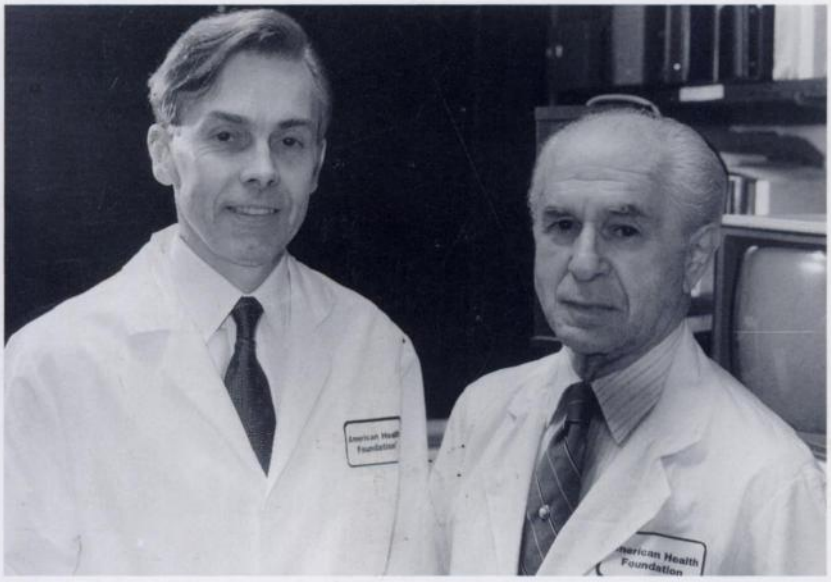
Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



April 15, 1995
Volume 55 • Number 8
PP. 1603–1810
ISSN 0008-5472 • CNREA 8

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 9 - July 16, 1995

- 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.

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Ann D. Thor, University of Vermont at Burlington, Burlington, VT
Frederick Waldman, University of California, San Francisco, CA

Additional Faculty to be Announced

**Member of the Workshop Executive Committee*

APPLICATION DEADLINE: MAY 5, 1995

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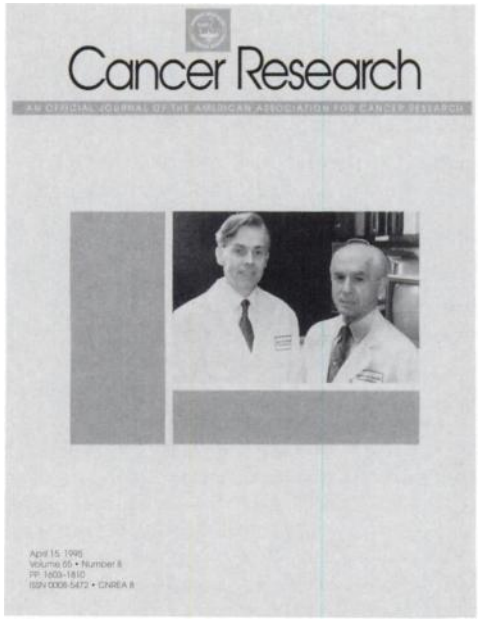
COVER LEGEND



This cover features Gary M. Williams and John H. Weisburger, who have investigated genotoxicity, a characteristic of some, but not all, carcinogens. Beginning in the 1950s, Elizabeth and James Miller, Peter Magee, Emmanuel Farber, and others established that a critical effect of carcinogens is interaction with DNA and alteration of its structure and function. At a 1971 meeting in Sweden on the Evaluation of Genetic Risks of Environmental Chemicals, a working group consisting of Lars Ehrenberg, Peter Brookes, Hermann Druckrey, Bengt Lagerlöf, Jack Litwin, and Dr. Williams introduced the term "genotoxic" as a general definition of such properties (Ambio Special Report No. 3, pp. 15–16. Stockholm: Royal Swedish Acad. Sci., 1973). Tests for bacterial mutagenicity as developed by Bruce Ames (Proc. Natl. Acad. Sci. USA, *70:* 2281, 1973) or for DNA repair in hepatocytes as established by Dr. Williams (Cancer Lett., *1:* 273, 1976) characterized the genotoxic properties of a chemical. However, not all carcinogens were found to be DNA-reactive. In 1977, Drs. Weisburger and Williams proposed an essential distinction (*Structural Correlates of Carcinogenesis and Mutagenesis,* Proc. FDA Sci. Symp., pp. 45–52. Rockville, MD: FDA Office of Health Affairs, 1978; J. Assoc. Off. Anal. Chem., *62:* 857, 1979). Genotoxic carcinogens have the structure typical of electrophiles or radical cations, and thus react with DNA, whereas epigenetic carcinogens were postulated to produce cancer through epigenetic cellular effects, which nevertheless ultimately could lead to the emergence of genetically abnormal neoplastic cells. Epigenetic agents include promoters that enhance the growth, development, and further genetic alterations of transformed cells. In 1980, Drs. Weisburger and Williams provided a comprehensive assignment of many types of carcinogens to these two categories based on mechanism of action (*Casarett and Doull's Toxicology,* Ed. 2, pp. 84–138. New York: Macmillan Co., 1980). Refinements in detection of the DNA reactivity, such as through the use of isotopically labeled carcinogens or the ^{32}P-postlabeling assay introduced by Kurt Randerath, provided further evidence for the basic distinction.

