

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

Molecular Oncology

Causes of Cancer and Targets for Treatment

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

Molecular Oncology

Causes of Cancer and Targets for Treatment

Edited by
Edward P. Gelmann
Chief, Division of Hematology/Oncology and Deputy Director for Clinical Research, Herbert Irving Comprehensive Cancer Center and Columbia University Medical Center, New York, NY, USA
Charles L. Sawyers
Chair, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, and Investigator, Howard Hughes Medical Institute, Chevy Chase, MD, USA
Frank J. Rauscher III
Professor, Gene Expression and Regulation Program; Professor, Tumor Microenvironment and Metastasis Program; Deputy Director for Basic Research, Wistar Institute Cancer Center, Philadelphia, PA, USA



Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

CAMBRIDGE
UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

Published in the United States of America by Cambridge University Press, New York

Cambridge University Press is part of the University of Cambridge.

It furthers the University’s mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org
Information on this title: www.cambridge.org/9780521876629

© Cambridge University Press 2014

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2014

Printed in the United Kingdom by MPG Printgroup Ltd, Cambridge

A catalog record for this publication is available from the British Library

Library of Congress Cataloging in Publication data
Molecular oncology : causes of cancer and targets for treatment /
edited by Edward P. Gelmann, Chief, Division of
Hematology/Oncology and Deputy Director for Clinical Research,
Herbert Irving Comprehensive Cancer Center and Columbia
University Medical Center, New York, NY, USA, Charles L. Sawyers,
Chair, Human Oncology and Pathogenesis Program, Memorial
Sloan-Kettering Cancer Center, New York, NY, USA, Frank J.
Rauscher III, Professor, Gene Expression and Regulation Program,
Professor, Tumor Microenvironment and Metastasis Program, Deputy
Director for Basic Research, Wistar Institute Cancer Center,
Philadelphia, PA, USA.

pages cm
Includes bibliographical references and index.
ISBN 978-0-521-87662-9 (hardback)

1. Cancer – Molecular aspects. 2. Tumor markers.
3. Carcinogenesis. I. Gelmann, Edward P., 1953– II. Sawyers,
Charles L. III. Rauscher, F. J. (Frank Joseph), 1957–
RC268.4.M675 2014
616.99’4 – dc23 2013012165

ISBN 978-0-521-87662-9 Hardback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

.....
Every effort has been made in preparing this book to provide accurate and up-to-date information which is in accord with accepted standards and practice at the time of publication. Although case histories are drawn from actual cases, every effort has been made to disguise the identities of the individuals involved. Nevertheless, the authors, editors, and publishers can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing through research and regulation. The authors, editors, and publishers therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this book. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

This book is dedicated to the scientists who made the discoveries,
to the members of industry who developed the pharmaceuticals,
to the clinicians whose trials turned medicines into therapies,
and to the patients whose participation in research is
essential and whose diseases we work to relieve.

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

Contents

<i>List of contributors</i>	xi
<i>Preface</i>	xxi
<hr/>	
Part 1.1 Analytical techniques: analysis of DNA	
1. Cancer genome sequencing	1
Abizar Lakdawalla, Jeffrey Fisher, Mostafa Ronaghi, and Jian-Bing Fan	
2. Genome-wide association studies of cancer predisposition	10
Zsofia K. Stadler, Sohela Shah, and Kenneth Offit	
3. Comparative genomic hybridization	21
Donna G. Albertson and Daniel Pinkel	
4. Chromosome analysis: molecular cytogenetic approaches	28
Thomas Ried	
5. DNA methylation	37
Marsha Reyngold and Timothy A. Chan	
Part 1.2 Analytical techniques: analysis of RNA	
6. The application of high-throughput analyses to cancer diagnosis and prognosis	46
Edward P. Gelmann	
7. Cancer proteomics	52
Samir Hanash and Ayumu Taguchi	
8. Tyrosine kinome profiling: oncogenic mutations and therapeutic targeting in cancer	58
Paramita Ghosh, Yun Qiu, Ling-Yu Wang, and Hsing-Jien Kung	
9. In situ techniques for protein analysis in tumor tissue	76
Valsamo K. Anagnostou and David L. Rimm	
Part 2.1 Molecular pathways underlying carcinogenesis: signal transduction	
10. HER	85
Wolfgang J. Köstler and Yosef Yarden	
11. The insulin–insulin-like growth-factor receptor family as a therapeutic target in oncology	110
Michael Pollak	
12. TGF-β signaling in stem cells and tumorigenesis	119
Ying Li, Ruth He, and Lopa Mishra	
13. Platelet-derived growth factor	135
Arne Östman and Carl-Henrik Heldin	
14. FMS-related tyrosine kinase 3	144
Soheil Meshinchi and Derek L. Stirewalt	
15. ALK: Anaplastic lymphoma kinase	162
Karen Pulford	
16. The FGF signaling axis in prostate tumorigenesis	190
Fen Wang, Yongde Luo, and Wallace L. McKeehan	
17. Hepatocyte growth factor/Met signaling in cancer	204
Fabiola Cecchi, Young H. Lee, and Donald P. Bottaro	
18. PI3K	218
Kevin D. Courtney and Lewis C. Cantley	
19. Intra-cellular tyrosine kinase	231
Rosalyn B. Irby and Timothy J. Yeatman	
20. WNT signaling in neoplasia	243
Masaru Katoh	
21. Ras	258
Adrienne D. Cox and Molly J. DeCristo	
22. BRAF mutations in human cancer: biologic and therapeutic implications	272
Moriah H. Nissan and David B. Solit	
23. Aurora kinases in cancer: an opportunity for targeted therapy	278
Vikas Sehdev, Altaf A. Dar, and Wael El-Rifai	
24. 14-3-3 proteins in cancer	293
Alexandra K. Gardino and Michael B. Yaffe	

