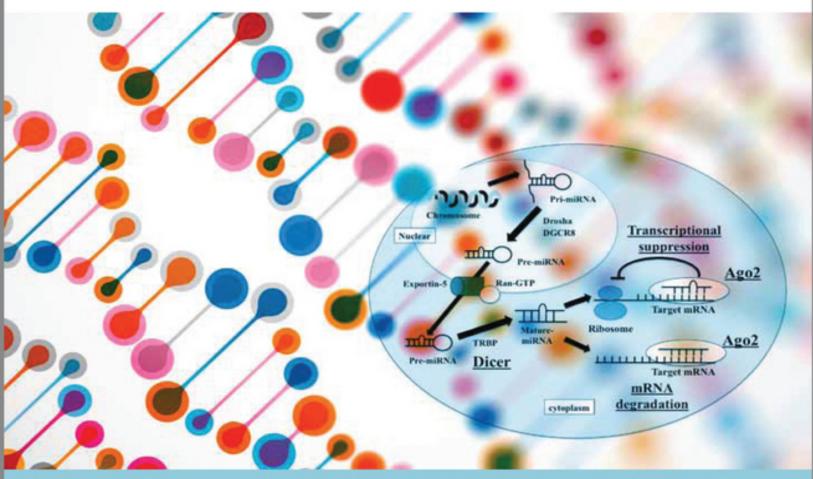
#### Editor SAURA C. SAHU

# microRNAs in Toxicology and Medicine





# Table of Contents

Title Page

<u>Copyright</u>

**Dedication** 

List of Contributors

**Preface** 

<u>Acknowledgments</u>

Part I: microRNAs and Toxicology

**Chapter 1: Introduction** 

<u>References</u>

<u>Chapter 2: Environmental Toxicants and</u> <u>Perturbation of miRNA Signaling</u>

2.1 Introduction
2.2 miRNAs: Description and Biological
Significance
2.3 Environmental Toxicant-Associated miRNA
Perturbations
2.4 Conclusions and Future Directions
Acknowledgments

**References** 

## <u>Chapter 3: microRNAs in Drug-Induced</u> <u>Liver Toxicity</u>

3.1 Introduction
3.2 miRNA Tissue Distribution and Abundance
3.3 miRNA and Drug-Induced Liver Toxicity
3.4 Circulating miRNAs as Potential Biomarkers
for Drug-Induced Liver Toxicity
3.5 Mechanistic Studies and Perspectives
Disclaimer
References

### <u>Chapter 4: Fishing for microRNAs in</u> <u>Toxicology</u>

4.1 microRNAs in Toxicology
4.2 Fish Models in Toxicology
4.3 Fish as Models for Studying miRNA Function
4.4 Application of Fish Models in Toxicity Studies of miRNA Alterations
4.5 Summary
Acknowledgments
References

## Part II: microRNAs and Disease States

Chapter 5: microRNAs and Inflammation

5.1 Introduction

5.2 miRNA Biogenesis and Functions

5.3 miRNAs in Hematopoietic Systems

5.4 miRNA and Inflammatory Diseases

5.5 Regulation of the Immune System

5.6 Regulation of miRNA Expression

5.7 Select miRNA Regulation of Inflammation

5.8 Conclusion

<u>References</u>

### <u>Chapter 6: Regulatory Role of microRNAs</u> <u>in Mutagenesis</u>

6.1 Introduction
6.2 miRNA Roles in Xenobiotic Metabolism
6.3 miRNA Roles in the Cell Cycle
6.4 miRNA Roles in DNA Repair
6.5 Apoptosis
6.6 miRNA Regulation and Mutation Formation
6.7 Conclusions
Disclaimer
References

### Chapter 7: microRNAs and Cancer

7.1 Introduction
7.2 miRNAs are Deregulated in Cancer
7.3 miRNAs Function as Oncogenes and Tumor
Suppressor Genes
7.4 miRNAs in Cancer Metastasis
7.5 miRNAs in Cancer Stem Cells

7.6 Mutations in miRNA Loci
7.7 Mutations in miRNA Target Genes
7.8 Prospective: miRNA as Biomarkers and Therapeutics
Acknowledgments
References

<u>Chapter 8: miRNAs in Cancer Invasion and</u> <u>Metastasis</u>

8.1 Introduction 8.2 miRNAs and Cancer Invasion and Metastasis 8.3 miRNAs as Useful Cancer Prognostic Markers 8.4 Future Perspectives References

