Methods in ENZYMOLOGY

Volume 346

Gene Therapy Methods

Edited by

M. Ian Phillips

ACADEMIC PRESS

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Volume 346
GENE THERAPY METHODS

METHODS IN ENZYMOLOGY

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COLLEGE OF MEDICINE
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

ACADEMIC PRESS

An Elsevier Science Imprint

San Diego San Francisco New York Boston London Sydney Tokyo

Academic Press
An Elsevier Science Imprint.
525 B Street, Suite 1900, San Diego, California 92101-4495, USA
http://www.academicpress.com

Academic Press
32 Jamestown Road, London NW1 7BY, UK
http://www.academicpress.com

International Standard Book Number: 0-12-182247-8

PRINTED IN THE UNITED STATES OF AMERICA
02 03 04 05 06 07 SB 9 8 7 6 5 4 3 2 1

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Contributors to Volume 346

Article numbers are in parentheses following the names of contributors.
Affiliations listed are current.

ANDREW H. BAKER (10), *Department of Medicine and Therapeutics, University of Glasgow, Glasgow G11 6NT, United Kingdom*

PARAMITA BANDYOPADHYAY (2), *ValiGen, Inc., Newtown, Pennsylvania 18940*

ANDREA BANFI (9), *Department of Molecular Pharmacology, Stanford University School of Medicine, CCSR 4215, Stanford, California 94305*

CATHERINE BARJOT (13), *Department of Human Genetics, University of Michigan, Ann Arbor, Michigan 48109*[*]

ARTHUR L. BEAUDET (11), *Department of Human and Molecular Genetics, Baylor College of Medicine, Houston, Texas 77030*

HELEN M. BLAU (9), *Department of Molecular Pharmacology, Stanford University School of Medicine, CCSR 4215, Stanford, California 94305*

P. BOROS (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

O. BOYER (17), *Laboratoire de Biologie et Thérapeutique des Pathologies Immunitaires, Université Pierre et Marie Curie, Hôpital de la Pitié-Salpétriére, 75651 Paris Cedex 13, France*

LARS J. BRANDÉN (6), *Center for BioTechnology, Department of Biosciences, Karolinska Institute, SE-141 57 Huddinge, Sweden*[†]

XANDRA BREAKEFIELD (34), *Molecular Neurogenetics Unit, Massachusetts General Hospital, Charlestown, Massachusetts 02129*

J. S. BROMBERG (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

VLADIMIR BUDKER (7), *Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin 53705*

MARK M. BURCIN (31), *Cardiogene, 40699 Erkrath, Germany*

MASSIMO BUVOLI (8), *Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder, Colorado 80309*

CHERYL A. CARLSON (16), *Department of Medicine, Division of Medical Genetics, University of Washington, Seattle, Washington 98195*

M. G. CASTRO (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*[‡]

[*]Current affiliation: UMR INRA 703, ENVN—Atlanpole La Chanterie, F-44307 Nantes Cedex 3, France

[†]Current affiliation: Clinical Research Center, Karolinska Institute, S-141 86 Stockholm, Sweden

[‡]Current affiliation: Gene Therapeutics Research Institute, Cedars-Sinai Medical Center, Los Angeles, California 90048

JEFFREY S. CHAMBERLAIN (13), *Department of Neurology, University of Washington School of Medicine, Seattle, Washington 98195*

JULIE CHAO (14), *Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, South Carolina 29425*

LEE CHAO (14), *Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, South Carolina 29425*

KYE CHESNUT (24), *Powell Gene Therapy Center, University of Florida, Gainesville, Florida 32610*

JAYANTA ROY CHOWDHURY (2), *Department of Medicine and Molecular Genetics, and Marion Bessin Liver Research Center, Albert Einstein College of Medicine, Bronx, New York 10461*

NAMITA ROY CHOWDHURY (2), *Department of Medicine and Molecular Genetics, and Marion Bessin Liver Research Center, Albert Einstein College of Medicine, Bronx, New York 10461*

YI CHU (15), *Cardiovascular Division, University of Iowa College of Medicine, Iowa City, Iowa 52242*

MARINEE K. L. CHUAH (33), *Flanders Interuniversity Institute of Biotechnology, Center for Transgene Technology and Gene Therapy, University of Leuven, B-3000 Leuven, Belgium*

DESIRE COLLEN (33), *Flanders Interuniversity Institute of Biotechnology, Center for Transgene Technology and Gene Therapy, University of Leuven, B-3000 Leuven, Belgium*

