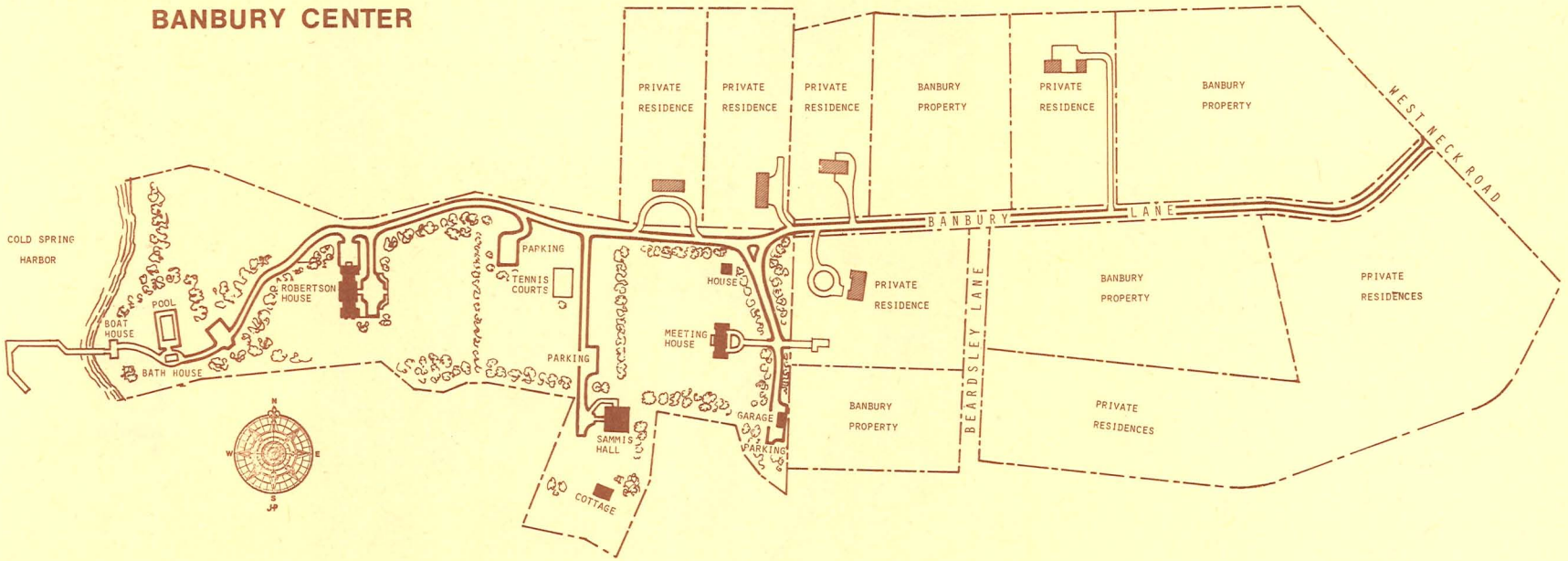
# Banbury Center

of Cold Spring Harbor Laboratory

Sammis Hall

1980

## BANBURY CENTER




*Mailing address:*
Banbury Center
P. O. Box 534
Cold Spring Harbor, New York 11724

# BANBURY CENTER

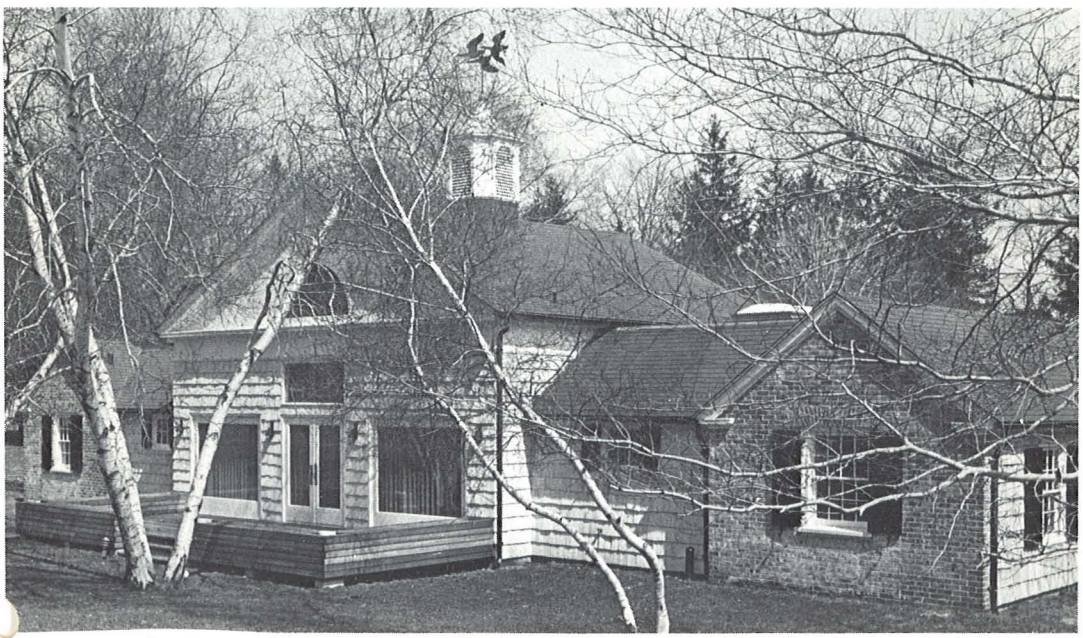
## OF COLD SPRING HARBOR LABORATORY

Founded in 1977 by the Cold Spring Harbor Laboratory, the Banbury Center is situated on a gracefully beautiful, 45-acre estate, located in the Village of Lloyd Harbor, New York, given to the Laboratory in 1976 by Mr. Charles Robertson, who died in May 1981. The Center provides a meeting house, housing and dining facilities for conference participants, and editorial offices which produce volumes of conference proceedings.

