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.
Contents

List of contributors xi
Preface xxi

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. Kölstler and Yousef Yarden

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

### Part 2.5 Molecular pathways underlying carcinogenesis: cell cycle

38. Cell cycle: mechanisms of control and dysregulation in cancer  452  
   Erik S. Knudsen, Ryan J. Bourgo, Elizabeth L. Gosnell, Jeffry 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 Bjornst

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  
   Allian D. Spigelman and Janindra Warusavitane

47. Colon and rectal cancer  547  
   Erin M. Perchiniak and Joanna Groden
### Contents

#### Part 3.7 Molecular pathology: pediatric solid tumors

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

#### Part 4 Pharmacologic targeting of oncogenic pathways

78. **Oncology drug discovery for biologics: antibody development strategies and considerations**  
Bryan C. Barnhart, Marco M. Gottardis, and Matthew V. Lorenzi

79. **Targeting the EGFR family of receptor tyrosine kinases**  
Siyuan Zhang and Dihua Yu

80. **Therapeutic approaches with antibodies to cell-surface receptors**  
Antonio Gualberto

81. **Signal transduction in tumor angiogenesis**  
Timothy Hla, Nasser Altorki, and Vivek Mittal

82. **Tyrosine-kinase inhibitors in oncology**  
Anne S. Tsao, Vassiliki Papadimitrakopoulou, and Roy S. Herbst

83. **Anti-estrogens and selective estrogen-receptor modulators**  
Ping Fan and V. Craig Jordan

84. **Therapeutic applications of anti-sense mechanisms for the treatment of cancer**  
A. Robert MacLeod and C. Frank Bennett

85. **Induction of apoptosis**  
Dario C. Altieri

86. **DNA-methylation inhibitors**  
Jean-Pierre Issa

87. **Histone deacetylase inhibitor**  
Paul A. Marks

88. **Drug resistance: as complex and diverse as the disease itself**  
Antonio Tito Fojo

89. **Molecular profiling and therapeutic decision-making: the promise of personalized medicine**  
Susan M. Henshall and Andrew V. Biankin

90. **DNA repair inhibition in anti-cancer therapeutics**  
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

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

Donald P. Bottaro
Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Ryan J. Bourgo
Kimmel Cancer Center, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, PA, USA

Edward M. Brown, MD
Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women’s Hospital, Boston, MA, USA

Dennis K. Burns
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Lisa M. Butler
Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia

Monica Buzzai
Novartis, Origgio, VA, Italy

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

Lewis C. Cantley, PhD
Weill Cornell Cancer Center, New York – Presbyterian Hospital, Weill Cornell Medical College, New York, NY, USA

Fabiola Cecchi
Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Margaret M. Centenera
Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia

DuyKhanh P. Ceppa, MD
Division of Thoracic Surgery, Indiana University School of Medicine, Indianapolis, IN, USA

Timothy A. Chan
Memorial Sloan Kettering Cancer Center, New York, NY, USA

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

Derek Y. Chiang, PhD
Novartis Institutes for Biomedical Research, Cambridge, MA, USA

Michael D. Cole
Departments of Pharmacology and Genetics, Dartmouth Medical School, Norris Cotton Cancer Center, Lebanon, NH, USA

Kevin D. Courtneyn, MD, PhD
Division of Hematology/Oncology, UT 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

Nicholas C. P. Cross
Wessex Regional Genetics Laboratory, University of Southampton, Salisbury District Hospital, Salisbury, UK

Thomas A. D’Amico, MD
Division of Thoracic Surgery, Duke University Health System, Durham, NC, USA

Alan D. D’Andrea
Department of Radiation Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

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

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

Altaf A. Dar
California Pacific Medical Center Research Institute, San Francisco, CA, USA

