



# 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

### Senior Staff Editors

Kathleen C. Assenmacher  
Pamela R. Arnold

### Staff Editors

Ronald M. Vitale  
Carolina Miranda

### Editorial Associate

Michelle K. Bruni

### Staff Assistant

Mary Ellen Perring

### 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

### Administrative Staff

#### Executive Director

Margaret Foti

#### Director of Administration

Adam D. Blistein

#### Controller

Joan D. Ritchie

#### Manager, Meetings and Exhibits

Jeffrey M. Ruben

#### Assistant Director,

**Administration**

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 Assistant

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

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 Cory

William M. Crist

Riccardo Dalla-Favera

Mary B. Daly

Nancy E. Davidson

Benoit de Crombrughe

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. Fojo

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. Germer

Eli Glatstein

David W. Golde

Joe W. Gray

J. W. Grisham

Lorraine J. Gudas

F. Peter Guengerich

Sen-itiroh Hakomori

Stanley R. Hamilton

Curtis K. 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. Kadlubar

Michael B. Kastan

John H. Kersey

Young S. Kim

Kenneth W. Kinzler

Hynda K. Kleinman

Alfred G. Knudson, Jr.

Richard D. Kolodner

Laurence N. Kolonel

Peter H. Kramer

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

Lynn M. Matrisian

W. Gillies McKenna

Beatrice 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 J. 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,

*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. Accelerated mailing of all AACR journals to AACR members in Japan is 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 (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 address changes to: AACR Member Services, Public Ledger Bldg., Suite 826, 150 South Independence Mall West, Philadelphia, PA 19106-3483. Nonmember 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 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, AACR, 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 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 Mall 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 subscription with *Clinical Cancer Research*. The combined 1998 institutional subscription price of \$795 includes a subscription to *Clinical Cancer Research*. Periodicals postage paid at Philadelphia, PA and additional mailing offices. POSTMASTER: Send address changes to AACR Subscription Office, P.O. Box 11806, Birmingham, AL 35202. Copyright 1998 by the American Association for Cancer Research, Inc. Printed in the U.S.A.