PLENARY SESSION
An Integrated View of the Cancer Cell (Donald S. Coffey)

SYMPOSIA
The Cell Cycle and Tumor Suppressor Genes (Thea D. Tilts)
DNA Damage and Repair (Philip C. Hanawalt)
Natural Products in Chemoprevention of Cancer (Michael B. Sporn)
Ribozymes and Antisense Oligonucleotides and the Alteration of Gene Expression (Kevin J. Scanlon)
Genetic Susceptibility to Cancer (Kenneth W. Kinzler)
Contributions of Environmental Factors to Cancer (Kenneth Olden)
Cell Surface Glycosylation Defining Malignancy (Sen-itiyoh Hakomori)
Peripheral Stem Cells and High-Dose Chemotherapy (Peter J. Quesenberry)
Apoptosis (Alan R. Eastman)
Biology of Radiation Oncology (H. Rodney Withers and C. Norman Coleman)
Biomarkers of Carcinogenesis (David Sidransky)
Transcription Factors and Carcinogenesis (Frank J. Rauscher III)
Gene Therapy in Cancer Clinical Trials
Telomeres and Telomerase (Carol W. Greider and Jerry W. Shay)
Extracellular Matrix, Gene Expression, and Cell Signalling (Hynda K. Kleinman)
Mechanistic Basis for Ethnic Differences in Cancer Risk (Kenneth Olden)
Signal Transduction and Gene Control and Development (James E. Darnell)
Angiogenesis (Judah Folkman and Adrian L. Harris)
Genes, Development, and Cancer (Eric N. Olson)
Growth Factors, Receptors, and Differentiation (Angie Rizzino)
New Strategies and Targets for Chemotherapy (Joseph R. Bertino and Eddie Reed)
Genetic Approaches to Invasion and Metastasis (Robert S. Kerbel and Patricia S. Steeg)
Immunotherapy: Tumor Vaccines (David A. Berd)
Graft versus Tumor Effects (Richard J. O'Reilly)
Dietary Intervention in Hormonal Carcinogenesis (Diane F. Birt and Lovell A. Jones)
The Role of Stromal-Epithelial Interactions in Growth and Neoplasia (Leland W. K. Chung)
Cancer Prevention and Intermediate Biomarkers (Peter Greenwald)
Combinatorial Chemistry for Anticancer Drug Discovery (Sydney E. Salmon)
Translational Research in Breast Cancer (Marc E. Lippman)
DNA Methylation (Peter A. Jones and Stephen B. Baylin)

METHODS WORKSHOPS
General, In Situ, and Quantitative PCR (including Differential Display) (Saraswati Sukumar)
Gene Targeting (Janet Rossant and Andras Nagy)

CONTROVERSY SESSIONS
Are Estrogens Implicated in Breast Cancer? (Lovell A. Jones)
Is Mammography Before Age 50 Beneficial? (Virginia L. Emster)
What Are the Limits and Benefits of PSA as a Screening Tool? (John Trachtenberg)
Breast Cancer Prevention: What Will We Advise Women with BRCA1? (Louise C. Strong)
What Are the Risks of Electromagnetic Fields in Causing Cancer? (Mark A. Israel)
Is Bone Marrow Transplantation Indicated for Breast Cancer? (Nancy E. Davidson)

MEET-THE-EXPERT SUNRISE SESSIONS
New Developments in Clinical Pharmacology (Merrill J. Egorin)
Site-specific Gene Expression in Transgenic Animals (Norman Greenberg)
Organ-specific Carcinogenesis (Cheryl Lyn Walker)
Modeling and Analyzing Clinical Trials (Steven Piantadosi)
Multivariate Determinants of Radiocurability (Richard P. Hill)
Multidrug Resistance (Victor Ling)
Cytokines, Vaccines, and Gene Therapy (Jonathan W. Simons)
Tyrosine Kinases and Phosphatases
Prostate Cancer (John T. Isaacs)
Lung Cancer (Stephen B. Baylin)
Colon Cancer (Ronald N. Buick)
Pediatric Malignancies (Joseph V. Simone)
Hematological Malignancies (Lee M. Nadler)
Stem Cell Transplantation (Elizabeth J. Shpall)
Molecular Determinants of Multidrug Resistance (Elizabeth W. Newcomb)
Is a Mutagenic Event Involved in Initiation? (Ann R. Kennedy)
Glutathione S-Transferase (Kenneth D. Tew)
Farnesyl Transferase as a Target for Therapy (Alexander W. Wood)
Liver Cancer Etiology and Prevention (John D. Groopman)
Biochemical Determinants of Carcinogenesis (Allan B. Okey)

