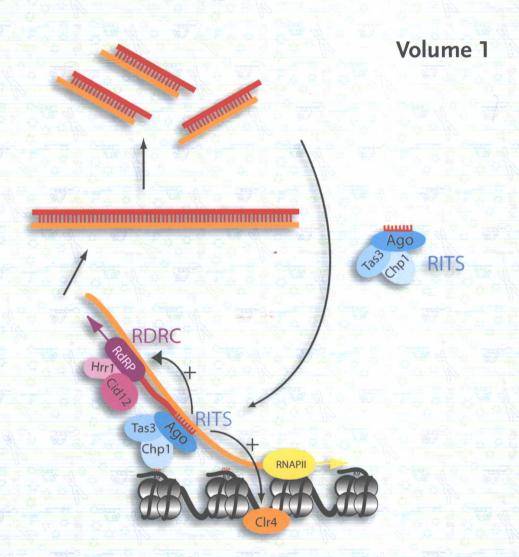


Robert A. Meyers

Epigenetic Regulation and Epigenomics







Epigenetic Regulation and Epigenomics

Advances in Molecular Biology and Medicine

Edited by Robert A. Meyers

Volume 1



WILEY-BLACKWELL

The Editor

Dr. Robert A. Meyers Editor in Chief RAMTECH Limited 122, Escalle Lane Larkspur, CA 94939

Cover

Simplified model of the interplay between histone modifications and small RNAs in the maintenance of pericentric heterochromatin in fission yeast (for more information see Chapter 19 "Histone Modifications", Figure 8)". Designed and drawn by Andrew Bannister and Blerta Xhemalce, The Gurdon Institute, University of Cambridge, CB2 10N, UK.

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. No warranty can be created or extended by sales representatives or written sales materials. The Advice and strategies contained herein may not be suitable for your situation. You should consult with a professional where appropriate. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at http://dnb.d-nb.de.

© 2012 Wiley-VCH Verlag & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

Wiley-Blackwell is an imprint of John Wiley & Sons, formed by the merger of Wiley's global Scientific, Technical, and Medical business with Blackwell Publishing.

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Composition Laserwords Private Limited, Chennai, India

Printing and Binding Strauss GmbH, Mörlenbach

Cover Design Adam Design, Weinheim, Germany

Printed in the Federal Republic of Germany Printed on acid-free paper

Print ISBN: 978-3-527-32682-2

Preface and Commentary

Epigenetics is the term given to heritable traits that occur over rounds of cell division and sometimes transgenerationally, in which the mechanisms are reversible, but do not involve changes to the underlying DNA sequence. This involves regulatory systems such as DNA methylation, histone modification, nucleosome location, and noncoding RNA. The *epigenome*, meanwhile, is a parallel to the word genome, refers to the overall epigenetic state of a cell and can be considered essentially a network of chemical switches within our cells.

Our compendium is written for university undergraduates, graduate students, faculty and investigators at research institutes. There are 33 articles with a combined length of over 1100 pages and as such is the largest in depth, up to date treatment of epigenetics presently available.

Epigenetics Regulation and Epigenomics differs in content and quality from all others available in five ways 1) the overall coverage was approved by our Board, which includes 11 Nobel Prize winners; 2) the selection of each article and author was validated by several reviewers from major university research centers; 3) each article was then reviewed by peers from other universities; 4) a glossary of terms with definitions is provided at the beginning of each article and 5) the articles average 35 print pages — which provides several times the depth of other such compendia.

The content is divided into five sections of articles covering key epigenetics areas. These sections are *Analytical Methods, Basic Molecular Mechanisms, The Epigenome, Medical Applications* and *Model Organisms*.

Analytical Methods articles range from chromatin immunoprecipitation (ChIP), to tag sequencing (impacting epigenomics), DNA methylation analysis, high throughput epigenotyping by mass spectrometry and includes RNA methodologies which provide an understanding of aspects of gene regulation. The Basic Mechanisms section covers the cell nucleus and chromatin organization and dynamics; epigenetics of stem cells; imprinting and histone modifications and methylation; as well as epigenetic aspects of prions, twins, cloning and RNA interference and all types of regulation of gene expression. The Epigenome coverage includes computational epigenetics and the human epigenome. Medical Applications include a comprehensive article on epigenetic medicine and additional detail in several articles on the of epigenetics of cancer, the immune system and aging as well as pharmaco-epigenomics to improve cancer therapies. In fact, drugs that inhibit the DNA methyltransferases, which place methyl groups on the

DNA, are now approved for clinical use in the United States for the treatment of certain cancers. This may be the beginning of a new era of cancer treatment involving epigenetic therapy. Pharmacology and emerging clinical application of RNA is also presented in this section. Model Organisms range from bacteria to protozoans as well as fungi and plants.

