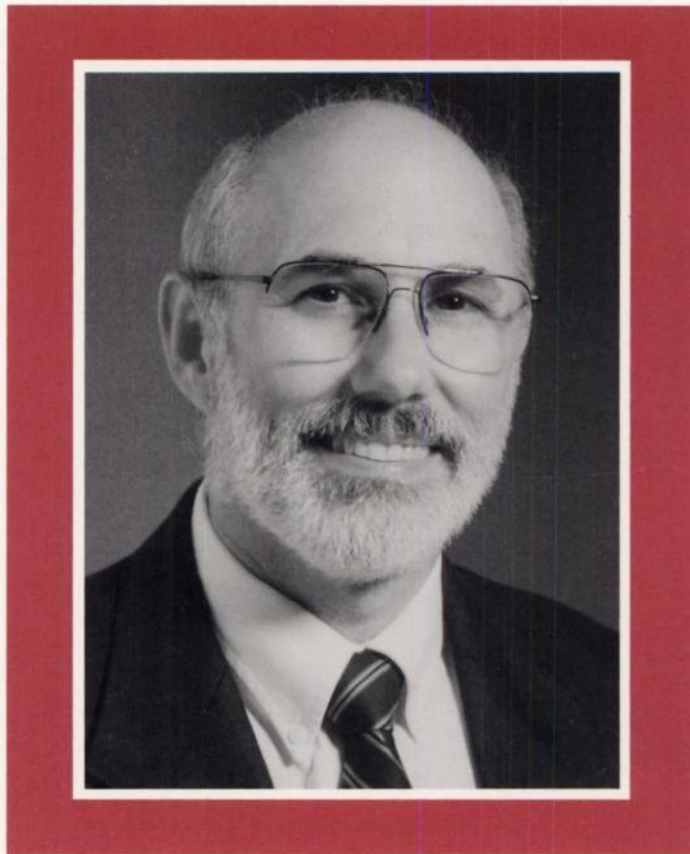




Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



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AMERICAN ASSOCIATION FOR CANCER RESEARCH
89th Annual Meeting



Frank J. Rauscher, III, Program Committee Chairperson

Morial Convention Center, New Orleans, Louisiana

March 28-April 1, 1998

Titles of Major Sessions

(Names of confirmed session organizers are in parentheses)

PLENARY SESSION

New Horizons in Cancer Research (Frank J. Rauscher, III)

SYMPOSIA

Molecular Determinants of Cellular and Tumor Responses to Radiation (Michael B. Kastan)

Successes in Oncogene-based Drug Targeting: Selectivity and Specificity (Alex Matter)

Cancer Gene Therapy: New Concepts and Clinical Applications (Jack A. Roth)

Reconstruction of Human Tumorigenesis and Progression: Cancer Genetics In Model Organisms

Tumor Angiogenesis: An Integrated Approach (Rakesh K. Jain)

Signaling by wnt-1, β -catenin, and the APC Tumor Suppressor in Cancer (Paul Polakis)

Prostate Cancer: Basic Science and Clinical Aspects (Leland W.K. Chung)

The Molecular Basis of Immune Recognition: Basic Concepts with Therapeutic Implications (Giorgio Trinchieri)

The bcl-2 Family: Regulation and Effectors (Stanley J. Korsmeyer)

The Latest in Telomere and Telomerase Function: Proof of Principle? (Ronald A. DePinho)

Inherited Cancer Susceptibility Syndromes: Genetics, Genes, and Function

New Concepts in Chemotherapeutics and Drug Resistance (Susan Band Horwitz)

Cell Death Signalling Pathways: Caspase Cascades and Effectors/Initiators of Apoptosis

p73/p53: An Emerging Gene Family (William G. Kaelin)

Breast Cancer: Basic Science and Clinical Aspects (Sofia D. Merajver)

Molecular Targets and Endpoints for Chemoprevention (Waun Ki Hong)

Tumor Physiology: Tumor-Stromal, Cell-Cell, and Microenvironment Interactions (Mina J. Bissell)

Gastrointestinal Cancer: Basic Science and Clinical Aspects

Tumor Virology: Molecular Biology and Etiology (Karl Münger)

Advances in Cancer Vaccine Development (Dorothee Herlyn)

