strong association between the extent of European ancestry and multiple sclerosis around the centromere of chromosome 1. However, they did not discover admixture associations elsewhere on the genome, including the MHC region.

Although further large-scale studies will be required to reconcile these findings and to further refine our knowledge of the particular genes that confer risk for multiple sclerosis, these studies highlight promising candidates for future exploration. Moreover, the success of admixture mapping suggests that it could be a powerful tool for identifying genetic risk factors in other complex disorders.

Alison Rowan

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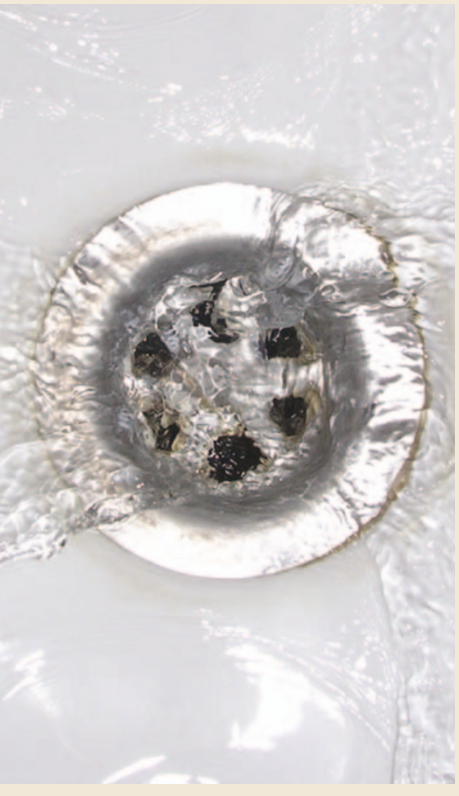

DEVELOPMENT

Throwing light on photoreceptor development

Colour vision in *Drosophila* depends on the responses of two types of colour-sensitive photoreceptor, R7 and R8. Two new studies provide important insights into the mechanisms that govern the cell fate and synaptic specificity of these neurons.

The compound eye is made up of 800 'unit eyes' or ommatidia, each of which contains eight photoreceptors (R1–R8) that project retinotopically to their targets in the optic ganglia. The centre of the unit eye is occupied by photoreceptors R7 and R8, which share the same optic path. These neurons express one of four rhodopsins — Rh3, Rh4, Rh5 or Rh6 — in three subtypes of ommatidium: p (pale), y (yellow) and DRA (dorsal rim area).

Colour vision depends on the p and y ommatidia, which discriminate long and short wavelengths, respectively. If R7 chooses the p fate, it expresses UV-sensitive Rh3 and instructs R8 to commit to the same fate, expressing the blue-sensitive Rh5. In the absence of a signal from R7, as when R7 commits to the y fate and expresses UV-sensitive Rh4, R8 defaults to the y fate and expresses the green-sensitive Rh6.

Desplan and colleagues explored the question of how R8 commits unambiguously to a p or y cell fate. They found that *warts* (*wts*, encoding large tumour suppressor, LATS) and *melted* (*melt*, encoding a pleckstrin homology (PH)-domain protein) have opposite roles in establishing pR8 or yR8 cell fates. *wts* is necessary and sufficient for yR8 specification, whereas *melt* suppresses *wts*, allowing *rh5* expression and preventing *rh6* induction. By repressing each other's transcription, *wts* and *melt* form a bistable loop that guarantees a firm commitment of R8 to a single fate. The authors propose that in the absence of an instruction from R7, the loop is biased in favour of *wts* expression, and that the system can amplify this signal to ensure that cell fate is unambiguous.

A report from Zipursky's group shows that the mechanisms underlying the synaptic specificity of photoreceptors are no less remarkable. The first step of R7 targeting requires the cell-adhesion molecule N-cadherin. Given that alternative splicing generates 12 isoforms of N-cadherin, which could explain how this widely expressed protein contributes to the differential cell recognition that leads to synaptic specificity, Zipursky and colleagues reasoned that isoform-specific mutants affecting only some N-cadherin functions probably exist.

They found that different subsets of N-cadherin isoforms act at early and late stages of R7 targeting. A mutant allele that eliminates the six isoforms containing alternative exon 18A was shown to disrupt the connections of R7 neurons. Whereas isoforms containing exon 18B were sufficient for the projection of R7 to a temporary target layer, 18A isoforms were necessary for R7 to terminate in the appropriate synaptic layer — M6 in the medulla — during the second phase of development.

These studies reveal some of the striking ways in which the cell fate and synaptic specificity of neurons are determined. They highlight the value of using relatively accessible invertebrate systems for studying the mechanisms of neurodevelopment.

Rebecca Craven

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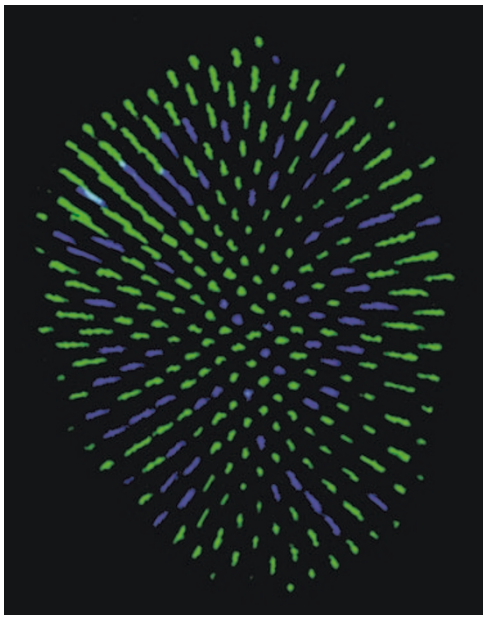

A *Drosophila* retina stained for R8 rhodopsins: blue-sensitive Rh5 (blue) and green-sensitive Rh6 (green). Image courtesy of C. Desplan, New York University, USA.