

nature insight

RNA interference



The most familiar role for RNA is as a relatively passive intermediary in the translation of information from genes into proteins. But other functions for this versatile molecule have been emerging. This Insight explores the surprising recent discovery that RNA can actively regulate gene expression.

RNA interference or RNAi is a remarkable process whereby small noncoding RNAs silence specific genes. Although the first hints about this silencing process were seen decades ago, the real breakthrough in mechanistic understanding came in 1998. A landmark paper by Fire and colleagues (*Nature* **391**, 806–811; 1998) showed that the trigger for gene silencing is double-stranded RNA. Since then, other components of the RNAi machinery have been identified at a startling rate, although the picture is still incomplete.

RNAi is a conserved mechanism that pervades the biological world (budding yeast being a notable exception). It was first observed in plants in the guise of a mysterious immune response to viral pathogens. But RNAi is more than just a response to exogenous genetic material. Small RNAs termed microRNAs regulate gene expression in organisms ranging from nematode to man. Hundreds of microRNAs have been identified *in silico*, and we are beginning to understand their diverse functions in development and physiology.

Another biological role of RNAi is in heterochromatin silencing. By silencing transcripts generated from repeat sequences, RNAi guides heterochromatin formation and represses transposable elements and other foreign DNA integrated into the genome.

As well as expanding our appreciation of how genes are regulated, RNAi has been harnessed as an experimental tool to explore gene function, is revolutionizing our ability to perform large-scale genetic screens, and even shows therapeutic potential. We hope that these reviews capture the excitement and promise of this fast-moving field. We are grateful to the authors for their contributions and to the reviewers for their valuable input.

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