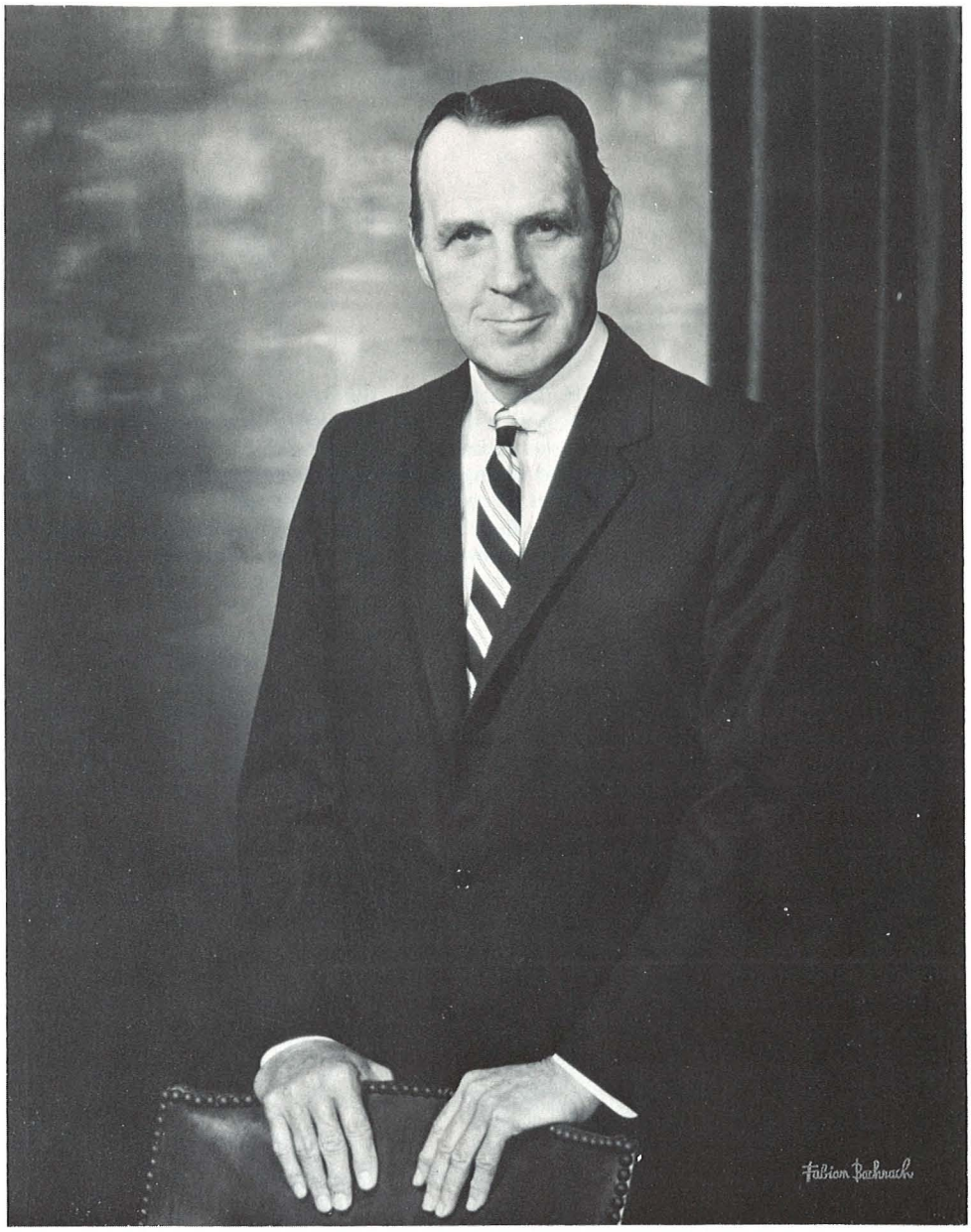
The Banbury Center extends the Laboratory's well-known activities in research and the holding of conferences and courses in fundamental biology in a new direction: the holding of small meetings for both specialists and nontechnical groups on issues of biology and public policy. The meetings concentrate on environmental health risks, chiefly environmental sources of cancer that point to opportunities for cancer prevention. The conferences consider risks affecting workers or consumers and such techniques of risk assessment as short-term testing of chemicals and human health data collection and analysis.

The meetings for specialists are intended to help mobilize scientific talent working on environmental health problems and to present these problems to a wider public in a factual, nonargumentative way. Separately funded meetings bring specialists together with nontechnical people doing policy-oriented jobs, such as journalists and congressional staff, for background workshops.

The Banbury Center includes Robertson House, a Georgian-style mansion, capable of offering meals to some 32 persons and overnight accommodations for 20; a meeting house, containing a conference room, library, and offices, which was converted from a garage in 1977; Sammis Hall, a new guest house with 16 single bedrooms, completed in early 1981; and such recreational facilities as a tennis court, a swimming pool, and a beach.



*Meeting House, rear view*




# Charles S. Robertson

**February 13, 1905–May 2, 1981**

On May 2, 1981, while meeting in the Banbury Meeting House, the Cold Spring Harbor Laboratory Board of Trustees learned of the imminent death of Mr. Charles S. Robertson at his home in Florida. The trustees stood in silent tribute after passing the following resolution: "The Board of Trustees of Cold Spring Harbor Laboratory wishes to record its affection and respect, and deep gratitude to Charles S. Robertson, whose gifts of endowment and of his home in Lloyd Harbor to the Laboratory, along with other gifts from his family, have made an invaluable contribution to the support of research and the conduct of numerous programs in the fields of neuroscience and biology and public policy. In addition, the Board wishes to express its deep appreciation for the friendship and close personal interest of a valued neighbor."

# BANBURY CENTER 1980 Activities

The third year of the Banbury Center program on the environmental health risks that are an urgent concern of biological science and public policy was a period of both fulfillment and difficulty.

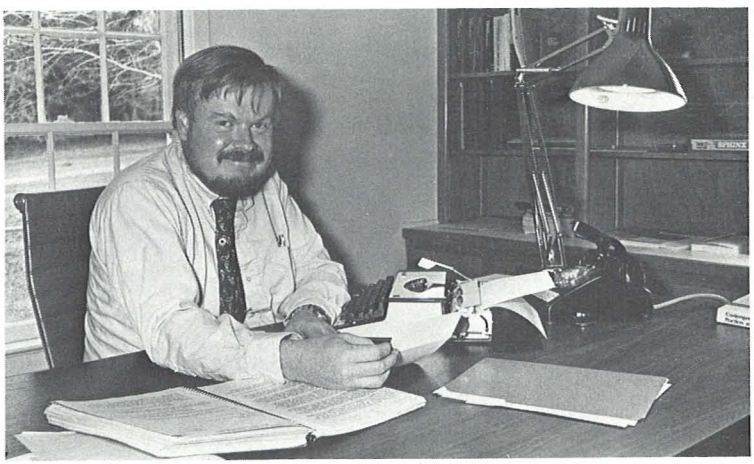
The sense of fulfillment came from several sources. Reports continued to emerge from meetings that participants found both focused and stimulating. There was continued praise from participants for the facilities at Banbury and the arrangements made by many people, most notably by Beatrice Toliver, the Banbury administrative assistant, and by Katya Davey, our hostess and cook in Robertson House. Further meetings were held in 1980 on topics likely to produce reports of even wider interest than those published previously. Response was excellent to an appeal for conference ideas made to leaders in research on environmental health risks. Small meetings at Banbury on rapidly developing fields of fundamental biology continued to proliferate. Planning for meetings in 1981 and 1982, several involving collaboration with other institutions including government agencies, pushed forward.

The difficulty came because early expectations of funding the Banbury program entirely from sources outside the Laboratory were not met. About 30 percent of the program's cost so far has come from appropriations of Laboratory funds by a Board of Trustees that vigorously endorses the public service goals of the Banbury program but insists, along with the Laboratory and Banbury administrations, that the deficits must be removed promptly through vigorous fund raising for both short-term and long-term needs.

### Environmental Health Risks

The three years since the start of the Banbury program have been a time of intensifying concern about the possibility that agricultural and industrial chemicals, or factors in the diet, or such pleasurable habits as smoking—things that other people do to us or that we do to ourselves—may contribute to variations in cancer rates between different localities or over time. In the same period, scientific studies of the linkages between the environment and cancer have intensified, in the hope of better understanding of how cancers may be prevented.

