

TABLE OF CONTENTS – BIOMARKERS IN TOXICOLOGY – 1st EDITION

- **Part I: General**

Chapter 1. Introduction

Chapter 2. Rodents model for toxicity testing and biomarkers

Introduction

The rat

The mouse

The hamster

Concluding Remarks and Future Directions

References

Chapter 3. Minipig models for toxicity testing and biomarkers

Introduction

Minipigs in Toxicological Testing

Biomarker Development and Qualification

Standard Biomarkers used in Minipig Toxicological Studies

Excipients and Vehicles

Future use and Challenges

Biomarkers

Concluding Remarks and Future Directions

References

Chapter 4. Nonhuman primates in preclinical research

Introduction

Nonhuman Primates as Animal Models

Clinical Pathology in Nonhuman Primates

Background Lesions in Nonhuman Primates

Concluding Remarks and Future Directions

References

Chapter 5. Biomarkers of toxicity in zebrafish

Introduction

Zebrafish Background

Ecotoxicological Biomarkers of Toxicity

Examples of Biomarkers of Fish Toxicity

An Example of an Established Biomarker: Vitellogenin

Cautions

Concluding Remarks and Future Directions

References

Chapter 6. *Caenorhabditis elegans* as a model for biomarkers of diseases and toxicities

Introduction

C. Elegans and Biomarkers

Biomarkers for General Organ Damage

Neurodegenerative Diseases

Cancers

Concluding Remarks and Future Directions

References

Chapter 7. Alternative animal toxicity testing and biomarkers

Introduction

Use of Alternatives to Animal Testing and Biomarkers

Reasons for Developing Alternatives to Animal Tests and the Role of Biomarkers

Examples of Organizations Researching and Funding Alternatives to Animal Testing and Biomarker Development

