

Gene determines whether male body odor smells pleasant

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To many, urine smells like urine and vanilla smells like vanilla. But androstenone, a derivative of testosterone that is a potent ingredient in male body odor, can smell like either - depending on your genes. While many people perceive a foul odor from androstenone, usually that of stale urine or strong sweat, others find the scent sweet and pleasant. Still others cannot smell it at all.

New research from Rockefeller University, performed in collaboration with scientists at Duke University in North Carolina, reveals for the first time that this extreme variability in people's perception of androstenone is due in large part to genetic variations in a single odorant receptor called OR7D4. The research is reported September 16 as an advance online publication of the journal *Nature*.

Androstenone, found in higher concentrations in the urine and sweat of men than of women, is used by some mammals to convey social and sexual information, and the ability to perceive androstenone's scent may have far-reaching behavioral implications for humans.

In the largest study ever conducted of its kind, researchers at Rockefeller University presented nearly 400 participants with 66 odors at two different concentrations and asked them to rate the pleasantness and intensity of each odor. When scientists at Duke University identified OR7D4 as a receptor that androstenone selectively activates, Leslie Vosshall, Chemers Family Associate Professor and head of the Laboratory of Neurogenetics and Behavior at Rockefeller University and Andreas Keller, a postdoc in her lab, formed a collaboration with them, and began collecting blood samples from participants and isolated their DNA. The Duke team, led by Hiroaki Matsunami, used DNA from each participant to sequence the gene that encodes the OR7D4 receptor.

"With this large dataset, we are able to say that people who express different variants of this receptor perceive this odor differently," says Vosshall.

Although it has long been suspected that the ability to perceive the odor of androstenone is genetically determined, this study is the first to identify variations in a single gene that account for a large part of why people perceive androstenone's scent so differently.

With their Duke collaborators, Vosshall and Keller identified two point mutations called single nucleotide polymorphisms along the gene, which gave rise to two variants of the odorant receptor: RT and WM, which differ by two amino acids. As a group, participants with the RT/RT genotype perceive androstenone's odor as foul and intense. Those with the RT/WM genotype, on the other hand, are more likely to perceive androstenone as less unpleasant. Many cannot smell androstenone at all. Although some participants with the RT/WM genotype can smell androstenone, they experience the smell very differently than those with two copies of the fully functional receptor: To them, androstenone doesn't smell like urine; it has a vanilla scent.

"There are two independent things that are interesting about this odor," says first co-author Keller. "One is that it is a potential social signal but the other one is that so many people cannot smell it."

Two additional point mutations in some of the participants influenced their sensitivity to androstenone, one of which may make humans hypersensitive to this odor. Vosshall and Keller are interested in what it is about these amino acid changes that alter one's perception of androstenone's scent, and in whether one's perception of this potent compound can influence behavior.

"Since some mammals clearly use androstenone to communicate sexuality and dominance within a social hierarchy, it's intriguing to think whether the same thing may happen in humans," Vosshall says. "If so, what happens to humans who can't get the signal because they have the nonfunctional copy of the gene? Or the hyperfunctional one? What could be the social and sexual implications of this on one's perception of the smell of fellow humans?"

Source: Rockefeller University

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