Development of a Recombinant Antibody-Based Treatment of Snakebites

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Improving Antivenom to Save Lives and Limbs

Antivenom for snakes is produced by immunization of large mammals with snake venom using a traditional and expensive method developed in the 1880s. 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 can 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.

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Figure 1 – The Sub-Saharan antivenom crisis. Overview of the vicious cycle fueled by the current production method of antivenom and dangerously inappropriate products of Indian origin marketed by unscrupulous manufacturers dominating the unregulated African market [4]. WHO describes snakebites as one of the World’s most neglected tropical diseases and the antivenom situation in Sub-Saharan Africa as a long standing crisis [5].

Figure 2 – Schematic overview of research approach.

Antigen analysis

Important residues for toxicity (modeling and validation)

Epitope analysis (peptide microarray)

Interspecies variation (transcription)