Contents

- 25. **STAT signaling as a molecular target for cancer therapy** 305
Hua Yu and Richard Jove
- 26. **The MYC oncogene family in human cancer** 313
Michael D. Cole
- 27. **Jun proteins and AP-1 in tumorigenesis** 319
Shira Anzi and Eitan Shaulian
- 28. **Forkhead box proteins: the tuning forks in cancer development and treatment** 328
Eric W.-F. Lam, Kyle W. Muir, and Chuay-Yeng Koo
- 29. **NF-κB and cancer** 336
Willscott E. Naugler and Michael Karin

Part 2.2 Molecular pathways underlying carcinogenesis: apoptosis

- 30. **Apoptosis: the extrinsic pathway** 353
Xinchen Teng and J. Marie Hardwick
- 31. **Apoptosis: the intrinsic pathway** 367
Jody White

Part 2.3 Molecular pathways underlying carcinogenesis: nuclear receptors

- 32. **Androgens and the androgen receptor (AR)** 378
Nicole L. Moore, Margaret M. Centenera, Lisa M. Butler, Theresa E. Hickey, and Wayne D. Tilley
- 33. **Emerging roles of peroxisome proliferator-activated receptor gamma in cancer** 392
Chenguang Wang, Xuemin Zhang, Lifeng Tian, and Richard G. Pestell

Part 2.4 Molecular pathways underlying carcinogenesis: DNA repair

- 34. **The ATM-mediated DNA-damage response** 403
Yosef Shiloh
- 35. **Werner syndrome: association of premature aging and cancer predisposition** 423
Byungchan Ahn, Tinna Stevnsner, and Vilhelm A. Bohr

- 36. **Hereditary disorders of DNA repair and DNA damage tolerance that predispose to neoplastic transformation** 434
Errol C. Friedberg and Roger A. Schultz
- 37. **Telomerase: target for cancer treatment** 442
Jerry W. Shay and Woodring E. Wright
- 38. **Cell cycle: mechanisms of control and dysregulation in cancer** 452
Erik S. Knudsen, Ryan J. Bourgo, Elizabeth L. Gosnell, Jeffrey L. Dean, and A. Kathleen McClendon
- 39. **DNA-damage-induced apoptosis** 465
Shun J. Lee, Benjamin F. O'Connor, Scott A. Stuart, and Jean Y. J. Wang

Part 2.6 Molecular pathways underlying carcinogenesis: other pathways

- 40. **The ubiquitin/proteasome pathway in neoplasia** 473
Robert C. A. M. van Waardenburg and Mary-Ann Bjornsti
- 41. **Small silencing non-coding RNAs: cancer connections and significance** 481
Milena S. Nicoloso and George A. Calin

Part 3.1 Molecular pathology: carcinomas

- 42. **Head and neck cancer** 497
Kelly Quesnelle, Jennifer Grandis, Karl Munger, and Marshall R. Posner
- 43. **Lung cancer** 506
Jill E. Larsen and John D. Minna
- 44. **Esophageal cancer** 526
DuyKhanh P. Ceppa and Thomas A. D'Amico
- 45. **Gastric cancer** 532
Yoshiaki Ito and Khay Guan Yeoh
- 46. **Small-bowel tumors: molecular mechanisms and targeted therapy** 542
Allan D. Spigelman and Janindra Warusavitarne
- 47. **Colon and rectal cancer** 547
Erin M. Perchiniak and Joanna Groden

48.	Pancreatic cancer	557
	Siong-Seng Liau and David A. Tuveson	
49.	Hepatocellular carcinoma	569
	Augusto Villanueva, Yujin Hoshida, Derek Y. Chiang, and Josep M. Llovet	
50.	Renal-cell carcinomas	579
	Kyle A. Furge and Bin T. Teh	
51.	Bladder cancer	584
	Robert S. Svatek and Colin P. Dinney	
52.	Prostate cancer	591
	Kaustubh Datta and Donald J. Tindall	
53.	Targeted therapies in breast cancer	598
	Nancy E. Hynes and Gwen MacDonald	
54.	Molecular targets for epithelial ovarian cancer	606
	Grace K. Suh, Bryan T. Hennessy, Roeland Verhaak, Ji-Yeon Yang, Gordon B. Mills, and Robert C. Bast, Jr.	
55.	Testicular cancer: germ-cell tumors (GCTs)	619
	J. Wolter Oosterhuis and Leendert H. J. Looijenga	
56.	Cervical cancer	630
	John Doorbar	

