Neuromethods 98

Springer Protocols

Xuenong Bo
Joost Verhaagen *Editors*

Gene Delivery and Therapy for Neurological Disorders

Humana Press

NEUROMETHODS

Series Editor
Wolfgang Walz
University of Saskatchewan
Saskatoon, SK, Canada

For further volumes:
http://www.springer.com/series/7657

Gene Delivery and Therapy for Neurological Disorders

Edited by

Xuenong Bo

Queen Mary University of London, London, UK

Joost Verhaagen

Netherlands Institute for Neuroscience, Amsterdam, The Netherlands

Humana Press

Editors
Xuenong Bo
Queen Mary University of London
London, UK

Joost Verhaagen
Netherlands Institute for Neuroscience
Amsterdam, The Netherlands

ISSN 0893-2336 ISSN 1940-6045 (electronic)
Neuromethods
ISBN 978-1-4939-2305-2 ISBN 978-1-4939-2306-9 (eBook)
DOI 10.1007/978-1-4939-2306-9

Library of Congress Control Number: 2015930046

Springer New York Heidelberg Dordrecht London

Printed on acid-free paper

Humana Press is a brand of Springer
Springer Science+Business Media LLC New York is part of Springer Science+Business Media (www.springer.com)

Series Preface

Experimental life sciences have two basic foundations: concepts and tools. The *Neuromethods* series focuses on the tools and techniques unique to the investigation of the nervous system and excitable cells. It will not, however, shortchange the concept side of things as care has been taken to integrate these tools within the context of the concepts and questions under investigation. In this way, the series is unique in that it not only collects protocols but also includes theoretical background information and critiques which led to the methods and their development. Thus it gives the reader a better understanding of the origin of the techniques and their potential future development. The *Neuromethods* publishing program strikes a balance between recent and exciting developments like those concerning new animal models of disease, imaging, in vivo methods, and more established techniques, including, for example, immunocytochemistry and electrophysiological technologies. New trainees in neurosciences still need a sound footing in these older methods in order to apply a critical approach to their results.

Under the guidance of its founders, Alan Boulton and Glen Baker, the *Neuromethods* series has been a success since its first volume published through Humana Press in 1985. The series continues to flourish through many changes over the years. It is now published under the umbrella of Springer Protocols. While methods involving brain research have changed a lot since the series started, the publishing environment and technology have changed even more radically. Neuromethods has the distinct layout and style of the Springer Protocols program, designed specifically for readability and ease of reference in a laboratory setting.

The careful application of methods is potentially the most important step in the process of scientific inquiry. In the past, new methodologies led the way in developing new disciplines in the biological and medical sciences. For example, Physiology emerged out of Anatomy in the nineteenth century by harnessing new methods based on the newly discovered phenomenon of electricity. Nowadays, the relationships between disciplines and methods are more complex. Methods are now widely shared between disciplines and research areas. New developments in electronic publishing make it possible for scientists that encounter new methods to quickly find sources of information electronically. The design of individual volumes and chapters in this series takes this new access technology into account. Springer Protocols makes it possible to download single protocols separately. In addition, Springer makes its print-on-demand technology available globally. A print copy can therefore be acquired quickly and for a competitive price anywhere in the world.

Saskatoon, Saskatchewan, Canada ***Wolfgang Walz***

Preface

Gene therapy, once labeled as a hype by skeptics, is now becoming a reality due to the development of safer and more efficient viral vectors. Three gene therapy drugs, two for cancer and one for lipoprotein lipase deficiency, have been approved in China and the European Union, and hundreds of clinical trials of gene therapies are in progress. Gene therapy can be used to treat not only the diseases caused by genetic defects but also medical conditions such as nerve injury and pain by manipulating gene expression. For most types of neurological disorders, there are currently no effective treatments based on conventional pharmaceuticals and surgical practice to slow or stop disease progression and regain normal neurological functions. Gene therapy is emerging as a powerful approach with potential to treat and perhaps even cure many neurological disorders. Better understanding of the underlying genetic and molecular mechanisms for neurological disorders and the development and improvement of gene delivery vectors and methods has made gene therapy clinically applicable. Development of gene therapy for different neurological disorders is at various stages, from lab-based research only to Phase II clinical trials. More and more neuroscientists and neurologists have employed or intend to employ gene-targeting techniques for the development of potential gene therapies for neurological disorders.