PIETER R. CULLIS (3), *Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z3, and Inex Pharmaceuticals Corporation, Burnaby, Canada V5J 5L8*

BEVERLY L. DAVIDSON (25), *Departments of Internal Medicine, Neurology, Physiology, and Biophysics, College of Medicine, University of Iowa, Iowa City, Iowa 52242*

MICHELE DE PALMA (29), *Institute for Cancer Research and Treatment, Laboratory for Gene Transfer and Therapy, University of Torino Medical School, 10060 Candiolo, Torino, Italy*

Y. DING (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

J. KEVIN DONAHUE (19), *Institute of Molecular Cardiobiology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*

JIAN-YUN DONG (30), *Department of Microbiology, Medical University of South Carolina, Charleston, South Carolina 29425*

DONGSHENG DUAN (20), *Department of Anatomy and Cell Biology, University of Iowa College of Medicine, Iowa City, Iowa 52242*

FIONA M. ELLARD (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

JOHN F. ENGELHARDT (20), *Department of Anatomy and Cell Biology, University of Iowa College of Medicine, Iowa City, Iowa 52242*

DAVID B. FENSKE (3), *Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z3*

TERRY FLOTTE (24), *Powell Gene Therapy Center, University of Florida, Gainesville, Florida 32610*

ANTONIA FOLLENZI (26), *IRCC, Institute for Cancer Research and Treatment, Laboratory for Gene Transfer and Therapy, University of Torino Medical School, 10060 Candiolo, Torino, Italy*

CORNEL FRAEFEL (34), *Institute of Virology, University of Zurich, CH-8057 Zurich, Switzerland*

JASON J. FRITZ (21), *Department of Molecular Genetics and Microbiology, College of Medicine, University of Florida, Gainesville, Florida 32610*

S. FU (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

MARK R. GALLAGHER (23), *Harvard/ Généthon Joint Laboratory, Harvard Institutes of Medicine, Boston, Massachusetts 02115*

CRAIG H. GELBAND (32), *Department of Physiology, University of Florida College of Medicine and Functional Genomics, Gainesville, Florida 32610*

C. A. GERDES (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*[*]

JILL GLASSPOOL-MALONE (4), *Gene Delivery Alliance, Inc., Rockville, Maryland 20850*

JOHN T. GRAY (23), *Harvard/Généthon Joint Laboratory, Harvard Institutes of Medicine, Boston, Massachusetts 02115*

WALTER H. GÜNZBURG (35), *Institute of Virology, University of Veterinary Sciences, A-1210 Vienna, Austria*

YUTAKA HANAZONO (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

KRISTINE HANSON (7), *Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin 53705*

DENNIS HARTIGAN-O'CONNOR (13), *Department of Neurology, University of Washington School of Medicine, Seattle, Washington 98195*

WILLIAM W. HAUSWIRTH (21), *Department of Ophthalmology and Powell Gene Therapy Center, College of Medicine, University of Florida, Gainesville, Florida 32610*

DONALD D. HEISTAD (15), *Cardiovascular Division, University of Iowa College of Medicine, Iowa City, Iowa 52242*

MIKKO O. HILTUNEN (18), *University of Kuopio, A. I. Virtanen Institute, FIN-70210 Kuopio, Finland*

MATTHEW J. HUENTELMAN (32), *Department of Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, Florida 32610*

NEIL JOSEPHSON (37), *Division of Hematology, University of Washington, Seattle, Washington 98195*

YASUFUMI KANEDA (36), *Division of Gene Therapy Science, Graduate School of Medicine, Osaka University, Suita City, Osaka 565-0871, Japan*

MICHAEL J. KATOVICH (32), *Department of Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, Florida 32610*

NOBUFUMI KAWAI (22), *Department of Physiology, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

SUSAN M. KINGSMAN (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

D. KLATZMANN (17), *Laboratoire de Biologie et Thérapeutique des Pathologies Immunitaires, Université Pierre et Marie Curie, CNRS, Hôpital de la Pitié-Salpétriére, 75651 Paris Cedex 13, France*

BETSY T. KREN (2), *Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota 55455*

[*]Current affiliation: GlycArt Biotechnology AG, 8093 Zurich, Switzerland

T. KU (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

AKIHIRO KUME (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

LESLIE A. LEINWAND (8), *Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder, Colorado 80309*

MICHELLE K. LEPPO (19), *Institute of Molecular Cardiobiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*

