WEB WATCH

The miRNA Registry

• http://www.sanger.ac.uk/Software/Rfam/mirna/index.shtml

The miRNA Registry was set up to manage the increasing number of microRNAs that are being discovered. It was developed by the team behind Rfam UK (the RNA Families Database of Alignments and Covariance Models) with support from several well-known RNA researchers.

The database provides researchers with a means of searching information on published miRNAs — both precursor and mature sequences — by accession number, identifier, reference details and by BLASTing with sequence data. You can also 'Browse miRNAs' by species. Each miRNA entry is well presented: relevant publications are listed, along with background information (including where the miRNA gene maps to) and links to related miRNAs and other databases, in addition to providing the precursor and mature sequences.

This registry also provides an invaluable naming scheme: miRNA sequences can be submitted for naming once a manuscript has been accepted for publication, the idea being that this will prevent distinct genes and miRNAs with the same names from being published.

The latest version of this database (Release 3.0), which was made available in January 2004, contains 719 entries — 213 more entries than Release 2.0, which was only made available in July 2003. And, in addition to the entries from *Caenorhabditis elegans*, *C. briggsae*, *Drosophila melanogaster*, human, mouse and *Arabidopsis thaliana*, Release 3.0 also contains miRNAs from both rat and rice.

As the number of miRNAs being discovered looks set to continue to rise rapidly, this site is sure to become an even more valuable resource for the miRNA community.

Natalie Wilson

FURTHER READING

Griffiths-Jones, S. The microRNA Registry. *Nucleic Acids Res.* 1 Jan 2004 (doi:10.1093/nar/gkh023)

DEVELOPMENTAL BIOLOGY

MicroRNAs surface in the leaf

Despite 70 million years of independent history, the same microRNA (miRNA) molecules could be responsible for distinguishing the top from the bottom side of leaves in two very different types of flowering plant — maize and *Arabidopsis thaliana*. Organ polarity — in this case, that of the leaf — therefore becomes the latest addition to the rapidly growing number of regulatory functions that have been found for small interfering RNAs. These conclusions are reported in two separate papers that are published in *Nature*.

The leaves of monocots such as maize are quite different from those of dicots such as *A. thaliana*, yet in both plants, the upper (adaxial) and the lower (abaxial) surfaces can be distinguished clearly — for example, in *A. thaliana*, the top surface is waxier and the lower surface contains pores for gaseous exchange. They also differ genetically, with the upper side expressing three genes, *PHABULOSA* (*PHB*), *PHAVOLUTA* (*PHV*) and *REVOLUTA* (*REV*), that are down-regulated in the lower surface.

How is this polarity controlled? The fact that *PHB*, *PHV* and *REV* transcripts can be cleaved *in vitro* by two complementary miRNAs (miRNA165 and miRNA166) indicates that the RNA interference (RNAi) pathway might define the expression domain of this family of genes. Michelle Juarez and colleagues confirmed this in maize by cloning and characterizing the expression of the maize homologue of *REV*, which is defined by the previously described *rolled leaf 1* (*rdl1*) mutant. miRNA166 and *RDL1* have complementary expression patterns; moreover, mutations that disrupt the miRNA target site cause dominant alleles of *rdl1*, *phb* and *phv*, in which transcripts persist in the lower leaf surface.

In the paper by Catherine Kidner and Rob Martienssen, the idea of a possible link between leaf polarity and RNAi was sparked by the observation that mutants in the *A. thaliana ARGONAUTE1* (*AGO1*) gene, which is required for RNAi, have leaf-polarity defects. More specifically, some *ago1* mutant phenotypes resemble those of the dominant *phb* alleles

STEM CELLS

Making more of yourself

Reporting in Science, Wang and Lin tackle one of the most fundamental problems in stem-cell biology: how does a stem cell decide that, when dividing, it should make at least one more of itself — rather than generating two more-specialized cell types? The authors find that a key to such 'self-renewal' is, at least for one type of stem cell, a translational repressor known as Nanos.

Recent years have seen much progress in understanding the extrinsic signals that regulate stem-cell self-renewal. But the intrinsic cues have, for most stem cells, been more of a mystery. Wang and Lin approached the problem by looking at fruitfly ovaries, and specifically germline stem cells (GSCs), which have certain benefits as a model system — including their distinctive morphology. GSCs are formed from primordial germ cells at the larval/pupal transition. In adult females, GSCs can both self-renew and generate differentiating cell types, namely cystoblasts, which go on to produce egg chambers.

It was already known that Nanos contributes to the production of eggs, but exactly what it does was less clear. To start to find out, Wang and Lin constructed a *nanos* transgene that is switched on by heat shock. They used this transgene to restore functional Nanos to female embryos with *nanos* mutations. Then, after the adults emerged from the pupa, they switched the transgene off. The result was that the number of GSCs dropped sharply in comparison with wild-type flies — as did the number of egg chambers (presumably because there were fewer GSCs to generate them). So, Nanos is required continuously for GSCs to self-renew.

In this experiment, Nanos was switched on and off in the whole fly. It cannot be seen from this, however, whether the Nanos signal is intrinsic or extrinsic to GSCs. To find out, the authors removed the protein only from GSCs. They concluded that Nanos is an intrinsic regulator of GSC self-renewal — and that it works by preventing these cells from differentiating. Moreover, it probably functions by forming