Editorial

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As the inaugural and continuing Editor-in-Chief of the journal *Neurotoxicity Research*, I feel compelled to reflect on the journal's development and the prospect for years ahead with the new owner, Springer Science + Business Media.

Neurotoxicity Research was originally conceived as a journal with a focus on neurotoxins, exogenous, and endogenous. Conceptually, the term “neurotoxicity” (as used in the context of the journal) reflects selective neurotoxicity—the origins of which can be traced to Rita Levi-Montalcini, the Nobel Laureate who with Stanley Cohen developed anti-Nerve Growth Factor (anti-NGF), an immunotoxin noted for its ability to produce permanent *immunosympathectomy* in developing mice. The status of neurotoxins in Neuroscience continued to broaden from this discovery in the 1950s, as Hans Thoenen and J.P. Tranzer discovered the catecholaminergic neurotoxin 6-hydroxydopamine (6-OHDA)—able to destroy with relative selectivity, discrete noradrenergic and dopaminergic nerves in either (or both) the peripheral and central nervous system. Hans Baumgarten, almost simultaneously, reported that the serotonin analogs 5,6- and 5,7-dihydroxytryptamine (5,6- and 5,7-DHT) produced selective destruction of serotonergic neurons. John Olney pioneered the unmasking of glutamate and analogs as selective toxins through action at assorted glutamate receptor subtypes. The next great discovery was made by J.W. Langston who found that MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) selectively

destroyed *substantia nigra par compacta* dopaminergic neurons, producing irreversible parkinsonian syndrome in primates. Not long afterwards prions became recognized as abnormally folded proteins able to produce gradual development of neurodegenerative disorders (e.g., Creutzfeldt-Jakob Disease). Abnormal protein deposits in brain (e.g., synuclein, A-beta) and their oligomers are principles now known to promote neurotoxicity. The series of findings on neurotoxic species has revived interest in putative environmental toxins which might account, in part, for the occurrence of a host of neurodegenerative disorders. More recent discoveries of endogenous neurotoxins and neuroprotectants have added to the expansiveness of neurotoxins as major principles in Neuroscience.

The terminology of a “selective neurotoxin” has similarly evolved over the past several decades. Botulinum neurotoxin represents a chemical entity producing prolonged inactivation of exocytosis primarily of cholinergic nerves. Now, long-term inactivation of a nerve without associated neuronal necrosis or apoptosis comes under the umbrella of a neurotoxin. A substance capable of destroying the astrocytic myelin sheath, and thus, altering nerve conduction with a semblance of amyotrophic lateral sclerosis, is now regarded as a neurotoxin, despite the fact that a non-neuronal cell is impaired. Similarly, because activated microglia have a prominent role in promotion of apoptosis, any agent promoting activation of microglia could be regarded as a neurotoxin. Today rotenone, an inhibitor of complex 1 in the mitochondrial respiratory chain, is used in low amount for prolonged periods to induce synuclein deposition in brain, which mimics the occurrence of this abnormal protein deposit in parkinsonian brain. Although very unselective in cell targeting, rotenone has come to be accepted as a ‘selective’ neurotoxin, primarily because the outcome of long-term low-dose rotenone treatment better

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mirrors the CNS pathology of Parkinson Disease. Neuroprotectants able to prevent programmed cell death during ontogeny would cause greater than normal neuronal survival in brain—an abnormal outcome. Consequently, a neuroprotectant could likewise be viewed as a neurotoxin.

As reflected in an Editorial in the first journal edition, volume 1 issue 1 of *Neurotoxicity Research*, the term *Neurotoxicity* is intended to be more expansive than what otherwise might be implied as a study of exogenous neurotoxic chemicals. *Neurotoxicity* also obviously encompasses the endogenous cellular chemical species attending cell survival and cell death, either apoptotic, necrotic, or necroptotic. The biologic templates of nerve degeneration and denervation are obvious starting points for experimentation in nerve regeneration and sprouting. Gene knockouts and transgenic animals are additional and natural templates of neurotoxicity research. *Neurotoxicity Research* is yet

more expansive, as behavioral abnormality and psychiatric-related studies additionally come under its purview.

Just as no one in the early 1900s could envision the host of developments of the 20th century, no one today can know the discoveries to be made over the next 50 to 100 years. The last 50 years of neuroscience research is a virtual revolution, or resurrection. Someone looking back 50 years from now may be confused by today's limited scope and foresight for the unknowns of neuroscience and the direction of *Neurotoxicity Research*. When tomorrow sees today's views as too narrow in scope, this will be the proof that the journal succeeded in melding new thought and in influencing the direction of neuroscience research. Neurotoxicity research is an open and wide door, barring no discipline into neuronal investigations intended to obviate neuronal disparity, towards the goal of warding off neurodegenerative and neuropsychiatric disorders.