Gene Transfer & Gene Therapy

Gene Transfer and Gene Therapy

Proceedings of an E.I. du Pont de Nemours — UCLA Symposium
Held at Tamarron, Colorado
February 6–12, 1988

Editors

Arthur L. Beaudet
Institute for Molecular Genetics
Baylor College of Medicine
Houston, Texas

Richard Mulligan
Biomedical Research Whitehead Institute
Cambridge, Massachusetts

Inder M. Verma
MBVL
Salk Institute
San Diego, California

Alan R. Liss, Inc. • New York

Address all Inquiries to the Publisher
Alan R. Liss, Inc., 41 East 11th Street, New York, NY 10003

The publication of this volume was facilitated by the authors and editors who submitted the text in a form suitable for direct reproduction without subsequent editing or proofreading by the publisher.

Library of Congress Cataloging-in-Publication Data

E.I. du Pont de Nemours-UCLA Symposium (1988 : Tamarron, Colo.)
Gene transfer and gene therapy : proceedings of an E.I. du Pont de Nemours-UCLA Symposium, held at Tamarron, Colorado, February 6-12, 1988 / editors, Arthur L. Beaudet, Richard Mulligan, Inder M. Verma.
p. cm. -- (UCLA symposia on molecular and cellular biology : new ser., v. 87)
Includes bibliographies and index.
ISBN 0-8451-2686-5
1. Gene therapy--Congresses. 2. Genetic engineering--Congresses. I. Beaudet, Arthur L. II. Mulligan, Richard. III. Verma, Inder M. IV. Title. V. Series.
[DNLM: 1. Genetic Engineering--congresses. 2. Hereditary Diseases--therapy--congresses. 3. Transfection--congresses. W3 U17N new ser. v. 87 / QZ 50 E11g 1988]
RB155.8.E18 1988
616'.042--dc20
DNLM/DLC
for Library of Congress

89-8306
CIP

Contributors

W. French Anderson, Laboratory of Molecular Hematology, N.H.L.B.I, N.I.H., Bethesda, MD 20892 **[365]**

Donald C. Anderson, Departments of Pediatrics and Cell Biology, Baylor College of Medicine, Houston, TX 77054 **[315]**

A.-C. Andres, Ludwig Institute for Cancer Research, 3010 Bern, Switzerland **[151]**

S.E. Antonarakis, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 **[293]**

M. Antoniou, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom **[35]**

D. Armentano, Department of Cell Biology, Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 **[355]**

Suzanne Atiee, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 **[67]**

M. Bakhanashvili, Department of Biochemistry, Tel Aviv University, Tel Aviv 69978, Israel **[215]**

J. Barber, The Salk Institute, San Diego, CA 92138; present address: Viagene, San Diego, CA 92112 **[129]**

John A. Barranger, Department of Pediatrics, Division of Medical Genetics, Childrens Hospital of Los Angeles, University of Southern California School of Medicine, Los Angeles, CA 90027 **[397]**

W. Bautsch, Cystic Fibrosis Research Group, Zentrum Biochemie, Federal Republic of Germany **[283]**

J.W. Belmont, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 **[375]**

John M. Belote, Department of Biology, Biological Research Laboratories, Syracuse University, Syracuse, NY 13210 **[1]**

Anton Berns, Division of Molecular Genetics, The Netherlands Cancer Institute and Department of Biochemistry, University of Amsterdam, 1066 CX Amsterdam, The Netherlands **[117]**

Alan Bernstein, Mount Sinai Hospital Research Institute and Department of Medical Genetics, University of Toronto, Toronto, Ontario, Canada **[189]**

R. Michael Blaese, Metabolism Branch, N.C.I., N.I.H., Bethesda, MD 20892 **[365]**

Patrice Blanchet, Unité de Génétique Cellulaire, Institut Pasteur, 75724 Paris Cedex 15, France [243]

G. Blom, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Russell T. Boggs, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

