OVARIAN CANCER

Cancer Treatment and Research

Steven T. Rosen, M.D., *Series Editor*

Kurzrock, R., Talpaz, M. (eds): *Cytokines: Interleukins and Their Receptors.* 1995. ISBN 0-7923-3636-4.
Sugarbaker, P. (ed): *Peritoneal Carcinomatosis: Drugs and Diseases.* 1995. ISBN 0-7923-3726-3.
Sugarbaker, P. (ed): *Peritoneal Carcinomatosis: Principles of Management.* 1995. ISBN 0-7923-3727-1.
Dickson, R.B., Lippman, M.E. (eds.): *Mammary Tumor Cell Cycle, Differentiation and Metastasis.* 1995. ISBN 0-7923-3905-3.
Freireich, E.J, Kantarjian, H. (eds.): *Molecular Genetics and Therapy of Leukemia.* 1995. ISBN 0-7923-3912-6.
Cabanillas, F., Rodriguez, M.A. (eds.): *Advances in Lymphoma Research.* 1996. ISBN 0-7923-3929-0.
Miller, A.B. (ed.): *Advances in Cancer Screening.* 1996. ISBN 0-7923-4019-1.
Hait , W.N. (ed.): *Drug Resistance.* 1996. ISBN 0-7923-4022-1.
Pienta, K.J. (ed.): *Diagnosis and Treatment of Genitourinary Malignancies.* 1996. ISBN 0-7923-4164-3.
Arnold, A.J. (ed.): *Endocrine Neoplasms.* 1997. ISBN 0-7923-4354-9.
Pollock, R.E. (ed.): *Surgical Oncology.* 1997. ISBN 0-7923-9900-5.
Verweij, J., Pinedo, H.M., Suit, H.D. (eds.): *Soft Tissue Sarcomas: Present Achievements and Future Prospects.* 1997. ISBN 0-7923-9913-7.
Walterhouse, D.O., Cohn, S. L. (eds.): *Diagnostic and Therapeutic Advances in Pediatric Oncology.* 1997. ISBN 0-7923-9978-1.
Mittal, B.B., Purdy, J.A., Ang, K.K. (eds.): *Radiation Therapy.* 1998. ISBN 0-7923-9981-1.
Foon, K.A., Muss, H.B. (eds.): *Biological and Hormonal Therapies of Cancer.* 1998. ISBN 0-7923-9997-8.
Ozols, R.F. (ed.): *Gynecologic Oncology.* 1998. ISBN 0-7923-8070-3.
Noskin, G. A. (ed.): *Management of Infectious Complications in Cancer Patients.* 1998. ISBN 0-7923-8150-5
Bennett, C. L. (ed.): *Cancer Policy.* 1998. ISBN 0-7923-8203-X
Benson, A. B. (ed.): *Gastrointestinal Oncology.* 1998. ISBN 0-7923-8205-6
Tallman, M.S. , Gordon, L.I. (eds.): *Diagnostic and Therapeutic Advances in Hematologic Malignancies.* 1998. ISBN 0-7923-8206-4
von Gunten, C.F. (ed.): *Palliative Care and Rehabilitation of Cancer Patients.* 1999. ISBN 0-7923-8525-X
Burt, R.K., Brush, M.M. (eds): *Advances in Allogeneic Hematopoietic Stem Cell Transplantation.* 1999. ISBN 0-7923-7714-1
Angelos, P. (ed): *Ethical Issues in Cancer Patient Care* 2000. ISBN 0-7923-7726-5
Gradishar, W.J., Wood, W.C. (eds): *Advances in Breast Cancer Management.* 2000. ISBN 0-7923-7890-3
Sparano, Joseph A. (ed.): *HIV & HTLV-I Associated Malignancies.* 2001. ISBN 0-7923-7220-4.
Ettinger, David S. (ed.): *Thoracic Oncology.* 2001. ISBN 0-7923-7248-4.
Bergan, Raymond C. (ed.): *Cancer Chemoprev*ention. 2001. ISBN 0-7923-7259-X.
Raza, A., Mundle, S.D. (eds): *Myelodysplastic Syndromes & Secondary Acute Myelogenous Leukemia; Directions for the new Millennium.* 2001. ISBN 0-7923-7396-0.
Talamonti, Mark S. (ed.): *Liver Directed Therapy for Primary and Metastatic Liver Tumors.* 2001 ISBN 0-7923-7523-8
Stack, M.S., Fishman, D.A. (eds.): *Ovarian Cancer.* 2001 ISBN 0-7923-7530-0

OVARIAN CANCER

edited by

M. Sharon Stack, Ph.D.
and
David A. Fishman, M.D.

Northwestern University Medical School
Chicago, IL, U.S.A.

