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Book Review

How to study neuroprotection?

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METHODS IN MOLECULAR BIOLOGY, vol. 399: NEUROPROTECTION METHODS AND PROTOCOLS. By T Borsello. Humana Press Inc., Totowa, NJ, 2007. pp 239. ISBN: 978-1-58829-666-5. 80.87 €.

Understanding the aetiology of major neurodegenerative diseases and identifying ways of early detection has become an increasingly important approach to treatment and prevention of such diseases. Most neurodegeneration-inducing insults ultimately lead to the initiation of a common signalling cascade of neuronal cell death, which is manifest clinically as loss in distinct neurological functions. Such degenerative events are usually accompanied by counteracting, compensatory regenerative mechanisms. Therefore, elucidation of the common mechanisms underlying neurodegeneration and regeneration would allow establishment of strategies to intervene in the progression of neurodegeneration and to support regenerative processes. As the pathogenesis involves several endogenous and exogenous aetiological stimuli with multiple molecular pathways leading to morphologically different types of dysfunction or death (apoptosis, necrosis, autophagy) and counteracting attempts to survive, the field of neurodegeneration is broad. Consequently the related methods are highly complex. But how to study neuroprotection at a time when the Material and Methods sections in papers are becoming less and less informative?

In this respect, the book *Neuroprotection Methods and Protocols* brings together leading experts from neurobiology, neurophysiology, neuropharmacology, neuroimmunology and clinical neuroscience to highlight the most recent milestones in this rapidly evolving field and focuses on the most important techniques needed by undergraduate and post-graduate students when undertaking research in this area. What is neuroprotection? Neuroprotection is the mechanism and strategy used to protect against neuronal injury or degeneration in the Central Nervous System (CNS) following acute disorders, such as stroke or nervous system injury/trauma, or as a result of chronic neurodegenerative diseases, including Parkinson's, Alzheimer's or Multiple Sclerosis. The goal of neuroprotection is to limit neuronal dysfunction/death after CNS injury in an attempt to maintain the highest possible integrity of cellular interactions in the brain thus minimising disturbance to neural function. Given the very limited capacity of regeneration in the brain, protecting neurons that are on the brink of death is a major challenge for basic and clinical neuroscience, with implications for a broad spectrum of acute and chronic neurological and psychiatric diseases.

The book of 15 chapters opens with a review by Repici, Mariani and Borsello, on the three main types of neuronal death: apoptosis, necrosis and autophagic cell death. Although these widely used methods do not need description, the authors indicate that, since multiple death pathways are often activated in response to a single stimulus, the optimal neuroprotective approach should include either combination treatments directed towards multiple cell death pathways or the use of single compounds that inhibit more than one cell death mechanism. The follow chapters are divided among four subject areas: (i) models to study neuronal injury and neuroprotection. In this context, chapters 2, 4 and 5 describe a model of NMDA-induced neurotoxicity that is believed to recapitulate some of the key damaging mechanisms that occur *in vivo* during brain ischaemia; a model of partial injury of the rat optical nerve and organotypic slice cultures of mouse entorhinal cortex and hippocampus to study axonal regeneration and collateral sprouting in the CNS *in vitro*. (ii) Methods to assess neuronal degeneration and death, such as the silver stain methods, as modified by Tenkova, to identify degenerating neurons in retina, cortex, and other nervous system regions of infants and adult rodents, illustrated in chapter 3; the method of astrocyte-based, Nrf2-dependent, antioxidant gene therapy that confers protection against malonate-induced neuronal cell death, and fixation of brain tissue by rapid freezing to study cerebral energy metabolism, as described respectively in chapters 6 and 7. (iii) Methods to identify genes involved in neuronal death and survival. Nuclear factor kappa B (NF-kB)/Rel proteins, as a dimeric transcription factor, control the expression of genes that regulate a broad range of biological processes through canonical and non-canonical pathways. In the central nervous system, NF-kB controls inflammatory reactions and apoptotic cell death following nerve injury. NF-kB activation is a part of a recovery process that may protect neurons against oxidative stresses or brain ischaemia-induced apoptosis and neurodegeneration. The identification of genes that mediate the prosurvival activity of NF-kB is therefore a topic of intense interest and is described in chapter 8, while the screening of libraries to identify genes involved in the cleavage of the β-amyloid precursor protein, a process associated with the neuronal degeneration characterizing Alzheimer's disease is well illustrated in chapters 9. Chapter 10 provides detailed protocols for harvesting RNA from single cells and its reverse transcription into cDNA for subsequent PCR or synthesis of amplified RNA. The last area (neuroprotection) discusses modern therapeutic approaches to acute focal brain ischaemia and basic strategies for neuroprotection, with particular attention to the DNA microarray technology to detect novel potential neuroprotective targets to counteract brain damage induced by hypoxia–ischaemia (chapter 11); to the

intracerebral infusion technology with neurotrophic factors, used to promote survival of cells in the CNS (chapter 12); cell-penetrating peptide purification and their use for neuronal rescue (chapter 13); and finally the basic and technical aspects of the handling and preparation of neural stem cells for experimental transplantation in rodent models of human pathologies (chapter 14). The final chapter is a review of two nuclear-based techniques, positron emission tomography and single-photon emission computed tomography, imaging methodologies to detect the loss of neurons, monitor the progression of the disease and validate the neuroprotective potential of therapeutic strategies.

All chapters are clearly written, in a logical order, and follow a uniform layout, with initial summary, keywords, introduction, materials, methods, abundant notes and discussion as well as extensive and updated reference lists. The protocols are described in full detail. This is a multi-authored text and as in many multi-author books, the individual chapters are of variable quality and there are some overlaps and redundancies. Throughout the book, each chapter stands alone, and although this results in some repetition of topics, it has the tremendous advantage that the reader can dive into any section of interest and feel at ease. The majority of the black-and-white figures in the book, while simple, clearly illustrate the authors'points. Tables, graphs and schemes, also presented in a black and white format, adequately illustrate the data on which the authors base their experimental protocols. However, in general, it is a technically oriented book that focuses particularly on those techniques that have led to recent advances in neuroprotection and is designed to help basic researchers understand the theory and practical principles behind those methods. Therefore, this is a comprehensive, practical, and user-friendly small manual both for inexperienced investigators and to experienced researchers and graduate students as a benchtop handbook, which without sacrificing scientific concepts, maintains the spirit of experimentation.

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