



The Molecular Biology of Cancer

A Bridge from Bench to Bedside

Edited by Stella Pelengaris and Michael Khan

SECOND EDITION

 WILEY-BLACKWELL



Table of Contents

[Title page](#)

[Copyright page](#)

[Contributors](#)

[Preface to the Second Edition](#)

[Reviews of the First Edition](#)

[Acknowledgments](#)

[Dedication](#)

[About the Companion Website](#)

[Introduction](#)

[1 Overview of Cancer Biology](#)

[Introduction](#)

[Cancer incidence and epidemiology](#)

[Towards a definition of cancer](#)

[Causes of cancer](#)

[Cancer is a genetic disease](#)

[Cancers \(and Darwin's finches\) evolve by mutation and natural selection](#)

[Blame the parents - inherited single gene defects and susceptibility to cancer](#)

[The cancer "roadmap" - What kinds of genes are epimutated in cancer?](#)

[Viruses and the beginnings of cancer biology](#)

[Hens and teeth or bears and woods? The hens have it - cancer is rare](#)

[The barriers to cancer](#)

[What is the secret of cancer developme . . . "timing"](#)

[Location, location, location - the cancer environment: nanny or spartan state](#)

[Cancer goes agricultural](#)

[Cancer superhighways - blood vessels and lymphatics](#)

[On your bike and turn the lights off before you go](#)

[Catching cancer](#)

[Hammering the hallmarks](#)

[Painting a portrait of cancer](#)

[The drugs don't work](#)

[Mechanism of origin rather than cell of origin - towards a new functional taxonomy of cancer](#)

[Is it worth it?](#)

[Conclusions and future directions](#)

[Appendix 1.1 History of cancer](#)

[2 The Burden of Cancer](#)

[Introduction](#)

[Lung cancer](#)

[Breast cancer](#)

[Colorectal cancer](#)
[Carcinoma of the prostate](#)
[Renal carcinoma](#)
[Skin cancer](#)
[Carcinoma of the cervix](#)
[Hematological malignancies](#)
[Conclusions and future directions](#)

[3 Nature and Nurture in Oncogenesis](#)

[Introduction](#)
[Risk factors](#)
[Preventing cancers](#)
[Cancer genetics - in depth](#)
[Cancer genomics](#)
[Gene-environment interactions](#)
[Mutations and treatment](#)
[Chemoprevention of cancer](#)
[Risk factors act in combination](#)
[Environmental causes of cancer](#)
[The clinical staging and histological examination of cancer](#)
[Screening and biomarkers](#)
[Somatic gene mutations, epigenetic alterations and multistage tumorigenesis](#)
[Conclusions and future directions](#)

[4 DNA Replication and the Cell Cycle](#)

[Introduction](#)
[The cell cycle - overview](#)

[Phases of the cell cycle](#)

[The cell-cycle engine: cyclins and kinases](#)

[Regulation by degradation](#)

[Regulation by transcription](#)

[MicroRNAs and the cell cycle](#)

[Chromatin](#)

[DNA replication and mitosis](#)

[Checkpoints - putting breaks on the cell-cycle engine](#)

[The DNA damage response \(DDR\)](#)

[The checkpoints](#)

[Cell-cycle entry and its control by extracellular signals](#)

[Changes in global gene expression during the cell cycle](#)

[Cell cycle and cancer](#)

[Drugging the cell cycle in cancer therapies](#)

[Conclusions and future directions](#)

[5 Growth Signaling Pathways and the New Era of Targeted Treatment of Cancer](#)

[Introduction](#)

[Growth factor regulation of the cell cycle](#)

[Growth homeostasis and tissue repair and regeneration](#)

[Regulated and deregulated growth](#)

[Cellular differentiation](#)

[Tissue growth and the “angiogenic switch”](#)

[Cancers and nutrients](#)

[Growth factor signaling pathways](#)
[A detailed description of signal transduction pathways and their subversion in cancer](#)
[Translational control and growth](#)
[Conclusions and future directions](#)

