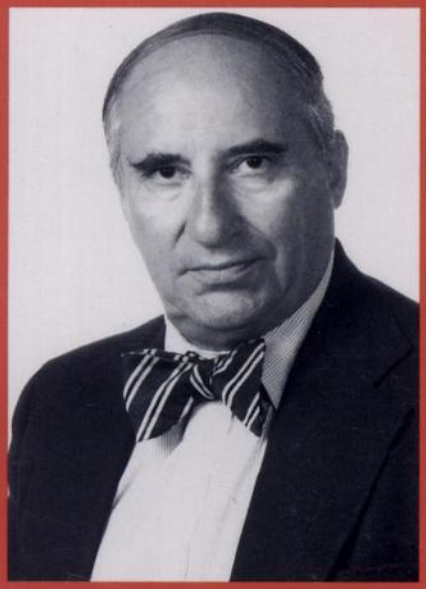
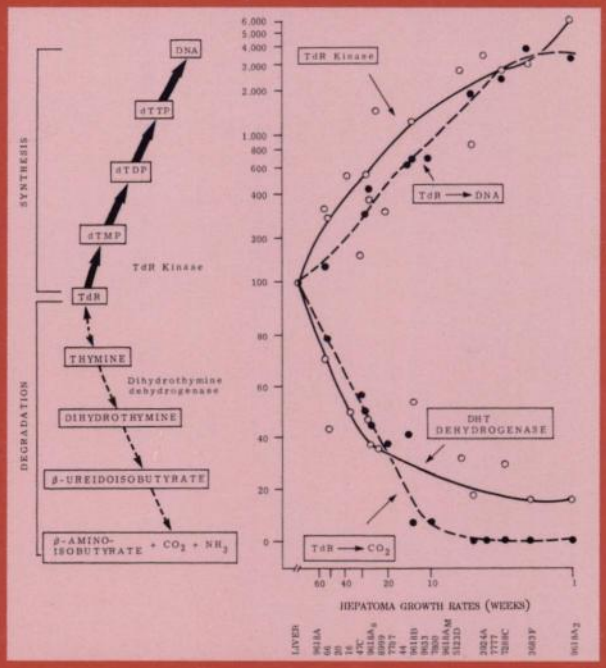
Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH





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AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Cytokines and Cytokine Receptors

October 14-18, 1995
The Sagamore, Bolton Landing (Lake George), New York

CONFERENCE CHAIRPERSONS

Steven Gillis / Seattle, WA
Douglas E. Williams / Seattle, WA

SCIENTIFIC PROGRAM

Keynote Address
Joost J. Oppenheim / Frederick, MD

Cytokines and Hematopoiesis
Manfred R. Keller / Ann Arbor, MI
Stewart D. Lyman / Seattle, WA
William P. Sheridan / Thousand Oaks, CA
Michael J.P. Lawman / Orlando, FL
Jonathan Drachman / Seattle, WA
Pamela Hunt / Thousand Oaks, CA
Connie J. Eaves / Vancouver, B.C, Canada
Katherine J. Turner / Cambridge, MA

Cytokines and Lymphopoiesis
Michael I. Lotze / Pittsburgh, PA
Serge LeBecque / Dardilly, France
David H. Lynch / Seattle, WA
Mary K. Kennedy / Seattle, WA
Teresa M. Foy / Lebanon, NH
John A. Schmidt / Rahway, NJ

Cytokines and Infectious Disease/ Cytokine Effects-Implications for Disease
Steven A. Miles / Los Angeles, CA
Steven G. Reed / Seattle, WA
William E. Paul / Bethesda, MD
Lawrence M. Lichtenstein / Baltimore, MD

Cytokine Receptors - Biological and Clinical Implications
Marc Feldmann / London, England
Thomas A. Waldmann / Bethesda, MD
Roy A. Black / Seattle, WA

Cytokine Signal Transduction
Tadamitsu Kishimoto / Osaka, Japan
Thomas J. Schall / Palo Alto, CA
Klaus Pfizenmaier / Stuttgart, Germany
Melanie K. Spriggs / Seattle, WA
David J. Pickup / Durham, NC

Additional Speakers to be Announced

Applicants are encouraged to submit abstracts for poster presentation.

Information and Application Forms

American Association for Cancer Research
Public Ledger Building, Suite 816
150 South Independence Mall West
Philadelphia, PA 19106-3483
215-440-9300 215-440-9313 (FAX)

AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Cancer Susceptibility Genes and Molecular Carcinogenesis

February 19-25, 1996
The Keystone Resort, Keystone, Colorado

CONFERENCE CHAIRPERSONS

Allan Balmain / Glasgow, Scotland
Curtis C. Harris / Bethesda, MD
Kenneth Olden / Research Triangle Park, NC

SCIENTIFIC PROGRAM

Keynote Address
Harold Varmus / Bethesda, MD

Genetic Susceptibility of Animal Models - Inbred Strains
William F. Dove / Madison, WI
Norman R. Drinkwater / Madison, WI
Cheryl Lyn Walker / Smithville, TX
Peter Demant / Amsterdam, The Netherlands

