

confirmed its involvement in sex determination. Although these results show that *DMY* is necessary for male development, whether it is also sufficient remains to be seen.

Magdalena Skipper

#### References and links

**ORIGINAL RESEARCH PAPER** Matsuda, M. *et al.* *DMY* is a Y-specific DM-domain gene required for male development in the medaka fish. *Nature* **417**, 559–562 (2002)

**FURTHER READING** Wittbrodt, J. *et al.* Medaka — a model organism from the Far East. *Nature Rev. Genet.* **3**, 53–64 (2002)

contain factors involved in X inactivation. However, chromosome-15 markers showed no association with the mutant phenotype in the 1.19 pedigree, indicating the presence of two distinct mutations. A lack of informative markers for the 1.19 pedigree prevented this mutation from being mapped further in this strain.

With this work, the authors show for the first time that autosomal factors are involved in the choice of which X chromosome to inactivate. But they still have some way to go before they can say what these factors are, and how they interact with each other and the X chromosome. Such future studies, however, are likely to be helped by new sequencing data from Chureau *et al.* on the mouse and bovine *Xic* regions. In a three-way comparison of this region between mouse, cow and human, these authors identified conserved coding and non-coding genes, conserved CpG islands and even conserved pseudogenes, in addition to four new genes. With Chureau *et al.*'s new insights into what the *Xic* consists of, Percec *et al.* should find themselves better placed to answer the questions that their results pose.

Jane Alfred

#### References and links

**ORIGINAL RESEARCH PAPERS** Percec, I. *et al.* Autosomal dominant mutations affecting X inactivation choice in the mouse. *Science* **296**, 1136–1139 (2002) | Chureau, C. *et al.* Comparative sequence analysis of the X-inactivation center region in mouse, human, and bovine. *Genome Res.* **12**, 894–908 (2002)

**FURTHER READING** Avner, P. & Heard, E. X-chromosome inactivation: counting, choice and initiation. *Nature Rev. Genet.* **2**, 59–67 (2001)

#### WEB SITES

Hunt Willard's lab:

<http://genetics.gene.cwru.edu/willard>

Marisa Bartolomei's lab: <http://www.med.upenn.edu/cellbio/faculty/bartolomei>



#### BEHAVIOURAL GENETICS

## An old lesson in behaviour

Picking up someone else's project is rarely top of a researcher's wish list, especially if it has been around for more than four decades. But if the project happens to be that of Jerry Hirsch, then perhaps the idea is worth reconsidering. In the 1950s and 1960s, this 'drosophilist' sought to analyse the genetic basis of behaviour by artificially selecting lines of *Drosophila* that had an extreme preference for moving towards or against gravity in a vertical maze. Although he was able to establish, for the first time, that this so-called geotactic behaviour — indeed any behaviour — has a genetic basis, getting to the underlying genes just wasn't possible at that time. However, by applying cDNA microarray experiments and mutant analysis to the original lines generated by Hirsch, Daniel Toma, along with Ralph Greenspan, Kevin White and Jerry Hirsch himself, have now partly realized the original researcher's aim by identifying three genes involved in fly geotactic behaviour. The genetic basis of any selected phenotype is rather impenetrable, even today, making this work all the more remarkable.

If Hi (flies that like to go 'up') and Lo (flies that like to go 'down') lines behave differently, then the genes involved in this divergent phenotype are probably differently expressed in the two lines. In a microarray experiment to assess this, the authors identified 250 genes whose expression levels differed at least twofold between the two lines.

Toma *et al.* decided to pursue only those candidates from their microarray analysis for which mutants with neurological defects already exist. This left them with four mutant lines — *cryptochrome* (*cry*), *Pendulin* (*Pen*), *Pigment-*

*dispersing factor* (*Pdf*) and *prospero* (*pros*) — which were tested for their preference to go up or down. The geotactic score of three of the mutants, the exception being *pros*, was significantly different from that of wild-type flies and correlated with the difference in mRNA levels seen in the selected Hi and Lo lines. The dosage effect of gene expression on behaviour was also tested by generating transgenic flies that expressed wild-type *Pdf* and *pros* in backgrounds with varying copies of the endogenous transcript. Although altering the level of *pros* had no significant effect on the geotactic score (as predicted from the mutant data), altering the dosage of *Pdf* produced a graded effect, which differed between the sexes.

This file might have been an old one but, despite the qualitative advance reported here, it still isn't closed. How do *Pen*, *Pdf* and *cry* influence behaviour, as their functions give us little clue? How do we identify the remaining genes, which are probably pleiotropic and of small effect? Regardless of the outstanding questions, this work shows that behaviour can be genetically dissected by combining classical quantitative analysis, genomic approaches and mutant characterization — a new 'modern synthesis' for understanding the genetic architecture of complex traits.

Tanita Casci

#### References and links

**ORIGINAL RESEARCH PAPER** Toma, D. P. *et al.* Identification of genes involved in *Drosophila melanogaster* geotaxis, a complex behavioral trait. *Nature Genet.* 3 June 2002 (10.1038/ng893)

#### WEB SITES

Kevin White's lab:

<http://www.med.yale.edu/bbs/gendev/faculty/white.html>

Jerry Hirsch's lab:

<http://www.psych.uiuc.edu/people/faculty/hirsch.html>

Ralph Greenspan's lab: [www.nsi.edu](http://www.nsi.edu)