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The structural and functional diversification of the Toxicofera reptile venom system

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ABSTRACT

The evolutionary origin and diversification of the reptilian venom system is described. The resolution of higher-order molecular phylogenetics has clearly established that a venom system is ancestral to snakes. The diversification of the venom system within lizards is discussed, as is the role of venom delivery in the behavioural ecology of these taxa (particularly *Varanus komodoensis*). The more extensive diversification of the venom system in snakes is summarised, including its loss in some clades. Finally, we discuss the contentious issue of a definition for "venom", supporting an evolutionary definition that recognises the homology of both the venom delivery systems and the toxins themselves.

1. Introduction

The first two higher-level squamate phylogenetic studies using multiple nuclear genes (C-mos and RAG-1) and broad taxonomic coverage (Vidal and Hedges, 2004; Townsend et al., 2004) suggested that most of the classical phylogeny based on morphology was incorrect. The interrelationships among a large novel clade containing i) snakes, ii) anguimorphs, iii) iguanians, and iv) amphisbaenians, lacertids and teiioids could not be resolved in either of these initial studies. Subsequently, it was demonstrated with the use of nine nuclear genes that venom has been a key evolutionary innovation underlying the diversification of the reptile clade Toxicofera including snakes, anguimorphs and iguanians (Fry et al., 2006; Vidal and Hedges, 2005). It has therefore only recently been determined that the single origin of venom in reptiles occurred approximately 170 million years ago during the Jurassic period (Fry et al., 2006; Vidal and Hedges, 2005). Advances in molecular systematics and venomics have thus provided the vital phylogenetic framework necessary for a reconstruction of the evolutionary history of all components of the reptilian venom-delivery system (Fry et al., 2006; Vidal et al., 2007; Vidal and Hedges, 2004, 2005).

2. Origin of venom proteins

Studies by us have demonstrated that a core set of venom genes were present in the common ancestor of all toxicoferans which subsequently evolved into the complex venoms observed in modern snakes and lizards following

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further toxin recruitment events (Fig. 1) (Fry, 2005; Fry et al., 2003a, 2003b, 2010a, 2008; Fry et al., 2006, 2009c, 2010b, in press). Venoms evolve via a process by which a gene encoding for a normal body protein, typically one involved in key regulatory processes or bioactivity, is duplicated and the copy selectively expressed in the venom gland. Venom proteins were recruited from disparate tissues (Table 1) with diverse ancestral activities (Table 2). Basal toxic activities varied widely too (Table 3) and some classes have mutated to form a myriad of new toxic

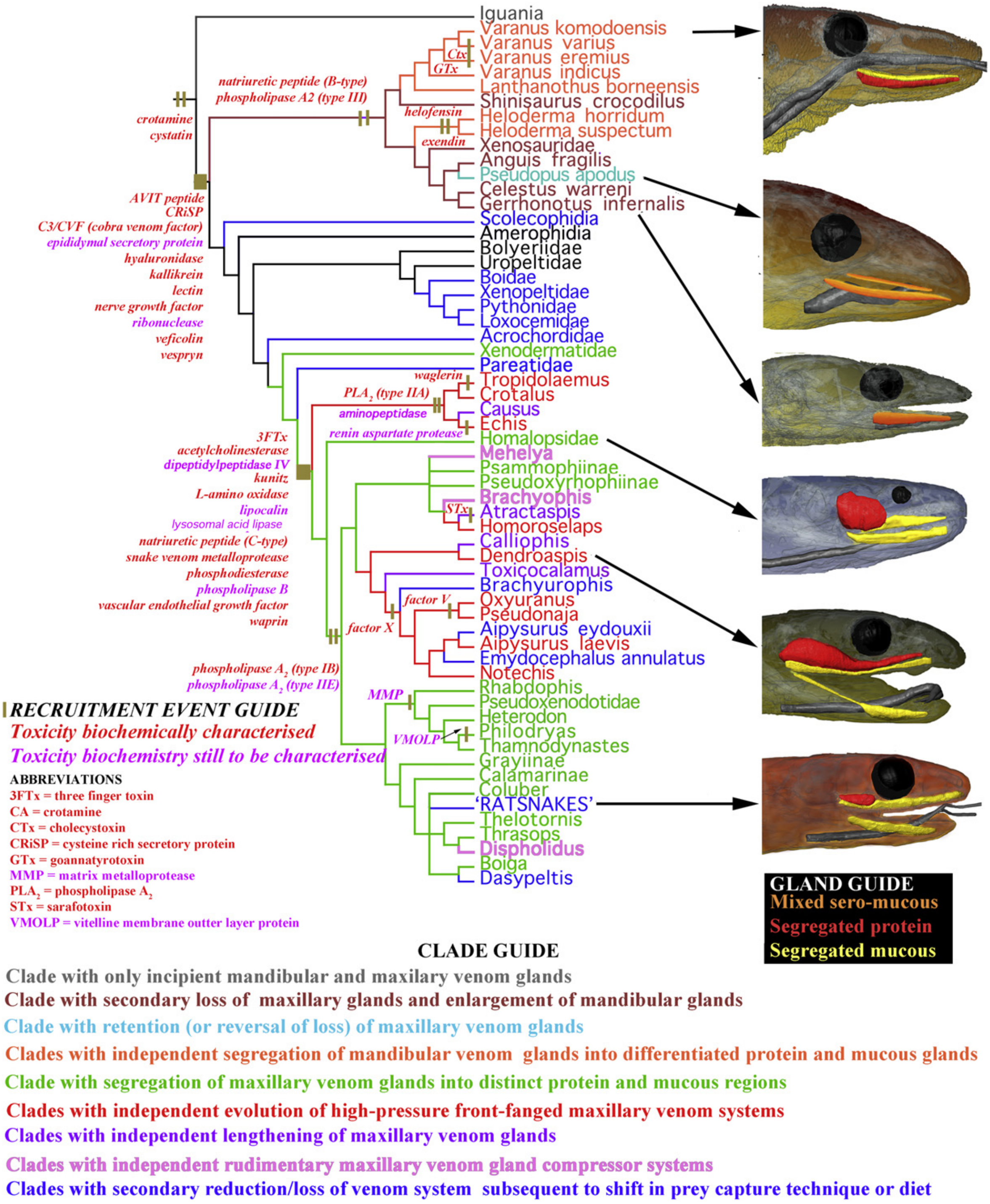

Fig. 1. Cladogram of evolutionary relationships of Toxicofera reptiles (Fry et al., 2006; Vidal and Hedges, 2002, 2004, 2005, 2009) showing relative timing of toxin recruitment events and derivations of the venom system. Magnetic resonance images are shown for representatives as per Fry et al., 2008, 2009a, 2009b, 2009c, 2010b.