Preface

*Molecular Toxicology Protocols, Second Edition* addresses a scientific field primed to explode upon the clinical and popular horizons. Toxicology, a subdiscipline of pharmacology, is actually the interface of chemistry and biology. This field also extends into nonchemical “agents” with deleterious biological effects, especially radiation, the purview of the radiobiologist and health physicist. With the huge increase in computational power now available over the last two decades, it has become possible to model and predict the potential toxicity of yet untested, and even unmade, chemicals. Perhaps, the greatest change in the recent practice of toxicology has been in applying the “tools of the trade” directly to the human population, in what are known “translational” studies, entering the realm of epidemiology. These studies expand the traditional public health aspect of toxicology from simple screening of agents for toxicological potential prior to their introduction into the environment to now include attempts to define “normal” or “background” exposures, elucidating the mechanistic basis of human disease and designing methods for preclinical intervention (“chemoprevention”).

Thus, for our purposes, we define “molecular” toxicology as either any study of toxicological mechanism, or any translation or application of such studies into the human population. Today, such “molecular” toxicology is mostly genetic toxicology, where the genetic material, DNA, is the target molecule. Of course DNA is found throughout the human body, such that all of the traditional modulators of toxicological effect, such as uptake, distribution, and metabolism, must be taken into account. Although genetic damage can have many outcomes, the one most clearly linking exposure and disease has been cancer.

During the past several years, important progress has been made in the understanding of the molecular biology of the cell, the cellular responses to genotoxic agents, and the molecular biology of human cancer. This progress has been rapidly achieved thanks to the development of new state-of-the-art techniques and continuous improvement of existing methods. Such advances permit not only the study changes of in cellular morphology but also the detection of changes occurring in the cellular genetic material (DNA), the cellular transcript (RNA), and the translated product (proteins). These molecular methods have now offered many potential areas of clinical applications. Therefore, following a successful publication of the first edition of *Molecular Toxicology Protocols* in 2005, this second volume contains several new chapters. Subjects of these new chapters range from preparation of fluid specimens for analysis of cellular inflammatory responses to genotoxic insults to sensitive methods for proteomic analysis and aberrant DNA methylation patterns.

Several books are currently available on the applications of molecular methods to various types of biotechnology. To our knowledge, however, there is no book emphasizing the application of molecular methods to genetic toxicology.

Therefore, the aim of *Molecular Toxicology Protocols* is to bring together a series of articles, each describing validated methods to elucidate specific molecular aspects of toxicology. With such content, this book addresses the needs of not only molecular biologists and toxicologists, but also all individuals interested in applying molecular methods to
clinical applications, including geneticists, pathologists, biochemists, and epidemiologists. The volume is divided into ten parts, roughly corresponding to the spectrum of biomarkers intermediate between exposure and disease outcomes as proposed in molecular epidemiology models.

Thus, Part I contains chapters describing methods to analyze global changes in protein expression and identify low-abundance proteins in cells and clinical samples, while the chapters in Part II describe methods for detecting cellular secretions in response to toxicant-induced inflammation. Part III describes methods for the analysis of an essential epigenetic modification, DNA methylation, which modulates gene expression and is frequently altered in toxicant-treated cells and clinical samples. Part IV addresses the application of the new array technologies to genetic toxicology, including methods for the analysis of individual variations in biotransformation and the effects of genetic exposure on gene expression. Part V includes chapters describing the sensitive and specific detection of pro-mutagenic lesions in the genetic material, while Part VI includes chapters assessing gross or macroscopic genetic damage. Parts VII and VIII focus on the detection and characterization of viable mutations in surrogate markers and cancer-related genes, respectively. The chapters of Part IX describe methods for the analyses of various pathways of DNA repair, an important modulator of genotoxicology. Finally, Part X describes methods for the analysis of cytotoxicity caused by the induction of apoptosis since cell death can either protect the organism from a transforming cell or cause distinct health effects itself.

As time goes by we believe that “molecular” approaches will play an increasingly important role in all types of toxicology, not just genetic toxicology. Moreover, genetic damage and dysfunction will undoubtedly be found to play a role in many more diseases of aging than just cancer and is probably a fundamental mechanism of aging itself. Therefore, the focus of this second edition, genetic toxicology, and more specifically, the genetic toxicology of cancer, represents just the “tip of the iceberg” as far as the field of molecular toxicology will eventually be understood.

