Genomics and Pharmacogenomics in Anticancer Drug Development and Clinical Response

Cancer Drug Discovery and Development™

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Edited by

Federico Innocenti, MD, PhD

University of Chicago,
Chicago, IL, USA

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Editor
Federico Innocenti, MD PhD
University of Chicago
Department of Medicine
Section of Hematology/Oncology
5841 South Maryland Avenue
Chicago IL 60637-1470
USA
finnocen@medicine.bsd.uchicago.edu

Series Editor
Beverly A. Teicher, PhD
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PREFACE

Genomics and Pharmacogenomics in Anticancer Drug Development and Clinical Response provides the most comprehensive body of knowledge available on the role of genetic and genomic variation in the individualization of drug therapies in cancer patients. As a consequence of the intrinsic chromosomal and genetic instability of the tumor genome, it is generally believed that tailoring of chemotherapy in cancer patients might be achieved by molecular analysis of patient tumor DNA. In addition, to reduce the toxicity risk of patients, the tumor DNA information should be integrated with the available data on polymorphic drug-metabolizing enzyme and transporter genes mediating the exposure of patients to active drugs and/or their active metabolites. The chapters of this book clearly show how DNA information from both the host (germline) and the tumor should be taken into account for rational selection of drug therapies in cancer patients, an aspect that received little attention, despite its importance.

The availability of new molecular approaches to the selection of drug therapy is an emerging need, because the traditional approach based on the evaluation of patient and tumor characteristics is clearly far from optimal. Many treated patients do not experience significant benefits from the treatment, while they often experience moderate to severe toxicities. In addition, the development and clinical use of novel molecularly targeted agents (alone or in combination with classical cytotoxic therapy) requires the understanding of the molecular features of the tumors and the identification of tumor markers of response.

In this book, the readers will find a series of chapters addressing the role of genomic information in cancer therapy and in drug development. Several books on pharmacogenomics are currently available, but this book represents a unique source, as it describes experimental approaches, statistical strategies, and clinical examples of the application of genomic medicine in oncology. Many outstanding scientists in the field of cancer pharmacogenomics have been invited to contribute, and I am grateful to have had the opportunity to work with them, learning a great deal from reading their chapters.

I have approached this book from both a basic and an applied perspective. Among three different sections, six chapters in the first section are focused on up-to-date genomic experimental approaches in oncology, including genome-wide phenotyping (microarray and proteomics) and genotyping methods, as well as novel cell-based models used for the identification of genetic markers of drug response.

The second section shows how genetic and genomic information is currently applied to treatment individualization and optimization: Eleven chapters describe some of the most elegant examples of genetic and genomic markers that are predictive of the survival and toxicity risk of cancer patients.

Finally, in the third section, readers will find four chapters that address the role of pharmacogenomics in drug development in oncology, including an industry perspective on this subject, as well as statistical aspects related to the discovery of pharmacogenomic biomarkers during drug development.

Because the discovery of genetic markers of response is of high relevance in oncology, we perceived the need that a collection of multidisciplinary topics be gathered together to discuss this important aspect of pharmacogenomics applied to cancer patients.

I believe that this book represents the first reference for researchers in the field of cancer pharmacogenomics and clinicians, from both the academia and industry.

Federico Innocenti

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Part III Pharmacogenomics in Clinical Drug Development in Oncology

CONTRIBUTORS

RICHARD APLENC, MD, MSCE • *Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA*

LUIGI CALZOLAI, PHD • *Medway School of Pharmacy, University of Kent, Kent, UK*

VINCENT CASTRANOVA, PHD • *The Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute of Occupational Safety and Health, Morgantown, West Virginia, USA*

JOSEPH CICCOLINI, PHARMD, PHD • *Pharmacokinetics—Medical Oncology, Université de la Méditerranée, Marseille, France*

DAVID G. COVELL, PHD • *Developmental Therapeutics Program, National Cancer Institute, Frederick, Maryland, USA*

LEA CUNNINGHAM, MD • *Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA*

M. EILEEN DOLAN, PHD • *Section of Hematology/Oncology, University of Chicago, Chicago, Illinois, USA*

JIAN GU, PHD • *Department of Epidemiology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas, USA*

NANCY L. GUO, PHD • *Mary Babb Randolph Cancer Center, Department of Community Medicine, West Virginia University, Morgantown, West Virginia, USA*

RUILI HUANG, PHD • *Developmental Therapeutics Program, National Cancer Institute, Frederick, Maryland, USA*

DONG HWAN KIM, MD, PHD • *Department of Hematology/Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*

FEDERICO INNOCENTI, MD, PHD • *Department of Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, Illinois, USA*

YASUHIRO KURAMITSU, MD, PHD • *Department of Biochemistry and Functional Proteomics, Yamaguchi University, Graduate School of Medicine, Yamaguchi, Japan*

