
Molecular Pathology Library

Series Editor
Philip T. Cagle, MD

For further volumes:
<http://www.springer.com/series/7723>

Antonia R. Sepulveda • John P. Lynch
Editors

Molecular Pathology of Neoplastic Gastrointestinal Diseases

 Springer

Editors

Antonia R. Sepulveda, MD, PhD
Department of Pathology & Cell Biology
Columbia University
New York, NY, USA

John P. Lynch, MD, PhD
Division of Gastroenterology
University of Pennsylvania
Philadelphia, PA, USA

ISSN 1935-987X ISSN 1935-9888 (electronic)
ISBN 978-1-4614-6014-5 ISBN 978-1-4614-6015-2 (eBook)
DOI 10.1007/978-1-4614-6015-2
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2012954430

© Springer Science+Business Media New York 2013

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

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

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Critical molecular mechanisms underlying gastrointestinal (GI) neoplasia have been substantially unraveled in recent years. This has resulted from technological advances such as the genome project data and large-scale “omic” methods, combined with the application of classic molecular and chemical testing approaches and established procedures for pathologic evaluation of tissue and cellular samples. This progress is leading to the development of new approaches for treatments and, in parallel, novel diagnostic workups of gastrointestinal cancers, integrating specific molecular testing in routine pathology practice. Moreover, identification of disease susceptibility genes has enabled the medical community to better manage and prevent diseases that have hereditary traits.

While significant advances have been harnessed, much remains to be learned in the spectrum of neoplastic diseases of the gastrointestinal tract. Critical elements of research that have allowed progress in the various fields of GI neoplastic disease include the availability of animal models, cell culture models, and basic and translational research approaches utilizing prospective or archived specimen material, and such advances are reviewed here.

In this book, we review the molecular aspects that characterize the spectrum of neoplasms that affect the GI tract, providing the reader with up-to-date knowledge at the level of (1) the molecular basis of the individual neoplasms, spanning the carcinomas of esophagus, stomach, small bowel, colon, and rectum; neuroendocrine tumors; and gastrointestinal stromal tumors; (2) molecular testing approaches for diagnosis or for characterization of target genes for selective targeted therapies, with a review of recommended guidelines for clinical application whenever available; (3) molecular testing for hereditary predisposition or disease risk for GI cancers.

The last three chapters in the book are forward-looking, focused on the molecular mechanisms of metastasis, detection of circulating tumor cells and nucleic acids, and the use of tumor markers for gastrointestinal cancers. These are current areas of research interest and future clinical practice and serve to complement the information reviewed for the individual neoplasms.

It is clear that the rapid pace of discovery is unmatched by the definitive validation of many molecular alterations that are identified through ongoing basic and translational research of cancer. Given this scenario we felt it would be impractical to provide coverage of all areas of research in each tumor type, and ultimately, authors for each of the chapters identified what in their opinion are the most relevant topics to cover for each tumor type at the time of writing, realizing that novel findings that may be clinically relevant may become a reality as the book is published. Nevertheless, basic principles of molecular pathogenesis and diagnosis of GI cancers are extensively covered and will remain a foundation for clinical practice as new knowledge emerges.

We expect that this book will be useful to a large spectrum of professionals, from pathologists, laboratorians, clinical gastroenterologists and oncologists, and trainees at various levels such as medical students, residents, fellows, and postdoctoral fellows, as well as investigators interested in the area of gastrointestinal cancer.

New York, NY, USA
Philadelphia, PA, USA

Antonia R. Sepulveda, MD, PhD
John P. Lynch, MD, PhD

Contents

Part I Introduction

- 1 Mechanisms of Gastrointestinal Carcinogenesis**..... 3
Frank I. Scott and John P. Lynch

