

American Association for Cancer Research, Inc. Publications Staff Managing Editor Margaret Foti **Assistant Managing Editor** Mary Anne Mennite Manager, Editorial Services Heide M. Pusztay Staff Editors Lisa A. Chippendale Pamela M. Grebow Michael J. Beveridge Kathleen C. Assenmacher Supervisor, Manuscript Processing
Margaret A. Pickels Assistant Supervisor,
Manuscript Processing
Theresa A. Griffith Staff Assistant Mary Ellen Pirring **Editorial Assistants** Valerie L. Taylor Andrea Conrad Katherine V. Pawlowski Bethann Massarella Charles W. Wells, Jr. Administrative Staff **Executive Director** Margaret Foti **Director of Administration** Adam D. Blistein Controller Joan D. Brokenshire Coordinator, Financial Operations George L. Moore **Meetings Coordinator** Jeffrey M. Ruben **Meeting Planner** Carole L. Kanoff **Public Information Coordinator** Jenny Anne Horst-Martz **Executive Assistant for Programs** Ruth E. Fortson **Administrative Assistant** Robin E. Felder Systems Specialist Lydia I. Rodriguez Staff Assistant Lori L. Holmes Secretary Malika L. Wright **Editorial Secretary** Diana F. Certo Financial Clerk Paul Perrault Office Clerk James J. Waters

Editor-in-Chief Carlo M. Croce

Associate Editors

Stuart A. Aaronson Jerry M. Adams David S. Alberts Carmen J. Allegra Frederick R. Appelbaum James O. Armitage William M. Baird Allan Balmain J. Carl Barrett Renato Baserga William T. Beck Joseph R. Bertino Mina J. Bissell Clara D. Bloomfield Gianni Bonadonna Ernest C. Borden G. Tim Bowden Edward Bresnick Samuel Broder Ronald N. Buick Paul A. Bunn, Jr. C. Patrick Burns Fernando Cabanillas Bruno Calabretta Eli Canaani Robert L. Capizzi Webster K. Cavenee Bruce D. Cheson David Colcher Robert L. Comis Allan H. Conney Neal G. Copeland Joseph G. Cory William M. Crist Benoit de Crombrugghe

Riccardo Dalla-Favera Richard L. Davidson Eugene R. DeSombre T. Michael Dexter Ralph E. Durand Alan Eastman Gertrude B. Elion Leonard C. Erickson Nelson Fausto Eric R. Fearon Isaiah J. Fidler Robert A. Floyd Judah Folkman Kenneth A. Foon Joseph F. Fraumeni, Jr. Stephen H. Friend Minoru Fukuda Philip Furmanski Eugene W. Gerner Eli Glatstein David W. Golde Michael M. Gottesman J. W. Grisham F. Peter Guengerich Sen-itiroh Hakomori Philip C. Hanawalt Curtis C. Harris John C. Harshbarger Stephen S. Hecht Carl-Henrik Heldin Brian E. Henderson Richard B. Hochberg Waun Ki Hong Tasuku Honjo Kay Huebner

John T. Isaacs Mark A. Israel Elaine S. Jaffe Rakesh K. Jain Peter A. Jones V. Craig Jordan John H. Kersey Young S. Kim Kenneth W. Kinzler Tadamitsu Kishimoto Alfred G. Knudson, Jr. Kurt W. Kohn Laurence N. Kolonel Donald W. Kufe John S. Lazo Jav A. Levv 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 Lvnn M. Matrisian W. Gillies McKenna Anna T. Meadows John Mendelsohn Christopher J. Michejda John D. Minna

Beatrice Mintz Malcolm S. Mitchell Ruth J. Muschel Yusuke Nakamura Garth L. Nicolson Kenneth Nilsson Susumu Nishimura Jeffrey A. Norton 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 Gordon L. Phillips Cecil B. Pickett Jacalyn H. Pierce Vito Ouaranta Frank J. Rauscher III Donald J. Reed Ralph A. Reisfeld Richard A. Rifkind Leslie L. Robison Igor B. Roninson Howard I. Scher Robert T. Schimke J. Schlessinger Manfred Schwab Joseph V. Simone Francis M. Sirotnak Anna Marie Skalka

Michael B. Sporn Martha R. Stampfer Eric J. Stanbridge Gary S. Stein Bernard S. Strauss Takashi Sugimura Saraswati Sukumar James A. Swenberg Paul Talalay Tadatsugu Taniguchi Steven R. Tannenbaum Masaaki Terada Kenneth D. Tew Donald J. Tindall George J. Todaro Jeffrey M. Trent Giorgio Trinchieri Takashi Tsuruo Axel Ullrich Peter Vaupel Giancarlo Vecchio 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 H. Rodney Withers Sheldon Wolff Stuart H. Yuspa Harald zur Hausen

Cover Editorial Board

Sidney Weinhouse, Cover Editor Hugh J. Creech Clark W. Heath, Jr. Edwin A. Mirand Raymond W. Ruddon Takashi Sugimura John H. Weisburger

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. Accelerated mailing of journals to AACR members in Japan is supported by a generous grant from the Banyu Pharmaceutical Company.