*Pittsburgh, PA, USA*  
*Phouthone Keohavong*  
*Fort Lauderdale, FL, USA*  
*Stephen G. Grant*
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Contributors

Volker M. Arlt • King’s College London, London, UK
Reetakshi Arora • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India
Narendra K. Bairwa • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India
Rameshwar N.K. Bamezai • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India
Michelle Barbi de Moura • Department of Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
Javed A. Bhalli • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA
Rahel Birru • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Grigory G. Borisenko • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Anne-Lise Børresen-Dale • Department of Genetics, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, and Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway
Shama C. Buch • Center for Clinical Pharmacology, University of Pittsburgh, Pittsburgh, PA, USA
Brian Cao • Van Andel Research Institute, Grand Rapids, MI, USA
Xuefei Cao • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA
Walter A. Deutsch • Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA, USA
Karen H. Dingley • Biology and Biotecnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA
Vasily N. Dobrovolsky • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA
James P. Fabisiak • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Amy Furda • Department of Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
James C. Fuscoe • Division of Systems Biology National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR, USA
Weimin Gao • Department of Environmental Toxicology, The Institute of Environmental and Human Health (TIEHH), Texas Tech University, Lubbock, TX, USA
Sailesh Gochhait • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India
Wolfgang Gödecke • Institute of Genetics, University of Essen, Essen, Germany
Contributors

Stephen G. Grant • Public Health Program, Nova Southeastern University, Fort Lauderdale, FL, USA
Madhu Gupta • Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC, USA
Vibhuti Gupta • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India
Brian Haab • Van Andel Research Institute, Grand Rapids, MI, USA
Kurt W. Haak • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA
Tomonori Hayashi • Laboratory of Immunology, Department of Radiobiology, Radiation Effects Research Foundation, Hiroshima, Japan
Robert H. Heflich • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA
Vijay Hegde • Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA, USA
Sai-Mei Hou • Department of Biosciences, Karolinska Institute, Huddinge, Sweden
Bennett van Houten • Department of Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
Hang-Kai Hsu • The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
Pei-Yin Hsu • The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
T. C. Hsu • Department of Cancer Biology, M.D. Anderson Cancer Center, Houston, TX, USA
Tim H.-M. Huang • The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
Yi-Wen Huang • Department of Obstetrics and Gynecology, Medical College of Wisconsin, Milwaukee, WI, USA
Kaori Shintani-Ishida • Department of Legal Medicine, Osaka City University Medical School, Osaka, Japan
Maria Jasin • Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; Cornell University Graduate School of Medical Sciences, New York, NY, USA
Hilde Johnsen • Department of Genetics, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway
Nina Joshi • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Valerian E. Kagan • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Crystal M. Kelly • Magee-Womens Research Institute, Pittsburgh, PA, USA
Phouthone Keohavong • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
Michael W. Killen • Markey Cancer Center, University of Kentucky, Lexington, KY, USA
Patrick P. Koty • Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC, USA
Steffi Kuhfittig-Kulle • Institute of Genetics, University of Essen, Essen, Germany
Kristen Kulp • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA
YOICHIRO KUSUNOKI • Laboratory of Immunology, Department of Radiobiology, Radiation Effects Research Foundation, Hiroshima, Japan

SEISHI KYOIZUMI • Laboratory of Immunology, Department of Radiobiology, Radiation Effects Research Foundation, Hiroshima, Japan

JEAN J. LATIMER • Department of Pharmaceutical Sciences, Nova Southeastern University, Fort Lauderdale, FL, USA

GURO ELISABETH LIND • Department of Cancer Prevention, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, and Centre for Cancer Biomedicine, Faculty of Medicine, University of Oslo, Oslo, Norway

RAGNHILD LOTHE • Department of Cancer Prevention, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, and Centre for Cancer Biomedicine, Faculty of Medicine, University of Oslo, Oslo, Norway

HITOSHI MAEDA • Department of Legal Medicine, Osaka City University Medical School, Osaka, Japan

SHIRLEY MCCREADY • School of Biological and Molecular Sciences, Oxford Brookes University, Oxford, UK

