

Technical and Biological Components of Marrow Transplantation

Technical and Biological Components of Marrow Transplantation

edited by

C. DEAN BUCKNER

R.A. CLIFT

*Fred Hutchinson Cancer Research Center
Seattle, Washington*

SPRINGER SCIENCE+BUSINESS MEDIA, LLC



Library of Congress Cataloging-in-Publication Data

Technical and biological components of marrow transplantation / edited by
C. Dean Buckner.

p. cm. – (Cancer treatment and research ; 76)

Includes bibliographical references and index.

ISBN 978-1-4613-5832-9 ISBN 978-1-4615-2013-9 (eBook)

DOI 10.1007/978-1-4615-2013-9

1. Bone marrow – Transplantation. 2. Hematopoietic stem cells –
Transplantation. I Buckner, C. Dean. II. Clift, R.A. III. Series.
[DNLM: 1. Bone Marrow Transplantation. 2. Hematologic
Diseases – therapy. 3. Neoplasms – therapy. 4. Metabolic Diseases –
therapy.

W1 CA693 v. 76 1995 / WH 380 T255 1995]

RD 123.5.T43 1995

617.4'4 – dc20

DNLM/DLC

for Library of Congress

95-1584

CIP

Copyright © 1995 Springer Science+Business Media New York

Originally published by Kluwer Academic Publishers in 1995

Softcover reprint of the hardcover 1st edition 1995

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher, Springer Science+Business Media, LLC.

Printed on acid-free paper.

Technical and Biological Components of Marrow Transplantation

Cancer Treatment and Research

- Muggia FM (ed): Cancer Chemotherapy: Concepts, Clinical Investigations and Therapeutic Advances. 1988. ISBN 0-89838-381-1
- Nathanson L (ed): Malignant Melanoma: Biology, Diagnosis, and Therapy. 1988. ISBN 0-89838-384-6
- Pinedo HM, Verweij J (eds): Treatment of Soft Tissue Sarcomas. 1989. ISBN 0-89838-391-9
- Hansen HH (ed): Basic and Clinical Concepts of Lung Cancer. 1989. ISBN 0-7923-0153-6
- Lepor H, Ratliff TL (eds): Urologic Oncology. 1989. ISBN 0-7923-0161-7
- Benz C, Liu E (eds): Oncogenes. 1989. ISBN 0-7923-0237-0
- Ozols RF (ed): Drug Resistance in Cancer Therapy. 1989. ISBN 0-7923-0244-3
- Surwit EA, Alberts DS (eds): Endometrial Cancer. 1989. ISBN 0-7923-0286-9
- Champlin R (ed): Bone Marrow Transplantation. 1990. ISBN 0-7923-0612-0
- Goldenberg D (ed): Cancer Imaging with Radiolabeled Antibodies. 1990. ISBN 0-7923-0631-7
- Jacobs C (ed): Carcinomas of the Head and Neck. 1990. ISBN 0-7923-0668-6
- Lippman ME, Dickson R (eds): Regulatory Mechanisms in Breast Cancer: Advances in Cellular and Molecular Biology of Breast Cancer. 1990. ISBN 0-7923-0868-9
- Nathanson, L (ed): Malignant Melanoma: Genetics, Growth Factors, Metastases, and Antigens. 1991. ISBN 0-7923-0895-6
- Sugarbaker, PH (ed): Management of Gastric Cancer. 1991. ISBN 0-7923-1102-7
- Pinedo HM, Verweij J, Suit HD (eds): Soft Tissue Sarcomas: New Developments in the Multidisciplinary Approach to Treatment. 1991. ISBN 0-7923-1139-6
- Ozols RF (ed): Molecular and Clinical Advances in Anticancer Drug Resistance. 1991. ISBN 0-7923-1212-0
- Muggia FM (ed): New Drugs, Concepts and Results in Cancer Chemotherapy. 1991. ISBN 0-7923-1253-8
- Dickson RB, Lippman ME (eds): Genes, Oncogenes and Hormones: Advances in Cellular and Molecular Biology of Breast Cancer. 1992. ISBN 0-7923-1748-3
- Humphrey G, Bennett Schraffordt Koops H, Molenaar WM, Postma A (eds): Osteosarcoma in Adolescents and Young Adults: New Developments and Controversies. 1993. ISBN 0-7923-1905-2
- Benz CC, Liu ET (eds): Oncogenes and Tumor Suppressor Genes in Human Malignancies. 1993. ISBN 0-7923-1960-5
- Freireich EJ, Kantarjian H (eds): Leukemia: Advances in Research and Treatment. 1993. ISBN 0-7923-1967-2
- Dana BW (ed): Malignant Lymphomas, Including Hodgkin's Disease: Diagnosis, Management, and Special Problems. 1993. ISBN 0-7923-2171-5
- Nathanson L (ed): Current Research and Clinical Management of Melanoma. 1993. ISBN 0-7923-2152-9
- Verweij J, Pinedo HM, Suit HD (eds): Multidisciplinary Treatment of Soft Tissue Sarcomas. 1993. ISBN 0-7923-2183-9
- Rosen ST, Kuzel TM (eds): Immunoconjugate Therapy of Hematologic Malignancies. 1993. ISBN 0-7923-2270-3
- Sugarbaker PH (ed): Hepatobiliary Cancer. 1994. ISBN 0-7923-2501-X
- Rothenberg ML (ed): Gynecologic Oncology: Controversies and New Developments. 1994. ISBN 0-7923-2634-2
- Dickson RB, Lippman ME (eds): Mammary Tumorigenesis and Malignant Progression. 1994. ISBN 0-7923-2647-4
- Hansen HH (ed): Lung Cancer. Advances in Basic and Clinical Research. 1994. ISBN 0-7923-2835-3
- Goldstein FJ, Ozols RF (eds): Anticancer Drug Resistance. Advances in Molecular and Clinical Research. 1994. ISBN 0-7923-2836-1
- Hong WK, Weber RS (eds): Head and Neck Cancer. Basic and Clinical Aspects. 1994. ISBN 0-7923-3015-3
- Thall PF (ed): Recent Advances in Clinical Trial Design and Analysis. 1994. ISBN 0-7923-3235-0