Subscription Information

Data Entry Clerk Robert A. Simms II

Cancer Research is published twice a month, one volume per year, by the American Association for Cancer Research, Inc. (AACR). Subscriptions include the Proceedings of the American Association for Cancer Research, issued in March of each year. Except for members of the AACR, all subscriptions are payable in advance to Cancer Research, P.O. Box 3000, Denville, NJ 07834 [Telephone: (800) 875-2997; FAX: (201) 627-5872], 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 1-chome, Minato-ku, Tokyo 105, Japan; Tel. (03) 502-6471. Individuals who are not AACR members may subscribe to Volume 55 (1995) of Cancer Research at the rate of \$460 U.S./\$520 foreign. Cancer Research is only available to institutions as a combined subscription with Clinical Cancer Research. The combined 1995 institutional subscription price of \$495 U.S./\$575 foreign includes a subscription to Clinical Cancer Research. Canadian subscribers should add 7% GST. 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: AACR Member Services, Public Ledger Bldg., Suite 816, 150 South Independence Mall West, Philadelphia, PA 19106-3483. Nonmember subscribers should send changes of address to: Cancer Research, P.O. Box 3000, Denville, NJ 07834. 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 1994-1995

President: Edward Bresnick, University of Massachusetts Medical Center, Worcester, MA 01655-0126
President Elect: Joseph R. Bertino, Memorial Sloan-Kettering Cancer Center, New York, NY 10021
Treasurer: Bayard D. Clarkson, Memorial Sloan-Kettering Cancer Center, New York, NY 10021

Executive Director: Margaret Foti, AACR, Public Ledger Bldg., Suite 816, 150 South Independence Mall West, Philadelphia, PA 19106-3483

Annual Dues

The annual dues of active members of the American Association for Cancer Research are \$160, \$80 of which may be applied to a subscription to Cancer Research. 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 Bldg., Suite 816, 150 South Independence Mall West, Philadelphia, PA 19106-3483. Telephone: (215) 440-9300; FAX: (215) 440-9313.

Back Issues and Single Copy Sales of the Journal

Copies of back stock of the journal Cancer Research may be ordered from Cancer Research, P.O. Box 3000, Denville, NJ 07834 [Telephone: (800) 875-2997; FAX: (201) 627-5872]. As long as supplies permit, single copies of Cancer Research will be sold at \$30 per copy for regular and Supplement issues, plus \$2 shipping for orders outside the U.S. The annual Proceedings of the American Association for Cancer Research is available at \$35 per copy, plus \$4 shipping for orders outside the U.S.

Advertisements in Cancer Research

Advertisement insertion orders and copy must be received approximately 5 weeks prior to the date of the issue in which the advertisement is to be published. The journal is mailed approximately 5 days preceding the date of issue. Inquiries about advertising should be directed to: M. J. Mrvica Associates, Inc., 155 South White Horse Pike, Berlin, NJ 08009 [Telephone: (609) 768-9360; FAX: (609) 753-0064].

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 Bldg., Suite 816, 150 South Independence Mall West, 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 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 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 handling fee to cover the cost of review.

Page Charges

Accepted manuscripts will be published with the understanding that the author(s) will pay a charge of \$65 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 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 0008-5472/94 \$02.00, to: Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923; (508) 750-8400. 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 Cadmus Journal Services for the opinions expressed by contributors or for the content of the advertisements.

Cancer Research (ISSN 0008-5472) is published twice a month by the American Association for Cancer Research, Inc., Public Ledger Bldg., Suite 816, 150 South Independence Mall West, Philadelphia, PA 19106-3483 for \$80 annually for members and \$460 for individual nonmembers. Cancer Research is only available to institutions as a combined subscription with Clinical Cancer Research. The combined 1995 institutional subscription price of \$495 includes a subscription to Clinical Cancer Research. Second-class postage paid at Philadelphia, PA and additional mailing offices. POSTMASTER: Send address changes to Cancer Research, P.O. Box 3000, Denville, NJ 07834. Copyright 1995 by the American Association for Cancer Research, Inc. Printed in the U.S.A.