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Editorial

This special issue of *Molecular Neurobiology* presents a series of mini-reviews resulting from an ISN satellite symposium entitled *Oxidative Mechanisms in Neurodegenerative Disorders* Held at the Guilin Park Hotel, Guilin, China on February 7–11, 2004. The timely topics in this symposium were contributed by more than 20 internationally acclaimed scientists and attended by more than 100 participants interested in this subject matter. This satellite symposium was also part of the 6th Biennial Asian-Pacific Society for Neurochemistry (APSN) meeting held in Hong Kong, China. Organizers included Dr. Piu Chan (Capital University of Medical Sciences and Beijing Institute of Geriatrics) Dr. Albert Y. Sun and Dr. Grace Y. Sun (University of Missouri, Columbia, MO). The satellite meeting was hosted by Xuanwu Hospital of Capital University of Medical Sciences and Guilin Medical College, and was generously supported by the following: the International Society of Neurochemistry (ISN), National Institutes of Health (USA) (1 R13 NS047414), the Geriatric Research, Education and Clinical Center (GRECC) VA Medical Center, Minneapolis, MN, USA, The Chinese Society of Neuroscience, Chinese Medical Association, Chinese Journal of Neurology, Shanghai Roche Pharmaceuticals Ltd., and Beijing QuiXave United Technology Ltd. Corporation.

By 2050, 25% of the general population will be more than 65 yr of age. Neurodegenerative disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), and stroke, are among the most prevalent diseases associated with aging and have created immense health problems and socioeconomical burdens to the society. Although not well understood, it is recognized that the high susceptibility of the central nervous system to oxidative stress is an important contributor to these age-related neurodegenerative diseases. Brain membranes are known to contain high levels of polyunsaturated fatty acids. In addition, although the brain utilizes a large amount of oxygen, it is relatively weak in oxidative defense mechanisms. In the brain, perturbation of the oxidative–antioxidative balance can be induced by a number of exogenous and endogenous factors, including excessive release of excitatory neurotransmitters and challenge by neurotoxic compounds. Increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) is known to perturb calcium homeostasis, cytoskeletal arrangements, mitochondrial function and intracellular trafficking that subsequently lead to the induction of apoptotic pathways. Oxidative stress is known to cause lipid peroxidation and generation of lipid mediators that alter proteins, DNA and signaling pathways, and mechanisms that are associated with progression of neurodegenerative diseases.

N. Bazan discusses the role of lipids in synaptic signaling and the discovery of a new lipid messenger, 10,17S-docosatriene, which is implicated in counteracting brain inflammatory results. Building on lipids and inflammation,

Sun examines the importance of phospholipase A_2 and arachidonic acid in astrocytes in response to oxidation, inflammation and G protein-coupled receptors. Cholesterol and its metabolites have been suggested to play a role in AD and Wood et al. review work on sterol levels in serum and brain of AD patients and control subjects concluding that there is little support for the hypothesis that elevated cholesterol is a risk factor for AD. Zhu discusses the important consequences of oxidative imbalance leading to activation of ERK, JNK/SAPK and p38 pathways in AD. Several of the papers focus on mitochondrial dysfunction in neurodegeneration. Gibson discusses the important involvement of α-ketoglutarate–dehydrogenase complex in mitochondria as a target of ROS leading to cell dysfunction and death. Naoi et al. discuss production of excess ROS/RNS and protein misfolding leading to mitochondrial dysfunction and cell death. Butterworth describes the contribution of mitochondrial dysfunction in the pathogenesis of Wernicke's encephalopathy.

Oxidative stress plays an important role in cerebral ischemic damage. The article by Chan summarizes oxidative stress as a molecular switch for cell death/survival in ischemia and neurodegeneration with substantial emphasis on mitochondrial dysfunction and caspase activation. Strosznajder presents the role of poly(ADP-ribose) polymerase as the nuclear target in brain ischemia injury. Sun presents kainic acid-mediated excitotoxicity as a model for neurodegeneration. Fan discusses effects of hypoxic preconditioning on proliferation of neural stem cells.

In the section on Parkinson's disease, Yu et al. discuss α-synuclein and dopamine metabolism and propose that inhibition of dopamine synthesis by this protein has pathological consequences. Yang et al. review environmental toxins on the α-synuclein. The next group of articles by Zhao, Lu, Simonyi, and Liu discuss the potential therapeutic efficacy and neuroprotective mechanisms of different compounds and conditions. Emphasis is on naturally occurring antioxidants and polyphenols from plant sources. Yao describes a new procedure using HPLC and a Coulometric Multi-Electrode Array System to simultaneously measure low molecular weight, redox-active compounds in a single column with binary gradient. Reiner examines the JNK pathway in neuronal migration and its interaction with the X-linked doublecortin genes.

Neuronal excitation and injury is associated with release of ATP and activation of the P2 nucleotide receptors. The article by Weisman et al. discusses molecular determinants and functioning of the P2Y2 nucleotide receptor, and its implications for proliferative and inflammatory pathways in astrocytes. Neary et al. present links between the P2 nucleotide receptors and protein kinase cascades induced by CNS injury. In conclusion Gonzalez et al. describe mechanisms for inhibition of P2 receptor.

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Guest Editors
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