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a wasp's sting

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Nature has always inspired humans. We extract scents from flowers to make perfume, and use pigments from minerals to reproduce colours. We copy the streamlined bodies of birds to build planes, and mimic the toughness of spider silk to design textiles. As our knowledge accumulates, and technology evolves, we have even reached a point where we are able to tamper with the very basics of Nature to twist it to our advantage. Take antimicrobial peptides (AMPs) for example. AMPs are used by organisms – humans included – across every kingdom to fight off viruses, bacteria, fungi and parasites. Despite this, millions of humans are infected each year by pathogens they are unable to fight off and for which no antidote exists. So researchers have turned to animal venom, which not only provides an easy way of isolating therapeutic toxins but also a precious source of AMPs into which scientists can dip. One particular AMP from the venom of a tropical wasp, *Polybia paulista,* appears not only to present anti-cancer properties but also to fight off an infection known as Chagas disease which affects millions of people every year and worldwide. Its name? Polybia-CP.

the wasp waist of *"La goulue"*

Henri Toulouse Lautrec (1864-1901)

Wasps populated our planet long before humans. The first traces date back to the Jurassic Period, about 200 million years ago and, by the Cretaceous (roughly 50 million years later), wasps had diversified into many superfamilies that are still around today. In fact, over 100,000 different species of wasp have been described, though there are undoubtedly hundreds of thousands more. With time, save for the polar regions, wasps have colonised every part of the planet and their size is as diversified as their habitat. The Asian giant hornet, found in Asian and parts of Russia, is the biggest wasp known to date, measuring 5cm in length. The smallest wasp, commonly known as the fairy wasp, happens to be the smallest flying insect known to date and barely the size of a grain of sand (0.15mm). As for *Polybia paulista*, it is one of the larger-sized wasps and lives in tropical areas of South America, specifically in São Paulo, hence its name.

There are social wasps and solitary wasps. The great majority are solitary, though they may still build a nest for their young. Many wasps are also parasitoid and lay their eggs on hosts they have initially paralysed by way of their sting, and off which the larvae slowly feed. Interestingly, Charles Darwin had observed this behaviour in wasps, and it was one phenomenon which made him question the existence of "a beneficent and omnipotent God" in the days when he sought to clarify his beliefs and thoughts on the theory of evolution. Social wasps, on the other hand, live in highly organised colonies – which may count thousands of wasps at a time – with one queen or multiple queens, and workers whose tasks are divided between nest building, foraging, looking after the young and defending the colony. *Polybia paulista* is a social wasp and, typically, kills prey via its sting to bring macerated portions back to its larvae.

A wasp's sting is therefore armed for two distinct purposes: as a means of defence and to subdue prey. As social and solitary wasps live very different lives, their venom – or its component parts – has also evolved differently and, though they may share similar toxins, over time, evolution has provided them with specific bioactive components. What exactly is venom? Venom is a cocktail of toxins synthesized by many different species – like scorpions, spiders, snakes, ants, jellyfish, fish, frogs, platypus and shrews to name a few – and injected into prey or predators by way of a sting. Wasp venoms, for example, are known to contain three major groups of molecules – namely proteins, small peptides and bioactive substances – which trigger off processes as diverse as paralysis, pain, inflammation, developmental arrest, immune suppression and antimicrobial activity.

Researchers are particularly intrigued by one specific peptide found in *P.paulista* venom: the antimicrobial peptide (AMP) polybia-CP. AMPs are small biologically active peptides, defined as being less than 100 amino acid residues long, and which adopt variable structures: alpha-helices, beta-sheets, extended structures or disordered loops. In invertebrates, AMPs constitute the organism's primary defense system and are very effective since they cause little resistance in pathogens. Why? Because, like making a gash in skin, many AMPs are able to disrupt the pathogen's membrane leaving it very little means to resist as, like blood flowing from a wound, its intracellular matter flows out. Other AMPs actually enter pathogen cells to interfere with vital metabolic pathways, such as DNA synthesis, ribosomal function, protein folding or ATP efflux.

Polybia-CP is itself a very small AMP – barely 10 amino acids long – yet it is a potent antimicrobial protein, particularly against Gram-positive bacteria. Gram-positive bacteria, unlike their Gram-negative counterparts, have no outer membrane and are only surrounded by a thick peptidoglycan wall. Polybia-CP is able to cross the wall and rupture the bacterial membrane possibly by adopting an alpha helical conformation upon contact, and edging its way in. This punctures the membrane, leading to the release of essential intracellular content and ultimately to cell death. Polybia-CP is also known as a chemotactic peptide as it causes an inflammatory response at the site of injury where host leukocytes are recruited.

There is a growing interest in AMPs as the world faces an increase in antimicrobial resistance. Drug-resistant bacteria have indeed become a major health problem around the globe. Even in developed countries, millions of people are infected by bacteria which now ignore traditional antibiotics, killing thousands of patients every year. Polybia-CP, for instance, is showing promise as an antichagasic agent. Chagas disease is caused by *Trypanosoma cruzi*, a protozoan injected by insects, which infects about 10 million people worldwide – and the only drugs currently available cause severe side effects in humans. Polybia-CP may be an ideal candidate as it could fight off *T.cruzi* while being less harmful to humans. What is more, polybia-CP also appears to have potent anti-cancer properties while being relatively harmless to healthy cells. Wasps and the power held within their sting have inspired the names of military ships and aircraft, such as HMS Wasp and USS Wasp. One of the British 'Wasps' which had fought successfully in two WW2 battles famously prompted Winston Churchill to say "Who said a Wasp couldn't sting twice?". Little did he know how true this is.

Cross-references to UniProt

Polybia paulista (Neotropical social wasp) (Swarm-founding polistine wasp): P0C1R0

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