



Cancer 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
Staff Editors
 Lisa A. Chippendale
 Pamela M. Grebow
 Michael J. Beveridge
 Kathleen C. Assenmacher
 Pamela R. Arnold
 Laurie B. Baker
Supervisor, Manuscript Processing
 Margaret A. Pickels
Assistant Supervisor, Manuscript Processing
 Theresa A. Griffith
Staff Assistant
 Mary Ellen Perring
Editorial Assistants
 Valerie L. Taylor
 Andrea Conrad
 Katherine V. Pawlowski
 Bethann Massarella
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
Secretary
 Malika L. Wright
Editorial Secretary
 Diana F. Certo
Office Clerk
 James J. Waters
Data Entry Clerk
 Robert A. Simms II

Editor-in-Chief
Carlo M. Croce

Associate Editors

Stuart A. Aaronson
 David S. Alberts
 Carmen J. Allegra
 Frederick R. Appelbaum
 Silvia Bacchetti
 William M. Baird
 Allan Balmain
 J. Carl Barrett
 Renato Baserga
 William T. Beck
 Joseph R. Bertino
 Diane F. Birt
 Mina J. Bissell
 Clara D. Bloomfield
 Ronald H. Blum
 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
 Ann F. Chambers
 Bruce D. Cheson
 David Colcher
 Robert L. Comis
 Allan H. Conney
 Neal G. Copeland
 Pelayo Correa
 Joseph G. Cory
 William M. Crist
 Benoit de Crombrughe
 Riccardo Dalla-Favera
 Nancy E. Davidson
 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
 Joe W. Gray
 J. W. Grisham
 F. Peter Guengerich
 Sen-itiroh Hakomori
 Philip C. Hanawalt
 Curtis C. Harris
 John C. Harshbarger
 Stephen S. Hecht
 Carl-Henrik Heldin
 Ingegerd Hellström
 Brian E. Henderson
 Richard B. Hochberg
 Waun Ki Hong
 Tasuku Honjo
 H. Robert Horvitz

Cover Editorial Board

Sidney Weinhouse, *Cover Editor*
 Hugh J. Creech
 Clark W. Heath, Jr.
 Edwin A. Mirand
 Raymond W. Ruddon

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
 Hynda K. Kleinman
 Alfred G. Knudson, Jr.
 Kurt W. Kohn
 Richard D. Kolodner
 Laurence N. Kolonel
 Donald W. Kufe
 John S. Lazo
 Jay A. Levy
 Victor Ling
 Lance A. Liotta
 Martin Lipkin
 Marc E. Lippman
 Gerald Litwack
 Leroy F. Liu
 Lawrence A. Loebl
 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.
 Luis F. Parada
 Peter L. Pedersen
 Anthony E. Pegg
 Pier Giuseppe Pellicci
 Angel Pellicer
 Bice Perussia
 Lester J. Peters
 Gordon L. Phillips
 Cecil B. Pickett
 Jacalyn H. Pierce
 Vito Quaranta
 Frank J. Rauscher III
 Donald J. Reed
 John C. 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
 Patricia S. Steeg
 Glenn Steele, Jr.
 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
 Thea D. Tlsty
 George J. Todaro
 Jeffrey M. Trent
 Giorgio Trinchieri
 Takashi Tsuruo
 Axel Ullrich
 Peter Vaupel
 Giancarlo Vecchio
 Peter K. Vogt
 Daniel D. Von Hoff
 Cheryl Walker
 Michael D. Waterfield
 Lee W. Wattenberg
 Ralph R. Weichselbaum
 I. Bernard Weinstein
 Bengt Westermark
 Raymond L. White
 Gordon F. Whitmore
 Alice S. Whittemore
 Max S. Wicha
 Wendell Wierenga
 Sheldon Wolff
 Stuart H. Yuspa
 Harald zur Hausen

Cancer Research is sponsored by the American Association for Cancer Research, 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

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 1995-1996

President: Joseph R. Bertino, Memorial Sloan-Kettering Cancer Center, New York, NY 10021

President Elect: Louise C. Strong, UT M. D. Anderson Cancer Center, Houston, TX 77030

Treasurer: Bayard D. Clarkon, 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 *Reference Update*. 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.