

METHODS IN MOLECULAR BIOLOGY™

Series Editor

John M. Walker

School of Life Sciences

University of Hertfordshire

Hatfield, Hertfordshire, AL10 9AB, UK

For other titles published in this series, go to
www.springer.com/series/7651

Molecular Imaging

Methods and Protocols

Edited by

Khalid Shah

*Massachusetts General Hospital,
Harvard Medical School,
Boston, Massachusetts, USA*

Editor

Dr. Khalid Shah

Molecular Neurotherapy and
Imaging Laboratory

Department of Radiology
and Neurology

Massachusetts General Hospital
Harvard Medical School
Charlestown, MA, 02129-2060, USA
kshah@helix.mgh.harvard.edu

ISSN 1064-3745

e-ISSN 1940-6029

ISBN 978-1-60761-900-0

e-ISBN 978-1-60761-901-7

DOI 10.1007/978-1-60761-901-7

Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2010935924

© Springer Science+Business Media, LLC 2011

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Humana Press, c/o Springer Science+Business Media, LLC, 233 Spring Street, New York, NY 10013, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden.

The use in this publication of trade names, trademarks, service marks, and similar terms, even if they are not identified as such, is not to be taken as an expression of opinion as to whether or not they are subject to proprietary rights. While the advice and information in this book are believed to be true and accurate at the date of going to press, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Humana Press is part of Springer Science+Business Media (www.springer.com)

Preface

From the first development of radioactive tracers in the early 1930s, it would take almost seven more decades for molecular imaging to evolve into a mature field of research. Since then, however, molecular imaging techniques have advanced and become invaluable tools for molecular biology research and – to a more modest extent – clinical medicine. Molecular imaging abandons the canonical imaging paradigm of detecting morphological contrasts and aims to explore the dynamics of molecules indicative of physiology and disease in a qualitative and quantitative manner. It allows longitudinal, noninvasive visualization of biological processes at the sub-cellular level, typically but not necessarily through the use of reporters with strong binding affinity to the molecular targets of interest. It follows from this rather unrestrictive definition that molecular imaging is not limited to specific image-capture methods but includes optical (near-infrared and visible spectrum fluorescence, bioluminescence), radio-scintigraphic modalities (PET, SPECT), magnetic resonance imaging (MRI), and magnetic resonance spectroscopy (MRS). All these imaging techniques progressively employ tagged probes with high affinity for molecules of interest, binding-activatable ‘smart’ probes and genetically engineered stably expressed reporters thus allowing optimized target visualization. Consequently, the list of biological processes that can be investigated is long and continues to expand.

The amount of possibilities offered by different molecular imaging techniques can be puzzling to biologists new to the field. Bearing this in mind, this book sets out to describe a rich variety of practical procedures and methods for diverging imaging technologies. Different sections are devoted to imaging of basic molecular and biochemical events, imaging in pre-clinical and finally in clinical settings and include sufficient practical details for students, established practitioners, and research fellows from different fields to become familiar with molecular imaging and incorporate imaging into their work.

Khalid Shah

Contents

Preface	v
Contributors	ix

SECTION I IMAGING BIOCHEMICAL PATHWAYS AND MOLECULAR EVENTS

1. Bioluminescence Resonance Energy Transfer (BRET) Imaging in Plant Seedlings and Mammalian Cells	3 <i>Qiguang Xie*, Mohammed Soutto*, Xiaodong Xu*, Yunfei Zhang, and Carl Hirschie Johnson (*equal contributors)</i>
2. Luciferase Protein Complementation Assays for Bioluminescence Imaging of Cells and Mice	29 <i>Gary D. Luker and Kathryn E. Luker</i>
3. Hybrid Raman-Fluorescence Microscopy on Single Cells Using Quantum Dots	45 <i>Henk-Jan van Manen and Cees Otto</i>
4. Labeling of Mesenchymal Stem Cells with Bioconjugated Quantum Dots	61 <i>Bhranti S. Shah and Jeremy J. Mao</i>
5. Quantification of miRNA Abundance in Single Cells Using Locked Nucleic Acid-FISH and Enzyme-Labeled Fluorescence	77 <i>Jing Lu and Andrew Tsourkas</i>

SECTION II IMAGING IN PRE-CLINICAL SETTINGS

6. Imaging Fate of Stem Cells at a Cellular Resolution in the Brains of Mice	91 <i>Khalid Shah</i>
7. Magnetic Resonance Imaging of Brain Inflammation Using Microparticles of Iron Oxide	103 <i>Martina A. McAteer, Constantin von Zur Muhlen, Daniel C. Anthony, Nicola R. Sibson, and Robin P. Choudhury</i>
8. Optical Characterization of Arterial Apoptosis	117 <i>Maarten F. Corsten and Abdelkader Bennaghmouch</i>
9. Intravital Fluorescence Microscopic Molecular Imaging of Atherosclerosis	131 <i>Farouc A. Jaffer</i>
10. MR Imaging of Transplanted Stem Cells in Myocardial Infarction	141 <i>Dara L. Kraitchman, Dorota A. Kedziorek, and Jeff W.M. Bulte</i>
11. In Vivo Imaging of the Dynamics of Different Variants of EGFR in Glioblastomas	153 <i>Khalid Shah</i>

12. Fluorescence Lifetime-Based Optical Molecular Imaging	165
<i>Anand T.N. Kumar</i>	
SECTION III IMAGING IN CLINICAL SETTINGS	
13. PET Imaging of $\alpha v\beta 3$ Expression in Cancer Patients	183
<i>Ambros J. Beer and Markus Schwaiger</i>	
14. Quantitative Approaches to Amyloid Imaging	201
<i>Victor L. Villemagne, Graeme O'Keefe, Rachel S. Mulligan, and Christopher C. Rowe</i>	
15. Molecular Imaging of Myocardial Remodeling After Infarction	227
<i>Johan W.H. Verjans, Susanne W.M. van de Borne, Leonard Hofstra, and Jagat Narula</i>	
16. Dual-Radionuclide Brain SPECT for the Differential Diagnosis of Parkinsonism . .	237
<i>Georges El Fakhri and Jinsong Ouyang</i>	
Index	247

