The medical threat of mamba envenoming in sub-Saharan Africa revealed by genus-wide analysis of venom composition, toxicity and antivenomics profiling of available antivenoms

Mambas (genus Dendroaspis) are among the most feared of the medically important elapid snakes found in sub-Saharan Africa, but many facets of their biology, including the diversity of venom composition, remain relatively understudied. Here, we present a reconstruction of mamba phylogeny, alongside genus-wide venom gland transcriptomic and high-resolution top-down venomic analyses. Whereas the green mambas, D. viridis, D. angusticeps, D. j. jamesoni and D. j. kaimosae, express 3Ftx-predominant venoms, black mamba (D. polylepis) venom is dominated by dendrotoxins I and K. The divergent terrestrial ecology of D. polylepis compared to the arboreal niche occupied by all other mambas makes it plausible that this major difference in venom composition is due to dietary variation. The pattern of intrageneric venom variability across Dendroaspis represented a valuable opportunity to investigate, in a genus-wide context, the variant toxicity of the venom, and the degree of paraspecific cross-reactivity between antivenoms and mamba venoms. To this end, the immunological profiles of the five mamba venoms were assessed against a panel of commercial antivenoms generated for the sub-Saharan Africa market. This study provides a genus-wide overview of which available antivenoms may be more efficacious in neutralising human envenomings caused by mambas, irrespective of the species responsible. The information gathered in this study lays the foundations for rationalising the notably different potency and pharmacological profiles of Dendroaspis venoms at locus resolution. This understanding will allow selection and design of toxin immunogens with a view to generating a safer and more efficacious pan-specific antivenom against any mamba envenomation.