AACR SPECIAL CONFERENCE IN CANCER RESEARCH

CHEMICALS, MUTATIONS, AND CANCER
Co-Sponsored by the National Cancer Institute of Canada

December 7-12, 1992
Banff Springs Hotel, Banff, Alberta, Canada

CONFERENCE CHAIRPERSON
Lawrence A. Loeb / Seattle, WA

SCIENTIFIC PROGRAM

Keynote Address
Lawrence A. Loeb / Seattle, WA

Lesion Structure
John M. Essigmann / Cambridge, MA
Kenneth Breslauer / Piscataway, NJ
Paul Hopkins / Seattle, WA
Dinesh J. Patel / New York, NY

The Biochemistry of Mutagenesis
G. Peter Beardsley / Cambridge, MA
Douglas E. Brash / New Haven, CT
Leonard C. Erickson / Maywood, IL
Arthur P. Grollman / Stony Brook, NY
B. Singer / Berkeley, CA

DNA Damage and Mutations by Oxygen Free Radicals
Robert A. Floyd / Oklahoma City, OK
Max Costa / Tuxedo, NY
Shosuke Kawanishi / Kyoto, Japan
Lawrence J. Marnett / Nashville, TN
Susumu Nishimura / Tsukuba, Japan

Replication and Transcription
Philip C. Hanawalt / Stanford, CA
Harrison Echols / Berkeley, CA
Myron F. Goodman / Los Angeles, CA
Thomas A. Kunkel / Research Triangle Park, NC
Daniel Reines / Atlanta, GA

DNA Repair Diseases
Veronica M. Maher / East Lansing, MI
R. Stephen Lloyd / Nashville, TN
Roger A. Schultz / Baltimore, MD
Christine A. Weber / Livermore, CA
Malcolm C. Paterson / Edmonton, Canada

Endogenous Mutagenesis
Leona D. Samson / Boston, MA
Mark Meuth / Salt Lake City, UT
Jeffrey H. Miller / Los Angeles, CA
Roeland M. Schaaper / Research Triangle Park, NC
Mutsuo Sekiguchi / Fukuoka, Japan

Genomic Instability
Thea D. Tisty / Chapel Hill, NC
Frederick W. Alt / New York, NY
Curtis C. Harris / Bethesda, MD
Bernard S. Strauss / Chicago, IL
Ted Weinert / Tucson, AZ

Genetic Homeostasis
Robert H. Haynes / Toronto, Canada
Bruce Demple / Boston, MA
Carol A. Gross / Madison, WI
Peter Herrlich / Karlsruhe, Germany
Miroslav Radman / Paris, France

Information and Application Forms
American Association for Cancer Research
Public Ledger Building
620 Chestnut Street, Suite 816
Philadelphia, PA 19106-3483

(215) 440-9300 (215) 440-9313 (FAX)

Application Deadline: October 26, 1992
AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Genetics of Cancer

November 4-8, 1992
Marriott Hilton Head Resort, Hilton Head, South Carolina

Supported by a Generous Grant from the General Motors Cancer Research Foundation

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Raymond L. White / Salt Lake City, UT

SCIENTIFIC PROGRAM

Keynote Address
Robert A. Weinberg / Cambridge, MA

Inherited Cancer Genes
Bruce A.J. Ponder / Cambridge, England
Raymond L. White / Salt Lake City, UT
Frank McCormick / Emeryville, CA
Arnold J. Levine / Princeton, NJ
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Genetic Mechanisms
Carmen Sepulvado / La Jolla, CA
Carlo M. Croce / Philadelphia, PA
Neal G. Copeland / Frederick, MD

Molecular Genetics of Mitosis
George F. Vande Woude / Frederick, MD
Carol Greider / Cold Spring Harbor, NY
Andrew Murray / San Francisco, CA
David Beach / Cold Spring Harbor, NY
Erich A. Nigg / Lausanne, Switzerland

Genetic Instability
Geoffrey Wahl / San Diego, CA
C. Thomas Caskey / Houston, TX
Walton Fangman / Seattle, WA

Genetics and Cell Commitment
Stuart A. Aaronson / Bethesda, MD
Mariano Barbacid / Princeton, NJ
M. Geoffrey Rosenfeld / La Jolla, CA
David Anderson / Pasadena, CA
Leo Sachs / Rehovot, Israel

Animal Models
Mario Capecchi / Salt Lake City, UT
Douglas Hanahan / San Francisco, CA
Erwin Wagner / Vienna, Austria

Programmed Cell Death
Stanley J. Korsmeyer / St. Louis, MO
H. Robert Horvitz / Cambridge, MA
John T. Isaacs / Baltimore, MD
Peter Kramer / Heidelberg, Germany

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Normal and Neoplastic Growth and Development

October 18-22, 1992
Chatham Bars Inn, Chatham (Cape Cod), Massachusetts

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PROGRAM COMMITTEE
Edward E. Harlow / Charlestown, MA
Peter M. Howley / Bethesda, MD
David M. Livingston / Boston, MA

SCIENTIFIC PROGRAM

Keynote Address
Robert A. Weinberg / Cambridge, MA

Hematopoiesis I
Irving L. Weissman / Stanford, CA
Charles J. Sherr / Memphis, TN
Alan Bernstein / Toronto, Canada
Elliott D. Kieff / Boston, MA

