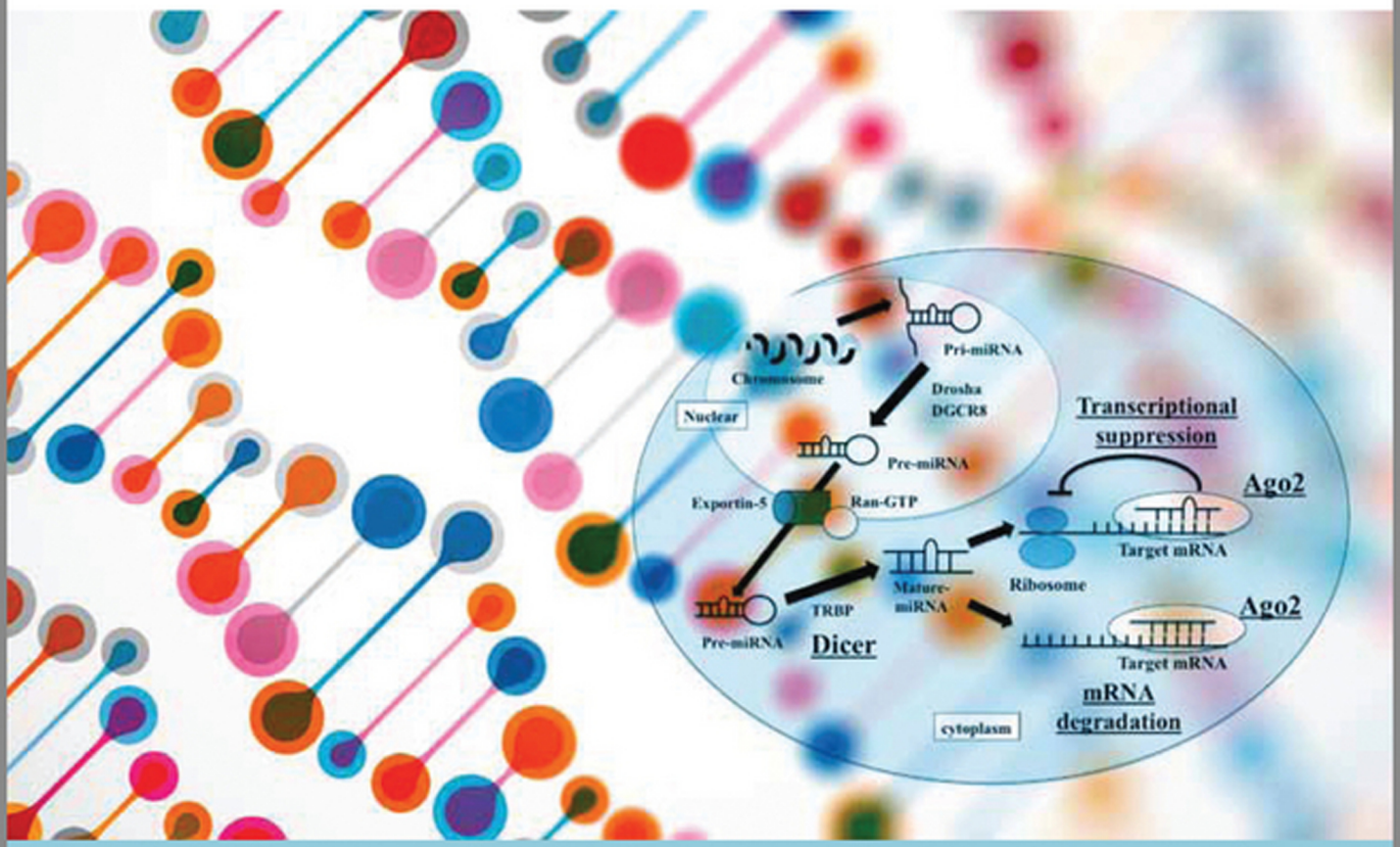
Editor SAURA C. SAHU

microRNAs in Toxicology and Medicine



WILEY

microRNAs in Toxicology and Medicine

microRNAs in Toxicology and Medicine

Editor

SAURA C. SAHU
Division of Toxicology, Center for Food Safety and Applied Nutrition,
Food and Drug Administration, USA

WILEY

This edition first published 2014

Registered office
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, United Kingdom

Library of Congress Cataloging-in-Publication Data

microRNAs in Toxicology and Medicine / editor, Saura C. Sahu.
pages cm
Includes bibliographical references and index.
ISBN 978-1-118-40161-3 (cloth)
1. Small interfering RNA. 2. Small interfering RNA – Therapeutic use. 3. Genetic regulation. I. Sahu, Saura C., editor of compilation.
QP623.5.S63M536 2014
572.8′8 – dc23

2013020036

A catalogue record for this book is available from the British Library.

