

THE AMERICAN ASSOCIATION FOR CANER RESEARCH

American Association for Cancer Research, Inc.

Publications Staff **Managing Editor** Margaret Foti

Assistant Managing Editor Mary Anne Mennite

Manager, Editorial Services Heide M. Pusztay

**Editorial Assistants** Susan L. Arns Grace Jeromski Margaret E. Pinto

Supervisor, Manuscript **Processing** Margaret A. Pickels

Assistant Supervisor, **Manuscript Processing** Theresa A. Griffith

**Editorial Secretaries** Mary Ellen Pirring June A. Holloway Valerie L. Taylor Luz M. Torres

Administrative Staff **Executive Director** Margaret Foti

Associate Director of Administration Adam D. Blistein

Senior Accountant Anthony P. Blengino

Financial Assistant George L. Moore

**Meetings Coordinator** Jeffrey M. Ruben

Meeting Planner Carole Kanoff

**Public Information** Coordinator Jenny-Anne Martz

Ruth E. Fortson

**Executive Assistant for Programs** 

Administrative Assistant Robin E. Felder

Systems Specialist

Lydia I. Rodriguez Secretary

Malika L. Wright

**Editorial Secretary** Diana F. Certo

Editor-in-Chief Carlo M. Croce

**Associate Editors** 

Stuart A. Aaronson Martin D. Abeloff Jerry M. Adams David S. Alberts Karen S. H. Antman Frederick R. Appelbaum James O. Armitage William M. Baird Allan Balmain J. Carl Barrett Renato Baserga William T. Beck Thomas L. Benjamin June L. Biedler Gianni Bonadonna G. Tim Bowden Norman Breslow Edward Bresnick Samuel Broder Ronald N. Buick Paul A. Bunn, Jr. C. Patrick Burns Bruno Calabretta Eli Canaani Robert L. Capizzi Webster K. Cavenee Bruce A. Chabner Yung-chi Cheng Bruce D. Cheson **David Colcher** Allan H. Conney Neal G. Copeland Joseph G. Cory Jeffrey Cossman

Frank Costantini

Cover Editorial Board

Sidney Weinhouse,

Cover Editor

Benoit de Crombrugghe Riccardo Dalla-Favera Richard L. Davidson Eugene R. DeSombre T. Michael Dexter Ralph E. Durand Alan Eastman Gertrude B. Elion Lois B. Epstein Leonard C. Erickson **Emmanuel Farber** Nelson Fausto Isaiah J. Fidler Robert A. Floyd Judah Folkman Kenneth A. Foon Joseph F. Fraumeni, Jr. Errol C. Friedberg Minoru Fukuda Philip Furmanski Eugene W. Gerner Leo E. Gerweck Eli Glatstein David W. Golde Michael M. Gottesman I W Grisham Sen-itiroh Hakomori Philip C. Hanawalt Curtis C. Harris Jules E. Harris John C. Harshbarger Stephen S. Hecht Brian E. Henderson Russell Hilf Richard B. Hochberg

Nancy H. Colburn Hugh J. Creech

Waun Ki Hong Tasuku Honjo Kay Huebner James N. Ihle John T. Isaacs Mark A. Israel Elaine S. Jaffe Rakesh K. Jain Peter A. Jones V. Craig Jordan Robert S. Kerbel Young S. Kim Tadamitsu Kishimoto Alfred G. Knudson, Jr. Kurt W. Kohn Laurence N. Kolonel Donald W. Kufe John S. Lazo Brigid G. Leventhal Jay A. Levy Frederick P. Li Victor Ling Lance A. Liotta Martin Lipkin Marc E. Lippman Gerald Litwack Leroy F. Liu Lawrence A Loeb Dan L. Longo Reuben Lotan David B. Ludlum Tak W. Mak Michael J. Mastrangelo W. Gillies McKenna

George H. Hitchings Edwin A. Mirand

Anna T. Meadows

John Mendelsohn Christopher J. Michejda John D. Minna Malcolm S. Mitchell Sharon B. Murphy Ruth J. Muschel Garth L. Nicolson Kenneth Nilsson Jeffrey A. Norton Peter C. Nowell Kenneth Olden Gilbert S. Omenn Richard J. O'Reilly Robert F. Ozols Michael A. Palladino, Jr. Peter L. Pedersen Anthony E. Pegg Angel Pellicer Bice Perussia Sidney Pestka Gordon L. Phillips Cecil B. Pickett Frank J. Rauscher III Donald J. Reed Ralph A. Reisfeld Richard A. Rifkind Igor B. Roninson Robert T. Schimke J. Schlessinger Manfred Schwab Joseph V. Simone Francis M. Sirotnak Anna Marie Skalka Michael B. Sporn Martha R. Stampfer

