

Organization and Policy

The Council for Tobacco Research—U.S.A., Inc. is the sponsoring agency of a program of research into questions of tobacco use and health. It is the outgrowth of an organization formed early in 1954 by tobacco manufacturers, growers and warehousemen. Research support has been mainly through a program of grants-in-aid supplemented by contracts for research with institutions and laboratories. The Council does not operate any research facility.

The Scientific Advisory Board to The Council meets regularly to evaluate applications for research support, judging them solely on the basis of scientific merit and relevance.

The Council awards research grants to independent scientists who are assured complete scientific freedom in conducting their studies. Grantees alone are responsible for reporting or publishing their findings in the accepted scientific manner—through medical and scientific journals and societies.

WILLIAM D. HOBBS
Chairman

1990 REPORT

of

THE COUNCIL FOR TOBACCO RESEARCH—U.S.A., INC.

THE COUNCIL FOR TOBACCO RESEARCH—U.S.A., INC.
900 Third Avenue, New York, N.Y. 10022

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to The Council for Tobacco Research—U.S.A., Inc.
as of December 31, 1990

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Harvard Medical School
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Fox Chase Cancer Center
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Professor and Chairman
Department of Preventive Medicine and Public Health
Professor of Medicine
President, Hereditary Cancer Institute
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Director
W. Alton Jones Cell Science Center
Lake Placid, New York

PETER K. VOGT, Ph.D.

Chairman
Department of Microbiology
University of Southern California School of Medicine
Los Angeles, California

Scientific Staff of The Council

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Associate Research Director

VINCENT F. LISANTI, D.M.D.
Associate Research Director

DAVID STONE, Ph.D.
Associate Research Director

CONTENTS

Introduction	5
Abstract Titles and Authors	7
Abstracts of Reports	19
I. Cancer-Related Studies	19
II. The Respiratory System	58
III. Heart and Circulation	75
IV. Neuropharmacology and Physiology	101
V. Pharmacology, Biochemistry and Cell Biology	115
VI. Immunology and Adaptive Mechanisms	163
Active Projects	181
Completed Projects	200
Index of Principal Investigators	221

Introduction

The Council continued to provide substantial funding for research in 1990, receiving \$16,000,000, an increase of \$2,000,000 from 1989, from its members. The sum brought to more than \$165,000,000 the Council's support of research since it was founded.

The funds have been for 1,174 original studies by 784 independent investigators in more than 300 medical schools, hospitals and research centers.

The research program continues to make contributions to the scientific literature. For example, this report contains 261 abstracts of documents published by Council grantees; these abstracts bring to at least 4,145 the total for such publications since the Council's organization in 1954.

Dr. Joseph D. Feldman became Chairman of the Scientific Advisory Board, succeeding Dr. Leon O. Jacobson. Dr. G. Barry Pierce was named Vice Chairman.

Dr. Roswell K. Boutwell retired from the Advisory Board after its April meeting. This distinguished scientist did much to advance the Council's research program during his service.

Joining the Board during the year was Dr. W. K. Joklik, Chairman of the Department of Microbiology and Immunology at Duke University Medical Center, Durham, North Carolina.

As for the Council itself, William D. Hobbs retired as Chairman at year's end after 10 years' service. He was succeeded in that position, effective the first of 1991, by Dr. James F. Glenn, Scientific Director of the Council. Replacing Dr. Glenn as Scientific Director, also as of January 1, 1991, is Dr. Harmon C. McAllister, currently the Council's Research Director.

agents had no effect on the proteolysis of the β chain but did prevent the degradation of ~25% of the δ subunit. In the presence of chloroquine the δ subunit could be detected in lysosomes. The experiments show that proteolysis in or close to the endoplasmic reticulum plays a major role in preventing the surface expression of single β and δ subunits of the T cell antigen receptor; nevertheless, some of the δ chain is able to evade this process. Interestingly, there is a second check on the transport of δ to the plasma membrane, and the subunit is removed from the secretory pathway and delivered to lysosomes for degradation.

Wileman, T., Pettey, C. and Terhorst, C.

International Immunology 2(8):743-754, 1990.

From Laboratory of Molecular Immunology, Dana Farber Cancer Institute, Boston, and Protein Expression Group, T-Cell Sciences, Cambridge, MA.

DIFFERENTIAL REGULATION OF THE HEPATITIS B VIRUS SURFACE GENE PROMOTERS BY A SECOND VIRAL ENHANCER

The hepatitis B virus surface gene is transcribed from two promoters, and the resulting mRNA species code for three distinct forms of the surface antigen. We show here that the viral transcriptional trans-activator, X protein, has no effect on either promoter. However, a cis-acting element in the downstream half of the X gene, distinct from the previously mapped viral enhancer, selectively activates the major surface gene promoter. Nuclease protection and gel-shift assays reveal that multiple cellular factors bind to two sites within this DNA fragment, both of which are necessary for enhancer activity. Since this region of the viral genome is frequently deleted upon integration into the host chromosome in chronic hepatitis B, loss of this second enhancer can alter the relative amounts of the three forms of the surface antigen in infected hepatocytes and thus possibly contribute to cellular damage.

Zhou, D.-X. and Yen, T. S. B.

The Journal of Biological Chemistry 265(34):20731-20734, December 5, 1990.

Other support: Cancer Research Coordinating Committee.

From the Department of Pathology, University of California School of Medicine, San Francisco, and the Anatomic Pathology Service, Veterans Affairs Medical Center, San Francisco.

Active Projects

Following is a list of the principal investigators, or institutions, whose projects are under way or were activated in the period since the previous Report, together with the respective project titles. Completed projects are listed in a later section.

PRINCIPAL INVESTIGATOR OR INSTITUTION

PROJECT TITLE

IAN Y. R. ADAMSON, Ph.D. Professor of Pathology, University of Manitoba, Winnipeg, Manitoba, Canada.	Cell interactions at the air blood barrier
BURT ADELMAN, M.D. Assistant Professor of Medicine, Medical College of Virginia, Richmond.	Effect of fibrinolytic activation on platelet function
JOHN J. ALBERS, Ph.D. Associate Director, Northwest Lipid Research Center, Harborview Medical Center, Seattle, WA.	High density lipoprotein quantitation
JORGE E. ALLENDE, Ph.D. Professor of Biochemistry, University of Chile, Santiago.	Biochemical signal transduction in oocytes Nuclear casein kinase II: its regulation and possible role in signal transduction
HARRY N. ANTONIADES, Ph.D. Professor of Biochemistry, Harvard University School of Public Health, Boston.	Biosynthesis and processing of PDGF-like polypeptides in human malignant cells in culture
SUSAN A. ASTRIN, Ph.D. Senior Member, Institute for Cancer Research, Philadelphia, PA.	Deregulation of c-myc in colon carcinoma
ALAN D. ATTIE, Ph.D. Assistant Professor of Biochemistry, University of Wisconsin, Madison.	Metabolism of low density lipoprotein from pigs with apolipoprotein-B mutations
KAREN J. AUBORN, Ph.D. Research Scientist, Long Island Jewish Medical Center, New Hyde Park, NY.	Regulatory factors associated with the malignant potential of HPV 6
DAVID E. AXELROD, Ph.D. Associate Professor of Microbiology, Waksman Institute, Rutgers University, Piscataway, NJ.	Ras oncogene: suppression/modification of cell transformation
ROBERT L. BARBIERI, M.D. Assistant Professor of Obstetrics and Gynecology, Harvard Medical School, Boston.	Effects of components of cigarette smoke on steroid production, metabolism and action
DAVID W. BARNES, Ph.D. Associate Professor of Biochemistry/Biophysics, Oregon State University, Corvallis.	Identification of oncogenes involved in human lung carcinoma

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- STEPHEN B. BAYLIN, M.D.
Associate Professor of Oncology and Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD.
- FREDERICK F. BECKER, M.D.
Professor of Pathology, University of Texas M. D. Anderson Cancer Center, Houston.
- A. DEAN BEFUS, Ph.D.
Professor, University of Calgary, Calgary, Alberta, Canada.
- TIMOTHY P. BENDER, Ph.D.
Assistant Professor of Microbiology, University of Virginia, Charlottesville.
- JOEL S. BENNETT, M.D.
Associate Professor of Medicine, Hospital of the University of Pennsylvania, Philadelphia.
- KAREN L. BENNETT, Ph.D.
Assistant Professor, University of Missouri, Columbia.
- MICHAEL BENNETT, M.D.
Professor of Pathology, University of Texas Southwestern Medical Center, Dallas.
- BRUCE BEUTLER, M.D.
Associate Professor of Internal Medicine, University of Texas Southwestern Medical Center, Dallas.
- RICHARD J. BING, M.D.
Professor of Medicine (emeritus), University of Southern California School of Medicine, Los Angeles; Visiting Associate, California Institute of Technology; Director of Experimental Cardiology and Scientific Development, Huntington Medical Research Institutes, Pasadena, CA.
- SUBAL BISHAYEE, Ph.D.
Associate Professor, Coriell Institute for Medical Research, Camden, NJ.
- J. EDWIN BLALOCK, Ph.D.
Professor, University of Alabama, Birmingham.
- DALE E. BOCKMAN, Ph.D.
Professor and Chairman, Department of Anatomy, Medical College of Georgia, Augusta.
- CONSTANTIN A. BONA, M.D.
Professor of Microbiology, Mount Sinai School of Medicine, New York.
- Gene hypermethylation in human tumors
- Defective DNA ligase I in Bloom's Syndrome
- Neuromodulation of pulmonary inflammation
- Expression of *c-myc* mRNA expression during B-lymphopoiesis
- Characterization of the platelet fibrinogen receptor
- Germ line-specific gene expression in early nematode development
- Immunoregulation of NK cells
- The role of cytoplasmic ribonuclease inhibitor in regulation of gene expression
- Coronary spasm; cerebral microcirculation
- Altered forms of PDGF-receptor in tumor cell lines
- Immunoregulatory role of endogenous opiates and their receptors
- Inhibition of thymic development by agents causing developmental syndromes
- Function and molecular studies of V genes encoding autoantibodies

