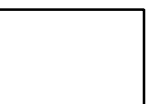
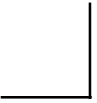


Expression Profiling of Human Tumors



EXPRESSION PROFILING OF HUMAN TUMORS

*Diagnostic and Research
Applications*

Edited by

Marc Ladanyi, MD

*Memorial Sloan-Kettering Cancer Center, New York, NY
and*

William L. Gerald, MD, PhD

Memorial Sloan-Kettering Cancer Center, New York, NY




Humana Press
Totowa, New Jersey

© 2003 Humana Press Inc.
999 Riverview Drive, Suite 208
Totowa, New Jersey 07512

www.humanapress.com

All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise without written permission from the Publisher.

The content and opinions expressed in this book are the sole work of the authors and editors, who have warranted due diligence in the creation and issuance of their work. The publisher, editors, and authors are not responsible for errors or omissions or for any consequences arising from the information or opinions presented in this book and make no warranty, express or implied, with respect to its contents.

This publication is printed on acid-free paper. 

ANSI Z39.48-1984 (American Standards Institute) Permanence of Paper for Printed Library Materials.

Cover illustrations:

Production Editor: Tracy Catanese
Cover design by Patricia F. Cleary.

For additional copies, pricing for bulk purchases, and/or information about other Humana titles, contact Humana at the above address or at any of the following numbers: Tel: 973-256-1699; Fax: 973-256-8341; E-mail: humana@humanapr.com, or visit our Website: <http://humanapress.com>

Photocopy Authorization Policy:

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Humana Press Inc., provided that the base fee of US \$20.00 per copy is paid directly to the Copyright Clearance Center at 222 Rosewood Drive, Danvers, MA 01923. For those organizations that have been granted a photocopy license from the CCC, a separate system of payment has been arranged and is acceptable to Humana Press Inc. The fee code for users of the Transactional Reporting Service is: [0-58829-122-7/03 \$20.00].

Printed in the United States of America. 10 9 8 7 6 5 4 3 2 1

Library of Congress Cataloging-in-Publication Data

Expression profiling of human tumors : diagnostic and research applications / edited by Marc Ladanyi and William L. Gerald.

p. cm.

Includes bibliographical references and index.

ISBN 0-58829-122-7 (alk. paper); 1-59259-386-0 (e-book)

1. Oncogenes. 2. Gene expression. 3. Cancer--Molecular aspects. I. Ladanyi, Marc. II. Gerald, William L.

RC268.42 .E976 2003
616.99'4042--dc21

2002032924

Preface

Advances in our knowledge of the molecular basis of cancer are at the heart of the present revolution in clinical oncology. The identification of tumor-specific molecular alterations has led to new means of diagnosis and classification, and the characterization of critical pathways regulating tumor growth is providing the potential for less toxic, more effective targeted therapy. Nonetheless, these advances had previously occurred at an agonizingly slow pace, i. e., one gene at a time. That investigative pace has now been dramatically altered by the completion of a draft of the entire human genome and the development of miniaturized high-throughput technology for genetic analysis. These extraordinary accomplishments now permit not only the monitoring of every gene sequence in a single experiment, but also a comprehensive analysis of the complex coordinated programs and pathways that contribute to the clinical phenotype of cancers. This rapid and comprehensive approach to the investigation of tumor biology has the potential to dramatically shape the future of clinical oncology.

Expression Profiling of Human Tumors is intended to provide an introduction and overview to comprehensive gene expression profiling of human tumors, one of the most promising new high-throughput investigative approaches in molecular biology. The intent was to provide not only a primer for the technology and analytical methods, but also an early assessment of the state-of-the-art with respect to both successes and pitfalls. These successes are significant and include methods of more precise diagnosis, and identification of prognostic markers, therapeutic targets, and gene expression patterns that predict therapeutic response. Nonetheless, there are significant challenges to further success, such as procurement and processing of appropriate samples, improvement and validation of technical approaches, and refinement of analytical methods for the resulting complex datasets. We have attempted to provide a balance between the basic science aspects of this work and its application to the clinical setting, but we have focused on the analysis of human tissue samples as providing the most direct means of translating findings to clinical practice. There are many complex issues that need to be considered as this type of work goes forward, and we hope this text will serve as a starting point for future discoveries.

