Molecular Cardiology

METHODS IN MOLECULAR MEDICINE™

John M. Walker, SERIES EDITOR

- 116 Interferon Methods and Protocols**, edited by Daniel J. J. Carr, 2005
- 115 Lymphoma: Methods and Protocols**, edited by Timothy Illidge and Peter W. M. Johnson, 2005
- 114 Microarrays in Clinical Diagnostics**, edited by Thomas Joos and Paolo Fortina, 2005
- 113 Multiple Myeloma: Methods and Protocols**, edited by Ross D. Brown and P. Joy Ho, 2005
- 112 Molecular Cardiology: Methods and Protocols**, edited by Zhongjie Sun, 2005
- 111 Chemosensitivity: Volume 2, In Vivo Models, Imaging, and Molecular Regulators**, edited by Rosalyn D. Blumethal, 2005
- 110 Chemosensitivity: Volume 1, In Vitro Assays**, edited by Rosalyn D. Blumethal, 2005
- 109 Adoptive Immunotherapy: Methods and Protocols**, edited by Burkhard Ludewig and Matthias W. Hoffman, 2005
- 108 Hypertension: Methods and Protocols**, edited by Jérôme P. Fennell and Andrew H. Baker, 2005
- 107 Human Cell Culture Protocols, Second Edition**, edited by Joanna Picot, 2005
- 106 Antisense Therapeutics, Second Edition**, edited by M. Ian Phillips, 2005
- 105 Developmental Hematopoiesis: Methods and Protocols**, edited by Margaret H. Baron, 2005
- 104 Stroke Genomics: Methods and Reviews**, edited by Simon J. Read and David Virley, 2005
- 103 Pancreatic Cancer: Methods and Protocols**, edited by Gloria H. Su, 2004
- 102 Autoimmunity: Methods and Protocols**, edited by Andras Perl, 2004
- 101 Cartilage and Osteoarthritis: Volume 2, Structure and In Vivo Analysis**, edited by Frédéric De Ceuninck, Massimo Sabatini, and Philippe Pastoureaux, 2004
- 100 Cartilage and Osteoarthritis: Volume 1, Cellular and Molecular Tools**, edited by Massimo Sabatini, Philippe Pastoureaux, and Frédéric De Ceuninck, 2004
- 99 Pain Research: Methods and Protocols**, edited by David Z. Luo, 2004
- 98 Tumor Necrosis Factor: Methods and Protocols**, edited by Angelo Corti and Pietro Ghezzi, 2004
- 97 Molecular Diagnosis of Cancer: Methods and Protocols, Second Edition**, edited by Joseph E. Roulston and John M. S. Bartlett, 2004
- 96 Hepatitis B and D Protocols: Volume 2, Immunology, Model Systems, and Clinical Studies**, edited by Robert K. Hamatake and Johnson Y. N. Lau, 2004
- 95 Hepatitis B and D Protocols: Volume 1, Detection, Genotypes, and Characterization**, edited by Robert K. Hamatake and Johnson Y. N. Lau, 2004
- 94 Molecular Diagnosis of Infectious Diseases, Second Edition**, edited by Jochen Decker and Udo Reischl, 2004
- 93 Anticoagulants, Antiplatelets, and Thrombolytics**, edited by Shaker A. Mousa, 2004
- 92 Molecular Diagnosis of Genetic Diseases, Second Edition**, edited by Rob Elles and Roger Mountford, 2004
- 91 Pediatric Hematology: Methods and Protocols**, edited by Nicholas J. Goulden and Colin G. Steward, 2003
- 90 Suicide Gene Therapy: Methods and Reviews**, edited by Caroline J. Springer, 2004
- 89 The Blood–Brain Barrier: Biology and Research Protocols**, edited by Sukriti Nag, 2003
- 88 Cancer Cell Culture: Methods and Protocols**, edited by Simon P. Langdon, 2003
- 87 Vaccine Protocols, Second Edition**, edited by Andrew Robinson, Michael J. Hudson, and Martin P. Cranage, 2003
- 86 Renal Disease: Techniques and Protocols**, edited by Michael S. Goligorsky, 2003
- 85 Novel Anticancer Drug Protocols**, edited by John K. Buolamwini and Alex A. Adjei, 2003
- 84 Opioid Research: Methods and Protocols**, edited by Zhizhong Z. Pan, 2003
- 83 Diabetes Mellitus: Methods and Protocols**, edited by Sabire Özcan, 2003
- 82 Hemoglobin Disorders: Molecular Methods and Protocols**, edited by Ronald L. Nagel, 2003

METHODS IN MOLECULAR MEDICINE™

Molecular Cardiology

Methods and Protocols

Edited by

Zhongjie Sun

*Departments of Medicine and Physiology and Functional Genomics,
College of Medicine, University of Florida, Gainesville, FL*

HUMANA PRESS TOTOWA, NEW JERSEY

© 2005 Humana Press Inc.
999 Riverview Drive, Suite 208
Totowa, New Jersey 07512

www.humanapress.com

All rights reserved.