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- H. LEON BRADLOW, Ph.D.
Institute for Hormone Research, New York.
- GARY R. BRIGHT, Ph.D.
Assistant Professor, Case Western Reserve University, Cleveland, OH.
- CONSTANCE E. BRINCKERHOFF, Ph.D.
Associate Professor of Medicine and Biochemistry, Dartmouth Medical School, Hanover, NH.
- THOMAS R. BROKER, Ph.D.
Associate Professor of Biochemistry, University of Rochester, Rochester, NY.
- MELISSA A. BROWN, Ph.D.
Research Assistant Professor of Medicine, Microbiology and Immunology, Oregon Health Sciences University, Portland.
- NANCY L. R. BUCHER, M.D.
Research Professor of Pathology, Boston University School of Medicine, Boston.
- KATHLEEN M. BUCKLEY, Ph.D.
Assistant Professor of Neurobiology, Harvard Medical School, Boston.
- DAVID E. BURSTEIN, M.D.
Assistant Professor of Pathology, New York University Medical Center, New York.
- MYLES CABOT, Ph.D.
Senior Scientist, W. Alton Jones Cell Science Center, Lake Placid, NY.
- EDWARD J. CAMPBELL, M.D.
Associate Professor of Medicine, University of Utah, Salt Lake City.
- J. DONALD CAPRA, M.D.
Professor of Microbiology and Internal Medicine, University of Texas Southwestern Medical Center, Dallas.
- DENNIS A. CARSON, M.D.
University of California, San Diego, La Jolla.
- JOHN J. CASTELLOT, JR., Ph.D.
Associate Professor, Tufts University, Boston.
- Smoking and estrogen metabolism in relation to cancer risk
- Role of second messengers in chemotaxis
- Autocrine control of collagenase synthesis
- Human papillomavirus replication and gene expression in primary human keratinocytes
- Mechanisms of interleukin 4 action: identification of IL-4 inducible genes
- Effects of hormones and extracellular matrices on cytoskeletal elements and proliferation of hepatocytes
- Function of synaptic vesicle proteins
- Suppression of neoplasia by N-ras oncogene
- A new pathway for diglyceride mediator production
- Human lung elastin turnover in emphysema
- Human V_HD_H segments
- Mechanism of immune dysfunction after oxidant exposure
- Growth regulation in pulmonary artery smooth muscle cells

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

FRANCO CELADA, M.D., Ph.D.
Senior Immunologist and Professor of Immunology, Hospital for Joint Diseases, Orthopedic Institute, New York.

JAMES C. CHAN, Ph.D.
Associate Professor, University of Texas, M. D. Anderson Cancer Center, Houston.

HAROLD A. CHAPMAN, M.D.
Associate Professor of Medicine, Brigham and Women's Hospital, Boston.

MORDECHAI CHEVION, Ph.D.
Chairman, Institute of Biochemistry, The Hebrew University of Jerusalem, Jerusalem, Israel.

DAVID W. CHRISTIANSON, Ph.D.
Assistant Professor of Chemistry, University of Pennsylvania, Philadelphia.

CHENG-MING CHUONG, M.D., Ph.D.
Assistant Professor of Pathology, University of Southern California, Los Angeles.

DOUGLAS CINES, M.D.
Associate Professor of Medicine, Hospital of the University of Pennsylvania, Philadelphia.

SUSAN CLASTER, M.D.
Assistant Research Hematologist, Children's Hospital, Oakland Research Institute, Oakland, CA.

GARY A. CLAWSON, M.D., Ph.D.
Associate Professor of Pathology, George Washington University, Washington, DC.

BERNICE H. COHEN, Ph.D.
Professor of Epidemiology, The Johns Hopkins University, Baltimore, MD.

STANLEY COHEN, Ph.D.
Professor of Biochemistry, Vanderbilt University School of Medicine, Nashville, TN.

ROBERT W. COLMAN, M.D.
Professor of Medicine and Pathology, Temple University School of Medicine, Philadelphia.

RONALD B. CORLEY, Ph.D.
Associate Professor of Immunology, Duke University Medical Center, Durham, NC.

PROJECT TITLE

Search for the T-epitopes utilized in anti-idiotypic antibody response

Molecular studies of a new transforming growth factor, "TAP"

Role of macrophages in lung injury

Zinc protects against free radical damage

X-ray studies of novel elastase-inhibitor complexes

Adhesion molecules in wound healing: model for tumor growth control and potential therapeutic value

Interaction of plasminogen activators with endothelial cells

Neutrophil-mediated membrane damage in inflammation—the red cell as model

Molecular mechanisms of response to injury

Airways obstruction and smoking in black and white adults

The role of lipocortin in the cellular response to EGF

Molecular cloning and regulation of human platelet cyclic AMP phosphodiesterase

Gene expression in LY-1+ B lymphocytes

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

ROBERT H. COSTA, Ph.D.
Assistant Professor of Biological Chemistry, University of Illinois, Chicago.

CARL E. CRUETZ, Ph.D.
Assistant Professor of Pharmacology, University of Virginia School of Medicine, Charlottesville.

SUSAN E. CULLEN, Ph.D.
Professor of Microbiology, Immunology and Genetics, Washington University School of Medicine, St. Louis.

GIDON CZAPSKI, M.Sc., Ph.D.
Professor of Physical Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel.

JEROME A. DEMPSEY, Ph.D.
Professor of Preventive Medicine, University of Wisconsin, Madison.

LAURENCE A. DOYLE, M.D.
Assistant Professor, University of Maryland Cancer Center, Baltimore.

ELLIS ENGLESBERG, Ph.D.
Professor of Microbiology, University of California, Santa Barbara.

DOUGLAS V. FALLER, M.D., Ph.D.
Associate Professor, Dana Farber Cancer Institute, Boston.

JAMES R. FERAMISCO, Ph.D.
Professor of Medicine, University of California, San Diego.

J. STEPHEN FINK, M.D., Ph.D.
Assistant Professor of Neurology, Massachusetts General Hospital, Charlestown.

JUDITH ANN FOSTER, Ph.D.
Professor and Chairperson, Department of Biology, Syracuse University, Syracuse, NY.

IRWIN FRIDOVICH, Ph.D.
Professor of Biochemistry, Duke University Medical Center, Durham, NC.

JOEL P. GALLAGHER, Ph.D.
Professor, University of Texas Medical Branch, Galveston.

PROJECT TITLE

Transcriptional regulation of the transthyretin gene in the choroid plexus of the brain

Role of protein phosphorylation in nicotine-induced catecholamine release

Synthesis and function of invariant chain proteoglycan

Role of metal ions on superoxide and vitamin C toxicity in biological systems

Loading and respiratory muscle recruitment

Peptides distinguishing classic and variant small cell lung cancer

Genetic studies of the insulin receptor's mitogenic signal

Molecular mechanisms controlling blood flow in the lung

Biological activity of the *fos* oncogene protein

cis-Acting genetic elements and transcriptional factors regulating transcription of the human VIP gene by cAMP and other second messengers

Involvement of elastin fibers in lung disease

Control of the biosynthesis of superoxide dismutases

Nicotine and its direct inhibitory action in the rat septal nuclei

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

ROBERT E. GALLAGHER, M.D.
Professor of Oncology and Medicine, Montefiore Medical Center, The Bronx, NY.

Retinoic acid receptor proteins in leukemia

JACK GAULDIE, Ph.D.
Professor of Pathology, McMaster University, Hamilton, Ontario, Canada.

The mast cell in interstitial pulmonary fibrosis.

MARTIN F. GELLERT, Ph.D.
Chief, Section on Metabolic Enzymes, Laboratory of Molecular Biology, National Institutes of Health, Bethesda, MD.

Mechanism of immunoglobulin gene rearrangement

CHOU ZEN GIAM, Ph.D.
Assistant Professor, University of Nebraska Medical Center, Omaha.

Immunoglobulin enhancer elements in tissue specific gene expression

GORDON NELSON GILL, M.D.
Professor of Medicine, University of California, San Diego, La Jolla.

Epidermal growth factor receptor gene in epidermoid carcinoma

GABRIEL C. GODMAN, M.D.
Professor of Pathology, Columbia University College of Physicians & Surgeons, New York.

Cytoskeletal organization of the endothelial cell in regulation of shape contractility and surface movement

BARRY GOLD, Ph.D.
Associate Professor, University of Nebraska Medical Center, Eppley Institute, Omaha.

