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on ants, bandicoots and Gilbertian mimicry

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Nature has its way of adapting to almost – if not every – known condition on Earth. It may take some time, but she gets there in the end. Adaptation has one sole aim: survival or, at the very least, a little more comfort. One of the most recent and dramatically rapid examples of biological adaptation occurred in Great Britain following the industrial revolution. Soot had begun to pollute cities which drove the peppered moth, *Biston betalaria*, to change its colour from speckled black to only black, making it far less conspicuous when resting against the soot-stained walls*. Many insects have devised ways to trick their predators through the art of mimicry. One ant, *Myrmecia gulosa*, commonly known as the giant bull ant makes use of a form of molecular mimicry: its body has not changed colour but the ant has acquired a protein that parodies a hormone which belongs to its predators, and is able to inflict lasting pain following a sting. The protein is known as OMEGA-myrmeciitoxin(02)-Mg1a, or simply Mg1a, and has recently been shown to mimic vertebrate epidermal growth factor.

The Mock Turtle's Story – The Lobster Quadrille

illustration by Arthur Rackham (1867-1939)

Myrmecia ants are found almost exclusively in Australia and its coastal islands. Commonly known as bull ants (not to be confused with bullet ants) or bulldog ants, they are at least 75 million years old and considered to be the most primitive group of ants living on our planet. Long and slender, with two characteristic large mandibles, they can be aggressive and ferocious creatures, sometimes reaching the gruesome length of 40mm – not the kind of ant you want to meet at close quarters when you know that its sting is one of the nastiest in the ant world. *Myrmecia* ants are also known as jack jumpers because of the way several species are able to jump repeatedly – sometimes reaching a height of 10cm – when they feel threatened. Their sting, however, is also frequently used for catching prey, which can be many times larger than the ants themselves, like bees for example – and dessert comes in the form of honey dew or nectar.

Their vision, too, is unlike that of other ants. Particularly sharp, *Myrmecia* ants can perceive UV light, which means that they are able to see more colours than humans can. Their eyesight may even be more acute than a dog's or a cat's. Excellent vision is important since *Myrmecia* ants do not lay pheromone trails to find their way but actually rely on visual cues for navigation, and can distinguish forms that are situated one to two metres away. Some species do release pheromones, however, though not to find their way around but as a territorial alarm. Where do they live? Largely in the same places as the ants you come across in other parts of the world: forests, woodlands, grasslands, heath and even urban areas.

The sting of *Myrmecia* ants is one of the most toxic in the insect world. Back in the 1950s, scientists began to take a closer look at sting venom and discovered that it was made up of several components, or toxins, each of

which caused a specific reaction in the ant's prey or predator – such as numbness or pain. This, however, was for bee and wasp venom; in those days, ant venom was believed to be simply formic acid. Then, in the 1960s, researchers discovered that bee, ant and wasp venom is composed of toxins, mostly of peptidic nature, i.e. peptides or proteins. Ever since, time and energy has been put into characterising them and defining their mode of action – because if we know how venom works then ways can be found to alleviate a painful sting. In some instances, even avoid death.

Myrmecia gulosa is a species of *Myrmecia* ant which produces a venom toxin of a particular nature. One of the first Australian insects to have been described by the larger than life British naturalist Sir Joseph Banks, all the way back in 1770, *M.gulosa* is abundant in the eastern part of Australia where it is known as the red bull ant or hoppy joe, as it is one of the *Myrmecia* ants that jumps when it feels at risk. The study of *M.gulosa* venom recently unveiled the existence of a peptide toxin which does not act in the same way as the other toxins and bears no structural resemblance to them either. Instead, this one had a secondary structure that seemed to echo, astonishingly, a mammalian epidermal growth factor, or EGF. Especially the EGFs of the wonderfully-named fat-tailed dunnart, long-nosed bandicoot and short-beaked echidna – to mention only three of these extraordinary Australian creatures who would not look out of place in Lewis Carroll's Lobster Quadrille.

Unlike other invertebrate and vertebrate EGF-like peptides, Mg1a has no propeptide, no transmembrane or cytoplasmic domain but simply a secretory signal peptide followed directly by the mature Mg1a – similar to most venom peptides. So, although its primary sequence is closer to that of a venom toxin, Mg1a adopts a secondary structure – namely an EGF-like fold – which mimics that of a mammalian EGF. In vertebrates, epidermal growth factors are mainly known to stimulate cell growth and differentiation and are active in instances such as wound healing. The process is triggered off when EGF binds to its receptor, itself lodged in the target cell's plasma membrane. Why would *M.gulosa* choose to produce a venom peptide that acts like EGF? Well, upon observation, it so happens that this EGF-like peptide hormone – called OMEGA-myrmeciitoxin(02)-Mg1a (Mg1a) – binds to the EGF receptors of the ants' mammalian predators thus inducing a long-lasting pain. A discovery which prompts the question: are mammalian EGFs involved in pain too?

Mg1a is very similar to the EGF-like peptide hormone sequences of marsupials – the Tammar wallaby, the koala bear, the common wombat, the fat-tailed dunnart and the long-nosed bandicoot – all of whom gladly make a meal out of *M.gulosa*. How does Mg1a cause pain? By specifically binding to the mammalian EGF receptor known as ErbB1, which triggers off a signal that ultimately activates sensory neurons and the perception of pain. In this case, long-lasting pain. Why long-lasting? No doubt to discourage predators from having another go. Perhaps, too, to give the ants sufficient time to make a run for it.

Here we have a startling example of adaptation where a creature mimics a model that belongs to its predator (here EGF) and promptly uses it to put its predator in danger – a form of mimicry that has been called Gilbertian mimicry. Of course, *M.gulosa* are far from the only living organisms to use mimicry for their survival. It is just another glorious example of time and biology working in unison to weave very specific needs into an existing tapestry.

**** read Protein Spotlight issue 183***

Cross-references to UniProt

OMEGA-myrmeciitoxin(02)-Mg1a, *Myrmecia gulosa* (Red bulldog ant) : P0DSL4

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