MicroRNA Interference Technologies

Bearbeitet von
Zhiguo Wang

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Preface

MicroRNAs (miRNAs), endogenous noncoding regulatory mRNAs of around 22-nucleotides long, have rapidly emerged as one of the key governors of the gene expression regulatory program in cells of varying species. Accumulating evidence suggests that miRNAs constitute a novel, universal mechanism for fine regulation of gene expression in all organisms, "fine tuning" the cellular phenotype during delicate processes. Owing to their ever-increasing number in the mammalian cells and their ever-increasing implication in the control of the fundamental biological processes (such as development, cell growth and differentiation, cell death, etc), miRNAs have now become a research subject capturing major interest of scientists worldwide. Moreover, with recent studies revealing the macro roles of miRNAs in the pathogenesis of adult humans, we have now entered a new era of miRNA research. The exciting findings in this field have inspired us with a premise and a promise that miRNAs will ultimately be taken to heart for the therapy of human disease. Yet these mysterious tiny molecules still remain mystifying in their cellular function and pathological role. While miRNAs have been considered potential therapeutic targets for disease treatment, it remains obscure what strategies we can use to achieve this goal. Thorough understanding of these molecules is obviously a prerequisite for realizing their rousing promise, which calls for an urgent need to develop apt technologies for the purpose.

In the past years, we have witnessed the rapid development of many creative, innovative, inventive techniques and methodologies pertinent to miRNA research and applications. These technologies have convincingly demonstrated their efficacy and reliability in producing gain-of-function or loss-of-function of miRNAs, providing new tools for elucidating miRNA functions and opening up a new avenue for the development of new agents targeting miRNAs for therapeutic aims. These stimulating advances prompted me to propose the concept of microRNA interference (miRNAi): *Manipulating the function, stability, biogenesis or expression of miRNAs to interfere with the expression of their target protein-coding mRNAs to alter the cellular functions.* This new thought motivated me to write this book entitled *MicroRNA Interference Technologies (miRNAi Technologies).*

The aim of this book is to provide comprehensive descriptions of the strategies and methodologies for interfering miRNA expression, biogenesis and function and their applications in miRNA research and new drug design using miRNAs as therapeutic targets. It is my expectation that from this book readers will be able to acquire a basic knowledge of miRNAs and the new concepts pertinent to miRNAi, gain insight into the principles of various miRNAi technologies and master the key steps of miRNAi protocols.

miRNAi Technologies contains 13 chapters. It begins with Chapter 1 on the updated knowledge of miRNA biology and their potential as therapeutic targets for human disease. Chapter 2 introduces four new concepts pertinent to miRNAs, which are of pivotal importance for our understanding and application of the miRNAi technologies. These new concepts are (1) the "miRNA Interference (miRNAi)" concept, (2) the "miRNA as a Regulator of a Cellular Function" concept, (3) the "One-Drug, Multiple-Target" concept and (4) the "miRNA Seed Family" concept. Chapter 2 also gives a laconic introduction of miRNAi strategies and the perspectives of miRNAi technologies in a general term. From Chaps. 3–13, each chapter introduces one of the miRNAi technologies with detailed descriptions of state-of-the-art design, step-by-step directive protocols, principles of action, applications to basic research, R&D and clinical therapy and advantages and limitations of the technologies. Chapters 3–6 describe various gain-of-function miRNAi technologies and chapters 7–13 introduce the loss-of-function miRNAi technologies.

Each chapter also contains illustrations, flowcharts and tables for easier and straightforward understanding of the contents. Though step-by-step protocols are provided for each miRNAi technology, it is not my attempt to give very detailed, problem-proof procedures by including information like compositions of solutions, conditions of reactions and materials. Instead, I intend to provide readers with a guideline for designing and setting up the protocols for their own particular uses. This also leaves room for readers to make their own improvements and innovations of the technologies.

This book is written for: (1) Fundamentalists (starting from graduate students to PI) in the field of studies involving miRNAs, in universities and research institutions; (2) Pharmacologists and gene therapists involving translational studies on drug development; (3) Pharmaceutical companies involving R&D in target searching and drug design and (4) Medical practitioners from residents to professors of various types of medical fields.

Canada Zhiguo Wang