Ellagic acid and DNA alkylation

IRA J. GOLDBERG, M.D.
Assistant Professor of Medicine, Columbia University, New York.

Regulation of plasma high density lipoprotein (HDL) catabolism

SANNA M. GOYERT, Ph.D.
North Shore University Hospital, Manhasset, NY.

Myeloid differentiation genes

KATHLEEN J. GREEN, Ph.D.
Assistant Professor of Pathology, Northwestern University of Medical School, Chicago.

Epithelial differentiation and neoplasia: desmoplakin expression and structure

MARK I. GREENE, M.D., Ph.D.
John Eckman Professor and Head of Immunobiology and the Center for Receptor Biology, University of Pennsylvania, Philadelphia.

Receptor interactions in cancer

PAUL J. HAGERMAN, M.D.
Associate Professor of Biochemistry, Biophysics and Genetics, University of Colorado, Denver.

The role of DNA methylation in gene expression

KATHERINE A. HAJJAR, M.D.
Assistant Professor of Pediatrics and Medicine, Cornell University Medical College, New York.

Assembly of fibrinolytic proteins on the endothelial cell surface

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

HIDESABURO HANAFUSA, Ph.D.
Professor, The Rockefeller University, New York.

Regulation of protein phosphorylation and cell transformation

MARIE H. HANIGAN, Ph.D.
Research Fellow, University of Virginia, Charlottesville.

The role of gamma-glutamyl transpeptidase in hepatocarcinogenesis

OLIVER HANKINSON, Ph.D.
Associate Professor of Pathology, University of California, Los Angeles.

Cloning and characterization of a repressor aryl hydrocarbon hydroxylase transcription

PETER C. HARPEL, M.D.
Professor of Medicine, Cornell University Medical College, New York.

Lipoprotein(a): structure and function

SUSAN P. HAWKES, Ph.D.
Associate Adjunct Professor of Pharmacy and Pharmaceutical Chemistry, University of California, San Francisco.

Purification and characterization of the 21K protein

ROBERT M. HOFFMAN, Ph.D.
Associate Professor of Pediatrics, University of California, San Diego, La Jolla.

Genes controlling methionine dependence in human cancer

JAMES C. HOGG, M.D., Ph.D.
Professor of Pathology, University of British Columbia, Vancouver, British Columbia, Canada.

Pathogenesis of airways obstruction in smokers

DEBORAH K. HOSHIZAKI, Ph.D.
Assistant Professor of Biological Chemistry, University of Illinois, Chicago.

Isolation and expression of a Drosophila lipid gene

RICHARD L. HUGANIR, Ph.D.
Associate Professor, The Johns Hopkins University School of Medicine, Baltimore, MD.

Mutagenesis of phosphorylation sites in the nicotinic acetylcholine receptor

MIEN-CHIE HUNG, Ph.D.
Assistant Professor, University of Texas M. D. Anderson Cancer Center, Houston.

Ligand isolation and its cDNA cloning for the neu-encoded receptor

PETER C. ISAKSON, Ph.D.
Assistant Professor of Pharmacology, University of Virginia School of Medicine, Charlottesville.

Lymphokine regulation of Ig isotype switch

KYOGO ITOH, M.D.
Assistant Professor of Surgery, University of Texas M. D. Anderson Cancer Center, Houston.

Characterization of the serum suppressive factor against induction of lymphokine-activated killer cells

BARBARA J. JACKSON, Ph.D.
Staff Scientist, Boston Biomedical Research Institute.

Adaptation of yeast to osmotic stress

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- SUSAN JAKEN, Ph.D.
Senior Scientist, W. Alton Jones Cell Science Center, Lake Placid, NY.
- KUAN-TEH JEANG, M.D., Ph.D.
Laboratory of Molecular Biology, National Institutes of Health, Bethesda, MD.
- JOLYON JESTY, Ph.D.
Associate Professor of Medicine, State University of New York at Stony Brook.
- JOHN P. JOHNSON, M.D.
Associate Director and Clinical Geneticist, Children's Hospital Medical Center, Oakland, CA.
- J.G. JOSHI, Ph.D.
Professor of Biochemistry, University of Tennessee, Knoxville.
- MARSHALL E. KADIN, M.D.
Associate Professor of Pathology, Harvard Medical School, Beth Israel Hospital, Boston.
- FA-TEN KAO, Ph.D.
Professor, Eleanor Roosevelt Institute for Cancer Research, Denver, CO.
- LEE M. KAPLAN, M.D., Ph.D.
Assistant Professor of Medicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA.
- MICHAEL KARIN, Ph.D.
Associate Professor of Medicine, University of California School of Medicine, San Diego, La Jolla.
- MANFRED L. KARNOVSKY, Ph.D.
Harold T. White Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston.
- MORRIS J. KARNOVSKY, M.B., B.Ch.
Shattuck Professor of Pathological Anatomy, Harvard Medical School, Boston.
- ERIC B. KMEC, Ph.D.
Assistant Professor of Biochemistry, Temple University, Philadelphia.
- HEINZ KOHLER, M.D., Ph.D.
Adjunct Professor of Pathology, University of California, San Diego, La Jolla.
- Transformation sensitive properties of protein kinase C
- Mechanistic analysis of the HTLV-I p40x protein
- Plasma inhibitors of factor X activation
- Mapping the gene for hyperalphalipoproteinemia
- Aluminum and ferritins in Alzheimer's disease
- Lymphomatoid papulosis: a cutaneous model of lymphomagenesis
- Fragile site 3p14 in small cell lung cancer
- Estrogen regulation of pituitary gene expression
- Isolation and characterization of a heritable fragile site on human chromosome
- Regulation of AP-1/Jun activity by tumor promoters
- Serotonin/peptidoglycan mimicry
- Characterization and therapy of rat vein graft lesions
- Transcriptional regulation by *cis-acting* elements
- Multitargeting with hybridomas on tumor cells

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- WILLEM KOPPENOL, Ph.D.
Associate Professor, Louisiana State University, Baton Rouge.
- ROBERT H. KRETSINGER, Ph.D.
Professor of Biology, University of Virginia, Charlottesville.
- ROBERT D. KUCHTA, Ph.D.
Assistant Professor, University of Colorado, Boulder.
- ARUN P. KULKARNI, Ph.D.
Associate Professor, University of South Florida, Tampa.
- STEVEN L. KUNKEL, Ph.D.
Associate Professor of Pathology, University of Michigan Medical School, Ann Arbor.
- MARTIN KUPIEC, Ph.D.
Assistant Professor, Tel Aviv University, Tel Aviv, Israel.
- ABEL LAJTHA, Ph.D.
Director, Center for Neurochemistry, Ward's Island, New York.
- THOMAS A. LANGAN, Ph.D.
Professor of Pharmacology, University of Colorado School of Medicine, Denver.
- STEPHEN LANIER, Ph.D.
Assistant in Pharmacology, Massachusetts General Hospital, Boston.
- PAUL LEBOWITZ, M.D.
Senior Research Scientist, Yale University, New Haven, CT.
- EVA LEE, Ph.D.
Assistant Professor in Residence, University of California, San Diego, La Jolla.
- VANDA A. LENNON, M.D., Ph.D.
Professor of Immunology and Neurology, Mayo Clinic, Rochester, MN.
- EDWARD B. LEOF, Ph.D.
Assistant Professor, Vanderbilt University, Nashville, TN.
- BEN-ZION LEVI, Ph.D.
Senior Lecturer, Technion, Haifa, Israel.
- Reactions of metal complexes with hydrogen peroxide
- Polyproline β -turn helices: syntheses and structures
- DNA primase as a target for chemotherapeutics
- Benzo(α)pyrene activation in human placenta
- Cytokine interactions between cells of the alveolar wall during inflammation
- Yeast mutants that affect recombination between repeated sequences
- Mechanisms of regionally specific nicotine effects
- Regulation of mitosis by CDC28/cdc2⁺ protein kinase substrates
- Molecular characterization of α_2 -adrenergic receptors
- c-Fos* cell proliferation and differentiation
- Biological function of the retinoblastoma gene in small cell lung carcinoma
- Novel ligands for small cell lung cancer
- TGF β 1 regulation of lung epithelial cell proliferation
- The cloning and characterization of human DNA binding protein which interacts with interferon consensus sequence

