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The selfish smell

Vivienne Baillie Gerritsen

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'Woman smelling coffee' by Gizem Saka

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OR7D4 is an olfactory G-coupled receptor similar to all those known to date. It is a transmembrane protein, with an extracellular loop, which acts as the binding pocket for its ligand, and a cytoplasmic domain which reacts with the G-protein. Androstenone, which is an odorous steroid derived from testosterone, lodges in the OR7D4 binding pocket thereby changing the receptor's conformation. This triggers off the formation of cAMP thanks to the G-protein, which in turn opens a channel protein. The opening of the channel lets in cations which change the neurone's membrane potential, and this is the very beginning of an electric signal which is relayed, along the sensory neurons' axons, all the way to the brain that will read the message as being part of a smell.

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The selfish smell

Vivienne Baillie Gerritsen

We are surrounded by smells. Pleasant ones and not so pleasant ones, hard to distinguish ones, mild ones and strong ones. Smells are not part of our everyday life for the simple sake of pleasure. They are there for a purpose. The perfume of a flower can be used as an attractant for a potential pollinator, for instance. The scent given off by a poisonous mushroom is a way of warding off a predator and, by the same token, can be instantly recognised as toxic by an animal, thereby saving both species. Special scents are also given off by males and females when mating is in the air, and no wine grower will ever argue that a wine's fragrance is not for the sole purpose of seduction. But what is a smell? More often than not, a scent is made up of a mixture of odorant molecules which, together, will trigger off a complex olfactory system that will ultimately let us perceive it and, if we wish to, put words to it. The very first step in such a system involves an odorant receptor to which an odorant molecule binds. Recently, a new human odorant receptor – OR7D4 – was discovered. OR7D4 is special in that it is the first receptor known to respond to a specific odorant molecule.



'Woman smelling coffee' by Gizem Saka

Courtesy of the artist

Discovering an odorant receptor is nothing new. Major discoveries of the like were made almost twenty years ago. What is singular, though, is that for the first time scientists are able to link an odorant receptor to a specific ligand. This is a breakthrough because, unlike our visual and senses hearing which are relatively straightforward, our olfactory senses are part of a highly complex system. We know what light frequency will give which colour. And what sound pitch will give which sound. But no one can say 'this molecular structure will give that smell' - which would be the perfume maker's Holy Grail. What is more, knowing a

molecule's structure is not sufficient. Any smell is the combination of more than one odorant molecule.

There are thousands of different smells and we are capable of discerning each one of them. Yet the human capacity to sniff out stuff has slackened over the millennia because we have put both our hearing facilities and our visual capacities to a greater use. As a result, our olfactory system is now one third of what it probably was in our ancestors. A rat, for instance, expresses about one thousand olfactory receptor genes, while we only express about three hundred. These olfactory receptors are found in ciliary membranes immersed in a film of mucus which lines the inner side of our nose. The cilia are the tips of sensory neurons which relay a smell along their axons to the brain. The brain will either recognise the smell it has just received - and consequently so will we - or it will discover a new smell and memorise it for the next time.

OR7D4 is an olfactory G-coupled receptor similar to all those known to date. It is a transmembrane protein, with an extracellular loop, which acts as the binding pocket for its ligand, and a cytoplasmic domain which reacts with the G-protein. Androstenone, which is an odorous steroid derived from testosterone, lodges in the OR7D4 binding pocket thereby changing the receptor's conformation. This triggers off the formation of cAMP thanks to the G-protein, which in turn opens a channel protein. The opening of the channel lets in cations which change the neurone's membrane potential, and this is the very beginning of an electric signal which is relayed, along the sensory neurons' axons, all the way to the brain that will read the message as being part of a smell.

Discovering a ligand's receptor is one thing. Attributing an actual smell to a specific ligand is another. It seems to be the case with androstenone though. This is a smell which is usually perceived as unpleasant (urine- or sweat-smelling), pleasant (sweet- or floral-smelling) or without a smell. That would make three smells, you're thinking. Not really. It is one smell perceived differently. What is it that makes people smell a smell differently? Is it innate? Or does it have something to do with something far less tangible, such as personality,

past experience, or even the subconscious? Many will answer that, though there is no doubt a genetic basis, much must be due to something which is not inherited. In the case of androstenone, however, there may be a case of an inherited difference in perception. Indeed, there is a common variant of the OR7D4 receptor and it seems that individuals that carry the same variant tend to smell androstenone in the same way...which would point to the genetic inheritance of a smell...

A lot of time and money is spent cracking the scent code. Besides the perfume industry, there are plenty of other industries that need smells to sell. Food, cosmetics, washing-up powders and beverages - to name a few - all make use of the power of fragrance. The industry has even learned how to trick our smelling senses. Take synthetic lemon juice, for instance, which only uses a few of the chemicals found in natural lemon scent and yet we can identify it as lemon. A handful of scientists have suggested that a crude quality of a smell, such as its pleasantness or unpleasantness, is simply a case of molecule compactness. So the more compact an odorant molecule is, the nicer it might smell. However, it is also known that one same odorant molecule can smell nice when there isn't too much of it. and awful when there is a lot. Take indole for example which is an odour molecule found abundantly in faeces and yet it is used in very small amounts in perfumes... Inherited or not, purely for our survival or not, what a smell will never be able to take away from us are the beautiful memories - and no doubt the bad they are able to stir in us.

Cross-references to Swiss-Prot

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