# Banbury Center

Of Cold Spring Harbor Laboratory



Sammis Hall



## **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

## BANBURY CENTER 1981 Activities

Banbury Center's fourth year of small conferences on environmental health risks, with the addition of small meetings focused on emerging areas of molecular biology and on the effects of molecular biological advances on society at large, took place as the national government rapidly changed its policies toward environmental regulation in particular and the support of science in general. The new tax-cutting Reagan administration began at once to ease restrictions on industry that had multiplied over a decade of mounting concern about the impact of advanced technology, particularly in the areas of mining and chemicals, on the health of workers and the general population. The changed political climate created problems for Banbury Center in achieving its goal of a reasonable balance of views in its conferences. Previously, the need was to assure adequate representation of scientific skepticism about the size of the environmental health risk problem. Now, the problem was assuring that what might be called an alarmist view would be heard, while continuing to concentrate on facts rather than opinions or ethical issues.

Such pressures merely forced us to redouble efforts to assure the objectivity of the spring conference on "Quantification of Occupational Cancer," whose proceedings came out in December as Banbury Report 9, and of our fall conference on "Environmental Effects on Maturation." The proceedings of the latter meeting, which considered possible special vulnerabilities of children to environmental chemicals, will be published in the spring of 1982 as Banbury Report 11.

The success of these meetings, and the expansion of the Banbury program to include such conferences on molecular biology as those on "Gene Amplification and Aberrant Chromosomal Structures" (October) and "Construction and Use of Mammalian Viral Vectors" (December), and on broader impacts of fundamental biology ("Patenting of Life Forms," October), reinforced confidence in the original view of the beautiful Robertson estate as an ideal place for meetings on urgent technical issues of biological science and public policy.

The establishment of the center, after the late Charles S. Robertson's magnificent gifts to the

Laboratory in 1973 and 1976, was dictated by an increasing awareness of the social importance and usefulness of molecular biology. Recombinant DNA techniques had been applied in an important way to short-term testing of possible dangers from chemicals in the environment. The techniques themselves were the subject of years of intense, and now largely resolved, debate about the possibility of health risks. Meanwhile, scientists became increasingly conscious of the power of recombinant DNA techniques for understanding mechanisms of cancer induction as well as normal cellular development and of the rapidly expanding opportunities for using the new techniques in industrial microbiology. All of these subjects are of intense interest to the scientists working at Cold Spring Harbor Laboratory.

#### Sammis Hall

The sense of fulfillment of earlier hopes sharpened feelings of loss at the death in Florida, on May 2, 1981, of Charles Robertson, who had maintained a lively interest in the new uses of what had been his family home for 40 years. A few days after his death, members of the Banbury Center and Laboratory staff considered it an honor to attend a beautiful service in memory of Mr. Robertson at St. John's Episcopal Church in Cold Spring Harbor.

Not long after, on July 19, a muggy, overcast Sunday, a landmark in the development of Banbury Center was passed with the dedication of our 16-bedroom guest house, Sammis Hall. The Palladian-style structure, designed in 1978-1979 by the architectural firm of Moore, Grover, and Harper, was named for Mr. Robertson's mother's family. Accompanied by occasional showers, the ceremonies were held under a yellow-and-whitestriped tent on the lawn next to the deck of the Banbury Meeting House. Among these attending were Mr. Robertson's sister, Mrs. Donald Rose, who has her summer home here, and such other members of the family as Mr. and Mrs. William Robertson and Dr. and Mrs. Walter Meier, who also are neighbors.

Built with the aid of grants of \$150,000 from the Kresge Foundation and \$225,000 from the Max Fleischmann Foundation, Sammis Hall pleasingly supplements the family comfort of Robertson House. Now, a total of 37 overnight guests can be accommodated on the Banbury estate, with our extra guests (already a usual feature of Banbury conferences) housed in Blackford Hall at the main Laboratory grounds across Cold Spring Harbor.

Excavation for Sammis Hall began in the fall of 1979, and the structure began rising in March 1980. A year later its first guests participated in the conference on "Quantification of Occupational Cancer." By the end of 1981, no less than 20 groups of conference and course participants had stayed in Sammis Hall for periods of from two days to three weeks, enjoying its charming views of surrounding trees and a unique central hall, stretching more than two stories up to a dozen skylights.