Takashi Sugimura

John H. Weisburger

Gary S. Stein Bernard S. Strauss Takashi Sugimura Saraswati Sukumar James A. Swenberg Paul Talalay Steven R. Tannenbaum Masaaki Terada Snorri S. Thorgeirsson Donald J. Tindall George J. Todaro Jeffrey M. Trent Giorgio Trinchieri Axel Ullrich Peter Vaupel Giancarlo Vecchio Ellen S. Vitetta Daniel D. Von Hoff Michael D. Waterfield Lee W. Wattenberg Ralph R. Weichselbaum I. Bernard Weinstein Bengt Westermark Raymond L. White Gordon F. Whitmore Max S. Wicha Walter Willett Sheldon Wolff Stuart H. Yuspa Harald zur Hausen

Eric J. Stanbridge

Cancer Research is sponsored by the American Association for Cancer Research, Inc. and receives major support from the American Cancer Society, Inc. Publication costs are also met by a grant from the Elsa U. Pardee Foundation.

# **Subscription Information**

Cancer Research is published twice a month, one volume per year, by the American Association for Cancer Research, Inc. Subscriptions include the Proceedings of the American Association for Cancer Research, issued in April of each year. Except for members of the American Association for Cancer Research, all subscriptions are payable in advance to Waverly Press, Inc., 428 E. Preston Street, Baltimore, MD 21202-3993, to which all business communications, remittances (in United States currency or its equivalent), and subscription orders should be sent. In Japan, send orders and inquiries to (sole agent): USACO Corporation, Tsutsumi Bldg., 13-12, Shimbashi-chome, Minato-ku, Tokyo 105, Japan; Tel. (03) 502-6471. Nonmembers of the American Association for Cancer Research within the United States may subscribe to Volume 53 (1993) of Cancer Research at the rate of \$390.00 (individual and institutional nonmembers), including postage. Institutional and individual nonmembers outside of the United States should add \$60.00 to their respective rates to offset second-class postage costs. Air mail and other means of delivery are available at extra charge; contact Waverly Press for information. Changes of address notification should be sent 60 days in advance and include both old and new addresses. Member subscribers should send address changes to: Member Services, American Association for Cancer Research, Inc., Public Ledger Building, 620 Chestnut St., Suite 816, Philadelphia, PA 19106-3483. Nonmember subscribers should notify Waverly Press of changes of address. Copies of the journal which are undeliverable because of address changes will be destroyed.

#### Notice to Members of the American Association for Cancer Research

Officers for 1992-1993

President: Lee W. Wattenberg, University of Minnesota, Minneapolis, MN 55455
President-Elect: Margaret L. Kripke, M.D. Anderson Cancer Center, Houston, TX 77030 Treasurer: Thomas J. King, Georgetown University Medical Center, Washington, DC 20007

Executive Director: Margaret Foti, AACR, Public Ledger Building, 620 Chestnut St., Suite 816, Philadelphia, PA 19106-3483

#### Annual Dues

The annual dues of active members of the American Association for Cancer Research are \$135.00 and they include a subscription to one AACR journal. The member rate for each additional journal is \$45.00. Corresponding members of the Association will be charged an appropriate fee to offset postage costs. Payment of dues and changes of address of members of the Association should be sent promptly to: Member Services, American Association for Cancer Research, Inc., Public Ledger Building, 620 Chestnut St., Suite 816, Philadelphia, PA 19106-3483. Telephone: (215) 440-9300.

# Back Issues and Single Copy Sales of the Journal

Copies of back stock of the journal Cancer Research may be ordered from Waverly Press, Inc. As long as supplies permit, single copies of Cancer Research will be sold by this company at \$30.00 per copy for regular issues and \$30.00 per copy for Supplement issues which contain material from conferences on topics related to cancer. The annual Proceedings of the American Association for Cancer Research is available at \$35.00 per copy. Orders outside the U. S. and Canada add \$2.00/copy to offset postage costs.

## Advertisements in Cancer Research

Advertisement insertion orders and copy must be received 60 days prior to the date of issue in which the advertisement is to be published. The journal is mailed approximately 7 days preceding the date of issue. Inquiries about advertising should be directed to: Elizabeth Mosko, Williams and Wilkins, 428 E. Preston Street, Baltimore, MD 21202-3993. Telephone: (410) 528-4005.