No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise without written permission from the Publisher. Methods in Molecular Medicine™ is a trademark of The Humana Press Inc.

All papers, comments, opinions, conclusions, or recommendations are those of the author(s), and do not necessarily reflect the views of the publisher.

For additional copies, pricing for bulk purchases, and/or information about other Humana titles, contact Humana at the above address or at any of the following numbers: Tel.: 973-256-1699; Fax: 973-256-8341; E-mail: humana@humanapr.com; or visit our Website: www.humanapress.com

This publication is printed on acid-free paper.
ANSI Z39.48-1984 (American Standards Institute) Permanence of Paper for Printed Library Materials.

Production Editor: Nicole E. Furia

Cover design by Patricia F. Cleary

Cover Illustration: Figure 1 from Chapter 11, "Autologous Mesenchymal Stem Cells for Post-Ischemic Myocardial Repair," by Yao Liang Tang.

Photocopy Authorization Policy:

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Humana Press Inc., provided that the base fee of US \$25.00 per copy is paid directly to the Copyright Clearance Center at 222 Rosewood Drive, Danvers, MA 01923. For those organizations that have been granted a photocopy license from the CCC, a separate system of payment has been arranged and is acceptable to Humana Press Inc. The fee code for users of the Transactional Reporting Service is: [1-58829-363-7/05 \$25.00].

Printed in the United States of America. 10 9 8 7 6 5 4 3 2 1

eISBN 1-59259-879-X
ISSN 1543-1894

Library of Congress Cataloging-in-Publication Data

Molecular cardiology : methods and protocols / edited by Zhongjie Sun.

p. ; cm. — (Methods in molecular medicine ; 112)

Includes bibliographical references and index.

ISBN 1-58829-363-7 (hardcover : alk. paper)

1. Heart—Diseases—Molecular aspects—Laboratory manuals. 2.

Heart—Molecular aspects—Laboratory manuals.

[DNLM: 1. Cardiovascular Diseases—therapy. 2. Gene Therapy. 3. Gene Transfer Techniques. 4. Heart—physiopathology. WG 166 M718 2005] I. Sun, Zhongjie. II. Series.

RC682.9. M648 2005

616.1'2042—dc22

2004012780

Preface

The aim of *Molecular Cardiology: Methods and Protocols* is to document state-of-the-art molecular and genetic techniques in the area of cardiology. These modern approaches enable researchers to readily study heart diseases at the molecular level and will promote the development of new therapeutic strategies. Methods for genetic dissection, signal transduction, and microarray analysis are excellent tools for the study of the molecular mechanisms of cardiovascular diseases. Protocols for transgenesis take advantage of recent advances in many areas of molecular and cell biology. Transgenic models of heart diseases (cardiac hypertrophy, cardiac dysfunction, and so on.) are powerful tools for the study of heart disease pathogenesis. Methods for gene transfer to heart tissue using viral and nonviral vectors form the basis of gene therapy for heart diseases. Heart-specific promoters containing a hypoxia-inducible cardioprotective gene switch are key for protection of the heart from ischemia. Gene and stem cell therapies open novel and exciting avenues for the prevention and treatment of heart diseases.

Molecular Cardiology: Methods and Protocols consists of 26 chapters dealing with various aspects of molecular cardiology, including gene transfer and gene therapy for cardiovascular disease, stem cell therapy for cardiovascular disease, gene analysis in the injured and hypertrophied heart, and transgenesis in cardiovascular research. This book provides step-by-step methods for the successful completion of experimental procedures, and would be useful for both experienced and new investigators in the field of molecular cardiology. The “Notes” section in each chapter contains the most critical information and provides valuable troubleshooting guides to help develop protocols for your research. This book, however, is not all-inclusive owing to the broad range and fast advances in molecular biological technology.

Molecular Cardiology: Methods and Protocols should be of general interest to both basic and clinical researchers and of special interest to cardiovascular researchers, cardiologists, and molecular biologists.

I have been very fortunate to enlist a group of renowned experts in molecular cardiology for this book. I would like to thank them for their dedication and contribution. I very much appreciate the constant guidance and support from Dr. John Walker, the series editor. Many thanks also go to Thomas Lanigan and Craig Adams at the Humana Press for their professional assistance in the successful completion of this book.

