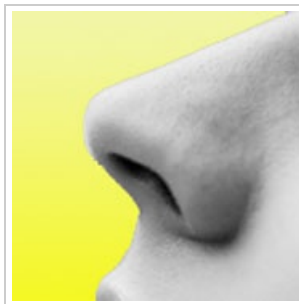


## FEATURED ARTICLES

**Smells like teen spirit***Neuroscience Gateway* (October 2007) | doi:10.1038/aba1785**Naturally occurring genetic variations in an odorant receptor alter the perception of a putative pheromone.**

What makes one man's trash another man's treasure? Perhaps people are genetically programmed to perceive things differently. For instance, olfactory perception differs across the population. Now Keller *et al.* report that variability in odor perception is influenced by genetic variation in odorant receptors in a recent article in *Nature*.



Approximately 30% of people cannot detect androstenone, which is a byproduct of testosterone that is released in urine and sweat and may be a human pheromone. People who can detect androstenone show wide variation in subjective rating of its scent, from pleasant to offensive.

The authors screened cultured cells expressing human odorant receptors for androstenone-induced alteration in transcriptional activity. Of 335 odorant receptors tested, cells expressing *OR7D4* showed the strongest response. Are there genetic variations in *OR7D4*? The authors found 13 single-nucleotide polymorphisms (SNPs) in *OR7D4*. Two of the SNPs, arginine-to-tryptophan (R88W) and threonine-to-methionine (T133M) substitutions, were in linkage disequilibrium, resulting in common (RT) and rare (WM) *OR7D4* alleles.

*OR7D4* alleles altered androstenone sensitivity. Although cells expressing the WM allele of *OR7D4* responded normally to other odors, they did not respond to even high doses of androstenone or the related compound androstadienone. Cells expressing either R88W or T133M showed intermediate responses relative to cells expressing the RT and WM alleles, suggesting that both SNPs affect *OR7D4* function. In contrast, a serine-to-asparagine substitution, S84N, present in more than 1% of the population, increased sensitivity to androstenone relative to *OR7D4* RT. Cells expressing the S84N variant showed more surface expression of *OR7D4* than cells expressing the RT or WM alleles, suggesting that receptor trafficking may contribute to variations in androstenone sensitivity.

How did the *OR7D4* alleles affect androstenone perception? In a test of 66 odors and 2 solvents, RT/WM and WM/WM individuals rated androstenone and androstadienone as less 'intense' than did RT/RT individuals. In all, 46% of RT/WM and 28% of RT/RT individuals could not detect the highest concentration of androstenone, suggesting that genetic variation in just one allele of an odorant receptor can affect odor detection. RT/RT and RT/WM individuals differed in their rating of androstenone and androstadienone valence (positive or negative). Relative to RT/RT individuals, nearly half as many RT/WM individuals rated the highest concentration of androstadienone as 'extremely unpleasant'. RT/WM individuals were 42% less likely to rate

androstenone as 'sickening' and 129% more likely to equate its scent to vanilla relative to RT/RT individuals.

In all, *OR7D4* genotype explained 19% of the variance in the valence and 39% of the variance in the intensity of androstenone odor perception. As potential pheromones, androstenone and androstadienone detection may have social and reproductive consequences. These data suggest that other perceptual differences, like taste preference, may also be genetically encoded.

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1. Keller, A., Zhuang, H., Chi, Q., Vosshall, L. B. & Matsunami, H. Genetic variation in a human odorant receptor alters odour perception. *Nature* **449**, 468–472 (2007). | [Article](#) | [PubMed](#) | [ISI](#) | [ChemPort](#) |