Development of a Recombinant Antibody-Based Treatment of Snakebites

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Improving Antivenom to Save Lives and Limbs

Antivenom for snakebites is produced by immunization of large mammals with snake venom using a traditional and expensive method developed in the 1880's. Due to the animal origin, the products are highly immunogenic and come with a high risk of adverse side effects such as serum sickness and anaphylaxis, possibly leading to death [1].

This project aims at replacing existing snake antivenoms with a mixture of recombinant, humanized antibodies produced by modern cell-based fermentation technology [2]. It is anticipated that such an antivenom will reduce the current high risk of severe side effects, reduce cost, and thereby be sold at 1/10 of the current price making the essential medicine available for > 700 M Africans [4].

Modern day technology allows development of monoclonal antibodies (mAbs) targeting snake toxins, however, identification, characterization of immunogenic features (B-cell epitopes), and availability of purified snake toxins or non-toxic analogs currently constitute major bottlenecks blocking the development of recombinant mAbs. We have set out to remove these bottlenecks starting by mapping antibody binding sites of existing horse-derived products and purified antibodies from snakebite victims using high-density peptide microarrays. Moreover, we are developing homology models of all relevant mamba toxins to map conserved sites and identify key residues for toxicity.

Challenges in the near future

- **Modeling of protein-protein interactions**: Validating the antibody affinity by competing of an essential site (i.e. α7 nAChR) with a toxic analog. (e.g., cobratoxin)
- **Expressing and purifying toxins and non-toxic analogs**: Investigating the specificity of an experimental monoclonal antibody (mAb) with the non-toxic analogs of a well-known snake toxin.
- **Validation of correct protein fold**: Testing the protein purity and stability by means of various methods.
- **Validation of physiological activity**: Determining the in vivo activity and selectivity of the recombinant antibody.
- **Sequence of binding antibodies**: Investigating the specificity of binding domains of the recombinant antibody.

Figure 5 – Schematic overview of upcoming challenges related to protein research.

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