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DISCOVERY OF HUMAN ANTIBODIES AGAINST SPITTING COBRA TOXINS

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The Snakebite Challenge

Current snakebite envenoming treatment options consist of animal-derived antisera [1] and are associated with severe adverse reactions due to the heterologous nature of the animal-derived antibodies present in these antisera, and the presence of therapeutically irrelevant antibodies [2]. The African spitting cobras are among the most medically important snakes in sub-Saharan regions due to the severity of the clinical outcomes caused by their cytotoxic venom, which is derived from cytotoxins of the 3FTx toxin family and PLA₂ [3]. Here we report the results of our progress in identifying human antibodies targeting relevant toxins from the venom of the black-necked spitting cobra (*Naja nigricollis*).

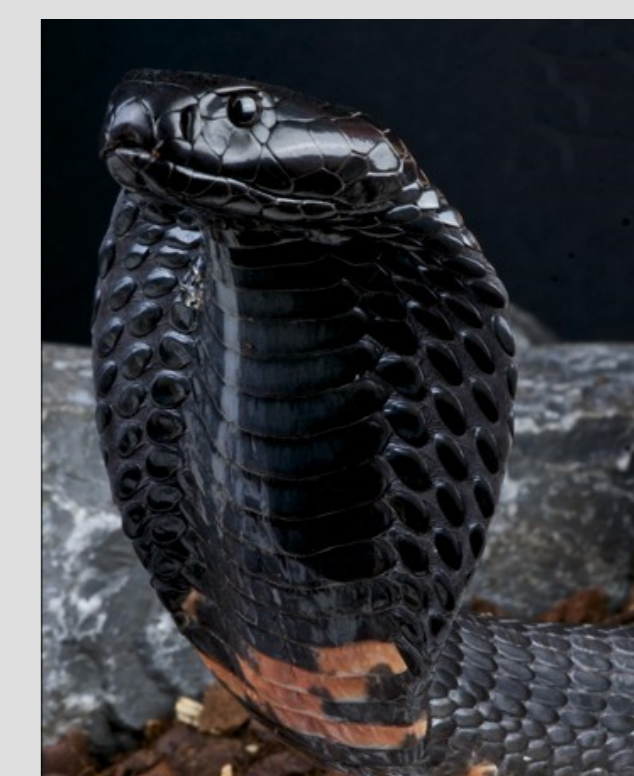


Fig. 1: *Naja nigricollis*

Selection of Medically Relevant Toxins

Selecting only medically relevant venom toxins for antibody discovery we avoid production of therapeutically irrelevant antibodies. Toxin fractionation was carried out with RP-HPLC.

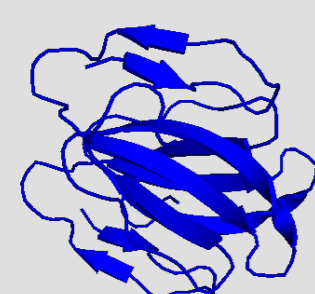


Fig. 2: 3FTx [4]