The emphasis here on gene expression profiling is not intended to suggest that this should be considered the ultimate view of the molecular biology of the cancer cell. On the contrary, we all look forward to the day when analysis at the protein level is as comprehensive and provides as much detail as the present attempts of global gene transcript measurements. Obviously, the closer we come to assessment of the actual func-

tion of each molecule, the more accurate our abilities to correlate those with the clinical phenotype. Proteomics holds the promise to better achieve that goal but is still in its infancy with even greater hurdles to overcome than we presently face with sequence-based expression analysis. We leave that topic for future publications.

We would like to express our deep appreciation to the many authors who have provided overviews of work in their fields. These individuals have contributed their time and effort to provide highly useful information for others (sometimes while being badgered by the Editors!). We would also like to thank Ms. Fabienne Volel and Ms. Shirley Tung for excellent assistance. Finally we thank our wives, Lucta Allen-Gerald and Maureen Zakowski, for their patience and support.

Expression Profiling in Human Tumors clearly depicts the rapid advances that are occurring in clinically important areas and that will no doubt increasingly impact clinical care. We sincerely hope that our book provides information useful to all basic or clinical investigators concerned with the molecular basis of cancer and the improvement of cancer care.

William L. Gerald, MD, PhD

Marc Ladanyi, MD,

Contents

Preface	<i>vii</i>
Contributors	<i>xiii</i>
PART I. INTRODUCTION	
1 Present and Anticipated Impact of Expression Profiling Studies of Human Tumors <i>Marc Ladanyi and William L. Gerald</i>	<i>xxx</i>
PART II. TECHNICAL ASPECTS	
2 cDNA Microarrays <i>Paul S. Meltzer</i>	<i>xxx</i>
3 Oligonucleotide Microarrays <i>Marina Chicurel and Dennise Dalma-Weizhausz</i>	<i>xxx</i>
4 Serial Analysis of Gene Expression (SAGE) in Cancer Research <i>C. Marcelo Aldaz</i>	<i>xxx</i>
5 Tissue Arrays <i>Cyrus V. Hedvat</i>	<i>xxx</i>
6 Microarray Data Analysis: Cancer Genomics and Molecular Pattern Recognition <i>Pablo Tamayo and Sridhar Ramaswamy</i>	<i>xxx</i>
7 The Role of Tumor Banking and Related Informatics <i>Stephen J. Qualman, Jay Bowen, Sandra Brewer-Swartz, and Mary France</i>	<i>xxx</i>
PART III. APPLICATIONS	
8 Characterization of Gene Expression Patterns for Classification of Breast Carcinomas <i>Irene L. Andrulis, Nalan Gokgoz, and Shelley B. Bull</i>	<i>xxx</i>

9	Microarray Analysis of Colorectal Cancer <i>Dan Notterman, Carrie J. Shawber, and Wei Liu</i>	xxx
10	Gene Expression Analysis of Prostate Carcinoma <i>William L. Gerald</i>	xxx
11	Classification of Human Lung Carcinomas by mRNA Expression <i>Arindam Bhattacharjee and Matthew Meyerson</i>	xxx
12	Molecular Profiling of Bladder Cancer Using High-Throughput DNA Microarrays <i>Marta Sánchez-Carbayo and Carlos Cordon-Cardo</i>	xxx
13	Gene Expression Profiling of Renal Cell Carcinoma and its Clinical Implications <i>Masayuki Takahashi and Bin Tean Teh</i>	xxx
14	Pancreatic Ductal Adenocarcinoma <i>Christine Iacobuzio-Donahue and Ralph H. Hruban</i>	xxx
15	Gene Expression in Ovarian Carcinoma <i>Garrett M. Hampton</i>	xxx
16	Classification of Pediatric Tumors Using DNA Microarrays <i>Javed Khan and Marc Ladanyi</i>	xxx
17	Transcriptomes of Soft Tissue Tumors: Pathologic and Clinical Implications <i>Sabine C. Linn, Rob B. West, and Matt van de Rijn</i>	xxx
18	Gene Expression Profiling in Lymphoid Malignancies <i>Wing C. Chan and Louis M. Staudt</i>	xxx
19	Gene Expression Profiling of Brain Tumors <i>Meena K. Tanwar and Eric C. Holland</i>	xxx
20	Expression Profiling of Bone Tumors <i>Deborah Schofield, Timothy J. Triche, and Daniel Wai</i>	xxx
	Index	xxx

