Advanced Delivery and Therapeutic Applications of RNAi

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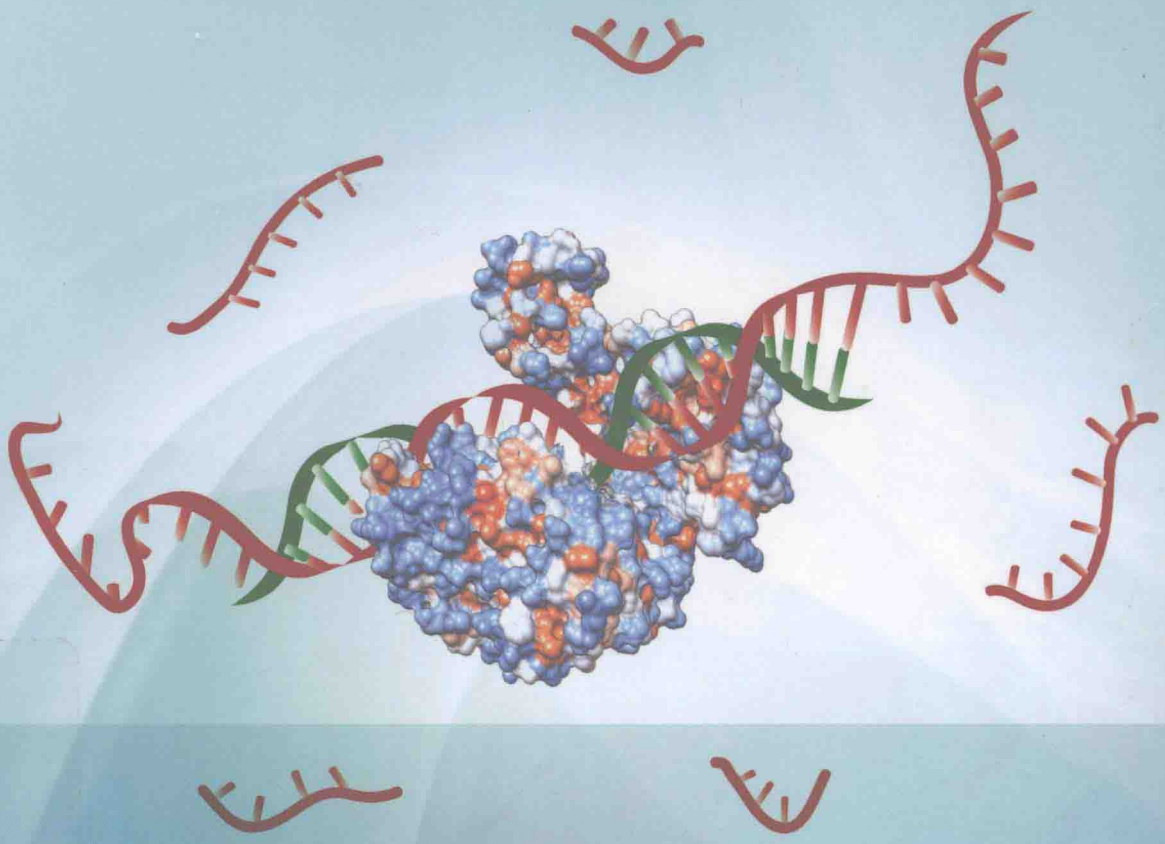

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Advanced Delivery and Therapeutic Applications of RNAi

I dedicate this book to my parents, Mr. Guangxiong Cheng and Mrs. Pingqing Xu, my wife Lizhi Sun, my children Daniel and Jessica for their love and continuous support, and to my mentors who have inspired me to pursue a career in science.

Kun Cheng

I dedicate this book to my wife Subhashini, my children Kalika and Vivek for their love and support; my late mother Sarswati for believing in me; and to my students and mentors who have always helped me in my quest for learning and in achieving higher goals.

Ram I. Mahato

Preface

RNA interference (RNAi) is one of the most dramatic findings since the beginning of the twenty-first century, and remarkable progress has been made in different aspects of the RNAi technology since its discovery in 1998. Generally, RNAi can be achieved by three strategies: chemical synthesized small interfering RNA (siRNA), long double-stranded RNA (dsRNA), and DNA-based (plasmid or viral vector) short hairpin RNA (shRNA). The versatility and specificity of RNAi have quickly evolved the technology from a powerful tool for studying the genetic function of a specific gene to a promising therapeutic paradigm for a variety of diseases. However, the field of RNAi therapy has a frustrating history that is similar to that of other nucleic acid-based therapies. Poor stability and cellular uptake are the two major limitations for the successful application of RNAi therapy. Since 2011, several major investors in RNAi technology have announced that they would close down their RNAi research after spending hundreds of millions of dollars in the past few years. Lack of an efficient delivery system for RNAi to overcome numerous biological obstacles *in vivo* is believed to be the major reason for these tough decisions. At the time of writing, there were 22 ongoing or completed clinical trials using RNAi for numerous diseases. The majority of these clinical trials employed naked siRNA for local treatment of ocular or respiratory diseases. This actually indicates *delivery* as the single most important challenge faced by siRNA therapeutics. All these facts clearly indicate that *efficient delivery* is the crucial step in transforming RNAi molecules from groundbreaking scientific discovery to successful therapeutics.

Advanced Delivery and Therapeutic Applications of RNAi aims to provide up-to-date information about the basics, delivery and therapeutic applications of RNAi. The book is divided into three parts, starting with fundamentals related to mechanisms, biological barriers, analysis, and regulatory perspectives of RNAi. Part II, on RNAi delivery strategies, discusses different strategies for RNAi delivery and targeting. The book ends with the current applications of RNAi for various diseases including cancer, liver disease, and ocular disease. The book presents a wide variety of aspects of the development of RNAi therapeutics from bench to clinic, which have not yet been addressed in a single book. We hope that this book will serve as a useful tool for scientists who are interested in exploring the therapeutic potential of RNAi technology.

We would like to express our sincere appreciation and gratitude to all contributors who have made time to share their knowledge, experience and expertise in different aspects of RNAi. We would also like to thank Paul Deards, Sarah Tilley, Jasmine Kao, and Emma Strickland at Wiley for their help in the planning, preparation and production of this book.

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Ram I. Mahato is a full time Professor of Pharmaceutics and Drug Delivery at the Department of Pharmaceutical Sciences, University of Tennessee Health Science Centre, Memphis. Dr Mahato has served as a Research Assistant Professor at the University of Utah, as Senior Scientist at GeneMedicine, Inc., and as a postdoctoral fellow at the University of Southern California, Washington University and Kyoto University. He received a PhD in pharmaceutics and drug delivery from the University of Strathclyde (Glasgow) in 1992. He has two issued United States patents and is author or co-author of more than 105 papers and book chapters. He has edited nine journal theme issues, and six books, and has written one textbook. He is a theme issue editor for *Pharmaceutical Research* and a member of the editorial board of eight journals. He is an AAPS and CRS Fellow and regular member of the BTSS Study section of the National Institutes of Health. His research includes delivery and targeting of small molecules, oligonucleotides, siRNA and genes.

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