Our team of authors and peer reviewers are located at top rated epigenetics departments at institutions including the University of Cambridge, the University of Southern California, the University of California at Los Angeles, Washington University, St. Louis, and the National Institutes of Health. The team is truly global with authors or coauthors from the U.S., Sweden, Belgium, Germany, France, the UK, Austria, Spain, Hungary, Japan, India, China, Singapore, Canada and Israel.

Our team hopes that you, the reader, will benefit from our hard work - finding the content useful in your research as well as educational. We wish to thank our Managing Editor, Sarah Mellor, as well as our Executive Editor, Gregor Cicchetti for both their advice and hard work in the course of this project.

Larkspur, California, March 2012

Robert A. Meyers **RAMTECH Limited**

List of Contributors

Julia Arand

University of Saarland Institute for Genetics/Epigenetics Uni Campus Bld. A2.4 66123 Saarbrücken Germany

Andrew J. Bannister

University of Cambridge Wellcome Trust/Cancer Research UK Gurdon Institute Tennis Court Road Cambridge, CB2 1QN UK

Sailen Barik

Cleveland State University
Center for Gene Regulation in Health and
Disease and Department of Biological,
Geological and Environmental Sciences
College of Sciences and Health
Professions
2121 Euclid Avenue
Cleveland, OH 44115
USA

Therese M. Becker

University of Sydney Westmead Institute for Cancer Research at Westmead Millennium Institute Westmead Hospital Westmead Sydney, New South Wales Australia

Sven Beichmanis

University of Heidelberg Kirchhoff-Institute for Physics and BioQuant Center 69120 Heidelberg Germany

Frédéric Berger

Temasek Life Sciences Laboratory (TLL) 1 Research Link Singapore 117604 Singapore

Yehudit Bergman

The Hebrew University Medical School Institute for Medical Research Israel-Canada Department of Developmental Biology and Cancer Research Jerusalem Israel

Autumn Bernal

Duke University Radiation Oncology 139 Environmental Safety DUMC Durham, NC 27710 USA

Vira Bitko

NanoBio Corporation 2311 Green Rd Ste A Ann Arbor, MI 48105 USA

Erin L. Bredeweg

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Romulo Martin Brena

University of Southern California USC Epigenome Center Harlyne Norris Medical Research Tower G511, 1450 Biggy Street Los Angeles, CA 90033 **USA**

Michael J. Buck

State University of New York at Buffalo Department of Biochemistry

and

The Center of Excellence in Bioinformatics and Life Sciences 701 Ellicott Street Buffalo, NY 14203 **USA**

Josep Casadesús

Universidad de Sevilla Departamento de Genética Facultad de Biología Apartado 1095 41080 Seville Spain

Douglas L. Chalker

Washington University in St Louis **Biology Department** 1 Brookings Drive St Louis, MO 63130 USA

Lingyi Chen

Nankai University The Ministry of Education Key Laboratory of Bioactive Materials Laboratory of Stem Cells and Developmental Biology College of Life Sciences 94 Weijin Road Tianjin 300071 China

Pao-Yang Chen

Department of Molecular Cell and Developmental Biology University of California 610 Charles Young Drive East Los Angeles, CA 90095 USA

Bart Claes

VIB Vesalius Research Center Herestraat 49 Box 912 3000 Leuven Belgium

and

KU Leuven Campus Gasthuisberg Vesalius Research Center Herestraat 49 Box 912 3000 Leuven Belgium

Nicole Cloonan

The University of Queensland Queensland Centre for Medical Genomics Institute for Molecular Bioscience 306 Carmody Road St Lucia, Queensland 4072 Australia

Lanelle R. Connolly

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Ignacio Cota

Universidad de Sevilla Departamento de Genética Facultad de Biología Apartado 1095 41080 Seville Spain

Marion Cremer

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Christoph Cremer

University of Heidelberg Kirchhoff-Institute for Physics and BioQuant Center 69120 Heidelberg Germany

Thomas Cremer

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Mark A. Dawson

University of Cambridge Wellcome Trust/Cancer Research UK Gurdon Institute Tennis Court Road Cambridge, CB2 1QN UK

and

University of Cambridge Cambridge Institute for Medical Research Department of Haematology Cambridge, CB2 0XY

Melvin L. DePamphilis

National Institute of Child Health and Human Development National Institutes of Health Building 6A Room 3A15 9000 Rockville Pike Bethesda, MD 20892-2753 USA

Andras Dinnyes

Szent Istvan University Molecular Animal Biotechnology Laboratory Hungary

and

BioTalentum Ltd 2100 Gödöllö Hungary

Jean-Sébastien Doucet

University of Toronto Centre for Addiction and Mental Health Department of Pharmacology Toronto, Ontario Canada

Karl Ekwall

Karolinska Institutet Department of Biosciences and Nutrition Center for Biosciences Novum Huddinge 141 57 Stockholm Sweden

Robert E. Farrell Jr.