[6 Oncogenes](#)

[Introduction](#)
[The oncogenes](#)
[The discovery of oncogenes ushers in the new era of the molecular biology of cancer](#)
[Overview of oncogenes](#)
[Types of oncogenes](#)
[Oncogene collaboration - from cell culture to animal models](#)
[The c-MYC oncogene](#)
[The RAS superfamily](#)
[SRC - the oldest oncogene](#)
[BCR-ABL and the Philadelphia chromosome](#)
[The BCL-2 family](#)
[Biologically targeted therapies in cancer and the concept of "oncogene addiction"](#)
[Conclusions and future directions](#)

[7 Tumor Suppressors](#)

[Introduction](#)
[The "two-hits" hypothesis: loss of heterozygosity \(LOH\)](#)
[Haploinsufficiency in cancer](#)
[Epigenetic events](#)

[Definition of a tumor suppressor](#)
[The retinoblastoma protein family](#)
[p53/TP53](#)
[INK4a/ARF](#)
[The p53 and RB pathways in cancer](#)
[Senescence and immortalization: Role of RB and p53](#)
[Tumor suppressors and the control of cell proliferation](#)
[Tumor suppressors and control of the DNA damage response and genomic stability](#)
[The microRNAs and tumor suppressors](#)
[Conclusions and future directions](#)
[Acknowledgments](#)

[8 Cell Death](#)

[Introduction](#)
[An historical perspective](#)
[Apoptosis in context](#)
[Apoptosis as a barrier to cancer formation](#)
[Apoptosis versus necrosis](#)
[Cell death by necrosis - not just inflammatory](#)
[The pathways to apoptosis](#)
[The apoptosome - "wheel of death"](#)
[Caspases - the initiators and executioners of apoptosis](#)
[The IAP family - inhibitors of apoptosis and much more](#)
[The central role of MOMP and its regulators in apoptosis - the BCL-2 family](#)

[Mitochondrial outer membrane permeabilization \(MOMP\)](#)

[Endoplasmic reticulum stress](#)

[Stress-inducible heat shock proteins](#)

[Tumor suppressor p53](#)

[Oncogenic stress: MYC-induced apoptosis](#)

[Autophagy – a different kind of cell death and survival](#)

[Cell death in response to cancer therapy](#)

[Exploiting cell death \(and senescence\) in cancer control](#)

[Conclusions and future directions](#)

[9 Senescence, Telomeres, and Cancer Stem Cells](#)

[Introduction](#)

[Senescence](#)

[Conclusions and future directions](#)

[10 Genetic Instability, Chromosomes, and Repair](#)

[Introduction](#)

[Telomere attrition and genomic instability](#)

[Sensing DNA damage](#)

[Repairing DNA damage](#)

[Checkpoints](#)

[Microsatellites and minisatellites](#)

[Chaperones and genomic instability](#)

[Cancer susceptibility syndromes involving genetic instability](#)

[Genomic instability and colon cancer](#)

[Conclusions and future directions](#)

[11 There Is More to Cancer than Genetics: Regulation of Gene and Protein Expression by Epigenetic Factors, Small Regulatory RNAs, and Protein Stability](#)

[Introduction](#)

[The language of epigenetics](#)

[Epigenetics](#)

[Methylation of DNA](#)

[Acetylation of histones and other posttranslational modifications](#)

[Epigenetics and cancer](#)

[CIMP and MIN and the “mutator phenotype”](#)

[Imprinting and loss of imprinting](#)

[Clinical use of epigenetics](#)

[Regulation of translation](#)

[Noncoding RNA and RNA interference](#)

[Therapeutic and research potential of RNAi](#)

[Treatments based on miRNA](#)

[Regulating the proteins](#)

[Therapeutic inhibition of the proteasome](#)

[Receptor degradation](#)

[Wrestling with protein transit - the role of SUMO and the promyelocytic leukemia \(PML\) body](#)

[Conclusions and future directions](#)

