Mechanisms of Action & Therapeutic Applications of Biologicals in Cancer & Immune Deficiency Disorders

Mechanisms of Action and Therapeutic Applications of Biologicals in Cancer and Immune Deficiency Disorders

Proceedings of a Hoffman-La Roche-
Smith Kline & French—UCLA Symposium
Held at Keystone, Colorado
April 23–30, 1988

Editors

Jerome E. Groopman
Hematology/Oncology
New England Deaconess Hospital
Boston, Massachusetts

David W. Golde
Department of Medicine
Hematology/Oncology
University of California
Los Angeles, California

Charles H. Evans
Laboratory of Biology
National Cancer Institute
Bethesda, Maryland

Alan R. Liss, Inc. • New York

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

Printed in United States of America

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

Mechanisms of action and therapeutic applications of biologicals in cancer and immune deficiency disorders : proceedings of a Hoffmann-La Roche-Smith Kline & French-UCLA symposium, held at Keystone, Colorado, April 23-30, 1988 / editors, Charles H. Evans, David W. Golde, Jerome E. Groopman.
p. cm. -- (UCLA symposia on molecular and cellular biology ; new ser., v. 100)
Includes bibliographies and index.
ISBN 0-8451-2699-7
1. Biological response modifiers--Congresses. 2. Antibodies, Monoclonal--Therapeutic use--Congresses. 3. Cancer--Immunotherapy--Congresses. 4. AIDS (Disease)--Immunotherapy--Congresses. I. Evans, Charles H. (Charles Hawes), 1897- . II. Golde, David W. III. Groopman, Jerome E. IV. Hoffmann-La Roche, Inc. V. Smith, Kline & French Laboratories. VI. University of California, Los Angeles. VII. Series.
[DNLM: 1. Acquired Immunodeficiency Syndrome--drug therapy--congresses. 2. Antibodies, Monoclonal--therapeutic use--congresses. 3. Colony-Stimulating Factor therapeutic use--congresses. 4. Hematopoietic Stem Cells--congresses. 5. Interleukins--therapuetic use--congresses. W3 U17n new ser. v. 100 / WD 308 M486 1988]
RC271.B53M43 1989
616.99'4061--dc20
DNLM/DLC
for Library of Congress 89-12128
CIP

Contributors

John W. Adamson, Division of Hematology, Department of Medicine, University of Washington, Seattle, WA 98195 **[1]**

Frederick R. Appelbaum, Department of Clinical Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA 98104 **[145]**

Richard A. Ashmun, Department of Hematology/Oncology, St. Jude's Children's Research Hospital, Memphis, TN 38101 **[39]**

Michael B. Atkins, Department of Hematology-Oncology, New England Medical Center, Tufts University School of Medicine, Boston, MA 02111 **[153]**

Patricia D. Baker, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Dean W. Ballard, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710 **[361]**

Jeffery A. Barker, Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20892 **[315]**

Peggy Barlow, Infectious Disease Unit, Massachusetts General Hospital, Boston, MA 02214 **[385]**

Susan C. Barnett, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892; present address: Ludwig Institute of Cancer Research, London, England W1P8BT **[315]**

Ernst Böhnlein, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710 **[361]**

Jeanne Bertonis, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Samuel Broder, Clinical Oncology Program, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 **[331, 343, 371]**

Carol Browne, Department of Immunology Research, Lilly Research Laboratories, Indianapolis, IN 46285 **[187]**

Elaine M. Bruin, Immunopharmacology Section, E.I. Du Pont de Nemours & Co., Wilmington, DE 19898 **[239]**

The numbers in brackets are the opening page numbers of the contributors' articles.