The chapters in this volume provide a brief overview of the latest developments in adeno-associated viral and lentiviral vectors as well as the gene therapy strategies for the most common neurological disorders, followed by a step-by-step guide on viral vector-based gene delivery in animal models used in the authors' laboratories. We hope this book will serve as a guide for researchers to explore the potentials of gene therapy for neurological disorders. Although safe gene manipulation in neural cells can be achieved, it may still be years away from efficacious gene-based treatment of neurological disorders such as Parkinson's and Alzheimer's diseases due to the complexity of the underlying genetic/molecular mechanisms and the lack of reliable animal models. However, such obstacles are being and will be overcome, and gene therapy will revolutionize medicine in the future.

London, UK — *Xuenong Bo*
Amsterdam, The Netherlands — *Joost Verhaagen*

Contents

Contributors

Wael Asaad • *Department of Neurosurgery and Brown Institute for Brain Science, Alpert Medical School and Rhode Island Hospital, Brown University, Providence, RI, USA*

Mariela A. Moreno Ayala • *Instituto de Investigaciones Biomedicas (INBIOMED), National Council for Science and Technology (CONICET), School of Medicine, University of Buenos Aires, Buenos Aires, Argentina*

Mimoun Azzouz • *Department of Neuroscience, Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, UK; Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia*

Christopher Binny • *Department of Neuroscience, Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, UK*

Bas Blits • *UniQure, Amsterdam, The Netherlands*

Xuenong Bo • *Centre for Neuroscience and Trauma, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK*

Imramsjah M.J. van der Bom • *Department of Radiology, University of Massachusetts Medical School, Worcester, MA, USA; New England Center for Stroke Research, University of Massachusetts Medical School, Worcester, MA, USA*

Allison M. Bradbury • *Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*

Marianela Candolfi • *Instituto de Investigaciones Biomedicas, National Council for Science and Technology, University of Buenos Aires School of Medicine, Buenos Aires, Argentina*

Maria G. Castro • *Department of Neurosurgery, School of Medicine, University of Michigan, Ann Arbor, MI, USA; Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI, USA*

Matthew J. During • *Department of Molecular Virology, Immunology and Medical Genetics, Neuroscience and Neurological Surgery, Comprehensive Cancer Center, The Ohio State University, Columbus, OH, USA*

Ruben Eggers • *Laboratory for Neuroregeneration, Netherlands Institute for Neuroscience, an Institute of the Royal Academy of Arts and Sciences, Amsterdam Zuidoost, The Netherlands*

Ioanna Eleftheriadou • *Gene Therapy, Division of Brain Sciences, Centre for Neuroinflammation and Neurodegeneration, Faculty of Medicine, Imperial College London, London, UK*

Nitish D. Fagoe • *Laboratory for Neuroregeneration, Netherlands Institute for Neuroscience, an Institute of the Royal Academy of Arts and Sciences, Amsterdam Zuidoost, The Netherlands*

Dahna M. Fong • *Department of Pharmacology and Clinical Pharmacology and Centre for Brain Research, School of Medical Sciences, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand*

Diane Golebiowski • *Department of Neurology, University of Massachusetts Medical School, North Worcester, MA, USA; Gene Therapy Center, University of Massachusetts Medical School, North Worcester, MA, USA*

Matthew Gounis • *Department of Radiology, University of Massachusetts Medical School, Worcester, MA, USA; New England Center for Stroke Research, University of Massachusetts Medical School, Worcester, MA, USA*
Heather L. Gray-Edwards • *Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
Mark W. Hankins • *Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK*
Stephan Hermening • *UniQure, Amsterdam, The Netherlands*
Judith A. Hudson • *Department of Clinical Sciences, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
Tsuneya Ikezu • *Department of Pharmacology and Experimental Therapeutics, Boston University School of Medicine, Boston, MA, USA; Department of Neurology and Graduate Program in Neuroscience, Boston University School of Medicine, Boston, MA, USA*
Jacob A. Johnson • *Department of Clinical Sciences, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
Aime K. Johnson • *Department of Clinical Sciences, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
Evangelia Karyka • *Department of Neuroscience, Sheffield Institute for Translational Neuroscience, The University of Sheffield, Sheffield, UK*
Deniz Kirik • *BRAINS Unit, Lund University, Lund, Sweden*
Tomomi Kiyota • *Department of Pharmacology and Experimental Neuroscience, University of Nebraska Medical Center, Omaha, NE, USA*
Carl Koschmann • *Division of Pediatric Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA*
Anna Luisa Kühn • *Department of Radiology, University of Massachusetts Medical School, Worchester, MA, USA; New England Center for Stroke Research, University of Massachusetts Medical School, Worchester, MA, USA*
Churl-Su Kwon • *Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA*
En-Ju D. Lin • *Department of Molecular Virology, Immunology and Medical Genetics, Neuroscience and Neurological Surgery, Comprehensive Cancer Center, The Ohio State University, Columbus, OH, USA*
Christian L. Lorson • *Department of Veterinary Pathobiology, Life Sciences Center, University of Missouri, Columbia, MO, USA; Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia, MO, USA*
Pedro R. Lowenstein • *Department of Neurosurgery, University of Michigan, Ann Arbor, MI, USA; Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI, USA*
John Lynes • *Department of Neurosurgery, School of Medicine, University of Michigan, Ann Arbor, MI, USA; Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI, USA*
Robert E. MacLaren • *Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK*
Douglas R. Martin • *Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, AL, USA; Department of Anatomy, Physiology, and Pharmacology, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*