ISBN: 9781118401613

Set in 10/12pt Times by Laserwords Private Limited, Chennai, India

1 2014

I lovingly dedicate this book to:

My parents, Gopinath and Ichhamoni, for their gifts of life, love and living examples

My wife, Jharana, for her life-long friendship, love and support, as well as for her patience and understanding of the long hours spent at home on planning, writing and editing this book.

My children, Megha, Sudhir and Subir, for their love and care

Saura C. Sahu
Laurel, Maryland, USA

Contents

List of Contributors

Aamir Ahmad Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA

Malin Åkerblom Department of Experimental Medical Science, Wallenberg Neuroscience Center *and* Lund Stem Cell Center, Lund University, Sweden

Nahid Akhtar Department of Anatomy and Neurobiology, Northeast Ohio Medical University (NEOMED), USA

Azfur S. Ali Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA

Shadan Ali Department of Oncology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA

Sumit Arora Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA

Kathryn A. Bailey Department of Environmental Sciences and Engineering, UNC Gillings School of Global Public Health, University of North Carolina at Chapel Hill, USA

Arun Bhardwaj Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA

Barbara Burwinkel Molecular Epidemiology C080, German Cancer Research Center, Germany *and* Molecular Biology of Breast Cancer, University Women's Clinic, Germany

Si Chen Division of Biochemical Toxicology, National Center for Toxicological Research/US Food and Drug Administration, USA

Tao Chen Division of Genetic and Molecular Toxicology, National Center for Toxicological Research, Food and Drug Administration, USA

Sang-Woon Choi Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, USA *and* Friedman School of Nutrition Science and Policy, Tufts University, USA

Pierre Cordelier INSERM U1037, Cancer Research Center of Toulouse, France and Université Paul Sabatier Toulouse III, France

Katarina Cuk Molecular Epidemiology C080, German Cancer Research Center, Germany and Molecular Biology of Breast Cancer, University Women's Clinic, Germany

Yang Dai Department of Bioengineering, University of Illinois at Chicago, USA

Christopher J. Davis WWAMI Medical Education Program and Program in Neuroscience, Sleep and Performance Research Center, Washington State University, USA

Joel Fontanarosa Department of Bioengineering, University of Illinois at Chicago, USA

Jennifer L. Freeman School of Health Sciences, Purdue University, USA

Simonetta Friso University of Verona School of Medicine, Italy

Rebecca C. Fry Department of Environmental Sciences and Engineering, UNC Gillings School of Global Public Health, University of North Carolina at Chapel Hill, USA

Luc Gailhouste Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Japan

Marion Gayral INSERM U1037, Cancer Research Center of Toulouse, France and Université Paul Sabatier Toulouse III, France

Samir N. Ghadiali The Ohio State University, Dorothy M. Davis Heart and Lung Research Institute, USA

Lei Guo Division of Biochemical Toxicology, National Center for Toxicological Research/US Food and Drug Administration, USA

Keitaro Hagiwara Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Japan and Department of Biological Sciences, Tokyo Institute of Technology, Japan

Tariq M. Haqqi Department of Anatomy and Neurobiology, Northeast Ohio Medical University (NEOMED), USA

Valerie W. Hu Department of Biochemistry and Molecular Medicine, The George Washington University School of Medicine and Health Sciences, USA

Yan Huang The Ohio State University, Dorothy M. Davis Heart and Lung Research Institute, USA

Brock Humphries Department of Physiology, Michigan State University, USA

Johan Jakobsson Department of Experimental Medical Science, Wallenberg Neuroscience Center and Lund Stem Cell Center, Lund University, Sweden

Matthias Jung Clinic for Psychiatry, Psychotherapy, and Psychosomatic medicine, Martin Luther University, Germany

Daniel B. Kay Department of Psychiatry and Human Behavior University of Mississippi Medical Center, School of Medicine, USA

Nobuyoshi Kosaka Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Japan

Zhenhua Liu School of Public Health and Health Sciences, University of Massachusetts, USA *and* Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, USA

Yang Luan School of Public Health, Shanghai Jiao Tong University, China

Dharanija Madhavan Molecular Epidemiology C080, German Cancer Research Center, Germany and Molecular Biology of Breast Cancer, University Women's Clinic, Germany

