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# What mosquitoes sniff

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**It is hardly the time to talk of mosquitoes when the cold winter winds are still blowing. In milder climates though, mosquitoes are out and about, causing millions of deaths every year through their ability to transmit diseases, such as encephalitis, dengue, yellow fever and, of course, malaria. According to the World Health Organization, malaria alone is the cause of over two million deaths in Africa, one million of which are children under the age of five. The mosquitoes that transmit the disease belong to more than one species and they are collectively known as the anopheline mosquitoes.**

The female member of *Anopheles gambiae* is the mosquito which transmits malaria to humans. The question is why does it choose humans? The answer is it may well have to do with body odour. And where odour is involved, so are odorant receptors. Female *A.gambiae* have odorant receptors on their olfactive tissues that are specific for certain chemicals found in human sweat. And this is why they make a mosquito-line, so to speak, for certain humans.

Anopheles gambiae



What causes malaria is neither a virus nor a bacteria but a plasmodium, i.e. a single-celled animal distantly related to an amoeba. *Plasmodium falciparum* and *Plasmodium vivax* are the two main vectors of malaria – the former being the more wicked of the two. When a mosquito sucks in blood from someone suffering from malaria, it also sucks in the plasmodia that cause the disease. The plasmodia then take advantage of the situation by reproducing inside the mosquito. When the mosquito digs its teeth into another host, plasmodia are released into the victim's blood and cause a novel infection. So besides shipping malaria from one host to another, *A.gambiae* becomes a cosy and quiet corner for the plasmodium to reproduce. And whilst the mosquito acts as a taxi, human blood acts as a highway for the plasmodium.

One way to eradicate malaria altogether would be to empty humans of all their blood – which is not an option. Research on ways to fight off the disease has come round in a full circle in the past 50 years. By the second half of the 20$^{th}$ century, entomologists were aware that it was the female mosquito that stung. A far cry from what was believed in the times of Julius Caesar. In those days, it had been noted that people who lived close to swamps and marshes were more susceptible to be struck down by malaria. Bereft of the knowledge of biology we possess today, the people assumed that the actual stench was the perpetrator of the disease. And this is where the word 'malaria' originates from: 'mal' meaning 'bad' and 'aria' meaning air.

By the 1950s, scientists worldwide were thinking up all sorts of experiments to understand not only why it was the female mosquitoes that were attracted but also how they were attracted. One of the experiments involved a human steel robot which was warmed to body temperature, imbibed in human sweat or even made to exhale $CO_2$. Research blossomed until DDT made its appearance in the 1960s. DDT was so effective as an insecticide that scientists' eagerness to grasp the vector-host interaction was dulled. Today however, resistance to DDT coupled with second thoughts on the uncontrolled use of insecticides has flared another interest in alternative modes of fighting off mosquitoes.

The *Anopheles gambiae* genome has been sequenced in its entirety, and about 100 different odorant receptor genes have been found. The receptors are dispersed all over the mosquito's olfactive tissues, one of which – odorant receptor Or1 – is only found on female mosquito antennae. Or1 is attracted to one – in particular – of the 300 chemical compounds found in human sweat: 4-methylphenol. It is a transmembrane G-protein coupled receptor whose role, like all odorant receptors, is to bind its specific odorant. Once bound, a number of downstream effector enzymes induce second messengers, which in turn stimulate odorant neurons. And the smell of human sweat is transmitted to the mosquito's brain thus giving it the drive to sting. Or1 may also have a role in turning off the process once the mosquito has had its fill of blood. Once the insect is replete, the odorant receptor is inhibited. Why exactly remains a mystery but it may have to do with belly distension.

The existence of Or1 in female mosquitoes and the discovery of its ligand should lead to biotechnological applications for the development of mosquito traps or repellents. Substitute ligands which would trick the odorant receptors – and hence the mosquitoes – could be synthesized. The insects would be disorientated and led into traps where they would be left to buzz aimlessly. Alternatively, ligands which would inhibit the receptors could be designed and thus act as insect repellents.

The field is promising though more research must be done to grasp in greater molecular detail the intricacies of vector-host interaction and to develop a cheap solution to help fight off a disease which is one of the scourges of developing countries. We cannot change the way we smell but biotechnology could invent a way for mosquitoes to seek out smells differently. And who would refuse a hot, humid summer night without the unrelenting whine of a mosquito?

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