SPRINGER SCIENCE+BUSINESS MEDIA, LLC

Library of Congress Cataloging-in-Publication Data

Ovarian cancer / edited by M. Sharon Stack and David A. Fishman.
p. ; cm. – (Cancer treatment and research ; 107)
Includes bibliographical references and index.
ISBN 978-1-4757-3589-5 ISBN 978-1-4757-3587-1 (eBook)
DOI 10.1007/978-1-4757-3587-1
1. Ovaries—Cancer. 2. Carcinogenesis. 3. Metastasis. I. Stack, M. Sharon, 1959- II. Fishman, David A., 1959- III. Cancer treatment and research ; v. 107.
[DNLM: 1. Ovarian Neoplasms—therapy. WP 322 09631 2001]
RC280.08 08832 2001
616.99'465—dc21

2001038790

Copyright © 2002 by Springer Science+Business Media New York
Originally published by Kluwer Academic Publishers in 2002
Softcover reprint of the hardcover 1st edition 2002
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, photo-copying, recording, or otherwise, without the prior written permission of the publisher, Springer Science+Business Media, LLC.

The Publisher offers discounts on this book for bulk purchases. For further information, send email to [laura.walsh@wkap.com]

Printed on acid-free paper.

To our spouses, parents and children,

for their strength, wisdom, and love.

CONTENTS

B. Growth Control

C. Cellular Regulation and Metastasis

Contributors

Ronald D. Alvarez, Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of Alabama, Birmingham, AL 35233

Junken Aoki, Graduate School of Pharmaceutical Sciences, University of Tokyo, 7-3-1 Hongo, Bunkyo-Ku, Tokyo 113-0033, Japan

Nelly Auersperg, Department of Obstetrics & Gynaecology, University of British Columbia, Vancouver, B.C., V6H 3V5, Canada

Mack N. Barnes, Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of Alabama, Birmingham, AL 35233

A.T. Baron, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905

B.A. Barrette, Department of Obstetrics & Gynecology, Mayo Clinic, Rochester, MN 55905

Robert C. Bast, Jr, Departments of Experimental Therapeutics, Molecular Therapeutics, Gynecologic Oncology and Anatomic Pathology, University of Texas M.D. Anderson Cancer Center, Houston, TX 77030

C.H. Boardman, Department of Obstetrics & Gynecology, Mayo Clinic, Rochester, MN 55905

Kenny Bozorgi, Section of Gynecologic Oncology, Department of Obstetrics & Gynecology, Northwestern University Medical School, Chicago, IL 60611

Pierre O. Chappuis, Division of Medical Genetics, Department of Medicine, McGill University Health Center, Montreal, QC, Canada

T.A. Christensen, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905

Leeber Cohen, Division of Ultrasound, Department of Obstetrics & Gynecology, Northwestern University Medical School, Chicago, IL 60611

Tim Compton, Atairgin Technologies, 101 Theory, Irvine, CA 92612

E.M. Cora, Department of Biochemistry & Nutrition, University of Puerto Rico, School of Medicine, PO Box 365067, San Juan, PR 00936

D.V.S. DeFrias, Department of Pathology, Northwestern University Medical School, Chicago, IL 60611

Louis Dubeau, Department of Pathology, Keck School of Medicine of the University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA 90033

Astrid Eder, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030

James R. Erickson, AGY Therapeutics, 290 Utah Ave., S. San Francisco, CA 94080

Xianjun Fang, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030

J.M. Faupel-Badger, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905

David A. Fishman, Section of Gynecologic Oncology, Department of Obstetrics & Gynecology, Northwestern University Medical School, Chicago, IL 60611
William D. Foulkes, Division of Medical Genetics, Department of Medicine, McGill University Health Center, Montreal, QC, Canada
Tatsuro Furui, Department of Obstetrics & Gynecology, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu, 500-8705, Japan
Douglas Gaudette, Department of Human Biology & Nutrition Science, University of Guelph, ANNU Building, Guelph, Ontario,Canada N1G2W1
Supurna Ghosh, Department of Cell & Molecular Biology, Northwestern University Medical School, Chicago, IL 60611
T. Greenwood, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Yutaka Hasegawa, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
Warner K. Huh, Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of Alabama, Birmingham, AL 35233
Mahrukh Hussain, National Cancer Institute, Laboratory of Pathology, Building 10, Rm 2A33, 10 Center Drive, Bethesda, MD 20892
Robert Jaffe, Department of Obstetrics, Gynecology, & Reproductive Sciences, University of California San Francisco, 513 Parnassus Ave., San Francisco, CA 94122
S.C. Juneja, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Barry Kascinski, Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT 06520
P.C. Keh, Department of Pathology, Northwestern University Medical School, Chicago, IL 60611
F. Joseph Kelly, Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of Alabama, Birmingham, AL 35233
Elise C. Kohn, National Cancer Institute, Laboratory of Pathology, Building 10, Rm 2A33, 10 Center Drive, Bethesda, MD 20892
J.M. Lafky, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Ruth Lapushin, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
H. Lee, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Jinsong Liu, Departments of Experimental Therapeutics, Molecular Therapeutics, Gynecologic Oncology and Anatomic Pathology, University of Texas M.D. Anderson Cancer Center, Houston, TX 77030
Karen Lu, Departments of Experimental Therapeutics, Molecular Therapeutics, Gynecologic Oncology and Anatomic Pathology, University of Texas M.D. Anderson Cancer Center, Houston, TX 77030
N.J. Maihle, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Muling Mao, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030