Josephine Malmevik Department of Experimental Medical Science, Wallenberg Neuroscience Center and Lund Stem Cell Center, Lund University, Sweden

William B. Mattes PharmPoint Consulting, USA

Fanxue Meng Division of Genetic and Molecular Toxicology, National Center for Toxicological Research, Food and Drug Administration, USA

S. Patrick Nana-Sinkam The Ohio State University, Dorothy M. Davis Heart and Lung Research Institute, USA

Takahiro Ochiya Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Japan

Philip A. Philip Department of Oncology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA

Barry A. Rosenzweig Division of Drug Safety Research, Center for Drug Evaluation and Research, US Food and Drug Administration, USA

Rodney L. Rouse Division of Drug Safety Research, Center for Drug Evaluation and Research, US Food and Drug Administration, USA

Saura C. Sahu Division of Toxicology, Center for Food Safety and Applied Nutrition, Food and Drug Administration, USA

William F. Salminen PAREXEL, USA

Tewarit Sarachana Department of Biochemistry and Molecular Medicine, The George Washington University School of Medicine and Health Sciences, USA

Fazlul H. Sarkar Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA *and* Department of Oncology, Karmanos Cancer Institute, Wayne State University School of Medicine, USA

Insa S. Schroeder Department of Biophysics, GSI Helmholtz Centre for Heavy Ion Research, Germany

Maria S. Sepúlveda Department of Forestry and Natural Resources, Purdue University, USA

Leming Shi School of Pharmacy, Fudan University, China

Qiang Shi Division of Systems Biology, National Center for Toxicological Research, Food and Drug Administration, USA

Ajay P. Singh Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA *and* Department of Biochemistry and Molecular Biology, College of Medicine, University of South Alabama, USA

Seema Singh Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA

Geir Skogerbø National Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, China

Stephanie A. Tammen Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, USA *and* Friedman School of Nutrition Science and Policy, Tufts University, USA

Karol L. Thompson Division of Drug Safety Research, Center for Drug Evaluation and Research, US Food and Drug Administration, USA

Jérome Torrisani INSERM U1037, Cancer Research Center of Toulouse, France and Université Paul Sabatier Toulouse III, France

Andrey Turchinovich Molecular Epidemiology C080, German Cancer Research Center, Germany *and* Molecular Biology of Breast Cancer, University Women's Clinic, Germany

Zhishan Wang Department of Physiology, Michigan State University, USA

Gregory J. Weber School of Health Sciences, Purdue University, USA

Zuquan Weng Division of Systems Biology, National Center for Toxicological Research, Food and Drug Administration, USA

Yaguang Xi Mitchell Cancer Institute, University of South Alabama, USA

Jiekun Xuan Division of Biochemical Toxicology, National Center for Toxicological Research/US Food and Drug Administration, USA

Dongsheng Yan School of Ophthalmology and Optometry, Wenzhou Medical College, China

Jian Yan Division of Genetic and Molecular Toxicology, National Center for Toxicological Research, Food and Drug Administration, USA

Chengfeng Yang Department of Physiology, Michigan State University, USA *and* Center for Integrative Toxicology, Michigan State University, USA

Xi Yang Division of Systems Biology, National Center for Toxicological Research, Food and Drug Administration, USA

Bin Yi Mitchell Cancer Institute, University of South Alabama, USA

Preface

During the past decade it has become increasingly obvious that microRNAs regulate gene expressions and control many developmental and cellular processes in the eukaryotic organisms. Recent studies strongly suggest that they are likely to play important roles in a wide range of human diseases including cancer. As a result they have become an important component of the molecular mechanisms of the disease processes. Also, published reports strongly suggest that they are expected to play important roles in cellular response to xenobiotic stress affecting expression of microRNA as a mechanism of adaptation and, therefore, they have attracted great interest in toxicology. Thus microRNAs play an important role in toxicogenomics.

The importance of this field of research is evidenced by the increasing number of contributions published each year. It becomes increasingly clear that developments in this field are moving so rapidly that new means are needed to report the status of current ongoing research activities. The contributions presented in this monograph represent a collaborative effort by international experts working in this emerging field of science.

The main purpose of this book is to assemble up-to-date, state-of-the-art information on microRNAs presented by internationally recognized experts in a single edition. Therefore, I sincerely hope that this book will provide an authoritative source of current information on microRNA research and prove useful to the scientists interested in this scientific discipline throughout the world. It is my sincere hope that the information presented in this book will serve as a stimulus to all the investigators interested in this area of research. Also it should be of interest to a variety of other scientific disciplines including toxicology, medicine, and pharmacology, as well as food, drug, and other regulatory sciences.

