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Recombinant antivenoms based on mixtures of human antibodies against *D. jamesoni* toxins

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The pressing problem of a snakebite

Each year, more than 5 million people worldwide are affected by a snakebite, resulting in 150,000 deaths, and 400,000 amputations1. The current medical treatment against envenoming is based on the administration of an animal-derived antiserum, containing antibodies against snake venom toxins. Due to the heterologous and immunogenic nature of antivenom, patients in up to 80% of the cases experience serum sickness and anaphylaxis, which in some cases leads to death2, 3.

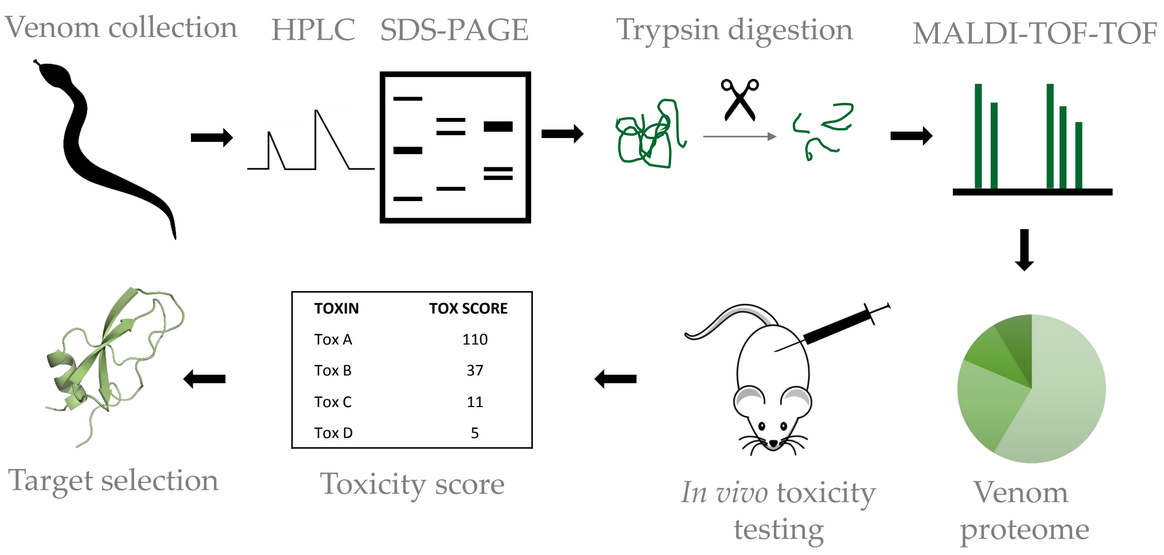
Clinical manifestations of *D. jamesoni* toxins

Early clinical signs
- Paralysis
- Fasciculation
- Vertigo
- Ataxia
- Sudden loss of consciousness

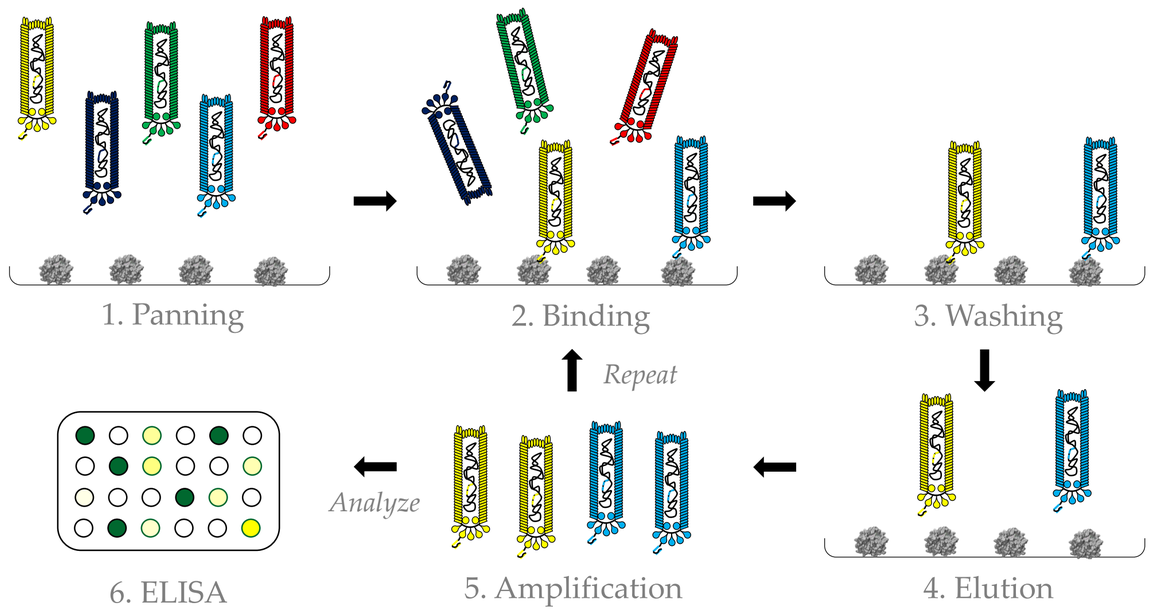
Late clinical signs
- Shock
- Hypotension
- Abdominal pain
- Epistaxis
- Pallor
- Increased sweating
- Nausea