Part II Epithelial Neoplastic Disease

- 2 Targeted Therapies and Molecular Diagnostics of Gastrointestinal Cancers**..... 33
Davendra Sohal, Antonia R. Sepulveda, and Weijing Sun
- 3 Molecular Pathology of Barrett’s Metaplasia and Esophageal Adenocarcinoma** 43
Mamoun Younes
- 4 Molecular Pathology of Squamous Carcinomas of the Esophagus** 53
Rohinton S. Tarapore and Jonathan P. Katz
- 5 Molecular Mechanisms and Pathology of Gastric Carcinogenesis: Sporadic Cancers** 67
Shuko Harada and Antonia R. Sepulveda
- 6 Hereditary Diffuse Gastric Cancer and Other Gastric Cancers Associated with Hereditary Predisposition Syndromes**..... 83
Fátima Carneiro, Carla Oliveira, and Raquel Seruca
- 7 Cancer Predisposition Syndromes of the Gastrointestinal Tract** 109
Ian S. Hagemann and Antonia R. Sepulveda
- 8 Molecular Pathology of Colon and Small Bowel Cancers: Sporadic Type**..... 131
Asif Rashid
- 9 Cancers of the Rectum and Anal Canal**..... 141
Jenia Jenab-Wolcott and Bruce Giantonio
- 10 Molecular Pathology of Inflammatory Bowel Disease-Associated Neoplasia**..... 173
Takeshi Uehara, Deqin Ma, and Antonia R. Sepulveda

Part III Non-epithelial Neoplastic Tumors

- 11 Molecular Biology and Pathology of Gastrointestinal Stromal Tumors**..... 181
Paul J. Zhang
- 12 Neuroendocrine Tumors**..... 193
Joseph R. Pisegna

Part IV Metastatic Disease and Tumor Markers

| | |
|---|-----|
| 13 Molecular Mechanisms of Tumor Metastasis | 213 |
| Andrew D. Rhim, Davendra Sohal, and Hiroshi Nakagawa | |
| 14 Circulating Tumor Cells and Nucleic Acids for Tumor Diagnosis | 229 |
| Loren Joseph | |
| 15 Serological Markers of Digestive Tract Cancers | 249 |
| Jorge L. Sepulveda | |
| Index | 271 |

Contributors

Fatima Carneiro, M.D., Ph.D. Department of Pathology and Cancer Genetics Group, Institute of Molecular Pathology and Immunology of the University of Porto, Porto, Portugal

Bruce Giantonio, M.D. Department of Hematology/Oncology, University of Pennsylvania, Philadelphia, PA, USA

Ian S. Hagemann, M.D., Ph.D. Department of Pathology and Immunology, Washington University, St. Louis, MO, USA

Shuko Harada, M.D. Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, USA

Jenia Jenab-Wolcott, M.D., Ph.D. Delaware County Memorial Hospital, Drexel Hill, PA, USA

Loren Joseph, M.D. Department of Pathology, The University of Chicago, Chicago, IL, USA

Jonathan P. Katz, M.D., Ph.D. Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA, USA

John P. Lynch, M.D., Ph.D. Department of Medicine, Division of Gastroenterology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

Deqin Ma, M.D., Ph.D. Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Hiroshi Nakagawa, M.D., Ph.D. Department of Medicine, Gastroenterology Division, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Carla Oliveira, Ph.D. Cancer Genetics Group, Institute of Molecular Pathology and Immunology of the University of Porto and Medical Faculty of the University of Porto, Porto, Portugal

Joseph R. Pisegna, M.D. Division of Gastroenterology and Hepatology, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA

Asif Rashid, M.D., Ph.D. Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

Andrew D. Rhim, M.D. Department of Medicine, Gastroenterology Division, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Frank I. Scott, M.D. Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA, USA

Antonia R. Sepulveda, M.D., Ph.D. Department of Pathology & Cell Biology, Columbia University, New York, NY, USA

Jorge L. Sepulveda, M.D., Ph.D. Department of Pathology & Cell Biology, Columbia University, New York, NY, USA

Raquel Seruca, M.D., Ph.D. Cancer Genetics Group, Institute of Molecular Pathology and Immunology of the University of Porto and Medical Faculty of the University of Porto, Porto, Portugal

Davendra Sohal, M.D., M.P.H. Solid Tumor Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA

Weijing Sun, M.D. Department of Medicine, Hematology-Oncology, University of Pittsburgh School of Medicine, UPMC Cancer Pavilion, Pittsburgh, PA, USA

Rohinton S. Tarapore, M.S., Ph.D. Department of Gastroenterology, University of Pennsylvania, Philadelphia, PA, USA

Takeshi Uehara, M.D. Department of Laboratory Medicine, Shinshu University School of Medicine, Matsumoto, Japan

Mamoun Younes, M.D. Department of Pathology, University of Texas Medical School at Houston, Houston, TX, USA

Paul J. Zhang, M.D. Department of Pathology and Lab Medicine, University of Pennsylvania Medical Center, Philadelphia, PA, USA