#### **Dissemination of Findings**

Publication of conference proceedings has been an integral part of the Banbury program from the beginning. The small size of the Banbury conference room necessarily limits attendance to between 40 and 50 people, most of them active researchers. There is little room for observers, such as members of the press, at our technical conferences. Thus, maximizing the usefulness of bringing together such groups of researchers, who do not meet together often, demands swift publication. Hence, Banbury Center strives to publish a Banbury Report six or seven months after each conference.

Our first Banbury Report was published in April 1979. Another followed by the end of that year

and four more were published in 1980. In 1981 we published another three. These were Banbury Report 7 on Endogenous Factors in Gastrointestinal Cancer, Banbury Report 8 on Hormones and Breast Cancer, and Banbury Report 9 on Quantification of Occupational Cancer. As always, we were grateful for the splendid cooperation of the scientists, organizers, and participants, who observed our tight deadlines. Preparations began for publication of Banbury Reports 10 and 11, covering our meetings on patenting and environmental risks for children.

With the aid of a \$25,000 purchase of copies of Banbury Reports 7 and 8 by the National Cancer Institute for distribution to grantees, total sales of Banbury Reports exceeded \$140,000 for the year and \$350,000 since the start of the publication program. The sales met most of the costs of book production and distribution.

Our second major informational program involves seminars specifically designed for groups, such as journalists and legislative aides, who have a major role in setting policy. Supported by a \$100,000 grant from the Alfred P. Sloan Foundation (which, along with the Esther A. and Joseph Klingenstein Fund financed the initial operations of Banbury Center), we began holding seminars for journalists in 1981.

The first of these, for the editorial staff of *Newsday*, the Long Island newspaper, covered such environmental health issues as ground water pollution, diet and cancer, and chemical waste disposal. The second, for the editorial staffs of the magazines of Time, Inc., covered the scientific background of current advances in genetic engineering and reviewed the initial steps in the creation of a genetic engineering industry. The aim of both seminars was to bring scientists together with editorial staffs at all levels to hear



Sammis Hall, rear view

informal presentations and ask many questions, so as to open the door to future contacts on specific news stories and allow managers of newsgathering efforts to confront sources usually seen only by reporters. We were gratified that the publisher and the president of *Newsday*, Mr. David Laventhol and Mr. Donald Wright, and Mr. Henry Anatole Grunwald, Editor-in-Chief of Time, Inc., were able to attend.

#### **Conferences and Courses**

The variety of meetings held at Banbury increased during 1981. Besides two informational seminars, two environmental health risk conferences, two conferences on emerging areas of molecular biology, and a conference on the social impact of molecular biology, Banbury also was the site of two conferences on neurobiology (as in 1980), two courses on neurobiology, and a workshop on tumor and transplantation antigens and provided housing for some of the participants in nine major conferences held at Cold Spring Harbor Laboratory.

The conference on "Neurobiology of the Leech," from June 29 to July 2, was organized by John Nicholls of Stanford University, Kenneth Muller of the Carnegie Institution of Washington, and Gunther Stent of the University of California at Berkeley (who also spoke at the dedication of Sammis Hall). The conference on "Methods for Measuring Global Neural Activity," from August 2 to 8, was organized by David Zipser of Cold Spring Harbor Laboratory and Peter Hand of the University of Pennsylvania School of Veterinary Medicine under a Sloan Foundation grant.

The workshop on "Tumor and Transplantation Antigens," from July 2 to 8, was organized (for the second year in a row) by Arnold Levine of the State University of New York at Stony Brook, who completed a term as an Institutional Trustee of the Laboratory.

The conference on "Gene Amplification and Aberrant Chromosomal Structures," supported by the National Institutes of Health and by a special fund established by Bankers Life of Chicago, was organized by Robert T. Schimke of Stanford University. It was held from October 4 to 7.

Organizing our second annual conference on "Construction and Use of Mammalian Viral Vectors," held from December 4 to 6, was Yakov Gluzman of the scientific staff of Cold Spring Harbor Laboratory.

Representing divergent views on the problem of quantification of occupational cancer, the organizers of the conference, held from March 29 to April 2, were Richard Peto of the University of Oxford, who doubts that cancer mortality due to environmental chemicals is rising among middleaged persons where trends can be most accurately measured, and Marvin Schneiderman of Clement Associates, who has analyzed studies indicating a rising trend of cancer incidence.