Achieving 3RS with Minimal to no Animal Testing by using Biomarkers

Applications of *In Vitro* Tests and Biomarkers

Concluding Remarks and Future Directions

References

Chapter 8. Toxicokinetic-toxicodynamic modeling

Introduction

Toxicokinetic Models

Toxicodynamic Models

Concluding Remarks and Future Directions

References

Part II: Systems Toxicity Biomarkers

Chapter 9. Central nervous system toxicity biomarkers

Introduction

Measuring CNS Dysfunctions

Biomarkers in Neurotoxicology

A Case Study: The Organophosphorus Insecticides

Concluding Remarks and Future Directions

References

Chapter 10. Peripheral nervous system toxicity biomarkers

Introduction

Organization of the Nervous System

Types of Biomarkers of the PNS

PNS Biomarkers Based on Mechanisms

PNS Biomarker Methodology

Autonomic Nervous System

Role of peripheral nervous system in Parkinson's disease and Lewy body disease

Biomarkers of Enteric Nervous System

Emerging Avenues of PNS Biomarker Developments: Exosomes

Personalized Medicine

Concluding Remarks and Future Directions

References

Chapter 11. Cardiovascular toxicity biomarkers

Introduction

Physiology of the Cardiovascular System

Cardiac Toxicity

Cardiac Biomarkers

Biomarker of Myocardial Ionic Dysfunction

Biomarkers of Wall Stretch

Biomarkers of Necrosis

Biomarkers of Inflammation

Remodeling

Neurohormonal Action

Vascular Biomarkers

Other Markers

Markers of Drug-Induced Toxicity

Cardiac Biomarkers of Illegal Drugs, Chemicals, and Terror Agents

Future Trends in Cardiovascular Biomarkers

Concluding Remarks and Future Directions

References

Chapter 12. Respiratory toxicity biomarkers

Introduction

The Respiratory System

Causes of Lung Injury and Disease

Types of Lung Injuries and Pathologies

Sampling Methods for Analysis of Biomarkers of Lung Toxicity

Types of Lung Toxicity Biomarkers

Concluding Remarks and Future Directions

References

Chapter 13. Hepatic toxicity biomarkers

Introduction to Liver Toxicity

Overview of Liver Physiology, Toxicity, and Pathology

Review of Existing Biomarkers of Liver Toxicity

Review of Emerging Biomarkers

Biomarker Qualification and Validation

Concluding Remarks and Future Directions

References

Chapter 14. Conventional and emerging renal biomarkers

Introduction

Characteristics of Biomarkers

Traditional Biomarkers

Newer Biomarkers

Concluding Remarks and Future Directions

References

Chapter 15. Gastrointestinal toxicity biomarkers

Introduction

Biomarkers for Gastrointestinal Damage

Concluding Remarks and Future Directions

References

Chapter 16. Biomarkers of acute and chronic pancreatitis

Introduction

Anatomical, Physiological, and Metabolic Considerations for Pancreatic Injury

Biomarkers of Acute and Chronic Pancreatitis

Biomarkers of endocrine and autoimmune pancreatitis

Biomarkers for Early Detection of Pancreatic Cancer

Concluding Remarks and Future Directions

References

Chapter 17. Skeletal muscle toxicity biomarkers

Introduction

Muscle Types

Pesticides

Metals

Therapeutic Drugs

Drugs of Abuse

Venoms and Zootoxins

Botulinum Toxin

Myotoxic Plants

Concluding Remarks and Future Directions

References

Chapter 18. Dermal toxicity biomarkers

Introduction

Why are biomarkers of dermal toxicity needed?

Biochemical Markers of Dermal Injury

Markers of Exposure

Histological/Ultrastructural Markers

Defining Skin Biomarkers

Concluding Remarks and Future Directions

References

Chapter 19. Ocular biomarkers in diseases and toxicities

Introduction

Ocular Biomarkers

Systemic Agents and Ocular Toxicity

Concluding Remarks and Future Directions

References

Chapter 20. Biomarkers of toxicity in human placenta

Introduction

Placental development and structure

Toxic and Hormonally Active Chemicals in Human Placenta

Placental Functions And Molecular Pathways Involved In Toxicity

Potential Biomarkers of Toxicity in Human Placenta

Use of Placenta in Regulatory Toxicology – Considerations by ecvam and other Organizations

CONCLUDING REMARKS AND FUTURE DIRECTIONS

References

Chapter 21. Blood and bone marrow toxicity biomarkers

Introduction

Hematopoietic System

Mechanisms of Hematotoxicity

Biomarkers of Hematotoxicity

Concluding Remarks and Future Directions

References

Chapter 22. Immunotoxicity biomarkers

Introduction

The Immune System

Mechanisms of Immunotoxicity

Biomarkers

Concluding Remarks and Future Directions

References

Part III: Agents Toxicity Biomarkers

Chapter 23. Insecticides

Introduction

Organophosphates and Carbamates

Chlorinated Hydrocarbons

Pyrethrins and Pyrethroids

Amitraz

Neonicotinoids

Fipronil

Ivermectin and Selamectin

Rotenone

Concluding Remarks and Future Directions

References

Chapter 24. Herbicides and fungicides

Introduction

Background

Toxicokinetics

Mechanism of Action

Biomarkers and Biomonitoring of Exposure

Herbicides

Fungicides

Concluding Remarks and Future Directions

References

Chapter 25. Polychlorinated biphenyls, polybrominated biphenyls, and brominated flame retardants

