Biochimica et Biophysica Acta 1779 (2008) 653–654

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

journal homepage: www.elsevier.com/locate/bbagrm

Preface

MicroRNAs: An exciting and open field calls for extensive study from initial and established investigators

It was not until the year 1998 that the Nobel Prize-winning discovery of RNA interference (RNAi) by Fire and Mello with their colleagues initiated the study of the expansive world of small RNAs. The discovery of short/small interfering RNAs (siRNAs) based on works from several pioneers, including Hannon, Zamore, Tuschl, Baulcombe, and their colleagues, further opened a big window for small RNAs. Shortly afterward, the hunt for various kinds of endogenous small RNAs by several leading investigators, including Bartel, Ambros, and their colleagues, led to the recognition of a large family of endogenous small RNAs, namely microRNAs (miRNAs). *lin-4* and *let-7*, discovered by Ambros and colleagues in 1993 and by Ruvkun and colleagues in 2000, respectively, are the two founding members of this big family. MiRNAs are small RNAs, only 21–25 nucleotides (nt); most of them are hidden in the neglected non-protein-coding regions of the genome and are widespread in plants and animals. Thousands of miRNAs have been identified, and many are highly conserved within the animal or the plant kingdoms but divergent between the two kingdoms. While siRNAs target mRNAs mainly for destruction, miRNAs regulate mRNAs through either destroying the targets or repressing the translation of the target RNAs (cover figure). The major difference between siRNA and miRNA in mammals is that the former targets very specific mRNAs that are fully complementary to the siRNAs for destruction, while the latter broadly targets many different mRNAs that are only partially complementary to the 5′ region of the miRNA. As a consequence, a miRNA has the potential to target hundreds of mRNAs, and many biological processes are thus potentially under the control of miRNAs.

Research on miRNAs also led the way to a series of small RNA technologies that allowed the discovery of the roles of miRNAs in normal and abnormal development and the pathogenesis of various human diseases, such as type-2 diabetes. One of the technologies was high-throughput miRNA arrays, which have been established over the past few years. With more miRNAs discovered, an entire set of miRNA atlases can be gathered. A miRNA atlas allows close comparison of miRNAs between normal and abnormal organs, tissues, or cells and provides various developmental landmarks and pathological biomarkers. Second, specific technologies for studying the roles of candidate miRNAs in various normal and abnormal developmental processes were developed. AntagomiRs, for example, are synthetic RNase-resistant modified RNA oligos that are fully complementary to their target miRNAs and act as potent miRNA inhibitors for functional analysis of miRNAs. Recent development of the so-called “miRNA sponges” or “target mimicry” in animals and plants provides an alternative but a long-lasting means of blocking miRNA functions *in vivo*. Validation of identified miRNAs and their targets can be fulfilled by various well-established approaches such as overexpression of miRNAs, expression of miRNA-resistant targets, or miRNA reporters that are fused with miRNA targeting sequences. Today, these small RNA technologies have been used extensively for functional genomics of miRNAs in plants and animals.

In this special issue on miRNAs, 17 corresponding authors, both established and initial investigators, contributed 19 reviews, minireviews, and original research papers on plant and animal miRNAs or their related technologies. These papers were selected after a strict peer-review process. Each was chosen because it provides a quality introductory or in-depth reading matter for readers who are working on, plan to work on, or have an interest in miRNAs. The 19 papers are roughly divided into four sections. The first section is composed of an introductory overview of miRNAs by Dr. Guiliang Tang. The second section of papers includes an in-depth discussion of animal miRNAs beginning with miRNA biogenesis by Dr. Feng Guo, followed by RISC-target interaction by Dr. Jiahuai Han, regulation of miRNAs by Dr. Neil Smalheiser, roles of miRNAs in specific development (skeletal muscle development) by Dr. John McCarthy, and beyond development (metabolism and neural plasticity) by Dr. Klaus Förstemann. This section also includes roles of miRNAs in diabetes by Dr. Xiaoqing Tang and Dr. Sabire Özcan, fragile X mental retardation by Dr. Peng Jin, and viral infection by Dr. Kuan-Teh Jeang. In addition, a paper on regulation of siRNA-mediated RNAi by Dr. Jiahuai Han is included. The third section includes discussion of plant miRNAs beginning with the description of various plant small RNA pathways by Dr. Zhixin Xie, followed by the evolutionary aspects of plant miRNAs and their targets by Dr. Michael Axtell. Also discussed are interspecies regulation of miRNAs and their targets by Dr. Jeffrey Chen and roles of miRNAs in abiotic stress by Dr. Ramanjulu Sunkar. The last section contains papers on technologies for miRNA study beginning with an evaluation of RNA isolation methods and technical variables for miRNA profiling by Dr. Peter Nelson. Other papers in this section are on the method of monitoring miRNA-mediated target regulation in *Drosophila* S2 cells by Dr. Klaus Förstemann, pol-III promoter-directed tight regulation of multiple miRNA-mediated gene silencing by Dr. Xu Gang Xia, and transcriptome analysis for identification of cold-induced miRNAs in plants by Dr. Weixiong Zhang.

It should be noted that this collection of papers is only a small part of the big miRNA field. Many aspects of miRNA-related research, such as roles of miRNAs in cancers, were not included in this special issue

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doi:10.1016/j.bbagrm.2008.10.003

because many excellent reviews on those aspects are currently available in other journals.

Finally, I thank all the contributors and their colleagues for their efforts in making this special issue publish on time. I especially thank all the outstanding reviewers, including several leading investigators of miRNA research, for their time, effort, and constructive comments to make this a valuable issue in the field. Sincere thanks to the BBA editorial staff, Jessica Abercrombie and Charity Houston, in particular, for their professional support and management of this issue. BBA editors Dr. Craig Peterson and Dr. Steven Triezenberg proposed, approved, and made this special issue on miRNA possible.

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