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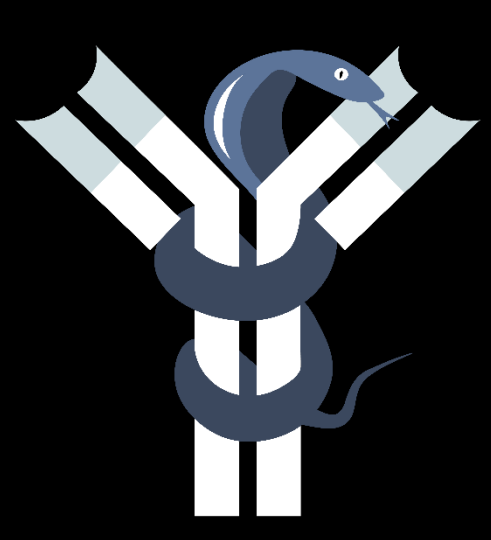
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Discovery of nanobodies for the development of recombinant antivenoms



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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

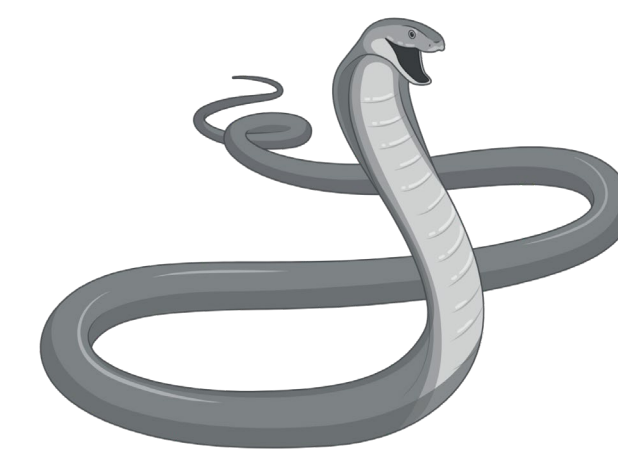
At the Center for Antibody Technologies, we apply such solutions to combat the snakebite crisis. Here, the pipeline for the discovery of neutralizing nanobodies (V_H Hs) against short-chain α -neurotoxins (sNTxs) from medically relevant *Elapidae* snake species in sub-Saharan Africa is presented as an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