Genetic Susceptibility of Animal Models - Transgenic and Knockout
Douglas Hanahan / San Francisco, CA
Tyler E. Jacks / Cambridge, MA
Michael P. Rosenberg / Research Triangle Park, NC

Genetic Susceptibility of Humans - Xenobiotic Metabolism
Frank J. Gonzalez / Bethesda, MD
Fred F. Kadlubar / Jefferson, AR
Peter G. Shields / Bethesda, MD
C. Roland Wolf / Dundee, Scotland

Genetic Susceptibility of Humans - DNA Repair
Isabel Mellon / Lexington, KY
Jan H. Hoeijmakers / Rotterdam, The Netherlands

Genetic Susceptibility of Humans - Tumor Suppressor Genes
David P. Lane / Dundee, Scotland
Louise C. Strong / Houston, TX
Curtis C. Harris / Bethesda, MD

Senescence and Terminal Differentiation
J. Carl Barrett / Research Triangle Park, NC
Carol W. Greider / Cold Springs Harbor, NY
Jennifer A. Pietenpol / Nashville, TN
Harold L. Moses / Nashville, TN

Apoptosis
Tona M. Gilmer / Research Triangle Park, NC
Judith Campisi / Berkeley, CA
Michael B. Kastan / Baltimore, MD
Eileen White / Piscataway, NJ
Scott W. Lowe / Cambridge, MA

Molecular Carcinogenesis in Animal Models and Humans - Skin
Allan Balmain / Glasgow, Scotland
Douglas E. Brash / New Haven, CT

Molecular Carcinogenesis in Animal Models and Humans - Liver and Breast
Henry C. Pitot / Madison, WI
Xin W. Wang / Bethesda, MD
Roger W. Wiseman / Research Triangle Park, NC
Mary-Claire King / Seattle, WA

Molecular Carcinogenesis in Animal Models and Humans - Brain
Terry A. Van Dyke / Chapel Hill, NC
Paul Kleihues / Lyon, France

Additional Speakers to be Announced

Applicants are encouraged to submit abstracts for poster presentation.

Application deadline: November 3, 1995

Information and Application Forms

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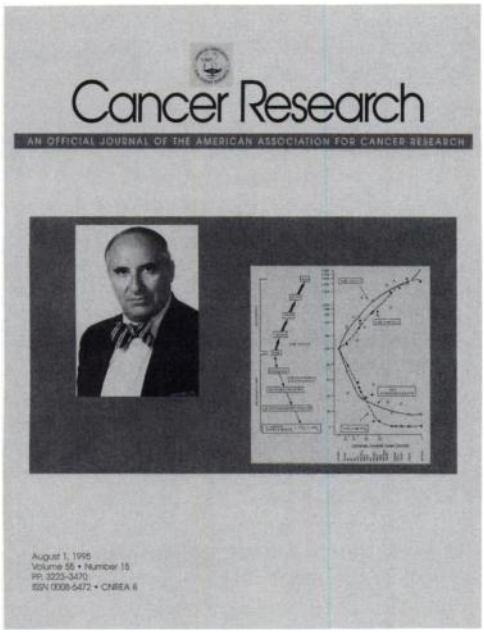
COVER LEGEND



George Weber (*cover*), was the first to demonstrate the absence of an enzyme activity, glucose-6-phosphatase, in chemically induced rat hepatoma (Cancer Res., *15:* 105–108, 1955), and he showed that glucose-6-phosphate utilization is profoundly altered in hepatomas (Cancer Res., *18:* 974–979, 1958). He is known for his introduction of the key enzyme concept, the molecular correlation concept, and the ideas of enzyme pattern-targeted chemotherapy (Adv. Cancer Res., *6:* 403–494, 1961; N. Engl. J. Med., *296:* 486–493 and 541–551, 1977; Cancer Res., *43:* 3466–3492, 1983). In hepatomas of different growth rates and degrees of differentiation, he showed that there is an ordered pattern of transformation- and progression-linked alterations in the activities of opposing key enzymes and metabolic pathways in carbohydrate, purine, and pyrimidine metabolism. (See illustration on cover, reproduced from Cancer Res., *43:* 3466–3492, 1983.) The biochemical imbalance is strongly conserved in murine, avian, and human neoplasms (*ibid.*; J. Biol. Chem., *257:* 432–438, 1982).

Dr. Weber suggested that the stringently linked enzymic alterations should be sensitive targets in chemotherapy. He was the first to report that the purine and pyrimidine salvage enzyme activities in cancer cells are higher than those of the key enzymes of *de novo* biosynthesis, and he designed combinations of drugs that inhibited both types of enzymes, yielding synergistic cytotoxicity (Cancer Res., *43:* 3466–3492 and 1616–1619, 1983; Biochem. Pharmacol., *36:* 3641–3646, 1987).

