Cancer Gene Profiling

Methods and Protocols

Edited by

Robert Grützmann and Christian Pilarsky

Department of Surgery, University Hospital Carl Gustav Carus,
University Dresden, Dresden, Germany
Preface

Science is the agent between imagination and reality

(Anonymous)

During the last few years, the methods for analysing cancer-related genes on a molecular level have changed rapidly. With the advent of automated sequencing, new and faster investigations have become possible. This has led to the collection of a large number of DNA samples, such as Expressed Sequence Tag (EST) libraries whose entries run into millions. The advances in DNA sequencing technologies resulted in rapid improvements in oligonucleotide synthesising technologies, which has allowed researchers to produce oligonucleotides for each and every imaginable sequence at a low cost. Finally, the method of polymerase chain reaction (PCR), and other improvements in enzymatic \textit{in vitro} amplification of nucleic acids, gave researchers the opportunity to use low amounts of nucleic acids for analysis. This enabled the research community to investigate the populations of cells in a given tissue.

Sometimes it takes only a few advances for a technology to be successful – for example, the concept of arraying biological probes in a reproducible manner, and the use of these arrays instead of a single probe, greatly advanced biomedical research, especially as it was discovered that everything is arrayable. It has also changed the landscape of science in another way: a reduction of costs. The costs of generating such an array are high, but the costs of replicating such arrays are not. This key fact has led to a growth in the number of biotech companies that design and produce arrays, and that today more and more researchers have access to and use. Such unrestricted access to these resources has really been the key to the biomedical research revolution we see today.

In this book, we have brought together the experiences of leading scientists in the discipline of cancer gene profiling. We have included several microarray techniques, as well as methods for arraying tissues and proteomics, because cancer genes can be profiled in different ways. Such different approaches are needed to understand the key stages of cancer development, because using only one technique would be insufficient. Therefore, we attempt to give an overview of the state-of-the-art methods that will enable the reader to perform these experiments successfully. It has been written for any student or practitioner with an interest in cancer gene profiling, and can be used in any well-equipped research laboratory. It may also serve as a demonstration of the kind of analysis that is possible today and will be complementary to other textbooks in the area of biomedical research.

This book has been divided into five main sections. The first section covers techniques to get clinically relevant cancer material through the best methods of sample collection and storage.

The second part begins with an overview of gene expression technology and gives an introduction to the latest cancer gene profiling technologies. Because cancer gene profiling is more then just the profiling of cancer gene expression, we have also included techniques for comparative genomic hybridisation (CGH) arraying and single-nucleotide polymorphism (SNP) analysis, and proteomic techniques.
vi Preface

The third section contains real-life examples for the different technologies, and shows the full potential of cancer gene profiling today. This potential can only be utilised by the use of adequate bioinformatics tools. These tools are covered in the fourth part of the book. Because a cancer gene profiling experiment will most often lead to numerous candidate genes, which, in turn, have to be further validated and analysed, examples of performing post profiling experiments can be found in the final section of the book. It should be noted that all of the chapters in the book are linked by the description of particular successful experiments that were performed within the field of gene expression profiling.

We offer our gratitude to all of the contributing authors and the staff of Humana Press – without their help, this book would not have been possible. We also thank our families for their love and patience. Finally, we are indebted to our mentor Hans Detlev Saeger for his unwavering support.

Science is not just a profession – it should also be fun. This fun comes from the inception of an idea that goes on to be proven through experimentation, or, as we found in a Chinese fortune cookie: “The impossible is only the untried.”

We hope that you will not only be successful, but will also have fun using our book in your research.

Dresden, Germany

Robert Grützmann
Christian Pilarsky
Contents

Preface ................................................................. v
Contributors ......................................................... ix

1. Organizational Issues in Providing High-Quality Human Tissues and Clinical Information for the Support of Biomedical Research ...................... 1
   Walter C. Bell, Katherine C. Sexton, and William E. Grizzle

2. Manual Microdissection ............................................. 31
   Glen Kristiansen

3. Laser Microdissection .............................................. 39
   Anja Rabien

4. Tissue Microarrays ................................................. 49
   Ana-Maria Dancau, Ronald Simon, Martina Mirlacher, and Guido Sauter

5. A Decade of Cancer Gene Profiling: From Molecular Portraits to Molecular Function ........................................ 61
   Henri Sara, Olli Kallioniemi, and Matthias Nees

6. Mining Expressed Sequence Tag (EST) Libraries for Cancer-Associated Genes ........................................ 89
   Armin O. Schmitt

   Jonathan D. Meade, Tong-jig Cho, Blake R. Shester, Jamie C. Walden, Zhen Guo, and Peng Liang

   Jutta Lüttges, Stephan A. Hahn, and Anna M. Heidenblut

9. Quantitative DNA Methylation Profiling on a High-Density Oligonucleotide Microarray ........................................ 155
   Anne Fassbender, Jörn Lewin, Thomas König, Tamás Rujan, Cecile Pelet, Ralf Lesche, Jürgen Distler, and Matthias Schuster