Part 3.2 Molecular pathology: cancers of the nervous system

57.	Brain tumors	641
	Chang-Hyuk Kwon, Dennis K. Burns, and Luis F. Parada	
58.	Mechanisms of pituitary tumorigenesis	652
	Shereen Ezzat and Sylvia L. Asa	
59.	Molecular oncology of neuroblastoma	669
	Vandana Batra, Rebecca J. Deyell, and John M. Maris	
60.	Neurofibromatosis type I	679
	Rachel S. Darken and David H. Gutmann	

Part 3.3 Molecular pathology: cancers of the skin

61.	Squamous-cell carcinoma	686
	Carter Van Waes, Yansong Bian, Clint T. Allen, John C. Morris, and Zhong Chen	
62.	Molecular oncology of basal cell carcinomas	693
	Ervin H. Epstein, Jr.	
63.	Melanoma	698
	Adina Vultur, Keiran Smalley, and Meenhard Herlyn	

Part 3.4 Molecular pathology: endocrine cancers

64.	Oncogenic events and therapeutic targets in thyroid cancer	704
	James A. Fagin and Julio C. Ricarte Filho	
65.	The parathyroid glands	712
	Edward M. Brown and Andrew Arnold	
66.	Multiple endocrine neoplasia type 2 (MEN2)	720
	Jo W. M. Höppener and C. J. M. Lips	

Part 3.5 Molecular pathology: adult sarcomas

67.	Sarcomas	731
	Lee J. Helman	

Part 3.6 Molecular pathology: lymphoma and leukemia

68.	Molecular pathology of lymphoma	738
	Christof Schneider, Laura Pasqualucci, and Riccardo Dalla-Favera	
69.	The molecular basis of acute myeloid leukemia	751
	Kim L. Rice, Monica Buzzai, Jessica Altman, and Jonathan D. Licht	
70.	Molecular oncology of acute promyelocytic leukemia (APL)	769
	Valérie Lallemand-Breitenbach and Hugues de Thé	
71.	Acute lymphoblastic leukemia (ALL)	777
	Ido Paz-Priel and Alan D. Friedman	
72.	B-cell chronic lymphocytic leukemia	786
	Francesco Bertoni, Francesco Forconi, Michele Dal-Bo, Antonella Zucchetto, Riccardo Bomben, Giovanni Del Poeta, and Valter Gattei	
73.	Chronic myeloid leukemia: imatinib and next-generation ABL inhibitors	793
	Charles L. Sawyers	
74.	Multiple myeloma	799
	W. Michael Kuehl and P. Leif Bergsagel	
75.	EMS: the 8p11 myeloproliferative syndrome	809
	Donald H. C. Macdonald, Andreas Reiter, and Nicholas C. P. Cross	
76.	JAK2 and myeloproliferative neoplasms	818
	Ross L. Levine	

Contents

Part 3.7 Molecular pathology: pediatric solid tumors

77. **Pediatric solid tumors: embryonal cell oncogenesis** 826
Jeffrey A. Toretzky and Aerang Kim

Part 4 Pharmacologic targeting of oncogenic pathways

78. **Oncology drug discovery for biologics: antibody development strategies and considerations** 836
Bryan C. Barnhart, Marco M. Gottardis, and Matthew V. Lorenzi
79. **Targeting the EGFR family of receptor tyrosine kinases** 843
Siyuan Zhang and Dihua Yu
80. **Therapeutic approaches with antibodies to cell-surface receptors** 854
Antonio Gualberto
81. **Signal transduction in tumor angiogenesis** 861
Timothy Hla, Nasser Altorki, and Vivek Mittal
82. **Tyrosine-kinase inhibitors in oncology** 872
Anne S. Tsao, Vassiliki Papadimitrakopoulou, and Roy S. Herbst

83. **Anti-estrogens and selective estrogen-receptor modulators** 884
Ping Fan and V. Craig Jordan
84. **Therapeutic applications of anti-sense mechanisms for the treatment of cancer** 893
A. Robert MacLeod and C. Frank Bennett
85. **Induction of apoptosis** 903
Dario C. Altieri
86. **DNA-methylation inhibitors** 908
Jean-Pierre Issa
87. **Histone deacetylase inhibitor** 912
Paul A. Marks
88. **Drug resistance: as complex and diverse as the disease itself** 921
Antonio Tito Fojo
89. **Molecular profiling and therapeutic decision-making: the promise of personalized medicine** 929
Susan M. Henshall and Andrew V. Biankin
90. **DNA repair inhibition in anti-cancer therapeutics** 936
Brian M. Alexander and Alan D. D’Andrea