C. Dean Buckner, Department of Clinical Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA 98104 **[145]**

Gordon F. Burns, Department of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

Larry Butler, Department of Immunology Research, Lilly Research Laboratories, Indianapolis, IN 46285 **[187]**

Judith Campisi, Department of Biochemistry, Boston University Medical School, Boston, MA 02218 **[229]**

Betty Chao, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Ben P. Chen, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Steve Clark, Genetics Institute, Cambridge MA 02140 **[65]**

Stanley Cohen, Department of Pathology, Hahnemann University, Philadelphia, PA 19102 **[249]**

Donna Costopoulos, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Francesco D'Alessandro, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

M. de Rie, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands 1066 CX **[293]**

Jan E. de Vries, Division of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX; present address: Unicet, Dardilly, France 69572 **[95]**

Theresa M. Di Meo, Immunopharmacology Section, E.I. Du Pont de Nemours & Co., Wilmington, DE 19898 **[239]**

Charles A. Dinarello, Department of Medicine, Tufts University School of Medicine, New England Medical Center Hospital, Boston, MA 02111 **[201]**

Pam Dyson, Department of Haematology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

Stefan Endres, Department of Medicine, Tufts University School of Medicine, New England Medical Center Hospital, Boston, MA 02111 **[201]**

Joseph W. Eschbach, Division of Hematology, Department of Medicine, University of Washington, Seattle, WA 98195 **[1]**

Charles H. Evans, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Barbara Fagg, Department of Biotechnology, Sandoz, Ltd., CH 4002 Basel, Switzerland **[135]**

Esme K. Farley, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Carl G. Figdor, Division of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[95]**

Paul Fisch, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Zvi Fishelson, Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel 76100 **[273]**

Richard Fisher, Department of Molecular Biology, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Richard Flavell, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Diane Fox, Immunopharmacology Section, E.I. Du Pont de Nemours & Co., Wilmington, DE 19898 **[239]**

B. Robert Franza, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY 11724 **[361]**

Jan-Erik Frödin, Department of Oncology, Karolinska Hospital, Stockholm, Sweden 104 01 **[263]**

Kerin Fresa, Department of Pathology, Hahnemann University, Philadelphia, PA 19102 **[249]**

Paulette M. Furbert-Harris, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Balázs A. Gelléri, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Jürg Gmür, Division of Oncology, Department of Medicine, University Hospital, CH-8091, Zürich, Switzerland **[219]**

Scott Graves, Department of Immunology, NeoRx Corporation, Seattle, WA 98119 **[283]**

Warner C. Greene, Department of Medicine, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710 **[361]**

Meera Hameed, Department of Pathology, Hahnemann University, Philadelphia, PA 19102 **[249]**

Jacquelyn A. Hank, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Stephen R. Hann, Department of Cell Biology, Vanderbilt University Medical School, Nashville, TN 37232 **[229]**

Seiji Hayashi, Clinical Oncology Program, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 **[371]**

A. Hekman, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

K. Hirai, Department of Clinical Immunology, University of Bern, Bern, Switzerland; present address: Department of Medicine and Physical Therapy, University of Tokyo, Tokyo, Japan **[135]**

Martin Hirsch, Infectious Disease Unit, Massachusetts General Hospital, Boston, MA 02114 **[385]**

Tasuku Honjo, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

A. Honselaar, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

Junko Horiguchi, Department of Medicine, Laboratory of Clinical Pharmacology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115 **[13]**

Kayo Inaba, Department of Zoology, Kyoto University Faculty of Science, Kyoto 606, Japan **[175]**

Yasumasa Ishida, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Carl Harald Janson, Department of Immunology, Karolinska Institute, Stockholm, Sweden 104 01 **[263]**

Boquan Jin, Department of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

Victoria Johnson, Infectious Disease Unit, Massachusetts General Hospital, Boston, MA 02114 **[385]**

Lorenz M. Jost, Division of Oncology, Department of Medicine, University Hospital, CH-8091, Zürich, Switzerland **[219]**

Kenneth Kaushansky, Division of Hematology, University of Washington, Seattle, WA 98195 **[29]**

Masashi Kawaichi, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Jan P.G. Klomp, Division of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[95]**

Peter C. Kohler, Departments of Human Oncology, Pediatrics and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Donald W. Kufe, Department of Medicine, Laboratory of Clinical Pharmacology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115 **[13]**

Sachiko Kuno, Department of Medicine, Research Institute, Ueno Fine Chemicals Industry, Ltd., Itami 664, Japan **[331]**