ALFRED S. LEWIN (21), *Department of Molecular Genetics and Microbiology, Powell Gene Therapy Center, College of Medicine, University of Florida, Gainesville, Florida 32610*

ANDRÉ LIEBER (16), *Department of Medicine, Division of Medical Genetics, University of Washington, Seattle, Washington 98195*

DEXI LIU (5), *Department of Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania 15261*

FENG LIU (5), *Department of Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania 15261*

J.-MATTHIAS LÖHR (35), *Department of Molecular Gastroenterology, Medical Clinic II, University of Heidelberg, D-68167 Mannheim, Germany*

P. R. LOWENSTEIN (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*[*]

IAN MACLACHLAN (3), *Protiva Biotherapeutics, Burnaby, British Columbia, Canada V5J 5L8*

ROBERT W. MALONE (4), *Gene Delivery Alliance, Inc., Rockville, Maryland 20850*

EDUARDO MARBÁN (19), *Institute of Molecular Cardiobiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*

ENCA MARTIN-RENDON (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

LYDIA C. MATHEWS (23), *Harvard/Généthon Joint Laboratory, Harvard Institutes of Medicine, Boston, Massachusetts 02115*

TAKASHI MATSUSHITA (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

NICHOLAS D. MAZARAKIS (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

PAUL B. MCCRAY, JR. (28), *Departments of Pediatrics and Internal Medicine, University of Iowa, Iowa City, Iowa 52242*

KYRIACOS A. MITROPHANOUS (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

HIROAKI MIZUKAMI (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

RYUICHI MORISHITA (36), *Division of Gene Therapy Science, Graduate School of Medicine, Osaka University, Suita City, Osaka 565-0871, Japan*

NICHOLAS MUZYCZKA (24), *Powell Gene Therapy Center, University of Florida, Gainesville, Florida 32610*

[*]Current affiliation: Gene Therapeutics Research Institute, Cedars-Sinai Medical Center, Los Angeles, California 90048

LUIGI NALDINI (26, 29, 33), *Institute for Cancer Research and Treatment, Laboratory for Gene Transfer and Therapy, University of Torino Medical School, 10060 Candiolo, Torino, Italy*

NATHALIE NEYROUD (19), *Institute of Molecular Cardiobiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*

STUART A. NICKLIN (10), *Department of Medicine and Therapeutics, University of Glasgow, Glasgow G11 6NT, United Kingdom*

TATSUYA NOMOTO (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

JAMES S. NORRIS (30), *Department of Microbiology and Immunology, Medical University of South Carolina, Charleston, South Carolina 29425*

H. BRADLEY NUSS (19), *Institute of Molecular Cardiobiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*

TAKASHI OKADA (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

BERT W. O'MALLEY (31), *Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas 77030*

KEIYA OZAWA (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

LUCIO PASTORE (11), *Department of Human and Molecular Genetics, Baylor College of Medicine, Houston, Texas 77030*[*]

M. IAN PHILLIPS (1), *Department of Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, Florida 32610*

MARK POTTER (24), *Powell Gene Therapy Center, University of Florida, Gainesville, Florida 32610*

L. QIN (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

PIPPA A. RADCLIFFE (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

MOHAN K. RAIZADA (32), *Department of Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, Florida 32610*

PHYLLIS Y. REAVES (32), *Department of Physiology, College of Medicine, University of Florida, Gainesville, Maryland 32610*

TERESA C. RITCHIE (20), *Department of Anatomy and Cell Biology, University of Iowa College of Medicine, Iowa City, Iowa 52242*

JONATHAN B. ROHLL (27), *Department of Biochemistry, Oxford BioMedica (UK) Limited, Oxford OX4 4GA, United Kingdom*

SEMYON RUBINCHIK (30), *Department of Microbiology, Medical University of South Carolina, Charleston, South Carolina 29425*

DAVID W. RUSSELL (37), *Division of Hematology, University of Washington, Seattle, Washington 98195*

ROBERT SALLER (35), *Bavarian Nordic, D-82152 Martinsried, Austria*

BRIAN SALMONS (35), *Austrian Nordic, A-1210 Vienna, Austria*

[*]Current affiliation: CEINGE-Biotecnologie Avanzate and Dipartimento di Biochima e Biotecnologie Mediche, Università degli Studi di Napoli "Federico II," 80131 Napoli, Italy

GIOVANNI SALVATORI (13), *Department of Human Genetics, University of Michigan, Ann Arbor, Michigan 48109*[*]

KURT SCHILLINGER (31), *Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas 77030*

