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Hidden powers

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We all take advantage of each other, one way or another. Cats hunt mice for food. Humans keep dogs for company. Flowers give off a scent to attract pollinators. Viruses use organisms to multiply. And ticks suck animal blood to stay alive. The tricks we use to these ends are varied and subtle. Flowers have put much effort into developing perfumes which are perceived by specific pollinators. Ticks have found ways of keeping blood fluid to be able to sip it. But it hasn't been easy. Adaptation has taken its time to fine-tune ways of making good use of another organism. Ticks, for instance, have thought up the finest of strategies not only to recognise an organism from which they can feed but also to land on it, fix itself to it and feed from it. Each step is crucial to a tick's survival. Understanding how a tick manages to shun its host's immune system – let alone keep its blood from coagulating – can be very informative for the development of therapeutic drugs.

Ixodes hexagonus

Source: Wikipedia

Ticks are parasites. And like all parasites, they take without giving back. At least nothing the host would have really liked. They not only feed on animal blood but if they are carrying bacteria or a virus in their system, there is a fair chance that they will inject it into their host's blood. Lyme disease, like other tick-borne diseases, is transmitted to humans in this way. Lyme disease is caused by the bacterium *Borrelia burgdorferi* which is found in many animals – dogs, cats, birds, mice, moles – that ticks are very fond of. When ticks suck their blood, the bacteria are sucked up too and are subsequently found in the tick's saliva. When it sinks its teeth into another host, it is highly probable that it will infect it with *Borrelia burgdorferi* too. One particular parasite, however, has had its powers twisted to serve the interests of humans. Leeches were used in the past centuries to suck 'excess' blood out of patients suffering from all sorts of ailments. Today, leeches are still used in microsurgery to drain blood which would otherwise clot. So far though, ticks have not proved to be of any particular use to humans. At least not directly.

About twenty years ago, researchers started making observations on the intricate processes ticks have had to develop just so that they can wine and dine: they have to recognise their host, clamber onto it, find a place from where they will be able to draw blood and cling firmly to their feeding spot for days. From a drug design point of view, any molecule involved in this series of actions could be used for a vaccine against ticks for instance, and consequently provide protection against Lyme disease. What is more, when feeding off its host's blood, not only have ticks found a way of keeping the blood fluid but they have also found a way of shunning an immune reaction. Any immune reaction triggers off the production of antibodies and causes inflammation where the host has been attacked. Both events would hinder a tick's dinner.

How does a tick manage to trick the immune system? By spitting molecules which can counter it into the host's organism. Scientists have discovered a family of proteins – known as 'evasins' – which are capable of shutting off the very first steps of an immune response brought about by chemokines. Ticks spit these proteins into whatever they bite so that – in the long run – they are not recognised as foreign. As a consequence, they can stick around for as long as they like, taking advantage of whatever it is they need.

It is not known how evasins really work. They are small proteins, barely one hundred amino acids long, and seem to be able to bind to chemokines. Interestingly, no other protein has been found which resembles them yet and they are highly specific for a certain class of chemokine. Indeed, up to now, such immunomodulatory proteins have proved to act upon a variety of molecules in the immune reaction. Such a finding is of great interest for the development of drugs which have a specific target.

How does evasin trick the immune system on a molecular level? It seems that one monomer of evasin clings onto a chemokine. As a result, the chemokines are not able to bind to their receptors, the binding of which would trigger off the first steps of an immune response. However, scientists are not sure that this is the only aspect at play. Evasins are highly glycosylated. Coating evasins with sugars may be one cunning way to hide from the immune system too thus minimizing the exposure of antigenic epitopes – which are critical regions used in host recognition of something foreign.

Though researchers are still not sure how ticks use their evasins to fool their host, they do know that evasins could give rise to wide-spread drugs. Besides being responsible for an immune response, chemokines cause inflammation. Such reactions are paramount for countering infection. However, inflammation can be the source of serious troubles – respiratory for one – and chemokines are involved in a number of auto-immune diseases such as dermatitis or arthritis for instance. If scientists can design drugs using evasins as their scaffold, they may prove to be invaluable. Once again though, we can only feel awe in the face of Nature and such cunning little creatures which, over the millennia, have perfected intricate schemes for the sake of dinner.

Cross-references to Swiss-Prot

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