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Review

Venomous snakes of Costa Rica: Biological and medical implications of their venom proteomic profiles analyzed through the strategy of snake venomics☆

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ABSTRACT

In spite of its small territory of ~50,000 km^2, Costa Rica harbors a remarkably rich biodiversity. Its herpetofauna includes 138 species of snakes, of which sixteen pit vipers (family Viperidae, subfamily Crotalinae), five coral snakes (family Elapidae, subfamily Elapinae), and one sea snake (Family Elapidae, subfamily Hydrophiinae) pose potential hazards to human and animal health. In recent years, knowledge on the composition of snake venoms has expanded dramatically thanks to the development of increasingly fast and sensitive analytical techniques in mass spectrometry and separation science applied to protein characterization. Among several analytical strategies to determine the overall protein/peptide composition of snake venoms, the methodology known as 'snake venomics' has proven particularly well suited and informative, by providing not only a catalog of protein types/families present in a venom, but also a semi-quantitative estimation of their relative abundances. Through a collaborative research initiative between Instituto de Biomedicina de Valencia (IBV) and Instituto Clodomiro Picado (ICP), this strategy has been applied to the study of venoms of Costa Rican snakes, aiming to obtain a deeper knowledge on their composition, geographic and ontogenic variations, relationships to taxonomy, correlation with toxic activities, and discovery of novel components. The proteomic profiles of venoms from sixteen out of the 22 species within the Viperidae and Elapidae families found in Costa Rica have been reported so far, and an integrative view of these studies is hereby presented. In line with other venomic projects by research groups focusing on a wide variety of snakes around the world, these studies contribute to a deeper understanding of the biochemical basis for the diverse toxic profiles evolved by venomous snakes. In addition, these studies provide opportunities to identify novel molecules of potential pharmacological interest. Furthermore, the establishment of venom

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proteomic profiles offers a fundamental platform to assess the detailed immunorecognition of individual proteins/peptides by therapeutic or experimental antivenoms, an evolving methodology for which the term 'antivenomics' was coined (as described in an accompanying paper in this special issue).

Biological significance
Venoms represent an adaptive trait and an example of both divergent and convergent evolution. A deep understanding of the composition of venoms and of the principles governing the evolution of venomous systems is of applied importance for exploring the enormous potential of venoms as sources of chemical and pharmacological novelty but also to fight the consequences of snakebite envenomings. Key to this is the identification of evolutionary and ecological trends at different taxonomical levels. However, the evolution of venomous species and their venoms do not always follow the same course, and the identification of structural and functional convergences and divergences among venoms is often unpredictable by a phylogenetic hypothesis. Snake venomics is a proteomic-centered strategy to deconstruct the complex molecular phenotypes the venom proteomes. The proteomic profiles of venoms from sixteen out of the 22 venomous species within the Viperidae and Elapidae families found in Costa Rica have been completed so far. An integrative view of their venom composition, including the identification of geographic and ontogenic variations, is hereby presented. Venom proteomic profiles offer a fundamental platform to assess the detailed immunorecognition of individual venom components by therapeutic or experimental antivenoms. This aspect is reviewed in the companion paper. This article is part of a Special Issue entitled: Proteomics of non-model organisms.

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1. Introduction

Gradually formed by the collision and separation of five crustal plates, the Central American isthmus reached its final closure nearly 3 million years ago, creating a barrier between two oceans and a bridge between two continents [1]. This closing enabled a massive exchange of terrestrial animals between North and South America, the 'great American biotic interchange', which created vast opportunities to generate evolutionary change and diversification in groups suddenly able to enter new environments [2]. Indeed, Central America, and particularly Costa Rica, holds one of the highest rates of biodiversity per km^2, and the 'Costa Rican System of Conservation Areas' is thought to protect an estimated half-million species of plants, animals, and microorganisms, representing not less than 4–5% of the terrestrial biological diversity [3].

The herpetofauna of Costa Rica — a nation of only 50,000 km^2 — includes 232 reptile species, of which 138 correspond to snakes [4]. Among these, sixteen species of pit vipers (Family Viperidae, subfamily Crotalinae), five of coral snakes (Family Elapidae, subfamily Elapinae), and a sea snake (family Elapidae, subfamily Hydrophiinae) are potentially life-threatening to humans and animals. Due to their medical relevance, these venomous species have been studied more intensively than non-venomous snakes, and their venoms have attracted the attention of local scientists since the pioneer work of Clodomiro Picado during the first decades of the XXth century [5]. Driven by the nation's need to have antivenoms available for the treatment of snakebite envenomings, the 'Instituto Clodomiro Picado' was founded in 1970, headed by another pioneer of Costa Rican toxinology, Róger Bolaños [6]. A significant quota of the research undertaken at this institute has since been devoted to the characterization of snake venoms