Although a regulatory problem underlay the interest of the United States Environmental Protection Agency and the U.S. Department of Labor in a Banbury conference on special environmental health risks for children, the conference focused on scientific work related to immature humans and animals in general. The conference, entitled "Environmental Effects on Maturation," was held from November 1 to 4 and was organized by Vilma Hunt of Pennsylvania State University, Kate Smith of EPA's Health Effects Research Laboratory in Cincinnati, and Dorothy Worth of Tufts University School of Medicine. The regulatory problem in the background is estimating the degree of risk for farm children entering fields that have been sprayed with pesticides.



Banbury staffers Lynda Moran (left) and Beatrice Toliver (right) with Banbury Center Director, Victor McElheny

The conference on "Patenting of Life Forms," held from October 18 to 21, grew out of the considerable confusion among both patent lawyers and scientists about the implications of the Supreme Court's 1980 decision that life forms themselves are patentable along with processes for creating them or using them. The organizers were Norton Zinder of Rockefeller University, an Institutional Trustee of Cold Spring Harbor Laboratory, Niels Reimers, Director of Technology Licensing of Stanford University, and David W. Plant, partner in the New York City patent law firm of Fish & Neave.

Courses and conferences at Banbury Center brought some 400 scientists, lawyers, and journalists to Banbury and Cold Spring Harbor Laboratory. A further 300 scientists were guests at Banbury during Laboratory conferences. Our guests came from the United States and 18 foreign countries.

#### **Support**

A wholly new enterprise like Banbury Center has to struggle for financing. During 1981 financial support strengthened notably.

The Environmental Protection Agency and Department of Labor joined in a cooperative agreement to support the conference on "Environmental Effects on Maturation." The National Institutes of Health and Bankers Life, following up their support of the International Symposium on Aging and Cancer in Washington, D.C., in September, 1980, sponsored the October conference on "Gene Amplification and Aberrant Chromosomal Structures."

Very gratifying was notification of the award by the National Cancer Institute of funds to hold a conference on the "Possible Role of Nitrosamines in Human Cancer," April 4 to 7, 1982. The Kaiser Family Foundation of Menlo Park, California, made a very generous grant to support the holding of the Banbury conference on "Prospects for Gene Therapy: Fact and Fiction," February 5 to 7, 1982, and publication of its findings. The Burroughs Wellcome Fund granted \$15,000 for a conference on hereditary factors in cancer, which will focus on probing for specific genes, to be held in October 1982.

Support from corporations, which had reached \$85,000 in 1980 (our first year of seeking such assistance), virtually doubled to \$169,500 in 1981. Of great help were letters of appeal from Alexander C. Tomlinson of our Board of Trustees which accompanied the Banbury proposal. Sustaining support in 1981 came from ten corporate sources: Bristol-Myers Fund, Dow Chemical, E.I. duPont deNemours, Exxon Education Foundation, Getty Oil, International Business Machines, Eli Lilly, New York Life, Phillips Chemical, and Texaco Philanthropic Foundation. Just after the turn of the year, Conoco joined the ranks with a contribution to the overall program.

A total of 15 companies, including Dow, du-Pont, and Lilly, contributed a total of \$43,000 toward the October conference on "Patenting of Life Forms." The other contributors were: Baxter Travenol Laboratories, Chevron Research Company, Exxon Research and Engineering Company, Hoffman LaRoche, Inc., Johnson and Johnson, Merck Sharp and Dohme Research Laboratories, Monsanto Company, National Distillers and Chemical Corporation, Pfizer, Inc., Schering-Plough Corporation, Smith Kline and French Laboratories, and The Upjohn Company.

For the December conference on "Construction" and Use of Mammalian Viral Vectors," two companies, Applied Molecular Genetics, Inc., and Bethesda Research Laboratories, joined 10 others, including duPont, Lilly, and Monsanto, which had contributed to the first mammalian vectors meeting in 1980. The other repeating contributors were Abbott Laboratories, Biogen N.V., Cetus Corporation, Collaborative Research, Inc., Genentech, Inc., Molecular Genetics, Inc., and New England BioLabs, Inc.

The roster of corporations contributing at least once to Banbury Center in the last two years has reached 32. Many of these companies have given generously to Cold Spring Harbor Laboratory over the last decade. It is a pleasure to record our gratitude to new and old contributors.



