Cellular and Molecular Targets of Cancer Therapy

The Forty-second Annual Symposium on Fundamental Cancer Research

October 24 - 27, 1989
Stouffer Presidente Hotel • Houston, Texas

Ernst W. Bertner Award Presentation and Memorial Lecture
Mechanisms of Selectivity of Antiviral Agents
Gertrude Elion, Wellcome Research Laboratories

Keynote Address
Novel Cytotoxic Agents Created by Gene Fusion
Ira Pastan, National Cancer Institute

PLASMA MEMBRANE TARGETS
Loss of Negative Growth Control by TGF-β in Malignancies: Mechanisms and Clinical Implications
Anita Roberts, NCI
Molecular Basis of Growth Suppression by Interferons
Adi Kimchi, Weizmann Institute
EGF and Its Receptor
Gordon Gill, UC at San Diego
Diversity of Multidrug Resistant Glycoproteins
Susan B. Horwitz, Albert Einstein

NUCLEAR TARGETS I
Role of the Nuclear Matrix
Donald S. Coffey, Johns Hopkins
Proto-oncogenes as Transcription Factors: Cooperativity between Fos and Jun at the AP-1 Binding Site
Thomas Curran, Roche
Nuclear Themes of Clinical Import
Mark A. Israel, NCI
Exploring the Therapeutic Potential of Topoisomerases
Warren E. Ross, University of Louisville
O*-methyl Guanine DNA Methyl Transferase: Its Role in Tumor Cell Drug Resistance and Strategies for Inhibition
Leonard C. Erickson, Loyola University
Wilson S. Stone Award Presentation and Memorial Lecture

CYTOPLASMIC TARGETS
Role of Protein Kinase C in Signal Transduction
Robert M. Bell, Duke
Control of ras Function by GAP
Frank McCormick, Cetus
Growth Regulation of Normal and Malignant Human Mammary Epithelium
Marc E. Lippman, Georgetown University
Oligodeoxynucleotides as Inhibitors of Gene Expression
Jack S. Cohen, NCI
Enzymatic Determinants of Cyclophosphamide Specificity and Resistance
O. Michael Colvin, Johns Hopkins

NUCLEAR TARGETS II
Molecular Mechanisms for Sequence Recognition of DNA: Biochemical and Biological Consequences
Laurence Hurley, University of Texas
Thymidylate Synthase as a Drug Target
Daniel V. Sant, UC at San Francisco
Molecular Models of Platinum – DNA Adducts
Stephen J. Lippard, MIT
DNA Repair at the Level of the Gene
Vilhelm A. Bohr, NCI

Special Lecture: Tumor Suppressor Genes
Robert A. Weinberg, MIT

Poster Session

NON-MALIGNANT TARGETS
Macrophage Recognition of Altered Self: Implications for Therapy of Cancer Metastasis
Israel J. Fidler, M. D. Anderson
A Multi-subunit Interleukin-2 Receptor: A Target for Immunotherapy of Cancer
Thomas A. Waldmann, NCI
Organ Matrix and Organ Growth Factors
Garth L. Nicolson, M. D. Anderson
Neovascularization as a Possible Target
Juliana Denkert, CRC Gray Laboratory
Molecular Biology of HIV
William A. Haseltine, Dana Farber

Symposium Cochairmen: William Plunkett, Ph.D. • William A. Brock, Ph.D.

THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

For registration information, please contact Pam Evans, Conference Services - HMB 131, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030. Phone: (713) 792-2222.
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Rules and official nomination forms are available from: Secretary, Award Committee, Bristol-Myers Award for Distinguished Achievement in Cancer Research, 345 Park Avenue, Suite 4100, New York, NY 10154, or (212) 546-5709.
The rapid advances that have occurred in the field of nitrosamine carcinogenesis since the pioneering discoveries by Magee and Barnes in London in the 1950s (Cancer Research cover, June 1970) and Druckrey in Freiburg, Germany, reported in the 1960s (Cancer Research cover, September 1973) were stimulated by the four scientists featured on this month’s cover.

In the late 1960s, Johannes Sander, at the School of Hygiene, University of Tübingen, Germany, found that nitrosamines could be formed in vivo, at the pH prevailing in the stomach, from nitrite and suitable precursor amines. He first demonstrated chemically (Z. Physiol. Chem., 349: 1691, 1968) and then through cancer induction in select organs (Z. Krebsforsch., 13: 54, 1969) that N-nitroso-N-methylbenzylamine or N-nitrosomorpholine was produced in vivo. Nitrate and nitrite are important food preservatives worldwide, and Sander’s discovery led to controls on the use of nitrite as a food additive. This reaction of nitrite on specific substrates may account for some human cancer in the stomach and esophagus (Banbury Rep., 12: 1982; Prev. Med., 16: 586, 1987).

It was held that tertiary amines do not react with nitrous acid (J. Chem. Ed., 40: 181, 1963), but Richard Loeppky, while working on his doctoral thesis at the University of Michigan under Professor P. A. S. Smith, showed that tertiary amines would form nitrosamines with nitrous acid (J. Am. Chem. Soc., 89: 1147, 1967). William Lijinsky, previously at the Epbley Institute for Research in Cancer, University of Nebraska Medical Center, and now at the Frederick Cancer Research Facility of the National Cancer Institute, is notable as one of the outstanding investigators of nitrosamines in recent years. Among his many contributions to this field was the discovery that a number of tertiary amine drugs and pesticides could react with nitrite to yield carcinogenic nitrosamines in vivo (Cancer Res., 34: 255, 1974).

Starting with a study of dimethylamine nitrosation (J. Natl. Cancer Inst., 44: 633, 1970), Sidney Mirvish, initially at the Weizmann Institute of Science in Israel and later at the Epbley Institute, compared the nitrosation kinetics of a series of amines and amides, thus evaluating which of these compounds was likely to yield significant amounts of nitrosamines or nitrosamides in vivo (Toxicol. Appl. Pharmacol., 31: 325, 1975). A major new discovery by Mirvish, Wallcave, Eagen, and Shubik was that the formation of hazardous nitrosamines in vivo could be blocked by vitamin C. The underlying mechanism was removal of nitrite [Science (Wash. DC), 177: 65, 1972; Cancer (Phila.), 58: 1842, 1986]. The addition of vitamin C when food is preserved with nitrite is now generally required worldwide. Overall, salting, pickling, and smoking of foods are declining, probably one reason for the decreasing incidence of stomach cancer in many parts of the world (J. Natl. Cancer Inst., 71: 629, 1975; Epidemiol. Rev., 8: 1, 1986).

Top left, Professor Johannes Sander, currently at the Staatliches Medizinuluntersuchungsamt, Hannover, Germany; bottom left, Richard N. Loeppky, Professor of Chemistry, University of Missouri, Columbia, MO; center, Professor Sidney Mirvish, Epbley Institute for Research in Cancer, University of Nebraska Medical Center, Omaha, NE; right, William Lijinsky, Director, Laboratory of Chemical and Physical Carcinogenesis, Frederick Cancer Research Facility, Frederick, MD. The formulations at top depict the formation of nitrosamines or nitrosamides from secondary amines or amides or of dimethyl-nitrosamine from a tertiary dimethylamine.

John H. Weisburger