



Cancer Research



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AMERICAN ASSOCIATION FOR CANCER RESEARCH SCIENTIFIC CONFERENCES

JULY 1-8, 1994

Molecular Biology In Clinical Oncology

A Workshop for Clinical Oncologists in Training
Supported by a Generous Grant from the National
Cancer Institute

Chairpersons: Stephen H. Friend, Charlestown,
MA; L. Michael Glode, Denver, CO
The Given Institute, Aspen, CO

JULY 17-24, 1994

Histopathobiology of Neoplasia

The Edward A. Smuckler Memorial Workshop for
Predoctoral and Postdoctoral Fellows
Contemplating Careers in Basic Cancer
Research

Supported by a Generous Grant from the National
Cancer Institute

Chairperson: Michael W. Lieberman, Houston, TX
Keystone Conference Center, Keystone, CO

OCTOBER 16-20, 1994

***Transcriptional Control of Cell Growth
and Differentiation***

Chairpersons: Eric N. Olson, Houston, TX; Bruce
M. Spiegelman, Boston, MA
Chatham Bars Inn, Chatham (Cape Cod), MA

NOVEMBER 7-11, 1994

***Modern Developments In Cancer
Therapeutics***

Joint Meeting with Academia Sinica
Chairperson: Yung-chi Cheng, New Haven, CT
Academia Sinica, Taipei, Taiwan, R.O.C.

NOVEMBER 29-DECEMBER 4, 1994

Translational Research In Cancer

Chairperson: Carlo M. Croce, Philadelphia, PA
Grove Park Inn, Asheville, NC

DECEMBER 8-13, 1994

***Basic and Clinical Aspects of
Prostate Cancer***

Chairperson: Donald S. Coffey, Baltimore, MD
Marriott's Rancho Las Palmas Resort, Rancho
Mirage (Palm Springs), CA

JANUARY 14-19, 1995

***Mechanism of Action of Retinoids,
Vitamin D, and Steroid Hormones***

Chairpersons: Michael B. Sporn, Bethesda, MD;
Ronald M. Evans, San Diego, CA; David
Mangelsdorf, San Diego, CA
Whistler Resort and Conference Center, Whistler,
B.C., Canada

FEBRUARY 13-18, 1995

***Molecular Biology of Cancer: Implications
for Prevention and Therapy***

Joint Meeting with Japanese Cancer Association
Chairpersons: Lee W. Wattenberg, Minneapolis,
MN; Masaaki Terada, Tokyo, Japan
Maui Marriott Hotel, Maui, HI

MARCH 19-22, 1995

86th Annual Meeting

Chairperson: Donald S. Coffey, Baltimore, MD
Metro Toronto Convention Centre, Toronto,
Ontario, Canada
(Abstract Deadline: October 14, 1994)

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

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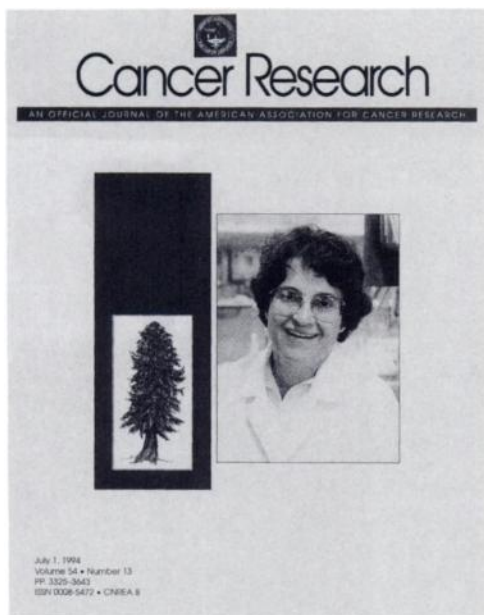
- METASTATIC MELANOMA AND KIDNEY CANCER •
- STAGE II OR LOCALLY ADVANCED BREAST CANCER •
- METASTATIC COLORECTAL CANCER TO THE LIVER •
- LOCOREGIONAL GASTRIC OR PANCREATIC CANCER •
- MESOTHELIOMA, PULMONARY METASTASES, STAGE III A, B LUNG CANCER OR ESOPHAGEAL CANCER •
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A Public Service Announcement Courtesy of this Publication

