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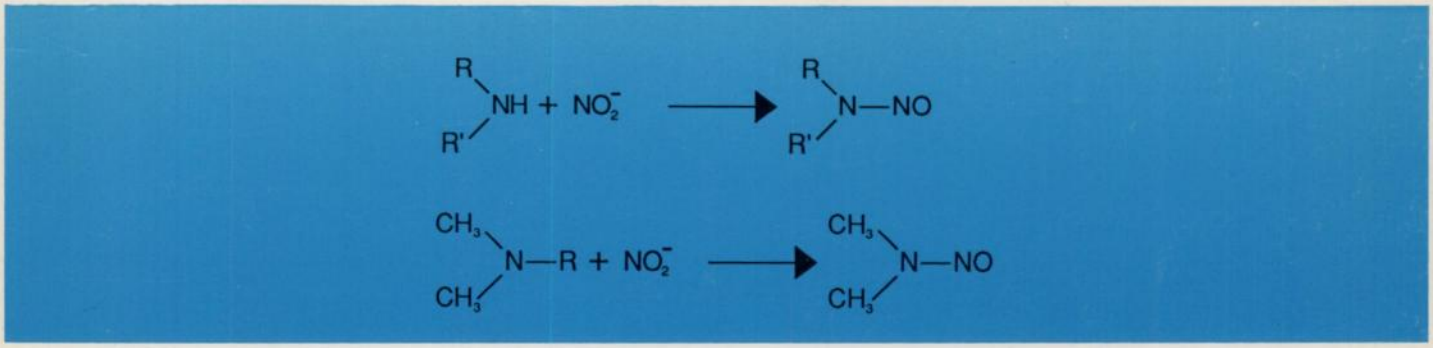

Cellular and Molecular Targets of Cancer Therapy

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-ß 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^6-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. Santi, 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 Supressor Genes
Robert A. Weinberg, MIT

Poster Session

NON-MALIGNANT TARGETS

Macrophage Recognition of Altered Self: Implications for Therapy of Cancer Metastasis
Isaiah 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

Neovasculature as a Possible Target
Juliana Denekamp, 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.

Thirteenth Annual Bristol-Myers Award for Distinguished Achievement in Cancer Research

Bristol-Myers Company presents an annual award to a scientist making an outstanding contribution in cancer research. The candidates for the award are to be nominated by medical schools, free-standing hospitals and cancer research centers.

Award: $50,000 U.S.

Deadline for Receipt of Nominations: **December 1, 1989**

Announcement of Award Recipient: **Spring 1990**

Selection Committee

Alan C. Sartorelli, Ph.D.	***Selection Committee Chairman,*** *Yale Comprehensive Cancer Center*
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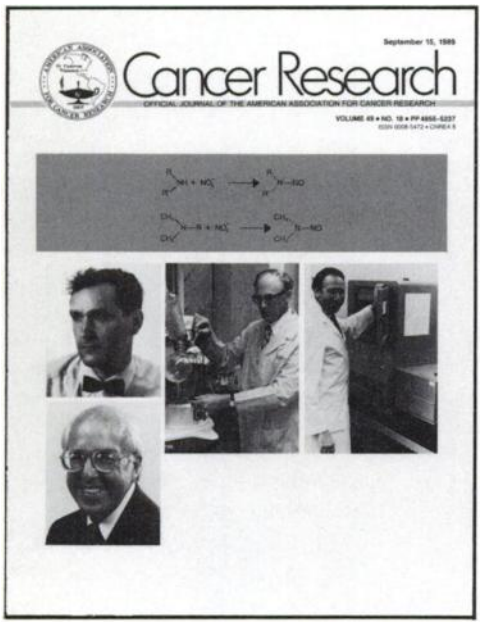
Rules and official nomination forms are available from: Secretary, Award Committee, Bristol-Myers Award for Distinguished Achievement in Cancer Research, 345 Park Avenue, Suite 4100, New York, NY 10154, or (212) 546-5709.

COVER LEGEND



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 Eppley 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 Eppley 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 Medizinaluntersuchungsamt, Hannover, Germany; *bottom left*, Richard N. Loeppky, Professor of Chemistry, University of Missouri, Columbia, MO; *center*, Professor Sidney Mirvish, Eppley 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 dimethylnitrosamine from a tertiary dimethylarylamine.

John H. Weisburger