## Journalists Workshop for Newsday: Environmental Health Risks January 16-18

#### Session 1 Water Resources and Human Health

- C.C. Johnson, C.C. Johnson and Associates, Silver Spring, Maryland: The numerous unknowns in making policy to assure water quality.
- J. Cotruvo, Environmental Protection Agency, Washington, DC: The Environmental Protection Agency's priorities in assuring water quality.
- M. Kavanaugh, Montgomery Engineers, Washington, DC: Engineering water treatment with a view to reuse.
- J. Tripp, Environmental Defense Fund, New York, New York: Legal struggles over watershed protection in the Northeast.

#### Session 2 The Health Effects of Chemical Waste Disposal

- J. Highland, Environmental Defense Fund, Washington, DC: Dimensions of the problem.
- R. Albert, New York University Medical Center, New York: Difficulties of measurement.

#### Session 3 Diet and Cancer

C. Mettlin, Roswell Park Memorial Institute, Buffalo, New York P. Newberne, Massachusetts Institute of Technology, Cambridge

## Quantification of Occupational Cancer, March 29-April 2

Varying viewpoints concerning the extent of the contribution of occupation to overall cancer incidence were presented against a background of epidemiological issues, study methods, statistical approaches, and cancer and chemical production trends. Precise evaluations were made about the role of asbestos exposure in lung cancer and mesothelioma incidence as well as radiation and lung cancer incidence, and the confounding factors of cigarette smoking and the healthy worker effect were considered. Industry-sponsored surveillance programs were discussed, as were classification systems, record linkage, exposure-based case-control studies, population-based large cohorts, and the use of standard-ized mortality ratios vs. proportional mortality ratios. A concluding roundtable explored the prospect of identifying high-risk groups and reducing cancer in industrial countries.

#### Session 1 Asbestos and Other Mineral Fibers

Chairperson: E.D. Acheson, University of Southampton, England

I.J. Selikoff, Mount Sinai School of Medicine, New York, New York: Constraints in estimating occupational contributions to current cancer mortality in the United States.

P.E. Enterline, University of Pittsburgh Graduate School of Public Health, Pennsylvania: Proportion of cancer due to exposure to asbestos.

W.J. Blot, National Cancer Institute, NIH, Bethesda, Maryland: Cancer among shipyard workers.



- J. Peto, Imperial Cancer Research Fund, Oxford, England: Trends in mesothelioma incidence in the United States and the forecast epidemic due to asbestos exposure during World War II.
- J.C. McDonald, London School of Hygiene and Tropical Medicine, England: Mesothelioma as an index of asbestos impact.
- W.J. Nicholson, Mount Sinai School of Medicine, New York, New York: Cancer from occupational asbestos exposure-Projections 1980-2000.

#### Session 2 Radiation Risks—Animal Experiments

Chairperson: M. Schneiderman, Clement Associates, Inc., Washington, DC

- S. Darby, National Radiological Protection Board, Harwell, England: Exposure to ionizing radiation and cancer mortality among workers.
- A.M. Stewart and George W. Kneale, University of Birmingham, England: Analysis of Hanford data-Delayed effects of small doses of radiation delivered at slow-dose rates.
- E.P. Radford, University of Pittsburgh Graduate School of Public Health, Pennsylvania: Radon daughters in the induction of lung cancer in underground miners.
- R. Saracci, International Agency for Research on Cancer, Lyon, France: The IARC monograph program on the evaluation of the carcinogenic risk of occupational carcinogens.
- G.M. Paddle, ICI Central Medical Group, Wilmslow, Cheshire, England: A strategy for the identification of carcinogens in a large, complex chemical company.

#### Session 3 Industry-wide Cancer Experience — Methodological Problems

Chairperson: M.A. Silverstein, International Union, United Auto Workers, Detroit, Michigan

- M.S. Gottlieb, Tulane University School of Medicine, New Orleans, Louisiana: Mortality studies on lung, pancreas, esophageal, and other cancers in Louisiana.
- R.R. Monson, Harvard University School of Public Health, Boston, Massachusetts: An estimate of the percentage of occupational cancer among a group of rubber workers.
- M. Karstadt, Mount Sinai School of Medicine, New York, New York: A survey of availability of epidemiologic data on humans exposed to animal carcinogens.
- M.E. Warshauer, Memorial Sloan-Kettering Cancer Center, New York, New York: A prospective study of morbidity and mortality in petroleum industry employees in the United States—A preliminary report.