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- EUGENE G. LEVIN, Ph.D.
Assistant Member, Scripps Clinic & Research Foundation, La Jolla, CA.
- RANDOLPH V. LEWIS, Ph.D.
Associate Professor and Head, Department of Molecular Biology, University of Wyoming, Laramie.
- MICHAEL R. LIEBER, M.D., Ph.D.
Assistant Professor, Stanford University, Stanford, CA.
- MICHAEL W. LIEBERMAN, M.D., Ph.D.
W. L. Moody, Jr., Professor and Chairman of Pathology, Baylor College of Medicine, Houston, TX.
- JON LINDSTROM, Ph.D.
Trustee Professor, University of Pennsylvania School of Medicine, Philadelphia.
- JOSEPH S. LIPSICK, M.D., Ph.D.
Associate Professor of Microbiology, State University of New York, Stony Brook.
- ZVI LIVNEH, Ph.D.
Scientist, The Weizmann Institute of Science, Rehovot, Israel.
- REUBEN LOTAN, Ph.D.
Professor and Deputy Chairman, University of Texas M.D. Anderson Cancer Center, Houston.
- RONALD J. LUKAS, Ph.D.
Director, Laboratory of Neurochemistry, St. Joseph's Hospital and Medical Center, Phoenix, AZ.
- JAN M. LUNDBERG, M.D.
Associate Professor of Pharmacology, Karolinska Institute, Stockholm, Sweden.
- HENRY T. LYNCH, M.D.
Professor and Chairman, Department of Preventive Medicine and Public Health, Creighton University School of Medicine, Omaha, NE.
- RICARDO B. MACCIONI, D.Sc.
Director General, International Center for Cancer & Developmental Biology, Santiago, Chile.
- HAIM MANOR, Ph.D.
Associate Professor, Technion Israel Institute of Technology, Haifa, Israel.
- Regulation of endothelial cell tissue plasminogen activator
- Physiologic effects of proenkephalin peptides
- The mechanism and regulation of site-specific recombination of antigen receptor genes in the vertebrate immune system
- Analysis of *Hras* function by homologous recombination in transgenic mice
- Neuronal nicotinic receptor structure
- Retroviral transduction of oncogenes *in vitro*
- Mechanism of S.O.S. error-prone repair
- Molecular basis for the antitumor action of retinoic acid
- Regulation of endogenous lectin expression in tumor cells
- Influences of nicotine on neuronal expression of acetylcholine receptors
- Neuronal and endothelial mechanisms upon airway irritation
- Genetic and biomarker studies of cancers of the respiratory tract, pancreas and urinary bladder
- Regulation of microtubule assembly in normal and transformed cells
- In vivo* and *in vitro* studies of induction and arrest of DNA amplification

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- BILLY R. MARTIN, Ph.D.
Associate Professor, Medical College of Virginia, Virginia Commonwealth University, Richmond.
- G. STEVE MARTIN, Ph.D.
Professor, University of California, Berkeley.
- ROBERT W. MASON, Ph.D.
Virginia Polytechnic Institute, Blacksburg.
- ROBERT G. MCKINNELL, Ph.D.
Professor of Genetics and Cell Biology, University of Minnesota, St. Paul.
- PAUL J. MEECHAN, Ph.D.
Assistant Professor of Biological Sciences, Northern Illinois University, DeKalb.
- EDWIN M. MEYER, Ph.D.
Associate Professor, University of Florida College of Medicine, Gainesville.
- ROBERT L. MILLETTE, Ph.D.
Professor of Biology, Portland State University, Portland, OR.
- JOHN G. MONROE, Ph.D.
Assistant Professor of Pathology, University of Pennsylvania School of Medicine, Philadelphia.
- BARBARA MROCZKOWSKI, Ph.D.
Assistant Professor of Biochemistry, Vanderbilt University, Nashville, TN.
- CHRISTOPHER MURLAS, M.D.
Associate Professor and Assistant Chairman, Department of Medicine, Rush University, Chicago.
- MOON H. NAHM, M.D.
Assistant Professor of Pathology, Washington University, St. Louis.
- SUSAN NAYLOR, Ph.D.
Associate Professor of Human Genetics, The University of Texas Health Science Center, San Antonio.
- DONALD J. NELSON, Ph.D.
Associate Professor of Chemistry, Clark University, Worcester, MA.
- STEVEN K. NORDEEN, Ph.D.
Assistant Professor, University of Colorado Health Sciences Center, Denver.
- Characterization of central nicotine receptors
- Proto-oncogenes, integrins and signal transduction
- Role of cathepsin L in emphysema
- Oocyte nuclear transfer to abrogate a malignant phenotype
- Isolation and injection of chromosome(s) complementing XP mutations
- Nicotine in a long-term model for Alzheimer's disease
- Regulation of herpesvirus late gene expression
- Developmental biology of B lymphocyte activation signaling
- Functional diversity of the EGF precursor: a study into the role of preproEGF in cell-to-cell communication
- Electromechanical properties of airway muscle
- Development of human B Cells
- Molecular and genetic analysis of small cell lung cancer
- Calmodulin interactions with target proteins and synaptic vesicles
- Regulation of expression of the *c-mos* proto-oncogene

PRINCIPAL INVESTIGATOR OR INSTITUTION

PROJECT TITLE

- SE-KYUNG OH, Ph.D.
Associate Professor of Microbiology, Boston University School of Medicine.
- JANET M. OLIVER, Ph.D.
Professor of Pathology, University of New Mexico School of Medicine, Albuquerque.
- SUZANNE OPARIL, M.D.
Professor of Medicine, University of Alabama, Birmingham.
- YOSHIO OSAWA, Ph.D.
Head, Department of Endocrine Biochemistry, Medical Foundation of Buffalo, Buffalo, N.Y.
- MARY D. OSBAKKEN, M.D.
Assistant Professor of Anesthesia and Biochemistry/Biophysics, University of Pennsylvania, Philadelphia.
- J. JAMES OU, Ph.D.
Assistant Professor, University of Southern California, Los Angeles.
- BEVERLY PAIGEN, Ph.D.
The Jackson Laboratory, Bar Harbor, ME.
- ROBERT E. PALAZZO, Ph.D.
Assistant Scientist, Marine Biological Laboratory, Woods Hole, MA.
- ISRAEL PECHT, Ph.D.
Professor, The Weizmann Institute of Science, Rehovot, Israel.
- ARTHUR PENN, Ph.D.
Research Professor of Environmental Medicine, New York University, New York.
- SCOTT W. PETERSON, Ph.D.
Associate Professor of Biology, Arkansas College, Batesville.
- G. BARRY PIERCE, JR., M.D.
Distinguished Centennial Professor of Pathology, University of Colorado Health Sciences Center, Denver.
- RAY C. PITTMAN, Ph.D.
Research Biochemist, University of California, San Diego, La Jolla.
- SALVATORE V. PIZZO, M.D., Ph.D.
Associate Professor of Pathology, Duke University Medical Center, Durham, NC.
- Role of the immunosuppressor SER in pulmonary inflammation and malignancy
- Regulation of the membrane oxidase of human polymorphonuclear leukocytes
- Role of atrial natriuretic peptide in the pathogenesis of hypoxic pulmonary hypertension
- Aromatase inhibitors in cigarette smoke and tobacco
- ³¹P NMR study of cardiac metabolism in health and disease
- Molecular analysis of hepatitis B virus X gene
- Mapping genetic determinants of atherosclerosis susceptibility
- Reactivation of isolated mitotic apparatus
- Mast cell membrane function-associated components
- An animal model for studying the molecular biology of atherosclerotic plaque development
- Insulin receptor down regulation in erythrocytes
- Mechanism underlying crisis and spontaneous transformation and immunologic reactions in tissue culture
- Quantitation *in vivo* of pathways involved in reverse cholesterol transport
- Protease regulation and cellular metabolism

PRINCIPAL INVESTIGATOR OR INSTITUTION

PROJECT TITLE

- CHRIS D. PLATSOUKAS, Ph.D.
Professor of Immunology and Deputy Chairman, University of Texas M.D. Anderson Cancer Center, Houston.
- JULIA M. POLAK, D.Sc., M.D.
Senior Lecturer in Histopathology, Royal Postgraduate Medical School, Hammer-smith Hospital, London, England.
- LINDA C. QUATTROCHI, Ph.D.
Assistant Research Scientist, University of California, San Diego, La Jolla.
- RAMI RAHAMIMOFF, M.D.
Professor of Physiology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
- TIMOTHY J. REGAN, M.D.
Professor and Director, Division of Cardiology, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark.
- LOLA M. REID, Ph.D.
Associate Professor, Albert Einstein College of Medicine of Yeshiva University, The Bronx, NY.
- MICHAEL A. REIDY, Ph.D.
Research Associate Professor, University of Washington, Seattle.
- SOLON L. RHODE, III, M.D., Ph.D.
Professor, University of Nebraska Medical Center, Omaha.
- A. ANGIE RIZZINO, Ph.D.
Associate Member, University of Nebraska Medical Center, Eppley Institute, Omaha.
- JOHN M. ROBINSON, Ph.D.
Associate Professor, Ohio State University College of Medicine, Columbus.
- LORNA W. ROLE, Ph.D.
Assistant Professor of Anatomy and Cell Biology, Columbia University College of Physicians & Surgeons, New York.
- GERALD M. ROSEN, Ph.D.
Professor of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore.
- NADIA ROSENTHAL, Ph.D.
Assistant Professor of Biochemistry, Boston University, Boston.
- Identification and molecular cloning of melanoma cell determinants recognized by tumor-specific, tumor-infiltrating lines
- Investigation of the role of regulatory peptides in human lung disease
- Human cytochrome P-450s: tissue distribution and regulation by chemical carcinogens
- Humoral effects of small cell carcinoma of the lung on neuromuscular transmission
- Cardiac arrhythmias after chronic nicotine and/or caffeine use
- In vitro* assay prediction of metastatic potential
- Regrowth of arterial endothelium
- Parvoviruses as transducing vectors for human cells
- Transforming growth factor beta and mammalian embryogenesis
- Neutrophil stimulation: biochemical and cell biological studies
- Modulation of neuronal nicotinic acetylcholine receptors
- Free radical mediated cytotoxicity
- Regulatory factors in muscle gene expression