Rachel S. Darken
Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA
<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaustubh Datta</td>
<td>Department of Urologic Research, Biochemistry and Molecular Biology, Mayo Clinic Cancer Center, Mayo Clinic Foundation, Rochester, MN, USA</td>
</tr>
<tr>
<td>Hugues de Thé</td>
<td>CNRS 7212, Université Paris Diderot, Paris, France</td>
</tr>
<tr>
<td>Jeffrey L. Dean</td>
<td>Kimmel Cancer Center, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Molly J. DeCristo</td>
<td>Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA</td>
</tr>
<tr>
<td>Giovanni Del Poeta</td>
<td>Department of Hematology, S. Eugenio Hospital and University of Tor Vergata, Rome, Italy</td>
</tr>
<tr>
<td>Rebecca J. Deyell MD</td>
<td>Center for Childhood Cancer Research, Department of Pediatrics, Childrens Hospital of Philadelphia, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Colin P. Dinney MD</td>
<td>Department of Urology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA</td>
</tr>
<tr>
<td>John Doorbar</td>
<td>Division of Virology, National Institute for Medical Research, London, UK</td>
</tr>
<tr>
<td>Wael El-Rifai, MD, PhD</td>
<td>Department of Surgery and Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN, USA</td>
</tr>
<tr>
<td>Ervin H. Epstein, Jr</td>
<td>Children’s Hospital Oakland Research Institute, Oakland, CA, USA</td>
</tr>
<tr>
<td>Shereen Ezzat</td>
<td>Department of Medicine, University of Toronto and the Princess Margaret Cancer Center, University Health Network, Toronto, Ontario, Canada</td>
</tr>
<tr>
<td>James A. Fagin, MD</td>
<td>Department of Medicine and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Jian-Bing Fan</td>
<td>Illumina, Inc., San Diego, CA, USA</td>
</tr>
<tr>
<td>Ping Fan</td>
<td>Vincent T. Lombardi Comprehensive Cancer Center, Georgetown University, DC, USA</td>
</tr>
<tr>
<td>Julio C. Ricarte Filho</td>
<td>Department of Medicine and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Jeffrey Fisher</td>
<td>Illumina, Inc., San Diego, CA, USA</td>
</tr>
<tr>
<td>Antonio Tito Fojo, MD, PhD</td>
<td>Medical Oncology Branch and Affiliates Head, Experimental Therapeutics Section, Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA</td>
</tr>
<tr>
<td>Francesco Forconi</td>
<td>Division of Hematology and Transplant, Department of Clinical Medicine and Immunological Sciences, University of Siena, Italy</td>
</tr>
<tr>
<td>Errol C. Friedberg</td>
<td>Laboratory of Molecular Pathology, Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA</td>
</tr>
<tr>
<td>Alan D. Friedman, MD</td>
<td>Departments of Oncology and Pediatrics, Division of Pediatric Oncology, Johns Hopkins University, Baltimore, MD, USA</td>
</tr>
<tr>
<td>Kyle A. Furge, PhD</td>
<td>Laboratory of Computational Biology, Van Andel Research Institute, Grand Rapids, MI, USA</td>
</tr>
<tr>
<td>Alexandra K. Gardino</td>
<td>David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, USA</td>
</tr>
<tr>
<td>Valter Gattei</td>
<td>Clinical and Experimental Onco-Hematology Unit, Centro di Riferimento Oncologico, I.R.C.C.S., Aviano, Pordenone, Italy</td>
</tr>
<tr>
<td>Edward P. Gelmann, MD</td>
<td>Departments of Medicine and Pathology, Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA</td>
</tr>
<tr>
<td>Paramita Ghosh</td>
<td>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</td>
</tr>
<tr>
<td>Elizabeth L. Gosnell</td>
<td>Kimmel Cancer Center, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Marco M. Gottardis</td>
<td>Oncology Drug Discovery, Bristol-Myers Squibb, Co., Princeton, NJ, USA</td>
</tr>
</tbody>
</table>
# List of contributors