10. Single-Nucleotide Polymorphism (SNP) Analysis to Associate Cancer Risk 171
    Julie Earl and William Greenhalf

11. Application of Proteomics in Cancer Gene Profiling: Two-Dimensional Difference in Gel Electrophoresis (2D-DIGE) .................. 197
    Deepak Hariharan, Mark E. Weeks, and Tatjana Crnogorac-Jurcевич

12. Search for and Identification of Novel Tumor-Associated Autoantigens ........... 213
    Karsten Conrad, Holger Bartsch, Ulrich Canzler, Christian Pilarsky, Robert Grützmann, and Michael Bachmann
13. Integrative Oncogenomic Analysis of Microarray Data in Hematologic Malignancies .............................................. 231
   Jose A Martínez-Climent, Lorena Fontan, Vicente Fresquet,
   Eloy Robles, María Ortiz, and Angel Rubio
   Felip Vilardell and Christine A. Iacobuzio-Donahue
15. Cancer Gene Profiling in Prostate Cancer ............................................. 293
   Adam Foye and Phillip G. Febbo
   B. Michael Ghadimi and Marian Grade
17. The EGFR Pathway as an Example for Genotype:
   Phenotype Correlation in Tumor Genes ............................................. 341
   Ulrike Mogck, Eray Goekkurt, and Jan Stoehlmacher
18. Quantitation Of CD39 Gene Expression in Pancreatic Tissue
   by Real-Time Polymerase Chain Reaction ..................................... 351
   Martin Loos, Beat Künzli, and Helmut Friess
19. Functional Profiling Methods in Cancer .............................................. 363
   Joaquin Dopazo
20. Calibration of Microarray Gene-Expression Data .................................... 375
   Hans Binder, Stephan Preibisch, and Hilmar Berger
21. Meta-analysis of Cancer Gene-Profiling Data ....................................... 409
   Xinan Yang and Xiao Sun
22. Target Gene Discovery for Novel Therapeutic Agents in Cancer Treatment ........................................... 427
   Ole Ammerpohl, Sanjay Tiwari, and Holger Kalthoff

Index ........................................................................................................ 447
Contributors

OLE AMMERMÖHL • Clinic for General Surgery and Thoracic Surgery, Division Molecular Oncology, University Hospital of Schleswig, Kiel, Germany

MICHAEL BACHMANN • Institute for Immunology, Technical University Dresden, Dresden, Germany

HOLGER BARTSCH • Institute for Immunology, Technical University Dresden, Dresden, Germany

WALTER C. BELL • Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, USA

HILMAR BERGER • Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Leipzig, Germany

HANS BINDER • Interdisciplinary Centre for Bioinformatics, University of Leipzig, Leipzig, Germany

ULRICH CANYLER • Institute for Immunology, Technical University Dresden, Dresden, Germany

YONG-JIG CHO • Department of Cell Biology, Vanderbilt-Ingram Cancer Center, School of Medicine, Vanderbilt University, Nashville, TN, USA

KARSTEN CONRAD • Institute for Immunology, Technical University Dresden, Dresden, Germany

TATJANA CRN OGORAC-JURCEVIC • Cancer Research UK Molecular Oncology Unit, Barts and The London Queen Mary’s School of Medicine and Dentistry, John Vane Science Centre, London, UK

ANA-MARIA DANCU • Institute of Pathology, University of Hamburg, Hamburg, Germany

JÜRGEN DISTLER • Science Department, Epigenomics AG, Berlin, Germany

JOAQUÍN DOPAZO • Bioinformatics Department, Centro de Investigación Príncipe Felipe, Valencia, Spain

JULIE EARL • Division of Surgery and Oncology, University of Liverpool, Liverpool, UK

ANNE FASSBENDER • Science Department, Epigenomics AG, Berlin, Germany

PHILLIP G. FEBBO • Departments of Medicine and Molecular Genetics and Microbiology, Duke Institute for Genome Science and Policy, Duke University, Durham, NC, USA

LORENA FONTAN • Division of Oncology, Center for Applied Medical Research, University of Navarra, Pamplona, Spain

ADAM FOYE • Departments of Medicine and Molecular Genetics and Microbiology, Duke Institute for Genome Science and Policy, Duke University, Durham, NC, USA

VICENTE FRESQUET • Division of Oncology, Center for Applied Medical Research, University of Navarra, Pamplona, Spain
Contributors

HELMUT FRIESS • Department of Surgery, Technische Universität München, Munich, Germany

B. MICHAEL GHADIMI • Department of General and Visceral Surgery, University Medical Center Göttingen, Georg-August-University, Göttingen, Germany

ERAY GOEKKURT • Department of Internal Medicine I, University Hospital Carl Gustav Carus, University Dresden, Dresden, Germany

MARIAN GRADE • Department of General and Visceral Surgery, University Medical Center Göttingen, Georg-August-University, Göttingen, Germany

WILLIAM GREENHALF • Division of Surgery and Oncology, University of Liverpool, Liverpool, UK

WILLIAM E. GRIZZLE • Department of Pathology, University of Alabama at Birmingham, Zeigler Research Building, Birmingham, AL, USA

