

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** Lisa A. Chippendale Pamela M. Grebow Michael J. Beveridge Supervisor, Manuscript **Processing** Margaret A. Pickels Assistant Supervisor, Manuscript Processing Theresa A. Griffith **Editorial Secretaries** Mary Ellen Pirring Valerie L. Taylor Andrea Conrad Katherine V. Pawlowski Shelley E. Perkins Administrative Staff **Executive Director** Margaret Foti Associate Director of Administration Adam D. Blistein Coordinator, Financial Operation 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

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 Thomas L. Benjamin Joseph R. Bertino June L. Biedler Mina J. Bissell 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 A. Chabner Yung-chi Cheng Bruce D. Cheson David Colcher Robert L. Comis Allan H. Conney Neal G. Copeland Joseph G. Cory Jeffrey Cossman Frank Costantini

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 Lois B. Epstein 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 Jules E. Harris John C. Harshbarger Stephen S. Hecht Carl-Henrik Heldin Samuel Hellman Brian E. Henderson Russell Hilf Richard B. Hochberg

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 Kenneth W. Kinzler Tadamitsu Kishimoto Alfred G. Knudson, Jr. Kurt W. Kohn Laurence N. Kolonel Donald W. Kufe John S. Lazo Jay A. Levy Frederick P. Li Victor Ling Lance A. Liotta Martin Lipkin Marc E. Lippman Gerald Litwack Lerov F. Liu Lawrence A. Loeb Dan L. Longo Reuben Lotan David B. Ludlum Tak W. Mak Michael J. Mastrangelo Lynn 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 Frederica P. Perera Bice Perussia Sidney Pestka Gordon L. Phillips Cecil B. Pickett Jacalyn H. Pierce Vito Quaranta 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 Stuart F. Schlossman 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 Louise C. Strong 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.

Subscription Information

Secretary Malika L. Wright

Editorial Secretary Diana F. Certo

Financial Clerk

Data Entry Clerk

Robert A. Simms II

Paul Perrault Office Clerk James J. Waters

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 March of each year. Except for members of the American Association for Cancer Research, all subscriptions are payable in advance to Waverly, 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 54 (1994) of Cancer Research at the rate of \$415.00 (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. Canadian subscribers should add 7% GST. Air mail and other means of delivery are available at extra charge; contact Waverly, Inc. 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, Inc. of changes of address. Copies of the journal which are undeliverable because of address changes will be destroyed. Printed in the U.S.A.

Notice to Members of the American Association for Cancer Research

Officers for 1994-1995

President: Edward Bresnick, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756

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 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 \$150.00, \$80.00 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 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, Inc. As long as supplies permit, single copies of Cancer Research will be sold by this company at \$30.00 per copy for regular and Supplement issues, plus \$2.00 shipping for orders outside the U.S. The annual Proceedings of the American Association for Cancer Research is available at \$35.00 per copy, plus \$4.00 shipping for orders outside the U.S.

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: Garth Thompson, Waverly, Inc., 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.

Page Charges

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 0008-5472/94 \$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 for \$80 per year (for members of the American Association for Cancer Research) or \$415 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, Inc., 428 E. Preston Street, Baltimore, MD 21202-3993.

Copyright 1994 by the American Association for Cancer Research, Inc.