Introduction

Polychlorinated Biphenyls

Polybrominated Biphenyls

Brominated Flame Retardants

Thyroid Hormone Disruption as a Biomarker of Exposure and Effect

Perturbed Calcium Homeostasis and Kinase Signaling as Biomarkers of Effect

Induction of Cytochrome P450 Enzymes as a Biomarker of Exposure and Effect

Concluding Remarks and Future Directions

References

Chapter 26. Polycyclic aromatic hydrocarbons

Introduction

Biomarkers of Exposure

Biomarkers of Effect

Biomarkers of susceptibility

Concluding Remarks and Future Directions

References

Chapter 27. Bisphenol A

Introduction

Mechanisms of Action

Hallmarks of Exposure to Bisphenol A at the Tissue Level

Bisphenol A Metabolites

Biomolecular Responses to Bisphenol A Exposure

Polymorphisms and Sensitivity to BISPHEENOL A Exposure

Risk Assessment

Concluding Remarks and Future Directions

References

Chapter 28. Melamine

Introduction and Historical Background

Toxicology of Melamine

Biomarkers

Concluding Remarks and Future Directions

References

Chapter 29. Metals

Introduction

Classification of Biomarkers

Selection of an Ideal Biomarker: Benefits and Drawbacks

Biomonitoring of Exposure to Heavy Metals

Lead

Arsenic

Mercury

Cadmium

Chromium

Thallium

Manganese

Current Concerns and Biological Relevance

Concluding Remarks and Future Directions

References

Chapter 30. Chemical and biological warfare agents

Introduction

Desirable Properties of Biomarkers

Chemical Warfare Agents

Classification of Chemical Warfare Agents

Biomarkers of Exposure to Chemical Warfare Agents

Nerve Agents

Blister Agents or Vesicants

Biological Warfare Agents

Classification of Biological Warfare Agents: Modes of Delivery and Possible Portals of Entry

Biomonitoring of Exposure to Biological Warfare Agents

Anthrax

Smallpox

Plague

Botulism

Concluding Remarks and Future Directions

References

Chapter 31. Freshwater cyanotoxins

Introduction

Hepatotoxins

Neurotoxins

Concluding Remarks and Future Directions

References

Chapter 32. Mycotoxins

Introduction

Aflatoxins

Ochratoxins

Fumonisin

Deoxynivalenol Trichothecene

Concluding Remarks and Future Directions

References

Chapter 33. Poisonous plants: biomarkers for diagnosis

Introduction

Astragalus and *Oxytropis* Species (Locoweeds, Nitrotoxin Spp., and Selenium Accumulators)

Larkspurs (*Delphinium* Spp.)

Lupines (*Lupinus* Spp.)

Poison Hemlock (*Conium Maculatum*)

Water Hemlock (*Cicuta* Spp.)

Ponderosa Pine Needles (*Pinus* Spp.)

Rayless Goldenrod (*Isocoma Pluriflora*) and White Snakeroot (*Ageratina Altissima*)

Halogeton (*Halogeton glomeratus*)

Pyrrolizidine Alkaloid-Containing Plants

Photosensitizing Plants

Death Camas

Knapweeds: *Centaurea* Spp.

Conclusions

References

Part IV: Pharmaceuticals and Nutraceuticals Biomarkers

Chapter 34. Biomarkers of drug toxicity

Introduction

Biomarkers of Drug-Induced Liver Toxicity

Biomarkers of Drug-Induced Kidney Toxicity

Biomarkers of Drug-Induced Vascular Injury

Biomarkers of Drug-Induced Cardiac Injury

Biomarkers of Drug-Induced Brain Injury

Concluding Remarks and Future Directions

References

Chapter 35. Biomarkers of toxicity for dietary ingredients contained in dietary supplements

Introduction

Overview of Regulation of Dietary Supplements in the USA

Biomarkers of Toxicity: Dietary Ingredients

Biomarkers of Toxicity: Toxic Compounds in New Dietary Ingredients

Biomarkers of Toxicity: Active Moiety of a Dietary Ingredient

Use of Biomarkers to Address Safety of Multiple Ingredients in New Dietary Ingredient Notifications

Concluding Remarks and Future Directions

References

Chapter 36. Nutriphenomics in rodent models: Impact of dietary choices on toxicological biomarkers

