Nature Reviews Molecular Cell Biology | AOP, published online 4 June 2008; doi:10.1038/nrm2429

DOI:
10.1038/nrm2429

SMALL RNAS

United in silence

> …translational inhibition is also widely used by plant miRNAs…

The degree of complementarity between microRNAs (miRNAs) and their targets is thought to determine the mechanism of silencing. Plant miRNAs, which have high complementarity, predominantly use endonucleolytic cleavage ('slicing'), whereas animal miRNAs, which are less complementary, also use a second silencing mechanism — translational repression. Olivier Voinnet and his team now report that translational inhibition is also widely used by plant miRNAs and small interfering RNAs (siRNAs).

The authors characterized *Arabidopsis thaliana* mutants that were identified in a screen for defective miRNA function, using a perfectly complementary miRNA. Some of the mutants had higher levels of target mRNA and protein compared with wild-type plants, suggesting defects in slicing activity. Intriguingly, two other mutants (*mad5* and *mad6*) showed higher protein levels but mRNA levels that were similar to that of wild-type plants, suggesting a defect in translational inhibition. These findings imply that RNA silencing that is mediated by a perfectly complementary miRNA can be mediated by two different mechanisms.

STOCKBYTE

To test whether miRNA-mediated translational inhibition of target mRNAs is widespread in *A. thaliana*, the authors analysed the mRNA and protein levels of several endogenous miRNA targets. *mad5* and *mad6* showed increased protein levels from all tested target transcripts, irrespective of the level of complementarity or the location of target sites within the mRNAs (5′ untranslated region (UTR), coding region or 3′ UTR). The analysis also suggested that certain recently evolved miRNAs might function solely at the level of translation even if they are perfectly matched to their targets.

Positional cloning showed that *mad5* has a mutation in the *KTN1* gene, which encodes a subunit of the microtubule-severing enzyme KATANIN. The idea that microtubule dynamics functions in miRNA-mediated translational repression is supported by several observations that have been made in animal studies.

Given the role of mRNA decapping factors in miRNA-guided translational repression in animals, Voinnet and colleagues tested whether the decapping component VCS is required in plants. Indeed, *vcs* mutants had increased protein levels of miRNA targets but not of non-miRNA targets, whereas corresponding mRNA levels remained the same.

So, which Argonaute (AGO) protein is involved in translational repression? AGO1 functions as a miRNA-mediated slicer enzyme, but an *ago1* mutant also showed disproportionally higher protein levels for some targets but not others. Translational repression was also defective in *ago10* mutants, but only for some miRNA targets. So it seems that both AGO1 and AGO10 function in translational repression.

Using *mad6* and a specific mutant allele of *ago1*, the authors also tested the contribution of translational repression to siRNA silencing. In both mutants, target protein levels were increased with little or no change in the mRNA levels, which implies that siRNAs can mediate translational repression as well as mRNA degradation.The silencing mechanisms in plants and animals are clearly more related than previously thought. The authors propose that "translational repression is the default mechanism by which small RNAs silence messages, both in plants and animals". The debate as to whether this is true and whether the two mechanisms coexist in the same cell, or whether they are spatially and/or temporally separated, will undoubtedly continue in the future.

Arianne Heinrichs

ORIGINAL RESEARCH PAPER Brodersen, P. *et al.* Widespread translational inhibition by plant miRNAs and siRNAs. *Science* 15 May 2008 (doi:10.1126/science.1159151)
FURTHER READING Rana, T. M. Illuminating the silence: understanding the structure and function of small RNAs. *Nature Rev. Mol. Cell Biol.* **8**, 23–36 (2007)