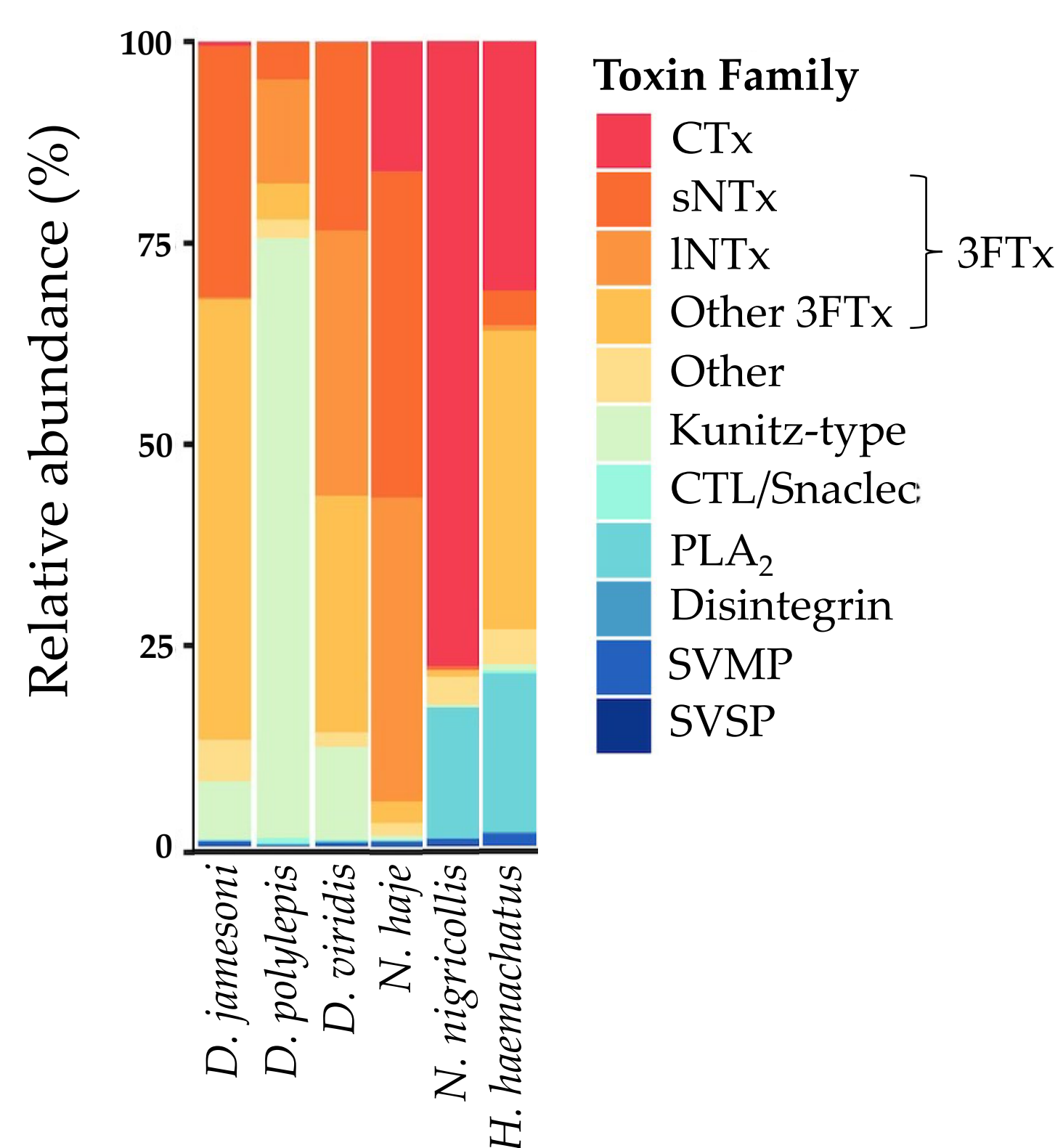
Naja haje



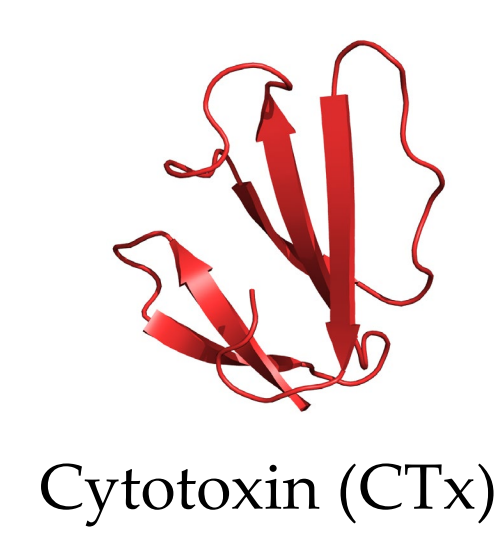
Hemachatus haemachatus

2 Proteomic characterisation of *Elapidae* venom

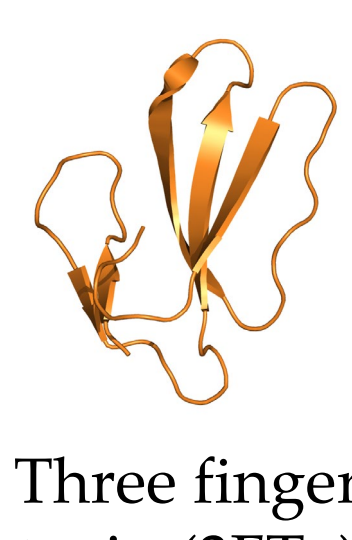
LC-MS/MS analysis³



Elapid venom mainly contains four toxin families



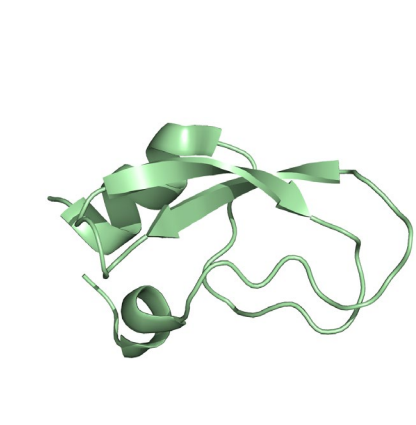
Cytotoxin (CTx)



