proteinspotlight
> ONE MONTH, ONE PROTEIN <

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# No one nose

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**Do we, or do we not, have a sixth sense? Yes say most. And it does seem to be the case. Like many animals, we are capable of responding to sensory chemicals of which we are quite unaware – pheromones – and that can modify our behaviour. However, we may also be in the process of losing the organ which was probably used by our ancestors to perceive such an obscure sense: the vomeronasal organ, which can be observed just in the inside of our nostrils. The intriguing part is that a subfamily of protein receptors, which suspiciously resemble known mammalian pheromone receptors, has been discovered in humans: the type 1 vomeronasal receptors. Could it be then that not only do we have a sixth sense but also an organ dedicated to it?**

Most living creatures depend upon a sense which we – for the most part – have lost: a sense that we can neither hear, see, taste, smell or feel. Such a sense is conveyed by molecules which were termed pheromones in the 1950s. Pheromones are chemical molecules of diverse and varied structure, which are used in the animal world within a same species – mostly to settle love affairs. In many of our mammalian counterparts, pheromones are detected by a small organ – the vomeronasal organ (VNO) which is distinct from the main olfactory system but, like it, lines the nasal cavities. Though the way messages are conveyed from the outside world to the inside one and ultimately influence an individual's behaviour is complex and demands a greater understanding, a general outline of the process is known. Neurons bathe within the VNO presenting specific pheromone receptors on their surface. A pheromone binds to its receptor, and a signal is transmitted down the length of the neuron and ends up in the olfactory bulb which, in turn, will transmit its dispatch to the brain where some sense will be made out of the initial signal.

The existence of a VNO in humans has met with much controversy. It was first mentioned about 300 years ago but was only given full attention in 1877 by a German professor Rudolf Albert von Kölliker (1817-1905). It seems that though the organ is clearly present in the human foetus, not all adult humans have it and when they do, it really is only vestigial. Despite this, claims that pheromones can act on human VNOs have been made. Androstadienone is an androstene found under a man's arm, on his skin and hair. According to some, if picogram quantities (quantities which could not stimulate the olfactory system) of androstadienone are presented to a woman's VNO – or where it is expected to be – she will experience a change of mood, i.e. a sense of well-being. As a result, it was not long before 'pheromone' perfumes boasting positive influences on those who wore them were put on the market…

'Blue Nose Special', Hal Mayforth

Courtesy of the artist, www.mayforth.com

Today, there is little doubt that human pheromones exist. Besides androstadienone, the best example of their existence is the synchronisation of a woman's menstrual cycle and the regulation of her ovulation with female colleagues, due to molecules found under their armpits. What no one agrees upon is how these pheromones act upon us. Are they just 'smelled' by the olfactory system and follow the classical transmission pathway of a smell? Pheromone sensing does occur in this fashion in pigs and rabbits for instance. Or do we really have a VNO in which are lodged specific pheromone receptors as in many reptiles and other mammals?

We do own pheromone receptors. However, they are few and far between and no one knows whether they are functional either. Despite this, they are very similar in sequence to pheromone vomeronasal receptors found in other animals, of which there are two subfamilies in rodents; one of them – V1R – is found in human olfactory mucosa. Proteins of the V1R type are integral membrane proteins and belong to the very large G-protein coupled receptor family. No one can say, though, whether V1Rs are indeed expressed in a human VNO.

So – as far as human V1R goes – there seems to be very little certainty about anything at all. What V1R has offered biology so far is a window onto the sexual behaviour of our ancestors and its evolution. Scientists assumed that our higher primate ancestor – which is believed to have existed 23 million years ago – probably had as many functional pheromone receptors as the mouse does today, i.e. about 140. If reproduction based on pheromones existed in our ancestor and we lost that capacity over the 23 million years which separate us from it, statistics inform us that we should only have about 5 intact pheromone sequences today due to 'functional relaxation'. And such is the case… So the fact that adult VNO is vestigial is hardly surprising. More amazing yet is that our VNOs are a live – so to speak – incarnation of a kind of behaviour we had and which we are in the process of losing.

Why is it we discarded pheromones in the first place anyway? Primate vision may have become more and more acute so as to be able to distinguish the colours of fruit for feeding. As a result, and with time, male primates may have acquired the ability to see when their female counterparts were ovulating because of changes in colour of their genitalia. Consequently, reproductive behaviour based on pheromones would have become less and less of an asset as primates counted more on vision to choose a mate. And slowly but surely, pheromone receptors such as V1Rs would have started to 'relax' since they were under less of a functional constraint. Such a theory gains strength when you know that bird reproductive behaviour is based solely on body colour, and that they do not have vomeronasal pheromone perception.

Besides not knowing what to think of what is left of the human VNO and its receptors, the knowledge that pheromones such as androstadienone could potentially modify human behaviour via the existing VNO has tickled scientists' fancies. Synthetic pheromones could have a therapeutic interest. Sprays that could free women from premenstrual mood shifts have already been thought up. The fight against prostrate cancer could perhaps be boosted by way of a pheromone that could check testosterone production.

And how about smearing gender-specific magazines with pheromones to lure men or women into buying them? Trials have been carried out already… Despite the obvious ethical issue, lab tests turned out to be quite conclusive but in a newsagent's, a potential buyer is submerged by so many cues that the emotional smear of a product would probably have no chance whatsoever. Pheromones certainly are mysterious molecules for the rational human and make us wonder yet again whether we really have been granted the power of free will or not (See Spotlight issue 52).

## Cross-references to Swiss-Prot

Type 1 vomeronasal receptors 1-5, *Homo sapiens* (human): Q9GZP7, Q8NFZ6, Q9BXE9, Q7Z5H5, Q7Z5H4

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