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jennifer Grandis</td>
<td>University of Pittsburgh Medical Center, Pittsburgh, PA, USA</td>
</tr>
<tr>
<td>Joanna Groden</td>
<td>Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University College of Medicine, Columbus, OH, USA</td>
</tr>
<tr>
<td>Antonio Gualberto MD PhD</td>
<td>Department of Pathology and Laboratory Medicine, The Alpert Medical School of Brown University, Providence, RI, USA</td>
</tr>
<tr>
<td>David H. Gutmann, MD, PhD</td>
<td>Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA</td>
</tr>
<tr>
<td>Samir Hanash</td>
<td>Fred Hutchinson Cancer Research Center, Seattle, WA, USA</td>
</tr>
<tr>
<td>J. Marie Hardwick</td>
<td>Feinstein Department of Molecular Microbiology and Immunology, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA</td>
</tr>
<tr>
<td>Ruth He</td>
<td>Lombardi Comprehensive Cancer Center, Georgetown University, Washington DC, USA</td>
</tr>
<tr>
<td>Carl Henrik Heldin</td>
<td>Ludwig Institute for Cancer Research, Uppsala University, Uppsala, Sweden</td>
</tr>
<tr>
<td>Lee J. Helman, MD</td>
<td>Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA</td>
</tr>
<tr>
<td>Bryan T. Hennessy, MD</td>
<td>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</td>
</tr>
<tr>
<td>Susan M. Henshall, PhD</td>
<td>Cancer Research Program, Garvan Institute of Medical Research, Darlinghurst, Sydney, NSW, Australia</td>
</tr>
<tr>
<td>Roy S. Herbst, MD, PhD</td>
<td>Yale University School of Medicine, New Haven, CT</td>
</tr>
<tr>
<td>Meenhard Herlyn</td>
<td>The Wistar Institute Melanoma Research Center, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Theresa E. Hickey</td>
<td>Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia</td>
</tr>
<tr>
<td>Timothy Hla</td>
<td>Center of Vascular Biology, Department of Pathology and Laboratory Medicine, Weill Medical College of Cornell University, New York, NY, USA</td>
</tr>
<tr>
<td>Jo W. M. Höppener</td>
<td>Department of Molecular Cancer Research, University Medical Center Utrecht, University Hospital, the Netherlands</td>
</tr>
<tr>
<td>Yujin Hoshida, MD, PhD</td>
<td>Liver Cancer Program, Tisch Cancer Institute, Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, USA</td>
</tr>
<tr>
<td>Nancy E. Hynes</td>
<td>Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland</td>
</tr>
<tr>
<td>Rosalyn B. Irby</td>
<td>Penn State Hershey Cancer Institute H046, Penn State University College of Medicine, Hershey, PA, USA</td>
</tr>
<tr>
<td>Jean-Pierre Issa</td>
<td>Fels Institute for Cancer Research, Temple University School of Medicine, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Yoshiaki Ito, MD PhD</td>
<td>Cancer Science Institute, National University of Singapore, Center for Translational Medicine, Singapore</td>
</tr>
<tr>
<td>V. Craig Jordan</td>
<td>Vincent T. Lombardi Comprehensive Cancer Center, Georgetown University, DC, USA</td>
</tr>
<tr>
<td>Richard Jove, PhD</td>
<td>Beckham Research Institute, City of Hope, Duarte, CA, USA</td>
</tr>
<tr>
<td>Michael Karin</td>
<td>Laboratory of Gene Regulation and Signal Transduction, Department of Pharmacology and Pathology, Moores Cancer Center, UCSD School of Medicine, La Jolla, CA, USA</td>
</tr>
<tr>
<td>Masaru Katoh, MD, PhD</td>
<td>Genetics and Cell Biology Section, National Cancer Center, Tokyo, Japan</td>
</tr>
<tr>
<td>Aerang Kim</td>
<td>Department of Pediatrics, Children's National Medical Center, George Washington University, Washington, DC, USA</td>
</tr>
<tr>
<td>Erik S. Knudsen</td>
<td>Department of Pathology, UT Southwestern Medical Center, Dallas, TX, USA</td>
</tr>
<tr>
<td>Chuay-Yeng Koo</td>
<td>Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London, UK</td>