Molecular Diversity-based Approaches to Anti-Cancer Drug Design (Jack D. Keene)

New Mechanisms of Action of Viral and Cellular Oncogenes (Elizabeth Moran)

Genetic Approaches to Diagnosis: The Impact of Molecular Medicine on Early Detection and Diagnosis (David Sidransky)

Tobacco and Lung Carcinogenesis: Genetics, Biology, and Etiology (Adi F. Gazdar)

Transcriptional Regulation of the Neoplastic Phenotype (Frank J. Rauscher, III)

Restoring Drug Sensitivity to Tumors: New Concepts from Tumor Biology and Physiology (William N. Hait)

Emerging Concepts in Individual Cancer Susceptibility (Fred F. Kadlubar)

CONTROVERSY SESSIONS

Have We Improved the Treatment of Cancer?

Environmental Estrogens and Cancer

Will Multidrug Resistance Modulators Be Effective in the Clinic?

**METHODS WORKSHOPS AND EDUCATIONAL SESSIONS
To Be Announced**

"MEET-THE-EXPERT" SUNRISE SESSIONS

Cancer Genome Anatomy Project (CGAP): Update and Potential (Paul S. Meltzer)

Cell Adhesion: Integrin Signaling, Membrane to Nucleus JAK-STATs: Dedicated Cytokine Signaling Pathways

Histone Acetylation and Transcriptional Regulation (Tony Kouzarides)

Molecular Genetics of Brain Tumors

Genetic Analysis of Tumor Suppression by COX-2 Inhibitors (Makoto M. Taketo)

Antisense-based Therapeutics: Basic and Clinical Studies (Thale Jarvis)

Gene Transfer to Hematopoietic Progenitors (Fulvio Mavilio)

Psychosocial Aspects of Genetic Diagnosis (Caryn E. Lerman)

B-Cell Lymphomas: Genetics and Biology (Riccardo Dalla-Favera)

Hormonal Regulation of Cell Proliferation and Differentiation (Lorraine J. Gudas)

Cell Cycle Control (Giulio Draetta)

Proteases in Cancer: Clinical Significance and Mechanisms in Metastasis (Henri Rochefort)

Inherited Cancers of the Kidney: Family Studies, Genes, and Biochemistry (W. Marston Linehan)

Strategies for Combining Chemotherapy and Biotherapy (Antonio C. Buzaid)

New Concepts in Antimetabolites: Basic Science and Clinical Trials (Steven Grant)

IL-12: Biological and Clinical Developments (Giorgio Trinchieri)

Chemoprevention Trials: Progress and Promise (Scott M. Lippman)

Nuclear Hormone Receptors in Development and Disease

Growth Factor Signaling: The IGF-1, IGF-2 System in Cancer (Haim Werner)

Genetics and Biology of Hematologic Malignancies (Pier Pellici)

Radiation Sensitization: Basic and Clinical Aspects

Advances in Mechanisms of Drug Resistance: Basic Science and Clinical Implications (Susan E. Bates)

Immunotherapy and Costimulatory Molecules

Emerging Issues in Molecular Epidemiology (Barbara S. Hulka)

Initiation of DNA Damage and Repair

Familial Cancer Syndromes: DNA Testing and Clinical Approaches (Ken Yamaguchi)

HIV Receptors and Co-Receptors: Basic Science and Clinical Implications

Chromosomal Translocations: Genetics, Biology, and Protein Function (James R. Downing)

Recent Advances in Mechanisms of Cancer Invasion and Metastasis (Isaiah J. Fidler)

From Slave to Master: The Biological Events During Melanoma Development and Progression (Meenhard Herlyn)

Biology and Genetics of Myelodysplastic Syndrome

Topoisomerases: Structure and Function

Progress in Antibody Therapy of Human Cancer (Nancy Hynes)

Animal Models for Chemoprevention (Michael N. Gould)

Further Information: AACR Office · Public Ledger Building · Suite 826 · 150 S. Independence Mall West · Philadelphia, PA 19106-3483 · **TELEPHONE:** (215) 440-9300 · **FAX:** (215) 440-9313 · **Email:** meetings@aacr.org · For up-to-date information visit the AACR Website at <http://www.aacr.org>

