

METHODS IN MOLECULAR BIOLOGY

Series Editor

John M. Walker

School of Life and Medical Sciences

University of Hertfordshire

Hatfield, Hertfordshire, AL10 9AB, UK

For further volumes:

<http://www.springer.com/series/7651>

MicroRNA and Cancer

Methods and Protocols

Second Edition

Edited by

Wei Wu

*Department of Medicine, Helen Diller Family Comprehensive Cancer Center, University of California
in San Francisco, San Francisco, CA, USA*

 **Humana Press**

Editor

Wei Wu

Department of Medicine, Helen Diller Family Comprehensive Cancer Center
University of California in San Francisco
San Francisco, CA, USA

ISSN 1064-3745 ISSN 1940-6029 (electronic)
Methods in Molecular Biology
ISBN 978-1-4939-7433-7 ISBN 978-1-4939-7435-1 (eBook)
DOI 10.1007/978-1-4939-7435-1

Library of Congress Control Number: 2017955683

© Springer Science+Business Media, LLC 2011, 2018

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Humana Press imprint is published by Springer Nature
The registered company is Springer Science+Business Media, LLC
The registered company address is: 233 Spring Street, New York, NY 10013, U.S.A.

Preface

The discovery of microRNAs (miRNAs or miRs) heralded an exciting era in biology and started a new chapter in regulation of human genes. The miRNAs are a class of small endogenous noncoding RNAs (~22 nt) that fine-tune gene expression at the posttranscriptional level, mainly through binding 3'-UTR of mRNAs. They are involved in stem cell self-renewal, cellular development, differentiation, proliferation, and apoptosis.

Small miRNAs have big impacts in cancer development. Among the many miRNAs, a subset was identified as regulators of neoplastic transformation and tumor progression, invasion and metastasis as well as tumor-initiating cells (cancer stem cells). The widespread deregulation of miRNomes has been unveiled in diverse cancers compared to normal tissues. The oncomirs (oncogenic miRNAs), TSmiRs (tumor-suppressive miRNAs), and MetastamiRs (cancer metastasis associated miRNAs) comprise an important part of the cancer genome and, hence, they have pivotal diagnostic and prognostic significance. Moreover, cancer-associated miRNAs are proving worthwhile as effective cancer biomarkers for individualized medicine and potential therapeutic targets.

Six years after publication of the first edition of our book about “microRNA and cancer,” it has become a very popular reference in colleges, universities, and research institutes and I was encouraged to publish a second edition. This second edition provides the latest information at the forefront of miRNAs biology as it is being applied worldwide to cancer research. It is organized in the same style as the first edition with a review section and a protocol section. The review section is focused on current cancer research topics related to microRNA functions, including the roles of microRNAs in DNA damage, cancer-immune system interaction, cancer cell resistance, APOBEC gene expression, and gene expression noise. The protocol section is focused on experimental applications of microRNAs in various types of cancer and the scope of research covers detection of circulating microRNA, discovery of microRNA signatures using miRseq technology, evaluation of microRNA delivery systems, microRNA-based therapeutics, and finally, microRNA sequencing analysis.

MicroRNA research is a fast growing field and microRNAs are pivotal elements in cancer biology. An individual miRNA interferes with a broad range of mRNAs and, conversely, a single mRNA could be targeted by a variety of miRNAs. The complexity of miRNA::mRNA interactions is far-reaching in our understanding to date. This book provides the basic principles of experimental and computational methods for the study of microRNAs in cancer research and, therefore, provides a firm grounding for those who wish to develop further applications.

I am especially indebted to Drs. Shu Zheng, Suzanne D. Conzen, and Trever Bivona for giving me the opportunity to gain substantial experience in cancer research and I thank Dr. Fred G. Biddle for all kinds of support. Heartfelt gratitude goes to my family, who continue to patiently support me as I put forward my efforts related to the publication. Without their confidence and continuous support, many things would not have been possible. Also, I thank Professor John Walker for his encouragement and all staff from Springer for their hard work to produce the book. Finally, I am grateful to all the contributing authors for providing their high quality manuscripts.

San Francisco, CA, USA

Wei Wu M.D., Ph.D.

