
Preface

The discovery that gene expression can be controlled via Watson-Crick base pairing of short RNAs to complementary target RNAs (RNA interference) has significantly advanced our understanding of eukaryotic gene regulation and function. The ability of short RNA sequences to modulate gene expression has provided a powerful new tool to study gene function and is about to revolutionize the treatment of disease. Endogenous small RNAs have been found in various organisms, including humans, mouse, flies, worms, fungi, and bacteria. In higher eukaryotes microRNAs may regulate as much as 50% of gene expression. The biogenesis and processing of these regulatory RNAs is an area of intense research interest since they act as cellular rheostats, subtly modulating gene expression.

Targeting cellular genes by exogenous introduction of small interfering RNAs (siRNAs) takes advantage of the endogenous posttranscriptional gene silencing (PTGS) mechanism. The siRNAs can be transfected directly into cells wherein they enter the RNA induced silencing complex (RISC) directly. Alternatively, they can be generated within the cell via gene expression by the use of vectors containing Pol II or Pol III promoters for expression. These RNAi triggers can be expressed in the form of microRNAs or as short hairpins (shRNAs), which are processed into 21-22 nt RNAi triggers. Transcriptional gene silencing (TGS) involves small RNAs complementary to promoter regions that recruit components of the RNAi machinery as well as chromatin remodeling proteins to promoter regions, resulting in transcriptional silencing. TGS has been demonstrated in lower eukaryotes, plants, and most recently in mammalian cells. In addition to the small RNA mechanisms in higher organisms, there are numerous small RNAs in prokaryotic organisms that posttranscriptionally regulate gene expression by a variety of different mechanisms, including Watson-Crick base pairing.

The chapters in this volume cover a wide variety of small RNA regulatory pathways in organisms ranging from bacteria to humans. The breadth of these regulatory pathways and their functional importance in the host organisms are also covered within the volume. Aside from the biological aspects of small RNA mediated regulation of gene expression, techniques for utilizing small RNAs to study gene function or as therapeutic modalities are also discussed. We believe that this volume captures the essence of the breadth and excitement surrounding the newly discovered regulatory roles of small RNAs.