

In Vitro Neurotoxicology

METHODS IN PHARMACOLOGY AND TOXICOLOGY

MANNFRED A. HOLLINGER, PhD, SERIES EDITOR

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METHODS IN PHARMACOLOGY AND TOXICOLOGY

In Vitro Neurotoxicology

Principles and Challenges

Edited by

Evelyn Tiffany-Castiglioni

*Department of Veterinary Anatomy and Public Health
Texas A&M University College of Veterinary Medicine
and Center for Environmental and Rural Health,
College Station, TX*

Foreword by

Mannfred A. Hollinger

*University of California
Davis, CA*

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Dedication

To Robert S. Tiffany, Jr. and Frances James Tiffany
In Memoriam

Foreword

Researchers in pharmacology and toxicology are constantly searching for relevant *in vitro* methods in order to obtain valid data without the use of whole animals with their attendant costs and ethical questions. This is particularly true for workers interested in neurotoxicology, where we continue to discover new neurotoxic effects of drugs and other xenobiotics. Over the years, a number of creative and useful methods have emerged. For someone entering the field of neurotoxicology, the decision regarding type of method most appropriate for his or her work can be a daunting one. For example, the time and effort required to search the literature and evaluate candidate systems can require weeks, if not months.

In Vitro Neurotoxicology: Principles and Challenges, edited by Dr. Evelyn Tiffany-Castiglioni, is a masterful contribution to the field of neurotoxicology. With each passing year the need for new and improved *in vitro* methods to help further our understanding of neurotoxicology will increase. This volume brings us up to date.

Mannfred A. Hollinger
Professor Emeritus
University of California
Davis, CA

Preface

Neurotoxicity assessment with *in vitro* systems is the focus of both increasing expectations and heightened challenges. Such systems prospectively offer a means to improve screening efficiency for potential neurotoxicants, a method for better understanding mechanisms of toxicant action, a decreasing use of animals, and a means to obtain data from human samples. On the other hand, *in vitro* systems have not yet been used in consistent, broadly applied formats that would validate and exploit their value for neurotoxicity testing. Inherent problems, such as test chemical concentration and delivery, lack of heterogeneous cell–cell interactions, immaturity of cell types available, phenotypic variations induced by culture techniques, and insensitivity of endpoints tested, significantly impede the use and interpretation of *in vitro* assays. In addition, standardized metrics and methods for comparing results across studies and laboratories, as well as benchmark criteria for linking *in vitro* to *in vivo* studies, are often lacking.

The purpose of *In Vitro Neurotoxicology: Principles and Challenges* is to synthesize principles and concepts of *in vitro* neurotoxicology that will facilitate the development of significantly improved methods and systems for *in vitro* neurotoxicity testing, with emphasis on their relevance to *in vivo* systems. An outstanding list of contributors has been assembled, including well-respected leaders in the field and new investigators who are exploring emerging frontiers in the area of genomic toxicology. Contributors have taken a fresh look at their own and others' work, critically and comparatively analyzed it across experimental systems and toxicants, and formalized essential principles for *in vitro* neurotoxicity testing. In most cases, chapters are arranged around major themes or central ideas, rather than around individual toxicants or specific *in vitro* models. Most chapters are collaborative efforts that address a theme and employ examples comprised of multiple experimental systems and endpoints. The chapters emphasize several neurotoxicants that are of prominent human health concern and about which metabolism and dose–responses are best understood, both *in vivo* and *in vitro*: lead, mercury, organophosphorus insecticides, polychlorinated biphenyls and dioxin, ethanol, and endogenous proteins.

There are already several excellent articles and monographs that describe materials and techniques applicable to *in vitro* neurotoxicology, such as cell lines, methods of primary cell culture, brain slice preparations, and *in vitro*

assays for viability and function. Rather than repeating the contents of these previous works, *In Vitro Neurotoxicology: Principles and Challenges* provides an Appendix containing a critically reviewed list of related works. The list, carefully selected and annotated by the contributors, includes important review articles, books on in vitro toxicology, neurotoxicology, and in vitro neurotoxicology, and chapters from methods manuals. The Appendix collects in one place references to most of the major reviews and seminal work related to in vitro neurotoxicology that have appeared in the past ten years.

Evelyn Tiffany-Castiglioni

Contents

<i>Dedication</i>	<i>v</i>
<i>Foreword</i>	<i>vii</i>
<i>Preface</i>	<i>ix</i>
<i>Contributors</i>	<i>xiii</i>
1 In Vitro Neurotoxicology: <i>Introduction to Concepts</i> <i>Evelyn Tiffany-Castiglioni</i>	1
2 Predictive Value of In Vitro Systems for Neurotoxicity Risk Assessment <i>Marion Ehrich and David C. Dorman</i>	29
3 Exposure–Dose–Response Paradigm as It Relates to Toxicogenomics <i>William H. Hanneman, Melvin E. Andersen, Marie E. Legare, Christine T. French, Tami S. McMullin, Carolyn Broccardo, and Ruth E. Billings</i>	41
4 In Vitro Studies of Neurotoxicant Effects on Cellular Homeostasis <i>Gerald J. Audesirk and Ronald B. Tjalkens</i>	59
5 Role of Apoptosis in Neurotoxicology <i>Lori D. White, Sid Hunter, Michael W. Miller, Marion Ehrich, and Stanley Barone, Jr.</i>	95
6 Impairment of Neurotransmitter Metabolism and Function by Neurotoxicants: <i>Enzyme Pathways in Neurons and Astroglia</i> <i>Michael Aschner and Ursula Sonnewald</i>	133
7 Cell-Type-Specific Responses of the Nervous System to Lead <i>Evelyn Tiffany-Castiglioni and Yongchang Qian</i>	151
8 Effects of Toxicants on Neural Differentiation <i>Stanley Barone, Jr., Prasada R. S. Kodavanti, and William R. Mundy</i>	187