COVER LEGEND



The discovery, structure elucidation, and synthesis of taxol, a natural product anticancer drug derived from the bark of the Pacific yew (*Taxus brevifolia*) (cover), are major achievements stemming from many years of effort, primarily sponsored by the National Cancer Institute. Taxol was discovered and isolated and its structure established by Monroe E. Wall, Mansukh C. Wani, and their collaborators (*J. Am. Chem. Soc.*, **93**: 2325–2327, 1971). Its antitumor action has been explored by many investigators, of whom Susan Band Horwitz (cover) is one of the leading figures [*Proc. Natl. Acad. Sci. USA*, **77**: 1561–1565, 1980; *Nature (Lond.)*, **277**: 665–667, 1979; *J. Cell Biol.*, **91**: 479–487, 1981; *Nature (Lond.)*, **367**: 593–594, 1994]. Its attraction for pharmacologists is its natural origin and unique diterpenoid structure. It proved to be a potent inhibitor of eukaryotic cell replication, blocking cells at the late G₂-M phase of the cell cycle, and promoting the stabilization of microtubules, thereby providing a novel approach to tumor chemotherapy.

The bad news has been the scarcity of taxol, for which a single 300-mg dose requires the sacrifice of a 100-year-old tree. The good news is that now taxol is readily available via partial synthesis from taxane precursors found in the needles of many *Taxus* species which constitute a renewable source. As a consequence, studies of the effects of taxol in combination with other cancer chemotherapeutic agents are currently under investigation at many clinical centers.

Of great interest have been the simultaneous reports of the total synthesis of taxol by two laboratories, that of R. C. Holton and collaborators at Florida State University, Tallahassee (*J. Am. Chem. Soc.*, **116**: 1597–1600, 1994) and that of K. C. Nicolaou *et al.* [*Nature (Lond.)*, **367**: 630–634, 1994] of the Scripps Institute and the University of California, San Diego. Different strategies were used, and the syntheses in both instances were long and complex, considered by experts to be “astonishing” and “fantastic” (*Chem. and Eng. News*, Feb. 21,

1994, pp. 32–36). At this time, neither synthesis is practical for large-scale production of taxol.

Taxol has significant activity against drug-refractory ovarian cancers and has been shown to have activity against breast and lung cancers (*J. Natl. Cancer Inst. Monogr.*, **15**: 1993). It offers novel, exciting prospects for the further development of antitumor agents and has set off major programs on the synthesis of derivatives (*Chem. and Eng. News*, May 9, 1994, p. 31).

Dr Horwitz is distinguished for her wide-ranging investigations into the pharmacology and therapeutic action of taxol and related agents. She received the B.A. from Bryn Mawr College and the Ph.D. in biochemistry from Brandeis University. After postdoctoral fellowships at Tufts and Emory Universities, she joined Albert Einstein College of Medicine in 1967. She is presently Falkenstein Professor of Cancer Research and an Associate Director of the Cancer Center. She has an impressive record of accomplishments in the pharmacology and therapeutics of anticancer agents, particularly camptothecin (*Biochem. Biophys. Res. Commun.*, **45**: 723–727, 1971), the epipodophyllotoxins (*Biochemistry*, **15**: 5443–5448, 1976), and bleomycin (*J. Biol. Chem.*, **256**: 11636–11644, 1981). Her outstanding work on taxol (*Pharmacol. & Ther.*, **25**: 83–125, 1984; *J. Biol. Chem.*, **269**: 3132–3134, 1994) has been a prime influence in understanding the nature and mechanisms of action of this drug on microtubule functions and its promising effects in ovarian, lung, and breast cancer. Dr. Horwitz has received many honors, including the Cain Memorial Award of the American Association for Cancer Research in 1992 and the American Society for Pharmacology and Experimental Therapeutics Award for Experimental Therapeutics in 1994. She has provided valuable service to the AACR, including membership on its Board of Directors from 1987 to 1990. She served as chairperson of the Rhoads Award Committee in 1991 and was on the AACR Special Conferences Committee from 1989 to 1992.

Dr. Wani received his Ph.D. in chemistry from the University of Indiana in 1950. Since 1962, he has been a member of the Research Triangle Institute in Research Triangle Park, N.C. In 1986, he advanced to Principal Scientist, chemistry and life sciences. His major efforts have been on the isolation and characterization of natural products, and the synthesis of anti-fertility and anticancer agents.

Dr. Wall was awarded the Ph.D. in 1939 in agricultural biochemistry from Rutgers University, N.J., and since 1960 has been at the same institute as Dr. Wani. Since 1983 he has held the title of Chief Scientist. Both have been recognized widely for their many important contributions. Drs. Wall and Wani were also featured on the March 15, 1994 cover of *Cancer Research* as winners of the 1994 Cain Memorial Award.

We are grateful to Drs. Horwitz, Wall, and Wani for their assistance in preparing the legend.

Sidney Weinhouse