Three finger toxin (3FTx)

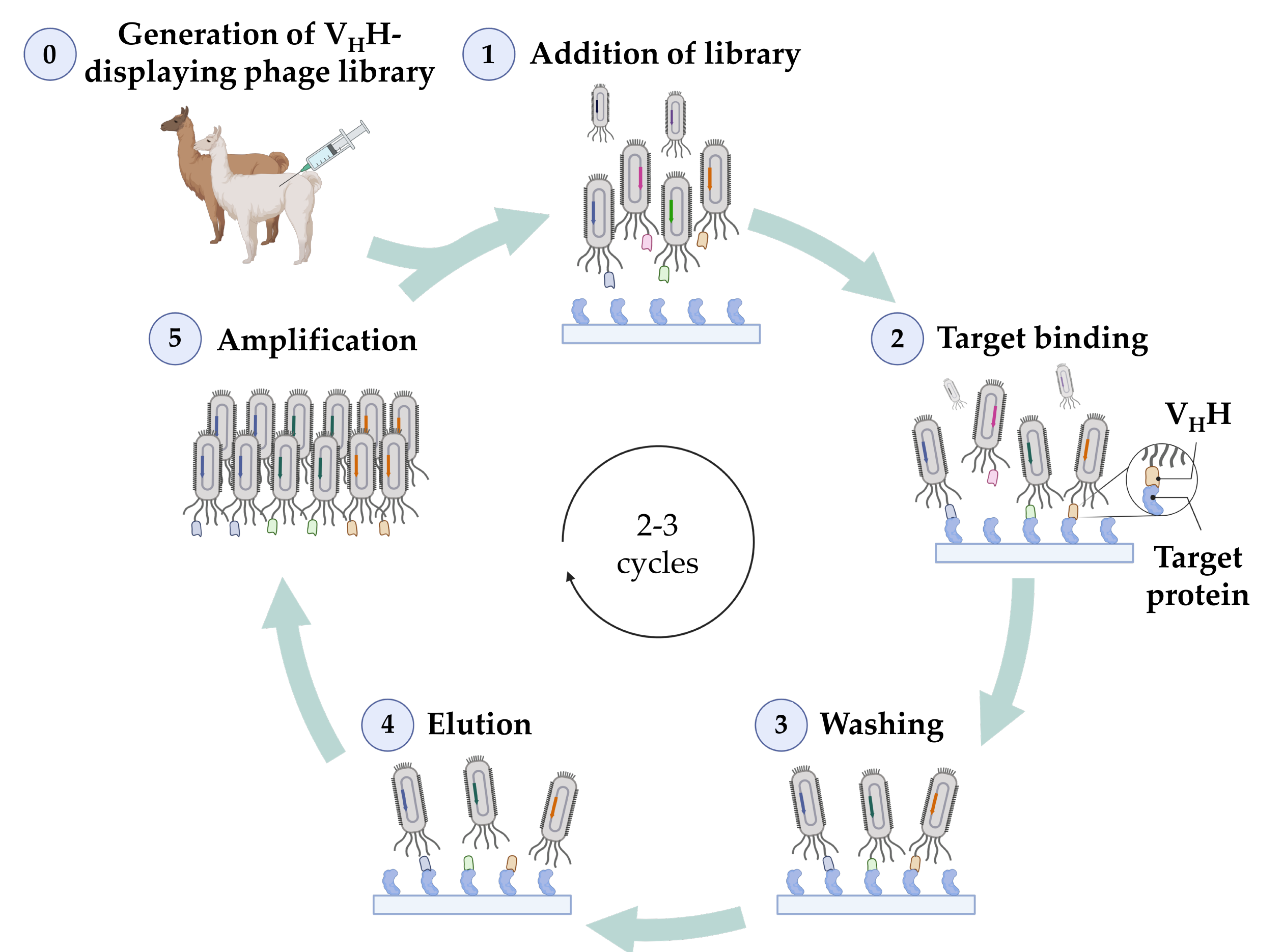


Phospholipase A₂ (PLA₂)



