

A sickly smell

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Words are not the only means of communication. Not only are they specific to the human species but there are many other ways of conveying messages, and – since the dawn of time – all kingdoms have shown great imagination in this area. Bacteria exchange information via chemical messages they secrete. Flowers produce scents to attract pollinators. Many animals are capable of turning on a possible partner by exuding pheromones. Releasing all sorts of molecules is one thing, but you also need something on the receiving end to sense them. These are receptors. There are many different kinds of receptors, found in many different tissues or cellular compartments, all of which are there to sense their matching molecule and relay the information further, i.e. the central nervous system in animals. Subsequently, the organism will be instructed to run away, let itself be seduced or avoid spoiled food, for instance. One particularly surprising receptor discovered in the nose of mice – a formyl peptide receptor – seems to have the ability to sniff out disease.



“The Nose” by Theo Gerritsen, 2010

Courtesy of the artist

The nose of a mammal is like a factory, sometimes of vital importance. All day long it receives all sorts of molecules with which it has to deal. Many different kinds of receptors are found in a mammal’s nasal cavity. The more obvious ones, perhaps, are those that ‘sniff’ scents – a bad one or a good one. These sensations are then relayed to the brain which will subsequently suggest how to behave, i.e. flee the situation or copulate for example. But

there are also receptors which are far more subtle – these are the receptors which are capable of ‘sniffing’ odourless substances, amongst which are the well-known pheromones that are capable of sexually arousing a potential mate or instilling a sense of fear. Most mammals are armed with the pheromone machinery; humans, however, seem only to carry the remains of such a system. Indeed, to date, no one has been able to demonstrate that we are still under the influence of pheromones. And, recently, yet another kind of receptor was discovered in the nose of mice – the formyl peptide receptor (FPR) – which seems to have the astonishing skill of detecting disease.

Formyl peptide receptors, *per se*, are nothing new really. They have been known for a long time. FPRs are found on the surface of immune cells and react in response to substances which are secreted by foreign bodies such as bacteria or viruses for example. However, FPRs inside a nose is something very novel. What is more, it seems that this particular type of FPR is probably only found in rodents and may well be the result of fairly recent evolution. So far, seven types of FPR have been characterized, five of which are found in the nose of mice. The other two only seem to belong to the immune system – a characteristic shared with the human immune system.

FPRs belong to the huge family of G-protein-coupled receptors and are lodged within a cell’s membrane. Like all odorant or non-odorant

nasal receptors, FPRs are found on the surface of chemosensory neurons whose dendrites extend into the nasal epithelium. Each chemosensory neuron has its specific receptor – hence a certain type of FPR is only found on the membrane of a certain type of chemosensory neuron. Any amount of chemosensory neurons – on which are attached not only FPRs but also all the other hundreds of receptors – are activated continuously and the brain sums up all the different messages it receives, processes the information and then says how to behave, or not to behave.

No one is really sure what kind of molecules FPRs actually bind in noses. If these particular receptors are capable of informing a mouse that disease is nigh, what could be the chemical nature of the warning? Formyl peptides are possibly the answer. As in the common immune response, the nasal FPR ligands could also be formyl peptides of the kind secreted by foreign bodies once they have invaded an organism. But how could such ligands reach a rodents' nose? An immune response typically occurs within an organism. One theory is that a sick animal may release some of the enemy formyl peptides in its bodily fluids, such as sweat or urine. Any animal in its close surroundings could then

easily pick them up simply by sniffing. Likewise, spoiled food can also be detected by way of a whiff, and hence avoided.

What is the point of being able to sniff out disease you might ask? The obvious answer is: avoidance. If and when an animal senses disease, the clear message is “keep your distance”. The motivation for such behaviour – more often than not completely unconscious – between members of the same species, for instance, is to protect it in the light of perpetuation. There have been intriguing stories of animals that can sense disease, if not death, in humans. One such story is that of Oscar, a young cat that haunts the corridors of an old people's nursing home in Rhode Island (USA) and invariably curls up on the bed of a person who is dying. The fact that something as seemingly insignificant as a 'scent' can bring about a given behaviour, and how this happens, has fascinated scientists for decades. Much has been discovered, but an awful lot remains to be understood. Certainly, the more we seem to unravel, the more Nature is showing how infinitely fine-tuned she is. And it will take more than Man's nose to perceive all its subtleties.

Cross-references to UniProt

Formyl peptide receptor-related sequence 1, *Mus musculus* (Mouse) : O08790
Formyl peptide receptor-related sequence 3, *Mus musculus* (Mouse) : O88537
Formyl peptide receptor-related sequence 4, *Mus musculus* (Mouse) : A4FUQ5
Formyl peptide receptor-related sequence 6, *Mus musculus* (Mouse) : Q3SXG2
Formyl peptide receptor-related sequence 7, *Mus musculus* (Mouse) : Q71MR7

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