Martha B. Ladner, Department of Molecular Biology, Cetus Corporation, Emeryville, CA 94608 **[29]**

Val Lam, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Regine Landmann, Division of Oncology, Departments of Internal Medicine and Research, Kantonsspital, Basel, Switzerland **[89]**

Nicolette Layman, Department of Immunology Research, Lilly Research Laboratories, Indianapolis, IN 46285 **[187]**

Mei-Ting Lee, Department of Cell Biology, Cetus Corporation, Emeryville, CA 94608 **[29]**

Roy A. Levine, Department of Biochemistry, Boston University Medical School, Boston, MA 02118 **[229]**

Margaret Liu, Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02142 **[385]**

Theresa Liu, Biogen Research Corp., Cambridge, MA 02142 **[385]**

A. Thomas Look, Departments of Hematology/Oncology and Tumor Cell Biology, St. Jude's Children's Hospital, Memphis, TN 38101 **[39]**

David J. Looney, Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, MD 20892, and Walter Reed Army Institute of Research, Washington, DC 20307 **[331]**

Angel F. Lopez, Department of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

John W. Lowenthal, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710 **[361]**

Bruce L. Maloff, Immunopharmacology Section, E.I. Du Pont de Nemours & Co., Wilmington, DE 19898 **[239]**

Randy Mandell, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

John Maraganore, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Paul A. Marks, DeWitt Wallace Research Laboratories, Memorial Sloan-Kettering Cancer Center, Sloan-Kettering Division of the Graduate School of Medical Sciences, Cornell University, New York, NY 10021 **[119]**

Giuseppe Masucci, Department of Oncology, Karolinska Hospital, Stockholm, Sweden 104 01 **[263]**

Makoto Matsukura, Clinical Oncology Program, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 **[371]**

Werner Meier, Biogen Research Corp., Cambridge, MA 02142 **[385]**

C.J.M. Melief, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

Håkan Mellstedt, Department of Oncology, Karolinska Hospital, Stockholm, Sweden 104 01 **[263]**

Rita Michalevicz, Department of Hematology, Ichilob Hospital, Tel-Aviv Medical Center, Tel-Aviv, Israel 64239 **[105]**

James W. Mier, Department of Hematology-Oncology, New England Medical Center, Tufts University School of Medicine, Boston, MA 02111 **[153]**

Malcolm Mitchell, University of Southern California, Los Angeles, CA 90033 **[283]**

Hiroaki Mitsuya, Clinical Oncology Program, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 **[331, 343, 371]**

Malcolm A. S. Moore, Laboratory for Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, New York, NY 10021 **[77]**

Alton C. Morgan, Jr., Department of Immunology, NeoRx Corporation, Seattle, WA 98119 **[283]**

Alan Mufson, Genetics Institute, Cambridge, MA 02140 **[283]**

K. Nakajima, Department of Clinical Immunology, University of Bern, CH 3010 Bern, Switzerland **[135]**

Miyuki Nishi, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan; present address: Department of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, CA 92037 **[175]**

Robert P. Numerof, Department of Medicine, New England Medical Center, Tufts University School of Medicine, Boston, MA 02111 **[153]**

Jean Paul Obrecht, Division of Oncology, Departments of Internal Medicine and Research, Kantonsspital, Basel, Switzerland **[89]**

Reto Obrist, Division of Oncology, Departments of Internal Medicine and Research, Kantonsspital, Basel, Switzerland **[89]**

Oswald Oelz, Division of Oncology, Department of Medicine, University Hospital, CH-8091 Zürich, Switzerland **[219]**

Masahiro Ohtsuka, Department of Tumor Cell Biology, St. Jude's Children's Research Hospital, Memphis, TN 38101 **[39]**

John R. Ortaldo, Laboratory of Experimental Immunology BRMP, DCT, National Cancer Institute, Frederick, MD 21701-1013 **[305]**

Shashikant Phadtare, Department of Chemistry, Meyer L. Prentis Cancer Center, Detroit, MI 48201 **[371]**