Index 945

Contributors

Byungchan Ahn
Department of Life Sciences, University of Ulsan, Ulsan, Korea

Donna G. Albertson
Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA

Brian M. Alexander
Department of Radiation Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Clint T. Allen, MD
Head and Neck Surgery Branch, National Institute on Deafness and Other Communication Disorders, NIH, Bethesda, MD, USA

Dario C. Altieri, MD
The Wistar Institute, Philadelphia, PA, USA

Jessica Altman
Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Nasser Altorki
Department of Cardiothoracic Surgery and Neuberger Berman Lung Cancer Research Center, Weill Medical College of Cornell University, New York, NY, USA

Valsamo K. Anagnostou, MD
Department of Pathology, Yale University School of Medicine, New Haven, CT, USA

Shira Anzi
Department of Developmental Biology and Cancer Research, IMRIC, The Hebrew University – Hadassah Medical School, Jerusalem, Israel

Andrew Arnold, MD
Center for Molecular Medicine and Department of Genetics and Developmental Biology, University of Connecticut School of Medicine, Farmington, CT, USA

Sylvia L. Asa
Department of Pathology and Laboratory Medicine, University of Toronto, Department of Pathology, University Health Network, Toronto, Ontario, Canada

Bryan C. Barnhart
Oncology Drug Discovery, Bristol-Myers Squibb, Co., Princeton, NJ, USA

Robert C. Bast, Jr., MD
Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Vandana Batra MD
Center for Childhood Cancer Research, Department of Pediatrics, Childrens Hospital of Philadelphia, Philadelphia, PA, USA

C. Frank Bennett
Department of Antisense Drug Discovery, Isis Pharmaceuticals, Inc., Carlsbad, CA, USA

P. Leif Bergsagel, MD
Division of Hematology-Oncology, Comprehensive Cancer Center, Mayo Clinic, Scottsdale, AZ, USA

Francesco Bertoni
Lymphoma and Genomics Research Program, Institute of Oncology Research, and Lymphoma Unit, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Yansong Bian, MD, PhD
Laboratory of Cell and Developmental Biology, National Institute of Dental and Craniofacial Research, NIH, Bethesda, MD, USA

Andrew V. Biankin MB, BS, FRACS, PhD
Cancer Research Program, Garvan Institute of Medical Research, Darlinghurst, Sydney, NSW, Australia

Mary-Ann Bjornsti
Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham AL, USA

List of contributors

Vilhelm A. Bohr Laboratory of Molecular Gerontology, Gerontology Research Center, National Institute on Aging, NIH, Baltimore, MD, USA	Timothy A. Chan Memorial Sloan Kettering Cancer Center, New York, NY, USA
Riccardo Bomben Clinical and Experimental Onco-Hematology Unit, Centro di Riferimento Oncologico, I.R.C.C.S., Aviano, Pordenone, Italy	Zhong Chen, MD, PhD Head and Neck Surgery Branch, National Institute on Deafness and Other Communication Disorders, NIH, Bethesda, MD, USA
Donald P. Bottaro Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA	Derek Y. Chiang, PhD Novartis Institutes for Biomedical Research, Cambridge, MA, USA
Ryan J. Bourgo Kimmel Cancer Center, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, PA, USA	Michael D. Cole Departments of Pharmacology and Genetics, Dartmouth Medical School, Norris Cotton Cancer Center, Lebanon, NH, USA
Edward M. Brown, MD Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women’s Hospital, Boston, MA, USA	Kevin D. Courtney, MD, PhD Division of Hematology/Oncology, UT Southwestern Medical Center, Dallas, TX, USA
Dennis K. Burns Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA	Adrienne D. Cox, PhD Departments of Radiation Oncology and Pharmacology, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
Lisa M. Butler Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia	Nicholas C. P. Cross Wessex Regional Genetics Laboratory, University of Southampton, Salisbury District Hospital, Salisbury, UK
Monica Buzzai Novartis, Origgio, VA, Italy	Thomas A. D’Amico, MD Division of Thoracic Surgery, Duke University Health System, Durham, NC, USA
George A. Calin, MA, PhD RNA Interference and Non-coding RNA Center and the Department of Experimental Therapeutics, University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA	Alan D. D’Andrea Department of Radiation Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
Lewis C. Cantley, PhD Weill Cornell Cancer Center, New York – Presbyterian Hospital, Weill Cornell Medical College, New York, NY, USA	Michele Dal-Bo Clinical and Experimental Onco-Hematology Unit, Centro di Riferimento Oncologico, I.R.C.C.S., Aviano, Pordenone, Italy
Fabiola Cecchi Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA	Riccardo Dalla-Favera, MD Department of Genetics and Development, Department of Pathology and Cell Biology, and Department of Microbiology and Immunology, Institute for Cancer Genetics and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA
Margaret M. Centenera Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia	Altaf A. Dar California Pacific Medical Center Research Institute, San Francisco, CA, USA
DuyKhanh P. Ceppa, MD Division of Thoracic Surgery, Indiana University School of Medicine, Indianapolis, IN, USA	Rachel S. Darken Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA

