

# Discovery of nanobodies for the development of recombinant antivenoms

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# Discovery of nanobodies for the development of recombinant antivenoms

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## 1 Snakebite envenoming

Snakebite envenoming is a major public health problem affecting millions of people, especially those living in poor developing countries.[1] Sub-Saharan Africa is one of the main hotspots, accounting for 25% of the cases, demanding urgent global attention. Although currently available antivenoms have saved countless lives, they come with considerable drawbacks, making room for innovative solutions.[2]

At the Center for Antibody Technologies, we apply such solutions to combat the snakebite crisis. Here, the pipeline for the discovery of neutralizing nanobodies ($V_HHs$) against short-chain $\alpha$-neurotoxins (sNTxs) from medically relevant *Elapidae* snake species in sub-Saharan Africa is presented as an example.

**Global numbers (per year)[1]**
1.8- 2.7 million envenomings
81,000- 138,000 deaths

**Africa & Middle East**
453,000-580,000 envenomings
20,000-32,000 deaths

400,000 cases of amputations, disabilities, blindness, or neurological sequelae worldwide

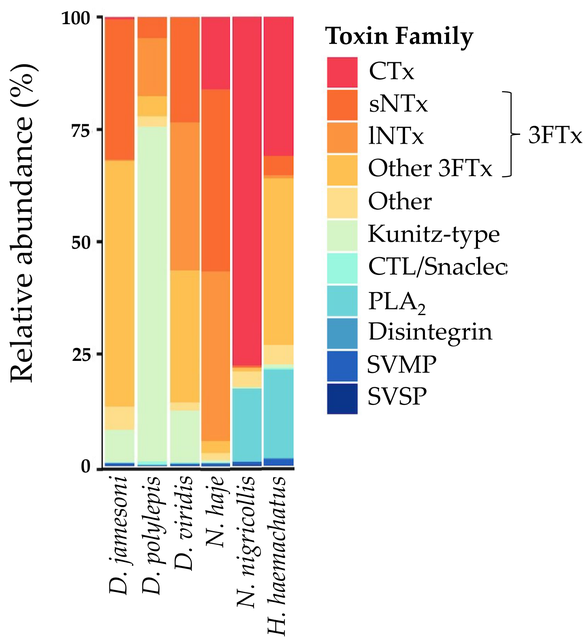
*Dendroaspis polylepis*

*Naja haje*

*Hemachatus haemachatus*

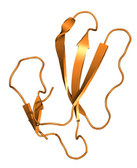
## 2 Proteomic characterisation of *Elapidae* venom

LC-MS/MS analysis[3]



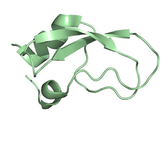

Elapid venom mainly contains four toxin families

Cytotoxin (CTx)



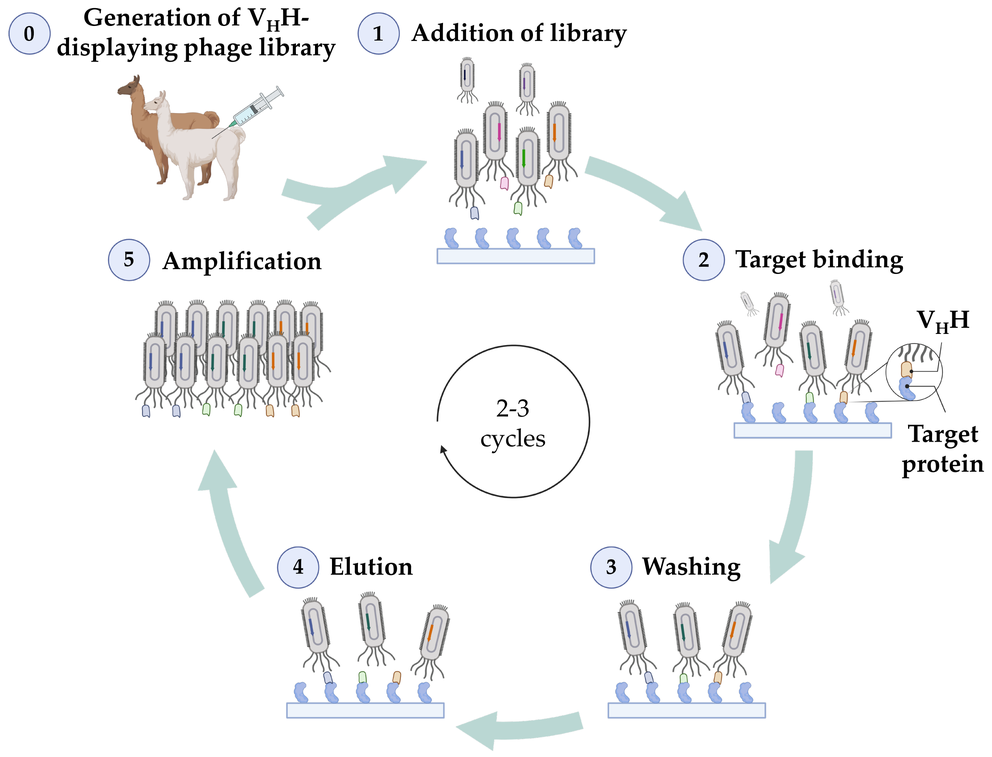
Three finger toxin (3FTx)

