

METHODS IN MOLECULAR BIOLOGY

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Molecular Toxicology Protocols

Second Edition

Edited by

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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.

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Contents

<i>Preface</i>	<i>v</i>
<i>Contributors</i>	<i>xi</i>
PART I TOXICOPROTEOMICS	
1 Array-Based Immunoassays with Rolling-Circle Amplification Detection <i>Katie Partyka, Shuangshuang Wang, Ping Zhao, Brian Cao, and Brian Haab</i>	3
2 Analysis of Protein Changes Using Two-Dimensional Difference Gel Electrophoresis <i>Weimin Gao</i>	17
PART II TOXICANT-INDUCED INFLAMMATION	
3 Assessment of Pathological and Physiological Changes in Mouse Lung Through Bronchoalveolar Lavage <i>Yuanpu Peter Di</i>	33
4 Analysis of Clinical and Biological Samples Using Microsphere-Based Multiplexing Luminex System <i>Yingze Zhang, Rabel Birru, and Yuanpu Peter Di</i>	43
PART III GENE PROMOTER METHYLATION	
5 Detection of DNA Methylation by MeDIP and MBDCap Assays: An Overview of Techniques <i>Hang-Kai Hsu, Yu-I Weng, Pei-Yin Hsu, Tim H.-M. Huang, and Yi-Wen Huang</i>	61
6 Screening of DNA Methylation Changes by Methylation-Sensitive Random Amplified Polymorphic DNA-Polymerase Chain Reaction (MS-RAPD-PCR) <i>Kamaleshwar P. Singh</i>	71
PART IV ARRAY TECHNOLOGIES	
7 Strategies for Measurement of Biotransformation Enzyme Gene Expression <i>Marjorie Romkes and Shama C. Buch</i>	85
8 Genotyping Technologies: Application to Biotransformation Enzyme Genetic Polymorphism Screening. <i>Marjorie Romkes and Shama C. Buch</i>	99

9	TaqMan™ Fluorogenic Detection System to Analyze Gene Transcription in Autopsy Material	117
	<i>Kaori Shintani-Ishida, Bao-Li Zhu, and Hitoshi Maeda</i>	
PART V ANALYSIS OF DNA ADDUCTS		
10	³² P-Postlabeling Analysis of DNA Adducts	127
	<i>David H. Phillips and Volker M. Arlt</i>	
11	Modification of the ³² P-Postlabeling Method to Detect a Single Adduct Species as a Single Spot.	139
	<i>Masako Ochiai, Takashi Sugimura, and Minako Nagao</i>	
12	DNA Isolation and Sample Preparation for Quantification of Adduct Levels by Accelerator Mass Spectrometry	147
	<i>Karen H. Dingley, Esther A. Ubick, John S. Vogel, Ted J. Ognibene, Michael A. Malfatti, Kristen Kulp, and Kurt W. Haack</i>	
13	Analysis of DNA Strand Cleavage at Abasic Sites	159
	<i>Walter A. Deutsch and Vijay Hegde</i>	
PART VI DETECTION OF CHROMOSOMAL AND GENOME-WIDE DAMAGE		
14	Premature Chromosome Condensation in Human Resting Peripheral Blood Lymphocytes Without Mitogen Stimulation for Chromosome Aberration Analysis Using Specific Whole Chromosome DNA Hybridization Probes	171
	<i>Rupak Pathak and Pataje G.S. Prasanna</i>	
15	Mutagen Sensitivity as Measured by Induced Chromatid Breakage as a Marker of Cancer Risk	183
	<i>Xifeng Wu, Yun-Ling Zheng, and T.C. Hsu</i>	
16	Pulsed-Field Gel Electrophoresis Analysis of Multicellular DNA Double-Strand Break Damage and Repair	193
	<i>Nina Joshi and Stephen G. Grant</i>	
PART VII DETECTION AND CHARACTERIZATION OF SURROGATE GENE MUTATION		
17	Detection of <i>Pig-a</i> Mutant Erythrocytes in the Peripheral Blood of Rats and Mice.	205
	<i>Vasily N. Dobrovolsky, Xuefei Cao, Javed A. Bhalli, and Robert H. Heflich</i>	
18	The Blood-Based Glycophorin A (<i>GPA</i>) Human In Vivo Somatic Mutation Assay	223
	<i>Nicole T. Myers and Stephen G. Grant</i>	
19	Flow Cytometric Quantification of Mutant T Cells with Altered Expression of the T-Cell Receptor: Detecting Somatic Mutants in Humans and Mice.	245
	<i>Seishi Kyoizumi, Yoichiro Kusunoki, and Tomonori Hayashi</i>	