HEINZ-JOSEF LENZ, MD, FACP • *Division of Medical Oncology, University of Southern California, Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, California, USA*

TERESA LETTIERI, PHD • *European Commission-DG Joint Research Centre, Institute for Environment and Sustainability, Ispra (VA), Italy*

MARK R. LITZOW, MD • *Division of Hematology Research, Mayo Clinic, Rochester, Minnesota, USA*

GEORG LURJE, MD • *Division of Medical Oncology, University of Southern California, Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, California, USA*

SHARON MARSH, PHD • *Washington University, Division of Molecular Oncology, St. Louis, Missouri, USA*

HOWARD L. MCLEOD, PHD • *University of North Carolina, Chapel Hill, Chapel Hill, North Carolina, USA*

CEDRIC MERCIER, MD, PHD • *Medical Oncology, Université de la Méditerranée, Marseille, France*

GERARD MILANO, PHD • *Laboratoire d'Oncopharmacologie, Centre Antoine Lacassagne, Nice, France*

HIRONOBU MINAMI, MD • *Division of Oncology/Hematology, National Cancer Center Hospital East, Kashiwa, Japan*

MIGUEL ANGEL MOLINA, PHD • *Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain*

KAZUYUKI NAKAMURA, PHD • *Department of Biochemistry and Functional Proteomics, Yamaguchi University, Graduate School of Medicine, Yamaguchi, Japan*

YASUSHI OKUNO, PHARMD • *Department of PharmacoInformatics, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan*

YONG QIAN, PHD • *The Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute of Occupational Safety and Health, Morgantown, West Virginia, USA*

JOSE LUIS RAMIREZ, PHD • *Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain*

RAFAEL ROSELL, MD • *Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain*

KIMIE SAI, PHD • *Division of Biosignaling, National Institute of Health Sciences, Tokyo, Japan*

YOSHIRO SAITO, PHD • *Division of Biochemistry and Immunochemistry, National Institute of Health Sciences, Tokyo, Japan*

FERNANDA SALAZAR, PHD • *Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain*

MARIACARMELA SANTARPIA, MD • *Department of Clinical Oncology and Innovative Therapy, University of Messina, School of Medicine, Messina, Italy*

JUN-ICHI SAWADA, PHD • *Division of Biochemistry and Immunochemistry, National Institute of Health Sciences, Tokyo, Japan*

ELKE SCHAEFFELER, PHD • *Margarete-Fischer-Bosch, Institute of Clinical Pharmacology, Stuttgart, Germany*

MATTHIAS SCHWAB, MD • *Department of Clinical Pharmacology, University Hospital Tuebingen, Tubingen, Germany*

JEFFREY SETTLEMAN, PHD • *Massachusetts General Hospital Cancer Center, Charlestown, Massachusetts, USA*

SREENATH V. SHARMA, PHD • *Massachusetts General Hospital Cancer Center, Charlestown, Massachusetts, USA*

XIANGLIN SHI, PHD • *The Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute of Occupational Safety and Health, Morgantown, West Virginia, USA*

RICHARD SIMON, DSC • *Biometric Research Branch, National Cancer Institute, Bethesda, Maryland, USA*

ANURAG SINGH, PHD • *Massachusetts General Hospital Cancer Center, Charlestown, Massachusetts, USA*

MARGARET R. SPITZ, MD, MPH • *Department of Epidemiology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas, USA*

MARTIN STANULLA, MD, MSC • *Pediatric Hematology Oncology, Hannover Medical School, Hannover, Germany*

NATALIE STICKLE, MSC • *UHN Microarray Centre, University Health Network, T. Robert Beamish Family Convergence Centre of Medical Discovery, Toronto, Ontario, Canada*

MIQUEL TARON, PHD • *Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain*

SOKEN TSUCHIYA, PHARMD • *Department of Genomic Drug Discovery Science, Department of PharmacoInformatics, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan*

GOZOH TSUJIMOTO, MD, PHD • *Department of Genomic Drug Discovery Science, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan*

ANDERS WALLQVIST, PHD • *Laboratory of Computational Technologies, SAIC-Frederick, Inc., Frederick, Maryland, USA*

NEIL WINEGARDEN, MSC • *UHN Microarray Centre, University Health Network, T. Robert Beamish Family Convergence Centre of Medical Discovery, Toronto, Ontario, Canada*

KWONG-KWOK WONG, PHD • *Department of Gynecologic Oncology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas, USA*

XIFENG WU, MD, PHD • *Department of Epidemiology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas, USA*

TAL ZAKS, MD, PHD • *Translational Medicine-Oncology, GlaxoSmithKline, Collegeville, Pennsylvania, USA*