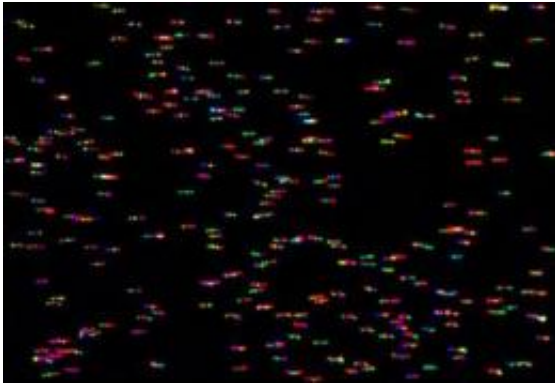


Gene switch for odorant receptors

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NanoString barcodes: Each barcode consists of six spots made out of four colors (green, blue, red, yellow), and is bound to a different type of RNA molecule. The barcodes are attached to a flat surface and stretched with an electrical current. This analytical method of gene expression is "digital": barcodes corresponding to different types of RNA molecules are, literally, counted. Credit: NanoString

The olfactory sensory neurons in the nasal mucosa perceive the myriad smells in the air with the aid of odorant receptors. Each sensory neuron chooses one and only one receptor gene for expression. The probability that a particular receptor gene is chosen for expression determines how many olfactory sensory neurons in total produce this receptor type. Scientists from the Max Planck Institute of Biophysics in Frankfurt have unveiled an aspect of how the probability of the choice of an odorant receptor gene is regulated in olfactory sensory neurons. Regulatory elements in the genome regulate the probability of the choice of individual odorant receptor genes within a gene cluster. These elements

act as on-off-switches for gene choice, but they do not regulate the number of receptor molecules that are produced by a cell once a particular gene is chosen for expression.

Odorant [receptor genes](#) form the largest gene family in the genome of many animals: for example, the mouse genome contains approximately 1200 of these genes. These genes are distributed across 40 [gene clusters](#) in the mouse genome, and clusters contain varying numbers of receptor genes. Nearby regulatory elements regulate the choice of individual genes within a cluster. Thus far, two such regulatory elements are known: the H element on chromosome 14 and the P element on [chromosome 7](#).

Using RNA analysis, the Max Planck researchers discovered that the P element regulates the choice of individual genes from a cluster of 24 odorant receptor genes: in genetically modified [mice](#) that lack the P element, the [probability](#) that an olfactory sensory neuron chooses one of the genes is affected. "The P element can only turn a gene on, and so determine whether or not a cell chooses a receptor gene for [expression](#). However, it has no influence on the number of [receptor molecules](#) produced by an individual cell. It works, therefore, like an on-off switch," says Peter Mombaerts from the Max Planck Institute of Biophysics. The P element does not influence genes from other clusters on the same or on other chromosomes.

The engineered loss of the P element has different effects on the choice of odorant receptor genes: some genes are no longer chosen, others are chosen by fewer olfactory [sensory neurons](#), and some genes remain completely unaffected by the absence of the P element. Thus the P element is not the only DNA sequence that regulates gene choice within this cluster of 24 genes. This is also indicated by the limited "reach" of the regulatory elements: the effect of the H and P elements is restricted to 200,000 base pairs. "We can estimate from the number of odorant

receptor genes and the average distance between these genes the potential number of regulatory elements. Each cluster is controlled by several elements. We speculate that there may be as many as 150 such [regulatory elements](#) for odorant receptor gene choice in the [mouse genome](#)," explains Mombaerts.

The scientists do not yet know how these elements regulate the choice of an odorant receptor gene within a cluster. It is possible that regulatory proteins dock to special binding sites on the DNA.

This discovery was made possible by the new method "NanoString" for measuring RNA levels in tissues. The Max Planck researchers were able to measure the levels of messenger RNA for half of all the odorant receptor genes in one go. With traditional methods, the RNA level could be analysed for only one odorant receptor gene at a time.

These findings have taken the scientists one step closer to figuring out how an olfactory sensory neuron selects one of 1200 genes for expression. "We still have a long way to go in solving this fascinating mystery. The arrangement in clusters may play a role. It is clear that this process does not just involve a single mechanism; odorant receptor gene choice is probably regulated at several levels", speculates Mombaerts.

More information: Mona Khan, Evelien Vaes, and Peter Mombaerts "Regulation of the Probability of Mouse Odorant Receptor Gene Choice" *Cell*, 11 November 2011, pp. 907-921 ([doi:10.1016/j.cell.2011.09.049](https://doi.org/10.1016/j.cell.2011.09.049))

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