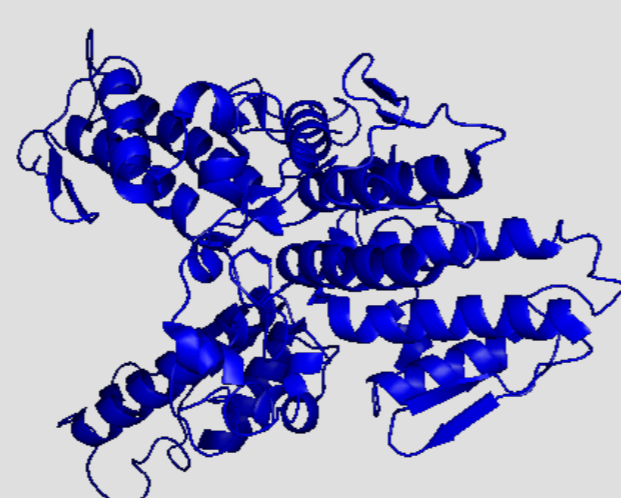
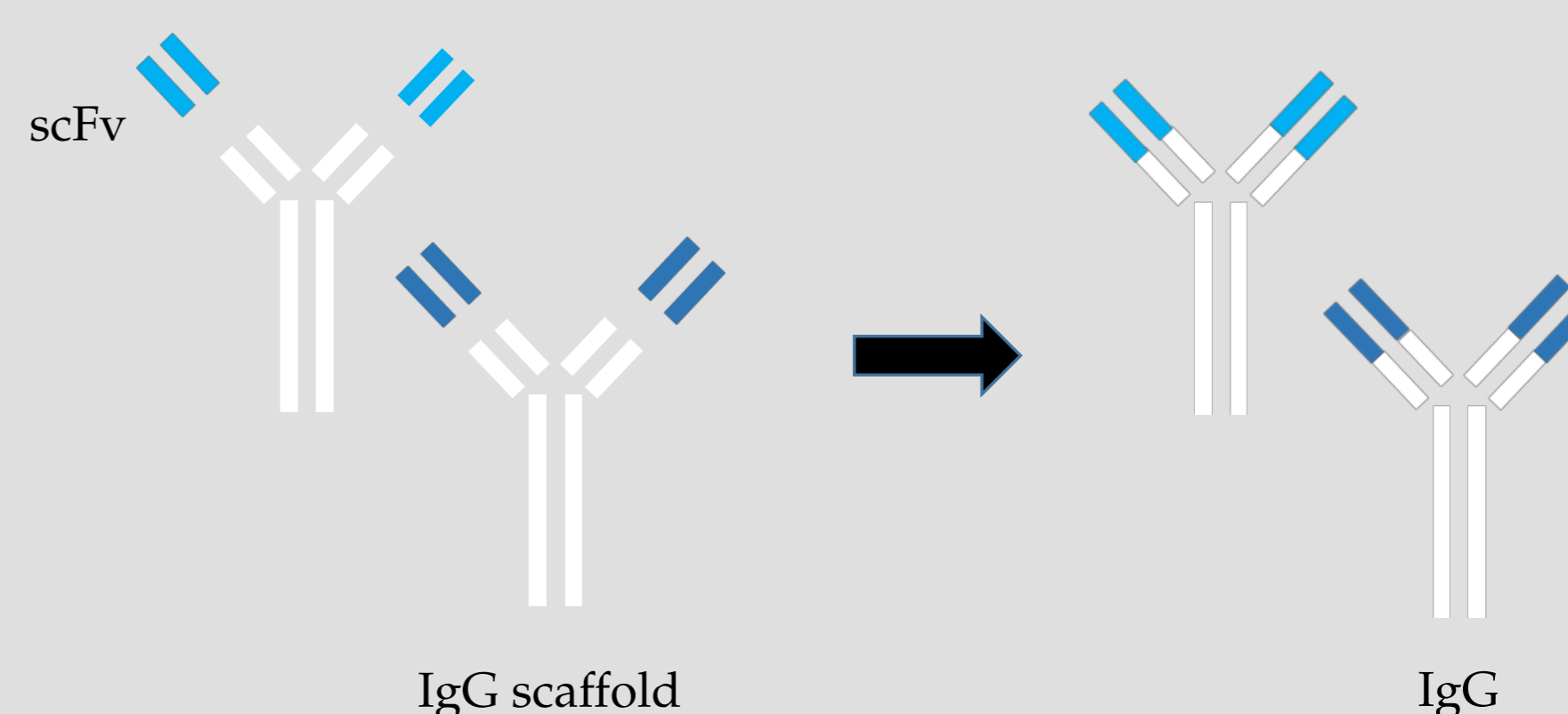
