

## ABSTRACT

Venomous snakes pose a significant global health challenge, affecting between 1.8 and 2.7 million people annually, with an estimated 81,000 to 138,000 deaths and 400,000 survivors left with permanent physical and psychological injuries. The World Health Organization (WHO) has recognized snakebite envenoming as a priority Neglected Tropical Disease, disproportionately impacting impoverished and rural communities in tropical regions, where access to healthcare and effective antivenoms is limited. This project addresses this urgent issue by focusing on snake species within the superfamily Colubroidea, integrating cutting-edge multi-omics approaches to study their systematics, evolution, and venom diversity. Our research will target vipers from Africa, Arabia, and Asia like members of the genera *Pseudocerastes*, *Bitis*, and *Echis* —the latter among the deadliest snakes globally— elapids such as *Walterinnesia aegyptia* and *Naja arabica*, the burrowing asp *Atractaspis andersonii*, mildly venomous species like *Telescopus dhara*, and non-venomous species of the genera *Coronella* and *Natrix*. These taxa represent a continuum of venom capabilities, ecological roles, and evolutionary diversity, providing an exceptional framework to explore key questions in venom evolution, ecological adaptation, and genetic diversity. By studying these species, we aim to address gaps in the understanding of venom composition and function while making significant advancements in systematics, evolution, and biogeographic research. We will generate high-quality chromosome-level reference genomes for 12 species, complemented by extensive transcriptomic and proteomic data. This interdisciplinary approach will enable the creation of a comprehensive catalog of venom-gland-specific toxin genes—the so-called venom-ome-specific toxins. These datasets will redefine the understanding of venom systems by identifying the molecular mechanisms driving the diversification and specialization of toxic arsenals, paving the way for next-generation synthetic antivenoms with defined compositions using recombinant technologies. Additionally, whole genome sequencing and transcriptomic analyses will resolve unresolved phylogenetic relationships, speciation events, hybridization patterns, and demographic histories across these groups, offering critical insights into their evolutionary trajectories. These analyses will also elucidate how venom systems have evolved in response to ecological pressures, providing a deeper understanding of the interplay between genetics, adaptation, and function. This project bridges evolutionary biology, systematics, toxinology, and applied genomics, generating high-resolution data critical for understanding venom systems and their broader applications. By integrating cutting-edge technologies, such as high-quality genome assemblies and multi-omics analyses, this research will establish a new standard in the study of venomous organisms and their ecological and evolutionary roles. The findings will have far-reaching implications beyond public health. By contributing valuable genomic resources, the project will advance fundamental evolutionary science while promoting the conservation of snake species, many of which play vital roles in their ecosystems as predators and prey. The data generated will also provide essential tools for policymakers and conservationists, enhancing efforts to protect biodiversity in areas where human-snake conflicts are most pronounced.