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A tropical tale: how *Naja nigricollis* venom beats *Trypanosoma brucei*

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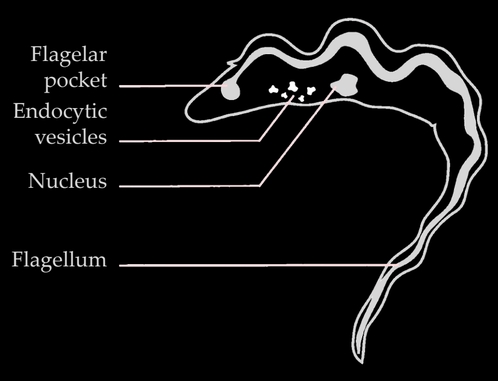
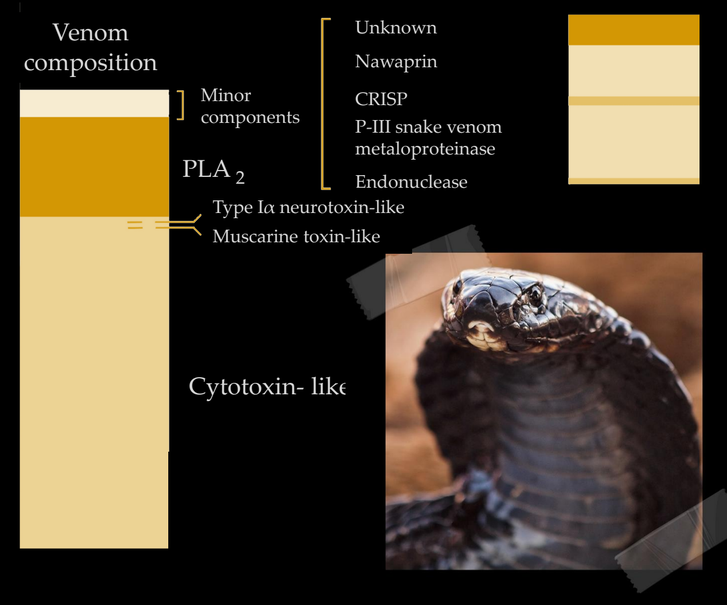
Sleeping sickness: a neglected tropical disease

Trypanosoma brucei is a parasitic protozoan species capable to infecting insect vectors whose bite further produces African sleeping sickness in human beings [1]. During the parasite's extracellular life in the mammalian host, its outer coat, mainly composed of Variable Surface Glycoproteins (VSGs) [2], undergoes enormous variation in its composition to avoid the host's lytic immune response [3].



A tropical tale of trypanosomes and snakes

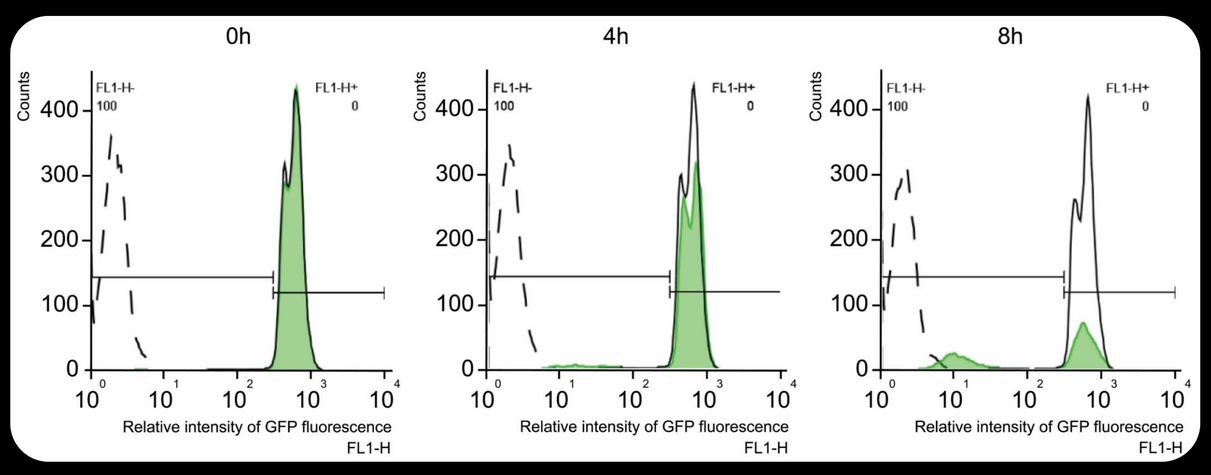
The elapid *N. nigricollis* is a large venomous snake from sub-Saharan Africa [4]. Since the origin of pharmacology, venoms have been used as medicines, since venom toxins target a myriad of different physiological processes with high specificity and selectivity.



