



## Discovery of nanobodies for the development of recombinant antivenoms

**Burlet, Nick J.; Ahmadi, Shirin; Benard Valle, Melisa; Thumtecho, Suthimon; Ljungars, Anne; Laustsen-Kiel, Andreas Hougaard**

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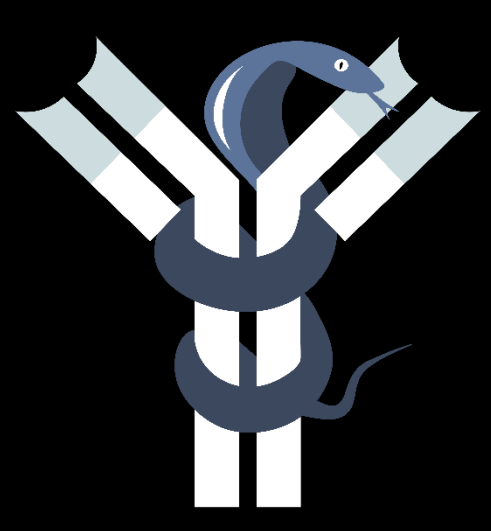
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# Discovery of nanobodies for the development of recombinant antivenoms



Nick J. Burlet, Shirin Ahmadi, Melisa Bénard-Valle, Suthimon Thumtecho, Anne Ljungars, and Andreas H. Laustsen

Department of Biotechnology and Biomedicine, Technical University of Denmark, Lyngby, Denmark

## 1 Snakebite envenoming

Snakebite envenoming is a major public health problem affecting millions of people, especially those living in poor developing countries.<sup>1</sup> 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.<sup>2</sup>

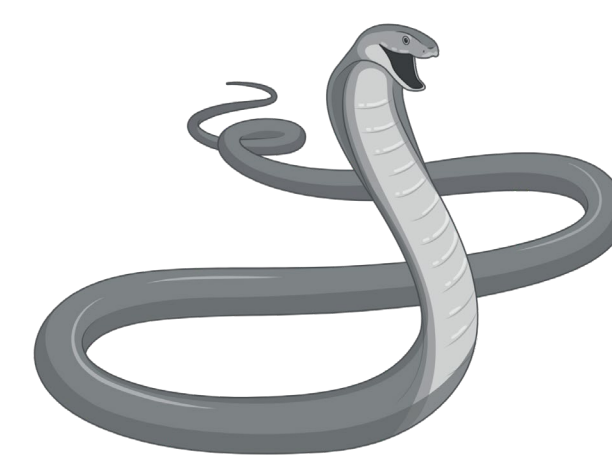
At the Center for Antibody Technologies, we apply such solutions to combat the snakebite crisis. Here, the pipeline for the discovery of neutralizing nanobodies (V<sub>H</sub>Hs) against short-chain  $\alpha$ -neurotoxins (sNTxs) from medically relevant *Elapidae* snake species in sub-Saharan Africa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

Global numbers (per year)<sup>1</sup>  
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*