But as the studies continue, the goal of cancer prevention is clouded by complications. Writing in *Nature* in January 1981, John Cairns, former Director of Cold Spring Harbor Laboratory, pointed out that few types of cancer fit a simple model of causation by damage to the genetic material in the nuclei of cells, as would be caused by



*Victor McElheny, Banbury Center Director*

mutagenic chemicals in the workplace or the general environment. Cairns, now at the Harvard School of Public Health and one of Banbury Center's scientific advisors, noted that more complex models, involving several stages, drastic rearrangements of chromosomes, the action of the body's metabolism and the action of so-called promoters, are thrusting themselves forward. The new complexity is not discouraging. Instead, it becomes clearer than ever that biology and genetics at the molecular level—the subjects that Cold Spring Harbor Laboratory works on—have a multi-faceted relevance to the understanding of the onset of cancer. Also clearer than ever is the relevance of an environmental health-risk program, focused on cancer prevention, at a fundamental biology laboratory.

### Four New Books

Publication of the first two Banbury Reports in 1979, covering environmental mutagens and mammalian-cell mutagenesis tests, was followed in 1980 by Banbury Reports 3 through 6, covering low-tar cigarettes, populations with low cancer rates, ethylene dichloride, and the labeling of dangers. The four books explore a wide range of issues: whether cigarette-linked lung cancer, the largest single environmental cancer cause, can be reduced; how we can improve our knowledge of such risks as dietary factors by studying defined populations with low cancer rates; how to resolve conflicts between two different cancer tests of the same substance; and whether labeling by itself can be heavily relied on for public health protection strategies.

The production of the four books was made smoother and faster by good relations with authors, typesetters, and printers, achieved by Lynda Moran and Judith Cuddihy, the Banbury editors, and Kathleen Kennedy, the Banbury editorial assistant. Conferences held in October and November of 1979 resulted in books published in May, June, and August of 1980. The conference on labeling in May 1980 produced a book in December. Our book on cancer risks in defined populations, appearing in June 1980, came out five months earlier than the proceedings of a conference involving many of the same people—held one year before our conference.

The availability of a professional transcript of each conference allowed us to increase the interest of each book by including lively discussion of the formal papers. Through strong sales, including those to the National Cancer Institute, the books came very close to meeting all publication expenses, including marketing and overhead.

### Conferences

The first 1980 conference, in May, on environmental health risks, represented a first foray into the social-science aspects of this field. The conference concluded that labeling could not handle the regulatory burden of public health protection single-handedly. The conference on gastrointestinal cancer in October focused new attention on substances formed inside the body, rather than those taken in, that may be important in causing cancer of the colon. The conference on hormones and breast cancer, also in October, explored the notion of a close linkage between total estrogen exposure and the risk of contracting breast cancer.

The uses of the Banbury estate continued to expand. At the beginning of March, James Hicks of the yeast group at the Laboratory, organized a workshop on the molecular biology of plants. In May, two members of the Laboratory's Neurobiology Advisory Committee organized a small conference on the molluscan nerve cell. To edit the book resulting from this conference, which received a very favorable review in the journal

*Katya Davey*

*Judith Cuddihy, Lynda Moran, Beatrice Toliver*

*Science*, on May 15, 1981, Judith Cuddihy of our staff temporarily shifted to the editorial group in Nichols. In November, Ron McKay of the scientific staff organized a workshop on monoclonal antibodies against neural antigens, which is expected to result in a book in 1981. In December, the Banbury staff worked with Joe Sambrook in organizing the conference on construction and use of mammalian vectors, which was summarized in the British journal, *Nature*, on March 5, 1981.

Planning continued for what has been undoubtedly the most difficult and controversial of the Banbury risk assessment conferences so far. This was the conference at the end of March 1981 on the quantification of occupational cancer. Elaborate consultations were held up to the last minute with all sides of the complex arguments about the true size of the cancer risk in the workplace, to assure that major viewpoints were represented. The 55 participants heard estimates of cancer attributable to occupation that were smaller than the most alarmist figures, but larger than those put forward by opponents of government regulation of workplace conditions.

In 1980, planning began for many meetings in 1981–82, including the conferences on gene amplification and aberrant chromosomal structures, scheduled for October, patenting of life forms, also scheduled for October, and environmental risks for developing organisms (including children), scheduled for Novemeber.

Funds were requested for conferences in February and March 1982 on the possible role of nitrosamines in human cancer and new techniques of chemical dosimetry.

### Courses

Occupying Banbury facilities almost continuously from the end of the spring conference season in early June to the beginning of the late-summer conference season in mid-August was a series of courses. The first of these, on the Neurobiology of Behavior, was taught by Eric Kandel and John Koester of the Columbia University College of Physicians and Surgeons and Keir Pearson of the University of Alberta. The second, called The Synapse: Cellular and Molecular Neurobiology, was taught by Rami Rahamimoff of the Hebrew University Medical School in Jerusalem, Jack McMahon of Stanford University, Bernard Katz of University College, London, Charles Stevens of Yale University and Doju Yoshikami of the University of Utah. The third course, on Principles of Neural Development, was taught by Dale Purves of Washington University in St. Louis and P. H. Patterson of Harvard Medical School. After these courses, Arnold J. Levine of the State University of New York organized, along with D. P. Lane of Imperial College, London, a former member of the Laboratory scientific staff, a workshop on Tumor and Development Antigens. Details on attendance and programs are printed in the

section on post-graduate training programs. Both Dr. Stevens and Dr. Levine are scientific trustees of Cold Spring Harbor Laboratory.

### Support

Through the year, plans were made for the first of our workshops for journalists under the $100,000 grant from the Alfred P. Sloan Foundation (noted in the report for 1979). This workshop, for the editorial staff of *Newsday,* was held in January 1981, and concerned issues of ground water pollution, the disposal of chemical wastes, and the influence of diet on cancer rates. The success of that workshop triggered planning for several more during 1981, including a highly successful workshop on DNA held for leading editorial managers and writers of Time Inc. magazines on May 3 and 4, 1981.

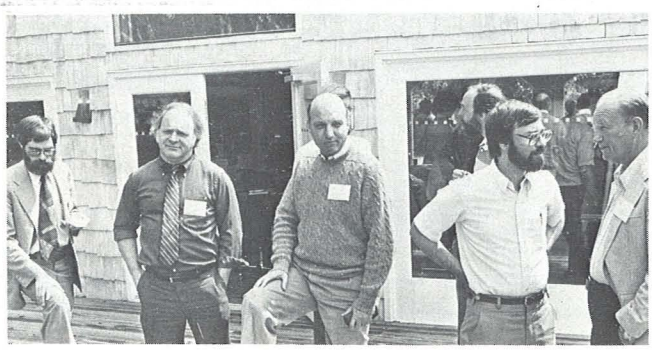
Our fund raising in 1980 was greatly assisted by the purchase of many books from four Banbury conferences by the National Cancer Institute, for wide distribution to institute grantees. Approaches to each United States government agency with a mission in the field of environmental health risks, aimed at joint sponsorship of conferences, bore fruit in the scheduling of two conferences in 1981. Gratifying support was received from the Exxon Education Foundation, the International Life Sciences Institute, and the Environmental Protection Agency for the labeling conference, and from Hoffmann-LaRoche, Inc. and Merck Sharp and Dohme Laboratories for the conference on gastrointestinal cancer. The conference on mammalian vectors drew contributions from nearly a dozen companies, including Abbott Laboratories, Cetus Corporation, Collaborative Genetics Inc., E.I. duPont de Nemours & Co., Genex Corporation, Genentech Inc., Lilly Research Laboratories, Molecular Genetics Inc., Monsanto Company, and New England BioLabs. Very welcome sustaining support was received from New York Life Insurance Company and the Bristol-Myers Foundation.

