

OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



May 1, 1994 Volume 54 • Number 9 PP. 2287–2525 ISSN 0008-5472 • CNREA 8

AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Transcriptional Control of Cell Growth and Differentiation

October 16-20, 1994 Chatham Bars Inn, Chatham (Cape Cod), Massachusetts



CONFERENCE CHAIRPERSONS

Eric N. Olson / Houston, TX
Bruce M. Spiegelman / Boston, MA

PROGRAM COMMITTEE

Elaine V. Fuchs / Chicago, IL Joan V. Ruderman / Boston, MA

SCIENTIFIC PROGRAM

Opening Lectures David Baltimore / New York, NY Robert Tjlan / Berkeley, CA

James E. Darnell, Jr. / New York, NY

Cell Cycle and Transcription - I

David M. Livingston / Boston, MA Stephen J. Elledge / Houston, TX Robert N. Elsenman / Seattle, WA Carol L. Prives / New York, NY

Cell Cycle and Transcription - II George F. Vande Woude / Frederick, MD

Mark Kirschner / Boston, MA
Steven I. Reed / La Jolla, CA

Signal Transduction Systems Influencing Transcription

Joan V. Ruderman / Boston, MA Marc Montminy / La Jolla, CA Jean Y. J. Wang / La Jolla, CA Spyridon Artavanis-Tsakonas / New Haven, CT

Transcription Factors Controlling Cell Growth

Michael Karin / La Jolla, CA Richard Treisman / London, England Michael Z. Gilman / Cold Springs Harbor, NY

Application Deadline: June 27, 1994

Transcription Factors Controlling Cell Differentiation - I

Bruce M. Spiegelman / Boston, MA Elaine V. Fuchs / Chicago, IL Michael G. Rosenfeld / La Jolla, CA Michael Levine / La Jolla, CA

Transcription Factors Controlling Cell Differentiation - II

Eric N. Olson / Houston, TX Stuart Orkin / Boston, MA Charles P. Emerson / Philadelphia, PA

Development

Eddy M. De Robertis / Los Angeles, CA Richard Behringer / Houston, TX Janet Rossant / Toronto, Ontario, Canada Clifford Tabin / Boston, MA

Applicants are encouraged to submit abstracts for poster presentation.

Information and Application Forms

American Association for Cancer Research Public Ledger Building 620 Chestnut Street, Suite 816 Philadelphia, PA 19106 (215) 440-9300 (215) 440-9313 (FAX)

ESSENTIAL RESEARCH FROM CAMBRIDGE

Clinical Bone Marrow Transplantation

A Reference Textbook

Kerry Atkinson

A balanced and uniquely detailed overview of both the scientific basis and clinical practice of bone marrow transplantation.

1994 700 pp. 42073-3 Hardcover about \$180.00

Molecular Genetics for the ClinicianD. J. H. Brock

A clear and concise explanation of the technology and applications of molecular genetics in clinical medicine.

applications of molecular genetics in clinical me 1993 301 pp. 41179-3 Hardcover \$69.95 42325-2 Paper \$24.95

Cancer of the Esophagus

Approaches to the Etiology

Valda Mary Craddock

Describes the variety of factors thought to cause cancer of the gullet i.e. dietary deficiencies and consumption of mouldy food in China and South Africa, alcohol and tobacco use in Europe and USA, and other hazards in relation to the frequency of the disease in different parts of the world.

Cambridge Monographs on Cancer Research 1993 291 pp. 37393-X Hardcover \$99.95

Blood Stem Cell Transplants

Edited by Robert Peter Gale,

Christopher A. Juttner, and Philippe Henon Examines the latest information in the area and includes an overview of the concepts behind and advantages of blood stem cell transplants.

1994 198 pp. 44210-9 Hardcover \$59.95

Cytokine Therapy

Edited by David W. Galvani and John C. Cawley

"...a concise and thoroughly readable account of important clinical specialities on which cytokine therapy has already made an impact."