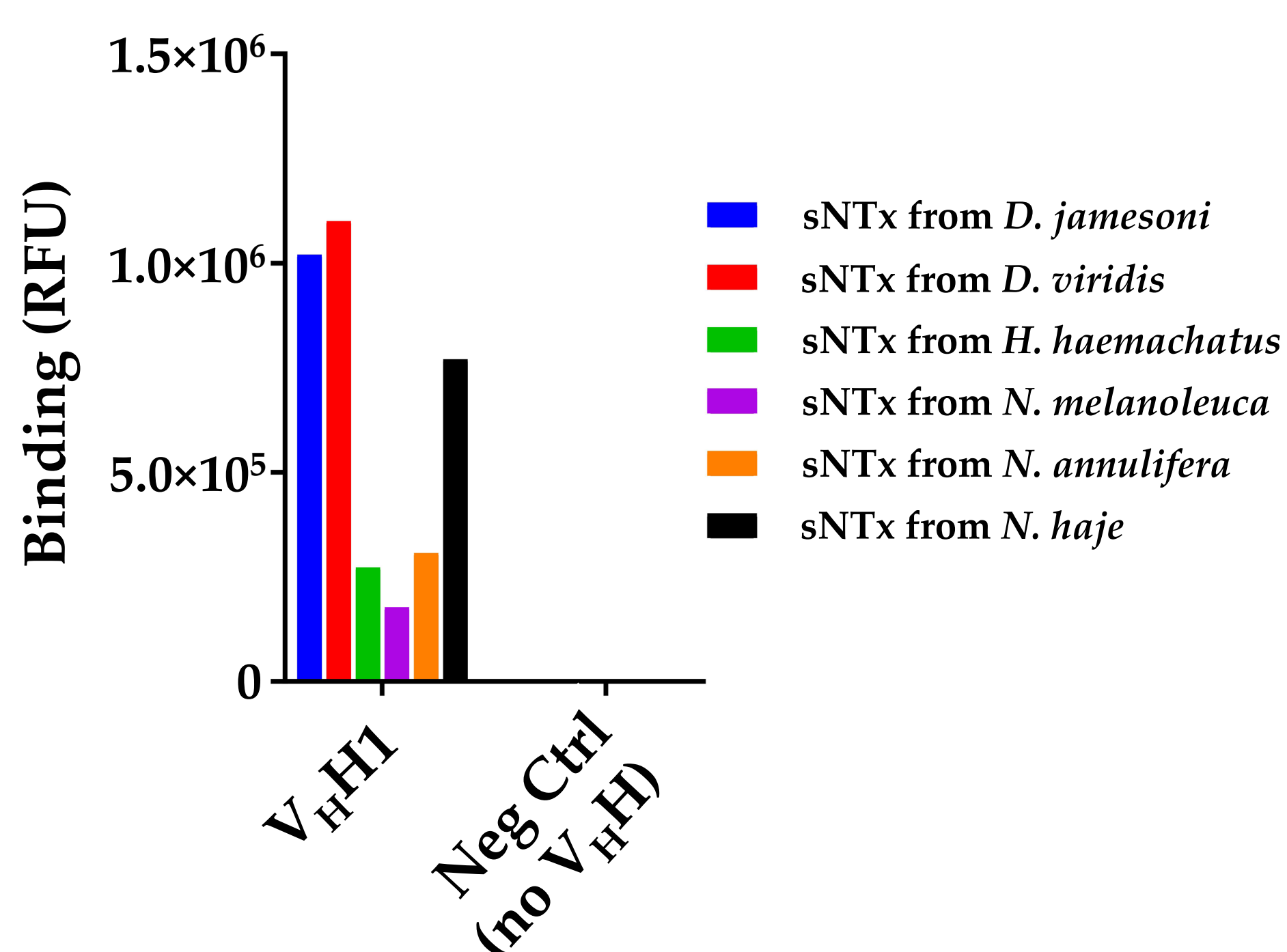
Kunitz-type serine protease inhibitor

3 Phage display campaign on sNTxs

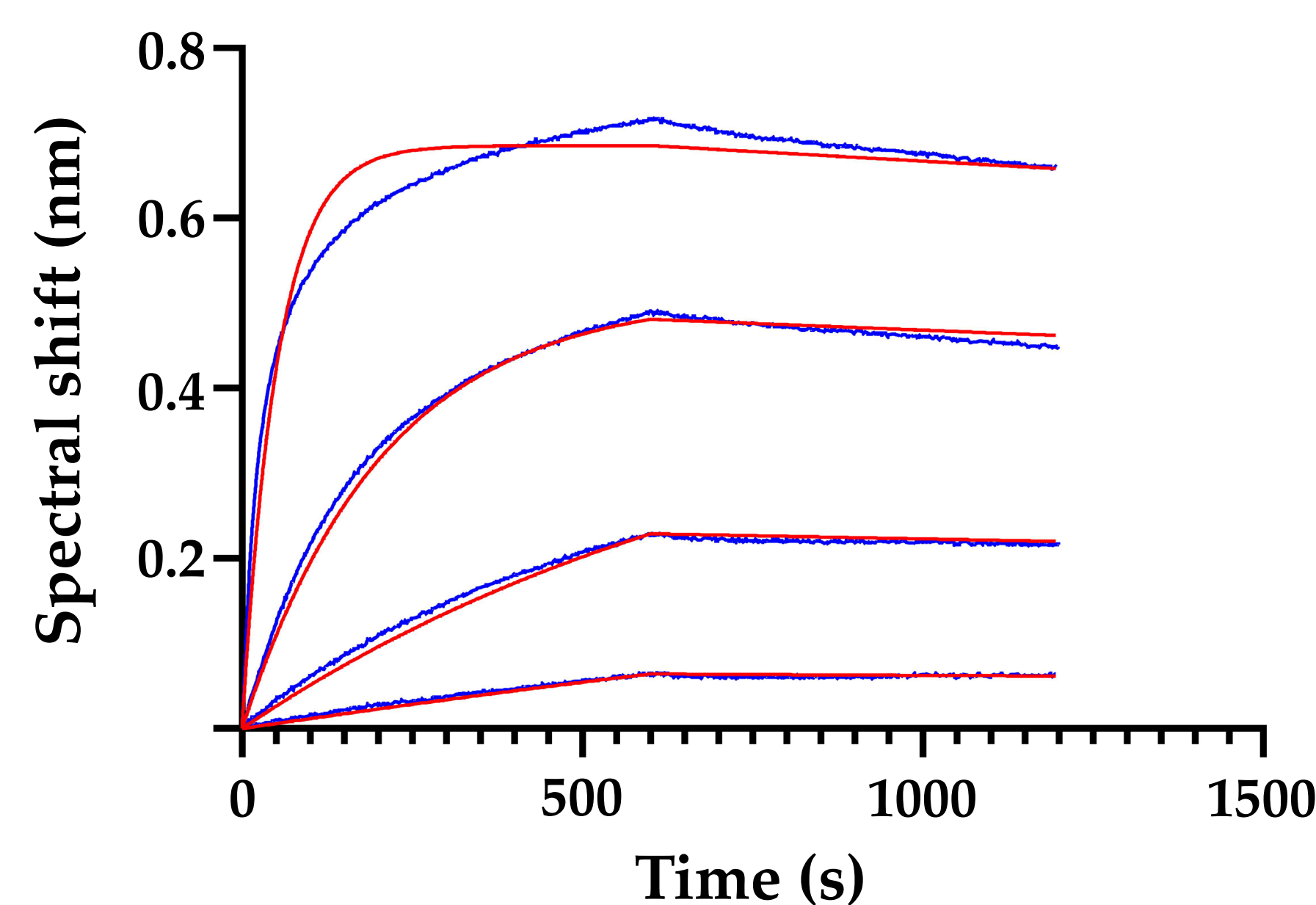


4 Screening and characterisation of sNTx-binding V_H Hs

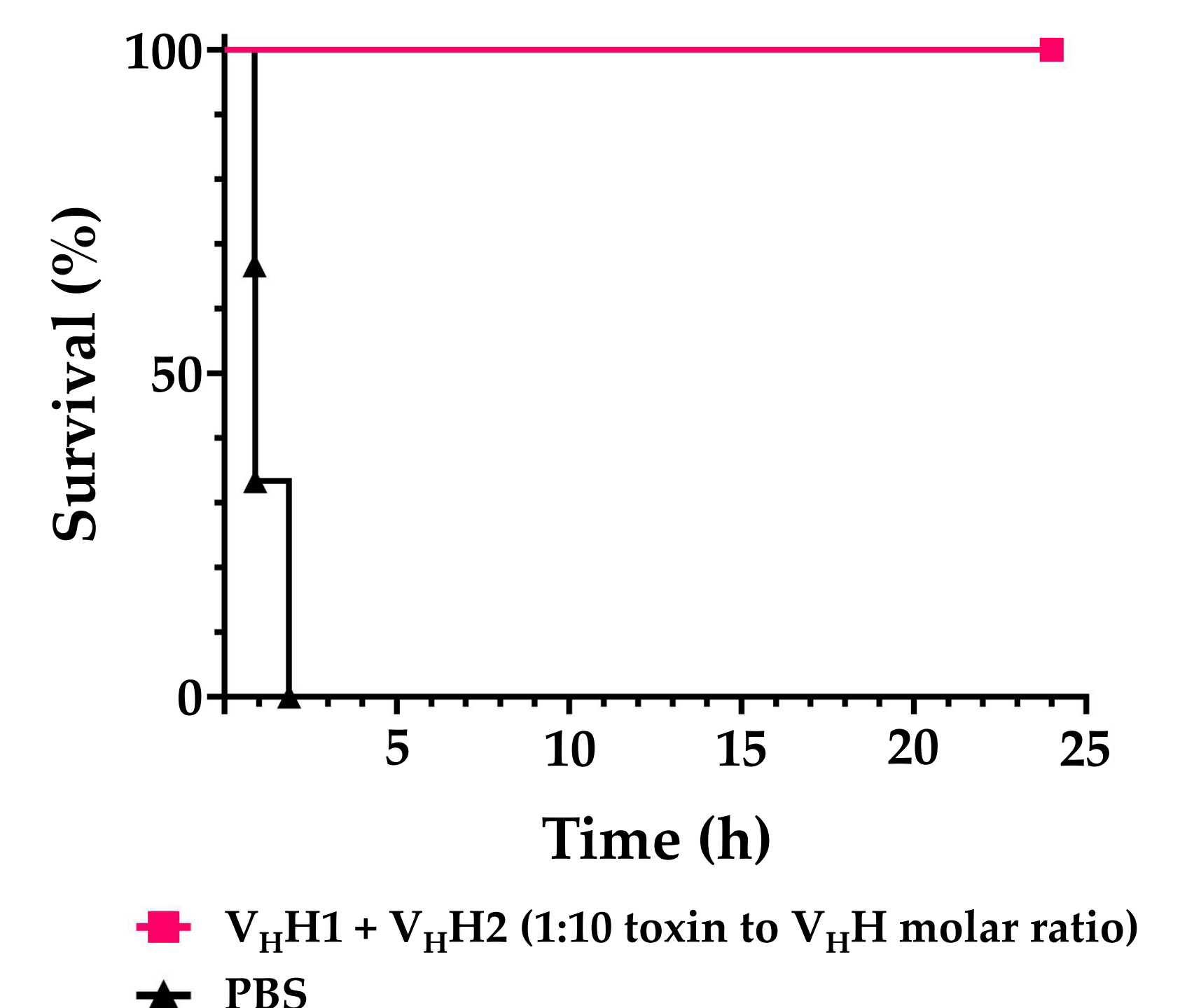
Representative discovered V_H H shows binding to sNTxs from three different elapid genera.



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



Mix of two V_H Hs prevents lethality of mice when pre-incubated with 3LD₅₀s of *N. haje* whole venom before *iv* administration.



5 Outlook

The pipeline shown here is currently being used for the discovery of V_H Hs 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*.
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- 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*.

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