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## **Platypus poison**

Vivienne Baillie Gerritsen

**P**latypuses (Ornithorhynchus anatinus) are the only mammals that squirt venom. They do this from a mobile calcaneus spur situated on the inside of each hind limb. It is a sophisticated system. The spur itself is attached at its base to a small bone which can articulate; when needed it moves at a right angle to the limb ready to fire. Strangely, only male platypuses have spurs; female platypuses lose theirs during development. Platypus venom has been under close scrutiny since 1895 when two naturalists Charles J. Martin and Frank Tidswell made their first account. We know today that platypus venom is a cocktail of toxins, most of which is a mixture of proteins which resemble no other to date. These have been named the defensin-like proteins, or DLPs, because their three dimensional structure resembles that of an antimicrobial peptide known as beta-defensin.

Venom is not the only feature which makes the platypus a unique mammal. Amongst the most noticeable are its duckbill and unique orifice for both excretion and reproduction – a reptilian trait. The first specimen of a platypus was sent to England in 1798. No one could make...bill or tail of it. Chinese taxidermists had been tricking European navigators for ages with mermaid figures which were in fact the trunks of monkeys stuck to the ends of fish. So when the first platypus arrived in England, the naturalist George Shaw described it as a possible fraud.

Another peculiar characteristic of platypuses is their ability to lay eggs. Such a skill – or indeed lack of skill – lay at the heart of heated discussions amongst illustrious 19<sup>th</sup> century scientists such as Johann Friedrich Meckel, Richard Owen, Jean-Baptiste Lamark and Etienne Geoffroy Saint-Hilaire. To calm the storm, they sent a young naturalist, W.H. Caldwell, to Australia to find a few. With the help of 150 aborigines and vicious colonial behaviour, Caldwell did end up discovering some though it was not an easy task since platypus eggs are usually only laid in pairs and are no longer than 2cm.

When a platypus feels inconvenienced, it digs its spur into its victim and releases its venom. Since it is only the male platypus that has the use of such artillery, it is thought that the spurs are probably used as an offensive weapon to assert dominance during the mating season and to lay down territorial boundaries. Venom production does indeed increase during the mating season, which sustains the theory. The venom has probably a defensive role too though the aim seems less to kill than to induce intensive pain. Human poisoning is not rare and results in excruciating pain accompanied by massive swelling. Snake venom and platypus venom do seem to cause the same physiological discomforts though snake venom is far more virulent. However, it has been shown that platypus venom can kill dogs when injected intravenously.



Ornithorhynchus anatinus (1863), John Gould

Four major toxins make up the protein components of platypus venom, three of which are unique to platypuses: the defensin-like proteins (DLPs). Named after a class of antimicrobial peptides - the mammalian beta defensins - DLP only seems to share a comparable three dimensional structure. They are small, compact, globular proteins packed with beta-bulges, hairpin loops and beta-sheets. The fine detail of the three dimensional structure is very different though, hinting that the two types of protein do not share the same biological activity. Indeed, neither an antimicrobial nor a myotoxic activity has been detected to date. However, these compact molecules do present a structural core which could support different functional groups and hence exhibit different pharmacological and physiological activities. One possible role of DLP may be to produce - in unison with other venom components - the pain so characteristic of platypus poisoning.

Platypus toxins must participate in the activation of pain receptors, be it indirectly or directly. That is why they - like all toxins - are of particular interest in the understanding of pain-inducing effects. Ultimately a finer knowledge of what pain actually is, and by what it is caused, can lead to the development of drugs such as painkillers, which could be used to inhibit chronic pain states. Some animal synthetic analogues of animal toxins have already entered clinical trials for the treatment of neuropathologies for instance. The interest in platypus venom is that the pain is long lasting and particularly intense. And if DLPs do have a role in triggering off pain, it could lead to the discovery of novel pharmacological targets where common analgesics are ineffective.

## **Cross-references to Swiss-Prot**

Defensin-like peptide 1, *Ornithorhynchus anatinus* (Duckbill platypus) : P82172 Defensin-like peptide 2, *Ornithorhynchus anatinus* (Duckbill platypus) : P82140 Defensin-like peptide 3, *Ornithorhynchus anatinus* (Duckbill platypus) : P82141

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