Trends in Microbiology

1993 205 pp. 41232-3 Hardcover \$69.95 42337-6 Paper \$27.95

Human Cancer

Epidemiology and Environmental Causes John Higginson, Calum S. Muir, and Nubia Munoz

Provides a global perspective on the epidemiology of cancer and its environmental causes by summarizing on a cancer-by-cancer basis.

Cambridge Monographs on Cancer Research 1992 602 pp. 41288-9 Hardcover \$125.00

A Practical Guide to Human Cancer Genetics

Shirley V. Hodgson and Eamonn R. Maher

Presents essential information about genetic predisposition to cancer. It introduces the basic concepts and mechanisms of tumorigenesis and then system by system, describes the incidence, significance, and management of individual cancers.

1993 258 pp. 40128-3 Hardcover \$79.95

1993 258 pp. 40128-3 Hardcover \$79.95 40951-9 Paper \$34.95

Cambridge Medical Reviews: Haematological Oncology

Volume 2

Edited by Armand Keating, James Armitage, Alan Burnett, and Adrian Newland

Provides a comprehensive and up-to-date review of current research and will be an important source of information for far-reaching implications for the understanding, diagnosis and management of haematological malignant disease.

Cambridge Medical Reviews: Haematological Oncology 2

1993 239 pp. 43190-5 Hardcover \$79.95

Colorectal Cancer

A Scientific Perspective

Anne R. Kinsella

with assistance of Philip F. Schofield

"Every doctor with an interest in colorectal cancer should read Kinsella and Schofield's book and refer to it as the story unfolds."

— Ř. J. Heald, British Medical Journal Cambridge Monographs on Cancer Research 1993 173 pp. 36199-0 Hardcover \$84.95

Cancer Screening

Edited by A. B. Miller, J. Chamberlain, N. E. Day, M. Hakama, and P. C. Prorok

Contains the most up-to-date available recommendations from international authorities on all cancers for which screening has potential, including some sites not previously investigated.

1991 456 pp. 41041-X Hardcover \$94.95

Cancer Patient Care

Psychosocial Treatment Methods Edited by Maggie Watson

"...this volume has the advantage of giving a comprebensive overview. I think the book will appeal both to newcomers to psychosocial oncology and to those with some experience who wish to acquire a broader knowledge of current techniques in intervention."

-Penelope Hopwood, Psychological Medicine Copublished with the British Psychological Society

1991 320 pp. 41632-9 Hardcover \$94.95 42631-6 Paper \$42.95

Please stop by our booth at the ASCO meeting to see these and other fine titles

Available in bookstores or from



40 West 20th Street, New York, NY 10011-4211 Call toll-free 800-872-7423 MasterCard/VISA accepted. Prices subject to change.

THE AMERICAN ASSOCIATION FOR CANCER RESEARCH PRESENTS



An Important Educational Opportunity for Predoctoral and Postdoctoral Fellows Contemplating Careers in Basic Cancer Research

HISTOPATHOBIOLOGY OF NEOPLASIA

The Edward A. Smuckler Memorial Workshop Supported by a Generous Grant from the National Cancer Institute

> Keystone Conference Center Keystone, Colorado July 17 - July 24, 1994

- Intensive training in the histopathology and biology of neoplasia.
- Twenty-eight hours of hands-on laboratory exercises directed by distinguished pathologists.
- An outstanding series of lectures on rapidly developing areas of cancer research by laboratory directors and other prominent investigators.
- Extensive written course materials that will serve as valuable references in the future.
- Full funding of participants' lodging and subsistence expenses during the workshop.

