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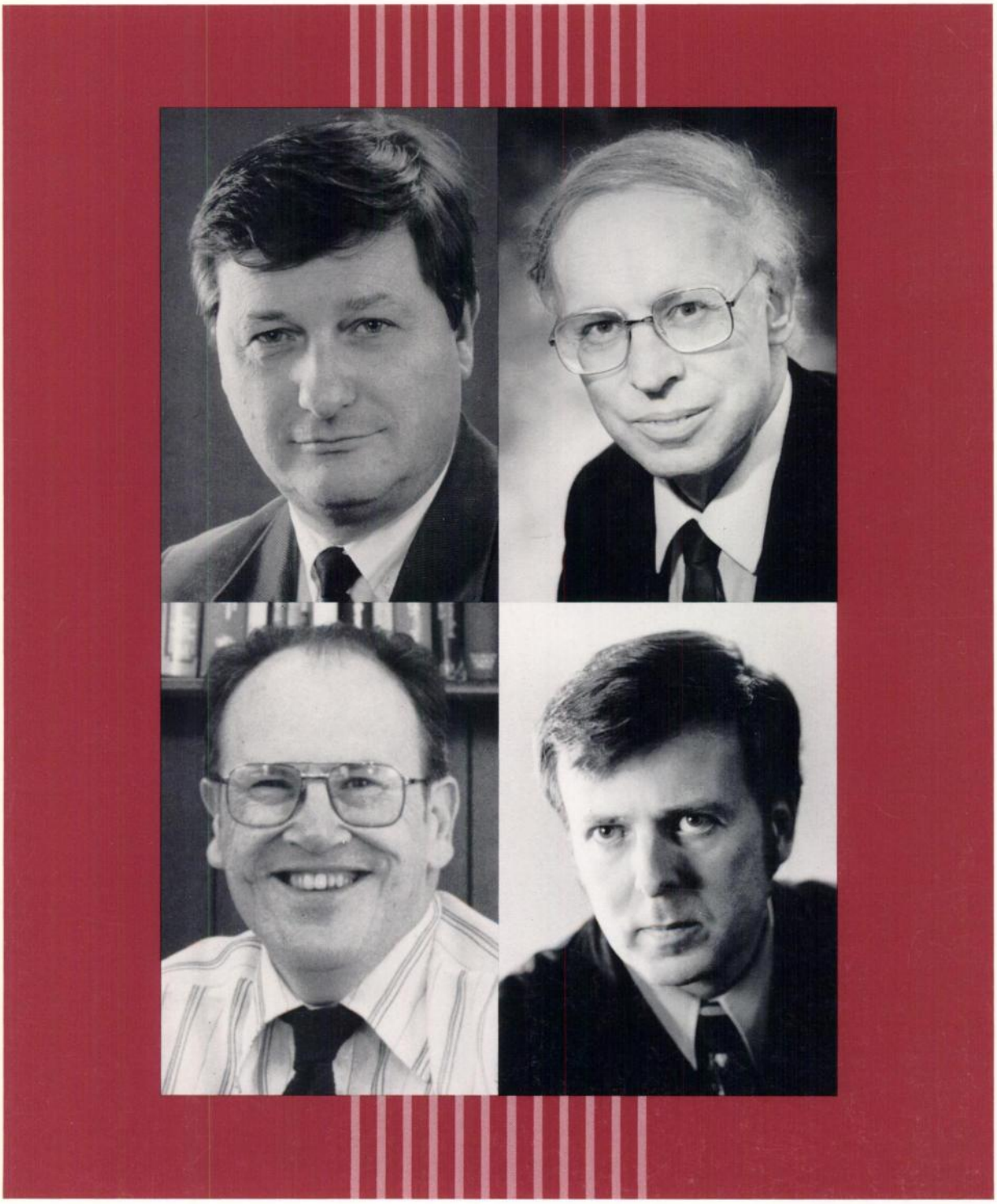

International Symposium on
PROGRESS AND PERSPECTIVES IN CHEMOPREVENTION OF CANCER
Milan, Italy, Istituto Nazionale Tumori, March 14-15, 1991

SUMMARY:

As thousands of chemical substances found in our environment can induce and/or promote cancer, why should other compounds able to inhibit cancerogenesis not exist as well? Chemoprevention, a term which really means the use of agents potentially capable of inhibiting or reversing the process of cancerogenesis, is a new branch of the medical science. This meeting of multi-disciplinary scientists will focus on this new branch from experimental to clinical research.

SCIENTIFIC COMMITTEE:

M. Baum (UK), C. Maltoni (I), R.C. Moon (USA), G. Peck (USA), M. Sporn (USA), and U. Veronesi (I).

SCIENTIFIC SECRETARY:

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MAIN TOPICS:

Experimental Aspects / Pharmacology and Toxicology / Clinical Experiences and Controlled Trials

REGISTRATION FEE:

Lit. 300.000

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FIRST INTERNATIONAL SYMPOSIUM ON HORMONAL CARCINOGENESIS

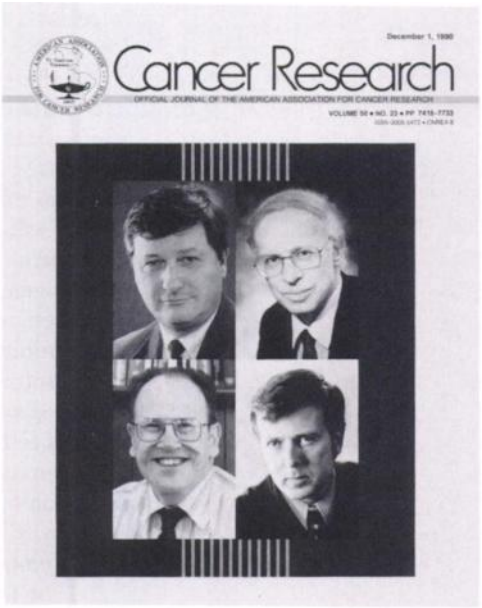
March 19-23, 1991
Hyatt Regency Cancun Hotel
Cancun, Mexico