Zhongjie Sun

Contents

Preface	v
List of Contributors	xi

PART I. INTRODUCTION

1 Introduction to Methods in Molecular Cardiology <i>Zhongjie Sun</i>	3
--	---

PART II. GENE TRANSFER AND GENE THERAPY FOR CARDIOVASCULAR DISEASE

2 Gene Therapy Approaches to Cardiovascular Disease <i>J. Mark Jones and Walter J. Koch</i>	15
3 Gene Therapy for Myocardial Ischemia Using the Hypoxia-Inducible Double Plasmid System <i>Yi Tang</i>	37
4 Cardiac Gene Delivery Using DNA–Adenoviral Constructs <i>J. Mark Jones and Walter J. Koch</i>	49
5 Manipulation of Neuronal Nitric Oxide Synthase Within the Paraventricular Nucleus Using Adenovirus and Antisense Technology <i>Yi-Fan Li, Yu Wang, Keith M. Channon, Harold D. Schultz, Irving H. Zucker, and Kaushik P. Patel</i>	59
6 TAT-Mediated Protein Transduction: <i>Delivering Biologically Active Proteins to the Heart</i> <i>Åsa B. Gustafsson, Roberta A. Gottlieb, and David J. Granville</i>	81
7 Expression of Human eNOS in Cardiac and Endothelial Cells <i>Xiuqing Wang, Robert Cade, and Zhongjie Sun</i>	91
8 Strategies of Conditional Gene Expression in Myocardium: <i>An Overview</i> <i>Heather L. Heine, Hon Sing Leong, Fabio M. V. Rossi, Bruce M. McManus, and Thomas J. Podor</i>	109
9 Gene Silencing Using Adenoviral RNAi Vector in Vascular Smooth Muscle Cells and Cardiomyocytes <i>Hideko Kasahara and Hiroki Aoki</i>	155

PART III. STEM CELL THERAPY FOR CARDIOVASCULAR DISEASE

- 10 Cardiac Commitment of Embryonic Stem Cells for Myocardial Repair
*Dana Zeineddine, Evangelia Papadimou, Annabelle Mery,
Claudine Ménard, and Michel Pucéat* 175
- 11 Autologous Mesenchymal Stem Cells for Post-Ischemic
Myocardial Repair
Yao Liang Tang 183
- 12 Cellular Therapy With Autologous Skeletal Myoblasts
for Ischemic Heart Disease and Heart Failure
Yao Liang Tang 193
- 13 Protocols for Myocardial Infarction Repair Using Fetal
Cardiac Myocytes
*Sharon Etzion, Radka Holbova, Liron Miller,
and Jonathan Leor* 205
- 14 Methods for Examining Stem Cells in Post-Ischemic
and Transplanted Hearts
*Nana Rezai, Hubert Walinski, Alexandra Kerjner,
Lubos Bohunek, Fabio M. V. Rossi, Bruce M. McManus,
and Thomas J. Podor* 223
- 15 Endothelial Progenitor Cell Culture and Gene Transfer
Hideki Iwaguro and Takayuki Asahara 239

PART IV. GENE ANALYSIS IN THE INJURED AND HYPERTROPHIED HEART

- 16 Delineation of Sequences Essential for Specific Promoter
Activation During Pressure Overloaded Hypertrophy
or Factor-Induced Hypertrophy
Chellam Rajamanickam and Radhakrishnan Jeejabai 251
- 17 Evaluation of the Cardiac Isoform of α_2 -Macroglobulin
as a Factor Inducing Cardiac Hypertrophy
Chellam Rajamanickam and Radhakrishnan Jeejabai 261
- 18 Detection of Apoptosis in Cardiovascular Diseases
Arwen L. Hunter, Jonathan C. Choy, and David J. Granville 277
- 19 Detection of Cardiac Signaling in the Injured
and Hypertrophied Heart
Xiaoning Si, Maziar Rahmani, Ji Yuan, and Honglin Luo 291
- 20 Affymetrix Oligonucleotide Analysis of Gene Expression
in the Injured Heart
*Bobby Yanagawa, Lydia Taylor, Theresa A. Deisher, Raymond Ng,
George F. Schreiner, Timothy J. Triche, Decheng Yang,
and Bruce M. McManus* 305

21 Identification and Validation of Loci and Candidate Genes
Linked to Cardiac Hypertrophy
Bastien Llamas and Christian F. Deschepper 321

22 Induction and Analysis of Cardiac Hypertrophy in Transgenic
Animal Models
Marcos E. Barbosa, Natalia Alenina, and Michael Bader 339

