



Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR

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

Senior Editorial Assistant
Theresa A. Griffith

Staff Assistant
Mary Ellen Pirring

Editorial Assistants
Valerie L. Samuel
Andrea Conrad
Katherine V. Pawlowski
Bethann Massarella
Edward L. Dodd III

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

Assistant to the Executive
Director

Ruth E. Fortson

Membership Development
Coordinator

Robin E. Felder

Administrative Assistant
Margaret A. Pickels

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
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
Ernest C. Borden
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

Cover Editorial Board

Sidney Weinhouse,
Cover Editor

Suzanne Cory
William M. Crist
Riccardo Dalla-Favera
Benoit de Crombrughe
Eugene R. DeSombre
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
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. Gray
J. W. Grisham
Lorraine J. Gudas
F. Peter Guengerich
Sen-itiroh Hakomori
Philip C. Hanawalt
Curtis C. Harris
John C. Harshbarger
Stephen S. Hecht
Carl-Henrik Heldin

Hugh J. Creech
Clark W. Heath, Jr.

Ingegerd Hellström
Brian E. Henderson
Richard B. Hochberg
Wu Ki Hong
Tasuku Honjo
H. Robert Horvitz
Kay Huebner
William B. Isaacs
Mark A. Israel
Elaine S. Jaffe
Rakesh K. Jain
Peter A. Jones
Fred F. Kadlubar
John H. Kersey
Kenneth W. Kinzler
Hynda K. Kleinman
Alfred G. Knudson, Jr.
Kurt W. Kohn
Richard D. Kolodner
Laurence N. Kolonel
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
Dan L. Longo
Reuben Lotan
David B. Ludlum
Lynn M. Matrisian
W. Gillies McKenna
Anna T. Meadows
Beatrice Mintz

Edwin A. Mirand
Raymond W. Ruddon

Malcolm S. Mitchell
Ruth J. Muschel
Yusuke Nakamura
Susan L. Naylor
Kenneth Nilsson
Susumu Nishimura
Jeffrey A. Norton
Kenneth Olden
Allen I. Oliff
Gilbert S. Omenn
Richard J. O'Reilly
Robert F. Ozols
Michael A. Palladino, Jr.
Luis F. Parada
Anthony E. Pegg
Pier Giuseppe Pelicci
Angel Pellicer
Bice Perussia
Lester J. Peters
Gordon L. Phillips
Cecil B. Pickett
Jacalyn H. Pierce
Jennifer A. Pietsenpol
Yves G. Pommier
Theresa P. Pretlow
Vito Quaranta
Frank J. Rauscher III
John C. Reed
Richard A. Rifkin
Leslie L. Robison
Igor B. Roninson
Howard I. Scher
Robert T. Schimke
J. Schlessinger
Manfred Schwab
David Sidransky
Joseph V. Simone

Takashi Sugimura
John H. Weisburger

Francis M. Sirotnak
Anna Marie Skalka
Helene S. Smith
Michael B. Sporn
Martha R. Stampfer
Eric J. Stanbridge
Patricia S. Steeg
Glenn Steele, Jr.
Bernard S. Strauss
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
Peter 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
Sheldon Wolff
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. Through the kind assistance of the Japanese Cancer Association, accelerated mailing of all AACR journals to AACR members in Japan is fully supported by a generous grant from the Banyu Pharmaceutical Company, Tsukuba, Japan.

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 or (201) 627-2427; 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 56 (1996) of *Cancer Research* at the rate of \$460 U.S./\$550 foreign. *Cancer Research* is only available to institutions as a combined subscription with *Clinical Cancer Research*. The combined 1996 institutional subscription price of \$595 U.S./\$725 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. 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 or (201) 627-2427; 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 \$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., 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 AACR, Inc. 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 \$75 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 \$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 0008-5472/96 \$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 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 1996 institutional subscription price of \$595 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 1996 by the American Association for Cancer Research, Inc. Printed in the U.S.A.