Session 4 Cancer in the US-Recent Trends and Proportion Due to Occupation Chairperson: M.H. Sloan, National Cancer Institute, NIH, Silver Spring, Maryland

R. Peto, University of Oxford, England: Trends in US cancer onset rates.

- D.L. Davis, Environmental Law Institute, Washington, DC: Estimating cancer causes-Problems in methodology, production, and trends.
- H.M. Rosenberg, National Center for Health Statistics, Hyattsville, Maryland: NCHS data resources for studying occupational cancer mortality.

#### Session 5 Special Problems of Methodology

Chairperson: B.W. Karrh, E.I. duPont deNemours & Company, Wilmington, Delaware

- M.S. Legator, University of Texas Medical Branch, Houston: A holistic approach to monitoring high-risk populations by short-term procedures.
- S.G. Austin, Union Carbide Corporation, New York, New York: An industry-sponsored mortality surveillance program.
- O. Wong, Biometric Research Institute, Inc., Washington, DC: An epidemiologic study of workers potentially exposed to brominated chemicals—With a discussion of multifactor adjustment.
- R.J. Waxweiler, National Institute for Occupational Safety and Health, Cincinnati, Ohio: Quantification of differences between proportionate mortality ratios and standardized mortality ratios.
- J.J. Beaumont, National Institute for Occupational Safety and Health, Cincinnati, Ohio: Occupational data sets appropriate for proportionate mortality ratio analysis.
- C.P. Wen, Gulf Oil Corporation, Houston, Texas: A population-based cohort study of brain tumor mortality among oil refinery workers with a discussion of methodological issues of SMR and PMR.

#### Session 6 Methodology

Chairperson: E. Bingham, University of Cincinnati Medical Center, Ohio

F.D. Hoerger, Dow Chemical Company, Midland, Michigan: Indicators of exposure trends.

- S.K. Hoar, National Cancer Institute, NIH, Bethesda, Maryland: Epidemiology and occupational classification systems.
- J. Siemiatycki, Institut Armand-Frappier, Laval-des-Rapides, Quebec, Canada: Exposure-based case control approach to discovering occupational carcinogens -- Preliminary findings.
- O. Axelson, Linkoping University, Sweden: Guiding experiences on the etiology of acute myeloid leukemia.
- S.W. Samuels, Industrial Union Department, AFL-CIO, Washington, DC: The international context of carcinogen regulation-Benzidine.
- S. Milham, Jr., Washington State Department of Social and Health Services, Olympia: Proportion of cancer due to occupation in Washington State.
- H. Tulinius, Icelandic Cancer Registry, Reykjavik: Cancer incidence and occupations in an area of low air pollution.
- H. Falk, Center for Disease Control, Atlanta, Georgia: Hepatic angiosarcoma registries—Implications for rare-tumor studies.

#### Session 7 Broad Approaches to Occupational Cancer Quantification

Chairperson: J. Cairns, Harvard School of Public Health, Boston, Massachusetts

- J.B. Swartz and S. Epstein, University of Illinois Medical Center, Chicago: Problems in assessing risk from occupational and environmental exposure to carcinogens.
- A.J. McMichael, Commonwealth Scientific and Industrial Research Organization, Adelaide, SA, Australia: Differentiating work from life-style in cancer causation.
- E.D. Acheson, University of Southampton, England: Towards a strategy for the identification of occupational carcinogens in England and Wales—A preliminary report.
- M.R. Alderson, Institute of Cancer Research, Royal Cancer Hospital, Sutton, Surrey, England: Occupational studies—The use of national and industrial comparisons or an internal analysis.
- H.B. Demopoulos, New York University Medical Center, New York: The value of contemporary demographic controls in evaluating cancer incidence and mortality rates in heavily industrialized urban areas in the United States.
- T. Hirayama, National Cancer Research Institute, Tokyo, Japan: Proportion of cancer attributable to occupation obtained from a census, population-based, large cohort study in Japan.

#### Session 8 Future Needs

Chairperson: G.W. Beebe, National Cancer Institute, NIH, Bethesda, Maryland

G.W. Beebe, National Cancer Institute, NIH, Bethesda, Maryland: Record linkage and needed improvements in existing data resources.

M.E. Smith, Health Division, Statistics Canada, Ottawa: Long-term medical follow-up in Canada.



## Journalists Workshop for Time, Inc.: DNA

#### May 3-4

Session 1 Scientific Successes with Recombinant DNA

- J.D. Watson, Cold Spring Harbor Laboratory, New York: Comments on the political and technical history of recombinant DNA.
- R. Roberts, Cold Spring Harbor Laboratory, New York: General introduction to the scientific techniques of working with DNA.
- P. Leder, National Institute of Child Health and Human Development, NIH, Bethesda, Maryland: Jumping genes.
- M. Ptashne, Harvard University, Cambridge, Massachusetts: Bacteria as factories.