Isabel Martins • *Department of Experimental Biology, Faculty of Medicine of Porto, University of Porto, Porto, Portugal; Instituto de Biologia Molecular e Celular, University of Porto, Porto, Portugal*
Matthew R.J. Mason • *Laboratory for Neuroregeneration, Netherlands Institute for Neuroscience, an Institute of the Royal Academy of Arts and Sciences, Amsterdam Zuidoost, The Netherlands*
Nicholas D. Mazarakis • *Gene Therapy, Division of Brain Sciences, Centre for Neuroinflammation and Neurodegeneration, Faculty of Medicine, Imperial College London, London, UK*
Michelle E. McClements • *Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK*
Pádraig J. Mulcahy • *Department of Neuroscience, Sheffield Institute for Translational Neuroscience, The University of Sheffield, Sheffield, UK*
Bartosz Muszynski • *Department of Neuroscience, Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, UK*
Erkan Y. Osman • *Department of Veterinary Pathobiology, Life Sciences Center, University of Missouri, Columbia, MO, USA; Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia, MO, USA*
Harald Petry • *UniQure, Amsterdam, The Netherlands*
Ashley N. Randle • *Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
James L. Sartin • *Department of Anatomy, Physiology and Pharmacology, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*
Vandana Saxena • *Department of Neurosurgery, School of Medicine, University of Michigan, Ann Arbor, MI, USA; Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI, USA*
Miguel Sena-Esteves • *Department of Neurology and Gene Therapy Center, University of Massachusetts Medical School, Worcester, MA, USA*
Monir Shababi • *Department of Veterinary Pathobiology, Life Sciences Center, University of Missouri, Columbia, MO, USA; Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia, MO, USA*
Fanxia Shen • *Department of Anesthesia and Perioperative Care, Center for Cerebrovascular Research, University of California San Francisco, San Francisco, CA, USA*
Samantha R. de Silva • *Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK*
Lorelei Stoica • *Department of Neurology, University of Massachusetts Medical School, Worcester, MA, USA; Gene Therapy Center, University of Massachusetts Medical School, Worcester, MA, USA*
Hua Su • *Department of Anesthesia and Perioperative Care, Center for Cerebrovascular Research, University of California San Francisco, San Francisco, CA, USA*
Isaura Tavares • *Department of Experimental Biology, Faculty of Medicine of Porto and Instituto de Biologia Molecular e Celular, University of Porto, Porto, Portugal*
Joost Verhaagen • *Laboratory for Neuroregeneration, Netherlands Institute for Neuroscience, an Institute of the Royal Academy of Arts and Sciences, Amsterdam Zuidoost, The Netherlands; Center for Neurogenomics and Cognition Research, Neuroscience Campus Amsterdam, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*

Brian K. Whitlock • *Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN, USA*

Mia Wibowo • *Department of Neurosurgery, School of Medicine, University of Michigan, Ann Arbor, MI, USA; Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI, USA*

Diane U. Wilson • *Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, AL, USA*

Maya Woodbury • *Department of Pharmacology and Experimental Therapeutics and Graduate Program in Neuroscience, Boston University School of Medicine, Boston, MA, USA*

Angela Wu • *Department of Pharmacology and Clinical Pharmacology, The University of Auckland, Auckland, New Zealand; Faculty of Medical and Health Sciences, Centre for Brain Research, School of Medical Sciences, The University of Auckland, Auckland, New Zealand*

Deborah Young • *Department of Pharmacology and Clinical Pharmacology, The University of Auckland, Auckland, New Zealand; Faculty of Medical and Health Sciences, Centre for Brain Research, School of Medical Sciences, The University of Auckland, Auckland, New Zealand*

Yi Zhang • *Centre for Neuroscience and Trauma, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary, University of London, London, UK*