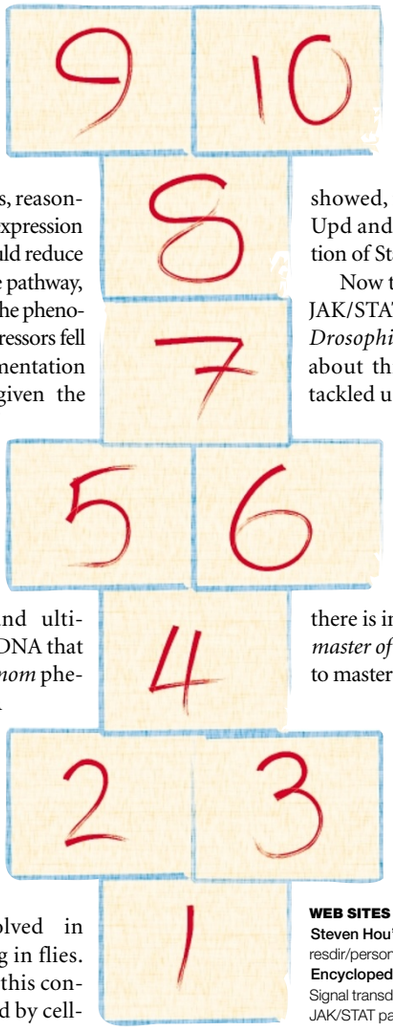
SIGNAL TRANSDUCTION

Mastering hopscotch

In mammals, the JAK/STAT signal transduction pathway mediates signalling by interferon and other cytokines. In *Drosophila*, the same signalling pathway is implicated in several processes, such as eye development, germ-cell differentiation and embryonic segmentation. However, there is one component of the pathway that has proved elusive in flies — that is until now. Using a genetic screen, Steven Hou's lab have found the pathway's missing receptor.

The basic mechanism of JAK/STAT signalling is as follows: a ligand (such as a cytokine) binds to a cell-surface receptor, which interacts with JAK, a non-receptor tyrosine kinase. JAK then phosphorylates the transcription factor STAT, which moves into the nucleus and regulates the expression of specific target genes. In *Drosophila*, the ligand is encoded by *unpaired* (*upd*; also known as *outstretched*), JAK is encoded by *hopscotch* (*hop*) and STAT by *Stat92E* (also known as *marelle*, the French word for hopscotch).

To hunt down a *Drosophila* receptor involved in JAK/STAT signalling, Hua-Wei Chen, Xiu Chen and their colleagues used a gain-of-function *upd* mutant, which had an abormal eye phenotype. They then screened a *P*-element insertion library for suppressor mutations, reasoning that reduction in expression of a Upd receptor would reduce signalling through the pathway, and thereby suppress the phenotype. Four of the suppressors fell into a single complementation group, which was given the name *master of marelle* (*mom*).



The authors cloned *mom* by characterizing the genomic DNA adjacent to the *P*-element insertions, and ultimately identified a cDNA that complemented the *mom* phenotype. The cDNA encodes a transmembrane protein with weak homology to mammalian cytokine receptors, and is therefore a strong candidate for the receptor involved in JAK/STAT signalling in flies. Further support for this conclusion was provided by cell-culture experiments, which showed, for example, that Mom binds Upd and is required for phosphorylation of Stat92E.

Now that this key component of the JAK/STAT pathway has been found in *Drosophila*, some important questions about this signalling pathway can be tackled using the full range of methods available to fly geneticists. Is Mom the only molecule required to mediate signalling from Upd to Hop, or are other molecules required? Is Mom the only receptor in flies, or is there a receptor family, like there is in mammals? Having found the *master of marelle*, can researchers expect to master JAK/STAT signalling?

Mark Patterson

References and links

ORIGINAL RESEARCH PAPER Chen, H.-W. *et al*. *mom* identifies a receptor for the *Drosophila* JAK/STAT signal transduction pathway and encodes a protein distantly related to the mammalian cytokine receptor family. *Genes Dev.* **16**, 388–398 (2002)

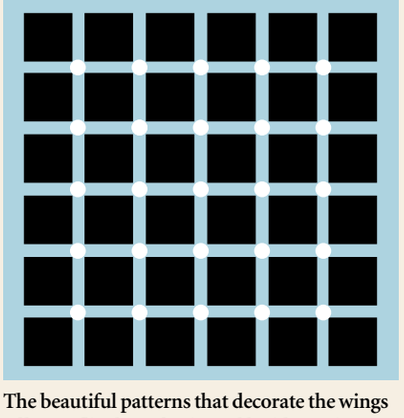
WEB SITES

Steven Hou's lab: http://www-dcs.nci.nih.gov/resdir/person_index.cfm?p_id=325

Encyclopedia of Life Sciences: http://www.els.net Signal transduction pathways in development: the JAK/STAT pathway

EVO–DEVO

Changing spots



The beautiful patterns that decorate the wings of butterflies have fascinated lepidopterists and evolutionary biologists alike for generations, both of them captivated by their incredible range of colours and shapes. For evolutionary biologists, however, the source of this variation — more precisely, the genetic variants on which natural selection acts to generate such variation — has often been quite elusive. In a new study, Patrícia Beldade and colleagues have used a candidate gene approach, together with artificial selection experiments, to get to the genetic basis of variation in wing eyespot size in the tropical butterfly *Bicyclus anynana*. Their work strongly implicates the *Distal-less* (*Dll*) gene in generating variation in eyespot size and highlights the strength of evo–devo for studying important adaptive features.

The authors chose to study *Dll*, which encodes a transcription factor, because of its previously reported organizing activity during eyespot development (see Highlights December 2001). But knowing that *Dll* is involved in determining the position of future eyespots and showing that variation at *Dll* is responsible for intra-individual variation in eyespot size are two different things. Rather than trying to match *Dll* variants to eyespot size in a natural population, the authors artificially selected butterflies for nine generations, and obtained two lines — one with large and one with small eyespots (high and low line, respectively) — in the expectation that *Dll* polymorphisms would segregate with one line or the other. That the selection experiment worked indicates that eyespot size is a highly heritable trait. Reassuringly for their hypothesis, Beldade *et al.* found not only that the domains of *Dll* expression correlated with eyespot size, but also that the phenotype of backcross progeny between a high–low hybrid and either a high or low parent segregated with a line-specific *Dll* polymorphism. Of course, as the authors point out, the linkage of *Dll* to this trait is not formal proof that *Dll* itself is involved, as their study does not rule out the involvement of linked loci. The case for the contribution of *Dll* to the difference in backcross phenotypes was further strengthened when it was found that the LOD score for a putative QTL peaks, or was very high, at *Dll*, compared with neighbouring regions.

Identifying which, if any, *Dll* alleles underlie variation in eyespot size is still some way away and, as the experiments revealed, more factors than *Dll* alone must be invoked to explain the phenotypic difference between the artificially selected lines. Even so, this work is a nice example of how a known developmental pathway can be linked to the standing quantitative varation in a population, made more significant in this case by involving a trait of known adaptive significance.

Tanita Casci

References and links

ORIGINAL RESEARCH PAPER Beldade, P. *et al*. Contribution of *Distal-less* to quantitative variation in butterfly eyespots. *Nature* **415**, 315–318 (2002)

WEB SITES

Paul Brakefield's lab: http://www.helsinki.fi/science/fragland/ldn_idx.html

Anthony Long's lab: http://hjmuller.bio.uci.edu/~labhome/