residues that are involved in the interaction with nAChRs.

### Future perspectives – Optimizing Peptide 1

Truncated and cyclic versions of Peptide 1 are expected to show increased affinity and neutralization capacity.

Other elapid venoms are rich in α-neurotoxins structurally similar to α-CTX, thus Peptide 1 and its optimized versions may provide protection against the neurotoxic effects exerted by α-neurotoxins present in a broad range of venoms.

References