List of contributors

Kaustubh Datta
Department of Urologic Research, Biochemistry and
Molecular Biology, Mayo Clinic Cancer Center, Mayo Clinic
Foundation, Rochester, MN, USA

Hugues de Thé
CNRS 7212, Université Paris Diderot, Paris, France

Jeffrey L. Dean
Kimmel Cancer Center, Department of Cancer Biology,
Thomas Jefferson University, Philadelphia, PA, USA

Molly J. DeCristo
Department of Biology, University of North Carolina at
Chapel Hill, Chapel Hill, NC, USA

Giovanni Del Poeta
Department of Hematology, S. Eugenio Hospital and
University of Tor Vergata, Rome, Italy

Rebecca J. Deyell MD
Center for Childhood Cancer Research, Department of
Pediatrics, Childrens Hospital of Philadelphia, Philadelphia,
PA, USA

Colin P. Dinney MD
Department of Urology, The University of Texas M. D.
Anderson Cancer Center, Houston, TX, USA

John Doorbar
Division of Virology, National Institute for Medical Research,
London, UK

Wael El-Rifai, MD, PhD
Department of Surgery and Vanderbilt-Ingram Cancer Center,
Vanderbilt University Medical Center, Nashville, TN, USA

Ervin H. Epstein, Jr
Children’s Hospital Oakland Research Institute, Oakland, CA,
USA

Shereen Ezzat
Department of Medicine, University of Toronto and
the Princess Margaret Cancer Center, University Health
Network, Toronto, Ontario, Canada

James A. Fagin, MD
Department of Medicine and Human Oncology and
Pathogenesis Program, Memorial Sloan-Kettering Cancer
Center, New York, NY, USA

Jian-Bing Fan
Illumina, Inc., San Diego, CA, USA

Ping Fan
Vincent T. Lombardi Comprehensive Cancer Center,
Georgetown University, DC, USA

Julio C. Ricarte Filho
Department of Medicine and Human Oncology and
Pathogenesis Program, Memorial Sloan-Kettering Cancer
Center, New York, NY, USA

Jeffrey Fisher
Illumina, Inc., San Diego, CA, USA

Antonio Tito Fojo, MD, PhD
Medical Oncology Branch and Affiliates Head, Experimental
Therapeutics Section, Center for Cancer Research, National
Cancer Institute, Bethesda, MD, USA

Francesco Forconi
Division of Hematology and Transplant, Department of
Clinical Medicine and Immunological Sciences, University of
Siena, Italy

Errol C. Friedberg
Laboratory of Molecular Pathology, Department of Pathology,
University of Texas Southwestern Medical Center, Dallas, TX,
USA

Alan D. Friedman, MD
Departments of Oncology and Pediatrics, Division of Pediatric
Oncology, Johns Hopkins University, Baltimore, MD, USA

Kyle A. Furge, PhD
Laboratory of Computational Biology, Van Andel Research
Institute, Grand Rapids, MI, USA

Alexandra K. Gardino
David H. Koch Institute for Integrative Cancer Research,
Massachusetts Institute of Technology, Cambridge, MA,
USA

Valter Gattei
Clinical and Experimental Onco-Hematology Unit, Centro di
Riferimento Oncologico, I.R.C.C.S., Aviano, Pordenone, Italy

Edward P. Gelmann, MD
Departments of Medicine and Pathology, Herbert Irving
Comprehensive Cancer Center, Columbia University, New
York, NY, USA

Paramita Ghosh
Departments of Biochemistry and Molecular Medicine, and
Urology, University of California David School of Medicine,
Sacramento, and VA Northern Health Care System, Mather,
CA, USA

Elizabeth L. Gosnell
Kimmel Cancer Center, Department of Cancer Biology,
Thomas Jefferson University, Philadelphia, PA, USA

Marco M. Gottardis
Oncology Drug Discovery, Bristol-Myers Squibb, Co.,
Princeton, NJ, USA

List of contributors

Jennifer Grandis

University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Joanna Groden

Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University College of Medicine, Columbus, OH, USA

Antonio Gualberto MD PhD

Department of Pathology and Laboratory Medicine, The Alpert Medical School of Brown University, Providence, RI, USA

David H. Gutmann, MD, PhD

Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA

Samir Hanash

Fred Hutchinson Cancer Research Center, Seattle, WA, USA

J. Marie Hardwick

Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA

Ruth He

Lombardi Comprehensive Cancer Center, Georgetown University, Washington DC, USA

Carl-Henrik Heldin

Ludwig Institute for Cancer Research, Uppsala University, Uppsala, Sweden

Lee J. Helman, MD

Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA

Bryan T. Hennessy, MD

Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Susan M. Henshall, PhD

Cancer Research Program, Garvan Institute of Medical Research, Darlinghurst, Sydney, NSW, Australia