20	Analysis of In Vivo Mutation in the <i>Hprt</i> and <i>Tk</i> Genes of Mouse Lymphocytes	255
	<i>Vasily N. Dobrovolsky, Joseph G. Shaddock, and Robert H. Heflich</i>	
21	Quantifying In Vivo Somatic Mutations Using Transgenic Mouse Model Systems	271
	<i>Roy R. Swiger</i>	
22	The Human T-Cell Cloning Assay: Identifying Genotypes Susceptible to Drug Toxicity and Somatic Mutation	283
	<i>Sai-Mei Hou</i>	
23	Molecular Analysis of Mutations in the Human <i>HPRT</i> Gene	291
	<i>Phouthone Keohavong, Liqiang Xi, and Stephen G. Grant</i>	
24	Simultaneous Quantification of t(14;18) and <i>HPRT</i> Exon 2/3 Deletions in Human Lymphocytes	303
	<i>James C. Fuscoe</i>	

PART VIII DETECTION AND CHARACTERIZATION
OF CANCER GENE MUTATION

25	Mutation Screening of the <i>TP53</i> Gene by Temporal Temperature Gel Electrophoresis (TTGE).	315
	<i>Therese Sorlie, Hilde Johnsen, Phuong Vu, Guro Elisabeth Lind, Ragnhild Lothe, and Anne-Lise Borresen-Dale</i>	
26	Detection of Point Mutations of K-ras Oncogene and p53 Tumor-Suppressor Gene in Sputum Samples	325
	<i>Weimin Gao and Phouthone Keohavong</i>	
27	ACB-PCR Quantification of Somatic Oncomutation	345
	<i>Meagan B. Myers, Page B. McKinzie, Yiyang Wang, Fanxue Meng, and Barbara L. Parsons</i>	
28	Gel-Based Nonradioactive Single-Strand Conformational Polymorphism and Mutation Detection: Limitations and Solutions	365
	<i>Vibhuti Gupta, Reetakshi Arora, Sailesh Gochhait, Narendra K. Bairwa, and Rameshwar N.K. Bamezai</i>	
29	Detection and Characterization of Oncogene Mutations in Preneoplastic and Early Neoplastic Lesions	381
	<i>Toshinari Minamoto</i>	
30	Detection of DNA Double-Strand Breaks and Chromosome Translocations Using Ligation-Mediated PCR and Inverse PCR	399
	<i>Sheetal Singh, Shyh-Jen Shih, and Andrew T.M. Vaughan</i>	

PART IX ANALYSIS OF DNA DAMAGE AND REPAIR MECHANISMS

31	Quantitative PCR-Based Measurement of Nuclear and Mitochondrial DNA Damage and Repair in Mammalian Cells	419
	<i>Amy Furda, Janine H. Santos, Joel N. Meyer, and Bennett Van Houten</i>	

32	The Sister Chromatid Exchange (SCE) Assay	439
	<i>Dawn M. Stults, Michael W. Killen, and Andrew J. Pierce</i>	
33	The Gene Cluster Instability (GCI) Assay for Recombination	457
	<i>Michael W. Killen, Dawn M. Stults, and Andrew J. Pierce</i>	
34	Measuring Recombination Proficiency in Mouse Embryonic Stem Cells.	481
	<i>Andrew J. Pierce and Maria Jasin</i>	
35	Microsatellite Instability: An Indirect Assay to Detect Defects in the Cellular Mismatch Repair Machinery.	497
	<i>Narendra K. Bairwa, Anjana Saha, Sailesh Gochhait, Ranjana Pal, Vibhuti Gupta, and Rameshwar N.K. Bamezai</i>	
36	Unscheduled DNA Synthesis: The Clinical and Functional Assay for Global Genomic DNA Nucleotide Excision Repair	511
	<i>Jean J. Latimer and Crystal M. Kelly</i>	
37	Analysis of Actively Transcribed DNA Repair Using a Transfection-Based System	533
	<i>Jean J. Latimer</i>	
38	An Immunoassay for Measuring Repair of UV Photoproducts.	551
	<i>Shirley McCready</i>	
39	Analysis of Double-Strand Break Repair by Nonhomologous DNA End Joining in Cell-Free Extracts from Mammalian Cells.	565
	<i>Petra Pfeiffer, Andrea Odersky, Wolfgang Goedecke, and Steffi Kuhfittig-Kulle</i>	
 PART X ANALYSIS OF CELLULAR BIOENERGETICS AND APOPTOSIS		
40	Bioenergetic Analysis of Intact Mammalian Cells Using the Seahorse XF24 Extracellular Flux Analyzer and a Luciferase ATP Assay	589
	<i>Michelle Barbi de Moura and Bennett Van Houten</i>	
41	Quantification of Selective Phosphatidylserine Oxidation During Apoptosis	603
	<i>James P. Fabisiak, Yulia Y. Tyurina, Vladimir A. Tyurin, and Valerian E. Kagan</i>	
42	Quantitative Method of Measuring Phosphatidylserine Externalization During Apoptosis Using Electron Paramagnetic Resonance (EPR) Spectroscopy and Annexin-Conjugated Iron	613
	<i>James P. Fabisiak, Grigory G. Borisenko, and Valerian E. Kagan</i>	
43	Detection of Programmed Cell Death in Cells Exposed to Genotoxic Agents Using a Caspase Activation Assay	623
	<i>Madhu Gupta, Madhumita Santra, and Patrick P. Koty</i>	
	<i>Index</i>	633

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