12 Cell Adhesion in Cancer

Introduction

Adhesive interactions with the extracellular matrix

Cell-cell interactions

Critical steps in the dissemination of metastases

E-cadherin downregulation in cancer leads to migration

Epithelial-mesenchymal transitions

Integrins, metalloproteinases, and cell invasion

Survival in an inappropriate environment

Conclusions

13 Tumor Immunity and Immunotherapy

Introduction

Endogenous immune response

Effector cells in tumor immunity

Tumor antigens

Antigen-specific therapy of cancer

Clinical trials in vaccine therapy

Cytokine therapy of cancer

Tumor immune evasion

Clinical trials in immunomodulatory therapy

Conclusions

14 Tumor Angiogenesis

Introduction

General principles of new vessel growth

Pathological neovascularization: tumor vessels

Basic concepts in tumor angiogenesis: the angiogenic switch

Vascular growth and differentiation factors: stimulators of the angiogenic switch

Role of inhibitors in angiogenesis

Clinical outcomes and future directions

Acknowledgments

15 Cancer Chemistry: Designing New Drugs for Cancer Treatment

Introduction

Historical perspective

The drug discovery process and preclinical development of a drug

Questions remaining

Conclusions and future directions

16 Biologically Targeted Agents from Bench to Bedside

Introduction

Targeted therapies

Cancer cell heterogeneity

Finding the molecular targets

Tumor regression in mice by inactivating single oncogenes

Targeted cancer therapies

Targeting oncogenes to treat cancer?

The concept of synthetic lethality and collateral vulnerability

[Clinical progress in biological and molecular targeted therapies](#)
[Molecular targeted drugs - an inventory](#)
[DNA damage responses](#)
[Transcription factors](#)
[Targeting epigenetic regulation of gene expression](#)
[Hitting the extrinsic support network and preventing spread](#)
[Gene therapy, antisense, and siRNA](#)
[Resistance to targeted therapies - intrinsic resistance and emergence of secondary pathways and tumor escape](#)
[Biomarkers to identify optimal treatments and tailored therapies](#)
[Pharmacogenetics and pharmacogenomics](#)
[Clinical trials in cancer](#)
[Conclusions and future directions](#)

[17 The Diagnosis of Cancer](#)

[Introduction](#)
[Clinical manifestations](#)
[Investigations in oncological practice](#)
[Non-invasive imaging techniques](#)
[Future novel uses of imaging](#)
[Proteomics and microarrays](#)
[Circulating tumor cells](#)
[Disease staging](#)
[Conclusions and future directions](#)

18 Treatment of Cancer: Chemotherapy and Radiotherapy

Introduction

Radiotherapy physics

Radiobiology

Treatment planning

Recent advances

Chemoradiation

Conclusion

19 Caring for the Cancer Patient

Introduction

Key concepts

Communication with the cancer patient

When is palliative care appropriate for cancer patients?

Palliative care assessment

Symptom control

Respiratory symptoms

Nausea and vomiting

Bowel obstruction

Constipation

Fatigue

Cachexia and anorexia

Psychological problems

The dying patient

Supportive care

An example of the care of a cancer patient

Questions remaining

[Conclusions and future directions](#)

[20 Systems Biology of Cancer](#)

[Introduction](#)

[Information flow in cells](#)

[Model organisms and cancer models](#)

[Array-based technologies: genomics, epigenomics, and transcriptomics](#)

[SNPs, the HapMap, and the identification of cancer genes](#)

[Cancer mRNA expression analysis](#)

[CGH arrays, CpG island microarrays, and CHIP-on-Chip](#)

[Next-generation sequencing](#)

[Proteomics](#)

[Posttranslational modifications](#)

[Protein complexes and cellular networks](#)

[Clinical applications of proteomics](#)

[Toponomics: investigating the protein network code of cells and tissues](#)

[Processing the images from the cyclical imaging procedures](#)

[Structure, code, and semantics of the toponome: a high-dimensional combinatorial problem](#)

[Detecting a cell surface protein network code: lessons from a tumor cell](#)