Session 2 Consequences of Damage to DNA

B.N. Ames, University of California, Berkeley: Mutagenesis.

M.S. Fox, Massachusetts Institute of Technology, Cambridge: DNA repair.

J.L. German III, New York Blood Center, New York: Chromsome damage.

W.S. Hayward, Rockefeller University, New York, New York: Viruses.

Session 3 Long Shots in Applications of DNA Technology

J. Schell, University of Cologne, Germany: Plants.

- R. Jaenisch, Heinrich-Pette-Institut, Hamburg, Federal Republic of Germany: The introduction of DNA into the germ lines of mice.
- M. Wigler, Cold Spring Harbor Laboratory, New York: Cancer genes.

Session 4 The Business of DNA

Chairperson: J. Tooze, European Molecular Biology Organization, Heidelberg, Federal Republic of Germany

#### Discussants:

N. Zinder, Rockefeller University, New York, New York R. Fildes, Biogen, Inc., Cambridge, Massachusetts E.G. Jaworski, Monsanto Company, St. Louis, Missouri R.E. Cape, Cetus Corporation, Berkeley, California

F. Pass, Molecular Genetics, Inc., Edina, Minnesota

## Neurobiology of the Leech, June 29-July 2

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 summer workshops and to make possible one or two specialized meetings each year at Banbury Center.



#### Opening Discussion: When is a neuronal circuit complete? Moderator: I. Parnas, Hebrew University of Jerusalem, Israel

#### Session 1

Chairperson: K.J. Muller, Carnegie Institution of Washington, Baltimore, Maryland

- S. Blackshaw, University of Glasgow, Scotland: Sensory cells and motoneurones.
- W.O. Friesen, University of Virginia, Charlottesville: Physiology and anatomy of sensillar movement receptors.
- J.Y. Kuwada, University of California, San Diego: Development of identified neurons in the leech CNS.
- A.P. Kramer, University of California, Berkeley: Development of morphological variation of mechanosensory cells in *Haementerial ghilianii*.
- I. Parnas, Hebrew University of Jerusalem, Israel: Expansion of the receptive fields of leech nociceptive cells following deletion of single neurons.

#### Session 2

Chairperson: J.G. Nicholls, Stanford University School of Medicine, California

D.A. Weisblat, University of California, Berkeley: Cell lineage in glossiphoniid neurogenesis.

- S.S. Blair, University of California, Berkeley: Alteration of cell patterning through single cell ablation in the early embryo of the leech.
- G.S. Stent, University of California, Berkeley: Somite formation in the leech embryo.
- J. Fernandez, University of Chile, Santiago: Organization of the germinal plate and formation of 32 body segments in embryos of *Hirudo medicinalis*.
- J. Hernandez, University of Chile, Santiago: Formation of ganglionic primordia in embryos of *Hirudo medicinalis*.

Evening Discussion: What use is the leech, if any?

Moderator: G.S. Stent, University of California, Berkeley

#### Session 3

Chairperson: K.J. Muller, Carnegie Institution of Washington, Baltimore, Maryland

- K.J. Muller, Carnegie Institution of Washington, Baltimore, Maryland: Leech synapses.
- E. Macagno, Columbia University, New York, New York: The close association of the intraganglionic dendritic fields of T cells.
- R. Stewart, Columbia University, New York, New York: Anatomy of leech segmental ganglia, with some comments about segmental and species differences.
- A. Mason, Carnegie Institution of Washington, Baltimore, Maryland: Modulatory effects of the retzius cells on longitudinal muscle of the leech *Hirudo medicinalis*.
- R.T. Sawyer, Penclawdd, West Glamorgan, South Wales: Leech biology and behavior.

#### Session 4

Chairperson: A.E. Stuart, University of North Carolina, Chapel Hill

G.S. Stent, University of California, Berkeley: Neuronal circuits.