Contents

| | |
|---|-----|
| Contribution Authors | vii |
| Preface | xi |
| 1. Marrow Transplantation for Chronic Myeloid Leukemia | 1 |
| REGINALD CLIFT | |
| 2. Bone Marrow Transplantation in Thalassemia | 43 |
| GUIDO LUCARELLI, and CLAUDIO GIARDINI | |
| 3. High-Dose Chemotherapy and Autologous Stem Cell Transplantation for Breast Cancer | 59 |
| CHARLES WEAVER, ROBERT BIRCH, LEE SCHWARTZBERG, and WILLIAM WEST | |
| 4. Bone Marrow Transplantation for Metabolic Diseases | 87 |
| ROBERTSON PARKMAN, GAY CROOKS, DONALD KOHN, CARL LENARSKY, and KENNETH WEINBERG | |
| 5. Cytomegalovirus Infection in Marrow Transplantation | 97 |
| MICHAEL BOECKH, and RALEIGH BOWDEN | |
| 6. Marrow Transplantation from Unrelated Volunteer Donors | 137 |
| CLAUDIO ANASETTI, EFFIE PETERSDORF, PAUL MARTIN, and JOHN HANSEN | |
| 7. Peripheral Blood Stem Cell Transplantation | 169 |
| WILLIAM BENSINGER | |
| 8. Umbilical Cord Blood Stem Cell Transplantation | 195 |
| JOHN WAGNER | |