</tr>
</tbody>
</table>
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-Breittenbach
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 Clinic, 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
<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soheil Meshinchi</td>
<td>Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA</td>
</tr>
<tr>
<td>Gordon B. Mills, MD, PhD</td>
<td>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</td>
</tr>
<tr>
<td>John D. Minna, MD</td>
<td>Hamon Center for Therapeutic Oncology Research, Simmons Cancer Center University of Texas Southwestern Medical Center, Dallas, TX, USA</td>
</tr>
<tr>
<td>Lopa Mishra</td>
<td>The University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA</td>
</tr>
<tr>
<td>Vivek Mittal</td>
<td>Department of Cardiac 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</td>
</tr>
<tr>
<td>Nicole L. Moore</td>
<td>Dame Roma Mitchell Cancer Research Laboratories, Adelaide University/Hanson Institute, Adelaide, South Australia</td>
</tr>
<tr>
<td>John C. Morris, MD</td>
<td>Metabolism Branch, National Cancer Institute, NIH, Bethesda, MD, USA</td>
</tr>
<tr>
<td>Kyle W. Muir</td>
<td>Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London, UK</td>
</tr>
<tr>
<td>Karl Munger</td>
<td>Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA</td>
</tr>
<tr>
<td>Willscott E. Naugler</td>
<td>Oregon Health and Sciences University, Department of Medicine, Division of GI and Hepatology, Portland, OR, USA</td>
</tr>
<tr>
<td>Milena S. Nicoloso</td>
<td>RNA Interference and Non-coding RNA Center and the Department of Experimental Therapeutics, University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA</td>
</tr>
<tr>
<td>Moriah H. Nissan</td>
<td>Human Oncology and Pathogenesis Program, and Louis V. Gerstner Jr. Graduate School of Biomedical Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Benjamin F. O’Connor</td>
<td>Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA</td>
</tr>
<tr>
<td>Kenneth Offit</td>
<td>Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>J. Wolter Oosterhuis</td>
<td>Department of Pathology, Erasmus MC – University Medical Center Rotterdam, Daniel den Hoed Cancer Center, Josephine Nefkens Institute, Rotterdam, the Netherlands</td>
</tr>
<tr>
<td>Arne Östman</td>
<td>Cancer Center Karolinska, Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden</td>
</tr>
<tr>
<td>Vassiliki Papadimitrakopoulou</td>
<td>University of Texas M.D. Anderson Cancer Center, Houston, TX, USA</td>
</tr>
<tr>
<td>Luis F. Parada</td>
<td>Department of Developmental Biology, University of Texas Southwestern Medical Center, Dallas, TX, USA</td>
</tr>
<tr>
<td>Laura Pasqualucci, MD</td>
<td>Institute for Cancer Genetics and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA</td>
</tr>
<tr>
<td>Ido Paz-Priel, MD</td>
<td>Departments of Oncology and Pediatrics, Division of Pediatric Oncology, Johns Hopkins University, Baltimore, MD, USA</td>
</tr>
<tr>
<td>Erin M. Perchiniak</td>
<td>Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University College of Medicine, Columbus, OH, USA</td>
</tr>
<tr>
<td>Richard G. Pestell</td>
<td>Department of Cancer Biology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Daniel Pinkel</td>
<td>Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA</td>
</tr>
<tr>
<td>Michael Pollak, MD</td>
<td>Department of Oncology, McGill University, Montreal, Quebec, Canada</td>
</tr>
<tr>
<td>Marshall R. Posner</td>
<td>Mount Sinai Medical Center, Tisch Cancer Institute, Icahn School of Medicine, New York, NY, USA</td>
</tr>
<tr>
<td>Name</td>
<td>Affiliation</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Karen Pulford</td>