23 Methods for the Detection of Altered β -Adrenergic Receptor
Signaling Pathways in Hypertrophied Hearts
Matthew J. Wolf, Hideo Tachibana, and Howard A. Rockman 353

PART V. TRANSGENES IN CARDIOVASCULAR RESEARCH

24 Transgenic Mouse Models for Cardiac Dysfunction
by a Specific Gene Manipulation
Gopal J. Babu and Muthu Periasamy 365

25 Cardiomyocyte Defects in Diabetic Models and Protection
With Cardiac-Targeted Transgenes
Xia Shen, Gang Ye, Naira S. Metreveli, and Paul N. Epstein 379

26 Cardiac-Specific Overexpression of Angiotensin II
Type 1 Receptor in Transgenic Rats
Sigrid Hoffmann 389

Index 405

Contributors

- NATALIA ALENINA • *Max-Delbrück-Center for Molecular Medicine, Berlin-Buch, Germany*
- HIROKI AOKI • *Department of Molecular Cardiovascular Biology, Yamaguchi University School of Medicine, Ube, Yamaguchi, Japan*
- TAKAYUKI ASAHARA • *Department of Regenerative Medicine, Institute of Biomedical Research and Innovation, RIKEN Kobe Center for Developmental Biology, Kobe, Japan*
- GOPAL J. BABU • *Department of Physiology and Cell Biology, The Ohio State University, Columbus, OH*
- MICHAEL BADER • *Max-Delbrück-Center for Molecular Medicine, Berlin-Buch, Germany*
- MARCOS E. BARBOSA • *Max-Delbrück-Center for Molecular Medicine, Berlin-Buch, Germany*
- LUBOS BOHUNEK • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital–University of British Columbia, Vancouver, British Columbia, Canada*
- ROBERT CADE • *Departments of Medicine and Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, FL*
- KEITH M. CHANNON • *Department of Cardiovascular Medicine University of Oxford, Oxford, United Kingdom*
- JONATHAN C. CHOY • *Department of Pathology and Laboratory Medicine, James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada*
- THERESA A. DEISHER • *Vascular Biology, Amgen Inc., Thousand Oaks, CA*
- CHRISTIAN F. DESCHEPPER • *Experimental Cardiovascular Biology Research Unit, Institut de recherches cliniques de Montréal, Montréal, Québec, Canada*
- SHARON ETZION • *Neufeld Cardiac Research Institute, Tel-Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*
- PAUL N. EPSTEIN • *Departments of Pediatrics and Pharmacology and Toxicology, School of Medicine, University of Louisville, Louisville, KY*
- ROBERTA A. GOTTLIEB • *Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, CA*

- DAVID J. GRANVILLE • *James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary, Research St. Paul's Hospital, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada*
- ÅSA B. GUSTAFSSON • *Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, CA*
- HEATHER L. HEINE • *The James Hogg iCAPTURE Center for Cardiovascular and Pulmonary Research/MRL, Department of Pathology and Laboratory Medicine, University of British Columbia–St. Paul's Hospital, Vancouver, British Columbia, Canada*
- SIGRID HOFFMANN • *Medical Research Center, Faculty for Clinical Medicine Mannheim, University of Heidelberg, Mannheim, Germany*
- RADKA HOLBOVA • *Neufeld Cardiac Research Institute, Tel-Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*
- ARWEN L. HUNTER • *Department of Pathology and Laboratory Medicine, James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada*
- HIDEKI IWAGURO • *Department of Regenerative Medicine, Division of Basic Clinical Science, Tokai University School of Medicine, Kanagawa, Japan*
- RADHAKRISHNAN JEEJABAI • *Center for Advanced Studies in Functional Genomics, Department of Biochemistry, School of Biological Sciences, Madurai Kamaraj University, Madurai, India*
- J. MARK JONES • *Department of Cardiac Surgery, Royal Victoria Hospital, Belfast, United Kingdom; formerly Department of Surgery, Duke University Medical Center, Durham, NC*
- HIDEKO KASAHARA • *Department of Physiology and Functional Genomics, University of Florida College of Medicine, Gainesville, FL*
- ALEXANDRA KERJNER • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital–University of British Columbia, Vancouver, British Columbia, Canada*
- WALTER J. KOCH • *Center for Translational Medicine, Thomas Jefferson University, Philadelphia, PA*
- HON SING LEONG • *The James Hogg iCAPTURE Center for Cardiovascular and Pulmonary Research/MRL, Department of Pathology and Laboratory Medicine, University of British Columbia–St. Paul's Hospital, Vancouver, British Columbia, Canada*
- JONATHAN LEOR • *Neufeld Cardiac Research Institute, Tel-Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*
- BASTIEN LLAMAS • *Experimental Cardiovascular Biology Research Unit, Institut de recherches cliniques de Montréal, Montréal, Québec, Canada*