<u>Chapter 9: The Role of microRNAs in</u> <u>Tumor Progression and Therapy</u>

9.1 Introduction
9.2 Tumor Progression
9.3 Key Signaling Pathways
9.4 The miRNAs as Regulators of Tumor
Progression
9.5 Regulation of miRNAs by Novel Anticancer
Compounds
9.6 Conclusions and Perspectives
References

<u>Chapter 10: Current Understanding of</u> <u>microRNAs as Therapeutic Targets in</u>

#### <u>Cancer</u>

10.1 Introduction on the Rationale of Using miRNAs as Therapeutics in Cancer 10.2 Current Approaches to Target miRNAs 10.3 Evidence of Successful miRNA Targeting in Experimental Cancer Models 10.4 Open Question: Targeting miRNA Processing in Cancer Cells 10.5 Concluding Remarks References

<u>Chapter 11: microRNAs, New Players in</u> <u>Cancer Chemoprevention</u>

11.1 Introduction 11.2 miRNA and the Natural Products 11.3 miRNA and Pharmaceuticals 11.4 Perspectives Acknowledgments References

<u>Chapter 12: microRNA and</u> <u>Neurodegenerative Diseases</u>

> 12.1 Introduction 12.2 miRNAs and Parkinson's Disease 12.3 miRNAs and Alzheimer's Disease 12.4 miRNAs and Huntington's Disease 12.5 Outlook Acknowledgments References

<u>Chapter 13: Sleep and microRNAs</u> (miRNAs) in Neurodegenerative Diseases

13.1 Sleep and microRNAs (miRNAs) in<br/>Neurodegenerative Diseases13.2 miRNAs and Sleep13.3 Aging13.4 Alzheimer's Disease13.5 Parkinson's Disease13.6 Creutzfeldt-Jakob Disease13.7 Huntington's Disease13.8 Multiple Sclerosis13.9 Fronto-Temporal Dementia13.10 SummaryAcknowledgmentsReferences

### <u>Chapter 14: Role of microRNAs in Autism</u> <u>Spectrum Disorder</u>

14.1 Introduction
14.2 Epidemiology of ASD
14.3 Etiology of ASD: Genetic Associations
14.4 ASD as Multigenic Systemic Disorders
14.5 Evidence for Epigenetic Contributions
14.6 The Role of microRNAs in Neurodevelopment
14.7 microRNAs in Neurodevelopmental and
Psychiatric Disorders: An Overview
14.8 microRNA Expression Profiles in Autism
Spectrum Disorder
14.9 Conclusions

<u>Acknowledgments</u> <u>References</u>

<u>Chapter 15: The Emerging Function of</u> <u>Natural Products as Regulators of miRNAs</u> <u>in Human Diseases</u>

15.1 Introduction 15.2 History of Natural Products as Drugs 15.3 Functions of miRNAs in Human Diseases 15.4 Regulation of miRNAs using Natural Products 15.5 Resveratrol and miRNAs 15.6 EGCG and miRNAs 15.7 Curcumin and miRNAs 15.8 Isoflavone and miRNAs 15.9 Metformin miRNA 15.10 Traditional Herbs and miRNAs 15.11 Polyphenol and miRNAs 15.12 Rice and miRNA 15.13 Human Breast Milk and miRNAs 15.14 Conclusion **Acknowledgments** References

## Part III: microRNAs and Stem Cells

<u>Chapter 16: Pluripotency and Early Cell</u> <u>Fate Decisions are Orchestrated by</u> <u>microRNAs</u> 16.1 Importance of microRNAs in ES and iPS Cells 16.2 Biogenesis and Function of microRNAs 16.3 microRNAs Mark ES Cell Identity 16.4 microRNAs Guide Induced Pluripotency 16.5 microRNAs Manipulate Cell Fate Decisions References

<u>Chapter 17: microRNAs in Cancer Stem</u> <u>Cells: Micromanagers of Malignancy</u>

<u>17.1 Introduction</u>
<u>17.2 Cancer Stem Cells</u>
<u>17.3 microRNAs: Biology and Mechanism</u>
<u>17.4 Role of microRNAs in the Regulation of</u>
<u>Genes and Signaling Pathways Associated with</u>
<u>Cancer Stem Cells</u>
<u>17.5 Translational Implications and Future</u>
<u>Perspectives</u>

<u>References</u>

## Part IV: microRNAs and Genomics

<u>Chapter 18: microRNAs: Tiny Regulators of</u> <u>Great Potential for Gene Regulation</u>