Penn State University Department of Biology 1031 Edgecomb Avenue NY, PA 17403 USA

Daniel M. Fass

Broad Institute of MIT and Harvard Stanley Center for Psychiatric Research 7 Cambridge Center Cambridge, MA 02142 USA

Robert Feil

Centre National de la Recherche Scientific and University of Montpellier CNRS, UMR 5535 Institute of Molecular Genetics (IGMM) 1919 route de Mende 34293 Montpellier France

Agustin F. Fernandez

Universidad de Oviedo Cancer Epigenetics Laboratory Instituto Universitario de Oncología del Principado de Asturias (IUOPA) Hospital Universitario Central de Asturias (HUCA) Bloque Polivalente A 33006 Oviedo Spain

Mario F. Fraga

National Center for Biotechnology (CNB) and Spanish National Research Council (CSIC) Department of Immunology and Oncology Cantoblanco 28049 Madrid Spain

Michael Freitag

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Neha Garg

Devi Ahilya University School of Biotechnology Khandwa Road Indore 452001 India

and

Barkatullah University Biotechnology Department Bhopal 462026 India

Sarika Garg

Devi Ahilya University School of Biotechnology Khandwa Road Indore 452001 India

and

Max Planck Unit for Structural Molecular Biology C/O DESY Gebäude 25b Notkestrasse 85 22607 Hamburg Germany

and

Present address: University of Saskatchewan Department of Psychiatry Rm B45 HSB 107 Wiggins Road Saskatoon, SK S7N 5E5 Canada

Sean M. Grimmond

The University of Queensland Queensland Centre for Medical Genomics Institute for Molecular Bioscience 306 Carmody Road St Lucia Queensland 4072 Australia

Ivo G. Gut

Centro Nacional de Analisis Genomico C/Baldiri Reixac 4 08028 Barcelona Spain

Thomas Haaf

Julius-Maximilians-University Würzburg Institute of Human Genetics Biozentrum Am Hubland 97074 Würzburg Germany

Martin Heß

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Ryutaro Hirasawa

Centre National de la Recherche Scientific and University of Montpellier CNRS, UMR 5535 Institute of Molecular Genetics (IGMM) 1919 route de Mende 34293 Montpellier France

Edward B. Holson

Broad Institute of MIT and Harvard Stanley Center for Psychiatric Research 7 Cambridge Center Cambridge, MA 02142 USA

Barbara Hübner

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Dean A. Jackson

University of Manchester Faculty of Life Sciences MIB 131 Princess Street Manchester M1 7DN UK

Randy Jirtle

Duke University Radiation Oncology 139 Environmental Safety DUMC Durham, NC 27710 USA

Kotaro J. Kaneko

National Institute of Child Health and Human Development National Institutes of Health Building 6A Room 3A15 9000 Rockville Pike Bethesda, MD 20892-2753 USA

Melissa M. Kemp

Broad Institute of MIT and Harvard Chemical Biology 7, Cambridge Center Cambridge, MA 02142 USA

Matthew J. Kohn

University at Albany Department of Biomedical Sciences School of Public Health and NYSTEM New York State Department of Health Empire State Plaza Biggs Laboratory C345 Albany, NY 12201 USA

Satya K. Kota

Centre National de la Recherche Scientific and University of Montpellier CNRS, UMR 5535 Institute of Molecular Genetics (IGMM) 1919 route de Mende 34293 Montpellier France

Keerthana Krishnan

The University of Queensland Queensland Centre for Medical Genomics Institute for Molecular Bioscience 306 Carmody Road St Lucia Queensland 4072 Australia

Anil Kumar

Devi Ahilya University School of Biotechnology Khandwa Road Indore 452001 India

Diether Lambrechts

VIB Vesalius Research Center Herestraat 49, Box 912 3000 Leuven Belgium

and

KU Leuven Campus Gasthuisberg Vesalius Research Center Herestraat 49, Box 912 3000 Leuven Belgium