AMERICAN ASSOCIATION FOR CANCER RESEARCH

The American Association for Cancer Research (AACR) is a professional society of over 11,000 scientists and physicians involved in all aspects of basic, clinical, and translational cancer research. Members of the AACR enjoy

- subscriptions to *Cancer Research*, *Cell Growth & Differentiation (CG&D)*, *Cancer Epidemiology, Biomarkers & Prevention*, and *Clinical Cancer Research* at reduced member rates
- reduced registration rates at the AACR Annual Meeting, Special Conferences, and International Meetings
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CALL FOR NOMINATIONS

Emil J Freireich Award and Lecture

Given annually to a physician scientist under the age of 45 years who has made a major contribution to the field of clinical cancer research which promises to have a major impact on malignant disease prevention, diagnosis or treatment.

Please contact: Dr. Evan M. Hersh, Assistant Director for Experimental Therapeutics & Translational Research, Chairman, Freireich Award Selection Committee, 1515 N. Campbell Ave., P.O. Box 245024, Tucson, AZ 85724-5024.

Office: (520) 626-2250

FAX: (520) 626-2225

hersh@azcc.arizona.edu

Committee: Bart Barlogie, MD, Margaret Foti, PhD, Emil Frei III, MD, James F. Holland, MD, Hagop Kantarjian, MD, Michael Keating, MD, John Mendelsohn, MD, William Plunkett, PhD



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DECEMBER 12-16, 1997

DNA Methylation, Imprinting, and the Epigenetics of Cancer

Chairpersons: Peter A. Jones, Los Angeles, CA;
Stephen B. Baylin, Baltimore, MD; Timothy H. Bestor, New York, NY
El Conquistador Resort and Country Club, Las Croabas, PR

JANUARY 9-13, 1998

Molecular Mechanisms of Apoptosis Regulation

Chairpersons: John C. Reed, La Jolla, CA; Vishva M. Dixit, Ann Arbor, MI
Renaissance Esmeralda Resort, Indian Wells (Palm Springs), CA

JANUARY 24-28, 1998

Angiogenesis and Cancer

Chairpersons: Judah Folkman, Boston, MA; Michael Klagsbrun, Boston, MA
Hyatt Orlando, Orlando, FL

FEBRUARY 16-21, 1998

Innovative Molecular Biology Approaches to the Prevention, Diagnosis, and Therapy of Cancer

Joint Meeting with the Japanese Cancer Association
Chairpersons: Edward Bresnick, Worcester, MA;
Kaoru Abe, Tokyo, Japan
Maui Marriott Resort, Maui, HI

MARCH 28-APRIL 1, 1998

89th Annual Meeting

Chairperson: Frank J. Rauscher III, Philadelphia, PA
Morial Convention Center, New Orleans, LA
Abstract Deadline: October 28, 1997

JUNE 14-18, 1998

Proteases and Protease Inhibitors in Cancer

Co-Sponsored by the Danish Society for Pathology
Chairpersons: Keld Dano, Copenhagen, Denmark;
Henri Rochefort, Montpellier, France; Lynn M. Matrisian, Nashville, TN; Nils Brunner, Copenhagen, Denmark
Nyborg Strand Conference Center, Nyborg, Denmark

SEPTEMBER 24-28, 1998

Viral Targets and Cellular Growth Control (tentative title)

Chairperson: Thea D. Tlsty, San Francisco, CA
(additional chairpersons to be announced)
Marriott's Laguna Cliffs Resort, Dana Point, CA

OCTOBER 14-18, 1998

Gene Regulation and Cancer (10th Anniversary of the AACR Special Conferences)

Chairpersons: Phillip A. Sharp, Cambridge, MA, and Steven L. McKnight, Dallas, TX
The Homestead, Hot Springs, VA

NOVEMBER 11-15, 1998

Endogenous Sources of Mutations

Chairpersons: Lawrence J. Marnett, Nashville, TN;
James A. Swenberg, Chapel Hill, NC; Tomas A. Lindahl, Herts, England
Sanibel Harbour Resort and Spa, Ft. Myers, FL

DECEMBER 2-6, 1998

Basic and Clinical Aspects of Prostate Cancer

Chairpersons to be announced
Hyatt Grand Champions Resort, Indian Wells (Palm Springs), CA