LABORATORY AND LECTURING FACULTY

Michael W. Lieberman*, Baylor College of Medicine, Houston, TX, **Course Director** Stephen Baird*, VA Medical Center, San Diego, CA

Helen Feiner*, New York University School of Medicine, New York, NY

Isaiah J. Fidler, UT M.D. Anderson Cancer Center, Houston, TX

Peter M. Howley, National Cancer Institute, Bethesda, MD

Mary-Claire King, University of California, Berkeley, CA

Margaret L. Kripke, UT M.D. Anderson Cancer Center, Houston, TX

John H. Lehman*, Albany College of Medicine, Albany, NY

Robert Low, University of Colorado School of Medicine, Denver, CO

Gary Miller*, University of Colorado School of Medicine, Denver, CO

Harold L. Moses, Vanderbilt University School of Medicine, Nashville, TN

Sharon B. Murphy, Children's Hospital, Chicago, IL G. Barry Pierce, University of Colorado School of Medicine, Denver, CO

Michael Prystowsky, University of Pennsylvania School of Medicine, Philadelphia, PA

Stewart Sell, University of Texas Medical School, Houston, TX

Saraswati Sukumar, The Salk Institute, La Jolla, CA Frederick Waldman, University of California, San Francisco, CA

Sandra R. Wolman, Oncor, Inc., Gaithersburg, MD

*Member of the Workshop Executive Committee

APPLICATION DEADLINE: APRIL 29, 1994

Further Information: American Association for Cancer Research • Public Ledger Building

620 Chestnut Street • Suite 816 • Philadelphia, PA 19106-3483

Telephone: (215) 440-9300 • FAX: (215) 440-9313

EACR XIII

The Thirteenth Meeting of the European Association for Cancer Research Berlin, Germany September 25-28, 1994

The EACR invites members and non-members to attend its next major meeting in Berlin. The meeting will cover theoretical and experimental approaches in cancer research as well as new aspects of clinical significance. Molecular and cell biology will be the main focus of the meeting.

Issues and Speakers to include:

Muhlbock Memorial Lecture: Charles Weissmann - Zurich Transgenic technology in medical research Plenary Lectures

Genetic epidemiology of breast cancer - T. Bishop, Leeds
Cell adhesion molecules and cytoakeletal elements in normal and
neoplastic cells - W. Franke, Heidelberg

Apoptosis - G. Evan, London

Cell signalling in cancer treatment - H. Grunicke, Innsbruck Suicide gene transfer and cancer therapy - M. Blaese, Bethesda Parallel Symposia and Chairpersons

Tumor suppressors in growth control and neoplasia - W. Deppert, Hamburg

Carrier systems for drug targetting - T.A. Connors, Belmont

Orthologous carcinogen-metabolizing enzymes: Confusion and progress - R. Wolf, Dundee

Molecular aspects of invasion and metastasis - W. Birchmeier, Berlin DNA repair deficiency syndromes and cancer - D. Bootsma, Rotterdam Minimal residual disease: risk factors and detection M.I. Colnaghi,

Significance of mutation spectra for carcinogenesis - E. W. Vogel, Leiden Immunotherapy: The new challenges - G. Riethmuller, Munchen Recent results in occupational carcinogenesis - S. Hernberg, Helsinki Cancer gene identification and gene therapy - M. Schwab, Heidelberg

Poster sessions will be organized. Interested participants are invited to submit poster abstracts on Symposium related topics. Deadline for abstract submission is June 15th, 1994.

For registration and abstract forms, contact the EACR XIII Secretariat:

Prof. Dr. G. Pasternak, Max Delbruck Center for Molecular Medicine Robert-Rossle-Str. 10, D-13122 Berlin, Germany Tel: +49-30/9406 2308 or 3740 Fax: +49-30/9494161

Reduced registration fees are available to members of the EACR. For further details and application form, please contact: Dr. M.R. Price, EACR Secretariat, Cancer Research Laboratory, University of Nottingham, Nottingham NG7 2RD, U.K. Tel: (0602) 513418, Fax: (0602) 515115.