DMITRY M. SHAYAKHMETOV (16), *Department of Medicine, Division of Medical Genetics, University of Washington, Seattle, Washington 98195*

KUNIKO SHIMAZAKI (22), *Department of Physiology, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

PATRICK L. SINN (28), *Departments of Pediatrics and Internal Medicine, Program in Gene Therapy, College of Medicine, University of Iowa, Iowa City, Iowa 52242*

C. I. EDVARD SMITH (6), *Center for BioTechnology, Department of Biosciences, Karolinska Institute, SE-141 57 Huddinge, Sweden*[†]

RICHARD O. SNYDER (23), *Harvard/Généthon Joint Laboratory, Division of Molecular Medicine, The Children's Hospital, Department of Pediatrics, Harvard Institutes of Medicine, Boston, Massachusetts 02115*[‡]

YOUNG K. SONG (5), *Department of Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania 15261*[§]

MATTHEW L. SPRINGER (9), *Department of Molecular Pharmacology, Stanford University School of Medicine, CCSR 4215, Stanford, California 94305*

HARMUT STECHER (16), *Department of Medicine, Division of Medical Genetics, University of Washington, Seattle, Washington 98195*

CLIFFORD J. STEER (2), *Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota 55455*

COLLEEN S. STEIN (25), *College of Medicine, University of Iowa, Iowa City, Iowa 52242*

DIRK S. STEINWAERDER (16), *Department of Medicine, Division of Medical Genetics, University of Washington, Seattle, Washington 98195*

R. SUNG (12), *Institute for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, New York 10029*

C. E. THOMAS (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*[‖]

KIYOTAKE TOBITA (22), *Department of Virology, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

S. TONDEUR (17), *Laboratoire de Biologie et Thérapeutique des Pathologies Immunitaires, Université Pierre et Marie Curie, Hôpital de la Pitié Salpétriére 75651 Paris Cedex 13, France*

GRANT TROBRIDGE (37), *Division of Hematology, University of Washington, Seattle, Washington 98195*

SOPHIA Y. TSAI (31), *Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas 77030*

[*]Current affiliation: Department of Immunology, Sigma-Tau S.P.A., 00040 Pomezia, Italy

[†]Current affiliation: Clinical Research Center, Karolinska Institute, S-141 86 Stockholm, Sweden

[‡]Current affiliation: Powell Gene Therapy Center, Department of Molecular Genetics and Microbiology, University of Florida, Gainesville, Florida 32610

[§]Current affiliation: Department of Pharmacology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261

[‖]Current affiliation: Department of Pediatrics and Genetics, Stanford University, Stanford, California 94305

MIKKO P. TURUNEN (18), *A. I. Virtanen Institute, University of Kuopio, FIN-70210 Kuopio, Finland*

P. UMANA (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*[*]

MASASHI URABE (22), *Division of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical School, Kawachi, Tochigi 329-0498, Japan*

THIERRY VANDENDRIESSCHE (33), *Flanders Interuniversity Institute of Biotechnology, Center for Transgene Technology and Gene Therapy, University of Leuven, B-3000 Leuven, Belgium*

GEORGE VASSILOPOULOS (37), *Division of Hematology, University of Washington, Seattle, Washington 98195*

T. VERAKIS (17), *Molecular Medicine and Gene Therapy Unit School of Medicine, University of Manchester, Manchester M13 9PT, United Kingdom*

JEAN-MICHEL H. VOS (deceased) (38), *Lineberger Comprehensive Cancer Center, Department of Biochemistry and Biophysics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599*

CINDY WANG (14), *Departments of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, South Carolina 29425*

GUOSHUN WANG (28), *Departments of Pediatrics and Internal Medicine, Program in Gene Therapy, College of Medicine, University of Iowa, Iowa City, Iowa 52242*[†]

JIANLONG WANG (38), *Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599*[‡]

SAM WANG (34), *Molecular Neurogenetics Unit, Massachusetts General Hospital, Charlestown, Massachusetts 02129*

D. ALAN WHITE (21), *Department of Molecular Genetics and Microbiology, College of Medicine, University of Florida, Gainesville, Florida 32610*

STEVE J. WHITE (10), *Department of Medicine and Therapeutics, University of Glasgow, Glasgow G11 6NT, United Kingdom*

PHILLIP WILLIAMS (7), *Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin 53705*

JON A. WOLFF (7), *Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin 53705*

LORRAINE M. WORK (10), *Department of Medicine and Therapeutics, University of Glasgow, Glasgow G11 6NT, United Kingdom*