| | | |
|-----|--|-----|
| 9. | In Vitro Expansion of Hematopoietic Cells for Clinical Application | 215 |
| | STEPHEN EMERSON, BERNHARD PALSSON, MICHAEL CLARKE, SAMUEL SILVER, PAUL ADAMS, MANFRED KOLLER, GARY VAN ZANT, SUSAN RUMMEL, R. DOUGLAS ARMSTRONG, JAMES MALUTA, JUDITH DOUVIUE, and LESLIE PAUL | |
| 10. | Recombinant Hematopoietic Growth Factors in Bone Marrow Transplantation | 225 |
| | JOHN NEMUNAITIS | |
| 11. | Detection of Minimal Residual Disease | 249 |
| | JOHN GRIBBEN and LEE NADLER | |
| 12. | Genetic Therapy Using Bone Marrow Transplantation | 271 |
| | RICHARD GILES, ELIE HANANIA, SIQING FU, and ALBERT DEISSEROTH | |
| 13 | Myeloablative Radiolabeled Antibody Therapy with Autologous Bone Marrow Transplantation for Relapsed B-Cell Lymphomas | 281 |
| | OLLIE PRESS, JANET EARY, FREDERICK APPLEBAUM, and IRWIN BERNSTEIN | |
| 14. | Graft Versus Leukemia in Humans | 299 |
| | ANNA BUTTURINI and ROBERT PETER GALE | |
| 15. | Interleukin-2 in Bone Marrow Transplantation | 315 |
| | UDIT VERMA, BISHAN CHARAK, CHITRA RASAGOPAL, and AMITABHA MAZUMDER | |
| 16. | Cellular Adoptive Immunotherapy after Bone Marrow Transplantation | 337 |
| | STAN RIDDELL and PHILIP GREENBERG | |
| | Index | 371 |

Contributing Authors

- ADAMS, Paul T., Department of Internal Medicine, University of Michigan
48105, 3105/Box 0368 Taubman Street, Ann Arbor, MI 48109
- ANASETTI, Claudio, Fred Hutchinson Cancer Research Center, Director,
Unrelated Donor Transplant Program, 1124 Columbia Street, Mailstop
E611, Seattle, WA 98104
- APPELBAUM, Frederick R., Fred Hutchinson Cancer Research Center,
1124 Columbia Street, M-127, Seattle, WA 98104
- ARMSTRONG, R. Douglas, Aastrom Biosciences, Inc., Domino Farms,
Lobby L, Ann Arbor, MI 48105
- BENSINGER, William I., Fred Hutchinson Cancer Research Center, 1124
Columbia Street, Mailstop E100, Seattle, WA 98104
- BERNSTEIN, Irwin D., Fred Hutchinson Cancer Research Center, 1124
Columbia Street, C1-169, Seattle, WA 98104
- BIRCH, Robert, Response Technologies, 1775 Moriah Woods Boulevard,
Memphis, TN 38117
- BOECKH, Michael, Fred Hutchinson Cancer Research Center, 1124
Columbia Street, Mailstop AC142, Seattle, WA 98104
- BOWDEN, Rowley, Fred Hutchinson Cancer Research Center, 1124
Columbia Street, Mailstop AC142, Seattle, WA 98104
- BUTTURINI, Anna, Salick Healthcare, Inc., 8201 Beverly Boulevard, Los
Angeles, CA 90048
- CHARAK, Bishan S., Georgetown University School of Medicine,
Department of Medical Oncology, 3800 Reservoir Road NW,
Washington, DC 20007-2197
- CLARKE, Michael F., Department of Hematology-Oncology, 102
Observatory Street, Ann Arbor, MI 48109
- CLIFT, Reginald, Fred Hutchinson Cancer Research Center, 1124 Columbia
Street, Mailstop E100, Seattle, WA 98104
- CROOKS, Gay, Instructor of Pediatrics, Children's Hospital, Los Angeles,
4650 Sunset Boulevard, Los Angeles, CA 90027
- DEISSEROTH, Albert, Department of Hematology, University of Texas,
MD Anderson Cancer Center, 1515 Holcombe Boulevard #24, Houston,
TX 77030-4009

DOUVILLE, Judith, Aastrom Biosciences, Inc., Domino Farms, Lobby L, Ann Arbor, MI 48105

EARY, Janet F., Department of Nuclear Medicine, University of Washington, 1959 NE Pacific Street, RC-70, Seattle, WA 98195

EMERSON, Stephen Chief, Division of Hematology/Oncology, University of Pennsylvania, School of Medicine, 3400 Spruce Street, Philadelphia, PA 19104-4283