- R.L. Calabrese, Harvard University, Cambridge, Massachusetts: Metastable coordination of the heartbeat in the leech *Hirudo medicinalis*.
- E.L. Peterson, Harvard University, Cambridge, Massachusetts: Coordination and phase control in the heartbeat timing oscillator of *Hirudo*.
- M. Pelligrino, University of Pisa, Italy: Effects of destruction of single HE cells in the CNS of the leech.
- C. Lent, Brown University, Providence, Rhode Island: Physiology and anatomy of the Leydig cells within the leech nervous system.
- B. Payton, Memorial University of Newfoundland, St. Johns, Canada: The giant leech of Newfoundland. Evening Discussion: Development and Regeneration

Moderator: J. Jansen, University of Oslo, Norway

#### Session 5

Chairperson: G.S. Stent, University of California, Berkeley

B. Wallace, Stanford University, California: Neurochemistry.

D. Stuart, University of California, Berkeley: Fluorescent staining of monoamine neurons in embryonic and adult leech.

- A.L. Kleinhaus, Yale University School of Medicine, New Haven, Connecticut: Variation of membrane properties and pharmacological sensitivities among identified leech neurons.
- W. Kristan, University of California, San Diego: Diversity of leech behavioral responses mediated by identified mechanosensory and motor neurons.
- J.C. Weeks, University of Washington, Seattle: Identified neurons mediating swim initiation and pattern generation in the leech.
- B.M. Salzberg, University of Pennsylvania, Philadelphia: Multiple-site optical recording of membrane potential-Prospects for optical recording from a reconstructed leech "nervous system."

#### Session 6

Chairperson: W. Kristan, University of California, San Diego

B. Zipser, Cold Spring Harbor Laboratory, New York: Specific neuron labeling.

- J.G. Nicholls, Stanford University School of Medicine, California: Regeneration and plasticity.
- L.P. Henderson, Stanford University School of Medicine, California: Serotonergic transmission between isolated leech neurones in culture.
- E.J. Elliott, Carnegie Institution of Washington, Baltimore, Maryland: Axon and synapse regeneration in the absence of glia.

## Workshop on Tumor and Transplantation Antigens, July 2-8

The development of DNA cloning and monoclonal antibody technologies has provided new research directions in the area of tumor and transplantation antigens. Both formal research presentations and extensive discussions were held with a group of scientists representing several disciplines: tumor virology, immunology, cell biology, genetics, and biochemistry. This workshop provided the group with an opportunity to compare and contrast observations from different experimental systems and to synthesize emerging general principles. The workshop was held at a time when new directions and ideas are emerging from an expanded research effort in this area.

#### Session 1

B. Bloom, Johns Hopkins University, Baltimore, Maryland: Mechanisms of tumor recognition and rejection.

#### Session 2

- R. Herberman, National Institutes of Health, Bethesda, Maryland: NK cells and tumor rejection.
- R. North, Trudeau Institute, Inc., Saranac Lake, New York: T-cell mediated suppression of tumor immunity.
- F. Lilly, Albert Einstein College, Bronx, New York: Genetic loci of the mouse involved in tumor rejection.
- S.-I. Shin, Albert Einstein College, Bronx, New York: Tumor growth and rejection in nude mice.
- W. Dove, University of Wisconsin, Madison: Teratocarcinoma transplantation rejection.
- T. Boon, Ludwig Institute for Cancer Research, Brussels, Belgium: New transplantation antigens of teratocarcinomas.



#### Session 3

- E. Blankenhorn, University of Pennsylvania, Philadelphia: MHL—Genetics and monoclonal antibodies. S. Weissman, Yale University, New Haven, Connecticut: H-2, HLA, DNA clones.
- M. Steinmetz, California Institute of Technology, Pasadena: H-2, HLA, DNA clones.
- L. Silver, Cold Spring Harbor Laboratory, New York: T-locus genetics and biochemistry.

#### Session 4

- R. Weinberg, Massachusetts Institute of Technology, Cambridge: Transformation antigens.
- N. Hopkins, Massachusetts Institute of Technology, Cambridge: DNA-mediated transfer of chemically transformed cell phenotype.
- D. Herlyn and M. Herlyn, Wistar Institute, Philadelphia, Pennsylvania: Melanoma antigens.
- O. Witte and N. Rosenberg, University of California, Los Angeles, and Tufts University Medical School, Boston, Massachusetts: Abelson virus transformation.
- M. Hayman, Imperial Cancer Research Fund Laboratories, London, England: Acute leukemia viruses.
- W. S. Hayward, Rockefeller University, New York, New York: Slow developing leukemias.