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- HARRY RUBIN, Ph.D., D.V.M.
Professor of Molecular Biology, University
of California, Berkeley.
- Adaptive vs. selective effects of alkylating
agents
- JEFFREY D. SAFFER, Ph.D.
Associate Staff Scientist, The Jackson Lab-
oratory, Bar Harbor, ME.
- HMG proteins in chromatin
- BARBARA M. SANBORN, Ph.D.
Professor, University of Texas Medical
School, Houston.
- The isolation and characterization of
hormonally-regulated sertoli cell
- AZIZ SANCAR, M.D., Ph.D.
Associate Professor of Biochemistry, Uni-
versity of North Carolina, Chapel Hill.
- Nucleotide excision repair
- DAVID A. SASSOON, Ph.D.
Assistant Professor of Biochemistry, Bos-
ton University.
- Molecular basis of limb development
- B. V. RAMA SASTRY, Ph.D.
Professor of Pharmacology, Vanderbilt
University, Nashville, TN.
- Mechanisms of smoking-induced compensa-
tory responses in human placenta
- GORDON H. SATO, Ph.D.
Director, W. Alton Jones Cell Science Cen-
ter, Lake Placid, NY.
- Isolation of growth factors from blue-green
algae
- WALTER SAUERBIER, Ph.D.
Professor of Microbiology, University of
Minnesota, St. Paul.
- Genetic studies of tumor suppressor genes in a
haploid cell/animal system
- CHARLES D. SCHER, M.D.
Professor of Pediatrics and Human Genet-
ics, Joseph Stokes Research Institute, Chil-
dren's Hospital of Philadelphia.
- PDGF modulated nuclear protein
- H. WILLIAM SCHNAPER, M.D.
Assistant Professor of Pediatrics, Washing-
ton University School of Medicine, St.
Louis.
- Purification and characterization of the lym-
phokine SIRS
- LUCIA SCHUGER, M.D.
Research Fellow, University of Michigan,
Ann Arbor.
- Role of laminin in mouse lung development
- DAVID W. SCOTT, Ph.D.
Professor of Immunology, University of
Rochester, Rochester, NY.
- B lymphomas in aging mice: role of idio-
type and tolerance
- ROBERT E. SCOTT, M.D.
Professor of Pathology, University of Ten-
nessee, Memphis.
- Commitment control and carcinogenesis in
normal, preneoplastic and malignant hu-
man epithelial cells
- SIDNEY A. SCUDDER, M.D.
Assistant Professor of Hematology/-
Oncology, University of California, Davis.
- Role of multidrug resistance in transition cell
carcinoma of the bladder

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- STEWART SELL, M.D.
Professor, University of Texas Health Sci-
ence Center, Houston.
- Rabbit AIDS
- GINETTE SERRERO, Ph.D.
Senior Scientist, W. Alton Jones Cell Sci-
ence Center, Lake Placid, NY.
- Characterization of adipose differentiation in-
hibitor
- JACQUELINE SHARON, Ph.D.
Assistant Professor, Boston University
School of Medicine.
- Antibodies as DNA-binding proteins
- JERRY W. SHAY, Ph.D.
Associate Professor, University of Texas
Health Science Center, Dallas.
- Role of cytoplasmic elements in the induction
and suppression of tumorigenicity
- ISAIAHU SHECHTER, Ph.D.
Associate Professor of Biochemistry, Tel
Aviv University, Tel Aviv, Israel.
- Coordinated regulation of hepatic cholesterol
synthesis
- ELLIOTT SIGAL, M.D., Ph.D.
Assistant Professor of Medicine, University
of California, San Francisco.
- Cellular biology of arachidonate 15-
lipoxygenase in airway epithelium
- MICHAEL SINENSKY, Ph.D.
Head, Lipid and Lipoprotein Metabolism
Division, Eleanor Roosevelt Institute for
Cancer Research, Denver, CO.
- Translational control of HMG-CoA reductase
- DAVID A. SIRBASKU, Ph.D.
Professor of Biochemistry and Molecular
Biology, University of Texas Health Sci-
ence Center, Houston.
- Estrogen-responsive and autonomous human
breast cancer growth
- FRANCES I. SMITH, Ph.D.
Assistant Professor of Microbiology,
Mount Sinai School of Medicine, New
York.
- Detection of mutations in genes involved in
human disease
- KENDALL A. SMITH, M.D.
Professor of Medicine, Dartmouth Medical
School, Hanover, NH.
- Dissection of the eukaryotic DNA replication
pathway
- STEVEN S. SMITH, Ph.D.
Assistant Research Scientist, City of Hope
National Medical Center, Duarte, CA.
- Selectivity of DNA methylation in normal and
oncogenically transformed cells
- ARTHUR K. SOLOMON, Ph.D.
Professor of Biophysics, Emeritus, Harvard
Medical School, Boston.
- Protein:protein and protein:cytoskeleton inter-
actions in the red cell membrane
- ASHWANI K. SOOD, Ph.D.
Cancer Research Scientist III, Roswell Park
Memorial Institute, Buffalo, NY.
- Mutant MHC class I antigens in antitumor im-
munity
- MOHAN SOPORI, Ph.D.
Scientist II, Lovelace Medical Foundation,
Albuquerque, NM.
- Cigarette smoke-induced alteration of im-
mune response

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- GEORGE D. SORENSON, M.D.
Professor of Pathology, Dartmouth Medical
School, Hanover, NH.
- Molecular genetic studies of metastases in pul-
monary carcinoma
- ELIOT R. SPINDEL, M.D., Ph.D.
Scientist, Oregon Regional Primate Re-
search Center, Beaverton.
- Structure and function of receptors for the
bombesin-like peptides
- ERIC J. STANBRIDGE, Ph.D.
Associate Professor of Microbiology, Uni-
versity of California, Irvine.
- Transfer of specific individual human chromo-
somes to recipient cells
- JEAN R. STARKEY, Ph.D.
Associate Professor of Microbiology, Mon-
tana State University, Bozeman.
- Adhesive receptor:ligand interactions in tu-
mor metastasis
- NEWMAN L. STEPHENS, M.D., F.R.C.P.
Professor of Physiology, University of
Manitoba, Winnipeg, Manitoba, Canada.
- Cellular mechanisms of airway smooth mus-
cle contraction
- DAVID M. STERN, M.D.
Associate Professor, College of Physicians
& Surgeons, Columbia University, New
York.
- Modulation of endothelial cell anticoagulant
mechanisms
- THOMAS P. STOSSEL, M.D.
Chief, Medical Oncology Unit, Massachu-
setts General Hospital, Boston.
- Functional anatomy of the lung macrophage
- FLEUR L. STRAND, Ph.D.
Professor of Biology, New York Univer-
sity, New York.
- Prenatal and postnatal effects of nicotine and
ACTH peptides on neuromuscular develop-
ment and motor behavior in rats
- DAVID S. STRAYER, M.D., Ph.D.
Associate Professor of Pathology, Univer-
sity of Texas Health Science Center, Hous-
ton.
- The role of EGF-like growth factors in onco-
genesis
- A. DONNY STROSBURG, Ph.D.
Chair Professor of Biochemistry and Immu-
nology, Pasteur Institute, Paris, France.
- Structure and function of the muscarinic re-
ceptors of a human embryonic lung
fibroblast
- SURESH SUBRAMANI, Ph.D.
Associate Professor of Biology, University
of California, San Diego, La Jolla.
- Recombination genes in *S. pombe* and mam-
malian cells
- MARY E. SUNDAY, M.D., Ph.D.
Assistant Professor of Pathology, Brigham
and Women's Hospital, Boston.
- Gastrin-releasing peptide gene expression in
lung growth
- JOHN P. SUNDBERG, D.V.M., Ph.D.
Staff Scientist, The Jackson Laboratory,
Bar Harbor, ME.
- Induced skin tumors of mice
- RAQUEL SUSSMAN, Ph.D.
Associate Scientist, Marine Biological Lab-
oratory, Woods Hole, MA.
- Molecular mechanism of mutagenesis

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PROJECT TITLE

- TORGNY H. SVENSSON, M.D.
Professor, Karolinska Institute, Stockholm,
Sweden.
- Cellular basis of smoking behavior
- MAKOTO TAKETO, M.D., Ph.D.
Associate Investigator, The McLaughlin
Research Institute, Great Falls, MT.
- Gene regulation in teratocarcinoma stem cells
- D. LANSING TAYLOR, Ph.D.
Professor of Biological Science, Carnegie-
Mellon University, Pittsburgh.
- The structural and metabolic chemistry of
cytoplasm
- KENNETH M. TAYLOR, M.D.
Professor and Chief of Cardiac Surgery,
Royal Postgraduate Medical School, Lon-
don, England.
- Regulatory peptides in the innervated and de-
nervated heart
- CORNELIS P. TERHORST, Ph.D.
Associate Professor of Pathology, Dana-
Farber Cancer Institute, Boston.
- Intracellular transport and assembly of the T
cell receptor
- VICTOR P. TERRANOVA, Ph.D.
Associate Professor, Columbia University,
New York.
- Directed migration of metastatic tumor cells
- MATTHEW L. THOMAS, Ph.D.
Assistant Professor of Pathology, Microbi-
ology and Immunology, Washington Uni-
versity School of Medicine, St. Louis.
- Leukocyte-common antigen, T200: changes
in carbohydrate structure
- ANNAMARIA TORRIANI-GORINI, Ph.D.
Professor of Biology, Massachusetts Insti-
tute of Technology, Cambridge.
- The regulatory control of phosphate metabo-
lism in *E. coli*: the *phoR* gene of the *pho*
regulon
- PHILIP W. TUCKER, Ph.D.
Professor of Microbiology, University of
Texas Southwestern Medical Center, Dal-
las.
- Role of 2p13 translocations in childhood leu-
kemia
- JOHN TURK, M.D.
Assistant Professor of Medicine and Pathol-
ogy, Washington University, St. Louis.
- Glycosyl-phosphatidylinositol hydrolysis in
insulin secretion
- JONATHAN W. UHR, M.D.
Professor and Chairman of Microbiology,
Professor of Internal Medicine, University
of Texas Southwestern Medical Center,
Dallas.
- Mechanisms underlying tumor dormancy
- THOMAS W. VICKROY, Ph.D.
Assistant Professor, University of Florida,
Gainesville.
- Neuropharmacological investigations of nico-
tine interactions with CNS cholinergic and
mesolimbic dopaminergic neurons
- LYDIA VILLA-KOMAROFF, Ph.D.
Associate Professor, Children's Hospital,
Boston.
- Control of neuropeptide synthesis in rodents