GENETIC PREDISPOSITION TO CANCER

Special Conference Sponsored by The General Motors Cancer Research Foundation June 14 & 15, 1994

> National Cancer Institute Bethesda, Maryland

June 14, 1994:

Keynote Address: Characteristics of Genetic Predisposition Syndromes - Raymond L. White

The Genetics of Breast Cancer - Mary Claire King; Genetics of Esophageal Cancer - Brian J. Reid; Genetics of Brain Cancer Progression - Webster K. Cavenee; Clinical & Molecular Genetics of MEM II - Bruce A. J. Ponder; The Genetics of Colorectal Cancer - Sir Walter F. Bodmer; Abrogation of Cell Cycle Checkpoint Control in Preneoplastic Cells - Thea Tlsty; Genome Instability & Its Relationship to Development of Cancer - Richard Fishel; Triplet Repeat Diseases - C. Thomas Caskey; Genetic & Environmental Interactions in the Development of Multiple Primary Tumors - Louise C. Strong; Molecular Basis of Hepatitis-Hepatoma Correlation - Christian Brechot; Mechanistic Role of Human Papilloma Viruses in Human Cancer - Peter Howley; Chemoprevention in Patients at Genetic Risk for Developing Invasive Cancer & Metastases - Lance Liotta; From Gene Defect to Therapy - Ron Evans; Social & Ethical Considerations - Francis Collins.

June 15, 1994:

Li-Fraumeni Syndrome - Stephen H. Friend; Transgenic Approaches to the Analysis of Multistage Carcinogenesis in Mice - Alan Balmain; Tumor Suppressor Gene Mutations in Mice - Tyler Jacks; Molecular Basis for Secondary Leukemia - Carlo Croce; Radiation-Genetic Interactions in the Development of Cancer - John Little.

Conference Summary - Robert A. Weinberg

1:30 P.M.. - Lectures by the 1994 Prizewinners of the General Motors Cancer Research Foundation Awards

Please preregister by contacting the General Motors Cancer Research Foundation - 767 Fifth Avenue, New York, NY 10153. Telephone (212) 418-6229, Fax (212) 418-6388. Additional information is available; no registration fee; attendance open.

THE UNIVERSITY OF TEXAS MOANDERSON CANCER CENTER

47th ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH

Chairmen:

William H. Klein, Ph.D., Raymond E. Meyn, Ph.D., William Plunkett, Ph.D.

J. W. Marriott Hotel - Houston, Texas October 11-14, 1994

CELL DEATH IN DEVELOPMENT AND CANCER

The 47th Annual Symposium on Fundamental Cancer Research sponsored by The University of Texas M. D. Anderson Cancer Center will focus on the programmed cell death (apoptosis) in developmental biology and cancer. In recent years, mechanisms responsible for programmed cell death have been found to be conserved throughout the animal kingdom, implying an ancient evolutionary process. The meeting will emphasize the latest findings on cell death in normal and malignant development in several experimental systems.

October 11, 1994, P.M.

Bertner Award: Andrew H. Wyllie, Ph.D. Keynote Address: H. Robert Horvitz, Ph.D.

October 12, 1994, A.M.

Cell Death in Development
Special Lecture: David Livingston, M.D.

October 12, 1994, P.M.

Cell Death and Transcription Senescence

October 13, 1994, A.M.

Cell Death and the Immune System Special Lecture: Luc Montagnier, M.D.

October 13, 1994, P.M.

Cell Death Oncogenes

Special Lecture: Frank McCormick, M.D.

October 14, 1994, A.M.

Cell Death and Cancer Therapeutics Special Lecture: Irving Weissman, M.D.

Call for Posters

One page abstracts (double spaced) may be submitted for the Poster Session by September 1, 1994. Abstracts should include a purpose, methods, results, and a conclusion.

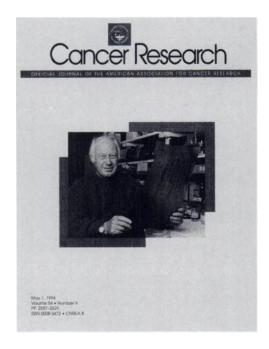
Wilson S. Stone Memorial Award

The award acknowledges outstanding research achievement by a junior investigator. Those eligible include postdoctoral fellows and faculty whose highest appointment has been Assistant Professor (or its equivalent) for no more than three years. The award consists of an inscribed plaque, an honorarium of \$1,000 and travel and per diem expenses to attend the symposium. Deadline for receipt of nominations is June 1, 1994. Nomination forms may be obtained by contacting Dr. Anthony J. Mastromarino at 713/792-3391 or by facsimile 713/795-0781.