EDUCATIONAL WORKSHOPS
To Be Announced

Further Information: AACR Office • Public Ledger Building • Suite 816 • 150 S. Independence Mall West Philadelphia, PA 19106-3483 • TELEPHONE (215) 440-9300 • FAX (215) 440-9313
Signal Transduction of Normal and Tumor Cells

Co-Sponsored by the National Cancer Institute of Canada
with Additional Support from the
National Institute of Environmental Health Sciences

April 1-6, 1995
The Banff Centre, Banff, Alberta, Canada

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SCIENTIFIC PROGRAM

Tyrosine Kinases
Michael Stern / New Haven, CT
Lewis C. Cantley / Boston, MA
William J. Muller / Hamilton, Ontario, Canada
Morag Park / Montreal, Quebec, Canada

Development
Mariano Barbacid / Princeton, NJ
Joseph Culotti / Toronto, Ontario, Canada
Michael Hoffman / Madison, WI
Ashley R. Dunn / Melbourne, Australia

Cell Cycle
Brenda J. Andrews / Toronto, Ontario, Canada
James M. Roberts / Seattle, WA
Edward E. Harlow / Charlestown, MA
Jeffrey L. Wrana / New York, NY

Tumor Suppressors
Alan Bernstein / Toronto, Ontario, Canada
Paul Polakis / Richmond, CA
Additional Speakers to be Announced

Immune System/Hematopoiesis
André Veillette / Montreal, Ontario, Canada
Tak W. Mak / Toronto, Ontario, Canada
Chaim Rolfman / Toronto, Ontario, Canada
James N. Ihle / Memphis, TN

DNA Viruses and the Immune System
Grant McFadden / Edmonton, Alberta, Canada
William S.M. Wold / St. Louis, MO
Thomas Schall / Palo Alto, CA
David C. Johnston / Hamilton, Ontario, Canada

Cytoplasmic Effectors
Anthony J. Pawson / Toronto, Ontario, Canada
Christopher J. Marshall / London, England
Sara A. Courtneidge / Heidelberg, Germany
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Robert N. Eisenman / Seattle, WA
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James Woodgett / Toronto, Ontario, Canada
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Applicants are encouraged to submit abstracts
for poster presentation.

Information and Application Forms
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Application Deadline: January 20, 1995
In 1992, nitric oxide (NO) was the Molecule of the Year in Science (258: 1861, 1992). How this gaseous free radical achieved this lofty summit is a lengthy story, but in part its origin and its relevance to cancer research began in studies in Steven R. Tannenbaum's laboratory in the mid-1970s. From those early years to the present, this substance has assumed an incredible versatility and importance in biology and medicine, only a few highlights of which can be covered in this brief history.

In the 1970s, Dr. Tannenbaum (cover) and others were studying endogenous nitrosation via microbial reduction of nitrate and acid-catalyzed formation of N-nitroso compounds. A key factor was the recycling of nitrate from the blood via active transport into saliva, but little was known about nitrate pharmacokinetics in humans. Urinary collections from individuals on low nitrate diets and tracer studies with $^{15}$NO$_3^-$ led to the inescapable conclusion that nitrate was being synthesized endogenously in humans and rodents [Science (Washington DC), 200: 1487, 1978; Science (Washington DC), 212: 56, 1981]. In effect, this was a rediscovery because a 1916 paper (J. Biol. Chem., 24: 461, 1916), hitherto unknown to Dr. Tannenbaum and colleagues, had come to similar conclusions. Dr. Tannenbaum's laboratory also showed that endogenous synthesis occurred in germfree animals and quantified the extent of synthesis in humans by reverse isotope dilution experiments [Science (Washington DC), 212: 56, 1981; Proc. Natl. Acad. Sci. USA, 78: 7764, 1981; Cancer Res., 43: 1921, 1983].