Executive Board: Jonathan J. Li, Ph.D., Washington State University, Pullman, WA
Satyabrata Nandi, Ph.D., University of California, Berkeley, CA
Sara Antonia Li, Ph.D., Washington State University, Pullman, WA

Symposium Speaker:	***DES Syndrome;*** H.A. Bern, U. of California, Berkeley
Session I:	***Carcinogenesis Risk Assessment of Sex Hormones;*** G. Lucier, NIEHS, NC
Session II:	***Hormones, Cell Proliferation, and Carcinogenesis;*** E.V. Jensen, Cornell Med. Ctr., NY
Session III:	***Estrogen Metabolism and Carcinogenicity;*** A. Conney, Rutgers U., NJ
Session IV:	***Hormones and Tumor Promotion;*** L. Lerner, Philadelphia, PA
Session V:	***Growth Factors and Oncogenes;*** C. Barrett, NIEHS, NC
Session VI:	***Androgen/Progestin Carcinogenesis;*** W. Bardin, Population Council, NY
Symposium Speaker:	***Future Perspectives on Hormonal Carcinogenesis;*** G. Mueller, U. Wisconsin

Each session will consist of four or five presentations. This, complemented with posters, discussions, and exhibits in the Mexican setting will provide a unique Symposium. *Registration: $840.00 before December 1, 1990.* Contact: Dr. Jonathan J. Li, Hormonal Carcinogenesis Laboratory, College of Pharmacy, Washington State University, Pullman, WA 99164-6510, (509) 335-1326.

COVER LEGEND



Barnes and Magee (cover, Cancer Research, June 1970), who discovered the carcinogenicity of dimethylnitrosamine, reported that chronic low-level administration led to liver cancer. Following a single large dose, there was no carcinogenicity to the liver, but after the long term, cancer occurred in the kidney. Druckrey and colleagues (cover, Cancer Research, September 1973) consistently induced brain cancer in rodents by injection of methyl- or ethylnitrosourea. Loveless [Nature (Lond.), *223*: 206, 1969] found that methylating agents alkylated DNA and specifically yielded O^6-methylguanine. Goth and Rajewsky (Proc. Natl. Acad. Sci. USA, *71*: 639, 1974) reported that O^6-ethylguanine persisted in rat brain DNA and induced brain cancer. Rajewsky's group demonstrated that the O^6 alkyl groups could be removed at a rate that varied as a function of host age and cell type (Z. Krebsforsch., *82*: 37, 1974). Kleihues and Margison (J. Natl. Cancer Inst., *53*: 1839, 1974) also observed that in rats given ^{14}C-labeled *N*-nitrosomethylurea the radioactivity at the O^6 position declined rapidly in liver and more slowly in kidney but remained with little change in the brain. Samson and Cairns [Nature (Lond.), *267*: 281, 1977] reported that the O^6-methyl group of guanine was removed by an inducible DNA repair system in *Escherichia coli*. In a cell-free extract, Lindahl found that the O^6-methyl group was lost [Nature (Lond.), *80*: 76, 1979], via transfer enzymatically to a cysteine residue in the purified enzyme [J. Biol. Chem., *257*: 13776, 1982].

This methyltransferase is the key to the differing stabilities of the O^6-methyl group *in vivo*. When transferred to cysteine, an unusual acceptor site, the enzyme undergoes "suicide inactivation" (EMBO J., *1*: 1359, 1982). There is a stoichiometric relationship between available enzyme in a tissue, its local synthesis rate, and its sensitivity to alkylating agents (Proc. Natl. Acad. Sci. USA, *79*: 5162, 1982; Cancer Res., *43*: 3247, 1983). The high sensitivity of the mammary gland of Sprague-Dawley rats to *N*-nitrosomethylurea was traced to a low transferase level [Carcinogenesis (Lond.), *11*: 411, 1990], and the sensitivity of patients to alkylating drugs and the likelihood of secondary neoplasms also depend on prevailing transferase levels. Tumor cell lines with high titers of transferase have a low response to alkylating agents (J. Neurosurg., *70*: 573, 1989). A molecular comparison between the active site regions in prokaryotic and eukaryotic cells, including those of humans, shows an amazing similarity (Proc. Natl. Acad. Sci. USA, *87*: 686, 1990). A recent review on this topic by Anthony E. Pegg appears in Cancer Res., *50*: 6119–6129, 1990. The properties of the transferase thus clarify the early findings of the specific organotropism of methylating carcinogens by Barnes and Magee, Rajewsky and Kleihues.

We are indebted to the individuals mentioned for background information and photographs. We are grateful to David Scicchitano for suggesting this topic.

Paul Kleihues, *top left*, is Professor of Neuropathology, Universitatshospital, University of Zurich, Switzerland; Tomas Lindahl, *top right*, is Head, Clare Hall Laboratories, and Associate Director, Imperial Cancer Research Fund, Potters Bar, Hertfordshire, Great Britain; Anthony E. Pegg, *bottom left*, is Evan Pugh Professor, Cellular and Molecular Physiology and Pharmacology, Penn State College of Medicine and University Hospital, Hershey, Pennsylvania; Manfred F. Rajewsky, *bottom right*, is Professor of Cell Biology, University of Essen, and Director, Institute of Cell Biology, West German Cancer Center, Essen, Germany.

John H. Weisburger