## Product Labeling and Health Risks, May 21–May 23

Because of increasing public discussion of the use of labeling as a substitute for banning products which might be hazardous to at least some people, Louis A. Morris of the Food and Drug Administration, Michael B. Mazis of the American University and Ivan Barofsky of the Johns Hopkins Medical Institutions were asked to organize a conference on the efficacy of labeling as the major reliance in schemes of warning. This sixth of the Banbury conferences on the assessment of environmental health risks brought a large number of behavioral scientists together with representatives of consumer-protection groups, regulatory agencies, industry and the legal profession. The conclusion of the conference was that it would be a mistake to rely wholly on labeling and voluntary action to handle a clearly identified risk.

*Session 1: Labeling Case Studies*

M. Mazis, The American University, Washington, DC: Introduction, classification, integration.
D. Murphy, Federal Trade Commission, Washington, DC: Cigarette warning labels.
L. Morris, Food and Drug Administration, Rockville, Maryland: Estrogenic drugs—PPIs.
A. Reich, Occupational Safety and Health Administration, Washington, DC: Carcinogens at the work place.
R. Staelin, Carnegie-Mellon University, Pittsburgh, Pennsylvania: Food, product safety, and performance labeling.
R. C. Stokes, Food and Drug Administration, Washington, DC: FDA's food labeling research program.



*Session 2: Labeling as a Communications Device*

W. McGUIRE, Yale University, New Haven, Connecticut: Communications model.
J. C. OLSON, Pennsylvania State University, University Park: Attention/memory factors.
P. LEY, Plymouth Polytechnic, Devon, England: Practical methods of improving communication.
D. KANOUSE, Rand Corporation, Santa Monica, California: Critical aspects of communication.
P. SLOVIC, Decision Research, Eugene, Oregon: Convening risk information.

*Session 3: Roundtable—Labeling Alcohol Bottles with Pregnancy Warnings*

*Chairperson:* P. WHITE, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland

H. BRESLAWEC, Food and Drug Administration, Rockville, Maryland
M. DRESSLER, Bureau of Alcohol, Tobacco and Firearms, Washington, DC
S. FABRO, George Washington University Medical Center, Washington, DC
P. GAVAGHAN, Distilled Spirits Council of the United States, Inc. (DISCUS), Washington, DC

*Session 4: Labeling as a Social Policy*

W. SCHULTZ, Public Citizens Litigation, Washington, DC: Labeling, consumer needs, consumer rights.
J. WALDEN, The Proprietary Association, Washington, DC: From the producers' perspective.
H. BEALES, Federal Trade Commission, Washington, DC: Cost/benefit; economic perspectives.
I. BAROFSKY, Johns Hopkins Medical Institutions, Baltimore, Maryland: Psychosocial consequences.
P. RHEINSTEIN, Food and Drug Administration, Rockville, Maryland: Labeling and the health environment.
R. COOPER, Williams & Connolly, Washington, DC: Labeling as a regulatory alternative.

## Carcinogen and Mutagen Formation in the Gastrointestinal Tract, October 12–October 15

New interest in the relationship between diet and gastrointestinal cancer has been stirred by the discovery of a mutagenic factor in human feces, possibly a bacterial product, and by the discovery that mutagenic substances such as nitrosamines can be formed in the gastrointestinal tract. To summarize current knowledge and to focus additional attention on the role that endogenous factors may play in gastrointestinal cancer, W. Robert Bruce of the Ludwig Institute (then of the Ontario Cancer Institute), Pelayo Correa of the Louisiana State University Medical Center, Martin Lipkin of the Memorial Sloan-Kettering Cancer Center, Steven R. Tannenbaum of the Massachusetts Institute of Technology, and Tracy Wilkins of the Virginia Polytechnic Institute, organized a conference of some 40 specialists to consider such topics as the chemical structure of the mutagen found in feces, and epidemiological studies indicating that, in Japan, daily meat consumption reduces the risk of colon and rectal cancer while increasing the risk of pancreatic cancer, and that daily intake of yellow and green vegetables, containing vitamin A, is protective against several types of cancer. The book reporting on this conference was published in April 1981, exactly six months after the meeting.

*Session 1: Gastrointestinal Microbiology*

*Chairperson:* T. D. WILKINS, Virginia Polytechnic Institute and State University, Blacksburg

T. D. WILKINS, Virginia Polytechnic Institute and State University, Blacksburg: Microbiological considerations in interpretation of data obtained with experimental animals.
W. E. C. MOORE, Virginia Polytechnic Institute and State University, Blacksburg: The effect of diet on the human intestinal flora.
P. GOLDMAN, Harvard Medical School, Boston, Massachusetts: Metabolism of xenobiotics by the gastrointestinal flora.
B. GOLDIN, Tufts University School of Medicine, Boston, Massachusetts: Factors that affect intestinal bacterial activity—Implications for colon carcinogenesis.

*Session 2: Fiber*

*Chairperson:* P. J. VAN SOEST, Cornell University, Ithaca, New York

P. J. VAN SOEST, Cornell University, Ithaca, New York: Some factors influencing the ecology of gut fermentation in man.
J. H. CUMMINGS, MRC Dunn Clinical Nutrition Centre, Cambridge, England: Implications of dietary fiber breakdown in the human colon.
N. D. NIGRO, Wayne State University School of Medicine, Detroit, Michigan: Fat, fiber, and other modifiers of intestinal carcinogenesis—A strategy for prevention.

*Session 3: Host Response to Carcinogens*

*Chairperson:* M. LIPKIN, Memorial Sloan-Kettering Cancer Center, New York, New York

M. LIPKIN, Memorial Sloan-Kettering Cancer Center, New York, New York: Susceptibility of high-risk populations.
P. CORREA, Louisiana State University Medical Center, New Orleans: Mutagenesis and adenomatous polyps of the colon.
M. E. BALIS, Sloan-Kettering Institute for Cancer Research, New York, New York: Enzymes in gastrointestinal cells in cancer.
H. W. STROBEL, University of Texas Health Science Center, Medical School, Houston: Role of cytochrome P-450 in the response of the colon to xenobiotics.
L. W. WATTENBERG, University of Minnesota Medical School, Minneapolis: Inhibitors of gastrointestinal neoplasia.
G. N. WOGAN, Massachusetts Institute of Technology, Cambridge, and others: Discussion.

