RNA SILENCING

Probing the silence

Reporting in *The Plant Cell*, Olivier Voinnet and colleagues show that viral silencing suppressors can be used to help unravel the complexity of RNA silencing.

In plants, RNA silencing is involved in the anti-viral adaptive immune response through post-transcriptional gene silencing (PTGS; known as RNA interference (RNAi) in animals). PTGS involves endonucleolytic cleavage of RNAs guided by sequence-specific small interfering RNAs (siRNAs). RNA silencing is also linked to development, in which sequence-specific microRNAs (miRNAs) either promote endonucleolytic cleavage of RNAs or inhibit the translation of target RNAs.

The similarities between the siRNA and miRNA pathways led the authors to investigate RNA silencing using the suppressor proteins that viruses use to counteract PTGS. Although viral silencing suppressors have been studied before, their mode and point of action in the PTGS pathway have remained unknown.

The authors devised an experimental system in *Arabidopsis thaliana* to allow the comparative side-by-side analysis of five distinct suppressors. They expressed the suppressors transgenically in the same *Arabidopsis* ecotype, in which PTGS of the endogenous chalcone synthase (CHS) transcript was activated.

All five suppressors inhibited PTGS of the CHS transcript, but only three altered miRNA accumulation or miRNA-guided functions. This indicates that, as in animals, the siRNA and miRNA pathways overlap only partially.

The three suppressors that altered the miRNA pathway are diverse, so the authors propose that their induction of similar developmental abnormalities might be secondary to the inhibition of the siRNA pathway. The authors also found that other *Arabidopsis* small silencing RNAs were resistant to all five silencing suppressors, which indicates that these RNAs have distinct biosynthetic and functional pathways. Furthermore, miRNAs were shown to fall into 2 size classes (as per siRNAs), and the authors suggest that 21-nucleotide miRNAs are incorporated into the RNA-induced silencing complex (RISC), whereas 24-nucleotide miRNAs might direct transcriptional silencing events.

Using this system, the authors showed that not all suppressors are equal — one partially reduces dsRNA processing by Dicer and prevents mRNA degradation, perhaps by inhibiting RISC activity, others might act downstream of Dicer, as they have no effect on dsRNA processing, and another functions by sequestering both siRNAs and miRNAs. Because one suppressor was also found to suppress RNAi in a human cell line, it is hoped that these results will ultimately help to decipher the mechanisms that underlie RNAi in animals, as well as in plants.

Natalie Wilson

References and links

ORIGINAL RESEARCH PAPER Dunoyer, P., Lecellier, C.-H. *et al.* Probing the microRNA and small interfering RNA pathways with virus-encoded suppressors of RNA silencing. *Plant Cell* **16**, 1235–1250 (2004)

WEB SITE

Institut de Biologie Moléculaire des Plantes: http://ibmp.u-strasbg.fr/

IN BRIEF

COMPARATIVE GENOMICS

Comparative genomics identifies a flagellar and basal body proteome that includes the *BBS5* human disease gene.

Li, J. B. *et al. Cell* **117**, 541–552 (2004)

Cilia and flagella are microtubule-based organelles that have been implicated in many developmental and disease processes. To identify conserved genes involved in eukaryotic cilia/flagella structure, the authors compared the proteome of *Chlamydomonas reinhardtii* and human to that of the non-flagellated *Arabidopsis thaliana*. One of the 688 conserved genes that they thoroughly characterized was a new gene for Bardet–Bieldl syndrome.

COMPUTATIONAL BIOLOGY

Programmable cells: interfacing natural and engineered gene networks.

Kobayashi, H. & Kærn, M. *et al. Proc. Natl Acad. Sci. USA* **101**, 8414–8419 (2004)

Although engineering cells to carry out specific tasks is useful, exploiting natural circuits offers greater potential and flexibility. These authors have generated a modular genetic circuit in which a genetic toggle switch — an artificial module that can alternate between two stable states — is combined with two natural circuits: the SOS signalling pathway, which responds to DNA damage, and a transgenic quorum-sensing pathway. Four *Escherichia coli* strains were created, one of which forms a biofilm in response to DNA damage.

GENE THERAPY

LARGE can functionally bypass α-dystroglycan glycosylation defects in distinct congenital muscular dystrophies.

Barresi, R. *et al. Nature Med.* 6 June 2004 (doi:10.1038/nm1059)

Mutations in glycosyltransferases can cause muscular dystropies. Kevin Campbell and colleagues show that overexpressing one of these glycosyltransferases, LARGE, alleviates the symptoms of a dystrophic mouse model. Similarly, gene transfer of *LARGE* into the cells of humans with congenital muscular dystrophy restored glycosylation of the α-dystroglycan receptor. These results indicate that *LARGE* gene therapy could be an effective treatment for these disorders.

GENE REGULATION

Intergenic transcription is required to repress the *Saccharomyces cerevisiae SER3* gene.

Martens, J. A. *et al. Nature* **429**, 571–574 (2004)

Widespread intergenic transcription has been found in humans and yeast. Joseph Martens and colleagues show that when yeast is grown in rich medium, one such transcript, *SRG1*, is highly transcribed. Their data indicate that *SRG1*, which is transcribed from the regulatory region of *SER3*, is required to repress this gene. It seems that the reading of this transcript interferes with activator binding. So, uniquely, it is this, rather than the transcript itself, that represses *SER3*.