that disrupts *IGF2* imprinting. By engineering a chromosome 7:11 translocation that separates *Cdkn1c* — and the genes telomeric to it — from *Kcnq1* and the *H19* cluster, Cleary *et al.* investigate this link. Their results show that genes centromeric to the breakpoint — including *Kcnq1* and the *H19* cluster genes — are not regulated by elements near or telomeric to *Cdkn1c*, as these genes are normally imprinted in mice carrying either translocated chromosome. However, in mice that carry a maternally inherited 7:11 chromosome, *Cdkn1c* and the genes telomeric to it are no longer imprinted, and the expression of these normally maternally expressed genes is drastically reduced. This decreased expression is probably caused by these genes being separated from *cis*-acting regulatory elements required for their maximal expression — position effects mediated by chromosome 11 heterochromatin seem unlikely as chromosome 7 genes on the translocated chromosome are not methylated.

These findings strongly indicate that an ICR for this region lies proximal to the translocation breakpoint — a possible candidate is a differentially methylated region (DMR) that lies in *Kcnq10t1*, which is expressed from the paternal chromosome and is methylated on the maternal one. This DMR, the authors propose, might act as an enhancer blocker on paternal chromosomes that prevents enhancers from interacting with *Cdkn1c*. Methylation of this DMR on the maternal chromosome, where *Cdkn1c* is expressed and *Kcnq10t1* is silent, would impair the blocker's function, allowing *Cdkn1c* access to enhancers. The authors also predict that the BWS phenotype could be caused by the loss of *CDKN1C* expression, rather than by the overexpression of *IGF2*, as previously believed. Further insights into this region are likely to come from studies into several elements in this region that are conserved between mice and humans.

Jane Alfred

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FURTHER READING Yu, Y. & Bradley, A. Engineering chromosomal rearrangements in mice. *Nature Rev. Genet.* **2**, 780–790 (2001)
WEB SITE
Shirley Tilghman's lab:
http://www.molbio.princeton.edu/labs/tilghman/

retention, which would be compensated for by retaining more sodium ions, leading to greater water retention, higher blood volume and consequently higher blood pressure.

But do variants in WNK1 and WNK4 contribute to hypertension in the general population? Intriguingly, the genomic region that contains *WNK4* has also been linked to blood-pressure variation in a large population by the Framingham Heart Study, hinting at this possibility. Whether or not this is the case, drugs targeting the pathway in which WNKs are involved could prove to be good antihypertensive agents.

Peter Kirkpatrick, Associate Editor,
Nature Reviews Drug Discovery

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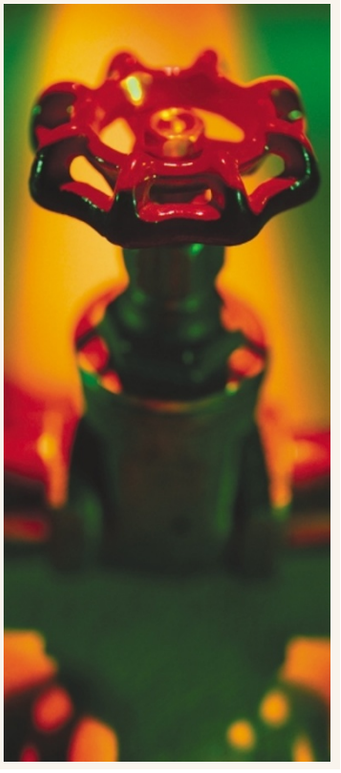

IN BRIEF

TECHNOLOGY

An oligonucleotide fingerprint normalized and expressed sequence tag characterized zebrafish cDNA library.

Clark, M. D. *et al. Genome Res.* **11**, 1594–1602 (2001)

Relatively few genomic resources are available to zebrafish researchers, despite the popularity of this organism among developmental biologists and geneticists. However, a new expressed-sequence-tag (EST) resource has been generated by a large collaborative effort, in which more than 25,000 unique cDNA clones were compiled following the normalization and subtraction of 75,000 clones from two cDNA libraries. Clone uniqueness was ensured by oligonucleotide fingerprinting, which identifies and preclusters similar clones before EST sequencing. Importantly for the zebrafish community, the complete set of clones is publicly available through The Resource Center of the German Human Genome Project (RZPD).

MOUSE GENETICS

Mutations in *Mlph*, encoding a member of the Rab effector family, cause the melanosome transport defects observed in *leaden* mice.

Matesic, L. E. *et al. Proc. Natl Acad. Sci. USA* **98**, 10238–10243 (2001)

Mammalian pigmentation requires specialized organelles called melanosomes, which synthesize melanin and are transported from melanocytes to, eventually, the hair shaft. Mouse coat-colour mutants have helped to identify components of this complex process, as indeed has the cloning of the gene mutated in *leaden* mice. *Mlph* encodes melanophilin, a novel Rab-effector-like protein involved in melanosome transport.

DEVELOPMENTAL BIOLOGY

Sightless has homology to transmembrane acyltransferases and is required to generate active Hedgehog protein.

Lee, J. D. & Treisman, J. E. *Curr. Biol.* **11**, 1147–1152 (2001)

Skinny hedgehog, an acyltransferase required for palmitoylation and activity of the Hedgehog signal.

Chamoun, Z. *et al. Science* 2 August 2001 (10.1126/science.1064437)

The conserved family of Hedgehog (Hh) proteins is responsible for important developmental signalling events in many species. Using different genetic screens, these papers identify a new *Drosophila* gene — called *sightless* (*sit*) in the first study and *skinny hedgehog* (*ski*) in the second — in the Hedgehog signalling pathway. They show that *sit*/*ski* is required in embryonic segmentation, and in eye and wing imaginal tissues, for effective signalling by Hh, but its absence does not affect Hh transcription or accumulation. *sit*/*ski* encodes a conserved 500-amino-acid transmembrane enzyme with homology to a family of membrane-bound acyltransferases. Genetic and biochemical experiments indicate that Sit/Ski catalyses an amino-terminal lipid modification of Hh that is essential for its patterning activity.