



# Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR 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

**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

### Administrative Staff

**Executive Director**  
Margaret Foti

**Associate 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

**Data Entry Clerk**  
Robert A. Simms II

### 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

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 Crombrughe

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

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

Leroy 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. Accelerated mailing of journals to AACR member 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. 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 *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. (0) 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 (individual at institutional nonmembers), including postage. Institutional and individual nonmembers outside of the United States should add \$60 to their respective rates to offset second-class postage costs. 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: Member Services, American Association for Cancer Research, Inc., 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.



FLF7-T2D-TYL2

## 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 \$150, \$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.

---

### 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 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: 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 for \$415 for nonmembers. 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 1994 by the American Association for Cancer Research, Inc. Printed in the U.S.A.