

The microRevolution

microRNAs (miRNAs) were initially considered a biological sideshow, the oddly interesting regulators of developmental timing genes in *Caenorhabditis elegans*. But in the past few years, studies have shown that miRNAs are a considerable part of the transcriptional output of the genomes of plants and animals, that they regulate a large part of their transcriptomes and that they serve important regulatory functions in widespread biological activities. Accordingly, miRNAs are now recognized as an additional layer of post-transcriptional control that must be accounted for if we are to understand the complexity of gene expression and the regulatory potential of the genome. Owing to this impressive progress in understanding the genomics and functions of miRNAs, we think this is an ideal time to examine the available evidence to see where this rapidly growing field is going.

In this Supplement, we have focused on approaches to detect the presence of miRNAs and their impact on genomes, and we explore the roles they play in regulating biological functions. The Supplement consists of five exploratory Perspectives and a comprehensive Review; the pieces generally follow a progressive logic from discovery to target prediction to function to systems perspective and finally to organismal perspective.

Plant and animal genomes have been shaped by miRNAs, as seen by the substantial number of conserved miRNAs that have accumulated through selection and the presence of miRNA target sites in genes of diverse functions. However, the true number of miRNAs and targets remains difficult to estimate. The detection of miRNAs is addressed in a Perspective from Eugene Berezikov, Edwin Cuppen and Ronald Plasterk (p S2), who discuss methods, both experimental and bioinformatic, for discovering new miRNAs. These authors wrangle with the question of how we define a 'true' miRNA and the implications this definition will have for future studies. Approaches to the prediction of targets of miRNAs are addressed by Nikolaus Rajewsky (p S8), who considers the case for combinatorial control of target expression by multiple miRNAs acting synergistically.

Some of the fundamental goals of investigations into genome function are to understand how the genome gives rise to different cell types, how it contributes to basic and specialized functions in those cells and how it contributes to the ways cells interact with the environment. The roles of miRNAs in each of those functions are touched on in three Perspectives. Jan Krützfeldt, Matthew Poy and Markus Stoffel (p S14) discuss approaches and technological advances useful to the investigator studying miRNA function. Eran Hornstein and Noam Shomron (p S20) take a systems approach to conceptualize a network of interacting miRNAs and targets and propose that miRNAs act to canalize developmental gene expression programs. And Bryan Cullen (p S25) discusses recent evidence for pathogenic roles of virally encoded miRNAs and proposes that cellular miRNAs influence the cell-type specificity of invading viruses.

In the last piece, Allison Mallory and Hervé Vaucheret (p S31) offer a view of the diverse biological roles of miRNAs from an organismal perspective in their Review of miRNAs and other endogenous regulatory RNAs in plants. This piece highlights the contributions of regulatory RNAs to developmental programs and stress responses.

Our hope is that you find strategic advice and insight in this Supplement. We invite you to access its contents online at <http://www.nature.com/ng/supplements/>, where it will be freely available for 3 months. In addition to the pieces featured here, online we provide links to related articles on miRNAs published by the Nature Publishing Group and an animation entitled 'Lifecycle of an miRNA' supplied by Rosetta Genomics.

We are grateful to our authors for their insightful contributions, as well as to our referees for their valuable comments during the review process. In addition, we gratefully acknowledge the support of our primary sponsors, Rosetta Genomics and Alnylam Pharmaceuticals, and our secondary sponsor, Santaris Pharma, for their help in producing this Supplement and making it freely available online.