Konstantin Lepikhov

University of Saarland Institute for Genetics/Epigenetics Uni Campus Bld. A2.4 66123 Saarbrücken Germany

Rena Levin-Klein

The Hebrew University Medical School Institute for Medical Research Israel-Canada Department of Developmental Biology and Cancer Research Ierusalem Israel

Shen Jean Lim

National University of Singapore Department of Biochemistry Yong Loo Lin School of Medicine 8 Medical Drive Singapore 117597 Singapore

Lin Liu

Nankai University The Ministry of Education Key Laboratory of Bioactive Materials Laboratory of Stem Cells

and

Developmental Biology College of Life Sciences 94 Weijin Road Tianjin 300071 China

Alexandra Lusser

Innsbruck Medical University Division of Molecular Biology Biocenter Fritz-Pregl Strasse 3 6020 Innsbruck Austria

Javier López-Garrido

Universidad de Sevilla Departamento de Genética Facultad de Biología Apartado 1095 41080 Seville Spain

Yolanda Markaki

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Jason A. Motl

Washington University in St Louis Biology Department 1 Brookings Drive St Louis, MO 63130 USA

Wesley R. Naeimi

University of Kent Kent Fungal Group School of Biosciences Stacey Building Canterbury Kent CT2 7NJ UK

Björn Oback

AgResearch Ruakura Research Centre East Street Private Bag 3123 Hamilton New Zealand

Matteo Pellegrini

Department of Molecular Cell and Developmental Biology University of California 610 Charles Young Drive East Los Angeles, CA 90095 USA

Pallavi A. Phatale

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Paolo Piatti

Innsbruck Medical University Division of Molecular Biology Biocenter Fritz-Pregl Strasse 3 6020 Innsbruck Austria

Kyle R. Pomraning

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Jason M. Rizzo

State University of New York at Buffalo Department of Biochemistry

and

The Center of Excellence in Bioinformatics and Life Sciences 701 Ellicott Street Buffalo, NY 14203 USA

Lothar Schermelleh

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Frederick A. Schroeder

Massachusetts General Hospital Harvard Medical School 185, Cambridge Street 6th Floor Boston, MA 02114 USA

Annie W. Shieh

Washington University in St Louis Biology Department 1 Brookings Drive St Louis, MO 63130 USA

Bernard Siebens

VIB Vesalius Research Center Herestraat 49 Box 912 3000 Leuven Belgium

and

KU Leuven Campus Gasthuisberg Vesalius Research Center Herestraat 49 Box 912 3000 Leuven Belgium

Mikiko C. Siomi

Keio University School of Medicine Department of Molecular Biology 35 Shinanomachi Shinjuku-ku Tokyo 160-8582 Japan

David Skaar

Duke University Radiation Oncology 139 Environmental Safety DUMC Durham, NC 27710 USA

Kristina M. Smith

Oregon State University Department of Biochemistry and **Biophysics**

and

Center for Genome Research and Biocomputing (CGRB) Corvallis, OR 97331-7305 USA

Jason A. Steen

The University of Queensland Queensland Centre for Medical Genomics Institute for Molecular Bioscience 306 Carmody Road St Lucia Queensland 4072 Australia

Hilmar Strickfaden

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Annelie Strålfors

Karolinska Institutet Department of Biosciences and Nutrition Center for Biosciences Novum Huddinge 141 57 Stockholm Sweden

Xiuchun Cindy Tian

University of Connecticut Department of Animal Science Center for Regenerative Biology Storrs, CT 06269 USA

Joo Chuan Tong

National University of Singapore Department of Biochemistry Yong Loo Lin School of Medicine 8 Medical Drive Singapore 117597 Singapore

and

Institute for Infocomm Research Data Mining Department 1 Fusionopolis Way No. 21-01 Connexis South Tower Singapore 138632 Singapore

Jörg Tost

Centre National de Génotypage CEA-Institut de Genomique Laboratory for Epigenetics Bâtiment G2 2 Rue Gaston Crémieux 91000 Evry France

and

Fondation Jean Dausset - CEPH Laboratory for Functional Genomics 27 rue Juliette Dodu 75010 Paris France

Mick F. Tuite

University of Kent Kent Fungal Group School of Biosciences Stacey Building Canterbury Kent CT2 7NJ UK

Rocio G. Urdinguio

Universidad de Oviedo Cancer Epigenetics Laboratory Instituto Universitario de Oncología del Principado de Asturias (IUOPA) Hospital Universitario Central de Asturias (HUCA) Bloque Polivalente A 33006 Oviedo Spain