<td>Nuffield Division of Clinical Laboratory Sciences, Radcliffe Department of Medicine, University of Oxford, Oxford, UK</td>
</tr>
<tr>
<td>Yun Qiu</td>
<td>Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, USA</td>
</tr>
<tr>
<td>Kelly Quesnelle</td>
<td>University of Pittsburgh Medical Center, Pittsburgh, PA, USA</td>
</tr>
<tr>
<td>Andreas Reiter</td>
<td>Medizinische Klinik, Universitätsmedizin Mannheim, Germany</td>
</tr>
<tr>
<td>Marsha Reyngold</td>
<td>Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Kim L. Rice</td>
<td>Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA</td>
</tr>
<tr>
<td>Thomas Ried, MD</td>
<td>Section of Cancer Genomics, Genetics Branch, Center for Cancer Research /NCI/NIH, Bethesda, MD, USA</td>
</tr>
<tr>
<td>David L. Rimm MD, PhD</td>
<td>Department of Pathology, Yale University School of Medicine, New Haven, CT, USA</td>
</tr>
<tr>
<td>Mostafa Ronaghi</td>
<td>Illumina, Inc., San Diego, CA, USA</td>
</tr>
<tr>
<td>Charles L. Sawyers, MD</td>
<td>Howard Hughes Medical Institute, Chevy Chase, MD, and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Christof Schneider, MD</td>
<td>Institute for Cancer Genetics and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA</td>
</tr>
<tr>
<td>Roger A. Schultz</td>
<td>Signature Genomics, Spokane, WA, USA</td>
</tr>
<tr>
<td>Vikas Sehdev</td>
<td>Department of Surgery and Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN, USA</td>
</tr>
<tr>
<td>Sohela Shah</td>
<td>Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Eltan Shaullan</td>
<td>Department of Biochemistry and Molecular Biology, IMRJC, The Hebrew University – Hadassah Medical School, Jerusalem, Israel</td>
</tr>
<tr>
<td>Jerry W. Shay</td>
<td>University of Texas Southwestern Medical Center, Department of Cell Biology, Dallas, TX, USA</td>
</tr>
<tr>
<td>Yousef Shiloh</td>
<td>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</td>
</tr>
<tr>
<td>Keiran Smalley</td>
<td>Department of Molecular Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA</td>
</tr>
<tr>
<td>David B. Solit, MD</td>
<td>Human Oncology and Pathogenesis Program, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Allan D. Spigelman</td>
<td>UNSW St Vincent's Clinical School, Cancer Services, St Vincent's &amp; Mater Health, Sydney, Hereditary Cancer Clinic, St Vincent's Hospital, The Kinghorn Cancer Centre, Sydney, NSW, Australia</td>
</tr>
<tr>
<td>Zsofia K. Stadler</td>
<td>Department of Medicine, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA</td>
</tr>
<tr>
<td>Tinna Stevnsner</td>
<td>Danish Centre for Molecular Gerontology and Danish Aging Research Center, University of Aarhus, Department of Molecular Biology, Denmark</td>
</tr>
<tr>
<td>Derek L. Stirewalt</td>
<td>Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA</td>
</tr>
<tr>
<td>Scott A. Stuart</td>
<td>Division of Hematology-Oncology, Department of Medicine, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA</td>
</tr>
<tr>
<td>Grace K. Suh, MD</td>
<td>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</td>
</tr>
<tr>
<td>Robert S. Svatok</td>
<td>Department of Urology, the University of Texas M. D. Anderson Cancer Center, Houston, TX, USA</td>
</tr>
<tr>
<td>Ayumu Taguchi</td>
<td>Fred Hutchinson Cancer Research Center, Seattle, WA, USA</td>
</tr>
<tr>
<td>Bin T. Teh, MD, PhD</td>
<td>National Cancer Centre of Singapore, Duke-NUS Graduate Medical School, Singapore, and Cancer Science Institute of Singapore</td>
</tr>
</tbody>
</table>
List of contributors

Xinchen Teng
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 Bioelectrics, 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
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
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.