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Discovery of human antibodies against sea snake venom phospholipase A_2s from *Aipysurus laevis*

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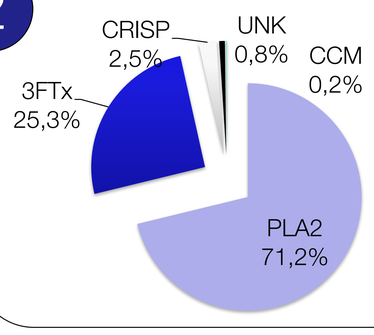
1 Addressing the problem of immunogenic antivenoms

Snakebite is one of the world's most neglected tropical diseases, with an estimated 5.5 million bites per year, resulting in 125.000 deaths [1]. The only current treatment for snakebite envenoming is antiserum derived from the blood of immunized mammals (typically horses) [2]. These antisera are expensive to produce and carry a high risk of causing hyper-allergic reactions in human recipients due to their heterologous origin [3]. Here we report the discovery of human scFvs against *Aipysurus laevis* toxins.

2 Composition of *A. laevis* venom

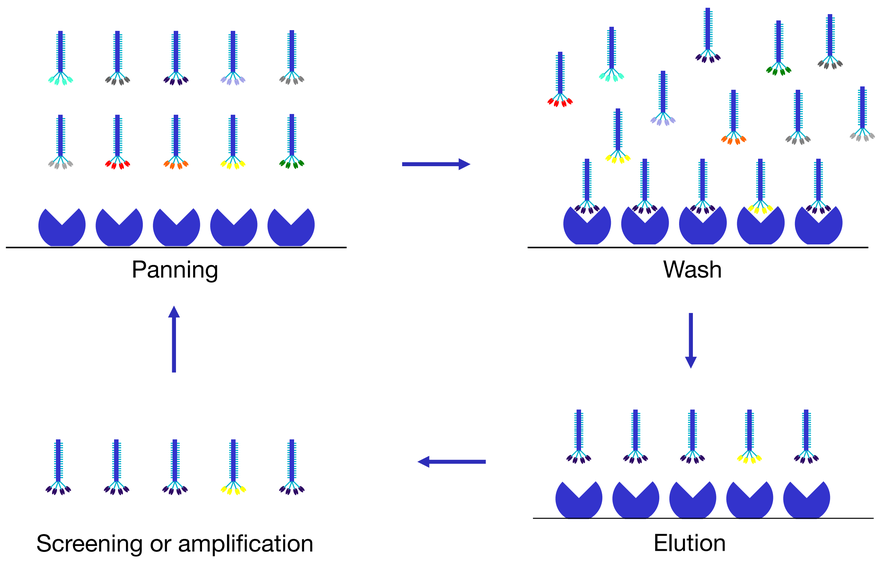


Composition of *A. laevis* venom according to protein families, expressed as percentages of the total protein content [4]:

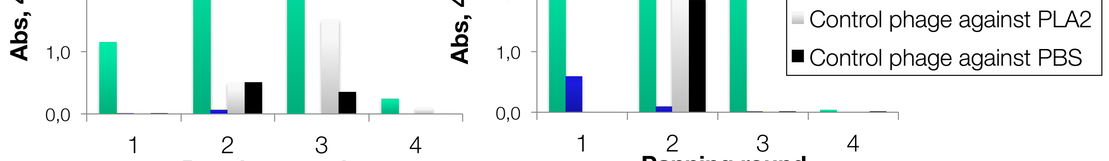
3FTx: three-finger toxin
PLA_2: phospholipase A_2
CRISP: cysteine-rich secretory protein
CCM: complement control module


Aipysurus laevis (Olive sea snake)

3 Selection using human scFv displaying phages

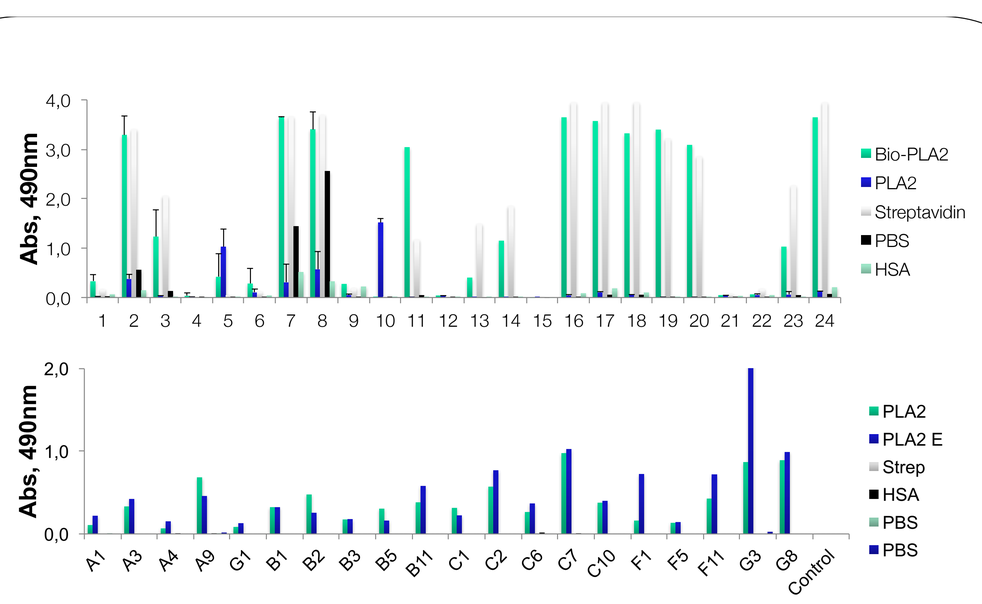


4 Panning rounds using Tomlinson libraries



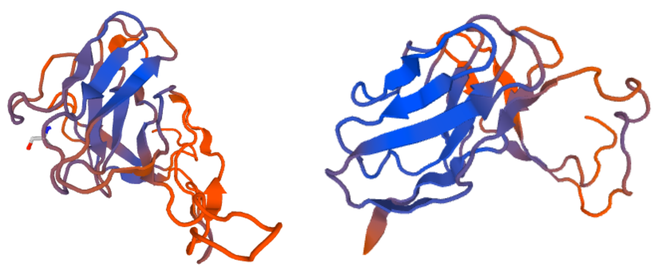
Polyclonal ELISA of four different panning rounds performed in the phage display selection using Tomlinson Library I & J against biotinylated-PLA_2.

5



Selected monoclonal phages expressing scFv were investigated by ELISA against Biotinylated-PLA_2, PLA_2, Streptavidin, HSA, & PBS. Top: Top 24 of 288 clones from first selection. Bottom: top 20 of 86 clones from second selection.

6



Isolated ssDNA from twelve promising binders was sequenced. Two of these sequences were modeled using SwissModel [6].

7 Next steps: Evaluation of scFv-toxin binding affinity

Soluble scFv fragments are to be expressed by *E. coli* for affinity studies using isothermal titration calorimetry (ITC) or surface plasmon resonance (SPR). We intend to expand our investigation of scFv cross-reactivity to PLA_2s from venoms of other snake species. We hope to develop human scFvs that may broadly neutralize snake venom PLA_2s across snake genera.

References

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