Emiliana Borrelli, Gene Expression Laboratory, Howard Hughes Medical Institute, The Salk Institute, La Jolla, CA 92037 [163]

C.D.K. Bottema, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

Florence Botteri, Cancer Biology and Gene Expression Laboratories, The Salk Institute, San Diego, CA 92138 [179]

Danielle Boullier, Unité de Génétique Cellulaire, Institut Pasteur, 75724 Paris Cedex 15, France [243]

Philippe Brûlet, Unité de Génétique Cellulaire, Institut Pasteur, 75724 Paris Cedex 15, France [243]

Martin L. Breitman, Mount Sinai Hospital Research Institute and Department of Medical Genetics, University of Toronto, Toronto, Ontario, Canada [189]

J-M. Buerstedde, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

Bruce Bunnell, Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL 35294 [225]

D. Canaani, Department of Biochemistry, Tel Aviv University, Tel Aviv 69978, Israel [215]

Charles R. Cantor, Department of Genetics and Development, College of Physicians and Surgeons, Columbia University, New York, NY 10032 [269]

C.T. Caskey, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [375]

F. Catala, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

S.M-W. Chang, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030; present address: Laboratory of Molecular Genetics, NINCDS, NIH, Bethesda, MD 20814 [375]

Shizhong Chen, Cancer Biology and Gene Expression Laboratories, The Salk Institute, San Diego, CA 92138 [179]

Jeffrey M. Chinsky, Department of Biochemistry and the Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX 77030 [255]

Daniel Chourrout, Laboratory of Fish Genetics, INRA, 78350 - Jouy-en-Josas, France [9]

A. Claass, Universitätskinderklinik Kiel, Federal Republic of Germany [283]

P. Collis, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Dawn-Marie Coulson, Mount Sinai Hospital Research Institute and Department of Medical Genetics, University of Toronto, Toronto, Ontario, Canada [189]

Ross Couwenhoven, Department of Pathology, University of Health Sciences, The Chicago Medical School, North Chicago, IL 60064 [205]

Nava Dalyot, Department of Hematology, Hadassah University Hospital, Jerusalem, Israel 91120 [47]

G.J. Darlington, Institute for Human Genetics, Baylor College of Medicine, Houston, TX 77030 [355]

E. deBoer, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Francesco J. DeMayo, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [67]

Zlatko Dembic, Central Research Units, Hoffman-la Roche, Basel, Switzerland [117]

P. DeTogni, The Salk Institute, San Diego, CA 92138 [129]

Michael Dexter, Paterson Institute for Cancer Research, Christie Hospital, Withington, Manchester, M20 9BX, United Kingdom [79]

D. Eli, Department of Biochemistry, Tel Aviv University, Tel Aviv 69978, Israel [215]

Glen A. Evans, Cancer Biology and Gene Expression Laboratories, The Salk Institute, San Diego, CA 92138 [179]

Ronald M. Evans, Gene Expression Laboratory, Howard Hughes Medical Institute, The Salk Institute, La Jolla, CA 92037 [163]

A. Fagan, Department of Neurosciences, School of Medicine, University of California, San Diego, La Jolla, CA 92093 [409]

William C. Fanslow, Department of Biochemistry, Rice University, Houston, TX 77251 [255]

A. Faras, Department of Microbiology, University of Minnesota, St. Paul, MN 55108; present address: Institute of Human Genetics, University of Minnesota, Minneapolis, MN 55455 [29]

Helen Fillmore, Department of Cell Biology and Anatomy, University of Alabama at Birmingham, Birmingham, AL 35294; present address: Department of Anatomy, University of Tennessee, Memphis, TN [225]

F.A. Fletcher, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [375]

F. Flueckiger, Ludwig Institute for Cancer Research, 3010 Bern, Switzerland [151]

E. Frömter, Medizinische Hochschule Hannover, D-3000 Hannover 61, Physiologisches Institut, Universität Frankfurt, Federal Republic of Germany [283]