Florence F. Wagner

Broad Institute of MIT and Harvard Stanley Center for Psychiatric Research 7 Cambridge Center Cambridge, MA 02142 USA

Joern Walter

University of Saarland Institute for Genetics/Epigenetics Uni Campus Bld. A2.4 66123 Saarbrücken Germany

Qiu Wang

Duke University Department of Chemistry French Family Science Center Durham, NC 27708-0354 USA

Albert H. C. Wong

University of Toronto Centre for Addiction and Mental Health Departments of Psychiatry and Pharmacology Faculty of Medicine 250 College Street Toronto Ontario, M5T 1R8 Canada

David L. A. Wood

The University of Queensland **Queensland Centre for Medical** Genomics Institute for Molecular Bioscience 306 Carmody Road St Lucia Queensland 4072 Australia

Mark Wossidlo

University of Saarland Institute for Genetics/Epigenetics Uni Campus Bld. A2.4 66123 Saarbrücken Germany

Blerta Xhemalce

University of Cambridge Wellcome Trust/Cancer Research UK Gurdon Institute Tennis Court Road Cambridge, CB2 1QN UK

Anette Zeilner

Innsbruck Medical University Division of Molecular Biology Biocenter Fritz-Pregl Strasse 3 6020 Innsbruck Austria

Andreas Zunhammer

Ludwig Maximilians University Biocenter Department of Biology II 82152 Martinsried Germany

Contents

Pre	Preface and Commentary			
List	List of Contributors			
Vol	ume 1			
Par	t I Analytical Methods	1		
1	RNA Methodologies Robert E. Farrell Jr.	3		
2	All Things ChIP: ChIP-Chip, ChIP-Seq, ChIP-PCR Jason M. Rizzo and Michael J. Buck	41		
3	Methods for DNA Methylation Analysis Agustin F. Fernandez, Rocio G. Urdinguio, and Mario F. Fraga	77		
4	DNA Methylation Analysis by MALDI Mass Spectrometry Jörg Tost and Ivo G. Gut	105		
5	Tag Sequencing Keerthana Krishnan, David L. A. Wood, Jason A. Steen, Sean M. Grimmond and Nicole Cloonan	145		
Par	t II Basic Molecular Mechanisms	169		
6	Heterochromatin and Euchromatin – Organization, Boundaries and Gene Regulation Annelie Strålfors and Karl Ekwall	171		
7	Regulation of Gene Expression Anil Kumar, Sarika Garg and Neha Garg	191		
8	Molecular Genetics of Genomic Imprinting Ryutaro Hirasawa, Satya K. Kota and Robert Feil	251		

9	Nuclear Transfer for Cloning Animals Andras Dinnyes, Xiuchun Cindy Tian and Björn Oback	279
10	Regulation of Gene Expression at the Beginning of Mammalian Development Matthew J. Kohn, Kotaro J. Kaneko and Melvin L. DePamphilis	325
11	RNA Interference in Animals Mikiko C. Siomi	365
12	The Cell Nucleus: Biogenesis, Structure and Function Dean A. Jackson	391
13	Chromosome Territory Organization within the Nucleus Thomas Cremer, Yolanda Markaki, Barbara Hübner, Andreas Zunhammer, Hilmar Strickfaden, Sven Beichmanis, Martin Heß, Lothar Schermelleh, Marion Cremer and Christoph Cremer	451
14	Epigenetic Reprogramming in Mammalian Development Konstantin Lepikhov, Julia Arand, Mark Wossidlo and Joern Walter	485
15	Histone Acetylation and Deacetylation Daniel M. Fass, Melissa M. Kemp, Frederick A. Schroeder, Florence F. Wagner, Qiu Wang and Edward B. Holson	515
16	Epigenetic Regulation in Pluripotent Stem Cells Lin Liu and Lingyi Chen	563
17	Imprinting and the Epigenetic Asymmetry between Parental Genomes Thomas Haaf	601
18	Chromatin Dynamics and Higher-Order Chromatin Organization Anette Zeilner, Paolo Piatti and Alexandra Lusser	629
19	Histone Modifications Blerta Xhemalce, Mark A. Dawson and Andrew J. Bannister	657
20	Monozygotic Twins and Epigenetics Jean-Sébastien Doucet and Albert H. C. Wong	703
21	Prions as Epigenetic Regulators of Phenotype in Fungi Wesley R. Naeimi and Mick F. Tuite	741
Vol	ume 2	
Par	t III The Epigenome	771
22	Computational Epigenetics Joo Chuan Tong and Shen Jean Lim	773