18.1 Introduction

<u>18.2 microRNAs: Biogenesis and Expression</u> <u>Criteria</u>

18.3 Mechanism of miRNA Mediated Regulation of Genes

18.4 Complexities of miRNA Regulation

18.5 microRNA and Epigenetics 18.6 Role of miRNAs in Biological Processes 18.7 microRNAs: Association with Disease Pathogenesis 18.8 microRNAs: Another Way to Unravel Disease Pathogenesis 18.9 microRNAs as Novel Therapeutic Targets 18.10 Concluding Remarks Competing Interests Conflict of Interest Statement Acknowledgments References

<u>Chapter 19: Exploration of microRNA</u> <u>Genomic Variation Associated with</u> <u>Common Human Diseases</u>

19.1 Introduction 19.2 Methods 19.3 Results 19.4 Discussion Acknowledgment References

Part V: microRNAs and Epigenomics

<u>Chapter 20: Crosstalk between microRNAs</u> and Epigenetics: From the Nutritional <u>Perspective</u> 20.1 Introduction 20.2 Epigenetic Regulation of microRNA Expression 20.3 Regulation of Epigenetic Machinery by microRNAs 20.4 microRNA and Epigenetics: Regulation by Nutrition 20.5 Summary References

## Part VI: microRNAs and Biomarkers

<u>Chapter 21: Body Fluid microRNAs as</u> <u>Toxicological Biomarkers</u>

21.1 microRNA History, Biogenesis and Functions 21.2 Differential Expression of miRNAs During Development and Diseases 21.3 Alterations of miRNA Expressions by Toxicant Exposures 21.4 Discovery of Body Fluid miRNAs 21.5 Body Fluid miRNAs as Toxicological Biomarkers 21.6 Challenges and the Future of Body Fluid miRNAs as Biomarkers References

<u>Chapter 22: Cell-free microRNAs as</u> <u>Biomarkers in Human Diseases</u> <u>22.1 Introduction</u> 22.2 Secretion and Transportation of Cell-Free miRNAs in Body Fluids 22.3 Technical Challenges in the Analysis of Cell-Free miRNAs 22.4 Cell-Free miRNAs as Novel Potential Biomarkers for Cancers and Tissue Injuries 22.5 Conclusion and Perspectives Disclaimer References

### <u>Chapter 23: Plasma microRNAs as</u> <u>Biomarkers of Human Diseases</u>

23.1 Introduction

23.2 Cancer

23.3 Cardiovascular Diseases and Disorders

23.4 Neurological Diseases and Disorders

23.5 Diabetes Mellitus

23.6 Infectious Diseases

23.7 Standardization of Circulating miRNA Analysis

23.8 Discovery, Origins and Functions of Circulating miRNAs

**References** 

<u>Chapter 24: Circulating microRNAs as</u> <u>Biomarkers of Drug-Induced Pancreatitis</u>

24.1 Introduction

24.2 Pancreatic Injury and Serum Biomarkers

24.3 Amylase and Lipase: Sensitivity and Specificity as Biomarkers of Pancreatic Injury 24.4 Pancreas Selective microRNAs as Circulating Biomarkers 24.5 Conclusions 24.6 Future Directions Acknowledgments Disclaimer References

## <u>Chapter 25: microRNA Profiling: Strategies</u> and Challenges

25.1 miRNA Biogenesis 25.2 Challenges of miRNA Profiling 25.3 miRNA Profiling Methodologies 25.4 Technical Challenges of Circulating miRNA Profiling 25.5 Quality Assessment and Data Normalization 25.6 Concluding Remarks Disclaimer References

Author Index

Subject Index

## 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

© 2014 John Wiley & Sons, Ltd.

Registered office

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

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at <u>www.wiley.com</u>.

The right of the author to be identified as the author of this work has been asserted in accordance with the Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book.

Limit of Liability/Disclaimer of Warranty: While the publisher and author have used their best efforts in preparing this book, they make no representations or warranties with respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. It is sold on the understanding that the publisher is not engaged in rendering professional services and neither the publisher nor the author shall be liable for damages arising herefrom. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The advice and strategies contained herein may not be suitable for every situation. In view of ongoing research, modifications. changes equipment in aovernmental regulations, and the constant flow of information relating to the use of experimental reagents, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each chemical, piece of equipment, reagent, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

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

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*

## 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

# **Chapter 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 by evolution (Christodoulou et al., 2010). conserved 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