WEB WATCH

Model databases

• http://www.gmod.org/

Model organism databases, such as FlyBase, Mouse Genome Database (MGD), *Saccharomyces* Genome Database (SGD) and WormBase are invaluable for teaching and research. Through expert curation, they integrate many types of information, including genetic maps, DNA sequence, gene structure and function, and the literature. But those who work on less popular experimental organisms are not so well served.

Enter the Generic Model Organism Database (GMOD) project. The idea of this project is to capitalize on the experience of the designers of the existing model organism databases to derive a set of tools that can be used to construct a database for any model organism. The project is being funded by the NIH, and is intended to reduce the costs of constructing individual databases, so that when the *Mymodelis tops* community decide to develop their own database, the tools are ready and waiting.

The GMOD project is at an early stage, and needs ideas from potential users and developers. What information should be included in the databases? Which tools are most valuable? To participate in these discussions go to the GMOD web site and visit the Forums section.

Seeing is believing

• http://vischeck.com/

Colour blindness is a relatively common genetic condition — particularly among males — and can obscure the message in coloured images. Vischeck allows users to view graphics and web pages as though they suffer from different types of colour blindness. Vischeck is therefore a valuable tool for considering the needs of colour-blind individuals and for improving the accessibility of any graphic.

Mark Patterson

EPIGENETICS

Breaking into imprinted regions

The expression of an imprinted gene is determined by which parent it is inherited from, and the mechanisms that mediate this are just beginning to be understood. A clue as to the nature of imprinting mechanisms comes from the frequent arrangement of imprinted genes into chromosomal clusters, an indication that they are controlled by shared regulatory elements. By using chromosome engineering technology — which allows non-homologous chromosome segments to be recombined together (see review by Yu and Bradley on p780) — Michele Cleary and colleagues have now disrupted a well-studied imprinted gene cluster on distal mouse chromosome 7 that contains, possibly, several imprinting control regions (ICRs). This genomic region is homologous to an imprinted region on human chromosome 11 that is involved in Beckwith–Wiedeman syndrome (BWS). By engineering a BWS-associated translocation in mice, Cleary *et al.* provide new evidence for gene dysregulation in this disorder and shed light on why this cluster has been maintained through evolution.

On mouse chromosome 7, the imprinted genes *H19*, *Igf2* and *Ins2* are controlled by an ICR in the 5′ region of *H19*. Around 300–800 kb telomeric to these genes lie the imprinted genes *Kcnq1*, *Kcnq10t1* and *Cdkn1c*. Although imprinting of these telomeric genes is unaffected by deletions in the *H19* cluster, the imprinting control of the two clusters has been linked by a BWS translocation within *KCNQ1*

HUMAN GENETICS

WNKs turn up the pressure

Hypertension affects ~25% of adults in industrialized societies, and significantly increases the risk of heart attacks, strokes and kidney failure. However, the molecular abnormalities that underlie the most common forms of hypertension are poorly understood. This situation is changing, though, as a result of research on several rare monogenic forms of high and low blood pressure. By studying one such disorder — pseudohypoaldosteronism type II (PHAII) — Wilson *et al.* have now provided evidence for a new pathway that governs blood pressure.

Previous work studying different families with PHAII had linked the disease to regions on chromosomes 1, 12 and 17, but no convincing candidate genes had been identified. The key breakthrough for Wilson *et al.* came from the identification of a new PHAII-affected family, in which it proved possible to link the disease to a deletion in the first intron of *WNK1*, which encodes a serine/threonine kinase. Confirmation of the role of *WNK1* in PHAII came from another family with chromosome-12-related PHAII with a different, but overlapping, intronic deletion in *WNK1*, which leads to a fivefold increase in its expression.

Next, by searching the human genome for genes related to *WNK1*, the authors found one such gene — *WNK4* — in the PHAII-linked region on chromosome 17. Screening families with PHAII linked to chromosome 17 revealed four families with missense mutations that cluster in a short, highly conserved segment of *WNK4*, which were suggested to result in a gain of function.

So, what might be the role of the identified WNK proteins? Hypertension in PHAII patients has been attributed to increased reabsorption of salt by the kidneys. Consistent with this, the mouse homologues Wnk1 and Wnk4 were both present in a region of the kidney that has a key role in maintaining the body's salt and water balance. Combining these observations with the fact that the features of PHAII are chloride dependent led the authors to propose that WNKs are part of a pathway that regulates chloride ion uptake by the kidney. Increased activity of WNKs could then result in greater chloride ion