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

PETER K. VOGT, PH.D.
Professor and Chairman, Department of
Microbiology, University of Southern Cali-
fornia, Los Angeles.

THOMAS J. WALDSCHMIDT, PH.D.
Assistant Professor of Pathology, Univer-
sity of Iowa, Iowa City.

THOMAS E. WEBB, PH.D.
Professor, Department of Physiological
Chemistry, Ohio State University College
of Medicine, Columbus.

DAVID B. WEINER, PH.D.
Research Associate Professor, University
of Pennsylvania, Philadelphia.

SAMUEL B. WEISS, PH.D.
Professor of Biochemistry and Molecular
Biology, University of Chicago.

JUDITH WEISZ, M.D.
Professor of Obstetrics and Gynecology,
Milton S. Hershey Medical Center, Penn-
sylvania State University, Hershey.

HOWARD G. WELGUS, M.D.
Assistant Professor of Medicine, Jewish
Hospital at Washington University Medical
Center, St. Louis.

NANCY K. WELLER, PH.D.
Assistant Professor of Medicine, Case
Western Reserve University, Cleveland,
OH.

SAMUEL A. WELLS, JR., M.D.
Bixby Professor of Surgery, Washington
University, St. Louis.

ÅKE WENNMALM, M.D.
Professor and Chairman, Department of
Clinical Physiology, University of Gothen-
burg, Gothenburg, Sweden.

DEAN F. WONG, M.D.
Assistant Professor, Johns Hopkins Hospi-
tal, Baltimore, MD.

RICHARD M. WRIGHT, PH.D.
Senior Instructor, Webb-Waring Lung In-
stitute, University of Colorado, Denver.

THOMAS C. WRIGHT, JR., M.D.
Assistant Professor of Pathology, Columbia
University College of Physicians & Sur-
geons, New York.

PROJECT TITLE

New *ONC* genes from acute retroviral leuke-
mias

The Fc R distinguishes Ly 1 from conventional
B cells

Biological synergism between glucarate and
retinoids

Structural basis for receptor activation in cel-
lular transformation

DNA recombinant events induced by acti-
vated hydrocarbons

Cytochromes P-450 and estrogen metabolism

Human macrophage collagenase and colla-
genase inhibitor

Molecular characterization of pulmonary al-
veolar type I cells and consideration of their
relationship to alveolar type II cells

Gene mapping of multiple endocrine neopla-
sia type I

Nicotine as inhibitor of prostaglandin forma-
tion: localization of the inhibitory step and
characterization of the cardiovascular im-
plications

In vivo studies of nicotine cholinergic recep-
tors in the human brain

Regulation of yeast xanthine oxidase gene ex-
pression

Characterization of heparin's growth inhibi-
tory activity

**PRINCIPAL INVESTIGATOR
OR INSTITUTION**

JOSEPH M. WU, PH.D.
Professor of Biochemistry, New York Med-
ical College, Valhalla.

REEN WU, PH.D.
Associate Adjunct Professor, California
Primate Research Center, University of
California, Davis.

LAWRENCE J. WYSOCKI, PH.D.
Staff Researcher, National Jewish Center
for Immunology and Respiratory Medicine,
Denver, CO.

ANDREW YEN, PH.D.
Associate Professor, New York State Col-
lege of Veterinary Medicine, Cornell Uni-
versity, Ithaca.

TIEN-SZE B. YEN, M.D., PH.D.
Assistant Professor of Pathology, Univer-
sity of California, San Francisco.

DONALD A. YOUNG, M.D.
Professor of Medicine, University of Roch-
ester, Rochester, NY.

MAURIZIO ZANETTI, M.D.
Associate Professor of Medicine, Univer-
sity of California School of Medicine, San
Diego, La Jolla.

PROJECT TITLE

Interferons and 2-5A expression in Al-
zheimer's disease fibroblasts

Genetic analysis of mucous cell defferentia-
tion

Immunogenicity of peptide fragments

Halting progression of neoplastic disease by
inducing terminal differentiation

Mechanisms of trans-activation by the hepati-
tis B virus X protein

Papilloma virus proteins and cell transforma-
tion

Idiotypic mapping by site-directed mutagen-
sis

Grantees of Completed Projects

Following is a list of the principal investigators, or institutions, whose projects have been completed prior to the period covered in this Report. A number of the individuals named are deceased. The titles and affiliations listed were those in effect at the time the work was in progress.

ROBERT H. ABELES, Ph.D.
Professor of Biochemistry, Brandeis University, Waltham, MA.

LEO G. ABOOD, Ph.D.
Professor of Brain Research and Biochemistry, Center for Brain Research, University of Rochester Medical Center, Rochester, NY.

MARIO D. ACETO, Ph.D.
Associate Professor of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond.

DOLPH O. ADAMS, M.D., Ph.D.
Professor of Pathology, Duke University Medical Center, Durham, NC.

KENNETH B. ADLER, Ph.D.
Assistant Professor of Pathology, University of Vermont College of Medicine, Burlington.

CLARENCE M. AGRESS, M.D.
Associate Clinical Professor of Medicine, University of California Medical Center, Los Angeles.

ANTHONY A. ALBANESE, Ph.D.
Director of Laboratories, The Burke Rehabilitation Center, White Plains, NY.

ANTHONY P. AMAROSE, Ph.D.
Instructor in Obstetrics and Gynecology, The Albany Medical College of Union University, Albany, NY.

E. T. ANGELAKOS, M.D., Ph.D.
Professor of Physiology, Boston University School of Medicine, Boston.

D. MURRAY ANGEVINE, M.D.
University of Wisconsin School of Medicine, Madison.

JOSEPH C. ARCOS, D.Sc.
Professor of Medicine, Tulane University School of Medicine, New Orleans, LA.

ALAN K. ARMITAGE, Ph.D.
Research Director, Hazleton Laboratories Europe, Harrogate, North Yorkshire, England.

MARILYN S. ARNOTT (RASCO), Ph.D.
Assistant Biologist and Assistant Professor of Biology, The University of Texas System Cancer Center, M.D. Anderson Hospital and Tumor Institute, Houston.

THOMAS M. AUNE, Ph.D.
Assistant Professor of Pathology, The Jewish Hospital of St. Louis.

DOMINGO M. AVIADO, M.D.
Professor of Pharmacology, University of Pennsylvania School of Medicine, Philadelphia.

IRIT AVIRAM, Ph.D.
Department of Biochemistry, The Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel.

STEPHEN M. AYRES, M.D.
Director, Cardiopulmonary Laboratory, Saint Vincent's Hospital, New York.

BERNARD M. BABIOR, M.D., Ph.D.
Head, Division of Biochemistry, Scripps Clinic and Research Foundation, La Jolla, CA.

LESLIE BAER, M.D.
Associate Professor of Medicine, Columbia University College of Physicians & Surgeons, New York.

OSCAR J. BALCHUM, Ph.D.
Hastings Professor of Medicine, University of Southern California School of Medicine, Los Angeles.

SAMUEL BALK, M.D., Ph.D.
Pathologist, New England Deaconess Hospital, Boston.

FREDERIK B. BANG, M.D.
Professor and Chairman, Department of Pathobiology, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD.

MICHAEL BÁRÁNY, M.D., Ph.D.
Professor of Biological Chemistry, University of Illinois, Chicago.

LAURIE BARCLAY, M.D.
University of South Florida, Tampa.

A. CLIFFORD BARGER, M.D.
Robert Henry Pfeiffer Professor of Physiology, Harvard Medical School, Boston.

BRODA O. BARNES, M.D., Ph.D.
Professor (Affiliate) of Physiology, Colorado State University, Fort Collins.

FREDERICK W. BARNES, Jr., M.D.
Associate Professor of Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD.

T. C. BARNES, D.Sc.
Research Scientist, Philadelphia State Hospital.

CARL G. BECKER, M.D.
Associate Professor of Pathology, Cornell University Medical College, New York.

R. FREDERICK BECKER, Ph.D.
Associate Professor of Anatomy and Director, Laboratory of Perinatal Science, Duke University Medical Center, Durham, NC.