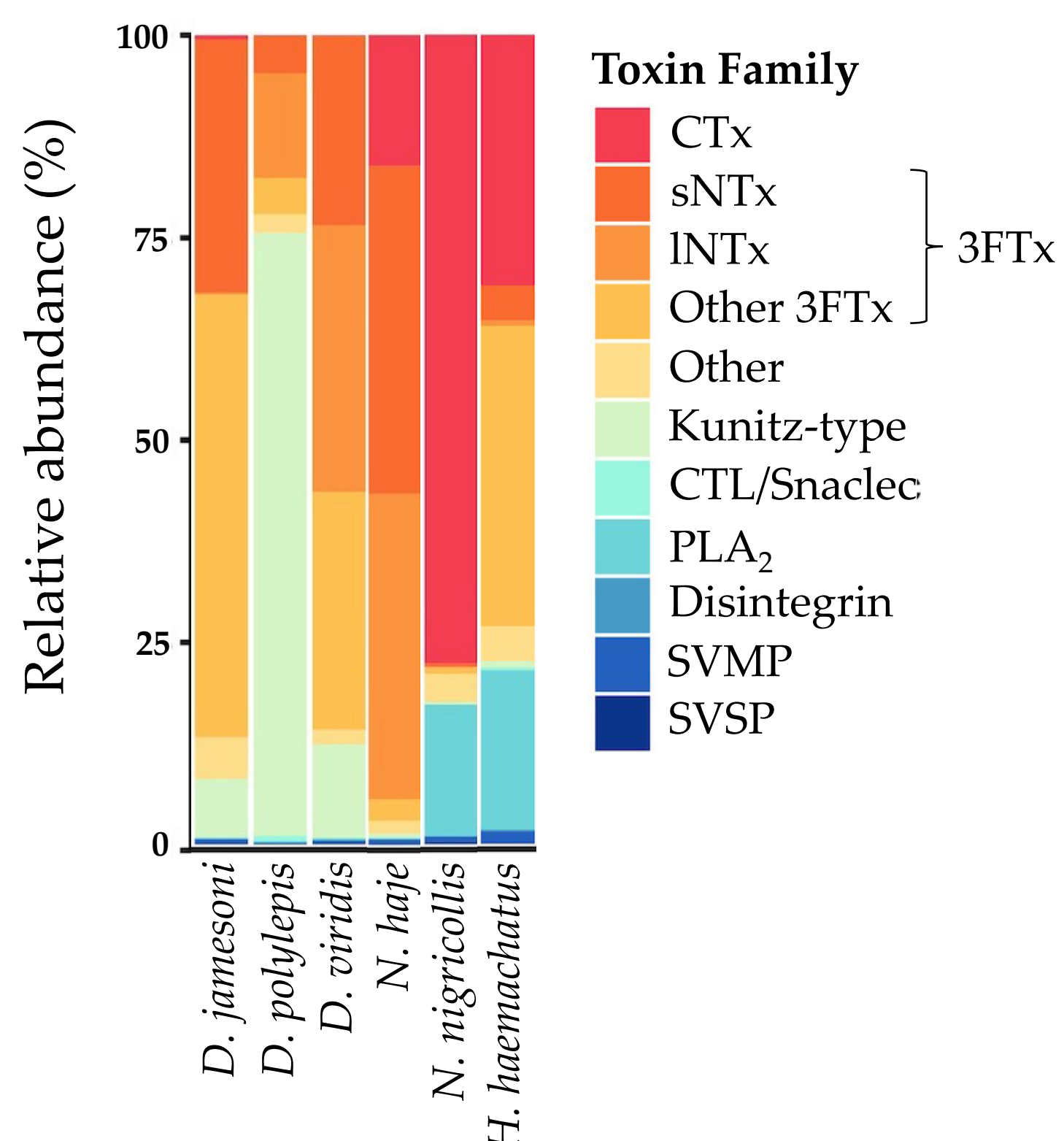
*Naja haje*



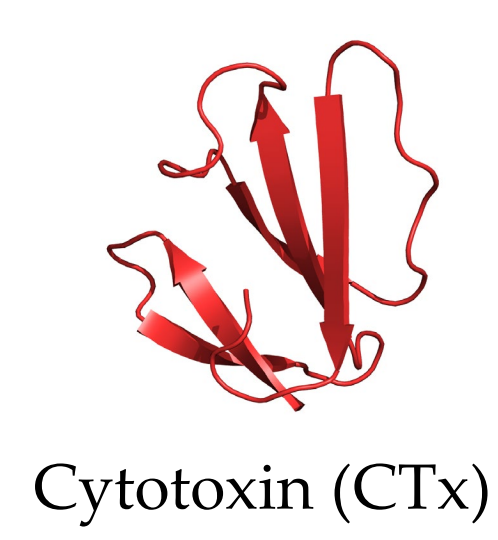
*Hemachatus haemachatus*

## 2 Proteomic characterisation of *Elapidae* venom

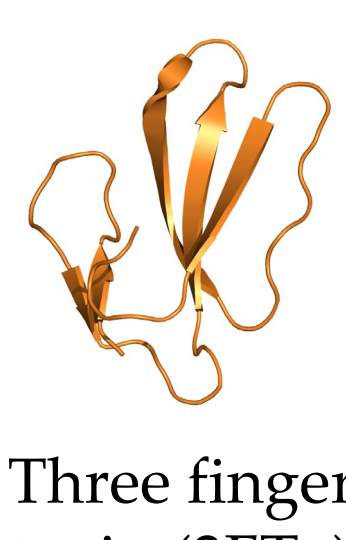
LC-MS/MS analysis<sup>3</sup>



Elapid venom mainly contains four toxin families



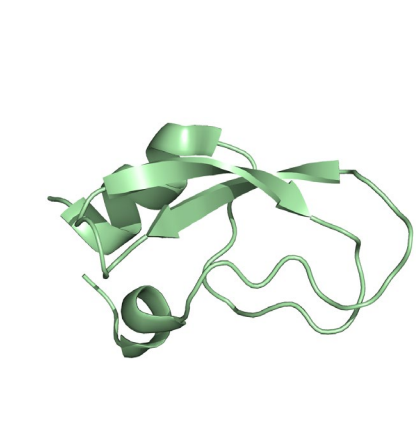
Cytotoxin (CTx)