Roy S. Herbst, MD, PhD

Yale University School of Medicine, New Haven, CT

Meenhard Herlyn

The Wistar Institute Melanoma Research Center, Philadelphia, PA, USA

Theresa E. Hickey

Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia

Timothy Hla

Center of Vascular Biology, Department of Pathology and Laboratory Medicine, Weill Medical College of Cornell University, New York, NY, USA

Jo W. M. Höppener

Department of Molecular Cancer Research, University Medical Center Utrecht, University Hospital, the Netherlands

Yujin Hoshida, MD, PhD

Liver Cancer Program, Tisch Cancer Institute, Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Nancy E. Hynes

Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

Rosalyn B. Irby

Penn State Hershey Cancer Institute H046, Penn State University College of Medicine, Hershey, PA, USA

Jean-Pierre Issa

Fels Institute for Cancer Research, Temple University School of Medicine, Philadelphia, PA, USA

Yoshiaki Ito, MD PhD

Cancer Science Institute, National University of Singapore, Center for Translational Medicine, Singapore

V. Craig Jordan

Vincent T. Lombardi Comprehensive Cancer Center, Georgetown University, DC, USA

Richard Jove, PhD

Beckham Research Institute, City of Hope, Duarte, CA, USA

Michael Karin

Laboratory of Gene Regulation and Signal Transduction, Department of Pharmacology and Pathology, Moores Cancer Center, UCSD School of Medicine, La Jolla, CA, USA

Masaru Katoh, MD, PhD

Genetics and Cell Biology Section, National Cancer Center, Tokyo, Japan

Aerang Kim

Department of Pediatrics, Children’s National Medical Center, George Washington University, Washington, DC, USA

Erik S. Knudsen

Department of Pathology, UT Southwestern Medical Center, Dallas, TX, USA

Chuay-Yeng Koo

Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London, UK

List of contributors

Wolfgang J. Köstler
Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel

W. Michael Kuehl, MD
Cancer Genetics Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA

Hsing-Jien Kung
Departments of Biochemistry and Molecular Medicine, and Urology, University of California David School of Medicine, Sacramento, CA, USA

Chang-Hyuk Kwon
Department of Developmental Biology, University of Texas Southwestern Medical Center, Dallas, TX, USA; Solid Tumor Program and Department of Neurological Surgery, James Comprehensive Cancer Center, The Ohio State University Wexner Medical Center, Columbus, OH, USA

Abizar Lakdawalla
Illumina, Inc., San Diego, CA, USA

Valérie Lallemand-Breitenbach
CNRS 7212, Université Paris Diderot, Paris, France

Eric W.-F. Lam
Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London, UK

Jill E. Larsen, PhD
Hamon Center for Therapeutic Oncology Research, Simmons Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX, USA

Shun J. Lee
Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA

Young H. Lee
Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Ross L. Levine, MD
Human Oncology and Pathogenesis Program, Leukemia Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Ying Li
The University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Siong-Seng Liau, MD, FRCS
Hepatopancreatobiliary Surgery Unit, Department of Surgery, Addenbrooke's Hospital, and Medical Research Council Cancer Cell Unit, Hutchison-MRC Research Center, University of Cambridge, Cambridge, UK

Jonathan D. Licht, MD
Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

C. J. M. Lips
Department of Internal Medicine, University Medical Center Utrecht, Utrecht, the Netherlands

Josep M. Llovet, MD
Liver Cancer Program, Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, USA; and BCLC Group, IDIBAPS, CIBEREHD, Liver Unit, Hospital Clínic, Barcelona, Spain

Leendert H. J. Looijenga
Department of Pathology, Erasmus MC – University Medical Center Rotterdam, Daniel den Hoed Cancer Center, Josephine Nefkens Institute, Rotterdam, the Netherlands

Matthew V. Lorenzi
Oncology Drug Discovery, Bristol-Myers Squibb, Co., Princeton, NJ, USA

Yongde Luo
Center for Cancer and Stem Cell Biology, Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston, TX, USA

Donald H. C. Macdonald
Department of Haematology, Imperial College, London, UK

Gwen MacDonald
Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

A. Robert MacLeod
Department of Antisense Drug Discovery, Isis Pharmaceuticals, Inc., Carlsbad, CA, USA

A. Kathleen McClendon
Kimmel Cancer Center, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, PA, USA

Wallace L. McKeehan
Center for Cancer and Stem Cell Biology, Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston, TX, USA

John M. Maris MD
Center for Childhood Cancer Research, Department of Pediatrics, Childrens Hospital of Philadelphia, Philadelphia, PA, USA

Paul A. Marks
Cell Biology and Genetics Program, Sloan-Kettering Institute for Cancer Research, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

List of contributors

Soheil Meshinchi

Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Gordon B. Mills, MD, PhD

Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

John D. Minna, MD

Hamon Center for Therapeutic Oncology Research, Simmons Cancer Center University of Texas Southwestern Medical Center, Dallas, TX, USA

