

American Association for Cancer Research, Inc.

Publications Staff Managing Editor Margaret Foti **Assistant Managing Editor** Mary Anne Mennite Manager, Editorial Services Heide M. Pusztay Senior Staff Editor Kathleen C. Assenmacher Staff Editors Ronald M. Vitale Carolina Miranda Editorial Associate Michelle K. Bruni **Staff Assistant** Mary Ellen Pirring Senior Editorial Assistant Theresa A. Griffith **Editorial Assistant** Brenda Roberson Journal Manager, Cancer Epidemiology, Biomarkers & Prevention Michael J. Beveridge Senior Editorial Assistant, Cancer Epidemiology, Biomarkers & Prevention Cecilia Gallo

**Executive Director** Margaret Foti **Director of Administration Adam D. Blistein** Controller Joan D. Ritchie ager, Meetings and Exhibits Jeffrey M. Ruben Assistant Director, **Adm**inistration Anne Horst-Martz Assistant to the Executive Director Ruth E. Fortson mbership Development Coordinator bin E. Felder ininistrative Assistant rearet A. Pickels s Specialist

Administrative Staff

Secretary
Maika L. Wright
Reitorial Assistant
Diana F. Certo
Office Clerk
James J. Waters
Data Entry Clerk
Robert A. Simms II

ydia I. Rodriguez

Editor-in-Chief Carlo M. Croce

**Associate Editors** Stuart A. Aaronson David S. Alberts Carmen J. Allegra Frederick R. Appelbaum Leonard H. Augenlicht Silvia Bacchetti William M. Baird Allan Balmain J. Carl Barrett Renato Baserga Stephen B. Baylin William T. Beck Nathan A. Berger Joseph R. Bertino Diane F. Birt Mina J. Bissell Clara D. Bloomfield Ronald H. Blum Gianni Bonadonna Rodrigo Bravo Edward Bresnick Garrett M. Brodeur Paul A. Bunn, Jr. C. Patrick Burns Fernando Cabanillas Bruno Calabretta Eli Canaani Robert L. Capizzi Webster K. Cavenee Ann F. Chambers Bruce D. Cheson **David Colcher** Robert L. Comis Allan H. Conney Neal G. Copeland Pelayo Correa Suzanne Corv William M. Crist

Benoit de Crombrugghe Albert B. Deisseroth Luigi M. DeLuca Eugene R. DeSombre Vincent T. DeVita, Jr. T. Michael Dexter Ralph E. Durand Alan Eastman Merrill J. Egorin Gertrude B. Elion Leonard C. Erickson Nelson Fausto Eric R. Fearon Andrew P. Feinberg Olivera J. Finn Robert A. Floyd Antonio T. Foio Judah Folkman Kenneth A. Foon Albert J. Fornace, Jr. Joseph F. Fraumeni, Jr. Stephen H. Friend Zvi Y. Fuks Minoru Fukuda Philip Furmanski Eugene W. Gerner Eli Glatstein David W. Golde Joe W. Grav J. W. Grisham Lorraine J. Gudas F. Peter Guengerich Sen-itiroh Hakomori Stanley R. Hamilton Curtis C. Harris Stephen S. Hecht Carl-Henrik Heldin Ingegerd Hellström Brian E. Henderson Richard B. Hochberg

Waun Ki Hong Tasuku Honjo H. Robert Horvitz Janet A. Houghton Kay Huebner Mark A. Israel Elaine S. Jaffe Rakesh K. Jain Peter A. Jones V. Craig Jordan Fred F. Kadluhar Michael B. Kastan John H. Kersev Young S. Kim Kenneth W. Kinzler Hynda K. Kleinman Alfred G. Knudson, Jr. Richard D. Kolodner Laurence N. Kolonel Peter H. Krammer David P. Lane Edmund C. Lattime John S. Lazo Victor A. Levin Jay A. Levy Victor Ling Lance A. Liotta Martin Lipkin Marc E. Lippman Gerald Litwack Leroy F. Liu David M. Livingston Lawrence A. Loeb Dan L. Longo Reuben Lotan David B. Ludlum Lvnn M. Matrisian W. Gillies McKenna Restrice Mintz James B. Mitchell

Malcolm S. Mitchell Ruth J. Muschel Yusuke Nakamura Susan L. Naylor Kenneth Nilsson Susumu Nishimura Jeffrey A. Norton Kenneth Olden Allen I. Oliff Richard J. O'Reilly Robert F. Ozols Michael A. Palladino, Jr. Takis S. Papas Luis F. Parada Drew M. Pardoll Ramon Parsons Anthony E. Pegg Pier Giuseppe Pelicci Angel Pellicer Bice Perussia Lester I Peters Gordon L. Phillips Cecil B. Pickett Jennifer A. Pietenpol Yves G. Pommier Bruce A. J. Ponder Theresa P. Pretlow Vito Quaranta Frank J. Rauscher III John C. Reed Richard A. Rifkind Leslie L. Robison Igor B. Roninson Eric K. Rowinsky Howard I. Scher Robert T. Schimke J. Schlessinger Manfred Schwab Jerry W. Shay **David Sidransky** 