9	Impairment of Synaptic Function by Exposure to Lead <i>Stephen M. Lasley and Mary E. Gilbert</i>	217
10	Aggregating Brain Cell Cultures for Neurotoxicological Studies <i>Marie-Gabrielle Zurich, Florianne Monnet-Tschudi, Lucio G. Costa, Benoît Schilter, and Paul Honegger</i>	243
11	Use of Complimentary In Vitro and In Vivo Methods for Assessing Neuroendocrine Disruptors <i>W. Les Dees, Jill K. Hiney, Robert K. Dearth, and Vinod K. Srivastava</i>	267
12	Establishing In Vitro Models to Study Endogenous Neurotoxicants <i>Heather D. Durham</i>	291
	Appendix: Annotated Reading List <i>Evelyn Tiffany-Castiglioni, Lucio G. Costa, Marion Ehrich, William R. Mundy, Gerald J. Audesirk, Michael Aschner, Prasada R. S. Kodavanti, and Stephen M. Lasley</i>	315
	Index	325

Contributors

MELVIN E. ANDERSEN • *Associate Professor, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*

MICHAEL ASCHNER • *Professor, Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC*

GERALD J. AUDESIRK • *Professor, Department of Biology, University of Colorado at Denver, Denver, CO*

STANLEY BARONE, JR. • *Research Biologist, Cellular and Molecular Toxicology Branch, Neurotoxicology Division/NHEERL/ORD US Environmental Protection Agency, Research Triangle Park, NC*

RUTH E. BILLINGS • *Research Associate, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*

CAROLYN BROCCARDO • *Research Assistant, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*

LUCIO G. COSTA • *Professor, Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA*

ROBERT K. DEARTH • *Technician I, Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University, College Station, TX*

W. LES DEES • *Professor, Department of Veterinary Anatomy Public Health, College of Veterinary Medicine, Texas A&M University, College Station, TX*

DAVID C. DORMAN • *Director of the Division of Biological Sciences, CIIT Centers for Health Research, Research Triangle Park, NC*

HEATHER D. DURHAM • *Professor, Department of Neurology and Neurosurgery, McGill University, Montreal Neurological Institute, Montreal, Quebec, Canada*

MARION EHRLICH • *Professor, Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA*

- CHRISTINE T. FRENCH • *Research Assistant, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*
- MARY E. GILBERT • *Assistant Professor, Neurotoxicology Division, US Environmental Protection Agency, Research Triangle Park, NC*
- WILLIAM H. HANNEMAN • *Assistant Professor, Head of Toxicology Section, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*
- JILL K. HINEY • *Research Assistant Professor, Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University, College Station, TX*
- PAUL HONEGGER • *Professeur Associe, Institute of Physiology, University of Lausanne, Lausanne, Switzerland*
- SID HUNTER • *Toxicologist, Reproductive Toxicology Division, US Environmental Protection Agency, Research Triangle Park, NC*
- PRASADA R. S. KODAVANTI • *Research Toxicologist, Neurotoxicology Division, US Environmental Protection Agency, Research Triangle Park, NC*
- STEPHEN M. LASLEY • *Professor, Department of Biomedical and Therapeutic Sciences, University of Illinois College of Medicine, Peoria, IL*
- MARIE E. LEGARE • *Assistant Professor, Department of Environmental and Radiological Health Science, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*
- TAMI S. McMULLIN • *Research Assistant, Department of Environmental and Radiological Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO*
- MICHAEL W. MILLER • *Professor, Department of Neuroscience and Physiology, State University of New York-Upstate Medical University, Syracuse, NY*
- FLORIANNE MONNET-TSCHUDI • *Maitre Assistant, Institute of Physiology, University of Lausanne, Lausanne, Switzerland*
- WILLIAM R. MUNDY • *Research Toxicologist, Neurotoxicology Division, US Environmental Protection Agency, Research Triangle Park, NC*
- YONGCHANG QIAN • *Research Assistant Professor, Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University, College Station, TX*

- BENOÎT SCHILTER • *Nestlé Research Centre, Vers-chez-les Blanc, Lausanne, Switzerland*
- URSULA SONNEWALD • *Professor, Department of Clinical Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway*
- VINOD K. SRIVASTAVA • *Research Assistant Professor, Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University, College Station, TX*
- EVELYN TIFFANY-CASTIGLIONI • *Professor and Head, Department of Veterinary Anatomy and Public Health, Associate Dean for Undergraduate Education, College of Veterinary Medicine, Texas A&M University, College Station, TX*
- RONALD B. TJALKENS • *Assistant Professor, Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University, and Center for Environmental and Rural Health, College Station, TX*
- LORI D. WHITE • *Biologist, Cellular and Molecular Toxicology Branch, Neurotoxicology Division, NHEERL/ORD US Environmental Protection Agency, Research Triangle Park, NC*
- MARIE-GABRIELLE ZURICH • *Premiere Assistante, Institute of Physiology, University of Lausanne, Lausanne, Switzerland*