

## Venom Evolution

### Genetic and External Factors

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The term venom is used for a variety of toxins that are injected by certain animals into a victim through a specialized apparatus. Though venom is most commonly employed as a means of defense and predation, it is also used as a means of asserting dominance over conspecifics. Venomous animals include sea anemones, jellyfish, gastropods, cephalopods, centipedes, insect groups, echinoderms, some species of amphibians, fish, snakes, reptiles and five species of mammals including shrews and platypus. Venom can be hemotoxic, neurotoxic and cytotoxic and produce symptoms that extend across the respiratory, muscular, renal and gastrointestinal systems.

Emily S W Wong and Katherine Belov studied the origin and diversification of venom genes through gene duplication which is known to be an important evolutionary force. Gene duplication is the process of duplicating a region of DNA; it is believed that the new copy of the gene mutates without deleterious consequences to the organism and potentially increases the fitness of the organism. In 2009, Fry *et al.*, suggested that venom sequences are similar at a molecular level. The complex cocktail of compounds that make up venom are believed to have arisen through gene duplication. The duplication of genes is a source of raw genetic substrate from which novel

functions arise. Once duplicated, some are retained by natural selection or genetic drift while the majority are lost due to the accumulation of deleterious mutations. Mutations are allowed to accumulate due to the presence of an additional gene copy which buffers against potential deleterious effects, allowing mutations to accrue over time for adaptive changes to occur. Immediately after a duplication event, duplicated toxins increase venom dosage and accelerate venom replenishment. Duplicates increase the functional diversity of venom through drift and selection allowing an animal to target a diverse range of molecules in many species. The duplicated genes can act cooperatively to induce synergistic effects in victims.

Although it is believed that gene duplication followed by adaptive selection is the primary driver of venom evolution, not much analysis has been possible due to the lack of fully sequenced genomes of venomous animals. Therefore, the platypus sequence was studied to quantify the role of gene duplication in the evolution of venom. 16 out of 107 platypus genes with known toxins evolved through gene duplication events. The lack of extensive gene duplications in platypus venom is at odds with the large venom gene expansion reported in snails and spiders implying that selective pressures vary based on venom function. Platypus venom is present only in males and is used for asserting dominance over competitors during the breeding season.

On the other hand, in species such as cone snails and snakes, where venom has have



evolved through extensive duplications, adaptive selection is likely to have played a much greater role, producing genes with a wide diversity of functions. Sites under selection in toxins may be influenced by a combination of factors, including an animal's feeding habits, their environment and biogeographical factors. Although elucidating the functional significance of these site-specific changes can be challenging, the identification of sites under positive selection represents the first step to fully characterizing the molecular actions of toxins and their evolution.

Certain toxin gene families are known to repeatedly evolve through gene duplications. The rapidly duplicating gene family which has a higher likelihood of generating potentially adaptive changes are large in size and are capable of adapting to a number of biological functions. The other kind belongs to gene families associated with immunity and defense which are co-opted to toxin roles. It is believed that genes involved in rapid response are more likely to be co-opted to become toxins than those involved in long term physiological processes.

The study of platypus venom shows that there are other evolutionary processes besides gene duplication involved in venom evolution, like mutations, gene fusions, alternative splicing and domain duplications. Venomous animals are known to use a diverse array of toxins. To date, most venom transcriptomic studies have used expression data to discover novel toxins, but next-gen sequencing will likely become the method of choice. Next-gen sequencing will advance our understanding of venom adaptation by allowing us to pose specific evolutionary questions about the evolutionary mechanisms responsible for venom adaptation, the biological networks involved in venom production and the adaptability of certain gene families for venom function.

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