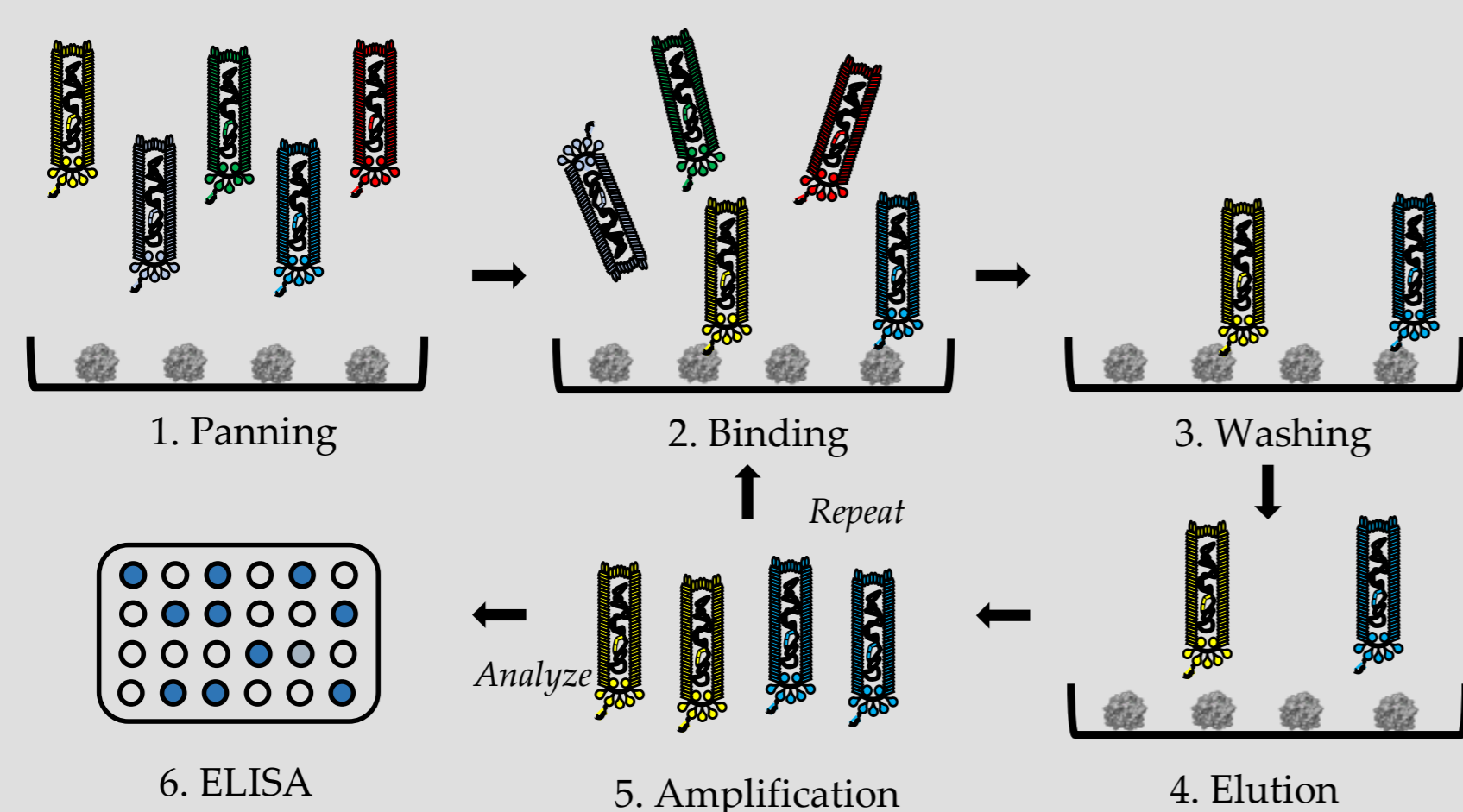