ROBERT GRÜTZMANN • Department of Surgery, University Hospital Carl Gustav Carus, University Dresden, Dresden, Germany

ZHEN GUO • GenHunter Corporation, Nashville, TN, USA

STEPHAN A. HAHN • Molecular GI-Oncology (MGO), Center for Clinical Research (ZKF), Ruhr-University Bochum, Bochum, Germany

DEEPAK HARIHARAN • Cancer Research UK Molecular Oncology Unit, Barts and The London Queen Mary’s School of Medicine and Dentistry, John Vane Science Centre, London, UK

ANNA M. HEIDENBLUT • Molecular GI-Oncology (MGO), Center for Clinical Research (ZKF), Ruhr-University Bochum, Bochum, Germany

CHRISTINE A. IACOBUZIO-DONAHUE • Department of Pathology, GI/Liver Division, Johns Hopkins Medical Institutions, The Sol Goldman Pancreatic Cancer Research Center, Baltimore, MD, USA

OLLI KALLIONIEMI • VTT Medical Biotechnology, Turku, Finland

HOLGER KALTHOFF • Clinic for General Surgery and Thoracic Surgery, Division Molecular Oncology, University Hospital of Schleswig-Holstein, Kiel, Germany

THOMAS KÖNIG • Science Department, Epigenomics AG, Berlin, Germany

GLEN KRISTIANSEN • Department of Pathology, University Hospital Zurich, Zurich, Switzerland

BEAT KÜNZLI • Department of Surgery, Technische Universität München, Munich, Germany

RALF LESCHE • Science Department, Epigenomics AG, Berlin, Germany

JÖRN LEWIN • Science Department, Epigenomics AG, Berlin, Germany

PENG LIANG • Department of Cell Biology, Vanderbilt-Ingram Cancer Center, School of Medicine, Vanderbilt University, Nashville, TN, USA

MARTIN LOOS • Department of Surgery, Technische Universität München, Munich, Germany

JUTTA LÜTTGES • Institute für Pathology, Saarbrücken Hospital, Saarbrücken, Germany

JOSE A. MARTINEZ-CLIMENT • Division of Oncology, Center for Applied Medical Research, University of Navarra, Pamplona, Spain
Jonathan D. Meade • GenHunter Corporation, Nashville, TN, USA
Martina Mirlacher • Institute of Pathology, University of Hamburg, Hamburg, Germany
Ulrike Mogck • Department of Internal Medicine I, University Hospital Carl Gustav Carus, University Dresden, Dresden, Germany
Matthias Nees • VTT Medical Biotechnology, Turku, Finland
María Ortiz • CEIT and TECNUN, University of Navarra, San Sebastián, Spain
Cecile Pelet • Science Department, Epigenomics AG, Berlin, Germany
Christian Pilarsky • Department of Surgery, University Hospital Carl Gustav Carus, University Dresden, Dresden, Germany
Stephan Preibisch • Max-Planck-Institute for Molecular Cell Biology and Genetics, Dresden, Dresden, Germany
Anja Rabien • Research Division, Department of Urology, Charité – Universitätsmedizin Berlin, Campus Charité Mitte, Berlin, Germany
Eloy Robles • Division of Oncology, Center for Applied Medical Research, University of Navarra, Pamplona, Spain
Angélu Rubio • CEIT and TECNUN, University of Navarra, San Sebastián, Spain
Tamas Rujan • Science Department, Epigenomics AG, Berlin, Germany
Henri Sara • VTT Medical Biotechnology, Turku, Finland
Guido Sauter • Institute of Pathology, University of Hamburg, Hamburg, Germany
Armin O. Schmitt • Institute for Animal Sciences, Humboldt-Universität zu Berlin, Berlin, Germany
Matthias Schuster • Science Department, Epigenomics AG, Berlin, Germany
Katherine C. Sexton • Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL, USA
Blake R. Shester • GenHunter Corporation, Nashville, TN, USA
Ronald Simon • Institute of Pathology, University of Hamburg, Hamburg, Germany
Jan Stoehelmacher • Department of Internal Medicine I, University Hospital Carl Gustav Carus, University Dresden, Dresden, Germany
Xiao Sun • Division of Bioinformatics, State Key Laboratory of Bioelectronics (Chien-Shiung Wu Laboratory), Southeast University, Nanjing, China
Sanjay Tiwari • Division Molecular Oncology, Clinic for General Surgery and Thoracic Surgery, University Hospital of Schleswig-Holstein, Kiel, Germany
Felip Vilardell • Department of Pathology, GI/Liver Division, Johns Hopkins Medical Institutions, The Sol Goldman Pancreatic Cancer Research Center, Baltimore, MD, USA
Jamie C. Walden • GenHunter Corporation, Nashville, TN, USA
Mark E. Weeks • Cancer Research UK Molecular Oncology Unit, Barts and The London Queen Mary’s School of Medicine and Dentistry, John Vane Science Centre, London, UK
Xinan Yang • Division of Bioinformatics, State Key Laboratory of Bioelectronics, (Chien-Shiung Wu Laboratory), Southeast University, Nanjing, Nanjing, China