Lopa Mishra

The University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Vivek Mittal

Department of Cardiothoracic Surgery and Neuberger Berman Lung Cancer Research Center, and Department of Cell and Developmental Biology, Weill Medical College of Cornell University, New York, NY, USA

Nicole L. Moore

Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia

John C. Morris, MD

Metabolism Branch, National Cancer Institute, NIH, Bethesda, MD, USA

Kyle W. Muir

Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London, UK

Karl Munger

Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Willscott E. Naugler

Oregon Health and Sciences University, Department of Medicine, Division of GI and Hepatology, Portland, OR, USA

Milena S. Nicoloso

RNA Interference and Non-coding RNA Center and the Department of Experimental Therapeutics, University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Moriah H. Nissan

Human Oncology and Pathogenesis Program, and Louis V. Gerstner Jr. Graduate School of Biomedical Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Benjamin F. O’Connor

Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA

Kenneth Offit

Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

J. Wolter Oosterhuis

Department of Pathology, Erasmus MC – University Medical Center Rotterdam, Daniel den Hoed Cancer Center, Josephine Nefkens Institute, Rotterdam, the Netherlands

Arne Östman

Cancer Center Karolinska, Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden

Vassiliki Papadimitrakopoulou

University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Luis F. Parada

Department of Developmental Biology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Laura Pasqualucci, MD

Institute for Cancer Genetics and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA

Ido Paz-Priel, MD

Departments of Oncology and Pediatrics, Division of Pediatric Oncology, Johns Hopkins University, Baltimore, MD, USA

Erin M. Perchiniak

Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University College of Medicine, Columbus, OH, USA

Richard G. Pestell

Department of Cancer Biology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA

Daniel Pinkel

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

Michael Pollak, MD

Department of Oncology, McGill University, Montreal, Quebec, Canada

Marshall R. Posner

Mount Sinai Medical Center, Tisch Cancer Institute, Icahn School of Medicine, New York, NY, USA

List of contributors

Karen Pulford Nuffield Division of Clinical Laboratory Sciences, Radcliffe Department of Medicine, University of Oxford, Oxford, UK	Jerry W. Shay University of Texas Southwestern Medical Center, Department of Cell Biology, Dallas, TX, USA
Yun Qiu Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, USA	Yosef Shiloh The David and Inez Myers Laboratory for Genetic Research, Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
Kelly Quesnelle University of Pittsburgh Medical Center, Pittsburgh, PA, USA	Keiran Smalley Department of Molecular Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
Andreas Reiter Medizinische Klinik, Universitätsmedizin Mannheim, Germany	David B. Solit, MD Human Oncology and Pathogenesis Program, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
Marsha Reyngold Memorial Sloan-Kettering Cancer Center, New York, NY, USA	Allan D. Spigelman UNSW St Vincent's Clinical School, Cancer Services, St Vincent's & Mater Health, Sydney, Hereditary Cancer Clinic, St Vincent's Hospital, The Kinghorn Cancer Centre, Sydney, NSW, Australia
Kim L. Rice Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA	Zsafia K. Stadler Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
Thomas Ried, MD Section of Cancer Genomics, Genetics Branch, Center for Cancer Research /NCI/NIH, Bethesda, MD, USA	Tinna Stevnsner Danish Centre for Molecular Gerontology and Danish Aging Research Center, University of Aarhus, Department of Molecular Biology, Denmark
David L. Rimm MD, PhD Department of Pathology, Yale University School of Medicine, New Haven, CT, USA	Derek L. Stirewalt Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
Mostafa Ronaghi Illumina, Inc., San Diego, CA, USA	Scott A. Stuart Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA
Charles L. Sawyers, MD Howard Hughes Medical Institute, Chevy Chase, MD, and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA	Grace K. Suh, MD Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
Christof Schneider, MD Institute for Cancer Genetics and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA	Robert S. Svatek Department of Urology, the University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
Roger A. Schultz Signature Genomics, Spokane, WA, USA	Ayumu Taguchi Fred Hutchinson Cancer Research Center, Seattle, WA, USA
Vikas Sehdev Department of Surgery and Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN, USA	Bin T. Teh, MD, PhD National Cancer Centre of Singapore, Duke-NUS Graduate Medical School, Singapore, and Cancer Science Institute of Singapore
Sohela Shah Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA	
Eitan Shaulian Department of Biochemistry and Molecular Biology, IMRIC, The Hebrew University – Hadassah Medical School, Jerusalem, Israel	

List of contributors

Xinchen Teng

Feinstein Department of Molecular Microbiology and Immunology, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA

Lifeng Tian

Department of Cancer Biology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA

Wayne D. Tilley

Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia

Donald J. Tindall

Department of Urologic Research, Biochemistry and Molecular Biology, Mayo Clinic Cancer Center, Mayo Clinic Foundation, Rochester, MN, USA

Jeffrey A. Toretsky

Departments of Oncology and Pediatrics, Georgetown University, Washington, DC, USA

Anne S. Tsao

University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

David A. Tuveson, MD, PhD

Department of Oncology, Addenbrooke’s Hospital, University of Cambridge, Cambridge, UK