PAGE B. MCKINZIE • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

FANXUE MENG • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

JOEL N. MEYER • Nicholas School of the Environment, Duke University, Durham, NC, USA

TOSHINARI MINAMOTO • Divisions of Translational and Clinical Oncology and Surgical Oncology, Cancer Research Institute, Kanazawa University and Hospital, Kanazawa, Japan

MEAGAN B. MYERS • Division of Genetic and Molecular Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

NICOLE T. MYERS • Department of Pharmaceutical Sciences, Nova Southeastern University, Fort Lauderdale, FL, USA

MICHAEL A. MALFATTI • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy Lawrence Livermore National Laboratory CA, USA

MINAKO NAGAO • Biochemistry Division, National Cancer Center Research Institute, Tokyo, Japan

MASAKO OCHIAI • Biochemistry Division, National Cancer Center Research Institute, Tokyo, Japan

ANDREA ODERSKY • Institute of Genetics, University of Essen, Essen, Germany

TED J. OGNIBENE • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA

RANJANA PAL • National Centre for Human Genetics, Jawaharlal Nehru University, Delhi, India

BARBARA L. PARSONS • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

KATIE PARTYKA • Van Andel Research Institute, Grand Rapids, MI, USA

RUPAK PATHAK • Armed Forces Radiobiology Research Institute, Bethesda, MD, USA

PETRA PFEIFFER • Institute of Genetics, University of Essen, Essen, Germany

DAVID H. PHILLIPS • King’s College London, London, UK

ANDREW J. PIERCE • Markey Cancer Center, University of Kentucky, Lexington, KY, USA

PATAJE G.S. PRASANNA • Armed Forces Radiobiology Research Institute, Bethesda, MD, USA
Contributors

Marjorie Romkes • Division of Clinical Pharmacology, University of Pittsburgh, Pittsburgh, PA, USA

Anjana Saha • National Centre of Applied Human Genetics, Jawaharlal Nehru University, Delhi, India

Janine H. Santos • Laboratory of Molecular Genetics, NIEHS, National Institutes of Health, Research Triangle Park, NC, USA; Laboratory of Signal Transduction, NIEHS, National Institutes of Health, Research Triangle Park, NC, USA

Madhumita Santra • Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC, USA

Joseph G. Shadduck • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

Shyh-Jen Shih • Department of Radiation Oncology, University of California Davis School of Medicine, Sacramento, CA, USA

Kamleshwar P. Singh • Department of Environmental Toxicology, The Institute of Environmental and Human Health (TIEHH), Texas Tech University, Lubbock, TX, USA

SHEETAL SINGH • Department of Radiation Oncology, University of California Davis School of Medicine, Sacramento, CA, USA

Therese Sorlie • Department of Genetics, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

Dawn M. Stults • Division of Hematology and Oncology, Department of Medicine, Vanderbilt University, Nashville, TN, USA

Takashi Sugimura • Biochemistry Division, National Cancer Center Research Institute, Tokyo, Japan

Roy R. Swiger • Midwest Research Institute, Palm Bay, FL, USA

Vladimir A. Tyurin • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA

Yuanpu Peter Di • Department of Environmental and Occupational Health University of Pittsburgh 100 Technology Drive, Bridgeside Point Pittsburgh PA, USA

Yulia Y. Tyurina • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA

Esther A. Ubick • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA

Andrew T.M. Vaughan • Department of Radiation Oncology, University of California Davis School of Medicine, Sacramento, CA, USA

John S. Vogel • Biology and Biotechnology Research Program, Center for Accelerator Mass Spectroscopy, Lawrence Livermore National Laboratory, Livermore, CA, USA

Phuong Vu • Department of Genetics, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

Shuangshuang Wang • Van Andel Research Institute, Grand Rapids, MI, USA

Yiying Wang • Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson, AR, USA

Yu-I Weng • The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA

Xifeng Wu • Department of Epidemiology, M.D. Anderson Cancer Center, Houston, TX, USA

Liqiang Xi • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
YINGZE ZHANG • Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
PING ZHAO • Van Andel Research Institute, Grand Rapids, MI, USA
YUN-LING ZHENG • Laboratory of Human Carcinogenesis, National Cancer Institute, Bethesda, MD, USA
BAO-LI ZHU • Department of Legal Medicine, Osaka City University Medical School, Osaka, Japan