They had found nitrate, but its origins were still a mystery. However, a lucky occurrence led to the correct path in the early 1980s. A subject in one of their studies produced extremely high levels of urinary nitrate as the result of an infection. Experiments in rodents demonstrated that nitrate was synthesized in a dose-related fashion when either Escherichia coli lipopolysaccharide or a variety of other immune stimulants simulated the human infection. At the same time, they showed that $^{15}$NH$_4^+$ was converted to $^{15}$NO$_3^-$ and that the incorporation of $^{15}$N was proportional to lipopolysaccharide dose (Proc. Natl. Acad. Sci. USA, 80: 4518, 1983).

They had thus established an origin and a precursor-product relationship for nitrate biosynthesis, but the chemistry was still obscure. Convinced that the conversion of a reduced nitrogen species such as glutamine or a nucleic acid base to the oxidation state of even hydroxylamine would require a strong oxidant on the order of hydroxyl radical, Dr. Tannenbaum persuaded a faculty colleague, Michael Marletta, to work on this problem. Dr. Marletta's research group, in a brilliant series of experiments, showed that the major immune cell in the mouse that carried out this reaction ($\text{NH}_4^+ \rightarrow \text{NO}_3^-$) was the macrophage (Cancer Res., 47: 5590, 1987). They also discovered that a new enzyme which utilized L-arginine as its sole substrate was the source of nitrate (Biochemistry, 27: 8706, 1988). This enzyme, named nitric oxide synthase, was shown in many laboratories to be a family of enzymes with different regulatory properties (FASEB J., 6: 3051, 1992).

The importance of nitric oxide synthase in cancer is still being explored. NO may inhibit or kill cancer cells or it may lead to mutations which cause cancer. Many types of cells are capable of extensive NO formation under complex cytokine control. It has been suggested that if NO causes C → T transitions in the p53 gene, it would constitute a direct causal link to cancer [Science (Washington DC), 262: 1980, 1993].

What began with a study of endogenous nitrosation continues as such with NO. Mutagenesis requires aromatic diazonium ion formation on purines and pyrimidines which occurs through the autoxidation of NO [Proc. Natl. Acad. Sci. USA, 89: 3030, 1992; Science (Washington DC), 254: 1001, 1991]. NO also reacts with the oxygen radical O$_2^-$ to form peroxynitrite, which causes DNA oxidation. Thus, what goes around comes around, but we do not yet know where it will end.

Dr. Tannenbaum was born in 1937 in New York, received a B.S. in 1958 and the Ph.D. in 1962 in Food Science and Technology at MIT. He stayed on at that institution, rising from Assistant Professor in Nutrition and Food Science in 1964 to Professor of Chemistry and Toxicology in the Department of Chemistry and the Division of Toxicology at MIT. He has over 300 original publications, books, and patents, has received many honors, and is a member of many professional organizations, editorial boards, and advisory groups. He has been a member of the American Association for Cancer Research (AACR) since 1981, serving on several committees, including the Awards Committee [American Cancer Society Award Committee (1992); Chairperson, Clowes Award Committee (1995)] and the Program Committee (1994). He also contributes his expertise as an Associate Editor for two AACR journals, Cancer Research and Cancer Epidemiology, Biomarkers & Prevention.

His laboratory continues efforts on quantitation of human exposures to carcinogens in food, air, and water on the pathophysiological consequences of nitric oxide and its action on DNA and its inhibition. His research on nitrite and NO has been supported for the past 20-plus years by the National Cancer Institute (CA26731).

We are greatly indebted to Dr. Tannenbaum for the information in this legend and for the photograph.

Sidney Weinhouse