ZIYING YAN (20), *Department of Anatomy and Cell Biology, University of Iowa College of Medicine, Iowa City, Iowa 52242*

XIANGCANG YE (31), *Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas 77030*

SEPPO YLÄ-HERTTUALA (18), *Department of Molecular Medicine, A. I. Virtanen Institute, University of Kuopio, FIN-70210 Kuopio, Finland*

JOSEPH ZABNER (28), *Departments of Pediatrics and Internal Medicine, Program in Gene Therapy, College of Medicine, University of Iowa, Iowa City, Iowa 52242*

[*]Current affiliation: GlycArt Biotechnology AG, 8093 Zurich, Switzerland

[†]Current affiliation: Departments of Medicine and Genetics, Gene Therapy Program, Louisiana State University Health Sciences Center, New Orleans, Louisiana 70112

[‡]Current affiliation: Division of Hematology/Oncology, Children's Hospital Boston, Boston, Massachusetts 02115

GUISHENG ZHANG (5), *Department of Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania 15261*

GUOFENG ZHANG (7), *Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin 53705*

HESHAN ZHOU (11), *Cell and Gene Therapy Center, Baylor College of Medicine, Houston, Texas 77030*

SERGEI ZOLOTUKHIN (24), *Department of Molecular Genetics and Microbiology, Powell Gene Therapy Center, University of Florida, Gainesville, Florida 32610*

Preface

Gene therapy is less than ten years old and still very much in its infancy. The first clinical gene therapy study was carried out in 1995 by Blaese and colleagues. Although early results on clinical efficacy were disappointing, the logic of gene therapy is irresistibly attractive. As science continues to evaluate the prospects for gene therapy, so the clinical benefits have begun to be demonstrated. Early results were hampered because of inadequate vectors for gene transfer. Most of the clinical studies involved gene addition. However, gene therapy allows both correction and replacement of defective genes. Ultimately, the goal is to have an *in vivo* somatic gene therapy that can deal with not only immediate life-threatening diseases, such as cancer and AIDS, but also chronic diseases that reduce the quality of life, such as hypertension and inflammatory diseases. The basis for gene therapy is understanding which genes are involved in diseased phenotypes and which vectors are appropriate for providing therapeutic genes. The rapid progress in gene discovery has been accelerated by the completion of the human genome project.

This book brings together, for the first time, methods in gene therapy that reflect the development of scientifically grounded systems for delivering genes. DNA can be engineered to carry a therapeutic gene in sufficient quantities for full-scale clinical trials. The methods can be classified as either viral or nonviral. Viral vectors are replication defective viruses with part of their coding sequences replaced by the therapeutic gene. These viral vectors include retroviruses, adenovirus, adeno-associated virus, herpes simplex virus, papillomavirus, and lentivirus. Nonviral vectors are simpler and easier to produce on the large scale. However, each has its advantage. Viral vectors can be engineered to be expressed in specific tissue and only under specific conditions. Nonviral vectors are less easy to control so precisely. Some diseases need gene therapy for a rapid effect, such as killing off tumor cells. Others need the presence of a stable, safe gene delivery system for chronic lifetime diseases. The use of gene therapy could eliminate the need for repeated administrations, improved therapeutic efficacy, and fewer side effects. In hypertension, for example, one of the major problems is the lack of patient compliance in taking current prescribed drugs that have to be administered once a day. The prospect of prolonged effective control of blood pressure and the subsequent reduction in heart attacks, stroke, and end-stage renal disease are an exciting possibility of the true benefits of gene therapy.

In this book we have brought together some of the leading researchers and research methods in gene therapy. There are many ways to classify these chapters: by disease, by the type of method, or the type of delivery system. We have chosen

to classify them under the main type of delivery system being investigated. However, each chapter stands on its own, offering scientific insight and experience with a particular approach. In some cases they cross the boundaries of these classifications. Although this is the first volume entitled "Gene Therapy Methods" for the *Methods in Enzymology* series, the increasing number of new methods and the progress of gene therapy will undoubtedly require more volumes in the future.

I wish to thank the authors for their contributions. I also wish to thank Ms. Gayle Butters of the University of Florida, Department of Physiology and Functional Genomics, for her excellent editorial assistance. My thanks also go to Shirley Light of Academic Press for her encouragement to do this volume.

M. IAN PHILLIPS

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Edited by SIDNEY P. COLOWICK AND NATHAN O. KAPLAN

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