- YI-FAN LI • *Department of Physiology and Biophysics, University of Nebraska Medical Center, Omaha, NE*
- HONGLIN LUO • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, Vancouver, British Columbia, Canada*
- BRUCE M. McMANUS • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, and Institute of Circulatory and Respiratory Health, Canadian Institutes of Health Research, Vancouver, British Columbia, Canada*
- CLAUDINE MÉNARD • *Centre de Recherches de Biochimie Macromoléculaire, CNRS, Montpellier, France*
- ANNABELLE MERY • *Centre de Recherches de Biochimie Macromoléculaire, CNRS, Montpellier, France*
- NAIRA S. METREVELI • *Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY*
- LIRON MILLER • *Neufeld Cardiac Research Institute, Tel-Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*
- RAYMOND NG • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, Vancouver, British Columbia, Canada*
- EVANGELIA PAPADIMOU • *Centre de Recherches de Biochimie Macromoléculaire, CNRS, Montpellier, France*
- KAUSHIK P. PATEL • *Department of Physiology and Biophysics, University of Nebraska Medical Center, Omaha, NE*
- MUTHU PERIASAMY • *Department of Physiology and Cell Biology, The Ohio State University, Columbus, OH*
- THOMAS J. PODOR • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital–University of British Columbia, Vancouver, British Columbia, Canada*
- MICHEL PUCÉAT • *Centre de Recherches de Biochimie Macromoléculaire, CNRS, Montpellier, France*
- MAZIAR RAHMANI • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, Vancouver, British Columbia, Canada*

- CHELLAM RAJAMANICKAM • *Center for Advanced Studies in Functional Genomics, Department of Biochemistry, School of Biological Sciences, Madurai Kamaraj University, Madurai, India*
- NANA REZAI • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital–University of British Columbia, Vancouver, British Columbia, Canada*
- HOWARD A. ROCKMAN • *Departments of Medicine, Cell Biology, and Molecular Genetics, Duke University Medical Center, Durham, NC*
- FABIO M.V. ROSSI • *Biomedical Research Centre, Department of Medical Genetics, University of British Columbia, Vancouver British Columbia, Canada*
- GEORGE F. SCHREINER • *SCIOS Inc., Fremont, CA*
- HAROLD D. SCHULTZ • *Department of Physiology and Biophysics, University of Nebraska Medical Center, Omaha, NE*
- XIA SHEN • *Departments of Pediatrics and Pharmacology and Toxicology, School of Medicine, University of Louisville, Louisville, KY*
- XIAONING SI • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, Vancouver, British Columbia, Canada*
- ZHONGJIE SUN • *Departments of Medicine and Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, FL*
- HIDEO TACHIBANA • *Pharmaceutical Development Division, Takeda Chemical Industries, Ltd., Chuo-ku, Osaka, Japan*
- YAO LIANG TANG • *Department of Pediatrics, All Children's Hospital, University of South Florida, St. Petersburg, FL*
- YI TANG • *Department of Surgery, Stanford University, Stanford, CA*
- LYDIA TAYLOR • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care–University of British Columbia, Vancouver, British Columbia, Canada*
- TIMOTHY J. TRICHE • *Children's Hospital Los Angeles, University of Southern California, CA*
- HUBERT WALINSKI • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital–University of British Columbia, Vancouver, British Columbia, Canada*
- XIUQING WANG • *Department of Medicine, College of Medicine, University of Florida, Gainesville, FL*

YU WANG • *Department of Physiology and Biophysics, University of Nebraska Medical Center, Omaha, NE*

MATTHEW J. WOLF • *Department of Medicine, Duke University Medical Center, Durham, NC*

BOBBY YANAGAWA • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care—University of British Columbia, Vancouver, British Columbia, Canada*

DECHENG YANG • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care—University of British Columbia, Vancouver, British Columbia, Canada*

GANG YE • *Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY*

Ji YUAN • *The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, Department of Pathology and Laboratory Medicine, St. Paul's Hospital/Providence Health Care—University of British Columbia, Vancouver, British Columbia, Canada*

DANA ZEINEDDINE • *Centre de Recherches de Biochimie Macromoléculaire, Montpellier, France*

IRVING H. ZUCKER • *Department of Physiology and Biophysics, University of Nebraska Medical Center, Omaha, NE*