[The molecular face of cells in diseases](#)

[Individualized medicine and tailored therapies](#)

[Discussion and conclusion](#)

[Internet resources](#)

[Appendix 20.1 Techniques for the generation of genetically altered mouse models of cancer](#)

[Glossary](#)

[Answers to Questions](#)

[Index](#)



The Molecular Biology of Cancer

A Bridge From Bench to Bedside

SECOND EDITION

EDITED BY

Stella Pelengaris

Pharmalogos Ltd, UK

and

Michael Khan

University of Warwick, UK

 **WILEY-BLACKWELL**

A John Wiley & Sons, Inc., Publication

This edition first published 2013 © 2013 by John Wiley & Sons, Inc.

© 2006 by Stella Pelengaris, Michael Khan, William P. Steward, Maria Blasco, Cassian Yee, David Shima, Charles Streuli, Norbert C.J. de Wit, Nicky Rudd, Christiana Ruhrberg, Anne Thomas, Esther Waterhouse, and Martine Roussel

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.

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, P019 8SQ, UK

Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK

The Atrium, Southern Gate, Chichester, West Sussex, P019 8SQ, UK

111 River Street, Hoboken, NJ 07030-5774, USA

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

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

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

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names,

service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

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 the respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. It is sold on the understanding that the publisher is not engaged in rendering professional services and neither the publisher nor the author shall be liable for damages arising herefrom. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

Library of Congress Cataloging-in-Publication Data

The molecular biology of cancer / edited by Stella Pelengaris and Michael Khan. – Second edition.

pages cm

Includes bibliographical references and index.

ISBN 978-1-118-02287-0 (hardback : alk. paper) – ISBN 978-1-118-00881-2 (pbk. : alk. paper) 1. Cancer–Molecular aspects. 2. Cancer–Genetic aspects. 3. Cancer cells. I. Pelengaris, Stella, editor of compilation. II. Khan, Michael, editor of compilation.

RC268.4.M65 2013

616.99'4042–dc23

2012031371

A catalogue record for this book is available from the British Library.

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

Cover image: 5 μm tissue section from a specimen of colorectal carcinoma, imaged using TIS microscopy for colocation of more than 15 different cancer-related proteins. Courtesy of Nasir Rajpoot, Adnan Mujahid, Shan-E-Amad Raza (all from the Department of Computer Science, University of Warwick) and Michael Khan.

Cover design by Design Deluxe

Contributors

About the Editors

Michael Khan, PhD, FRCP, is Associate Professor of Medicine at the University Hospitals of Coventry and Warwickshire and former Head of Molecular Medicine at the University of Warwick. He was elected as a fellow of the Royal College of Physicians in 2002 and as a member of the Association of Physicians in 2004. His main research interests have been in the regulation of tissue growth and plasticity during development and in adult tissue homeostasis. Currently, he is collaborating with mathematicians and others in a systems biology approach to define key functional gene and protein networks involved in regulating cell fate and to identify new biomarkers for colorectal cancer. Dr. Khan teaches cancer biology to undergraduates and runs postgraduate training courses at masters level and beyond in cancer biology and metabolism. Michael is Chief Medical Advisor to Silence Therapeutics PLC. He has co-authored four textbooks.

Stella Pelengaris, PhD, was a Senior Research Fellow in Molecular Medicine in the Department of Biological Sciences at the University of Warwick and Warwick Medical School. While working at the Imperial Cancer Research Fund, she established a series of unique model systems for studying the role of c-Myc and apoptosis in cancer initiation and reversal. From 1999 to 2008 she and Michael Khan jointly ran the Cancer Research Group at the University of Warwick, where, in collaboration with Gerard Evan, they confirmed the inherent tumor suppressor activity of c-Myc (apoptosis) as a major barrier to oncogenic activity of c-Myc. Stella is now director of Pharmalogos Ltd, in which capacity she

provides advice to biotechnology and pharmaceutical companies on promising novel targets for future oncology therapy developments.

About the Co-Authors

Maria A. Blasco PhD is Director of the Spanish National Cancer Research Centre (CNIO) and Head of the Telomeres and Telomerase Group. She obtained her PhD from Universidad Autónoma de Madrid (Spain) in 1993. That same year, she joined Carol W. Greider's lab at Cold Spring Harbor Laboratory (New York, USA). In 1997 she returned to Spain and joined the CNIO in 2003 as Director of the Molecular Oncology Programme and Leader of the Telomeres and Telomerase Group. She was appointed CNIO Director in 2011.

Norbert C.J. de Wit PhD is a clinical chemist at Maastricht University Medical Center (The Netherlands) with a subspecialization in laboratory hematology. He undertook a PhD at Warwick University (UK) in clinical proteomics and his current research interests are in laboratory hematology and hemato-oncology.

Bruno Morgan is Professor of Cancer Imaging at the University of Leicester and University Hospitals Leicester. He studied at Oxford Medical School and subsequently has trained in both hospital medicine and radiology. He has an active research program in developing CT and MRI applications to monitor drug therapy.

Ana M. Pizarro PhD obtained her doctorate at the Universidad Autónoma de Madrid (Spain). She was awarded an Intra-European Marie Curie Fellowship to work at The University of Edinburgh, and in 2007 became a research fellow at The University of Warwick (UK).

Martine F. Roussel PhD is Professor of Molecular Oncogenesis and Co-Director of the Cancer Center Signal Transduction Program at St. Jude, USA. She is also a Professor in the Department of Molecular Sciences at UT Memphis. She is a major figure in global cancer education and research with nearly 200 publications, many in the area of tumor suppression.

Nicky Rudd is Clinical Lead, Cancer & Haematology Services and Consultant in Palliative Medicine at the Leicester Royal Infirmary and LOROS, UK. She is also chair of the Specialist Training Committee for Palliative Medicine for the UK. Her main interests are hospital palliative care teams, communication skills training and teaching.

Christiana Ruhrberg obtained her PhD in biochemistry from Imperial College London and trained as a postdoctoral fellow in neuronal biology at the National Institute for Medical Research and in vascular biology at the Imperial Cancer Research Fund, both in London. Being awarded a Career Development Fellowship from the UK Medical Research Council and then a Lectureship from University College London, she now heads a research group that investigates the mechanisms of physiological angiogenesis and neural development.

Peter J. Sadler FRS obtained his BA, MA, and DPhil at the University of Oxford. Subsequently he was an MRC Research Fellow at the University of Cambridge and National Institute for Medical Research, and Professor at Birkbeck College, University of London, Crum Brown Chair of Chemistry at the University of Edinburgh, and from 2007 Chair of Chemistry at the University of Warwick. He is a Fellow of the Royal Society of Edinburgh (FRSE) and the Royal Society of London (FRS), and a European Research Council Advanced Investigator. His research interests are centered on the design and mechanism of action of metal-based anticancer compounds.

Walter Schubert MD is Associated Professor (HD) for Medical Neurobiology and Head of the Molecular Pattern Recognition Research (MPRR) group at Otto-von-Guericke-University Magdeburg, Germany. He studied neurology/psychiatry, histology, and molecular cell biology at universities of Bonn and Heidelberg (Center for Molecular Biology), Germany and is Visiting Professor of Toponomics at the Max-Planck-CAS (CAS-MPG) Partner Institute of Computational Biology, Shanghai, China. He also founded the field of toponomics and invented the topomome imaging technologies MELC and TISTM.

William P. Steward is Professor of Medical Oncology and Head of the Department of Cancer Studies and Molecular Medicine at the University of Leicester and an oncologist at the Leicester Royal Infirmary, UK. He has a major interest in new drug development, particularly in the fields of colorectal and hepatobiliary/pancreas cancers, and is working in an extensive translational research program in chemoprevention focusing on biomarker development and identification of novel agents.

Charles H. Streuli PhD is Professor of Cell Biology at the University of Manchester, UK and Director of the Wellcome Trust Centre for Cell-Matrix Research. He is also a founding member of the Manchester Breast Centre and the Breakthrough Research Unit in Manchester. His research focuses on how cellular adhesion regulates breast epithelial cell proliferation, differentiation, and polarity.

Anne L. Thomas PhD FRCP is Reader and Consultant in Medical Oncology at the University of Leicester and an oncologist at the Leicester Royal Infirmary, UK.

Peter Walden is a biochemist with specialization in molecular and cellular immunology. He received his PhD from Tübingen University, Germany worked at MIT, Cambridge, USA and MPI for Biology, Tübingen and is Head

of the Tumor Immunology Translational Research Group at Charité – Universitätsmedizin Berlin, Germany.

Esther Waterhouse is a consultant in palliative medicine at University Hospitals Leicester and LOROS Hospice in Leicester, UK. She has a particular interest in communication skills training and education.

Cassian Yee MD, PhD is an associate member of the Program in Immunology in the Clinical Research Division at Fred Hutchinson Cancer Research Center and an Associate Professor at the University of Washington School of Medicine (USA). He is a world authority on immunotherapy of melanoma and ovarian cancer.

Preface to the Second Edition

Based on our extensive experience of teaching undergraduates and postgraduates, it became clear that no single current resource covered in detail the cellular and molecular changes that give rise to cancer alongside the basic principles of biology and clinical practice, without which these cannot be readily understood. We had not intended to write a textbook at this stage in our careers, but realized that there was a real need for such a work for undergraduates, medical students, and even established researchers in the field. Very few cancer molecular biology textbooks were available that started at the beginning, using a format and language easy to digest, and included not only a comprehensive description of all aspects of cancer biology but also important chapters on diagnosis, treatment, and care of cancer patients.

Much has changed since the first edition and we have responded to the explosion in knowledge around targeted therapies and how these are developed and tested. Moreover, the emergent field of systems biology has impacted strongly on cancer biology, and may well revolutionize the way in which we view, study, and treat cancer in the near future, in particular with the inextricable association with concepts such as individualized and tailored therapies. We follow a similar structure to the first edition, but all chapters have been extensively revised, new chapters have been added, and an even stronger up-front emphasis has been placed on first presenting easy-to-digest models served up in plain English.

Students are first introduced to an overview of the cancer cell and important new concepts and those which are only just emerging (Chapter 1), and of selected human cancers

(Chapter 2), following which the textbook covers in depth those key cellular processes of greatest relevance to cancer. Thus, Chapters 3–14 cover the full range of cancer-relevant biology, including highly topical and important areas such as apoptosis, telomeres, DNA damage and repair, cell adhesion, angiogenesis, immunity, epigenetics, and the proteasome, as well as traditionally important areas such as cell-cycle control, growth regulation, oncogenes, and tumor suppressors. A major improvement on the first edition has been the inclusion of a detailed account of how cancer drugs are developed and brought to market. Moreover, the great strides forward in targeted treatments have allowed us to introduce Chapter 16, specifically to link the subject of each of the scientific chapters to classes of newly available treatments or to those in various stages of development. The result is that the science is put firmly into the context of treating cancer patients – the relevance becomes crystal clear.

The book then gives a description of cancer diagnosis, treatment, and care of cancer patients, which is not only essential to medical students but also important for cancer researchers and biology students who need to have a broader view of cancer and its impact. Finally, Chapter 20 concludes with a vision of how the future of cancer biology and oncology may be directed by interdisciplinary sciences, such as the exciting field of systems biology and the new technologies that underpin it.