RALPH S. BECKER, Ph.D.
Professor of Chemistry, University of Houston.

BENJAMIN BELL, M.D.
Director Emeritus, Normative Aging Study, Veterans Administration Outpatient Clinic, Boston.

SAMUEL BELLET, M.D.
Director, Division of Cardiology, Philadelphia General Hospital, Philadelphia.

BARUJ BENACERRAF, M.D.
Fabyan Professor and Chairman, Department of Pathology, Harvard Medical School, Boston.

WILLIAM F. BENEDICT, M.D.
Assistant Professor of Pediatrics, University of Southern California School of Medicine, Division of Hematology and Medical Genetics, Children's Hospital of Los Angeles, Los Angeles.

BARBARA J. van den BERG, M.D.
Research Pediatrician, Adjunct Professor in Biostatistics, University of California School of Public Health, Oakland.

JOHN A. BEVAN, M.D.
Professor of Pharmacology, University of California School of Medicine, Los Angeles.

BUDHDEV BHAGAT, Ph.D.
Professor of Physiology, Saint Louis University School of Medicine, St. Louis.

CESARE BIANCIFIORI, M.D.
Division of Cancer Research, University of Perugia, Perugia, Italy.

HYLAN A. BICKERMAN, M.D.
Assistant Professor of Medicine, and ALVAN L. BARACH, M.D., Consultant in Medicine, Columbia University College of Physicians & Surgeons, Goldwater Memorial Hospital, New York, NY.

BIO-RESEARCH CONSULTANTS, INC.
Cambridge, MA.

BIO-RESEARCH INSTITUTE, INC.
Cambridge, MA.

DEBAJIT K. BISWAS, Ph.D., D.Sc.
Associate Professor of Oral Biology, Laboratory of Pharmacology, Harvard School of Dental Medicine, Boston.

IRA B. BLACK, M.D.
Professor and Chief, Division of Developmental Neurology, Cornell University Medical College, New York.

PHYLLIS B. BLAIR, Ph.D.
Professor of Immunology, University of California, Berkeley.

FRED G. BOCK, Ph.D.
Associate Cancer Research Scientist, Biological Station, Roswell Park Memorial Institute, Springville, NY.

GUENTHER BODEN, M.D.
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INDEX OF PRINCIPAL INVESTIGATORS

Adamson, I. Y. R., 58
Adelman, B., 75, 76
Allende, J. E., 115
Antoniades, H. N., 19, 20
Attie, A. D., 77
Barnes, D., 20, 115
Baylin, S. B., 21, 22
Befus, A. D., 59, 78, 163
Bennett, J. S., 79
Bing, R. J., 79-81
Blalock, J. E., 101, 163-165
Bockman, D. E., 166
Bona, C. A., 166, 167
Broker, T. R., 22
Bucher, N. L. R., 116
Burch, J. W., 81
Burstein, D. E., 23-25
Cabot, M. C., 116, 117
Campbell, E. J., 60-63
Capra, J. D., 167
Castellot, J. J., Jr.
(with Wright, T. C., Jr.), 82
Celada, F., 168
Chapman, H. A., Jr., 64
Chevion, M., 83, 84, 118
Cines, D. B., 85-87
Clawson, G. A., 119
Cohen, S., 120
Colman, R. W., 88, 121
Conhaim, R. L., 65
Dempsey, J. A., 65
Doyle, L. A., 26
Faller, D. V., 66
Feramisco, J. R., 121
Fink, J. S., 122
Fridovich, I., 122-126
Fuxe, K., 101
Gauldie, J., 67, 168
Giam, C.-Z., 169
Gill, G. N., 26, 127
Godman, G. (with Stern, D.), 88
Goldberg, I. J., 89
Goyert, S. M., 127
Green, K. J., 128, 129
Hajjar, K. A., 90
Hanafusa, H., 28-30

Hung, M.-C., 30
Isakson, P. C., 169
Jaken, S., 129
Jeang, K.-T., 31
Jesty, J., 91
Kadin, M. E., 31
Kao, F.-T., 170
Karin, M., 32-34, 130, 131
Kohler, H., 171
Koppenol, W. H., 131-135
Kretsinger, R. H., 135
Kuchta, R. D., 135
Kulkarni, A. P., 34, 68, 136-138
Lanier, S. M., 139
Lee, E. Y.-H. P., 35, 36
Leighton, J., 36
Lindstrom, J., 103-105
Lipsick, J. S., 37
Lotan, R., 38
Lukas, R. J., 106, 107, 140
Lundberg, J. M., 69-71, 91, 173
Lynch, H. T., 39
Maccioni, R. B., 141
Martin, G. S., 39, 92, 142
Mason, R. W., 143
Nahm, M. H., 174
Naylor, S. L., 40
Nelson, D. J., 144, 145
Nordeen, S. K., 40, 145
Oh, S.-K., 176
Oparil, S., 71, 72
Osawa, Y., 146
Osbakken, M. D., 93
Paigen, B., 94
Pierce, G. B., 41, 42, 147
Pizzo, S. V., 148, 149
Polak, J. M., 72
Rahamimoff, R., 107, 108
Richmond, V. L., 150
Robinson, J. M., 150-152
Rosen, G. M., 153
Rubin, H., 42, 43, 154
Saffer, J. D., 43
Sancar, A., 44, 155
Schnaper, H. W., 177
Schuger, L., 73

REPORT
of
THE COUNCIL FOR
TOBACCO RESEARCH - U.S.A., Inc.

1986

Abstracts of Reports

Following are abstracts, approved by the authors, of reports on new research acknowledging support from The Council that have appeared in scientific journals since publication of the 1985 Report. The name of the grant recipient is in italics.

The abstracts are grouped under these headings: I. Cancer-Related Studies, II. The Respiratory System, III. Heart and Circulation, IV. Neuroparmacology and Physiology, V. Pharmacology and Biochemistry, VI. Immunology and Adaptive Mechanisms, VII. Metabolic Studies, VIII. Epidemiology.

I. Cancer-Related Studies

IDENTIFICATION OF PROCESSING EVENTS IN THE SYNTHESIS OF PLATELET-DERIVED GROWTH FACTOR-LIKE PROTEINS BY HUMAN OSTEOSARCOMA CELLS

The human osteosarcoma-derived cell line U-2 OS expresses *c-sis* mRNA and synthesizes platelet-derived growth factor (PDGF)-like proteins. Pulse-chase experiments indicate the proteins of 23 kDa and 180 kDa are synthesized first. The 23-kDa protein undergoes dimerization and proteolysis, giving rise to the 30-kDa dimeric protein secreted by the cells. The 180-kDa protein is proteolytically cleaved in a complex series of steps that give rise to several intracellular species. It is also the likely precursor of high molecular mass PDGF-like or PDGF-associated proteins secreted by these cells. The processing and secretion of the 180-kDa protein is slower than that of the 23-kDa protein. Subcellular fractionation and studies with the antibiotic monensin indicate that the processing events occur in the Golgi-endoplasmic reticulum compartment of U-2 OS cells.

Graves, D. A., Owen, A. J., Williams, S. R., and *Antoniades, H. N.*

Proceedings of the National Academy of Sciences, USA **83**:4636-4640, July 1986.

Other support: National Institutes of Health and the American Cancer Society.

From the Center for Blood Research and Department of Nutrition, Harvard School of Public Health, Boston.

HUMAN LEUKEMIA CELLS SYNTHESIZE AND SECRETE PROTEINS RELATED TO PLATELET-DERIVED GROWTH FACTOR

Human leukemia cells in culture (HL-60) synthesize and secrete proteins that are recognized by antiserum to human platelet-derived growth factor (PDGF). The molec-

SUPPRESSION OF TUMORIGENICITY WITH CONTINUED EXPRESSION OF THE c-Ha-ras ONCOGENE IN EJ BLADDER CARCINOMA-HUMAN FIBROBLAST HYBRID CELLS

A human tumor cell line (EJ) expressing an activated c-Ha-ras oncogene was fused with a normal human fibroblast cell line. This fusion resulted in hybrids that behaved as transformed cells in culture but failed to form tumors in nude (athymic) mice. After repeated cell passage, two tumorigenic segregants of the hybrids arose in culture. The levels of expression of activated c-Ha-ras mRNA and its protein product, p21, were similar in the EJ cell line, the nontumorigenic hybrids, and the tumorigenic segregants. DNA transfections of the hybrids were performed with activated c-Ha-ras plasmid constructs, and transfectants expressing a 2-fold level of c-Ha-ras relative to the hybrid cells were found to maintain the nontumorigenic phenotype. We suggest that expression of the active c-Ha-ras oncogene is insufficient for the malignant transformation of these human cells.

Geiser, A. G., Der, C. J., Marshall, C. J., Stanbridge, E. J.

Proceedings of the National Academy of Sciences, USA 83:5209-5213, July 1986.

Other support: National Cancer Institute and the Philip and Clarisse Fay Fund.

From the Department of Microbiology and Molecular Genetics, College of Medicine, University of California, Irvine.