*Session 4: Mutagens*

*Chairperson:* W. R. BRUCE, Ontario Cancer Institute, Toronto, Canada

G. M. STEMMERMANN, Japan-Hawaii Cancer Study, Honolulu, Hawaii: Mutagens in extracts of gastrointestinal mucosa.
T. D. WILKINS, Virginia Polytechnic Institute and State University, Blacksburg: Isolation of a mutagen produced in the human colon by microbial action.
D. G. I. KINGSTON, Virginia Polytechnic Institute and State University, Blacksburg: Structural studies on a mutagenic bacterial product from human feces.
W. R. BRUCE, Ontario Cancer Institute, Toronto, Canada: Studies of a mutagen from human feces.
S. VENITT, Institute of Cancer Research, Chalfont St. Giles, Buckinghamshire, England: Detection of mutagens in feces.
H. F. STICH, British Columbia Cancer Research Centre, Vancouver, Canada: Intake formation and release of mutagens by man.

*Session 5:* N-*nitroso Compounds*

*Chairperson:* S. R. TANNENBAUM, Massachusetts Institute of Technology, Cambridge

S. R. TANNENBAUM, Massachusetts Institute of Technology, Cambridge: Metabolism of nitrates.
S. R. TANNENBAUM, Massachusetts Institute of Technology, Cambridge: Endogenous formation of *N*-nitroso compounds.
G. EISENBRAND, Deutsches Krebsforschungszentrum, Heidelberg, Federal Republic of Germany: Assessment of exposure.
H. NEWMARK and W. J. MERGENS, Hoffmann-La Roche Inc., Nutley, New Jersey: Blocking nitrosamine formation using ascorbic acid and alpha-tocopherol.
E. BALISH, University of Wisconsin Medical School, Madison: Distribution of metabolism of nitrate and nitrite in rodents.

M. C. Archer, Ontario Cancer Institute, Toronto, Canada: Nitrate, nitrite, and *N*-nitroso compounds in the human intestine.
D. H. Fine, New England Institute of Life Sciences, Waltham, Massachusetts; L. K. Keefer, National Cancer Institute, Bethesda, Maryland; P. N. Magee, Temple University School of Medicine, Philadephia, Pennsylvania: Discussion.

*Session 6: Bile Acids and Other Lipids*

*Chairperson:* B. S. Reddy, American Health Foundation, Valhalla, New York

B. S. Reddy, American Health Foundation, Valhalla, New York: Bile salts and other constituents of the colon as tumor promoters.
M. J. Hill, Central Public Health Laboratory, London, England: Bile acids and colorectal cancer.
S. Hecht, Naylor Dana Institute for Disease Prevention, Valhalla, New York: Analysis of feces for benzo[a]pyrene after consumption of charcoal-broiled meat.

*Session 7: Epidemiology and Design of Future Studies*

*Chairperson:* P. Correa, Louisiana State University Medical Center, New Orleans

S. Graham, State University of New York at Buffalo: Epidemiologic tests of hypotheses of diet and cancer.
H. F. Mower, University of Hawaii, Manoa, Honolulu: Identification of mutagens found in gastric mucosa.
T. Hirayama, National Cancer Center Research Institute, Tokyo, Japan: A cohort study of life-style variables in gastrointestinal cancer in Japan.
W. Haenszel, University of Illinois, Chicago: The methodology for analysis of the relationship between mutagens and gastrointestinal cancer.

## Hormones and Breast Cancer, October 26–October 28

Breast cancer, which tragically accounted for 19% of the 183,000 female cancer deaths recorded in the United States in 1978, presents some of the most tangled puzzles faced by the researchers attempting to sort out the influences of genetic endowment and the environment in cancer causation. Still unidentified environmental factors apparently influence the sharp differences in breast cancer rates between Japan and the United States. Work by epidemiologists and experiments on rodents have underlined the importance of total exposure to estrogens in influencing the risk of breast cancer. But the organizers of the conference, Malcolm Pike of the University of Southern California, Pentti K. Siiteri of the University of California at San Francisco, and Clifford Welsch of Michigan State University, felt there was a strong need for a joint review of what is known about the etiology of breast cancer by epidemiologists, endocrinologists, and animal experimenters. They and the other conference participants surveyed the exogenous and endogenous factors affecting breast cancer incidence, summarized the underlying mechanisms by which hormones and carcinogens induce and promote tumor growth, and projected future directions for epidemiological and clinical research in the field.

*Session 1: Review of Epidemiology of Breast Cancer*

M. C. Pike, University of Southern California Medical School, Los Angeles: Epidemiology of breast cancer as it relates to menarche, pregnancy, and menopause.
F. de Waard, University of Utrecht, The Netherlands: Body size as a risk factor for breast cancer.

*Session 2: Endocrinology of Women at Risk to Breast Cancer*

J. B. Brown, University of Melbourne, Victoria, Australia: Hormone profiles in young women at risk.
R. Vihko, University of Oulu, Finland: Endocrine maturation in the course of female puberty.
S. S. Korenman, University of California, Los Angeles School of Medicine, Sepulveda: Abnormal ovarian function and breast cancer risk.
P. K. Siiteri, University of California, San Francisco: Estrogen production and transport following the menopause.

*Session 3: Review of Studies Attempting to Establish Endogenous Hormones as Important in Human Breast Cancer*

P. Cole, University of Alabama, Birmingham: Estrogens and progesterone.
B. E. Henderson, University of Southern California Medical School, Los Angeles: Prolactin.

R. D. Bulbrook, Imperial Cancer Research Fund Laboratories, London, England: Androgens and thyroid.
B. Zumoff, Montefiore Hospital and Medical Center, Bronx, New York: Hormonal studies in women with breast cancer.

*Session 4: In Vitro Studies of Human Breast Tissue*

M. E. Lippman, National Cancer Institute, Bethesda, Maryland: Hormonal regulation of breast cancer cells.
R. P. C. Shiu, University of Manitoba Faculty of Medicine, Winnipeg, Canada: Prolactin regulation of breast cancer cells.
R. Ottman, University of California, Berkeley, and P. K. Siiteri, University of California, San Francisco: Analysis of estrogen receptor assay data.

*Session 5: Exogenous Hormones and Breast Cancer*

J. L. Kelsey, Yale University School of Medicine, New Haven, Connecticut: Epidemiological studies of exogenous estrogens.
A. Segaloff, Alton Ochsner Medical Foundation, New Orleans, Louisiana: Hormonal therapy of breast cancer.

*Session 6: Other Exogenous Factors and Breast Cancer*

N. L. Petrakis, University of California Medical School, San Francisco: Epidemiological studies of mutagenicity of breast fluids—Relevance to breast cancer risk.
P. Hill, American Health Foundation, Valhalla, New York: Diet and hormone levels.

*Session 7: Hormones and the Genesis and Progression of Murine Mammary Tumors*

T. L. Dao, Roswell Park Memorial Institute, Buffalo, New York: Role of ovarian and adrenal steroids in mammary carcinogenesis.
C. W. Welsch, Michigan State University, East Lansing: Prolactin and growth hormone in murine mammary tumorigenesis.
R. Hilf, University of Rochester Medical Center, New York: Insulin.
C. J. Shellabarger, Brookhaven National Laboratory, Upton, New York: Pituitary and steroid hormones in radiation-induced mammary tumors.
R. C. Moon, Illinois Institute of Technology Research Institute, Chicago: Pregnancy, lactation, and thyroid hormones.
J. Meites, Michigan State University, East Lansing: Relation of neuroleptic drugs to mammary tumorigenesis.
Y. N. Sinha, Scripps Clinic and Research Foundation, La Jolla, California: Plasma prolactin analysis as a potential predictor of murine mammary tumorigenesis.

