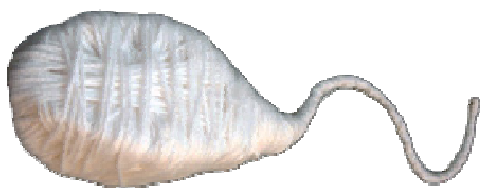


love at first smell

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The making of life is demanding. Take any form – from fungus to bacteria, and plants to humans – the creation of progeny does not just happen. It takes a lot of molecular dialogue to divide *E.coli* into two, to cloak pistils with pollen or to get sperm to wriggle its way into the egg. The most complex biochemical pathways are triggered off so that life can not only start to exist but also develop in the best way possible. Lately, some intriguing discoveries have been made regarding human sperm and how it finally makes it to the egg. The ongoing theory is that it may well sniff its way there. So do spermatozoa have noses? No. But they do have receptors on their surface, which are very like – if not identical – to olfactory receptors we have in our noses, and which can pick up scents. These odorant receptors are known as hOR 17-4. Could it be then that the egg exudes some kind of perfume to lure the sperm towards it? Perhaps.



Sperm in yarn by Ian Trask

Photo courtesy of the artist

It has been known for centuries that millions of spermatozoa are ejaculated at a time for the benefit of just one egg, and a very natural deduction to such a phenomenon would be: “surely one will make it”. But there seems to be more to fertilization than meets the eye. Sperm do not enter a woman’s womb blindfolded, simply counting on fate to do the rest. The path is far too tortuous and long a one for that. Indeed, sperm have to make their way up the uterus, where they must locate and enter the oviduct. They then travel through the tube and reach a mucus-filled constriction in which awaits the ovule.

Some species, such as sea urchins and fish, use external fertilization which has already been

extensively studied by scientists. External fertilization seems to be a very careless and haphazard means of ensuring offspring. Both the sperm and the egg are flung into an open and hostile environment in which they have to find one another. And fast. In order to do this, nature has larded the gametes with systems that will enable them to recognise one another. In this way, the egg shoots out chemical ligands that the sperm will identify, and towards which it will swim. Considering this, is there not a chance then that mammalian sperm and eggs communicate and meet in a similar way? It seems so. And the olfactory receptor hOR 17-4 may well help to unravel the mystery.

There are many different kinds of olfactory receptors, the great majority of which are found in the olfactory epithelium in the nose. They all belong to the vast family of G protein-coupled receptors which, once bound to their specific ligand or scent, are stimulated and trigger off signal transduction pathways, opening and shutting calcium ion channels in olfactory neurons, which end up telling the brain what it is smelling. The same kind of olfactory receptors are also found on the surface of sperm membranes. hOR 17-4 seems particularly promising in that *in vitro* studies have shown that it can be stimulated – and inhibited – by specific scents.

Although the signal transduction pathways may be similar to those which occur when we smell

something, sperm have neither a nose nor a brain. So how does it work? What is it that makes sperm swim towards the egg? In other words, is there a smell which is actually capable of causing movement? A mind-blowing concept in itself. It so happens that hOR 17-4 is situated on the sperm's tail – midway – just where it waggles. In vitro, hOR 17-4 is potently stimulated by bourgeonal, a small aromatic aldehyde used in the perfume industry and which mimics the floral scent of lilies of the valley. This particular ligand causes the sperm not only to head in the direction of an increasing gradient of the scent but also to swim there faster by beating its flagellum more actively. Does the egg – or do cells in its vicinity – exude the same kind of ligand to attract sperm? Is the egg actually...perfumed?

Another very curious and more recent discovery has been made: hOR 17-4 is also found in our noses. And responds to bourgeonal too! A question arises: is our sense of smell coupled to fertility? Does a woman attract a man by way of her scent which, in turn, will attract the sperm to her egg? It is a very intriguing thought. What is more, a second ligand known as undecanal has

the exact opposite effect on sperm, in vitro, by inhibiting the olfactory receptor. Undecanal mimics a leafy smell and when inhaled by human noses, it also dulls the smell of bourgeonal! The notion that a man is attracted to a woman in the same way that his sperm is attracted to her egg is beguiling. But it is all hypothetical. Nothing to date has been proved in vivo. Furthermore, no one has found the ligand which stimulates – if indeed one does – hOR 17-4 on the sperm's flagellum.

Besides uncovering who sniffs who and what, the results of such studies could prove to be very useful for contraception and procreation. Assuming that all sperm carry the same olfactory receptors, novel contraceptive methods could be designed where ligand antagonists – such as undecanal – bind to the receptors, thus hindering sperm movement towards the egg. In contrast, sterility could be detected depending on whether a male subject is capable of smelling a ligand such as bourgeonal or not. It is all very hypothetical but very intriguing. Does “love at first sight” really exist for example? Or is it more “love at first smell”?

Cross-references to UniProt

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