Introduction

Dietary Choices

Diet-Induced Metabolic Disorders

Control Diet Influence on Phenotype

Concluding Remarks and Future Directions

References

Part V: Biomarkers of Petroleum Products and Mixtures Toxicity

Chapter 37. Biomarkers of petroleum products toxicity

Introduction

Chemical Markers

Biochemical Biomarkers

Tissue and Body Fluid Levels of Petroleum Hydrocarbons

Histopathology

Biomarkers in Birds

Dispersants

Concluding Remarks and Future Directions

References

Chapter 38. Biomarkers of chemical mixture toxicity

Introduction

Potential Chemical Mixtures

Biomonitoring for Assessing Human Exposure to Chemical Mixtures

Risk Assessment of Combined Actions of Chemical Mixtures

Biomarkers of Target Organ Toxicity of Chemical Mixtures

Nonspecific Biomarkers of Toxic Response

Concluding Remarks and Future Directions

References

Part VI: Biomarkers of Radiation, Nanoparticles, and Carcinogenesis

Chapter 39. Biomarkers of radiation injury and response

Introduction

Background

Interaction of Radiation with Matter

Biological Consequences of Radiation

Effects of Radiation on Organisms

Biomonitoring of Exposure to Radiation

Biomarker Selection and Use

DNA: Chromosome, Single Nucleotide Polymorphism, and Methylation

RNA

Protein Biomarkers

Metabolomics

Microbiome

Concluding Remarks and Future Directions

References

Chapter 40. Biomarker analysis for nanotoxicology

Introduction

Nano–Bio Interface

Biomarkers Used for Nanotoxicity

Concluding Remarks and Future Directions

References

Chapter 41. Engineered nanomaterials: Biomarkers of exposure and effect

Introduction and Background

Classification and Characteristics of Nanomaterials

Definition and Meaning of Biological Monitoring and its Application to Engineered Nanomaterials

Biological Interactions Relevant to Biomarkers of Exposure to Engineered Nanomaterials at Molecular, Cellular, and Organ Level

Concluding Remarks and Future Directions

References

Chapter 42. Epigenetic biomarkers in toxicology

Introduction

DNA Methylation

Histone Modifications

Epigenetics and Disease

Concluding Remarks and Future Directions

References

Chapter 43. Genotoxicity biomarkers: Molecular basis of genetic variability and susceptibility

Introduction

Genotoxic Biomarker Detection Methods

Biomarkers and Mechanism of Action

Molecular Basis of Genetic Variability and Susceptibility

Concluding Remarks and Future Directions

References

Chapter 44. Risk factors as biomarkers of susceptibility in breast cancer

Introduction

Life Stage Susceptibility

Concluding Remarks and Future Directions

References

Chapter 45. Pancreatic and ovarian cancer biomarkers

Introduction

Currently used Clinical Biomarkers

Diagnostic Biomarkers

Prognostic Biomarkers

Predictive Biomarkers

Concluding Remarks and Future Directions

References

Chapter 46. Prostate cancer biomarkers

Introduction

Biomarkers and Cancer Biomarkers

Screening for Prostate Cancer

Criteria and Validation of Prostate Cancer Biomarkers

History of Prostate Cancer Biomarkers

Candidate Biomarkers for Prostate Cancer

Concluding Remarks and Future Directions

References

Chapter 47. Biomonitoring exposures to carcinogens

Introduction

Assessing Exposures

Assessing Effects

Assessing Susceptibility

Discovery and Validation of New Biomarkers

Concluding Remarks and Future Directions

References

Part VII: Special Topics

Chapter 48. Biomarkers of Alzheimer's disease

Introduction

Genetic Risk Factors for ALZHEIMER'S DISEASE

Mechanisms of Synaptic Dysfunction and Neuronal Loss

Biomarkers

Concluding Remarks and Future Directions

References

Chapter 49. Biomarkers of Parkinson's disease

Introduction

Genetic Biomarkers

Biochemical Markers

Neuroimaging Markers

Concluding Remarks and Future Directions

References

Chapter 50. Cytoskeletal disruption as a biomarker of developmental neurotoxicity

Introduction

Microtubules

Microfilaments

Intermediate Filaments

Concluding Remarks and Future Directions

References

Chapter 51. Biomarkers of mitochondrial dysfunction and toxicity

Introduction

Mitochondrial Function: General Overview

Mitochondrial Toxicity

Xenobiotics and Mitochondrial Dysfunction

Mitochondria and Disease

Concluding Remarks and Future Directions

References

Chapter 52. Biomarkers of oxidative/nitrosative stress and neurotoxicity

Introduction

Lipid Peroxidation and Markers of Oxidative Stress

Excitotoxicity and Oxidative Damage

Neuroinflammation and Oxidative Injury

Metal Toxicity and Oxidative Injury

Concluding Remarks and Future Directions

References

Chapter 53. Citrulline: Pharmacological perspectives and role as a biomarker in diseases and toxicities