FU, Siqing, Department of Hematology, University of Texas, MD Anderson Cancer Center, 1515 Holcombe Boulevard #24, Houston, TX 77030-4009

GALE, Robert Peter, Salick Healthcare, Inc., 8201 Beverly Boulevard, Los Angeles, CA 90048

GIARDINI, Claudio, Department of Hematology, Hospital of Pesaro, 6110 Pesaro, ITALY

GILES, Richard, Department of Hematology, University of Texas, MD Anderson Cancer Center, 1515 Holcombe Boulevard #24, Houston, TX 77030-4009

GREENBERG, Philip, Fred Hutchinson Cancer Research Center, Director, Unrelated Donor Transplant Program, 1124 Columbia Street, Mailstop AC100, Seattle, WA 98104

GRIBBEN, John, Tumor Immunology Division, Dana-Farber Cancer Institution, 44 Binney Street, Boston, MA 02115

HANANIA, Elie G., Department of Hematology, University of Texas, MD Anderson Cancer Center, 1515 Holcombe Boulevard #24, Houston, TX 77030-4009

HANSEN, John A., Fred Hutchinson Cancer Research Center, 1124 Columbia Street, M-718, Seattle, WA 98104

KOHN, Donald B., Associate Professor of Clinical Pediatrics and Microbiology, Children's Hospital, Los Angeles, 4650 Sunset Boulevard, Los Angeles, CA 90027

KOLLER, Manfred R., Aastrom Biosciences, Inc., Domino Farms, Lobby L, Ann Arbor, MI 48105

LENARSKY, Carl, Associate Professor of Clinical Pediatrics, Children's Hospital, Los Angeles, 4650 Sunset Boulevard, Los Angeles, CA 90027

LUCARELLI, Guido, Department of Hematology, Hospital of Pesaro, 6110 Pesaro, ITALY

MALUTA, James, Aastrom Biosciences, Inc., Domino Farms, Lobby L, Ann Arbor, MI 48105

MARTIN, Paul J., Fred Hutchinson Cancer Research Center, 1124 Columbia Street, M-718, Seattle, WA 98104

MAZUMDER, Amitabha, Georgetown University School of Medicine, Department of Medical Oncology, 3800 Reservoir Road NW, Washington, DC 20007-2197

NADLER, Lee, Tumor Immunology Division, Dana-Farber Cancer Institution, 44 Binney Street, Boston, MA 02115

NEMUNAITIS, John, Director of Clinical Research, Texas Oncology, P.A.,
Director of Cytokine Research, Baylor University Medical Center, PA
Research #400, 3320 Live Oak, Dallas, TX 75204

PALSSON, Bernard O., University of Michigan, Department of Chemical
Engineering, 2300 Hayward Street, Ann Arbor, MI 48109-2136

PARKMAN, Robertson, Children's Hospital of Los Angeles, Department
of Immunology MS62, 4650 Sunset Boulevard, Los Angeles, CA 90027

PAUL, Leslie, Aastrom Biosciences, Inc., Domino Farms, Lobby L, Ann
Arbor, MI 48105

PETERSDORF, Effie W., Fred Hutchinson Cancer Research Center, 1124
Columbia Street, M-718, Seattle, WA 98104

PRESS, Ollie, Assistant Professor of Medicine, University of Washington
Medical Center, Mailstop ED-08, 1959 NE Pacific, Seattle, WA 98111

RAJAGOPAL, Chitra, Georgetown University School of Medicine, Depart-
ment of Medical Oncology, 3800 Reservoir Road NW, Washington, DC
20007-2197

RIDDELL, Stan, Fred Hutchinson Cancer Research Center, Director,
Unrelated Donor Transplant Program, 1124 Columbia Street, Mailstop
AC100, Seattle, WA 98104

RUMMEL, Susan, Aastrom Biosciences, Inc., Domino Farms, Lobby L,
Ann Arbor, MI 48105

SCHWARTZBERG, Lee S., Response Technologies, 1775 Moriah Woods
Boulevard, Memphis, TN 38117

