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.

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