Joseph V. Simone Francis M. Sirotnak Anna Marie Skalka Michael B. Sporn Martha R. Stampfer Eric J. Stanbridge Patricia S. Steeg Glenn Steele, Jr. Gary S. Stein Gary D. Stoner Takashi Sugimura Saraswati Sukumar Paul Talalay Tadatsugu Taniguchi Steven R. Tannenbaum Masaaki Terada Kenneth D. Tew Donald J. Tindall Thea D. Tlsty Jeffrey M. Trent Giorgio Trinchieri Takashi Tsuruo Axel Ullrich George F. Vande Woude Peter W. Vaupel Giancarlo Vecchio Peter K. Vogt Daniel D. Von Hoff Cheryl Walker Michael D. Waterfield Lee W. Wattenberg Ralph R. Weichselbaum Bengt Westermark Raymond L. White Alice S. Whittemore Max S. Wicha Wendell Wierenga Roger Wiseman Sheldon Wolff Harald zur Hausen

Cover Editorial Board Sidney Weinhouse,

Riccardo Dalla-Favera

Nancy E. Davidson

Mary B. Daly

Cover Editor

Clark W. Heath, Jr.

Hugh J. Creech

Raymond W. Ruddon

Takashi Sugimura
John H. Weisburger

Cancer Research is sponsored by the American Association for Cancer Research, Inc. Accelerated mailing of all AACR journals to AACR members in Japan is supported by a generous grant from the Banyu Pharmaceutical Company, Tsukuba, Japan.

Edwin A. Mirand

# Subscription Information

Cancer Research is published twice a month, one volume per year, by the American Association for Cancer Research (AACR), Inc. 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 AACR, Subscription Office, P.O. Box 11806, Birmingham, AL 35202 [Telephone: (800) 633-4931 or (205) 995-1567; FAX: (205) 995-1588], 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 58 (1998) of Cancer Research at the rate of \$495 U.S./\$585 foreign. Cancer Research is only available to institutions as a combined subscription with Clinical Cancer Research. The combined 1998 institutional subscription price of \$795 U.S./\$925 foreign includes \$210 U.S./\$250 foreign for a subscription to Clinical Cancer Research. (Foreign subscription cost includes cost of surface mail. For faster delivery, expedited mailing rates are available by contacting the AACR Publications Department.) 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 changes to: AACR Member Services, Public Ledger Bldg., Suite 826, 150 South Independence Mall West, Philadelphia, PA 19106-3483. Nonnember subscribers should send changes of address to: AACR Subscription Office, P.O. Box 11806, Birmingham, AL 35202. Copies of the journal which are undeliverable because of address changes will be destroyed.

### Notice to Members of the American Association for Cancer Research (AACR)

Officers for 1998-1999

President: Webster K. Cavenee, Ludwig Institute for Cancer Research, La Jolla, CA 92093-0660 President-Elect: Daniel D. Von Hoff, Institute for Drug Development, San Antonio, TX 78245 Treasurer: Bayard D. Clarkson, Memorial Sloan-Kettering Cancer Center, New York, NY 10021

Executive Director: Margaret Foti, AACR, Public Ledger Bldg., Suite 826, 150 South Independence Mall West, Philadelphia, PA 19106-3483

#### Annual Dues

The annual dues of active members of the AACR are \$175, \$90 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, AACR, Public Ledger Bldg., Suite 826, 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 AACR Subscription Office, P.O. Box 11806, Birmingham, AL 35202 [Telephone: (800) 633-4931 or (205) 995-1567; FAX: (205) 995-1588]. As long as supplies permit, single copies of Cancer Research will be sold at \$30 per copy for regular and Supplement issues, plus \$4 shipping for orders outside the U.S. The annual Proceedings of the American Association for Cancer Research is available at \$45 per copy, plus \$6 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., 2 West Taunton Avenue, 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, Public Ledger Bldg., Suite 826, 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 and prevention, 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.) For other submission requirements, consult the "Instructions for Authors" printed in the January 1 issue of the journal and available through the AACR Website at http://www.aacr.org/caninst.htm. Reprints of the "Instructions" are available also 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) for \$75 in U.S. currency, payable to AACR, Inc., or credit card information (VISA, Mastercard, or American Express) should be supplied. 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 \$80 per printed page. Under exceptional circumstances, when no grant or other source of 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 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, AACR, Inc. It is understood by this transfer that the authors relinquish all exclusive rights of copyright ownership, including the rights of reproduction, 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 AACR, Inc., is required. The federal government may retain a nonexclusive license to publish or republish such material.

Copies of articles for which AACR, Inc. owns the copyright may be made for personal or internal use, provided that the copier pay the per-copy fee of \$4 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 0008-5472/98 \$04.00, 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 Reference Update. This journal is printed on acid-free paper.

No responsibility is accepted by the Editors, by AACR, 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 826, 150 South Independence 16 West, Philadelphia, PA 19106-3483 for \$90 annually for members and \$495 for individual nonmembers. Cancer Research is only available to institutions as a combined subscript with Clinical Cancer Research. The combined 1998 institutional subscription price of \$795 includes a subscription to Clinical Cancer Research. Periodicals postage philadelphia, PA and additional mailing offices. POSTMASTER: Send address changes to AACR Subscription Office, P.O. Box 11806, Birmingham, AL 35202. Copyright 1991 the American Association for Cancer Research, Inc. Printed in the U.S.A.