T. Friedmann, Department of Pediatrics, School of Medicine, University of California, San Diego, La Jolla, CA 92093 [409]

F. Gage, Department of Neurosciences, School of Medicine, University of California, San Diego, La Jolla, CA 92093 [409]

Eli Gilboa, Department of Molecular Biology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021 [365]

Edward I. Ginns, Molecular Neurogenetics Section, Clinical Neuroscience Branch, DIRP, NIMH, Bethesda, MD 20892 [345]

L. Michael Glode, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, CO 80262 [189]

Katherine Gordon, Integrated Genetics, Framingham, MA 01701 [57]

Paula Gregory, Department of Cell Biology and Anatomy, University of Alabama at Birmingham, Birmingham, AL 35294 [225]

K.O. Greulich, Physikalisch-Chemisches Institut, Universität Heidelberg, Federal Republic of Germany [283]

D. Greaves, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

B. Groner, Ludwig Institute for Cancer Research, 3010 Bern, Switzerland [151]

F. Grosveld, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

D. Grothues, Cystic Fibrosis Research Group, Zentrum Biochemie, Federal Republic of Germany [283]

K.S. Guise, Department of Animal Science, University of Minnesota, St. Paul, MN 55108 [29]

René Guyomard, Laboratory of Fish Genetics, INRA, 78350 - Jouy-en-Josas, France [9]

P.B. Hackett, Department of Genetics and Cell Biology, University of Minnesota, St. Paul, MN 55108 [29]

O. Hanscombe, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Gail S. Harrison, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, CO 80262 [189]

Lothar Hennighausen, Laboratory of Biochemistry and Metabolism, National Institute of Diabetes, Digestive, and Kidney Diseases, Bethesda, MD 20892 [57]

Richard Heyman, Gene Expression Laboratory, Howard Hughes Medical Institute, The Salk Institute, La Jolla, CA 92037 [163]

Howard R. Higley, Department of Experimental Biology, Baylor College of Medicine, Houston, TX 77030; present address: Collagen Corporation, Palo Alto, CA 94303 [255]

Yorio Hinuma, Institute for Virus Research, Kyoto University, Kyoto 606, Japan [103]

Chang Mu Hong, Department of Pediatrics, Division of Medical Genetics, Childrens Hospital of Los Angeles, University of Southern California School of Medicine, Los Angeles, CA 90027 [397]

Leroy Hood, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125 [235]

Arthur L. Horwich, Department of Human Genetics, Yale University School of Medicine, New Haven, CT 06510 [325]

Louis Houdebine, Cell Differentiation Unit, INRA, 78350 - Jouy-en-Josas, France [9]

Mary Hsi, Gene Expression Laboratory, Howard Hughes Medical Institute, The Salk Institute, La Jolla, CA 92037 [163]

J. Hundrieser, Cystic Fibrosis Research Group, Zentrum Humangenetik, Federal Republic of Germany [283]

J. Hurst, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Ursula Just, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany [79]

Philip Kantoff, Laboratory of Molecular Hematology, N.H.L.B.I., N.I.H., Bethesda, MD 20892 [365]

A.R. Kapuscinski, Department of Fisheries and Wildlife, University of Minnesota, St. Paul, MN 55108 [29]

Makoto Katsumo, Paterson Institute for Cancer Research, Christie Hospital, Withington, Manchester, M20 9BX, United Kingdom [79]

H.H. Kazazian, Jr., Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

Rodney E. Kellems, Department of Biochemistry and the Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX 77030 [255]

Vincent J. Kidd, Departments of Cell Biology and Anatomy and Microbiology, University of Alabama at Birmingham, Birmingham, AL 35294 [225]

Karl Klingler, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany; present address: Cancer Research Unit, Walter and Eliza Hall Institute of Medical Research, Victoria, 3050, Australia [79]

Norbert Kluge, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany [79]

Thomas B. Knudsen, Department of Anatomy, Quillen-Dishner College of Medicine, East Tennessee State University, Johnson City, TN 37614-0002 [255]