Most human carcinogens are genotoxic, leading to mutations in oncogenes and tumor suppressor genes. The rate of cell turnover is key to the fixation of the genetic lesion. Nongenotoxic agents also play a role in human carcinogenesis. For example, dietary fat enhances the risk of cancer of the breast or colon through promoting actions. A vital aspect of cancer prevention is to minimize exposure to DNA-reactive carcinogens as well as to reduce exposure to nongenotoxic carcinogens to levels below their thresholds.

Dr. Williams earned an M.D. degree from the University of Pittsburgh School of Medicine, where he was influenced by Dr. Farber to pursue studies in pathology and cancer research. After 2 years at the Massachusetts General Hospital, he joined Dr. Weisburger at the National Cancer Institute where they developed effective procedures for growing and transforming epithelial rat liver cells *in vitro.* Dr. Williams earned an IARC fellowship at the Wenner Gren Institute in Stockholm, then rejoined Dr. Farber at Temple University, Philadelphia, PA. In 1975, he became Chief of the Division of Pathology and Toxicology at the American Health Foundation in Valhalla, NY, where he has pursued research on the pathogenesis of chemically induced cancers and the relevant mechanisms. In 1986, he was appointed Director of Medical Sciences at the Foundation. Dr. Williams has published more than 350 papers and has served on many advisory and editorial boards. He is Editor-in-Chief of *Cell Biology and Toxicology.* The Society of Toxicology recognized him with the Arnold J. Lehman Award in 1982 for investigations on the mechanisms of action of carcinogens. Dr. Williams has been a member of the American Association for Cancer Research (AACR) since 1974.

Dr. Weisburger earned a Ph.D. degree in Organic Chemistry and Cancer Research under Francis E. Ray at the University of Cincinnati in 1949. He and Elizabeth Weisburger were USPHS officers in the Laboratory of Biochemistry, National Cancer Institute, in Bethesda, MD. They did pioneering research on the mechanisms of the carcinogen 2-acetylaminofluorene. As Head of the Carcinogen Screening Section, Experimental Pathology Branch, Etiology, and later as Director of the Bioassay Segment, Carcinogenesis Programs, Dr. Weisburger explored improved methods of testing chemicals for carcinogenicity. In 1972, Dr. Weisburger became Vice President for Research at the American Health Foundation in New York City and later in Valhalla, NY. He established a research program in nutrition and cancer on heterocyclic amines in cooked foods and on tea as a chemopreventive agent. He has published over 450 pages and has served on a number of editorial boards. The University of Umeå, Sweden, awarded him an honorary M.D., and the Society of Toxicology presented him with the Merit Award, while the Mid-Atlantic chapter of the Society honored him with the Ambassador of Toxicology Award. In addition, he received the Meyer and Anna Prentice Award from the Michigan Cancer Center, and the Japanese Cancer Association made him an Honorary Life Member. The American Society of Preventive Oncology, the American Health Foundation, and the New Jersey Commission for Cancer Research awarded him Distinguished Service Medals. Dr. Weisburger has been a long-standing member of the AACR, lending his time and talents to various facets of the organization by serving on AACR committees and contributing to AACR publications (*Cancer Research* Cover Editorial Board and *Cancer Epidemiology, Biomarkers & Prevention* Editorial Advisory Board).

We are indebted to those featured for the information and photograph for this cover.

Sidney Weinhouse