The role of textbooks as information repositories is increasingly under threat. Yet even now that we are well into the new millennium, with students and researchers alike bathed in seemingly limitless available information on the World Wide Web, textbooks still exist. Why is this? With the near-universal availability of Internet access to students and researchers, the most current information is potentially available to any interested party almost instantaneously. No

printed source can hope to provide the same immediacy of the latest breakthroughs or experimental findings, although they are free of the distractions of online gambling, 24-hour shopping, and less savory diversions that plague the Internet. However, limitless information creates new problems, namely how to evaluate, correlate, and place into context this wealth of knowledge. More than a million cancer-related publications are referenced on Medline alone, and even for the initiated it can prove daunting to attempt to construct a balanced overview of the many aspects of cell and molecular biology that impact on cancer. Because of these difficulties, one of the key aims of this book is to provide in a single source the necessary framework within which new information can subsequently be aligned and a more comprehensive, but still contextual, understanding of cancer achieved. In particular, we have taken the opportunity to highlight controversial areas and to identify areas of research promise, while establishing potential links between often diverse subdisciplines in a coordinated and accessible way. It is hoped that, having read this book, the reader will be suitably equipped to understand the significance and relevance to cancer of a new publication and be able to place the work into an overall picture of the disease. Moreover, the book should also provide established cancer researchers with valuable insights into the important questions that remain to be addressed.

The issue of references, how many and where to cite, is often difficult to judge for a textbook. One has to balance the flow of the text with the need to give pointers to the reader for further information and to highlight key studies. This textbook can be used by undergraduates in biology and medical students and can be used alongside cancer biology courses structured either for a quarter or semester system. Moreover, the book will be of value to those preparing for professional exams in medicine and oncology and for

established cancer researchers seeking a single-source overview of all aspects of cancer.

Features

We have included a number of features to facilitate the use of this textbook to teach cancer biology:

- Each chapter begins with a series of bullet points which explain the key concepts and illustrate areas of controversy in plain English. This is the platform on which the more complicated and detailed processes and models will be built throughout the rest of the chapter.
- Each chapter builds on concepts learned in previous chapters and is organized in a similar fashion, starting with an introduction and ending with a “Conclusions and future directions” section, a list of key outstanding questions remaining in the field, suggestions for further reading, and questions for student review.
- All the chapters contain textboxes that provide additional and relevant information as it relates to a described concept and are fully illustrated throughout.

Reviews of the First Edition

“Pelengaris, Khan, and the contributing authors are to be applauded. The Molecular Biology of Cancer is a comprehensive and readable presentation of the many faces of cancer from molecular mechanisms to clinical therapies and diagnostics. This book will be welcomed by neophyte students, established scientists in other fields, and curious physicians.”

Dean Felsher, Stanford University

“The explosion of information on the molecular biology of cancer, and its widespread and immediate availability via the internet, provides major challenges for those engaged in cancer treatment and research. A single up-to-date reference textbook on this topic is needed more than ever. This book will go a long way towards meeting this need, providing a valuable resource for a range of individuals and departments.”

Stan Kaye, Royal Marsden Hospital, London

Acknowledgments

An enormous number of talented scientists contributed to the knowledge described in this textbook. We acknowledge the many colleagues past and present whose important work could not be referenced in the text due to space constraints. In addition, we apologize if we failed to adequately identify contributions in the reference section at the end of this text. This oversight was not intentional, but rather a reflection of the overwhelming number of contributors to this field.

We thank mentors past and present for their help and encouragement: Martin Raff and Anne Mudge for making cell biology interesting and intelligible and Gerard Evan for introducing us to the world of cancer research. We thank our friends and colleagues who took time from their hectic research and clinical commitments to contribute to this book. In addition to those mentioned in the first edition, we especially thank our dedicated research team, Sylvie, Luxian, Yi-Fang, Elena, and Liam for bearing with us while we were writing and editing this book and for their patient reading and suggestions for improving the text. A special thanks is due to David Epstein FRS, our friend and colleague, for taking on too many tasks while we were occupied with this venture as well as for reading several chapters. We also greatly appreciate the suggestions and the gentle way in which these were presented by our friend Anthony Parker. Finally, we thank freelance project manager Nik Prowse and freelance copy-editors Cheryl Adam and Harriet Stewart-Jones, who have painstakingly teased out our many abuses of English and have helped us eliminate every tortured metaphor and incomprehensible sentence. Any that remain are entirely our fault. We are also very