AACR members will receive brochures on the above conferences as soon as they are available. Nonmembers should call or write:

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AMERICAN ASSOCIATION FOR CANCER RESEARCH (AACR)

AACR-HBCU Faculty Award in Cancer Research

*Supported by a generous grant provided by the
Comprehensive Minority Biomedical Program of the National Cancer Institute*

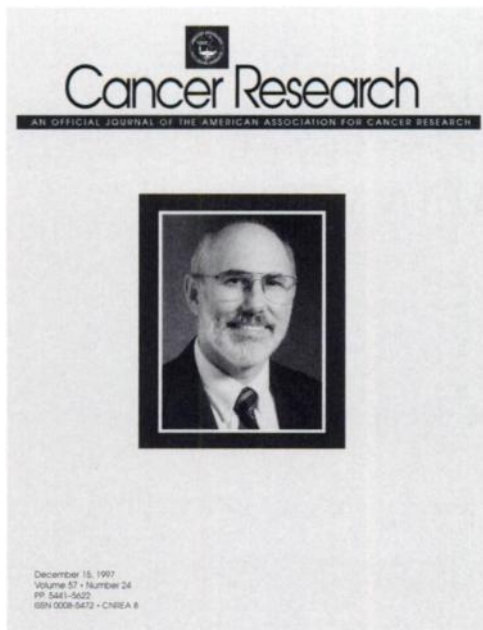
The American Association for Cancer Research (AACR) is extremely pleased to announce the availability of Awards in Cancer Research for full-time faculty members of Historically Black Colleges and Universities (HBCU's). Supported by a generous grant provided by the Comprehensive Minority Biomedical Program of the National Cancer Institute, AACR-HBCU Faculty Awards in Cancer Research will be presented annually by the American Association for Cancer Research to 20 scientists at the level of Assistant Professor or above engaged in meritorious basic, clinical, or translational cancer research at a non-government, not-for-profit research facility.

The purpose of this Award program is to increase the scientific knowledge base of faculty members at Historically Black Colleges and Universities, and to encourage them and their students to pursue careers in cancer research. Awardees will receive financial support for their participation in the 89th AACR Annual Meeting, March 28-April 1, 1998, in New Orleans, LA. The 1998 AACR Annual Meeting will attract approximately 7,500 scientists from around the world; will provide the latest findings in the most rapidly developing areas of basic, clinical, and translational cancer research; and will feature major presentations from prominent scientists who are making important advances in the field.

The American Association for Cancer Research, a scientific society of more than 13,500 researchers working in all subfields of basic, clinical and translational cancer research, is extremely pleased to sponsor this faculty award.

For Further Information

If after reading the enclosed information you have any questions concerning the application process or Award criteria, or if you have not received the Official Application Form, contact: HBCU Award Coordinator, American Association for Cancer Research, Telephone: (215) 440-9300, FAX: (215) 440-9412, E-mail: felder@aacr.org.



Even before the exact function of chromosomal DNA was recognized, both Herman Muller in 1939 and Barbara McClintock in 1941 recognized that the chromosome ends (telomeres) were special structures essential for the maintenance of chromosomal stability. In the early 1970s, James Watson and Alexy Olovnikov independently suggested that conventional DNA polymerases would not fully replicate linear eukaryotic chromosomes. Loss of a portion of the chromosome ends would occur each time a cell divided. This led to the hypothesis that a special mechanism to maintain the ends of chromosomes had to exist in immortal single cell organisms and the germline of higher organisms. In the late 1970s, Elizabeth Blackburn and Joe Gall discovered that the telomeres of the ciliated protozoa, *Tetrahymena*, consisted of TTGGGG hexameric repeats. This set the stage for Carol Greider, a student in Dr. Blackburn's laboratory, to discover the molecular mechanism that apparently solved the chromosome end replication problem. They isolated and characterized a ribonucleoprotein enzyme, called telomere terminal transferase or telomerase. They showed that it was required for telomeric repeat synthesis and that it utilized a portion of its RNA component as a template for adding telomeric sequences *de novo* to telomere ends by a reverse transcriptase mechanism. In 1988, Bob Moyzis reported that human telomeres contained TTAGGG repeats, and in 1989, Gregg Morin detected telomerase in a human tumor cell line. Thus, the stage was set for rapid progress in the field of human telomeres and telomerase.