D.D. Koeberl, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

Donald B. Kohn, Metabolism Branch, N.C.I., N.I.H., Bethesda, MD 20892; present address: Department of Pediatrics, Division of Research Immunology and Bone Marrow Transplantation, Childrens Hospital of Los Angeles, University of Southern California, Los Angeles, CA 90027 [365,397]

G. Kollias, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Paul Krimpenfort, Division of Molecular Genetics, The Netherlands Cancer Institute, and Department of Biochemistry, University of Amsterdam, 1066 CX Amsterdam, The Netherlands [117]

B. Kroll, Medizinische Hochschule Hannover, D-3000 Hannover 61, Physiologisches Institut, Universität Frankfurt, Federal Republic of Germany [283]

Gracia Kruppa, Clinical Research Group BRWTI, Max-Planck-Society, University of Göttingen, 3400 Göttingen, Federal Republic of Germany [89]

Christine Laker, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany [79]

Yvan Lallemand, Unité de Génétique Cellulaire, Institut Pasteur, 75724 Paris Cedex 15, France [243]

W.W. Lamph, The Salk Institute, San Diego, CA 92138 [129]

Carlisle P. Landel, Cancer Biology and Gene Expression Laboratories, The Salk Institute, San Diego, CA 92138 [179]

Fred D. Ledley, Department of Cell Biology, Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [335,355]

Eric Lee, Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, Bethesda, MD 20892 [57]

Kuo-Fen Lee, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [67]

Hervé Le Mouellic, Unité de Génétique Cellulaire, Institut Pasteur, 75724 Paris Cedex 15, France [243]

Z. Liu, Department of Genetics and Cell Biology, University of Minnesota, St. Paul, MN 55108 [29]

G. Maass, Cystic Fibrosis Research Group, Zentrum Biochemie, Federal Republic of Germany [283]

G.R. MacGregor, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [375]

L. MacKenzie-Graham, Department of Cell Biology, Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [355]

Anthony Manly, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

Brian M. Martin, Molecular Neurogenetics Section, Clinical Neuroscience Branch, DIRP, NIMH, Bethesda, MD 20892 [345]

Françoise Maxwell, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, CO 80262 [189]

Ian H. Maxwell, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, CO 80262 [189]

Michael McKeown, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

James V. McMurray, Institute of Neuroscience, University of Oregon, Eugene, OR 97403 [19]

V. Mignotte, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

K.A. Moore, Institute for Molecular Genetics and Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [375]

T. Naiman, Department of Biochemistry, Tel Aviv University, Tel Aviv 69978, Israel [215]

Masataka Nakamura, Institute for Virus Research, Kyoto University, Kyoto 606, Japan [103]

Kevin Nash, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

Jan A. Nolta, Department of Pediatrics, Division of Research Immunology and Bone Marrow Transplantation, Childrens Hospital of Los Angeles, University of Southern California, Los Angeles, CA 90027 [397]

Risa Ohkawa, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

Kiyoshi Ohtani, Institute for Virus Research, Kyoto University, Kyoto 606, Japan [103]

Ariella Oppenheim, Department of Hematology, Hadassah University Hospital, Jerusalem, Israel 91120 [47]

Wolfram Ostertag, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany [79]

H. Peng, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [355]

K. Pfizenmaier, Clinical Research Group BRWTI, Max-Planck-Society, University of Göttingen, 3400 Göttingen, Federal Republic of Germany [89]

D.G. Phillips, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

N. Ponelies, Physikalisch-Chemisches Institut, Universität Heidelberg, Federal Republic of Germany [283]

Brian Popko, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125 [235]

V. Ramamurthy, Department of Biochemistry, Baylor College of Medicine, Houston, TX 77030 [255]

Carol Readhead, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125 [235]

Hector Rombola, Mount Sinai Hospital Research Institute and Department of Medical Genetics, University of Toronto, Toronto, Ontario, Canada [189]