Three finger toxin (3FTx)

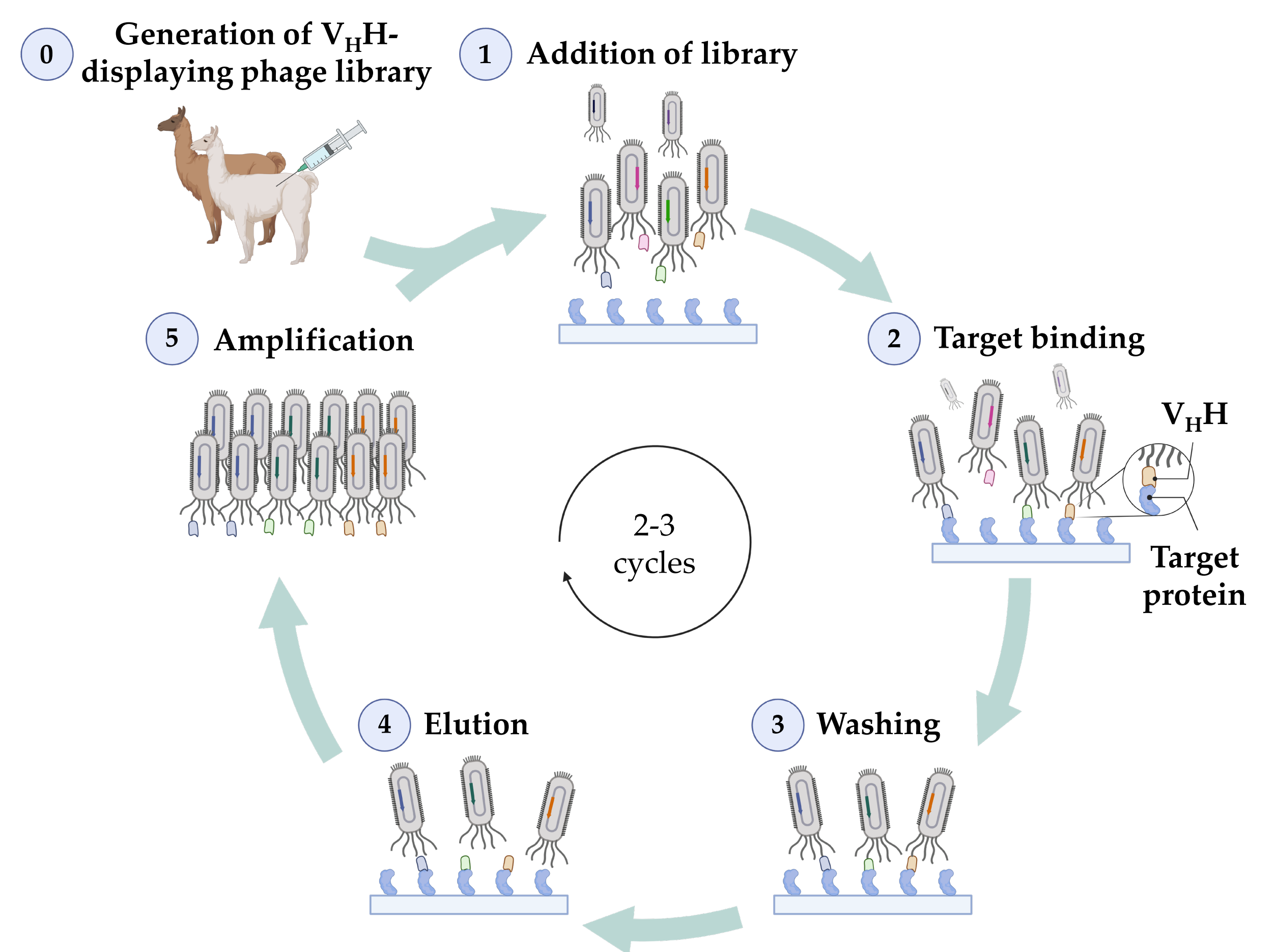


Phospholipase A<sub>2</sub> (PLA<sub>2</sub>)