Contributors

- IRENE L. ANDRULIS, PhD • *Departments of Molecular and Medical Genetics, Fred A. Litwin Centre for Cancer Genetics, Toronto, ON, Canada*
- C. MARCELO ALDAZ, MD, PhD • *Science Park Research Division, Department of Carcinogenesis, M. D. Anderson Cancer Center, The University of Texas, Smithville*
- ARINDAM BHATTACHARJEE, PhD • *Agilent Technologies, Andover, MA*
- JAY BOWEN, MS • *Department of Laboratory Medicine, Columbus Children's Hospital, Columbus, OH*
- SANDRA BREWER-SWARTZ, MEd • *Department of Laboratory Medicine, Columbus Children's Hospital, Columbus, OH*
- SHELLEY B. BULL, PhD • *Public Health Sciences, Samuel Lunenfeld Research Institute, University of Toronto, Toronto, ON, Canada*
- WING C. CHAN, MD • *Department of Pathology and Microbiology, University of Nebraska Medial Center, Nebraska Medical Center, Omaha, NE*
- MARINA CHICUREL, PhD • *Affymetrix, Inc., Santa Clara CA*
- CARLOS CORDON-CARDO, MD, PhD • *Division of Molecular Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- DENNISE DALMA-WEISZHAUSZ, PhD • *Affymetrix, Inc., Santa Clara, CA*
- MARY FRANCE, BS • *Department of Laboratory Medicine, Columbus Children's Hospital, Columbus, OH*
- CYRUS V. HEDVAT, MD, PhD • *Department of pathology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- WILLIAM L. GERALD, MD, PhD • *Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- NALAN GOKGOZ, PhD • *Departments of Laboratory Medicine, and Pathobiology, Fred A. Litwin Centre for Cancer Genetics, Mount Sinai Hospital, Toronto, ON, Canada*
- GARRET M. HAMPTON, PhD • *Genomics Institute of Novartis Research Foundation, San Diego, CA*
- ERIC C. HOLLAND, MD, PhD • *Departments of Neurosurgery, Neurology, and Cell Biology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- RALPH H. HRUBAN, MD • *Department of Pathology, the Johns Hopkins Hospital, Baltimore, MD*
- CHRISTINE A. IACOBUZIO-DONAHUE, MD, PhD • *Departments of Pediatrics and Molecular Genetics, Microbiology, and Immunology, Robert Wood Johnson Medical School, New Brunswick, NJ*

- JAVED KHAN, MD • *Oncogenomics Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD*
- MARC LADANYI, MD • *Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- SABINE C. LINN, MD, PhD • *Department of Medical Oncology, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands*
- WEI LIU, MD, PhD • *Departments of Pediatrics and Molecular Genetics, Robert Wood Johnson Medical School, New Brunswick, NJ*
- PAUL S. MELTZER, MD, PhD • *Section of Molecular Genetics, Cancer Genetics Branch, Human Genome Research Institute, Bethesda, MD*
- MATTHEW MEYERSON, MD, PhD • *Department of Adult Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA*
- DANIEL A. NOTTERMAN, MD • *Departments of Pediatrics and Molecular Genetics, Microbiology, and Immunology, Robert Wood Johnson Medical School, New Brunswick, NJ*
- STEPHEN J. QUALMAN, MD • *Department of Laboratory Medicine, Columbus Children's Hospital, Columbus, OH*
- SRIDHAR RAMASWAMY, MD • *Department of Adult Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA*
- MATT VAN DE RIJN, MD, PhD • *Department of Pathology, Stanford University Medical Center, Stanford, CA*
- MARTA SÁNCHEZ-CARBAYO, PhD • *Division of Molecular Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- DEBORAH SCHOFIELD, MD • *Clinical Associate Professor of Pathology and Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA*
- CARRIE J. SHAWBER, PhD • *Weill Medical College, Cornell University, New York, NY*
- LOUIS M. STAUDT, MD • *Metabolism Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD*
- MASAYUKI TAKAHASHI, MD • *Department of Urology, The University of Tokushima School of Medicine, Tokushima, Japan*
- PABLO TAMAYO, PhD • *Cancer Genomics Group, Whitehead Institute, Massachusetts Institute of Technology Center for Genome Research Cambridge, MA*
- MEENA K. TANWAR, BA • *Departments of Surgery (Neurosurgery), neurology, and Cell Biology, Memorial Sloan-Kettering Cancer Center, New York, NY*
- BIN TEAN TEH, MD, PhD • *Laboratory of Cancer Genetics, Van Andel Research Institute, Grand Rapids, MI*
- TIMOTHY J. TRICHE, MD, PhD • *Professor of Pathology and Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA*
- DANIEL WAI, MS • *Keck School of Medicine, University of Southern California, Los Angeles, CA*
- ROB B. WEST, MD, PhD • *Department of Pathology, Stanford University Medical Center, Stanford, CA*