As understanding of the telomerase mechanism progressed so did knowledge of the importance of telomere shortening in its absence. For example, Howard Cooke's group demonstrated that human chromosome ends were shorter in peripheral blood lymphocytes than in germline (sperm) DNA from the same individual. Calvin Harley, Bruce Futcher, and Dr. Greider found that telomeres progressively shortened with division of normal diploid cells in culture, while Nick Hastie and Robin Allshire showed that the telomeres in human colonic tissues were shorter in older donors when compared to those obtained from younger ones. These researchers and Titia deLange speculated that loss of telomeric sequences could eventually destabilize chromosomes and restrict the lifespan of somatic cells. Models that implicated telomerase repression and telomere loss in cellular senescence and telomerase reactivation in immortal and cancer cells soon appeared.

However, testing these ideas in human cancer was difficult since

the assay for detecting telomerase required large amounts of tissue. Despite this impediment, there were reports demonstrating that telomerase could be detected in human cancer. In 1994, scientists at the Geron Corporation with Woody Wright developed a simplified PCR-based telomerase activity assay, called TRAP (telomere repeat amplification protocol). Mieczyslaw Piatyszek in the group headed by Jerry W. Shay then applied the TRAP assay to the detection of telomerase in a large number of tumor biopsies. The TRAP assay allowed fast and efficient detection of telomerase activity in a large number of samples. It was also useful for following telomerase activity during the biochemical purification of telomerase components. This eventually led to the identification of human telomerase RNA in 1995 by scientists at Geron Corporation, and in 1997, to the identification of the human reverse transcriptase catalytic protein subunit of telomerase by Thomas Cech's laboratory in collaboration with Geron and independently by Robert Weinberg's group.

The following model has emerged from the telomere and telomerase studies conducted during the last few years: 1) progressive telomere loss in somatic cells is normal and can be viewed as a "clock" or timing mechanism that regulates how many times an individual cell can divide; 2) inhibition of cellular proliferation (senescence) occurs when telomeres are short; 3) telomerase is downregulated/repressed in most human tissues during development, but is detected in over 85% of more than 2,000 primary human tumor tissues examined; and 4) telomerase activity correlates with the stabilization of telomere length. Thus, upregulation or reactivation of telomerase activity appears to be necessary for the continued proliferation of cells and may be a critical, even rate-limiting, step in cancer progression.

Why is all this so exciting for the cancer community? At the 1997 Annual Meeting of the American Association for Cancer Research (AACR), there were over 150 presentations on telomerase and cancer and there is growing momentum in the field. Some of the critical questions being addressed include: Will inhibition of telomerase activity *in vivo* be effective in treating cancer or preventing cancer relapse? What is the role of telomerase RNA in cancer progression? Will routine telomerase screening be useful as a diagnostic tool for the early detection of cancer? Does the amount of telomerase activity have prognostic utility? What regulates telomerase activity during human development and during cancer progression? What are the structures and functions of the components of the telomerase ribonucleoprotein complex? What are the proteins that maintain telomere stability? Can experimentally manipulating (elongating) telomere length in normal cells result in their increased proliferation capacity?

That telomerase is almost universally detected in tumors has attracted many scientists to investigate some of the questions posed above. We are still in the early stages of this field and much remains to be done. However, even at this early stage, the excitement and optimism in the field appears warranted.

Jerry W. Shay (*cover*) received his B.A. and M.A. from the University of Texas at Austin in 1966 and 1968, respectively, and his Ph.D. from the University of Kansas at Lawrence in 1972. He did his postdoctoral work at the University of Colorado at Boulder from 1972-75. In 1975, he joined the University of Texas Southwestern Medical Center at Dallas as Assistant Professor in the Department of Cell Biology and Neuroscience, where he later rose to Associate Professor, before becoming Professor in 1993. He is active on many committees and in editorial activities in cell science, including service on the *Cancer Research* Editorial Board since 1997. He is also a member of the AACR and has chaired several symposia and educational sessions on telomerase at recent AACR Annual Meetings. In addition, Dr. Shay has authored over 50 book chapters/editorials and over 200 peer-reviewed articles, including more than 50 telomerase-related papers since 1994.

Sidney Weinhouse