Ph. Rümke, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

Yoram Reiter, Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel 76100 **[273]**

Michel Revel, Department of Virology, Weizmann Institute of Science, Rehovot, Israel **[105]**

Pamela Riedl, Department of Immunology Research, Lilly Research Laboratories, Indianapolis, IN 46285 **[187]**

Richard A. Rifkind, DeWitt Wallace Research Laboratories, Memorial Sloan-Kettering Cancer Center, Sloan-Kettering Division of the Graduate School of Medical Sciences, Cornell University, New York, NY 10021 **[119]**

S. Rodenhuis, Department of Clinical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

Margaret Rosa, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Martine F. Roussel, Department of Tumor Cell Biology, St. Jude's Children's Research Hospital, Memphis, TN 38101 **[39]**

Elhanan Sahar, Biotechnology Center, Tel-Aviv University, Tel-Aviv, Israel 69978 **[105]**

Eric Sariban, Department of Medicine, Laboratory of Clinical Pharmacology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115 **[13]**

Vicki Sato, Biogen Research Corp., Cambridge, MA 02142 **[385]**

Christian Sauter, Division of Oncology, Department of Medicine, University Hospital, CH-8091 Zürich, Switzerland **[219]**

Robert Schooley, Infectious Disease Unit, Massachusetts General Hospital, Boston, MA 02114 **[385]**

J. J. Seinen, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX [293]

Tara Seshadri, Department of Biochemistry, Boston University Medical School, Boston, MA 02118 [229]

Joan E. Shaw, Medical Products Department, E.I. Du Pont de Nemours & Co., Wilmington, DE 19898 **[239]**

Paul A. Sheehy, Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20892 **[315]**

Charles J. Sherr, Department of Tumor Cell Biology, St. Jude's Children's Research Hospital, Memphis, TN 38101 **[39]**

Paschalis Sideras, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Charles Sidman, The Jackson Laboratory, Bar Harbor, ME 04609 **[187]**

Miriam Siekevitz, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710; present address: Mt. Sinai Medical Center, New York, NY 10029 **[361]**

Paul M. Sondel, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Jeff A. Sosman, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

B. Stadler, Department of Clinical Immunology, University of Bern, CH 3010 Bern, Switzerland **[135]**

Rolf A. Stahel, Division of Oncology, Department of Medicine, University Hospital, CH-8091 Zürich, Switzerland **[219]**

Rainer Storb, Department of Clinical Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA 98104 **[145]**

Wendy Sullivan, Department of Immunology, NeoRx Corporation, Seattle, WA 98119 **[283]**

Shigetoshi Suzuki, Department of Medical Chemistry, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Osamu Taguchi, Aichi Cancer Center Research Institute, Nagoya 464, Japan **[175]**

Eiji Takeuchi, Department of Pathology, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Anje A. te Velde, Division of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[95]**

E. Donnall Thomas, Department of Clinical Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA 98104 **[145]**

Luen B. To, Department of Haematology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

Ryuji Ueno, Department of Medicine, Research Institute, Ueno Fine Chemicals Industry, Ltd., Itami 664, Japan **[331]**

Gloria Vachino, Department of Hematology-Oncology, New England Medical Center, Tufts University School of Medicine, Boston, MA 02111 **[153]**

Mathew A. Vadas, Department of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, Australia 5000 **[65]**

Stephen Voss, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

W. Vuist, Department of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[293]**

Nobutaka Wakamiya, Department of Medicine, Laboratory of Clinical Pharmacology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115; present address: Department of Pathology, Research Institute of Microbiological Diseases, Osaka University, Osaka, Japan **[13]**

Bruce Walker, Infectious Disease Unit, Massachusetts General Hospital, Boston, MA 02114 **[385]**

Yuji Wano, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710; present address: Fukui Medical School, Fukui 910-11, Japan **[361]**

David J. Warren, Laboratory for Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, New York, NY 10021 **[77]**

Gilda Weil-Hillman, Departments of Human Oncology, Pediatrics, and Genetics, University of Wisconsin, Madison, WI 53792 **[163]**

