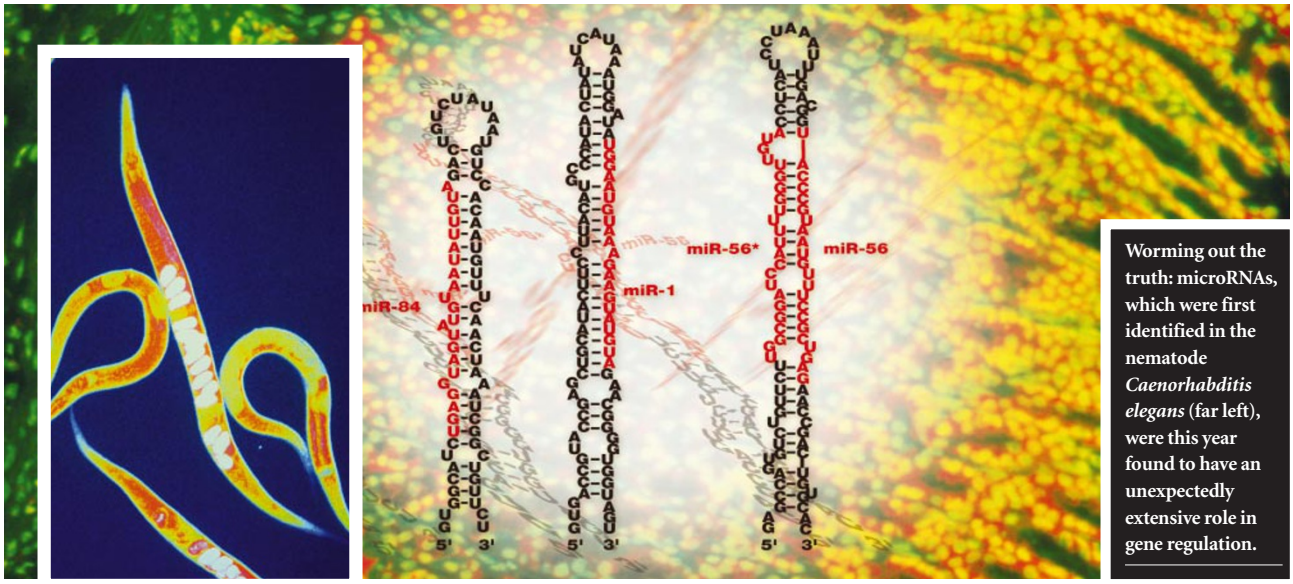

J. KING-HOLMES/SPL; INSET, M. YERIDAT/SPL

Worming out the truth: microRNAs, which were first identified in the nematode *Caenorhabditis elegans* (far left), were this year found to have an unexpectedly extensive role in gene regulation.

ization sometime early next year. But the polarization may retain a secret. The energy waves are thought to have been triggered by a rapid enlargement of the early Universe, known as inflation. This would also have created gravity waves, which would lead to tiny whirlpools in the CMB polarization. Detecting these whirlpools would provide the best evidence yet for inflation. Measuring such vortices will require more sensitive instruments, however. "No one knows for sure exactly how to do it — yet," says Lyman Page, a cosmologist at Princeton University in New Jersey. ■

Geoff Brumfiel

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Small RNAs

The genome's guiding hand?

They can be thought of as biology's 'dark matter': tiny RNAs that don't encode any protein. But 2002 has seen an avalanche of discoveries about their roles in influencing gene activity — lending some credence to the radical idea that small RNAs hover 'above' the genome, providing a matrix of regulatory control.

MicroRNAs (miRNAs) are about 22 nucleotides long, and were first identified in the nematode *Caenorhabditis elegans*[1,2]. In *C. elegans*, they regulate the activity of specific genes by binding to messenger RNAs (mRNAs) and preventing their translation to proteins.

Until recently, many experts thought that such examples were interesting anomalies. But they are now realizing that miRNAs are involved in gene regulation in a wide variety of organisms, and researchers are finding links between miRNAs and the phenomenon of RNA interference (RNAi). The latter mechanism, which is exploited by biologists for gene-silencing studies, is thought to be a natural defence against invading viruses. It uses an enzyme called Dicer to cut double-stranded viral RNA into small interfering RNAs (siRNAs), again about 22 nucleotides long. These then bind to other viral RNA, targeting it for destruction.

Dicer also creates miRNAs, by cutting them from longer, hairpin-shaped RNAs transcribed from the genome, but that was where the similarity was thought to stop. In August, however, it emerged that miRNAs can also function in the RNAi pathway and cause their target mRNAs to be degraded, if they perfectly match its target sequence[3].

Speculation was mounting that miRNAs represented an unexplored layer of gene regulation but, without knowing the identity of their targets, their role remained unclear. This again changed in the summer, when the mRNA targets of miRNAs were identified in the weed *Arabidopsis thaliana* — most of those studied seem to be involved in early plant development[4,5]. This was remarkable progress, given that miRNAs were only identified in plants a few months earlier[6,7].

At the same time, new functions for small RNAs were being found. Tiny RNAs now appear to do a whole lot more than just target mRNAs. They seem to be associated with various 'epigenetic' phenomena — the inheritance of features that do not involve genetic sequence changes. For instance, a startling connection has been made between small RNAs and the silencing of gene activity in tightly packed regions of the genome: deleting genes that encode components of the RNAi pathway led to a loss of gene silencing in the fission yeast *Schizosaccharomyces pombe*[8,9].

Small RNAs also seem to be capable of reshaping the genome. The ciliated protozoan *Tetrahymena thermophila* possesses two nuclei, the larger of which loses roughly 15% of its DNA during the cell's development — and this seems to be guided by small RNAs[10].

Finally, some researchers are taking a lead from the presumed natural function of RNAi by exploring the use of small RNAs as anti-viral agents. siRNAs targeted at viral genes can inhibit the replication of HIV-1 or polio-virus in cultured cells[11–13]. What's more, siRNAs targeted at the host receptors used by HIV to enter the cell can also block infection[13].

Of course, results in cultured cells don't always translate to the clinic. "The challenge will be in the delivery," says Andy Fire of the Carnegie Institution of Washington in Baltimore, co-discoverer of RNAi in *C. elegans*. But there are early signs that siRNAs targeted at human hepatitis C virus can function when injected into mice[14]. These small nucleotide strings could yet be big news for medicine. ■

Carina Dennis

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