Phospholipase $A_2$ ($PLA_2$)



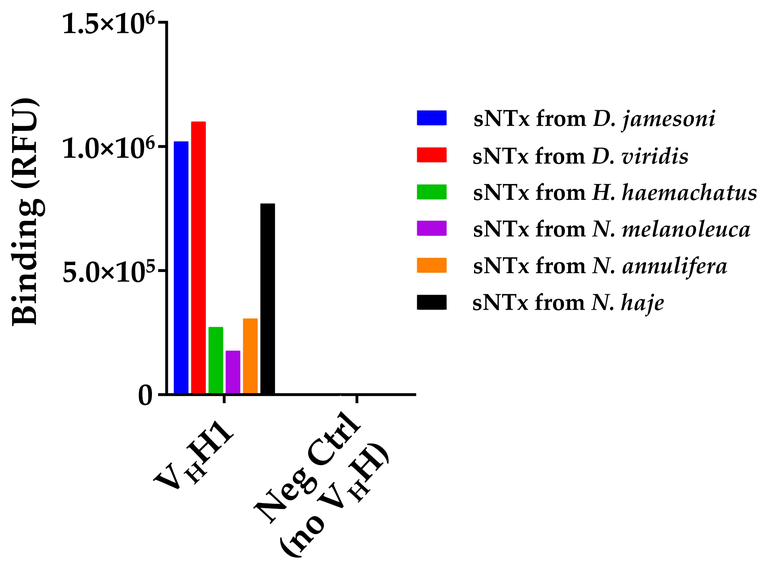
Kunitz-type serine protease inhibitor

## 3 Phage display campaign on sNTxs

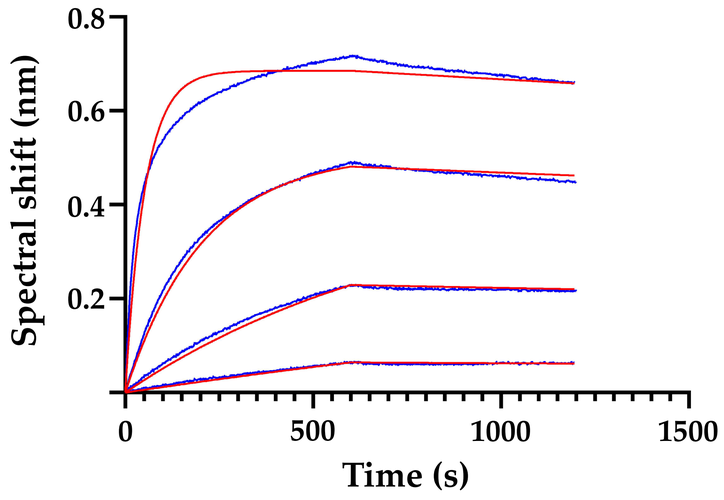



## 4 Screening and characterisation of sNTx-binding $V_HHs$

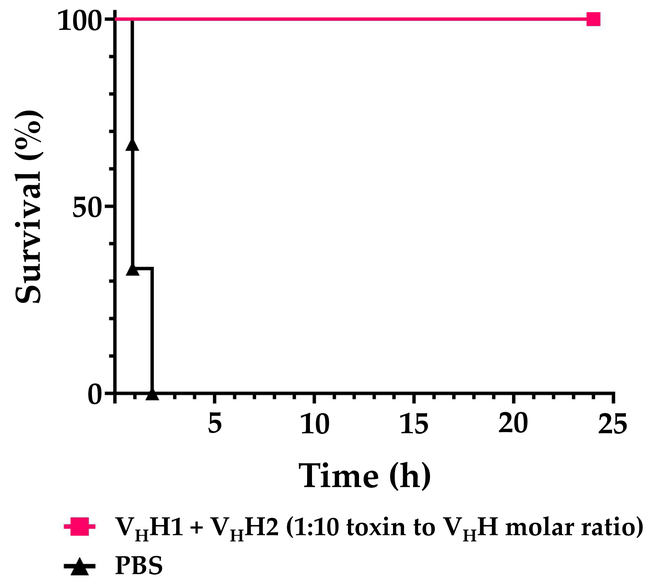
Representative discovered $V_HH$ shows binding to sNTxs from three different elapid genera.




Representative discovered $V_HH$ shows low nanomolar affinity to sNTx from *N. haje* in BLI experiments.




Mix of two $V_HHs$ prevents lethality of mice when pre-incubated with $3LD_{50}$s of *N. haje* whole venom before *iv* administration.




## 5 Outlook

The pipeline shown here is currently being used for the discovery of $V_HHs$ against additional toxin families in the venoms from medically relevant snake species in sub-Saharan Africa with the aim of making a recombinant antivenom for treatment of Elapid snakebites in the region.

**References:**

[1] Gutiérrez, J. M. *et al.* (2017). Snakebite envenoming. *Nat Rev Dis Primers.*

[2] Thumtecho, S. *et al.* (2023). Towards better antivenoms: navigating the road to new types of snakebite envenoming therapies. *J Venom Anim Toxins Incl Trop Dis.*

[3] Giang, T. T. N. *et al.* (2022). High-throughput proteomics and in vitro functional characterization of the 26 medically most important elapids and vipers from sub-Saharan Africa. *GigaScience.*

**Supported by:**

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