IN BRIEF

FUNCTIONAL GENOMICS

Open-reading frame sequence tags (OSTs) support the existence of at least 17,300 genes in *C. elegans*.

Reboul, J. *et al*. *Nature Genet*. **27**, 332–336 (2001)

Homology-based annotation yields 1,042 new candidate genes in the *Drosophila melanogaster* genome.

Gopal, S. *et al*. *Nature Genet*. **27**, 337–340 (2001)

The sequencing of several eukaryotic organisms' genomes has allowed new estimates of their gene number to be made — and there have been some surprises. Humans have fewer genes than expected, and worms have 50% more genes than flies have. The problem is that the tools used to make the predictions are not 100% reliable. Reboul *et al*. use an experimental strategy to test ~1,000 of the gene predictions in *C. elegans*, and find supporting evidence for 70%. Gopal *et al*. use a bioinformatic strategy to closely look at the *Drosophila* genome and find evidence for 1,000 more genes. So, the difference (in gene number) between flies and worms might not be so large after all.

PLANT GENETICS

Self incompatibility in the genus *Arabidopsis*: characterization of the *S* locus in the outcrossing *A. lyrata* and its autogamous relative *A. thaliana*.

Kusaba, M. *et al*. *Plant Cell* **13**, 1–18 (2001)

Molecular studies of self incompatibility in the *Brassica* species have identified a gene complex, *S*, that controls their inability to self pollinate. To address how this complex evolved, these authors sequenced two *S*-locus genes from the self-incompatible (SI) *A. lyrata* plant. A phylogenetic analysis of these genes and their orthologues in the self-compatible *A. thaliana* and other SI *Brassica* species revealed that this locus has undergone several duplications since the *Arabidopsis–Brassica* split, and that self compatibility in *A. thaliana* is due to the inactivation of *S*-locus genes.

EXPRESSION PROFILING

Delineating developmental and metabolic pathways *in vivo* by expression profiling using the RIKEN set of 18,816 full-length enriched mouse cDNA arrays.

Mika, R. *et al*. *Proc. Natl Acad. Sci. USA* **27**, 2199–2204 (2001)

In one of the first large-scale uses of this recently published resource (see In Brief in last month's issue), RIKEN researchers have arrayed almost 19,000 full-length, mouse cDNAs to analyse the expression profiles of 49 adult and embryonic mouse tissues. Cluster analysis identified sets of genes that were expressed ubiquitously or in similar groups of tissues and revealed that metabolic pathways are coordinately regulated throughout the mouse during development and adulthood. These expression profiles are available at a RIKEN database called READ.

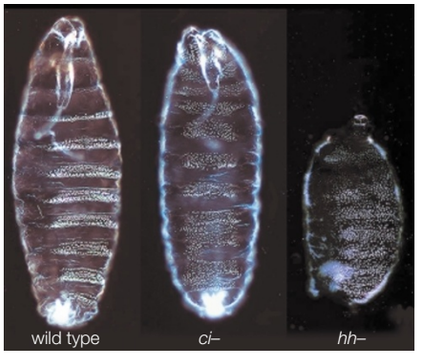
SIGNAL TRANSDUCTION

Genetics rules!

When it comes to dissecting signalling pathways, genetic analysis has sometimes had a rough time in asserting itself. To those seeking to understand which, and how, proteins physically interact in a signalling cascade, the rough sketch presented by analysing phenotypic mutants might seem a little disappointing. In this respect, Méthot and Basler's work is particularly satisfying, because it solves a longstanding problem that biochemistry alone could not address. By using an exclusively genetic approach, this research proves that the Hedgehog (Hh) signalling cascade converges on the activity of a single transcription factor and does not proceed, as some had proposed, through a branched pathway.

In vertebrates and invertebrates, signalling initiated by the secreted peptide Hh influences many developmental choices. The binding of Hh to the transmembrane protein Ptc (Patched) relieves the inhibition of Ptc on Smo (Smoothened), which then activates an intracellular signalling cascade. In *Drosophila*, the most distal element of this cascade is a zinc-finger transcription factor encoded by the *Gli*-homologue, *ci* (*cubitus interruptus*).

Five studies in the chick and in flies provided grounds for claims that Hh signalling outputs could occur independently of Ci/Gli. Among this evidence is the stronger mutant phenotype of hh^- fly embryos compared with their ci^- counterparts (see picture). The strategy used by Méthot and Basler to disprove such a claim is elegant and simple, and involves studying the phenotype of *ptc ci* double-mutant cells. The removal of *ptc* causes maximal Hh signalling; if Ci were the only outlet for the Smo signal, then every effect of Hh signalling caused by the *ptc* mutant should be reversed by the *ci* mutation. In a thorough genetic analysis, the authors monitored the behaviour of *ptc ci* double-mutant cells in *Drosophila* adults, larvae and



Cuticle preparations of *Drosophila* embryos. Courtesy of Konrad Basler, University of Zurich, Switzerland.

embryos. In every case examined, the evidence for a linear Hh pathway was unambiguous. For instance, in the larval wing disc (the epithelial pouch that develops into the adult structure), Ci is absolutely required for the Ptc-induced (and therefore Hh-dependent) expression of the marker genes *decapentaplegic*, *patched* and *engrailed*.

If Hh signalling absolutely needs Ci, then why should *hh* mutations have more severe effects than those in *ci*? The activator form of Ci that is induced in response to Hh has a nemesis in the form of a transcriptional repressor (Ci[rep]), which acts in the absence of Hh input. This repressor form of Ci might inhibit the expression of some Hh-target genes. The derepression of these genes in a *ci* null mutant (which produces no Ci[rep]) means that *ci* mutants express Hh-target genes that remain switched off in *hh* mutants. Thus, the effects of losing Ci seem milder than those of losing Hh.

In recognizing this, the authors have made a second discovery; although Ci is indispensable for signalling by Hh, Ci can have a separate function — as a repressor — in the absence of Hh signalling. It is probably this double life of Ci that led to the mistaken belief that Hh signalling has a branched output.

The results of this work are clear-cut but its implications are puzzling. How to explain the diversity of cellular responses of such a crucial pathway with just a single outlet? The solution to this problem might lie even beyond the power of genetics.

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References and links

ORIGINAL RESEARCH PAPER Méthot, N. & Basler, K. An absolute requirement for Cubitus interruptus in Hedgehog signaling. *Development* **128**, 733–742 (2001)

ENCYCLOPEDIA OF LIFE SCIENCES Hedgehog signalling