

Preface

The 2006 Nobel Prize in Medicine or Physiology was awarded to Andrew Fire and David Mello for their 1998 discovery of double-stranded RNA-mediated gene silencing by the process of RNA interference (RNAi). The capability to control and study cellular gene expression has opened up completely new research areas, shed exciting new light on existing fields, and provided researches with an unprecedented tool for investigating functional genomics and the potential to harness the RNAi mechanism as a potent therapeutic. This has resulted in an explosion of activity in both academia and industry.

Understanding the molecular mechanisms of RNAi is crucial for its transformation into a therapeutic modality. This dependency is the focus of “RNA Interference from Biology to Therapeutics”, a concept applied to a Controlled Release Society (CRS) Educational Workshop at the 2009 CRS Annual meeting organised by the Editor.

The volume is structured to introduce the reader to the biological principles of RNAi followed by therapeutic delivery and disease treatment; however, integration of these aspects is a common thread running throughout. Education was an important consideration in the book preparation; therefore, the text provides sufficient background of the subject matter to allow utilisation as a learning tool for students.

The opening chapter gives an overview of RNAi pathways and the ground rules for therapeutic exploitation using synthetic small interfering RNA (siRNA) and vector-based approaches highlighted in subsequent chapters. SiRNA design towards RNAi pathway engagement is continued into chapter 2, focused on the development of Dicer-substrate therapeutics. The rapid emergence of the microRNA (miRNA) field, fuelled by its inherent role in regulation of cellular processes in normal and disease states, is highlighted in chapters 3, 13, and 14 dedicated to this subject. Chapter 3, for example, describes miRNA biology in tissue development and repair. In keeping with the “biology-therapeutic” link, the second part of this chapter describes its therapeutic exploitation in tissue regenerative medicine.

The clinical translation of RNAi therapeutics is dependent on enabling technologies to overcome both extracellular and intracellular delivery requirements; this is the focus of chapters 4–10. A number of delivery solutions and RNAi applications

are covered that include nanoparticle-based systems composed of polymer, lipid, or exosomes. Systemic and mucosal routes of administration are addressed as well as stealth and targeting strategies.

Chapters 11–14 focus on RNAi treatment for specific disease types. Chapters 11 and 12 discuss target site selection within the viral RNA genome, viral escape, and solutions such as targeting cellular host factors in the treatment of HIV and influenza. Chapters 13 and 14 describe the application of miRNA in cancer such as deregulated miRNA expression for the identification of novel diagnostic and prognostic biomarkers and novel therapeutic targets as well as a description of miRNA-based anticancer therapies.

The clinical translation of RNAi-based treatments is an ultimate goal. Chapter 15 describes Alnylam's clinical development of a siRNA therapeutic for Respiratory Syncytial Virus (RSV) lung infections. Preclinical steps including siRNA screen, antiviral efficacy, toxicology, and immune studies are presented before an overview of recent Phase 1 and 2 clinical trials.

This book is highly relevant for experts in, or at the interface of, RNAi, delivery science, and medicine from a personal field perspective as well as opening up new interdisciplinary research possibilities. An attractive feature is the “Future Perspectives” section ending each chapter that gives global experts the opportunity to express a personal view on where the field is going, offering potential new research directives to the reader.

“RNA Interference from Biology to Therapeutics” is a comprehensive and truly unique text for those involved or interested in this extremely exciting, important, and high impact field.

Aarhus, Denmark

Kenneth A. Howard



<http://www.springer.com/978-1-4614-4744-3>

RNA Interference from Biology to Therapeutics

Howard, K.A. (Ed.)

2013, XVI, 340 p.,

ISBN: 978-1-4614-4744-3