Introduction

Citrulline: More Efficacious than Arginine – Justification

Salient Aspects of NITRIC OXIDE

Biochemical Aspects

Pharmacokinetics and Pharmacodynamics of Citrulline

Citrulline as a Biomarker in Diseases

Conditions in Which Citrulline May Prove to Be a Biomarker in the Future

Citrulline as a Biomarker in Toxicities

Concluding Remarks and Future Directions

References

Chapter 54. Pathological biomarkers in toxicology

Introduction

Diagnostic Pathology

Morphologic (Gross and Microscopic) Pathology

Concluding Remarks and Future Directions

References

Part VIII: Applications of Biomarkers in Toxicology

Chapter 55. Biomarkers in drug safety evaluation

Introduction

Use of Biomarkers in Drug Safety Evaluation

Traditional Indicators for Drug Toxicity Assessment

Translation and Qualification of Safety Biomarkers

Biomarker Validation and Qualification

Integration and Use of Safety Biomarkers in Drug Development

Safety Biomarkers for Preclinical and/or Clinical Perspectives

Genetic Biomarkers

Importance of Understanding Specific Mechanisms of Toxicity in Drug Development

Concluding Remarks and Future Directions

References

Chapter 56. Membrane transporters and transporter substrates as biomarkers for drug pharmacokinetics, pharmacodynamics, and toxicity/adverse events

Introduction

Membrane Transporters as Biomarkers for Drug Pharmacodynamics: Example of Multidrug Resistance in Cancers

Membrane Transporters as Biomarkers for Drug Pharmacokinetics: The Role of Polymorphisms in Drug ABSORPTION, DISPOSITION, METABOLISM, AND EXCRETION

Physiological Substrates of Transporters as Biomarkers

Concluding Remarks and Future Directions

References

Chapter 57. Biomarkers in biomonitoring of xenobiotics

Introduction

Requirements of a Biomarker for Toxicological Testing and Biomonitoring of Xenobiotics Exposure

Biological Samples Used for Biomonitoring Exposure Through Biomarkers

Biomarkers of Exposure for Monitoring Xenobiotics Exposure

Biomarkers of Effect in Toxicology Testing

Biomarkers of Susceptibility

Concluding Remarks and Future Directions

References

Chapter 58. Biomarkers of susceptibility: Pharmacogenomics and toxicogenomics

Introduction

Biomarkers Defined

Biomarkers of Susceptibility

Concluding Remarks and Future Directions

References

Chapter 59. Biomarkers for drugs of abuse and neuropsychiatric disorders: Models and mechanisms

Introduction

Drugs of Abuse

Amphetamine

Cocaine

Opioids

Cannabinoids/Marijuana

Alcohol

Abused Substances and Neuropsychiatric Disorders

Animal Models in Neuropsychiatry

Biomarkers of bipolar disorder and schizophrenia

Concluding Remarks and Future Directions

References

Chapter 60. MicroRNA expression as an indicator of tissue toxicity

Introduction

Standard Toxicity Measurements (Tissue and Circulating Biomarkers)

Nomenclature

Database

Sample Preparation

Kinetics and Pharmacokinetics/Pharmacodynamics

Organ Systems

Concluding Remarks and Future Directions

References

Chapter 61. Percellome toxicogenomics project as a source of biomarkers of chemical toxicity

Introduction

Animal Studies and Percellome Data Generation

Comprehensive Selection of Responding mRNAs

Merging of Toxicogenomics Project Data to Percellome Database

Estragole Study

Pentachlorophenol Study

Merging the Toxicogenomics project Data into the Percellome Database

Concluding Remarks and Future Directions

References

Chapter 62. Transcriptomic biomarkers in safety and risk assessment of chemicals

Introduction

Transcriptomics in Biomarker Discovery

Concluding Remarks and Future Directions

References

Chapter 63. Biomarkers in computational toxicology

Introduction

Exposure Modeling

Concluding Remarks and Future Directions

References

Chapter 64. Biomarkers in toxicology, risk assessment, and environmental chemical regulations

Introduction

Biomarkers

Toxicology and Risk Assessment

Biomarkers of Exposure

Biomarkers of Effect

Cancer-Related Biomarkers

Biomarkers of Susceptibility

Molecular Mechanisms and Risk Assessment

Integration with Environmental Regulations

Concluding Remarks and Future Direction

References

Index.