Robert C. A. M. van Waardenburg

Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, AL, USA

Carter Van Waes, MD, PhD

Head and Neck Surgery Branch, National Institute on Deafness and Other Communication Disorders, NIH, Bethesda, MD, USA

Roeland Verhaak, PhD

Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Augusto Villanueva, MD

Institute of Liver Studies, Division of Transplantation Immunology and Mucosal Biology, King’s College London, UK

Adina Vultur

The Wistar Institute Melanoma Research Center, Philadelphia, PA, USA

Chenguang Wang

Department of Stem Cell Biology and Regenerative Medicine, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA

Fen Wang

Center for Cancer and Stem Cell Biology, Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston, TX, USA

Jean Y. J. Wang

Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA

Ling-Yu Wang

Departments of Biochemistry and Molecular Medicine, University of California David School of Medicine, Sacramento, CA, USA

Janindra Warusavitarne

Department of Surgery, St Mark’s Hospital, Harrow, Middlesex, UK

Jody White

Frank Reidy Research Center for Bioelectronics, Old Dominion University, Norfolk, VA, USA

Woodring E. Wright

University of Texas Southwestern Medical Center, Department of Cell Biology, Dallas, TX, USA

Michael B. Yaffe

David H. Koch Institute for Integrative Cancer Research and Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA

Ji-Yeon Yang, PhD

Departments of Experimental Therapeutics, Gynecologic Medical Oncology, Bioinformatics and Computational Biology, and Systems Biology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Yosef Yarden

Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel

Timothy J. Yeatman, MD

Gibbs Cancer Center and Research Institute, Spartanburg, SC, USA

Khay Guan Yeoh, MBBS, FRCP, FRCP (Glasg)

Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore

Dihua Yu, MD, PhD

University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Hua Yu, PhD

Beckham Research Institute, City of Hope, Duarte, CA, USA

Siyuan Zhang, MD PhD

University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

List of contributors

Xuemin Zhang
State Key Laboratory of Proteomics, Institute of Basic Medical
Sciences, National Center of Biomedical Analysis, Beijing,
China

Antonella Zucchetto
Clinical and Experimental Onco-Hematology Unit, Centro di
Riferimento Oncologico, I.R.C.C.S., Aviano, Pordenone,
Italy

Cambridge University Press
978-0-521-87662-9 - Molecular Oncology: Causes of Cancer and Targets for Treatment
Edited by Edward P. Gelmann, Charles L. Sawyers and Frank J. Rauscher III
Frontmatter
[More information](#)

Preface

This book was conceived more than five years before its publication date. It was intended to provide a resource that summarized technology, biochemistry, molecular pathophysiology, and targeted therapeutics. As contributors were being recruited and chapters written the field that was being described changed at an accelerating pace. It is a tribute to scientific progress that volumes like this are out-of-date as they are published, but books like this are not meant to contain the most current laboratory discovery or report the most recent FDA approval.

While this book was being written there have been major advances in molecular oncology. The Cancer Genome Atlas (cancergenome.nih.gov) has demonstrated the broad spectrum of mutations in an expanding list of cancers. DNA sequence analysis alone has demonstrated that as cancers grow, metastasize, and develop treatment resistance, individual tumor sites within a single patient evolve differently and demonstrate increasingly complex spectra of driver and passenger mutations. These findings alone strongly support the Darwinian view of tumor progression. The complexities of cellular dysregulation in cancer may arise from DNA sequence changes, but extend to other levels of gene regulation. During the writing of this book the role of micro-RNAs (miRNAs) in cancer was elucidated. Aberrations in epigenetics such as DNA methylation and histone acetylation were demonstrated. Cancer drug development has also proceeded at increasing rates. In the period 2008–2012 there were 51 approvals of new drugs for cancer treatment by the US Food and Drug Administration. Many of these approvals

resulted from impressive data in Phase II trials that clearly demonstrated efficacy where no agents have worked before.

As we have assembled the contributions for this volume we have watched as more and more information is provided and accessed in electronic format, replacing the printed word. It is not hard to predict that younger generations of investigators will dispense entirely with books and access all information on electronic screens. Clearly a volume like this is meant to provide rapid reference when accessed from a shelf in someone's office.

We the editors took on the task of assembling this volume to provide background for active researchers, to provide meaningful lists of important citations that form the foundation of the molecular pathophysiology of cancer, and to define the context in which current investigation is pursued. This book is intended for students and professionals in academia and industry. Where electronic databases are non-discriminatory and web-based searches can be overwhelming in their download lists, volumes like this provide the perspective and judgment of experts who have spent a very long time in a path of study and therefore share their understanding and viewpoints that are missed in database or electronic literature searches. Volumes like this collect the experience and wisdom of the contributors and therefore provide value and perspective. As journal titles proliferate and the scientific literature expands, it is books like this that guide knowledge and help organize the work in a field into a comprehensible narrative. We hope you find these pages useful.