Fig. 3: PLA₂ [4]

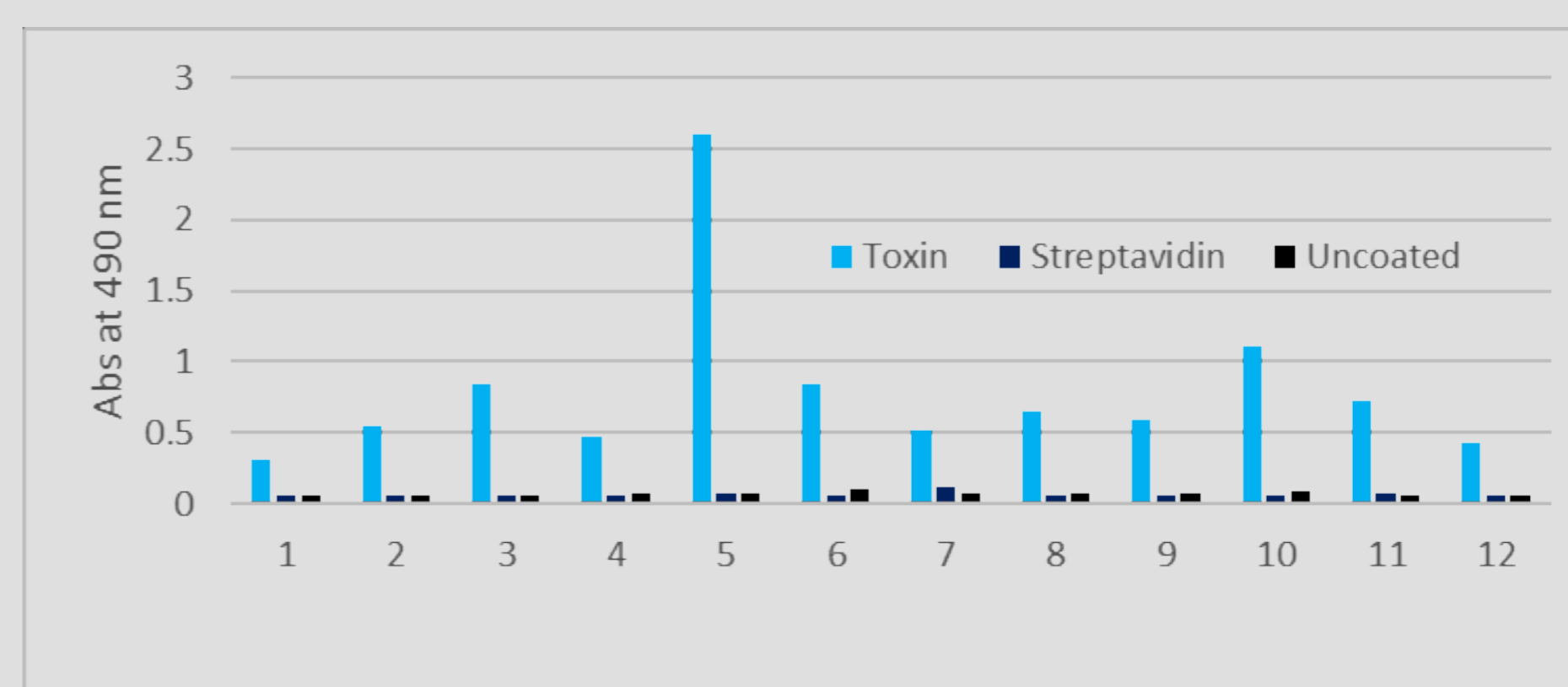
Conversion of scFvs to IgG Format



Discovery of scFvs with Phage Display



Strong Binders after 3 Rounds of Panning



References

- [1] Williams, DJ, et al. Ending the drought: new strategies for improving the flow of affordable, effective antivenoms in Asia and Africa. *Journal of proteomics* 74.9 (2011): 1735-1767.
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- [3] Petras, D, et al. Snake venomics of African spitting cobras: toxin composition and assessment of congeneric cross-reactivity of the pan-African EchiTAB-Plus-ICP antivenom by antivenomics and neutralization approaches. *Journal of proteome research* 10.3 (2011): 1266-1280.
- [4] Structures obtained from PDB.org

Future perspectives

It is our hope that this work will advance the development of recombinant antivenoms based on oligoclonal human antibodies that are compatible with the human immune system, and provide better treatment options for snakebite victims in rural parts of the tropical world.

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