*Session 8: Mechanism of Hormone Action*

J. Rosen, Baylor College of Medicine, Houston, Texas: Regulation of casein gene expression in hormone-dependent mammary cancer.
D. A. Sirbasku, University of Texas Medical School, Health Science Center, Houston: Mechanism of estrogen action—Estrogen-induced growth factors.
S. Nandi, University of California, Berkeley: Role of hormones in carcinogenesis.

# Construction and Use of Mammalian Vectors

## December 10–December 13

Expression of foreign genes in mammalian cells was the focus of this early example of what are expected to be many small conferences on molecular aspects of biology to be held at Banbury Center. Organized with support from a dozen industrial companies by Joseph Sambrook, the Laboratory's Assistant Director for Research, the conference heard reports from academic, industrial, and government scientists on progress with complementary methods of introducing foreign genes into cultured mammalian cells. These methods include 1) microinjection; 2) attachment of the genes to segments of viral DNA; and 3) the simultaneous transformation of the cells with two separate pieces of DNA, one carrying the gene of interest and the other carrying a genetic marker, such as the gene for the enzyme thymidine kinase, which confers a selective advantage on cells receiving the foreign genes. Successes were reported in obtaining constitutive expression of microinjected genes and in obtaining expression through viral transmission of such foreign genes as human growth hormone, hepatitis surface antigen and human genomic globin sequences. The conference heard that some disadvantages with the most commonly employed virus vector, simian virus 40, such as a sometimes-small proportion of an SV40 population carrying the foreign genes and limits on how much foreign DNA can be packed into SV40 particles, are being overcome. New selective markers were discussed, along with the possibility that cotransformed genes can continue to respond to hormones.

*Session 1: Delivery Systems*

*Chairperson:* W. C. Summers, Radiobiology Laboratories, New Haven, Connecticut

W. C. Summers, Radiobiology Laboratories, New Haven, Connecticut: Structure and expression of the HSV-TK locus.

F. Ruddle, Yale University, New Haven, Connecticut: Gene transfer in mammalian cells.

M. Wigler, Cold Spring Harbor Laboratory, New York: The stable transformation of animal cells with biochemically selectable vectors.

G. Milman, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland: Efficient DNA transfection and rapid detection of DNA expression.

M. L. Pearson, Frederick Cancer Research Center, Maryland: Clonal analysis of the efficiency of *tk* and *oua* DNA-mediated gene transfer in mouse L cell recipients.

M. Capecchi, University of Utah, Salt Lake City: The expression and stable integration of EDN injected into nuclei of cultured mammalian cells.

C. Lo, University of Pennsylvania, Philadelphia: Iontophoretic injection and integration of DNA into mouse L cells.

W. F. Anderson, National Heart, Lung, & Blood Institute, Bethesda, Maryland: Fate of eukaryotic genes microinjected into mouse L cells.

*Session 2: Papovaviruses as Vectors*

*(i) Replication/Integration/Excision*

*Chairperson:* C. Basilico, New York University Medical Center, New York

C. Basilico, New York University Medical Center, New York, New York: Requirements for integration, excision, and amplification of polyoma virus genomes.
Y. Gluzman, Cold Spring Harbor Laboratory, New York: An SV40 host-vector system for carrying pure population of recombinant viruses.
M. Botchan, University of California, Berkeley: The stable transformation of animal cells with biochemically selectable vectors.
W. Jelinek, Rockefeller University, New York, New York: Interspersed repetitious sequences in mammalian DNA.
J. T. Elder, Yale University School of Medicine, New Haven, Connecticut: Structural and transcriptional analysis of interspersed repetitive polymerase III transcription units in human DNA.
J. Hassell, McGill University, Montreal, Canada: The organization, expression, and recovery of transfected genes—The polyoma transforming gene as a model.
M. Fried, Imperial Cancer Research Fund Laboratories, London, England: Polyoma virus expression.
C. Rogers, Oregon State University, Corvallis: The construction of recombinant DNA molecules containing the yeast leucine gene for use as eukaryotic vectors.
R. Breathnach, Faculté de Médecine, Strasbourg, France: SV40 and polyoma based vectors.
A. Weissbach, Roche Institute of Molecular Biology, Nutley, New Jersey: The construction of recombinant DNA molecules containing the yeast leucine gene for use as eukaryotic vectors.

*(ii) Expression of Cloned Genes*

*Chairperson:* T. Shenk, State University of New York, Stony Brook

P. Gruss and G. Khoury, National Cancer Institute, Bethesda, Maryland: Expression of preproinsulin genes carried in SV40.
P. T. Lomedico, Hoffmann-La Roche Inc., Nutley, New Jersey: Programming mammalian cells to synthesize insulin.
P. J. Southern, Stanford University Medical Center, California: SV40 vector systems.
S. Subramani, Stanford University Medical Center, California: Expression of the mouse dihydrofolate reductase cDNA in SV40-based vectors.
P. Mellon, California Institute of Technology, Pasadena: Two assays correlating available structural and genetic information with in vivo expression of globin genes.
G. Pavlakis, National Cancer Institute, Bethesda, Maryland: Expression of eukaryotic genes cloned in SV40 vectors.

*Session 3: Adenoviruses*

*Chairperson:* T. Grodzicker, Cold Spring Harbor Laboratory, New York

D. Solnick, Cold Spring Harbor Laboratory, New York: Adenovirus recombinants containing an ectopic copy of the major late promoter which directs the expression of downstream genes.
C. S. Thummel, University of California, Berkeley: An adenovirus vector system for the expression of foreign eukaryotic proteins.
M. Rossini, Cold Spring Harbor Laboratory, New York: A study of expression and regulation of the adenovirus genome using microinjection of mammalian cells.

*Session 4: Retroviruses*

*Chairperson:* G. Vande Woude, National Cancer Institute, Bethesda, Maryland

J. Sorge and S. Hughes, Cold Spring Harbor Laboratory, New York: Uses of an avian sarcoma virus vector.
W. McClements, National Cancer Institute, Bethesda, Maryland: Long terminal repeat (LTR) of Moloney sarcoma virus.
I. M. Verma, Salk Institute, San Diego, California: Retroviral DNAs as eukaryotic cloning vectors.

*Session 5: Specialized Systems*

*Chairperson:* G. Khoury, National Cancer Institute, Bethesda, Maryland

M. J. Cline, University of California School of Medicine, Los Angeles: Use of a mutant dihydrofolate reductase gene to transform bone marrow cells of intact mice.
M. J. Gething, Imperial Cancer Research Fund Laboratories, London, England: Expression of influenza virus hemagglutinin in eukaryotic cells.
A. Pellicer, Columbia University College of Physicians & Surgeons, New York, New York: Control of expression of transforming genes.
D. T. Kurtz, Cold Spring Harbor Laboratory, New York: Hormonal control of the expression of the rat $\alpha_{2u}$ globin genes.
P. Howley, National Institutes of Health, Bethesda, Maryland: Bovine papilloma virus DNA—A novel eukaryotic cloning vector.

