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Beauty is in the nose of the beholder

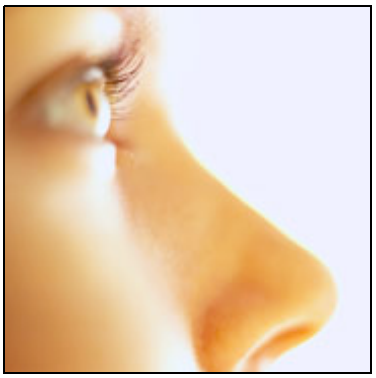
Gene found that determines if putative human pheromone smells naughty or nice.

Heidi Ledford

The compound androstenone can induce many reactions, depending on who is on the receiving end. For some, it smells sweet, like flowers or vanilla; to others it is foul, like sweat or urine. And then there are those who can't smell it at all.

Now researchers have found the molecular receptor responsible for sensing androstenone, and the genetic variations behind its assorted olfactory impacts. The finding may one day help to settle the debate over whether the compound, which is a breakdown product of testosterone, acts as a pheromone in humans.

Androstenone is known to be a key mating pheromone for pigs. "If you were a female pig who could not smell this, you would have a hard time on a date," says Leslie Vosshall, a neurobiologist at Rockefeller University in New York and an author on the study. "It's a very exciting odour for pigs." Whereas the compound clearly fans the flames of porcine passion, its effect on humans is a matter of debate.



Some smell it sour, some smell it sweet.

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Smell that?

Vosshall and her co-workers tested 335 putative human odorant receptors — more than 85% of the estimated full human complement — for responses to 66 different odours. One receptor, with the decidedly unsexy name OR7D4, yielded the strongest response to androstenone and it's close relative, androstadienone. It did not respond to the other 64 odorous compounds[1].

To work out if and how this receptor differs in different people, the team looked at the genetic sequence of the gene that codes for it. Vosshall and her colleagues sequenced the *OR7D4* gene from 391 people, and found two common gene variants to focus on.

> **“It has got to beat online dating.”**
>
> Jeffry Isaacson

It turned out that people with two copies of the most common *OR7D4* variant tended to find the smell of androstenone stronger and describe it as 'sickening'. Those with one or two copies of the second common variant were more likely to perceive the scent as 'extremely weak', and to label it 'sweet'. People with a third, less common variant were more likely to be unable to detect androstenone at all. In all of these cases, perception of other odours was not affected.

"We always thought the mechanism had to be due to receptor differences," says Gary Beauchamp, director of the Monell Chemical Senses Center in Philadelphia, Pennsylvania, who began studying androstenone more than 25 years ago but was not affiliated with the present study. "What's wonderful about this is proving it."

Chemical attraction

Now that the receptor is known, it will be easier for researchers to address lingering questions about androstenone's possible role as a human pheromone, says Jeffry Isaacson, a neurobiologist at the University of California, San Diego. "On that level, this is a major breakthrough," he says. "It's been quite a controversial area of research."

Pheromones are chemicals that serve as messengers to members of the same species. Sex pheromones are the most famous example, but other forms of olfactory communication exist as well.

Sniffing androstadienone has been shown to produce physiological effects in both men and women. Whether such responses qualify the compound as a pheromone has been hotly debated, in part because its mechanism of action is unclear, says Vosshall.

Sold on the idea

Meanwhile, scientific debates have done nothing to slow the inevitable march of capitalism. Love-scent.com, one of many purveyors of androstenone sprays, has already declared androstenone a human pheromone and a "scientifically proven sex-attractant".

The commercial and media rush to declare these compounds human pheromones has set some researchers on edge. "It's been overhyped a lot as a pheromone," says Vosshall. "So I think there's been a lot of backlash."

Now that the receptor has been identified, Vosshall hopes to find out whether variations in OR7D4 are also linked to physiological effects, or even human behaviour.

Such research would be welcome, says Isaacson. As a 45-year-old, single neurobiologist, he says he would personally grateful for any new insight into human pheromones: "They've sure got to beat online dating."

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References

1. Keller, A., *et al*. *Nature* doi:10.1038/nature06162 (2007).

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