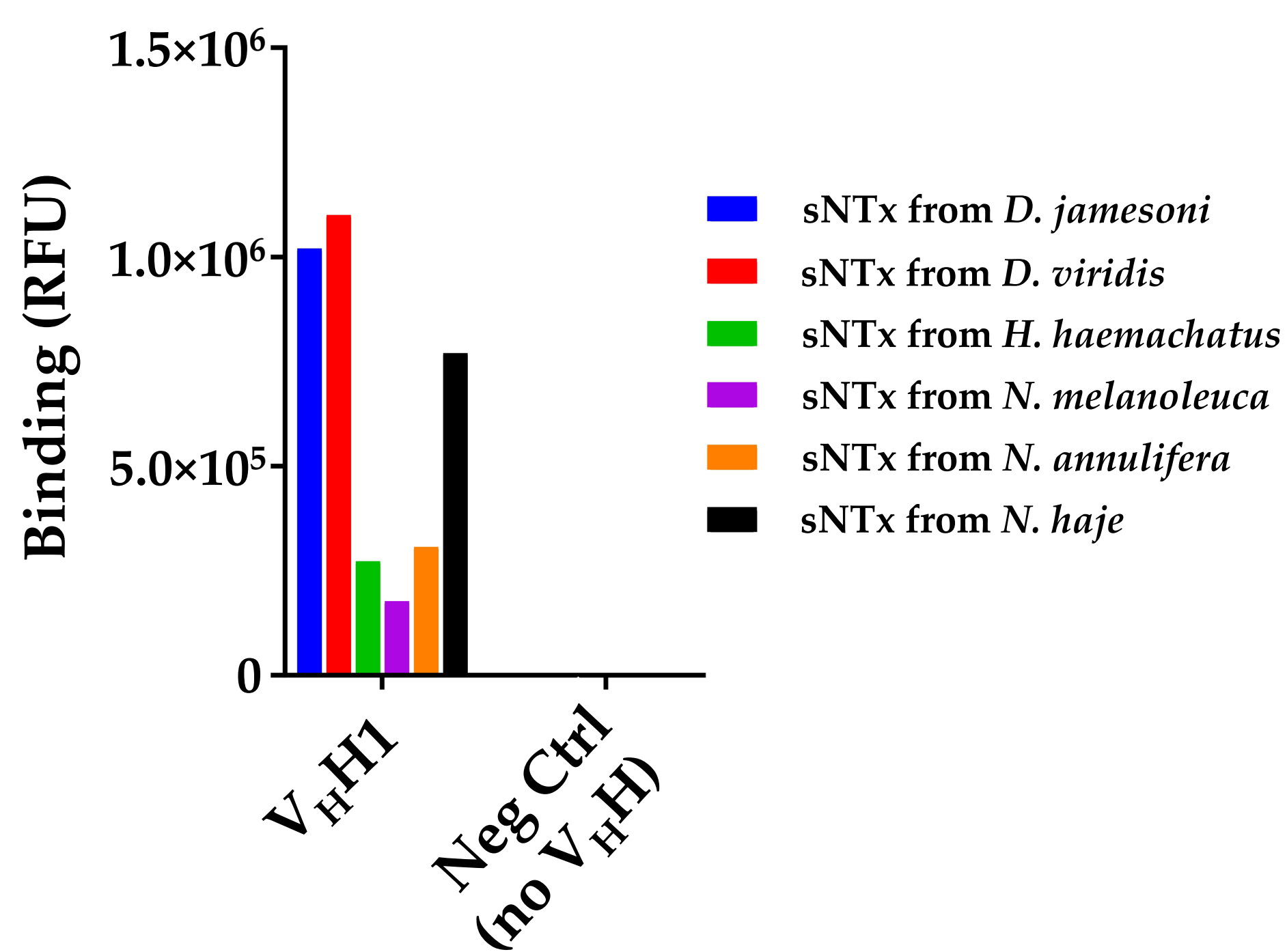
Kunitz-type serine protease inhibitor

## 3 Phage display campaign on sNTxs

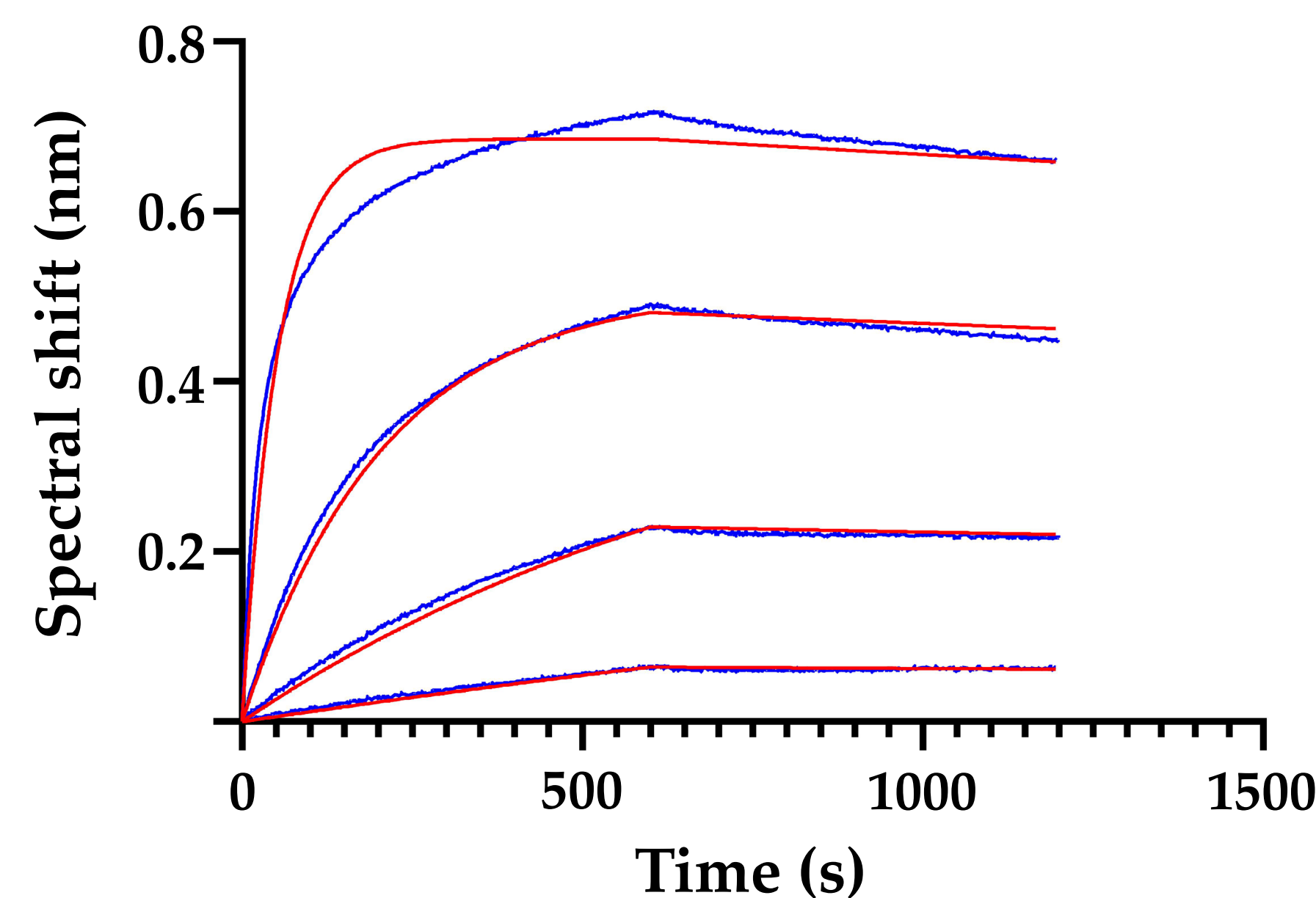


## 4 Screening and characterisation of sNTx-binding V<sub>H</sub>Hs

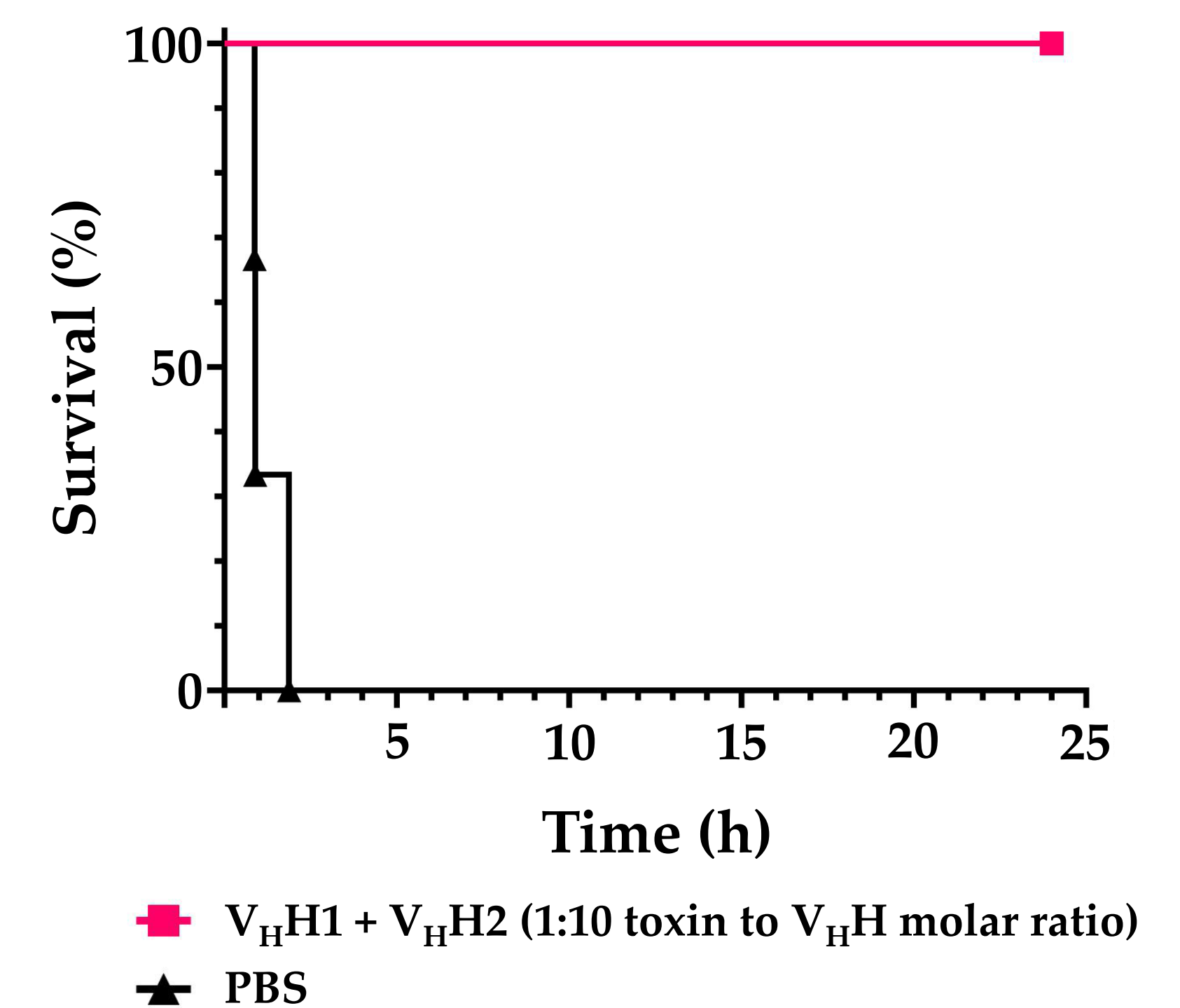
Representative discovered V<sub>H</sub>H shows binding to sNTxs from three different elapid genera.



Representative discovered V<sub>H</sub>H shows low nanomolar affinity to sNTx from *N. haje* in BLI experiments.



Mix of two V<sub>H</sub>Hs prevents lethality of mice when pre-incubated with 3LD<sub>50</sub>s of *N. haje* whole venom before *iv* administration.



## 5 Outlook

The pipeline shown here is currently being used for the discovery of V<sub>H</sub>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:

- Gutiérrez, J. M. *et al.* (2017). Snakebite envenoming. *Nat Rev Dis Primers*.
- 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*.
- 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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Ph.D. student Nick J. Burlet

[nickbur@dtu.dk](mailto:nickbur@dtu.dk)

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