SILVER, Samuel M., Department of Hematology-Oncology, 102 Observa-
tory Street, Ann Arbor, MI 48109

VAN ZANT, Gary, Aastrom Biosciences, Inc., Domino Farms, Lobby L,
Ann Arbor, MI 48105

VERMA, Udit, Georgetown University School of Medicine, Department of
Medical Oncology, 3800 Reservoir Road NW, Washington, DC 20007-
2197

WAGNER, John, Department of Pediatrics, University of Minnesota, Box
366 UMHC, 420 Delaware Street, SE, Minneapolis, MN 55455

WEAVER, Charles, Response Technologies, 1775 Moriah Woods
Boulevard, Memphis, TN 38117

WEINBERG, Kenneth, Associate Professor of Pediatrics, Children's
Hospital, Los Angeles, 4650 Sunset Boulevard, Los Angeles, CA 90027

WEST, William H., Response Technologies, 1775 Moriah Woods
Boulevard, Memphis, TN 38117

Preface

This is not a textbook and it is not intended to be a work of reference. We hope it is a book that can be read from cover to cover by physicians and scientists involved with, or interested in, bone marrow transplantation. The objective is to present up-to-date information and recent citations. For the most part, the contributions are directed at scientific and technologic advances designed to extend and improve the clinical application of treatment usually described as bone marrow transplantation.

Two chapters deal with the treatment of chronic myeloid leukemia (CML) and thalassemia, which are spectacularly successful applications of allogeneic marrow transplantation that have now become conventional therapy. These therapies are still being fine tuned, particularly with a view to increasing the number of patients who can avail themselves of this treatment. The use of volunteer unrelated donors is clearly an option favored by the pace of disease progression in these diseases, and it is already widely used for CML. Autologous marrow transplantation is an option that will be studied for both diseases. In the case of CML, the rapidly increasing understanding of the molecular biology of the underlying genetic flaw will add special opportunities to studies of *in vivo* or *in vitro* purging. In the case of thalassemia, autologous transplantation will provide the vehicle for introducing the genetic revisions needed for cure.

The term *bone marrow transplantation* is not always an accurate description of the field we cover. Increasingly it is applied to the reinfusion of autologous hematopoietic progenitors, either as part of a strategy of *ex vivo* marrow protection or as a vehicle for introducing genetic change. Indeed, it is likely that even allogeneic marrow transplantation soon will be routinely accomplished by the transfer of peripheral blood stem cells rather than bone marrow. However, bone marrow transplantation has a nice old-fashioned ring to it, and the phrase will probably continue in use to describe any manipulation that involves the reconstitution of the hematopoietic system.

The development of this field was made possible by advances in supportive care, including platelet transfusions and powerful antibiotics, and these advances have continued to the point where allogeneic transplants can now be performed with very little morbidity and mortality in patients who do not

have a big legacy of organ damage from intensive prior therapy. Improved management of cytomegalovirus infection should have a dramatic impact on survival after allogeneic transplantation. The chapters dealing with cytokines and progenitor expansion indicate that the time is not far distant when marrow transplantation can be contemplated as an outpatient procedure. This will undoubtedly have an influence on the timing of transplantation. We may soon be able to define circumstances in which early transplantation for leukemia will be less dangerous and more effective than initial remission induction without the support of early marrow reconstitution from a transplant. The genetic implantation of resistance factors into stem cells could enable a survival advantage over resident hematopoiesis for modified, reinfused stem cells, permitting the exploitation of selection pressures favoring the modified cell population over an extended time scale. This may encourage the development of chronic therapy removing some of the cataclysmic associations that history has bestowed on marrow transplantation.

Enthusiastic investigators of cord blood stem cell technology clearly contemplate global depositories of stem cells collected at the time of birth and, perhaps, outliving the unwitting donors: A brave new world indeed.

Soon more patients will receive marrow transplants as part of the treatment of solid tumors and metabolic diseases than for the treatment of hematologic disease. The contributions in this volume explicitly describe some of these applications and contain hints of other exciting possibilities. Marrow transplantation is clearly here to stay.

Dean Buckner
Reg Clift