For additional information contact: Conference Services, HMB 131 U.T. M. D. Anderson Cancer Center 1515 Holcombe Boulevard Houston, TX 77030-4095 Telephone: 713/792-2222

Facsimile: 713/794-1724

COVER LEGEND



The revolution in molecular biology now under way is again exemplified by the 1993 Nobel Awards in Chemistry. Kary B. Mullis was honored for the discovery of the polymerase chain reaction (PCR). In its beautiful simplicity, PCR has in 10 years already been adopted as the motor that is driving many of the most notable advances in molecular biology, and its future promise is impossible to exaggerate. The PCR technology is basically simple. It requires the action of DNA polymerase in the presence of an excess of the four DNA nucleotides, a minute amount of DNA, and primers that bind to the DNA and instruct the polymerase where to copy. Alternate heating and cooling separate the double strands, and repetition of the reaction on the original and new DNA strand yields four strands. By continued repetition, literally billions of new DNA strands can be synthesized [Science (Washington DC), 230: 1350, 1985]. Automation of this procedure has already made an indelible mark in a wide range of problems. One of the most striking has been the amplification of sequences of virtually trace amounts of DNA from archeological specimens. It has already become routine in the identification and sequence of genes involved in many aspects of cancer, as well as virtually every branch of biology. Dr. Mullis conceived the reaction while employed at the Cetus Corporation, Emeryville, California. According to a recent article (Science, 262: 506-507, 1993), he was not surprised at the call from Stockholm, after witnessing the tremendous impact of the reaction in such a short time.

Dr. Mullis received the B.S. in chemistry at the Georgia Institute of Technology in 1966 and the Ph.D. in biochemistry at the University of California at Berkeley in 1973. After postdoctoral work at the University of California at San Francisco and the University of Kansas, he joined the Cetus Corporation as a scientist, 1979–1986, where he perfected the PCR reaction. He is now Director of Molecular Biology at Xytronyx, Inc., in San Diego, California. He is a consultant for many firms and has received numerous awards besides the Nobel Prize.

Dr. Mullis shares the prize with Dr. Michael Smith (cover), Director of the Biotechnology Laboratory and Professor in the Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, Canada. His award honors his contribution of another technique, known as site-directed mutagenesis, which like PCR is of great importance in both conception and utility in molecular biology. His work has been applied to the use of oligonucleotides to detect specific genes, specific detection of mutations generated by oligonucleotide mutagenesis, and the use of synthetic oligonucleotides as specific in vitro mutagens for the analysis of gene and protein function. The basic principle involves the extension by a DNA polymerase of an oligonucleotide primer hybridized to a single-stranded circular template derived from a virus or plasmid into which a gene has been cloned. The primer is complementary to the region of DNA of interest except for a mismatch, addition, or deletion of one or more nucleotides. The resulting product is converted to a closed circular DNA and is used to transform a host cell. On replication, the DNA strand containing the mismatch to the mutated gene is propagated as a double-stranded vector, which can then be isolated and manipulated to yield large quantities of a mutated protein. The enzymatic properties of the protein can thus be related to specific alterations in its amino acid composition.

This work began during 1971–1975 when Dr. Smith developed methods for preparation of short-chain nucleotides and studied the stability of those with mismatched bases. His work has opened up a whole new approach to the study of functional changes in enzymes related to mutation at specific sites. Much promise is held for the process of "engineering" new enzymes.

Dr. Smith was born in Blackpool, England, and received the Ph.D. in 1956 from the University of Manchester. He joined the University of British Columbia in 1966.

We thank Drs. Smith and Mullis for providing material for this legend. A photograph of Dr. Mullis was not available at the time of publication.

Sidney Weinhouse