J.M. Rosen, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [67]

M. Rosenberg, Department of Pediatrics, School of Medicine, University of California, San Diego, La Jolla, CA 92093 [409]

Raul Saavedra, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125 [235]

P. Woods Samuels, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

G. Sarkar, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

P. Sassone-Corsi, The Salk Institute, San Diego, CA 92138 [129]

C.-A. Schoenenberger, Ludwig Institute for Cancer Research, 3010 Bern, Switzerland [151]

Stephen A. Schwartz, Department of Pathology, University of Health Sciences, The Chicago Medical School, North Chicago, IL 60064 [205]

A.F. Scott, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

Brent Seaton, Department of Biology and Center for Molecular Genetics, University of California, San Diego, La Jolla, CA 92093 [417]

M. Seh, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [355]

Barbara Seliger, Clinical Research Group BRWTI, Max-Planck-Society, University of Göttingen, 3400 Göttingen, Federal Republic of Germany [89]

R.F. Shen, Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030 [355]

S. Shimohama, Department of Neurosciences, School of Medicine, University of California, San Diego, La Jolla, CA 92093 [409]

H. David Shine, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125; present address: Departments of Neuropathology and Neuroscience, Harvard Medical School, Boston, MA 02115 [235]

Richard L. Sidman, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125; present address: Departments of Neuropathology and Neuroscience, Harvard Medical School, Boston, MA 02115 [235]

L-K. Siew, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Cassandra L. Smith, Departments of Microbiology and Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY 10032 [269]

S.S. Sommer, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

Barbara A. Sosnowski, Molecular Biology and Virology Laboratory, The Salk Institute, San Diego, CA 92138 [1]

Elaine Spooncer, Paterson Institute for Cancer Research, Christie Hospital, Withington, Manchester, M20 9BX, United Kingdom [79]

Michael Steinmetz, Central Research Units, Hoffman-la Roche, Basel, Switzerland [117]

Carol Stocking, Heinrich-Pette-Institut an der Universität Hamburg, 2000 Hamburg 20, Federal Republic of Germany [79]

E.S. Stoflet, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN 55905 [307]

Gary W. Stuart, Institute of Neuroscience, University of Oregon, Eugene, OR 97403 [19]

Suresh Subramani, Department of Biology and Center for Molecular Genetics, University of California, San Diego, La Jolla, CA 92093 [417]

Kazuo Sugamura, Department of Bacteriology, Tohoku University School of Medicine, Sendai 980, Japan [103]

Naoki Takahashi, Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125; present address: Department of Medicine, Tokyo University, Faculty of Medicine, Tokyo, Japan [235]

D. Talbot, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

B. Tümmler, Cystic Fibrosis Research Group, Zentrum Biochemie, West Germany, Federal Republic of Germany [283]

T. Teitz, Department of Biochemistry, Tel Aviv University, Tel Aviv 69978, Israel [215]

John J. Trentin, Department of Experimental Biology, Baylor College of Medicine, Houston, TX 77030 [255]

Shoji Tsuji, Molecular Neurogenetics Section, Clinical Neuroscience Branch, DIRP, NIMH, Bethesda, MD 20892; present address: Department of Neurology, Brain Research Institute, Niigata University, Niigata 951, Japan [345]

Yasushi Uematsu, Basel Institute for Immunology, CH-4005 Basel, Switzerland [117]

Herman van der Putten, Cancer Biology and Gene Expression Laboratories, The Salk Institute, San Diego, CA 92138; present address: Department of Biotechnology, Ciba-Geigy A.G., CH-4002 Basel, Switzerland [179]

M.A. van der Valk, The Netherlands Cancer Institute, CX1066, Amsterdam, The Netherlands [151]

I.M. Verma, The Salk Institute, San Diego, CA 92138 [129]

J. Visvader, The Salk Institute, San Diego, CA 92138 [129]

James Vitale, Integrated Genetics, Framingham, MA 01701 [57]

