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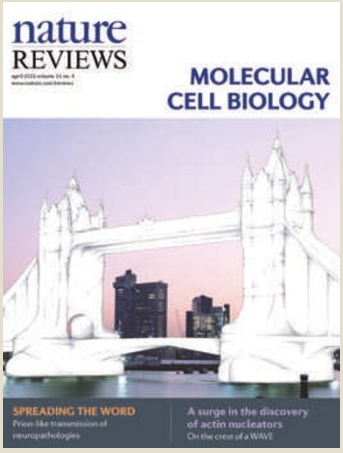

► **COVER:** 'Wrap artist' by Vicky Summersby, inspired by the Review on p264, and the work of the artists Christo and Jeanne-Claude.


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When, in 1993, the groups of Victor Ambros and Gary Ruvkun reported that the development of *Caenorhabditis elegans* is modulated by a 22-nucleotide RNA, now called *lin-4* microRNA (miRNA), the significance of their finding was initially under-appreciated. However, the field of miRNA research took off when Ruvkun and colleagues discovered a second miRNA, *let-7*, which exists in several species. Almost 20 years on, we have gained considerable insight into how miRNAs are made (see Kim, V. N. *et al. Nature Rev. Mol. Cell Biol.* **10**, 126–139 (2009)) and how miRNAs recognize and regulate the expression of target genes at the post-transcriptional level (see Brodersen, P. and Voinnet, O. *Nature Rev. Mol. Cell Biol.* **10**, 141–148 (2009)). But what are the true physiological targets of miRNAs?

In this issue, Stefano Piccolo and colleagues (page 252) propose that, as they are highly dose-sensitive, signalling pathways are ideal targets for the degree of fine-tuning that miRNAs are likely to achieve in nature. They describe how miRNAs might confer signalling robustness, alter the cellular milieu to influence gene expression induced by various signalling cascades and regulate crosstalk between signalling pathways. As miRNAs modulate signalling cascades that are important in disease, understanding their role in cell signalling might also help us to identify therapeutically relevant miRNAs.

Also in this issue, Kenneth G. Campellone and Matthew D. Welch describe how the discovery of mammalian proteins that regulate actin nucleation and dynamics helps us to understand how the actin cytoskeleton influences cellular functions (page 237), and Paul B. Talbert and Steven Henikoff explain that, whereas core histone particles are spools for wrapping DNA, histone variants have diverse additional roles in chromosome metabolism (page 264).