Contents

<i>Preface</i>	<i>v</i>
<i>Contributors</i>	<i>ix</i>

PART I REVIEW

1 Noncoding RNAs in DNA Damage Response: Opportunities for Cancer Therapeutics	3
<i>Wani Arjumand, Asia Asiaf, and Shiekh Tanveer Ahmad</i>	
2 MicroRNAs in Breast Cancer: Diagnostic and Therapeutic Potential	23
<i>Asia Asiaf, Shiekh Tanveer Ahmad, Wani Arjumand, and Mohammad Afzal Zargar</i>	
3 Involvement of miRNAs and Pseudogenes in Cancer	45
<i>Lütfi Tutar, Aykut Özgür, and Yusuf Tutar</i>	
4 MicroRNAs Reprogram Tumor Immune Response	67
<i>Wei Cao, Wenfang Cheng, and Wei Wu</i>	
5 Apolipoprotein B mRNA Editing Enzyme, Catalytic Polypeptide-Like Gene Expression, RNA Editing, and MicroRNAs Regulation	75
<i>Wei Cao and Wei Wu</i>	
6 MicroRNAs Change the Landscape of Cancer Resistance	83
<i>Jun Zhu, Wei Zhu, and Wei Wu</i>	
7 MicroRNA, Noise, and Gene Expression Regulation	91
<i>Wei Wu</i>	

PART II PROTOCOL SECTION

8 Deep Sequencing Reveals a MicroRNA Expression Signature in Triple-Negative Breast Cancer	99
<i>Yao-Yin Chang, Liang-Chuan Lai, Mong-Hsun Tsai, and Eric Y. Chuang</i>	
9 Detection of Plasma MicroRNA Signature in Osteosarcoma Patients	113
<i>Wendy Allen-Rhoades and Jason T. Yustein</i>	
10 Identification of E6/E7-Dependent MicroRNAs in HPV-Positive Cancer Cells	119
<i>Anja Honegger, Daniela Schilling, Holger Sültmann, Karin Hoppe-Seyler, and Felix Hoppe-Seyler</i>	
11 Combination of Anti-miRNAs Oligonucleotides with Low Amounts of Chemotherapeutic Agents for Pancreatic Cancer Therapy	135
<i>Marta Passadouro and Henrique Faneca</i>	

12	Evaluation of MicroRNA Delivery In Vivo	155
	<i>Rikki A.M. Brown, Kirsty L. Richardson, Felicity C. Kalinowski, Michael R. Epis, Jessica L. Horsham, Tasnuva D. Kabir, Marisa H. De Pinho, Dianne J. Beveridge, Lisa M. Stuart, Larissa C. Wintle, and Peter J. Leadman</i>	
13	Angiogenesis Analysis by In Vitro Coculture Assays in Transwell Chambers in Ovarian Cancer	179
	<i>Ali Flores-Pérez, Dolores Gallardo Rincón, Erika Ruiz-García, Raquel Echavarría, Laurence A. Marchat, Elizabeth Álvarez-Sánchez, and César López-Camarillo</i>	
14	Application of Individual qPCR Performance Parameters for Quality Control of Circulating MicroRNA Data	187
	<i>Anna Brunet-Vega, María Elisa Quílez, María José Ramírez-Lázaro, and Sergio Lario</i>	
15	Construction of Multi-Potent MicroRNA Sponge and Its Functional Evaluation	201
	<i>Subwan Chang</i>	
16	MicroRNA Sequencing Data Analysis Toolkits	211
	<i>Wei Wu</i>	
	<i>Index</i>	217

Contributors

- SHIEKH TANVEER AHMAD • *Clarke H. Smith Brain Tumour Centre, Arnie Charbonneau Cancer Institute, Cumming School of Medicine, 2A25 HRIC, University of Calgary, Calgary, AB, Canada*
- ELIZBETH ALVAREZ-SÁNCHEZ • *Posgrado en Ciencias Genómicas, Universidad Autónoma de la Ciudad de México, Benito Juarze, CDMX, Mexico*
- WENDY ALLEN-RHOADES • *Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA*
- WANI ARJUMAND • *Robson DNA Science Centre, Arnie Charbonneau Cancer Institute, Cumming School of Medicine, 2A32 HRIC, University of Calgary, Calgary, AB, Canada*
- ASIA ASIAF • *Department of Biochemistry, Faculty of Science, University of Kashmir, Hazratbal Srinagar, J&K, India*
- DIANNE J. BEVERIDGE • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- RIKKI A.M. BROWN • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- ANNA BRUNET-VEGA • *Oncology Service, Hospital de Sabadell, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Fundació Parc Taulí, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain*
- WEI CAO • *Translational Medical Center, Zhengzhou Central Hospital, Affiliated to Zhengzhou University, Zhengzhou, People's Republic of China*
- SUHWAN CHANG • *Department of Biomedical Sciences, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea*
- YAO-YIN CHANG • *Department of Electrical Engineering, Graduate Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, Taipei, Taiwan; Bioinformatics and Biostatistics Core, NTU Center of Genomic Medicine, Taipei, Taiwan*
- WENFANG CHENG • *Department of Gastroenterology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China*
- ERIC Y. CHUANG • *Department of Electrical Engineering, Graduate Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, Taipei, Taiwan; Bioinformatics and Biostatistics Core, NTU Center of Genomic Medicine, Taipei, Taiwan*
- MARISA H. DE PINHO • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- RAQUEL ECHAVARRIA • *Posgrado en Ciencias Genómicas, Universidad Autónoma de la Ciudad de México, Benito Juarze, CDMX, Mexico*
- MICHAEL R. EPIS • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- HENRIQUE FANECA • *Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal; Department of Life Sciences, Faculty of Science and Technology, University of Coimbra, Coimbra, Portugal*