Dr. Weber and his associates discovered 60 enzymic and metabolic alterations from the normal controls in rat hepatomas and sarcomas, in human ovarian, kidney, and colon carcinomas, and in breast carcinoma cells. His current studies show 31- to 95-fold increases in the steady-state activities of signal transduction enzymes in human ovarian and breast carcinoma cells. The increased signal transduction enzyme activities can be down-regulated by tiazofurin or quercetin (Cancer Res., *54:* 2611–2614 and 5574–5578, 1994; Life Sci., *55:* 1487–1492, 1994; Biochem. Biophys. Res. Commun., *208:* 425–431, 1995).

Born in Budapest, Hungary, Dr. Weber received the B.A. in 1950 and the M.D. in 1952 from Queen's University, Kingston, Ontario, Canada. While early in his career he worked at Harvard Medical School and at the Radcliffe Infirmary in Oxford, United Kingdom, Dr. Weber has spent most of his scientific life at Indiana University School of Medicine, Indianapolis, IN. He joined the University staff as Associate Professor of Biochemistry and Microbiology in 1959 and then rose to Professor of Pharmacology in 1961. In 1974, he was appointed Professor and Director of the Laboratory for Experimental Oncology, a research department at the University where he could thus pursue his original purpose in studying medicine.

His objective in elucidating the biochemical strategy of cancer cells for a rational design of chemotherapy was realized in 1987 when he and his clinical colleagues at Indiana University started a clinical trial for end-stage leukemic patients. The treatment was based on observations made with his associates that the activity of IMP dehydrogenase, the rate-limiting enzyme of *de novo* GTP biosynthesis, markedly increased in all cancer cells, particularly in rapidly proliferating ones such as leukemic blast cells [Nature (Lond.), *256:* 331–333, 1975; Adv. Enzyme Regul., *27:* 405–433, 1988]. Using tiazofurin, an inhibitor of IMP dehydrogenase, Dr. Weber and his associates designed a clinical protocol that yielded a 77% response rate, including complete responses, in patients with chronic granulocytic leukemia in blast crisis (Int. J. Cell Cloning, *8:* 161–170, 1990; Adv. Exp. Med. Biol., *309:* 287–292, 1991). Tiazofurin induced differentiation and, through decreasing GTP concentration, resulted in down-regulation of *ras* oncogene expression in the blast cells of leukemic patients (Cancer Commun., *3:* 61–66, 1991). Tiazofurin also reduced the concentration of the *ras*-GTP complex in K562 cells (Oncol. Res., *5:* 161–164, 1993). Dr. Weber and his associates reported that the increased IMP dehydrogenase activity in the blast cells of human leukemic patients (J. Biol. Chem., *265:* 5292–5295, 1990; *ibid.*, *266:* 506–509, 1991) was due to up-regulation of type II mRNA production (Cancer Res., *51:* 3886–3890, 1991; *ibid.*, *52:* 258–261, 1992).

Dr. Weber has published 261 primary peer-reviewed research papers and 80 reviews. He has trained over 100 postdoctoral students, who are currently active primarily in the field of cancer research and many of whom now occupy Professorships and Chairs in universities around the world. He served as Chairperson of the Experimental Therapeutics Study Section at the NIH, and he has been active on many other national and international committees, including representing the AACR on the USA National Committee of the International Union Against Cancer (1989–1993) and in the General Assembly of the 15th International Cancer Congress (1990–1991). He has been an active member of the AACR since 1956, contributing his time and talents to its committees and programs, including the Publications Committee, Clowes Award Committee, Program Committee, and Special Memberships Committee. He also served with distinction as an Associate Editor for *Cancer Research* for nearly 20 years. And, in 1988–1989, he assumed the duties of Chairperson of the Selection Committee for the Editor-in-Chief of the journal.

Dr. Weber is internationally known for his annual symposium, entitled "Advances in Enzyme Regulation," and the publication of the same name emanating from the meeting, which he edits with Associate Editor, Catherine E. Forrest Weber, his wife. The conference, which is held at Indiana University School of Medicine each year, and *Advances in Enzyme Regulation* (Pergamon Press, Oxford, United Kingdom), which is now in its 36th volume, have a significant impact on research in enzymology, metabolic regulation, and molecular biology in normal and cancer cells.

Dr. Weber's accomplishments have been recognized with various awards including the G. H. A. Clowes Memorial Award of the AACR (1982), the G. F. Gallanti Prize in Enzymology of the International Society of Clinical Chemists (1984), and the J. H. Wilkinson Award of the International Society for Clinical Enzymology (1987). He received an Outstanding Investigator Award from the National Cancer Institute (1987–1994) and honorary doctoral degrees from universities in Italy, Hungary, Germany, and Japan. The medical students at Indiana University have honored him twice with the Golden Apple Award for "Best Preclinical Professor." In 1990, Indiana University promoted him to the Distinguished Professor rank. Recently, he was awarded a 3-year M. Panic Professorship in Oncology (1995–1997) and a Wellcome Professorship (1995–1996).

We are indebted to Joseph G. Cory for the material for this cover feature.

Sidney Weinhouse