SELECTIVE TRANSFER OF INDIVIDUAL HUMAN CHROMOSOMES TO RECIPIENT CELLS

Two hypoxanthine phosphoribosyltransferase-deficient human cell lines, D98/AH-2 and HT1080-6TG, were stably transfected with pSV2 *gpt*, a plasmid containing the selectable marker *Escherichia coli* xanthine-guanine phosphoribosyl transferase (Eco *gpt*). Hypoxanthine-aminopterin-thymidine-resistant transformants arose with a frequency of ca. 10^{-6} and contained mostly single, but occasional multiple, copies of the plasmid sequences. These transformants actively express the Eco *gpt* marker. Single chromosomes from two different HT1080 *gpt* transformants and one D98 *gpt* transformant, containing the integrated plasmid sequences, were transferred via microcell-mediated chromosome transfer to hypoxanthine phosphoribosyl transferase-deficient mouse A9 cells. The transferred human chromosomes were identified as 2, 4 and 22 by using a combination of G-I staining, G-banding, isoenzyme analysis, and *in situ* hybridization. This system is being used to create a library of interspecies microcell hybrid clones, each containing a unique single human chromosome in a mouse background. The complete library will represent the entire human karyotype.

Saxon, P. J., Srivatsam, E. S., Leipzig, G. V., Sameshima, J. H., and Stanbridge, E. J.

Molecular and Cellular Biology 5(1):140-146, 1985.

Other support: National Cancer Institute and National Institutes of Health.

From the Department of Microbiology and Molecular Genetics, College of Medicine, University of California, Irvine.

PHAGOCYTES AS CARCINOGENS: MALIGNANT TRANSFORMATION PRODUCED BY HUMAN NEUTROPHILS

In a study of the relation between chronic inflammation and carcinogenesis, C3H mouse fibroblasts of the 10T 1/2 clone 8 line (10T 1/2 cells) were exposed to human neutrophils stimulated to synthesize reactive oxygen intermediates or to a cell-free enzymatic system generating superoxide (xanthine oxidase plus hypoxanthine). After exposure, the 10T 1/2 cells were either placed in tissue culture or immediately injected into athymic nude mice. Both malignant and benign tumors developed in the mice injected with treated cells, but not in those injected with control cells; in one instance cells grown from one benign tumor subsequently developed a malignant phenotype. Malignant transformation was also observed in treated cells in the experiments *in vitro*.

Weitzman, S. A., Weitberg, A. B., Clark, E. P., and Stossel, T. P.

Science 227:1231-1233, 1985.

Other support: American Cancer Society, National Institutes of Health, Edwin Hiam, and the Edwin Webster Foundation.

From the Hematology-Oncology Unit, Massachusetts General Hospital Cancer Center, and Department of Medicine, Harvard Medical School, Boston.

AUGMENTED EXPRESSION OF NORMAL c-myc IS SUFFICIENT FOR COTRANSFORMATION OF RAT EMBRYO CELL WITH A MUTANT ras GENE

The authors studied the effect of altered c-myc structure and expression upon the ability of c-myc to promote the transformation of normal rat embryo cells when it was supplemented by EJras (the mutant c-H-ras/ gene from EJ/T24 bladder carcinoma cells). We tested several c-myc alleles cloned from normal and tumor tissues of chicken and human origin and found that only LL4myc (derived from a bursal lymphoma in which an avian leukosis virus long terminal repeat resides within the first c-myc intron in the same transcriptional orientation) had cotransforming activity. No activity was observed with normal chicken and human c-myc alleles, two other bursal lymphoma c-myc alleles (LL3myc and LL6myc) and two human c-myc genes (HSR^{myc} and DM^{myc}) from human neuroectodermal tumor cell line COLO320, in which c-myc is amplified. Some of these inactive alleles had the following alterations that are frequently found in tumor-derived c-myc: point mutations affecting the encoded protein (LL3myc): a truncated structure with loss of the first, noncoding exon (LL3myc and DM^{myc}); and proviral integration within or near the myc locus (LL3myc and LL6myc). The following two experimental approaches indicated that cotransforming activity was directly related to the transcriptional activity of the alleles in cultured rat cells: (i) when cotransfected into Rat-2 cells, LL4myc was more highly expressed than the other (inactive) alleles; and (ii) augmented expression of HSR^{myc}, DM^{myc}, or normal human or normal chicken c-myc placed under the transcriptional control of retroviral long terminal repeats or increased expression of normal human c-myc under the in-

fluence of a retroviral enhancer element was accompanied by cotransformation activity. We concluded that augmented expression of even a normal *c-myc* gene is sufficient for cotransforming activity and that additional structural alterations frequently found in tumor-derived alleles are neither necessary nor sufficient for the gene to acquire rat embryo cell cotransforming properties.

Lee, W. F., Schwab, M., Westaway, D., and Varmus, H. E.

Molecular and Cellular Biology 5(12):3345-3356, 1985.

Other support: The George Hooper Research Foundation, National Institutes of Health and American Cancer Society.

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A DE-GLUCURONIDATION INHIBITOR REDUCES THE INDUCTION BY BENZO[α]PYRENE OF A 60-KILODALTON ONCOFETAL PROTEIN AND DNA BINDING *IN VIVO*

The objective of the present study was to evaluate the possibility of reducing carcinogenicity of benzo[α]pyrene (BP) in rats by the use of 2,5-di-O-acetyl-D-glucaro-1,4:6,3-dilactone (DAGDL). Our previous study demonstrated that DAGDL, a precursor of D-glucaro-1,4-lactone, known to be a natural inhibitor of β -glucuronidase, caused a 70% reduction in the incidence of mammary tumor induction in rats by 7,12-dimethylbenz[α]anthracene (DMBA). Coadministration of DAGDL also reduced the induction of a 60 kd oncofetal protein shown to be associated with carcinogenesis and tumorigenesis, and markedly reduced binding of DMBA to organ DNA. In the present study we have examined the effect of DAGDL coadministration on the induction of the oncofetal protein and its binding to organ DNA in the rat. DAGDL suppressed by 75% the induction of the oncofetal protein by a carcinogenic dose of BP. DAGDL also reduced BP binding to organ DNA, i.e. by 50–70%, depending on the organ examined. DAGDL appears to act as an anti-carcinogen depending on the organ examined. DAGDL appears to act as an anti-carcinogen by inhibiting deglucuronidation of hydroxylated metabolites of PAH, thereby increasing detoxification and carcinogenic clearance.

Walaszek, Z., Hanausek-Walaszek, M., and Webb, T. E.

In: Cooke, M. W. and Dennis, A. J. (eds.): *Polynuclear Aromatic Hydrocarbons: Ninth International Symposium on Chemistry, Characterization and Carcinogenesis*, Columbus, OH: Battelle Press, 1984, pp. 947-959.

Other support: National Cancer Institute.

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DIETARY GLUCARATE-MEDIATED REDUCTION OF SENSITIVITY OF MURINE STRAINS TO CHEMICAL CARCINOGENESIS

Serum β -glucuronidase activity is shown to differ quantitatively in the following strains of mice, listed in order of increasing activity: C3H, C57BL/6 < BALB/c, DBA/2, ICR < SENCAR, A/He. The level of the enzyme in the murine strains is shown to correlate with the urinary excretion of 17-ketosteroids, which in turn reflects the endogenous level of androgens. Dietary calcium D-glucarate, an *in vivo* β -glucuronidase inhibitor, reduced the steady state level of both β -glucuronidase and 17-ketosteroid excretion in the highly susceptible A/He and SENCAR strains to that of strains known to be resistant to chemical carcinogenesis. Sensitivity of the A/H strain is significantly reduced by dietary calcium glucarate, which is shown to inhibit DNA binding and the induction of pulmonary adenomas by benzo[α]pyrene.

Walaszek, Z., et al.

Cancer Letters 33:25-32, 1986.

Other support: National cancer Institute.

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USE OF SHORT DNA OLIGONUCLEOTIDES FOR DETERMINATION OF DNA SEQUENCE MODIFICATIONS INDUCED BY BENZO[α]PYRENE DIOL EPOXIDE

Various organic agents that alkylate DNA are known to induce mutations in bacterial and animal cells. The precise nature and location of modified DNA sequences in such mutants are often difficult to ascertain. In this report, a 10-base-pair oligomer (*Bam*HI linker) is treated with (\pm)-*trans*-benzo[α]pyrene-7,8-dihydrodiol-9,10-epoxide and inserted into replicative form DNA of phage M13 by ligation at a specific restriction site. *Escherichia coli* are transfected with the recombinant DNA containing the alkylated target, progeny viral plaques are selected, and their DNAs are subjected to DNA sequence analysis at the region of oligomer insertion. For the alkylated inserts used in this study, the DNA sequence analysis of progeny viral DNA showed that nucleotide deletions were present in every clone examined. These deletions occurred primarily, but not exclusively, at G-C cluster regions, varied from 1 to 24 base pairs in length, and include both target and nontarget nucleotides. A second type of repair, which restores most of the original nucleotide bases in the alkylated insert, is also implied by the DNA sequence data obtained.

Wei, S.-J. C., Desai, S. M., Harvey, R. G., and Weiss, S. B.

Proceedings of the National Academy of Sciences, USA 81:5936-5940, 1984.

Other support: U. S. Department of Energy, American Cancer Society and National Cancer Institute.

From the Franklin McLean Memorial Research Institute, the Department of Biochemistry and the Ben May Laboratory for Cancer Research, University of Chicago.