- ALI FLORES-PÉREZ • *Posgrado en Ciencias Genómicas, Universidad Autónoma de la Ciudad de México, Benito Juarze, CDMX, Mexico*
- ANJA HONEGGER • *Molecular Therapy of Virus-Associated Cancers (F065), German Cancer Research Center (DKFZ), Heidelberg, Germany*
- FELIX HOPPE-SEYLER • *Molecular Therapy of Virus-Associated Cancers (F065), German Cancer Research Center (DKFZ), Heidelberg, Germany*
- KARIN HOPPE-SEYLER • *Molecular Therapy of Virus-Associated Cancers (F065), German Cancer Research Center (DKFZ), Heidelberg, Germany*
- JESSICA L. HORSHAM • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- TASNUVA D. KABIR • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- FELICITY C. KALINOWSKI • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- CÉSAR LÓPEZ-CAMARILLO • *Posgrado en Ciencias Genómicas, Universidad Autónoma de la Ciudad de México, Benito Juarze, CDMX, Mexico*
- LIANG-CHUAN LAI • *Department of Physiology, College of Medicine, National Taiwan University, Taipei, Taiwan*
- SERGIO LARIO • *Digestive Diseases Service, Hospital de Sabadell, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Fundació Parc Taulí, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain*
- PETER J. LEEDMAN • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia; School of Medicine and Pharmacology, The University of Western Australia, Nedlands, WA, Australia*
- LAURENCE A. MARCHAT • *Programa en Biomedicina Molecular y Red de Biotecnología, Escuela Nacional de Medicina y Homeopatía, Instituto Politécnico Nacional, Ciudad de México, CDMX, Mexico*
- AYKUT ÖZGÜR • *Division of Biochemistry, Department of Basic Sciences, Faculty of Pharmacy, Cumhuriyet University, Sivas, Turkey*
- MARTA PASSADOURO • *Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal; Department of Life Sciences, Faculty of Science and Technology, University of Coimbra, Coimbra, Portugal*
- MARÍA ELISA QUÍLEZ • *Oncology Service, Hospital de Sabadell, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Digestive Diseases Service, Hospital de Sabadell, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Fundació Parc Taulí, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain*
- MARÍA JOSÉ RAMÍREZ-LÁZARO • *Digestive Diseases Service, Hospital de Sabadell, Corporació Sanitària Parc Taulí, Institut Universitari Parc Taulí-UAB, Sabadell, Spain; Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain*

- KIRSTY L. RICHARDSON • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- DOLORES GALLARDO RINCÓN • *Laboratorio de Medicina Translacional, Instituto Nacional de Cancerología, Tlalpan, CDMX, Mexico*
- ERIKA RUIZ-GARCÍA • *Laboratorio de Medicina Translacional, Instituto Nacional de Cancerología, Tlalpan, CDMX, Mexico*
- HOLGER SÜLTMANN • *Cancer Genome Research (B063), German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany*
- DANIELA SCHILLING • *Cancer Genome Research (B063), German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany*
- LISA M. STUART • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- MONG-HSUN TSAI • *Institute of Biotechnology, College of Bio-resources and Agriculture, National Taiwan University, Taipei, Taiwan*
- LÜTFI TUTAR • *Department of Molecular Biology and Genetics, Faculty of Arts and Sciences, Abi Evran University, Kırşehir, Turkey*
- YUSUF TUTAR • *Division of Biochemistry, Department of Basic Sciences, Faculty of Pharmacy, Cumhuriyet University, Sivas, Turkey; Department of Nutrition and Dietetics, Health Sciences Faculty, University of Health Sciences, Üsküdar, Istanbul, Turkey*
- LARISSA C. WINTLE • *Laboratory for Cancer Medicine, Harry Perkins Institute of Medical Research, University of Western Australia Centre for Medical Research, Nedlands, WA, Australia*
- WEI WU • *Department of Medicine, Helen Diller Family Comprehensive Cancer Center, University of California in San Francisco, San Francisco, CA, USA*
- JASON T. YUSTEIN • *Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA*
- MOHAMMAD AFZAL ZARGAR • *Department of Biochemistry, Faculty of Science, University of Kashmir, Hazratbal Srinagar, J&K, India*
- JUN ZHU • *Jiangsu Cancer Hospital, Nanjing, Jiangsu, China*
- WEI ZHU • *Department of Oncology, First Affiliated Hospital of Nanjing Medical University, Nanjing, PR China*