# Marie H. Robertson Fund for Neurobiology

Crucial support for Cold Spring Harbor Laboratory's program of conferences, courses and year-round research in the neurosciences is provided by the Marie H. Robertson Fund for Neurobiology. This fund, established in 1976 through the Banbury Foundation by the family of Mr. Charles S. Robertson, honors the memory of Mr. Robertson's wife, who died in 1972. At first the fund, which provides $75,000 annually, was used largely to support the summer teaching program in neurobiology, which includes laboratory courses given on the main Laboratory grounds in the village of Laurel Hollow and lecture courses given at Banbury Center in the village of Lloyd Harbor. But in 1979, after receipt of a substantial training grant from the National Institutes of Health, and added support from the National Science Foundation, it was decided to use some of the Marie H. Robertson funds to support specific summer workshops and to make possible one or two specialized meetings each year at Banbury Center. The first two of these Marie H. Robertson meetings were held in 1980. The programs are listed below.

## Lessons from the Study of Molluscan Nerve Cells
**May 18—May 20**

To stimulate interaction between investigators of membrane biophysics and of neural control of behavior, Eric Kandel of the College of Physicians and Surgeons of Columbia University and Charles Stevens of the Yale University School of Medicine, both members of the Neurobiology Advisory Committee of Cold Spring Harbor Laboratory, organized a three-day conference of 20 specialists and five graduate-student rapporteurs who summarized the presentations and discussion for what became, a few months later, the first of the Cold Spring Harbor Reports in the Neurosciences. The meeting was designed to summarize what now appears to be a revolution in knowledge that allows neuroscience researchers "to relate the biophysical properties of individual neurons to the features of the behavior that they mediate," as John Koester of Columbia Physicians and Surgeons and John H. Byrne of the University of Pittsburgh School of Medicine, the editors of the conference report, wrote in their introduction.

Arranged by
**Charles F. Stevens,** *Yale University, New Haven, Connecticut*
**Eric R. Kandel,** *Columbia University, College of Physicians & Surgeons, New York, New York*

27 participants

*Session 1*

*Chairperson:* C. F. STEVENS, Yale University, New Haven, Connecticut

C. F. STEVENS, Dept. of Physiology, Yale University, New Haven, Connecticut: Introduction.
R. C. THOMAS, Dept. of Physiology, Yale University School of Medicine, New Haven, Connecticut: Ion pumps in nerve cells.

S. THOMPSON, Dept. of Biology, and Hopkins Marine Station, Stanford University, California: The delayed $K^+$ channel and its inactivation.
J. CONNOR, Dept. of Physiology and Biophysics, University of Illinois, Urbana: The fast $K^+$ channel and repetitive firing.

*Session 2*

*Chairperson:* S. HAGIWARA, University of California School of Medicine, Los Angeles

R. W. MEECH, Dept. of Physiology, University of Utah Medical School, Salt Lake City: The calcium-dependent $K^+$ channel.
H. D. LUX, Max-Planck-Institut für Psychiatrie, Munich, Federal Republic of Germany: The calcium-dependent $K^+$ channel.

*Session 3*

*Chairperson:* A. M. BROWN, University of Texas Medical Branch, Galveston

S. HAGIWARA, Dept. of Physiology, University of California School of Medicine, Los Angeles: The calcium channel—Introduction.
D. TILLOTSON, Dept. of Physiology, Boston University Medical School, Massachusetts: Inactivation of the calcium channel.

*Session 4*

*Chairperson:* F. J. BRINLEY, NINCDS, National Institutes of Health, Bethesda, Maryland

A. M. BROWN, Dept. of Physiology, University of Texas Medical Branch, Galveston: Noise analysis.
F. J. BRINLEY, Neurological Disorders Program, NINCDS, National Institutes of Health, Bethesda, Maryland: Transmembrane flux and buffering of $Ca^{++}$—Axon.
S. SMITH, Dept. of Physiology and Anatomy, University of California, Berkeley: Transmembrane flux and buffering of $Ca^{++}$—Cell body.
T. G. SMITH, JR., National Institutes of Health, Bethesda, Maryland: Ionic channels in burst-generating cells.

*Session 5*

*Chairperson:* R. LLINAS, New York University, New York

W. A. WILSON, Epilepsy Center, Veterans Administration Hospital, Durham, North Carolina: Synaptic transmission—Postsynaptic channels: Voltage sensitivity.
A MARTY, Laboratoire de Neurobiologie, Ecole Normale Superieure, Paris, France: Synaptic transmission—Postsynaptic channels: Noise analysis.
R. LLINAS, Dept. of Physiology, New York University, New York: Synaptic transmission—Presynaptic channels: $Ca^{++}$ channels and transmitter release.

*Session 6*

*Chairperson:* E. R. KANDEL, Columbia University College of Physicians & Surgeons, New York, New York

E. SHAPIRO, Division of Neurobiology and Behavior, Columbia University College of Physicians & Surgeons, New York, New York: Modulation of presynaptic calcium channels.
M. KLEIN, Division of Neurobiology and Behavior, Columbia University College of Physicians & Surgeons, New York, New York: Biophysics of behavior—Molecular mechanisms of habituation and sensitization.
J. KOESTER, Division of Neurobiology and Behavior, Columbia University College of Physicians & Surgeons, New York, New York: Biophysics of behavior—Control of inking in *Aplysia I.*
J. BYRNE, Dept. of Medicine, University of Pittsburgh School of Medicine, Pennsylvania: Biophysics of behavior—Control of inking in *Aplysia II.*
R. LLINAS, Dept. of Physiology, New York University, New York: Applicability of channel analyses in molluscs to vertebrate central neurons.

# Usage of Monoclonal Antibodies in Neurobiology
**November 5—November 8**

Our ability to generate specific immunoglobulin and nucleic acid probes allows quite new questions to be answered in many complex biological systems. The nervous system is particularly open to study with these new molecular tools. This meeting was the first gathering of scientists studying the nervous system with monoclonal antibodies. We heard antibodies described which distinguish central and peripheral neurons, subtypes of neurons in the neural crest, antigenic gradients in the retina, many tens of neuronal types in the leech, the synaptic sites at the neuromuscular junction, neurotransmitters and their enzymes.

Arranged by
**Ron McKay,** *Cold Spring Harbor Laboratory, New York*
**Martin Raff,** *University College London, England*
**Louis F. Reichardt,** *University of California, San Francisco*

*39 participants*

*Session 1*

M. Raff, University College London, England: Introduction.

*Session 2: Defining Cell Types and Cell Lines*

*Chairperson:* H. Karten, State University of New York, Stony Brook

M. Schachner, Dept. of Neurobiology, University of Heidelburg, Federal Republic of Germany: Monoclonal antibodies recognizing subpopulations of glial cells in mouse cerebellum.

K. Fields, Dept. of Neurology, Albert Einstein College of Medicine, Bronx, New York: Indication for the use of monoclonal antibodies against brain filament proteins.

Y. Berwald-Netter,[1] F. Couraud,[2] and A. Koulakoff,[2] [1]College of France, Paris; [2]Faculty of Medicine, Marseille, France: Specific surface membrane markers as probes for neuronal evolution in vivo and in vitro.