Saura C. Sahu
Laurel, Maryland, USA

Acknowledgments

Editing this book has been a challenging journey. I express my sincere gratitude to all the individuals who have helped me, directly or indirectly, on this journey.

I am indebted to the internationally recognized experts, who shared my enthusiasm for this field of science and contributed generously to this book. They were selected from academia, industry, and government for their expertise in their own areas of research. Their work speaks for itself and I am grateful to them for their strong commitment, cooperation and excellent contributions in their own areas of expertise.

I thank the staff of the publisher, John Wiley & Sons, Ltd, especially Rebecca Ralf and Sarah Tilley for their excellent help, cooperation, support, and editorial assistance in the timely publication of this book.

Saura C. Sahu
Laurel, Maryland, USA

Part I

microRNAs and Toxicology

1

Introduction

Saura C. Sahu

Division of Toxicology, Center for Food Safety and Applied Nutrition, Food and Drug Administration, USA.

The microRNA, found in eukaryotic cells, belongs to a family of small, single-stranded noncoding regulatory ribonucleic acid (RNA) molecules with an average of 22 nucleotides conserved by evolution (Christodoulou *et al*., 2010). Discovered in 1993 (Lee *et al*., 1993), they regulate gene expressions, and control many developmental and cellular processes in eukaryotic organisms. The physiological function of the majority of microRNAs is unknown. However, recent studies strongly suggest that they likely to play important roles in a wide range of human diseases, including cancer. As a result they have become an important component to study in the molecular mechanisms of disease processes. However, challenges remain in the understanding of their involvement in various disease processes. Therefore, microRNA research has become a hot new discipline in biology and medicine: microRNAs are promising important biomarkers of diseases.

The microRNAs have attracted great interest in toxicology. Published reports provide evidence that toxic exposures and cellular stress can affect microRNAs (Lema and Cunningham, 2010). Therefore, they are expected to play an important role in cellular responses to xenobiotic exposure. They bind to target messenger RNAs (mRNA) and suppress their translation into proteins. Exposure of cells to xenobiotics leads to altered microRNA expressions, as do other genes that play important roles in toxicology. Altered microRNA expression affects protein translation, which alters cellular physiology leading to adverse biological effects. Also cellular stress affects expression of microRNAs as a mechanism of adaptation (Lema and Cunningham, 2010). Thus microRNAs play an important role in toxicogenomics. Their potential as biomarkers of toxicity appears to be promising.

It is becoming increasingly clear from the rate of published literature that developments in microRNA research are moving rapidly. Therefore, new means are needed to report the current status of this new developing area of research. The purpose of this book, *microRNAs in Toxicology and Medicine*, is the timely dissemination of information on current interests in this emerging field of science. As the Editor, it gives me great pride to introduce this unique book which encompasses many aspects of microRNA research never

microRNAs in Toxicology and Medicine, First Edition. Edited by Saura C. Sahu.

published together before. It is only recently that this exciting area of research has attracted the attention of toxicologists. This book deals with information on microRNAs at a level designated to take the reader to the borderline of research in this newly developing scientific discipline. The microRNA research work, actively pursued throughout the world, will lead to major discoveries of fundamental importance and of great clinical significance. This book brings together the ideas and work of investigators of international reputation who have pioneered this exciting area of research in toxicology and medicine. The book provides up-to-date information as well as new challenges in this exciting research area, and reflects the remarkable blossoming of this research in recent years. New ideas and new approaches are brought to bear on exploration of the role played by microRNAs in toxicology and medicine. Therefore, exciting times are ahead for future research. The up-to-date techniques, ideas, applications, and bibliographies are presented in this book in sufficient detail to enable newcomers to this scientific discipline to apply them in their studies and pursue them to any depth. I sincerely hope that the book will provide authoritative information as well as new ideas and challenges on microRNA research for stimulating the creativity of graduate students and investigators who are actively engaged in this rapidly developing field. The extensive collection of current information presented here will make it a valuable reference source for all scientists working in the microRNA area.

References

Christodoulou F, Raible F, Tomer R, Simakov O, Trachana K, Klaus S, *et al*. 2010. Ancient animal microRNAs and the evolution of tissue identity. *Nature* **463**, 1084–1088.

Lee RC, Feinbaum RL, Ambros V. 1993. The *C. elegans* heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. *Cell* **75**(5):843–854.

Lema C and Cunningham MJ. 2010. MicroRNAs and their implications in toxicological research. *Toxicol Lett.* **198**(2):100–105.