Handbook of Neurochemistry and Molecular Neurobiology

Acute Ischemic Injury and Repair in the Nervous System
Abel Lajtha (Ed.)

Handbook of Neurochemistry and Molecular Neurobiology
Acute Ischemic Injury and Repair in the Nervous System

Volume Editor: Pak H. Chan

With 55 Figures and 16 Tables

Springer
Stroke is a global health problem affecting approximately 15 million people annually in the world and about 700,000 people in the USA. It is the third leading cause of death and the most common cause of disability in most developed countries. The majority of strokes are ischemic (the blood flow to the brain is blocked), whereas a small percentage of strokes are hemorrhagic (the blood vessels burst). The molecular and cellular mechanisms of neuronal death that lead to brain injury and infarction after ischemic stroke have been intensively investigated over the past several decades. These investigations have led to our current understanding of the neurobiology of the disease at the molecular and cellular levels and have provided an impetus for the development of therapeutic strategies to treat brain injury in patients after an ischemic stroke.

This volume is intended to provide state-of-the-art and the most up-to-date knowledge on the mechanisms of neuronal death and repair after stroke. It begins with an overview of gene expression profiling in ischemic brain injury and ischemic tolerance for identification of the genes/proteins that are involved in neuronal death and neuroprotection. This chapter is followed by major discussions by leading experts in the field on the chosen gene/protein candidates that may affect neuronal death and survival. These candidate proteins include apoptotic-inducing factor (AIF) and poly(ADP-ribose) polymerase-1 (PARP-1), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), endothelial nitric oxide synthase (eNOS), and neuronal nitric oxide synthase (nNOS). Activation or expression of these proteins is known to induce DNA damage that leads to neuronal apoptosis. A succinct overview of the mechanisms of DNA damage and repair in ischemic neurons follows.

Protein synthesis, folding, aggregation, and degradation are known to play major roles in mediating the fate of ischemic neurons and this aspect is discussed, followed by a chapter that describes the neuroprotective or apoptotic role of heat shock protein. The neurobiology of superoxide dismutase, the key endogenous antioxidant enzyme in free radical detoxification and signaling in neuronal death or survival after cerebral ischemia is reviewed, and this basic research provided mechanistic support to the recent success of spin trap NXY-059 in a clinical stroke trial.

The neurovascular unit, which consists of many cell types, and its interaction and integrity have recently evolved as prime targets for therapeutic intervention in stroke. Thus, the two chapters that describe the biology of glial and cerebral endothelial cells and their role in the integrity and repair of the neurovascular unit are of major importance. This is followed by reviews on sex steroids and gender in ischemic pathobiology and the mechanisms of ischemic cell death in the developing brain. A review of the molecular mechanisms of cell death following subarachnoid hemorrhage is presented. The basic molecular and cellular mechanisms of neuroprotection of the antibiotic minocycline, a potential therapeutic agent in clinical stroke, are clearly reviewed by experts in the field. This chapter is followed by the concluding chapter, an outstanding review of the roles of matrix metalloproteinases and tissue plasminogen activator in reperfusion therapy that target the neurovascular unit in stroke.

It is our belief that this volume provides an excellent review of the tremendous advances of the past decades in neurochemical and molecular biological aspects of cerebral ischemia. We hope that these advances, as communicated through this volume, will provide an impetus for basic scientists and clinicians to further their translational research and to promote the insights for development of therapeutic interventions for stroke.

Pak H. Chan, Ph.D.
Preface ................................................................. v

Contributors ........................................................... ix

1 Gene Expression Profiling in Ischemic Brain Injury and Ischemic Tolerance . . . 1
   C. A. Harrington · S. Stevens · M. Stenzel-Poore · R. P. Simon

2 Neurobiology of AIF and PARP in Cerebral Ischemia ................................. 19
   D. W. Koh · T. M. Dawson · V. L. Dawson

3 iNOS and COX-2 in Ischemic Stroke ..................................................... 33
   P. Zhou · C. Iadecola

4 eNOS and nNOS in Stroke ............................................................... 47
   P. L. Huang

5 Molecular Mechanisms of DNA Damage and Repair in Ischemic Neuronal Injury .................................................. 65
   F. Sun · G. Gobbel · W. Li · J. Chen

6 Heat-Shock Protein Regulation of Protein Folding, Protein Degradation, Protein Function, and Apoptosis .......................... 89
   R. Ran · A. Lu · H. Xu · Y. Tang · F. R. Sharp

7 Cotranslational Protein Folding and Aggregation after Brain Ischemia .... 109
   B. R. Hu

8 Superoxide Dismutases in Stroke ......................................................... 121
   C. M. Maier · P. H. Chan