W. Stallcup, J. Levine, and W. Raschke, Salk Institute, San Diego, California: Monoclonal antibody against the NG2 marker.

G. Giotta, J. Heitzmann, and M. Cohen, Developmental Biology Laboratory, Salk Institute, San Diego, California: Monoclonal antibodies and the identification of cerebellar cell.

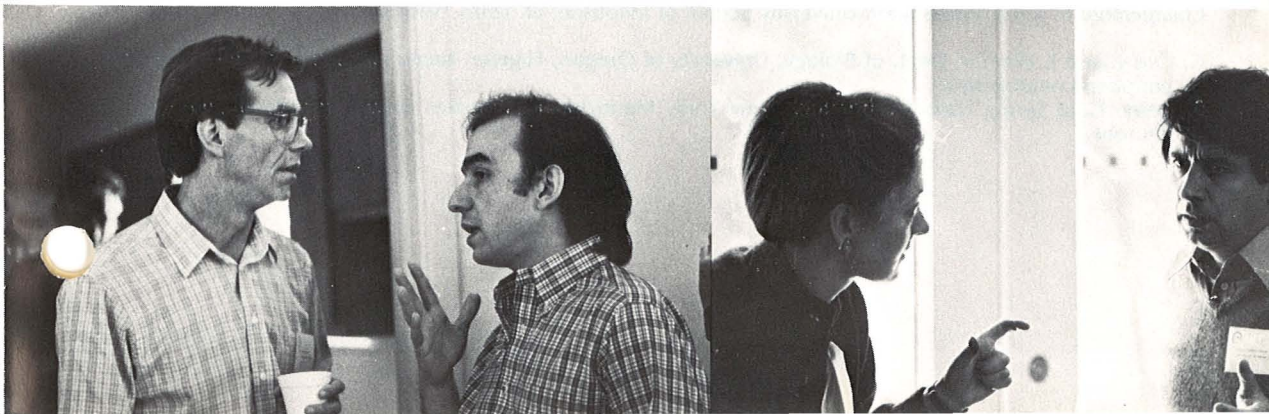
J. Cohen, R. Mirsky, S. Selvendren, and T. Vulliamy, Dept. of Zoology, University College London, England: Monoclonal antibodies which define neuron-specific cell surface molecules in the mammalian central and peripheral nervous system.

L. Lampson, Dept. of Anatomy, University of Pennsylvania, Philadelphia: Expression of the major histocompatibility antigens in the human nervous system.

*Session 3: The Synapse*

*Chairperson:* C. F. Stevens, Yale University School of Medicine, New Haven, Connecticut

R. Kelly, Dept. of Biochemistry, University of California, San Francisco: Antibodies to cholinergic synaptic vesicles.



W. MATTHEW, Dept. of Biochemistry, University of California, San Francisco: Monoclonal antibodies to synaptic membranes and vesicles.
A. DE BLAS, N. BUSIS, and M. NIRENBERG, NHLBI, National Institutes of Health, Bethesda, Maryland: Monoclonal antibodies to synaptic membrane molecules.
S. FUCHS, D. MOCHLY-ROSEN, M. SOUROUJON, and Z. ESHHAR, Dept. of Chemical Immunology, Weizmann Institute, Rehovot, Israel: Monoclonal antibodies against the nicotinic acetylcholine receptor.

*Session 4: The Retina*

*Chairperson:* M. NIRENBERG, NHLBI, National Institutes of Health, Bethesda, Maryland

H. KARTEN and N. BRECHA, State University of New York, Stony Brook: Biochemical and morphological specificity of retinal amacrine cells—Immunohistochemical findings.
G. EISENBARTH, K. SHIMIZU, M. CONN, B. MITTLER, and S. WELLS, Duke University Medical Center, Durham, North Carolina: Monoclonal antibody F12A2B5-reaction with a plasma membrane antigen of vertebrate neurons and peptide secreting endocrine cells.
C. BARNSTABLE, Dept. of Neurobiology, Harvard Medical School, Boston, Massachusetts: Developmental studies of rat retina cells using cell-type specific monoclonal antibodies.
D. TRISLER, M. SCHNEIDER, and M. NIRENBERG, NHLBI, National Institutes of Health, Bethesda, Maryland: A gradient of molecules in avian retina with dorsoventral polarity.

*Session 5: Defined Antigens*

*Chairperson:* L. F. REICHARDT, University of California, San Francisco

M. E. ROSS, E. E. BAETGE, D. J. REIS, and T. H. JOH, Dept. of Neurobiology, Cornell University Medical College, New York, New York: Monoclonal antibodies against catecholamine neurotransmitter synthesizing enzymes can be used for immunochemistry and immunocytochemistry.
A. C. CUELLO[1] and C. MILSTEIN,[2] [1]Dept. of Pharmacology and Human Anatomy, University of Oxford, England; [2]Medical Research Council Molecular Biology Unit, Cambridge, England: Monoclonal antibodies against neurotransmitter substances.
R. AKESON, J. S. RADMAN, K. GRAHAM, and A. ROBERTS, Children's Hospital Research Foundation, Cincinnati, Ohio: Identification of a rat nervous system specific polypetide.
R. PRUSS,[1] R. MIRSKY,[1] M. C. RAFF,[1] R. THORPE,[2] and B. H. ANDERTON,[2] [1]University College London, England; [2]St. George's Hospital Medical School, London, England: A monoclonal antibody recognizes a determinant present on common as well as class-specific intermediate filament subunits.
G. E. LEMKE and J. P. BROCKES, Dept. of Biology, California Institute of Technology, Pasadena: An immunochemical approach to the purification and characterization of glial growth factor.
E. YAVIN,[1,2] Z. YAVIN,[1] M. D. SCHNEIDER,[3] and L. D. KOHN,[1] [1]NIAMDD, National Institutes of Health, Bethesda, Maryland; [2]Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel; [3]NHLBI, National Institutes of Health, Bethesda, Maryland: Monoclonal antibodies to the thyrotropin receptor—Implications for receptor structure and the action of autoantibodies in Graves' disease.

*Session 6: The Neuromuscular Junction*

*Chairperson:* M. RAFF, University College London, England

S. BURDEN, Dept. of Anatomy, Harvard Medical School, Boston, Massachusetts: Monoclonal antibodies directed against the frog nerve-muscle synapse.
E. BAYNE, J. GARDNER, and D. M. FAMBROUGH, Dept. of Embryology, Carnegie Institution of Washington, Baltimore, Maryland: Monoclonal antibodies against extracellular matrix antigens in chicken skeletal muscle.
D. GOTTLIEB and J. GREVE, Department of Anatomy/Neurobiology, Washington University School of Medicine, St. Louis, Missouri: Effects of monoclonal antibodies to the cell surface on cultured myogenic cells.

*Session 7: Ganglia*

*Chairperson:* E. JONES, Washington University School of Medicine, St. Louis, Missouri

G. CIMENT and J. WESTON, Dept. of Biology, University of Oregon, Eugene: Immunochemical studies of avian peripheral neurogenesis.
B. ZIPSER, Cold Spring Harbor Laboratory, New York: Monoclonal antibodies specific for identifiable leech neurons.

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