Gordon B. Mills, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
R. Nayar, Department of Pathology, Northwestern University Medical School, Chicago, IL 60611
A.M. Okonkwo, Department of Pathology, Northwestern University Medical School, Chicago, IL 60611
Susan M. Pando, Department of Obstetrics & Gynecology, Yale University School of Medicine, New Haven, CT 06520
Jeff A. Parrott, Atairgin Technologies, 101 Theory, Irvine, CA 92612
K. C. Podratz, Department of Obstetrics & Gynecology, Mayo Clinic, Rochester, MN 55905
J.L. Reiter, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905
Peter E. Schwartz, Yale University School of Medicine, Department of Obstetrics & Gynecology, 333 Cedar St., New Haven, CT 06520
Viji Shridhar, Mayo Clinic, Rochester, MN 55905
Gregory J. Sieczkiewicz, National Cancer Institute, Laboratory of Pathology, Building 10, Rm 2A33, 10 Center Drive, Bethesda, MD 20892
Steven Skates, Massachusetts General Hospital, Boston, MA 02144
Amy P.N. Skubitz, Department of Laboratory Medicine & Pathology, University of Minnesota Medical School, Minneapolis, MN 55455
David Smith, Mayo Clinic, Rochester, MN 55905
M. Sharon Stack, Department of Cell & Molecular Biology, Northwestern University Medical School, Chicago, IL 60611
Fazal Haq Tabassam, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
Janos Tanyi, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
Hugh S. Taylor, Department of Obstetrics & Gynecology, Yale University School of Medicine, New Haven, CT 06520
Walter Tribley, Atairgin Technologies, 101 Theory, Irvine, CA 92612
Nicole Urban, The Fred Hutchinson Cancer Center, Seattle, WA 98101
John Wiener, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
Alice S.T. Wong, Department of Obstetrics & Gynaecology, University of British Columbia, Vancouver, B.C., V6H 3V5, Canada
Teresa K. Woodruff, Department of Neurobiology & Physiology, Northwestern University, Evanston, IL 60208
Yi Wu, Department of Cell & Molecular Biology, Northwestern University Medical School, Chicago, IL 60611
Jiamei Yu, Department of Pathology, Keck School of Medicine of the University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA 90033

Shiangxing Yu, Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030
Zhen Shang, Medical University of South Carolina, Charleston, SC 29425

Foreword

Ovarian carcinoma continues to be responsible for more deaths than all other gynecologic malignancies combined due to our continued inability to achieve detection of early (rather than advanced) stage disease and the lack of effective tumor-specific therapeutics. Despite many diagnostic imaging, surgical, medical, and therapeutic advances, little has changed over the past 40 years, as 70-75% of women newly diagnosed with epithelial ovarian carcinoma present with disseminated carcinomatosis (stage III or IV disease) with a resultant 5-year survival of 12 %. However, if disease is identified when confined to the ovary (Stage I), surgical intervention is less morbid, chemotherapy may not be required, and the resultant 5-year survival approaches 90%. Therefore the most effective means for improving survival requires detection of early stage rather than advanced stage disease.

Ovarian carcinogenesis, invasion and metastatic dissemination require a complex cascade of interrelated genetic, molecular, and biochemical events that regulate the neoplastic transition of normal ovarian surface epithelium. Ovarian cancers accumulate genetic aberrations that alter cell cycle control, DNA repair, genomic stability, apoptosis, transmembrane signaling, adhesion, and angiogenesis. Metastatic dissemination is influenced by numerous regulatory molecules and requires diverse biologic processes including cellular adhesion, migration, extracellular matrix degradation, directed invasion into host parenchyma, proliferation, and neovascularization. Many of these genetic aberrations and/or regulatory molecules are detectable in women with ovarian cancer and may ultimately serve as both novel tumor-specific biomarkers for early detection and for unique tumor-specific therapeutics. This volume summarizes recent advances in ovarian cancer detection and treatment and provides an analysis of current research into aspects of malignant transformation, growth control, and metastasis. A more detailed understanding of these processes may ultimately translate into the development of novel approaches for the detection and control of ovarian cancer.