Local tissue damage appears to be relatively infrequent and of minor severity in most cases, whereas the accumulative effect of symptoms may lead to death if not treated[4].

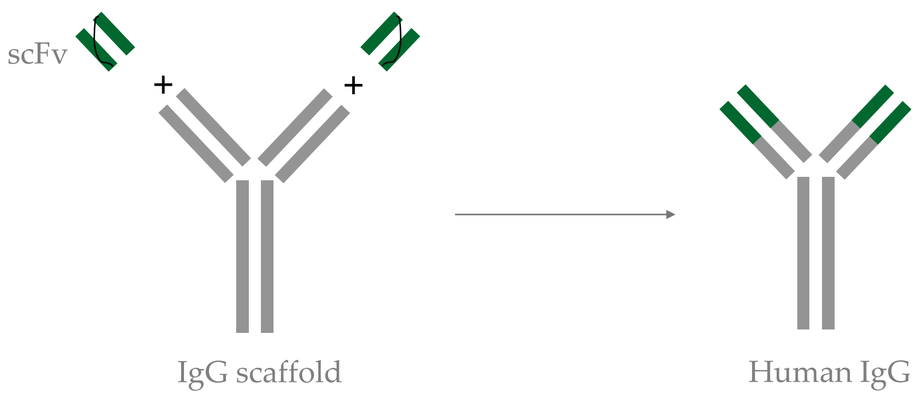
Toxicovenomics



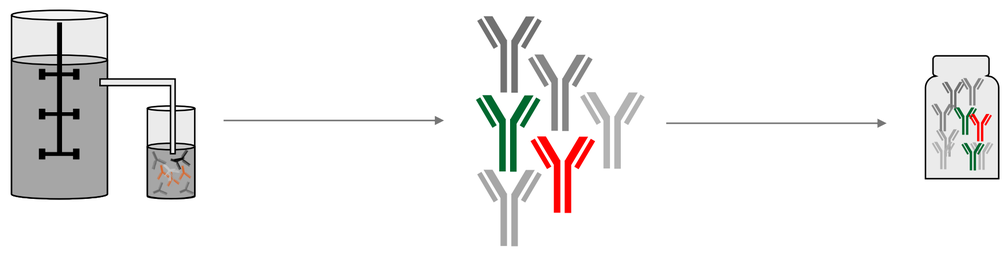
Selection of scFvs by phage display



Format conversion of scFv to IgG



Production of recombinant antibody mixtures



Perspectives

This project aims to develop a fully recombinant snakebite antivenom against the potent venom of *D. jamesoni*. This antivenom will be based on selected human IgG antibodies, compatible with the human immune system and with proven specificity. It is the ambition of this project to contribute to the development of safer, more effective, and inexpensive treatment options against snakebite envenoming.

References

[1] WHO, http://www.who.int/mediacentre/factsheets/fs337/en/

[2] Gutierrez JM, Leon G, Lomonte B, Angulo Y. (2011) Antivenoms for snakebite envenomings. Inflammation & Allergy-Drug Targets 10(5): 369-80.

[3] World Health Organization W. WHO guidelines for the production, control and regulation of snake antivenom immunoglobulins. Geneva: WHO, 2010; 134.

[4] UCSD, http://toxicology.ucsd.edu/Snakebite%20Protocols/Dendroa2.htm

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