R. Vogels, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

L. Wall, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

Stanley Welch, Department of Pathology University of Health Sciences, The Chicago Medical School, North Chicago, IL 60064 [205]

Monte Westerfield, Institute of Neuroscience, University of Oregon, Eugene, OR 97403 [19]

Heiner Westphal, Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, Bethesda, MD 20892 [57]

J. Wolff, Department of Pediatrics, School of Medicine, University of California San Diego, La Jolla, CA 92093 [409]

C. Wong, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

S.L.C. Woo, Department of Cell Biology, Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030 [355]

N. Wrighton, Laboratory of Gene Structure and Expression, National Institute for Medical Research, London NW7 1AA, United Kingdom [35]

S.J. Yoon, Department of Animal Science, University of Minnesota, St. Paul, MN 55108 [29]

H. Youssoufian, Department of Pediatrics, Genetics Unit, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 [293]

James Zwiebel, Laboratory of Molecular Hematology, N.H.L.B.I., N.I.H, Bethesda, MD 20892 [365]

Preface

The articles in this volume describe presentations at a meeting entitled **Gene Transfer and Gene Therapy** held at Tamarron, Colorado, February 6–12, 1988. Additional presentations of abstracts can be found in the *Journal of Cellular Biochemistry*, Supplement 12B:158, 1988. The planning for the meeting arose as an outgrowth of the highly successful 1986 UCLA Workshop **Vectors for Gene Transfer in Animals.** The aim of the meeting was to review research in the area of gene expression and gene transfer as it might relate to the goal of conducting somatic gene therapy in humans. The meeting effectively brought together basic researchers and human geneticists working with diseases.

Progress in gene transfer has been made in various species: mouse, *Drosophila,* zebra fish, rat, and other animals. Numerous examples of germ line gene transfer and somatic gene transfer in the mouse were reported. Important new information regarding control of gene expression, including the delineation of distant elements controlling human β-globin expression was presented. There has been a proliferation of knowledge on the cis-regulatory sequences and trans-acting factors which control gene expression. A detailed understanding of these mechanisms will be required for more sophisticated gene transfer and gene therapy efforts.

The meeting provided an up-to-date overview of vectors for gene transfer. Retroviral vector's predominated by a wide margin, although work with other vectors such as vaccinia virus was reported. Retroviral vectors continue to be modified to improve titer and expression. New retroviral packaging cell–lines designed to minimize production of replication–competent virus were reported. Efforts to carry out somatic gene therapy in animals might be viewed as encouraging or discouraging depending on whether one views the cup as half full or half empty. Significant expression in reimplanted bone marrow cells or fibroblasts was reported by a number of groups, but meaningful expression for the remainder of the life of all animals remains elusive.

Extensive time was devoted to discussions on human genetic diseases. Detailed molecular delineation of mutations is available in near innumerable amounts. Important diseases involving liver, bone–marrow derived cells,

central nervous system, muscle and other tissues were described. Although diagnosis for single gene disorders in extremely powerful, there is little ability to treat them. The feasibility of somatic gene therapy varies widely from disease to disease. Strategies for cloning disease genes prior to identification of the gene product represent an important new approach to human genetic diseases. A roundtable discussion was devoted to the ethical considerations for human somatic gene therapy.

Exciting progress was reported for homologous recombination in mammalian cells. Homologous recombination would offer major advantages for somatic gene therapy if it could be achieved. In the shorter term, use of homologous recombination in embryonic stem cells might lead to the development of mouse models for numerous human genetic diseases.

It will be of interest to observe whether the promise of somatic gene therapy bears fruit, and if so, what form such treatment might take. Hopefully, progress in the field will someday justify an additional UCLA symposium.

We gratefully acknowledge E.I. du Pont de Nemours & Company for generous sponsorship of this meeting. Additional support was received from: Genentech, Inc. and Pel-Freez Clinical Systems.

Arthur L. Beaudet
Richard Mulligan
Inder M. Verma

Contents