9 The Role of Glia in Excitotoxicity and Stroke .................................... 145
   T. M. Kauppinen · R. A. Swanson

10 Cerebral Endothelial Cell Reaction to Ischemic Insults ......................... 165
    D.-I Yang · T.-N. Lin · K.-J. Yin · C.-J. Hu · S.-D. Chen · J. Xu · C. Y. Hsu

11 Gender, Sex Steroids, and Cerebral Ischemic Pathobiology .................. 185
    I. P. Koerner · S. J. Murphy · P. D. Hurn

© Springer-Verlag Berlin Heidelberg 2007
Contributors

A. M. Buchan
Clinical Proteomics Research for the Brain Massachusetts General Hospital Harvard Medical School, USA

P. H. Chan
Department of Neurosurgery, Department of Neurology and Neurological Sciences, and Program in Neurosciences, Stanford University School of Medicine, Stanford, California 94305-5487, USA

S.-D. Chen
Department of Neurology, Chang Gung Memorial Hospital, Kaohsiung, Taiwan

J. Chen
Department of Neurology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213 Geriatric Research, Educational and Clinical Center, V.A. Pittsburgh Health Care System, Pittsburgh, PA 15261, USA

A. R. T. Colohan
Department of Physiology, Division of Neurosurgery, Department of Surgery, Loma Linda University, Loma Linda, California, USA

T. M. Dawson
Institute for Cell Engineering, Departments of Neurology, Neuroscience, and Physiology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA

V. L. Dawson
Institute for Cell Engineering, Departments of Neurology, Neuroscience, and Physiology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA

D. M. Ferriero
Department of Neurology and Pediatrics, University of California San Francisco, Box 0663, 521 Parnassus Ave. C215, San Francisco, CA 94143-0663, USA

G. Gobbel
Department of Neurological Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA

C. A. Harrington
Vaccine & Gene Therapy Institute, OHSU 505 NW 18th Avenue, Beaverton OR 97006, USA

C. Y. Hsu
Chi-Ching Huang Stroke Research Center, Taipei Medical University, Taipei, Taiwan

B. R. Hu
Dept of Neurology, University of Miami School of Medicine, Miami, FL 33136, USA

C.-J. Hu
Department of Neurology, Taipei Medical University, Taipei, Taiwan

P. L. Huang
Cardiovascular Research Center and Cardiology Division, Medical Services, Massachusetts General Hospital, Boston, MA 02114, USA

P. D. Hurn
Department of Anesthesiology and the Center for Research in Gender-based Medicine, Oregon Health and Sciences University 3181 S.W. Sam Jackson Park Rd, Portland OR 97239-3098, USA

C. Iadecola
Division of Neurobiology Weill Medical College of Cornell University New York, New York, USA

T. M. Kauppinen
Department of Neurology, University of California at San Francisco, and Veterans Affairs Medical Center, (127) Neurology, VAMC, 4150 Clement St., San Francisco, CA 94121, USA

© Springer-Verlag Berlin Heidelberg 2007
Contributors xi

R. A. Swanson
Department of Neurology, University of California at San Francisco, and Veterans Affairs Medical Center, (127) Neurology, VAMC, 4150 Clement St., San Francisco, CA 94121, USA

Y. Tang
M.I.N.D. Institute and Department of Neurology, University of California at Davis, 2805 50th Street, Sacramento, California 95817, USA

E. Tejima
Clinical Proteomics Research for the Brain Massachusetts General Hospital Harvard Medical School, USA

K. Tsuji
Clinical Proteomics Research for the Brain Massachusetts General Hospital Harvard Medical School, USA

Z. S. Vexler
Department of Neurology, University California San Francisco, Department of Neurology Box 0663, 521 Parnassus Ave. C215, San Francisco, CA 94143-0663, USA

X. Wang
Clinical Proteomics Research for the Brain Massachusetts General Hospital Harvard Medical School, USA

H. Xu
M.I.N.D. Institute and Department of Neurology, University of California at Davis, 2805 50th Street, Sacramento, California 95817, USA

J. Xu
Department of Neurology, Washington University School of Medicine, St. Louis, Missouri, USA

D.-I Yang
Institute of Neuroscience, Tzu Chi University, Hualien, Taiwan

K.-J. Yin
Department of Neurology, Washington University School of Medicine, St. Louis, Missouri, USA

J. H. Zhang
Department of Physiology, Division of Neurosurgery, Department of Surgery, Loma Linda University, Loma Linda, California, USA

P. Zhou
Division of Neurobiology Weill Medical College of Cornell University New York, New York, USA