N. nigricollis venom is able to kill *T. brucei* by targeting GPI anchoring of VSG

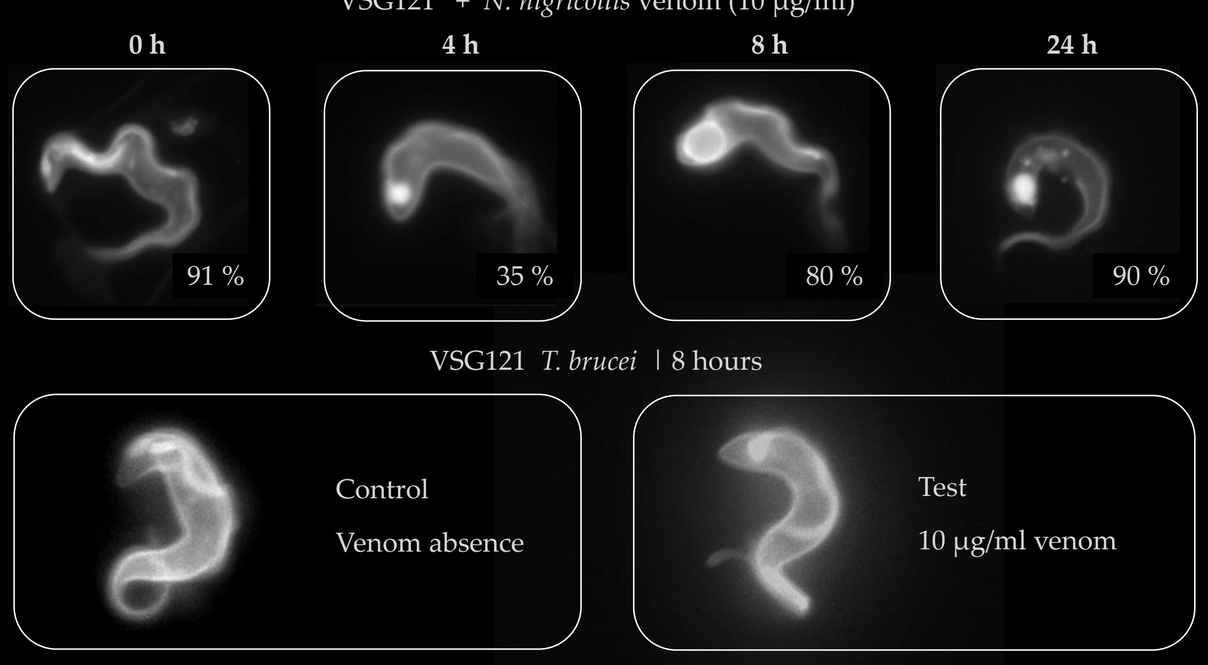
Phospholipases A_2 are one of the major enzymatically active components in *N. nigricollis* venom, which could be targeting the GPI anchor of VSG. Lyophilized whole venom was diluted in HMI-9 cell culture media, in which we cultured *T. brucei* parasites expressing eGFP attached to GPI (VSG121) with 10 µm/ml of *N. nigricollis* venom during 24 hours. Then, we study the surveillance and the GFP-GPI release by flow cytometry.