Richard H. Weisbart, Department of Medicine, Division of Rheumatology, Veterans Administration Medical Center, Sepulveda, CA 91343 **[57]**

Hans Wigzell, Department of Immunology, Karolinska Institute, Stockholm, Sweden 104 01 **[263]**

Anna C. Wilson, Laboratory of Biology, National Cancer Institute, Bethesda, MD 20892 **[315]**

Flossie Wong-Staal, Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, MD 20892 **[331]**

Clive Woodhouse, Department of Immunology, NeoRx Corporation, Seattle, WA 98119 **[283]**

Yu-Chung Yang, Genetics Institute, Cambridge, MA 02140 **[65]**

Benito A. Yard, Division of Immunology, Netherlands Cancer Institute, Amsterdam, The Netherlands 1066 CX **[95]**

Haruyoshi Yoshida, Department of Pathology, Kyoto University Faculty of Medicine, Kyoto 606, Japan **[175]**

Jiri Zemlicka, Department of Chemistry, Meyer L. Prentis Cancer Center, Detroit, MI 48201 **[371]**

Preface

We are witnessing a period of extraordinary progress in the understanding of growth factors. The application of recombinant DNA technology has allowed for the molecular and biochemical characterization of a wide range of polypeptides that modulate cell growth and function. These have been rapidly moved from the laboratory to the bedside and are showing considerable clinical promise in augmenting host defense. This symposium, **Mechanisms of Action and Therapeutic Applications of Biologicals in Cancer and Immune Deficiency Disorders,** was held at Keystone, Colorado, April 23–30, 1988, and formed an opportunity for interdisciplinary communication among basic science and clinical investigators. The proceedings in this volume represent the state-of-the-art in understanding the basic biology and clinical application of hematopoietic growth factors, the interleukins, and monoclonal antibody therapy. The complexity of the acquired immunodeficiency syndrome is such that one or several of these biologic modalities may prove to be of benefit in its treatment, and therefore AIDS served as a focus for much of the work and research.

The consensus of the meeting was that by manipulating number and/or function of immune effector cells of myeloid or lymphoid lineage, disorders that previously were not amenable to therapy may ultimately emerge as responsive. With such therapeutic approaches there are concerns and considerations that focus on the potential toxicities or negative effects that biologics might have on the host. An improved understanding of the physiological role of these mediators may allow us to use them in a selective and intelligent fashion with minimal and tolerable side effects. We are only at the threshold in benefiting from the applications of biologicals to malignant and immunodeficiency disorders.

We are indebted to Hoffmann-La Roche, Inc. and Smith Kline & French Laboratories for their support in sponsoring this meeting. Additional support was received from Biogen Research Corporation, Cetus Corporation, NeoRx Corporation, and the Genetics Institute.

Jerome E. Groopman
David W. Golde
Charles H. Evans

Contents

Mechanisms of Action and Therapeutic Applications of Biologicals in Cancer and Immune Deficiency Disorders, pages 1-11

EXPERIENCE WITH RECOMBINANT HUMAN ERYTHROPOIETIN IN MAN: AN UPDATE[1]

John W. Adamson and Joseph W. Eschbach

Division of Hematology,
Department of Medicine
University of Washington
Seattle, Washington 98195

ABSTRACT End-stage renal disease (ESRD) typically is associated with severe anemia. The major contributor to the anemia appears to be the absolute or relative deficiency of erythropoietin (Epo) production by the kidney. A series of clinical trials have been conducted in the United States using recombinant human Epo (rHuEpo) to treat anemic patients with ESRD. The encouraging results of the Phase I-II clinical trials have been confirmed in a multicenter trial in which over 250 patients have been treated. The rHuEpo was well tolerated, produced few or no direct side effects, and was effective in greater than 95 percent of the patients. rHuEpo should have a major role in the management of patients with ESRD and contribute significantly to their rehabilitation.

---

[1]This work was supported by research grants DK 19410 and DK 33488, and Clinical Research Center grant FR 0037 from the National Institutes of Health, DHHS, and patient support funds from AMGen Corporation to the Northwest Kidney Center.