Contributors

DANIEL C. ANTHONY • *Department of Pharmacology, University of Oxford, Oxford OX1 3QX, UK*

AMBROS J. BEER • *Department of Nuclear Medicine, Klinikum rechts der Isar, Technische Universität München, Munich 81675, Germany*

ABDELKADER BENNAGHMOUCH • *Maastricht Molecular Imaging and Therapeutics Laboratory (MMIT Laboratory), Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht 6224 ER, The Netherlands*

JEFF W.M. BULTE • *Division of MR Research, Russell H. Morgan Department of Radiology and Radiological Science; Cellular Imaging Section and Vascular Biology Program, Institute for Cell Engineering; Department of Chemical and Biomolecular Engineering; Department of Biomedical Engineering, Whiting School of Engineering, Johns Hopkins University, Baltimore, MD, USA*

ROBIN P. CHOUDHURY • *Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, Oxford OX3 9DU, UK*

MAARTEN F. CORSTEN • *Maastricht Molecular Imaging and Therapeutics Laboratory (MMIT Laboratory), Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht 6224 ER, The Netherlands*

GEORGES EL FAKHRI • *Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114, USA*

LEONARD HOFSTRA • *Maastricht Molecular Imaging and Therapeutics Laboratory (MMIT Laboratory), Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, The Netherlands*

FAROUC A. JAFFER • *Cardiovascular Research Center and Cardiology Division, Center for Molecular Imaging Research, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*

CARL HIRSCHIE JOHNSON • *Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA*

DOROTA A. KEDZIOREK • *Division of MR Research, Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, USA*

DARA L. KRAITCHMAN • *Division of MR Research, Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, USA*

ANAND T.N. KUMAR • *Athinoula A Martinos Center for Biomedical Imaging, Harvard Medical School, Massachusetts General Hospital, Charlestown, MA 02129, USA*

- JING LU • *Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104, USA*
- GARY D. LUKER • *Department of Radiology, University of Michigan, Ann Arbor, MI 48109-2200, USA; Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI 48109-2200, USA*
- KATHRYN E. LUKER • *Department of Radiology, Ann Arbor, MI, USA*
- JEREMY J. MAO • *Tissue Engineering and Regenerative Medicine Laboratory, Department of Biomedical Engineering, College of Dental Medicine, Columbia University Medical Center, New York, NY 10032, USA*
- MARTINA A. MCATEER • *Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, Oxford OX3 9DU, UK; Department of Pharmacology, University of Oxford, Oxford OX1 3QX, UK*
- RACHEL S. MULLIGAN • *Department of Nuclear Medicine, Centre for PET, Austin Health, Heidelberg, VIC 3084, Australia*
- JAGAT NARULA • *Department of Cardiology, University of California, Irvine, CA, USA*
- GRAEME O'KEEFE • *Department of Nuclear Medicine, Centre for PET, Austin Health, Heidelberg, VIC 3084, Australia; School of Physics and Department of Medicine, University of Melbourne, Melbourne, VIC, Australia*
- CEES OTTO • *Department of Science and Technology, Medical Cell BioPhysics, MIRA Institute for Biomedical Technology and Technical Medicine P.O. Box 217, 7500, AE Enschede, The Netherlands*
- JINSONG OUYANG • *Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114, USA*
- CHRISTOPHER C. ROWE • *Department of Nuclear Medicine, Centre for PET, Austin Health, Heidelberg, VIC 3084, Australia; Department of Medicine, University of Melbourne, Melbourne, VIC, Australia*
- MARKUS SCHWAIGER • *Department of Nuclear Medicine, Klinikum rechts der Isar, Technische Universität München, Munich 81675, Germany*
- BHRANTI S. SHAH • *Tissue Engineering and Regenerative Medicine Laboratory, Department of Biomedical Engineering, College of Dental Medicine, Columbia University Medical Center, New York, NY 10032, USA*
- KHALID SHAH • *Molecular Neurotherapy and Imaging Laboratory, Department of Radiology and Neurology, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114, USA*
- NICOLA R. SIBSON • *Experimental Neuroimaging Group, Gray Institute for Radiation Oncology and Biology, Churchill Hospital, University of Oxford, Oxford OX3 7LJ, UK*
- MOHAMMED SOUTTO • *Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA*
- ANDREW TSOURKAS • *Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104, USA*
- SUSANNE W.M. VAN DE BORNE • *Maastricht Molecular Imaging and Therapeutics Laboratory (MMIT Laboratory), Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, The Netherlands*

- HENK-JAN VAN MANEN • *AkzoNobel Research, Development & Innovation Measurement & Analytical Science Molecular Spectroscopy Group, Zutphenseweg 10, 7418 AJ, Deventer, The Netherlands*
- JOHAN W.H. VERJANS • *Division of Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands*
- VICTOR L. VILLEMAGNE • *Department of Nuclear Medicine, Centre for PET, Austin Health, Heidelberg, VIC 3084, Australia; The Mental Health Research Institute of Victoria, Parkville, VIC, Australia*
- CONSTANTIN VON ZUR MUHLEN • *Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, Oxford OX3 9DU, UK; Department of Pharmacology, University of Oxford, Oxford OX1 3QX, UK*
- QIGUANG XIE • *Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA*
- XIAODONG XU • *Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA*
- YUNFEI ZHANG • *Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA*