Olfactory receptor neurons select which odor receptors to express

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It may appear difficult to reconcile the fact that almost every cell in the body of an animal has an identical dose of genes with the variety of different appearances and properties cells can display—bone, skin, hair, muscle, and many more. This may seem even more complex given that all of these tissue types derive originally from a single fertilized egg cell. Understanding the many regulatory mechanisms that create different cells from a single template is the work of developmental biology.

A new paper published this week in the open-access journal *PLoS Biology* looks at this problem in the olfactory system of the fruit fly, where the ability to discriminate odors depends on receptor cells expressing different patterns of receptor genes, despite each cell having the same set of genes to choose from. The paper, by Anandasankar Ray and colleagues at Yale University, shows that receptor patterns are controlled by DNA sequences upstream of the receptor genes.

In the fruit fly Drosophila, there are two organs involved in smell: the antennae and the maxillary palps—the latter being part of the mouth. In these palps, there are always six types of neurons, cells that transmit information from the sensing part to the brain. Each type of neuron has a different, predictable pattern of olfactory receptors. How a neuron knows which receptors to express was, until now, a mystery.

By comparing the recently published genetic sequences of 12 species of Drosophila, Ray and colleagues identified regions of DNA near the receptor genes that are almost identical in all species. They hypothesized that these represented control regions, which are important for determining how genes are expressed. By altering the control regions experimentally, they have shown that this is true; these highly conserved regions act like zip codes, determining where the receptors end up. Interestingly, some regions positively regulate gene expression: when they are damaged, the receptor fails to be expressed in neurons where it would normally appear. Other regions negatively regulate receptor expression (stopping receptors from appearing in the wrong neurons) so that when the regulator is experimentally blocked, the related receptor appears in more neurons than it should.

Interestingly, the regulatory sequences identified in this study may also have another role in the nervous system. These controlling elements might also be apparent in the process of axon guidance, which connects the olfactory neurons to neurons in the antennae. This complex connection suggests that the process goes beyond the expression of olfactory neurons, and also contributes to the design and development of the fruit fly's greater nervous system.

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