VISUAL SYSTEM

Pick a colour

Trichromatic vision is one of the characteristics that set humans and higher primates apart from our ancestors. The evolution of our visual system from an earlier dichromatic system seems to have started with the duplication of a visual pigment gene, which subsequently gave rise to the genes that code for red and green pigments. Expression of the two pigments is usually mutually exclusive, but how does a cone cell decide which gene to express? The 'standard' model suggests that this is pre-determined by the differential expression of transcription factors between red and green cones, but Smallwood *et al.* now present evidence for a simpler 'stochastic' model, in which the pigment gene promoters compete to pair with a *cis*-acting regulatory sequence.

The red and green pigment genes are arranged in tandem on the X chromosome, and they share a locus control region (LCR), which is situated at the 5′ end, adjacent to the red pigment gene. Smallwood *et al.* generated a series of transgenic mouse lines, using the red and green pigment gene promoters to drive the expression of histochemical reporter genes (alkaline phosphatase for red and β-galactosidase (*lacZ*) for green). By arraying the genes in different configurations, they examined how proximity to the LCR and gene order influence the relative expression of the two genes.

First, they showed that if a 9-kb spacer was inserted between the genes, the proportion of *lacZ*-expressing cones was reduced, indicating that the distance of the gene from the LCR can bias promoter selection. On the other hand, if the gene order was swapped so that the green pigment gene was adjacent to the LCR, there was a large increase in the proportion of cones that expressed *lacZ* only. This implies that the green pigment promoter has a higher affinity for the LCR than the red pigment promoter, but presumably this difference is usually negated by the effect of distance.

The LCR clearly has a strong influence on pigment gene expression, but is competition for the LCR the main factor that drives promoter choice? To test this, the authors removed the element of competition by duplicating the LCR, and they found that a large proportion of cones now expressed both pigment genes simultaneously. This indicates that, contrary to the standard model, the cells are intrinsically able to express both pigment genes, but only one promoter can interact with the LCR at any given time.

So, the data from these experiments strongly support the stochastic model. Perhaps most remarkable was the fact that the transgenic retinal cells were able to choose whether to express the red or the green pigment gene, a decision that they are never faced with in real life. The beauty of the stochastic model is that it does not require any pre-existing differences in transcription factor expression between red and green cones. Instead, all of the information that determines promoter choice is designed into the gene array. This also has important evolutionary implications, as it shows how the ability to express a new visual pigment in a distinct cone population could have resulted from a single gene-duplication event.

Heather Wood

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SENSORY TRANSDUCTION

Out in the cold

We know surprisingly little about our sense of cold. It is mediated by small sensory fibres that project from the dorsal root and trigeminal ganglia, but these fibres have been very difficult to study and, consequently, it has been hard to pin down the molecular events responsible for transducing cold sensation. Two new studies have attempted to answer the question of how cold is detected, but they have come up with very different answers.

The first study, by McKemy *et al.*, reports the identification of a receptor for cold. The authors cloned a receptor from trigeminal sensory neurons that is activated both by cool or cold stimuli and by menthol, which is often used in studies of cold because it gives a similar sensation. The 'cold- and menthol-sensitive receptor', or CMR1, is a member of the transient receptor potential (TRP) family of excitatory ion channels. Other members of this family include the heat-sensitive vanilloid receptors VR1 and VRL1. When CMR1 is activated by menthol or cold, it opens and allows the influx of calcium ions, leading to depolarization and the generation of action potentials.

So far, so good. But the second study, by Viana *et al.*, comes to a very different conclusion. The authors cultured trigeminal ganglion neurons and studied their electrophysiological properties. In the subset of neurons that responded to cold or menthol, they found no evidence for an excitatory cold receptor. Rather, Viana *et al.* conclude that cooling these neurons causes depolarization and firing by closing a background potassium channel. The same channel also closes in cold-insensitive neurons, but firing is prevented by a transient potassium current that acts as an excitability brake.

Only time — and further research — will reveal how the findings of these two studies relate to each other. But it looks as though researchers that are searching for the mechanism of cold transduction will be out in the cold for a while yet.

Rachel Jones

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WEB SITES

Encyclopedia of Life Sciences: http://www.els.net/somatosensory systems