## **Historical Cover Themes**

Readers are invited to submit themes (events, persons, institutions) for consideration for the illustrated covers of Cancer Research. Correspondence regarding suggested cover themes, or other matters regarding covers, should be addressed to the Cover Editor, AACR Publications Department.

## Submission of Manuscripts

Manuscripts should be sent to the attention of: Dr. Carlo M. Croce, Editor-in-Chief, AACR Publications Department, American Association for Cancer Research, Public Ledger Building, 620 Chestnut St., Suite 816, Philadelphia, PA 19106-3483. Telephone: (215) 440-9300. If accepted, they will be listed under one of ten categories in the Table of Contents. Please specify in a covering letter which category applies to your submission: biochemistry and biophysics, carcinogenesis, clinical investigations; endocrinology, epidemiology; experimental therapeutics; immunology, molecular biology and genetics, tumor biology, and virology. (Final categorization in the Table of Contents is at the discretion of the Editor-in-Chief.) Consult the "Instructions for Authors" printed in the January 1 issue of the journal for other submission requirements. Reprints of the "Instructions" are available upon request.

Manuscript Processing Fee

Journal policy requires that a manuscript processing fee of \$75.00 be assessed for each paper to defray the expenses incurred in the editorial review process. Each manuscript submitted for publication should be accompanied by a check (drawn on a U.S. bank) or purchase order for \$75.00 in U. S. currency, payable to Cancer Research at the above address. Note: If an author resubmits a manuscript that our Editors previously found unacceptable for publication, it is journal policy to consider it a new submission, assign it a new manuscript number, and charge the author another \$75.00 handling fee to cover the cost of review.

Accepted manuscripts will be published with the understanding that the author(s) will pay a charge of \$65.00 per printed page. Under exceptional circumstances, when no source of grant or other support exists, the author(s) may apply to Dr. Carlo M. Croce, Editor-in-Chief, at the time of submission, for a waiver of the page charges. All such applications must be countersigned by an appropriate institutional official stating that no funds are available for the payment of page charges.

Copyright and Copyright Clearance Center

The Copyright Revision Act (PL 94-553), which became effective January 1, 1978, states that the copyright of a work is vested in the author from the moment of creation. Therefore, all authors who wish to publish in Cancer Research must formally transfer copyright to the proprietor of the journal, the American Association for Cancer Research, Inc. It is understood by this transfer that the authors relinquish all exclusive rights of copyright ownership, including the rights of reproduction, derivation, distribution, sale, and display.

Authors who prepared their articles as part of their official duties as employees of the U.S. Federal Government are not required to transfer copyright to the American Association for Cancer Research, Inc., since these articles are considered to be in the public domain. However, it is necessary for these authors to sign the appropriate section of the transfer form. In the case of articles supported by federal grants or contracts, copyright transfer to the American Association for Cancer Research, Inc., is required. The federal government may retain a nonexclusive license to publish or republish such material.

Copies of articles for which the American Association for Cancer Research, Inc. owns the copyright may be made for personal or internal use, provided that the copier pay the per-copy fee of \$2.00 through the Copyright Clearance Center, Inc. This Center is a nonprofit organization through which individuals and institutions may reimburse a copyright owner for photocopying journal articles beyond what is defined as "fair use" in Sections 107 and 108 of the Copyright Revision Act of 1978. Those who wish to photocopy Cancer Research articles may report the number of copies they have made, together with the fee code 0008-5472/93 \$02.00, to: Copyright Clearance Center, Inc., 27 Congress St., Salem, MA 01970. Remittances may be sent to the Center at the time of reporting or the Center will bill the user on a monthly basis. Deposit accounts and prepayment plans may also be arranged.

Between June 1978 and August 1983, a fee code appeared on the first page of all articles for which Cancer Research owned the copyright. For those issues, it is

understood that any articles which did not carry this code are in the public domain.

Cancer Research is abstracted or indexed in Biological Abstracts, Chemical Abstracts, Index Medicus, MEDLINE, Current Contents, and CancerLit. This journal is printed on acid-free paper.

No responsibility is accepted by the Editors, by the American Association for Cancer Research, Inc., or by Waverly, Inc. for the opinions expressed by contributors or for the content of the advertisements.

Cancer Research (ISSN 0008-5472) is published twice a month for \$80 per year (for members of the American Association for Cancer Research) or \$390 per year (for nonmembers) by the American Association for Cancer Research, Inc. Second-class postage paid at Baltimore, MD and additional mailing offices. POSTMASTER: Send address changes to Cancer Research, c/o Waverly Press, Inc., 428 E. Preston Street, Baltimore, MD 21202-3993.

Copyright 1993 by the American Association for Cancer Research, Inc.