Hematopoiesis II
Ihor Lemischka / Princeton, NJ
Bruce Mayer / New York, NY
Irvin S. Chen / Los Angeles, CA
Flossie Wong-Staal / La Jolla, CA

Hematopoiesis III
Irwin D. Bernstein / Seattle, WA
Jerry M. Adams / Melbourne, Australia
Joseph B. Bolon / Princeton, NJ
Anton Berns / Amsterdam, The Netherlands

DNA Tumor Viruses
Peter M. Howley / Bethesda, MD
Don Ganem / San Francisco, CA
Joseph R. Nevins / Durham, NC
Sara A. Courtneidge / Heidelberg, Germany

Colon Cancer
Arnold J. Levine / Princeton, NJ
Eric R. Fearon / Baltimore, MD
Steven Powell / Baltimore, MD
Frank McCormick / Emeryville, CA

Myogenesis
Stephen J. Tapscott / Seattle, WA
Peter K. Vogt / Los Angeles, CA
Webster K. Cavenee / La Jolla, CA

Tumor Suppressor Genes
Edward E. Harlow / Charlestown, MA
David M. Livingston / Boston, MA
David E. Housman / Cambridge, MA
Carol L. Prives / New York, NY

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Early attempts at understanding the age profiles of cancer incidence are now assuming renewed interest as the genes causing and preventing cancer are bringing new insights into the processes of cancer initiation and development. Some cancers, such as retinoblastoma, Wilms' tumor, and some leukemias, peak early in life, whereas cancers of the testis, cervix, brain, and, in certain populations, liver occur in late adulthood or middle age. However, most cancers, including colon, breast, prostate, and others, increase steeply as a function of advanced age. In one of two classes of models proposed by Armitage and Doll in the late 1950s (Br. J. Cancer, 11: 161–169, 1957), cancer arises from \( n \) mutations in critical genes, either in any order, i.e., the multitif model, or in a particular sequence, i.e., the multistage model. In the second class of models, the clonal growth model, a first mutation produces a clone of susceptible cells the population expansion of which leads to a second mutation. Cancer arises early with a high frequency of either or both mutations.

In a series of mathematical analyses of selected epidemiological data, Wilfred Donald Stein, pictured on this issue's cover, has brought out some extremely interesting clues to human cancer development based on age-incidence profiles, as described recently in *Advances in Cancer Research* (56: 161–213, 1991). Highlights of his findings are illustrated in the three figures reproduced on the cover. The figure on the left, analyzing data from Waterhouse et al. (Cancer Incidence in Five Continents, IARC Vol. 4, 1982), shows that, for bladder cancer and multiple myeloma, a clonal growth model in which a limited fraction of the whole population is at risk gives the best fit. This is not the case for leukemia. Similar treatment for stomach cancer, shown in the bottom figure, analyzing data of Manton and Stallard (Int. J. Epidemiol., 11: 49–61, 1982) for white American males, exhibits a striking feature. Whereas the data for the cohorts born in 1880, 1890, and 1900 show a similar age incidence profile, peaking at 80 years, the susceptibility declines markedly with the cohorts born most recently. Panel b of this figure, which plots data for 5 cohorts born over 5 decades, from 1890 to 1920, indicates that the risk for cancer declines according to the ratios 1:0.62, 0.40, 0.26, and 0.15 as the cohorts advance from 1880 to 1920. Evidently some factor in cancer development is being reduced as these cohorts advance. Similar analyses for cancer of the cervix also indicate decreased susceptibility in more recent cohorts but increased incidence at earlier ages, suggesting that exposure to a causative agent has occurred at an earlier period.

The figure on the top right, analyzing data of Lubin et al. (Br. Med. J., 288: 1953–1956, 1984), sheds interesting light on the effect of smoking cessation on lung cancer risk as a function of years elapsed since cessation of smoking, after varying periods of smoking. For the longest term smokers, 50+ years, the risk of subsequent lung cancer drops little after cessation whereas after a shorter period of smoking the risk drops markedly; for those who smoked 1 to 19 years, the subsequent risk falls to that of nonsmokers. These data are consistent with the clonal growth model in which smoking enhances the rate of initiation of transformed cells. For long-term smokers, clones of transformed cells are already large and susceptible to further spontaneous mutations, even in the absence of further smoking (Moolgavkar and Knudson, J. Natl. Cancer Inst., 66: 1037–1052, 1981).

These analyses emphasize the potential of the mutual benefits of epidemiological information considered in terms of the rapidly accumulating identification of the nature and sequence of mutations underlying cancer development.

Dr. Stein was born in Durban, South Africa, and after his early education in that country he received the Ph.D. degree in biophysics from the University of London. Since 1970, he has been a member of the faculty of the Hebrew University, Jerusalem, Israel, where he is now Professor of Biophysics. He has lectured widely and conducted research in the United States and Britain, principally in the field of membrane transport, and has published a long list of original papers, book chapters, and three books, the latest of which is "Channels, Carriers and Pumps: An Introduction to Membrane Transport," Academic Press, 1990. He is now pursuing his interest in the multidrug transporter and in cancer epidemiology at the National Cancer Institute, Bethesda, MD.

The figure on the left was obtained through the courtesy of the *Journal of Theoretical Biology* (165: 95–122, 1990) and the figures on the bottom and on the top right from *Advances in Cancer Research* (57: 161–213, 1991).

Sidney Weinhouse