Parasite cells counts by flow cytometry



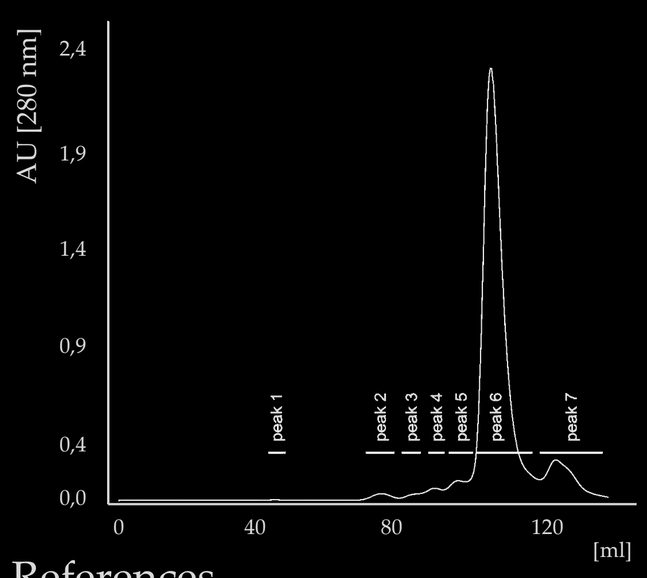
N. nigricollis venom provokes the flagellar pocket enlargement by accumulating GPI

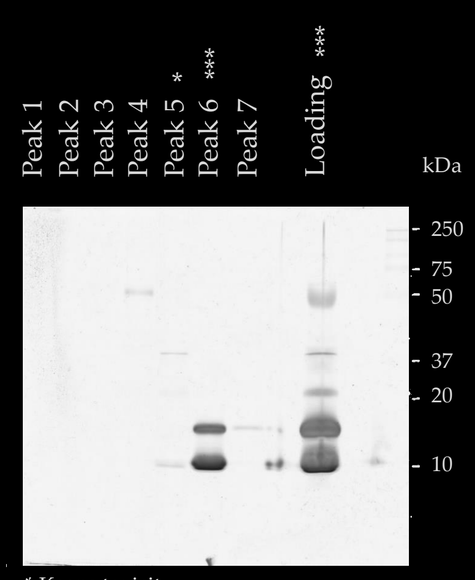
We observed VSG121 parasites using the fluorescence microscope. Contrarily to the parasites' phenotype during venom absence, parasites cultured with the *N. nigricollis* venom show a greener and enlarged flagellar pocket over the time.



PLA_2 and cytotoxins are potentially the toxins responsible of the parasite death

After gel filtration of 20 mg of *N. nigricollis* whole venom, we tested each venom fraction in culture and ran a SDS-PAGE, which was developed by silver-staining.

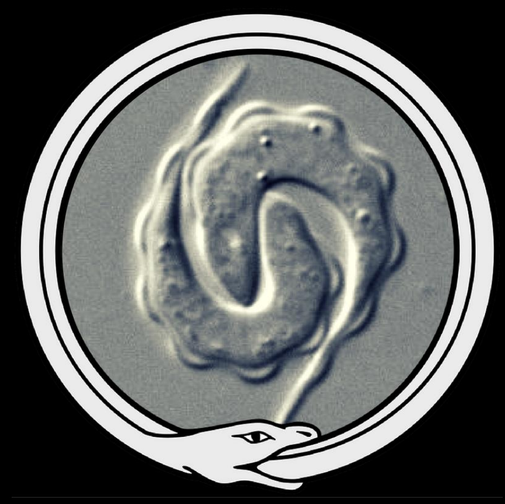




* Keeps toxicity
*** Kills

Impact

I. **First report of using snake venom to effectively kill effectively *T. brucei*.**



II. Novel molecular target antigenic variation-independent, allowing to bypass the main challenge of developing a successful treatment for the neglected tropical disease, African sleeping sickness.

III. Unveiling of the mechanism of parasite lethality may help pave the way for novel molecular tools for drug discovery against trypanosome related diseases.

References

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