#### Session 5

- J. Brugge, State University of New York, Stony Brook: RSV src.
- E. Racker, Cornell University, Ithaca, New York: Cellular sarc.
- B. Sefton, Salk Institute, San Diego, California: Cellular substrates of src.
- E. M. Scolnick, National Cancer Institute, Bethesda, Maryland: Rodent src.
- T.V. Rajan, Albert Einstein College, Bronx, New York: Antibody immunoselection of cell surface antigens.
- A. Linnenbach, Wistar Institute, Philadelphia, Pennsylvania: Human monoclonals.

#### Session 6

- D. Lane<sup>1</sup> and E. Tucker Gurney<sup>2</sup>, <sup>1</sup>Imperial College of Science and Technology, London England; <sup>2</sup>University of Utah, Salk Lake City: Monoclonal antibodies to SV40 tumor antigens.
- S. Tevethia, Pennsylvania State University, Hershey: SV40-T-transplantation antigens.
- K. Choudhury and Y. Ito, National Institutes of Health, Bethesda, Maryland: Polyoma T-antigens.
- A.J. Levine, State University of New York, Stony Brook: p50-54 cellular tumor antigen.

Session 7 Roundtable Discussion: New and Old Concepts of Tumor and Transplantation Antigens Discussants:

I. Weissman, Yale University, New Haven, Connecticut

B. Sefton, Salk Institute, San Diego, California

T. August, Johns Hopkins University, Baltimore, Maryland

R. Weinberg, Massachusetts Institute of Technology, Cambridge

T.V. Rajan, Albert Einstein College, Bronx, New York



# Methods for Measuring Global Neural Activity Workshop

August 2-6

The last of three workshops in the Sloan Foundation-supported series devoted to the interface between neuro- and cognitive sciences was held this summer at Banbury Center. The workshop topic was motivated by the growing realization that in order to better understand the functioning of the brain, information must be obtained about the coherence of neural activity in many brain structures. Extraordinary technical difficulties confront studies of this kind and the workshop was devoted to a variety of new approaches which have promise for overcoming these barriers. Among the topics discussed extensively were the use of the deoxyglucose method for labeling active neurons; the use of arrays of multiple electrodes for recording from many places simultaneously; the measurement of the microblood flow in the brain which has been found to be indicative of the level of neural activity; and use of specialized dyes and optical techniques to follow the functioning of large arrays of neurons. The general tenor of the workshop was that a real beginning had been made on the problem of measuring global neural activity, but that a large amount of technical innovation and developmental work still remains to be done.

#### Session 1

- D. Zipser<sup>1</sup> and P. Hand<sup>2</sup>, <sup>1</sup>Cold Spring Harbor Laboratory, New York; <sup>2</sup>University of Pennsylvania School of Veterinary Medicine, Philadelphia: Welcoming and introductory remarks.
- S. Kety, McLean Hospital, Belmont, Massachusetts: Estimation of circulation and metabolism of the brain by means of inert diffusible tracers.

#### Session 2

- G. Gerstein, University of Pennsylvania, Philadelphia: Simultaneous recording from many neurons—A cost/benefit analysis.
- L. Sokoloff, National Institutes of Health, Bethesda, Maryland: Metabolic mapping of local functional activity in the central nervous system with radioactive deoxyglucose.
- M. P. Stryker, University of California, San Francisco, School of Medicine: Measurements of the relationship between glucose utilization and neural activity in the cat's visual cortex.
- M. Mishkin, National Institutes of Health, Bethesda, Maryland: The visual system visualized with the 2-DG technique.
- C. Kennedy, National Institutes of Health, Bethesda, Maryland: Local metabolic responses during motor activity.
- D. Flood, University of Rochester Medical Center, New York: Methods of examining the response of neural population applied to the modification of orientation preferences of cats reared in striped cylinders.
- P. Hand, University of Pennsylvania, Philadelphia: Functional plasticity produced by sensory disuse or enrichment.
- C.R. Gallistel, University of Pennsylvania, Philadelphia: Objective quantitative data reduction with computer-assisted image analysis.

#### Session 3

- M. Des Rosiers, University of Montreal, Quebec, Canada: An overview of the various difficulties (technical and biological) encountered in attempting to apply the DG method at the cellular level while respecting the physiological prerequisites of the method.
- D.B. Kelley, Princeton University, New Jersey: Measuring activity in single neurons with [<sup>3</sup>H] 2-deoxy-D-glucose.
- C. Smith, National Institutes of Health, Bethesda, Maryland: A method for the determination of local rates of protein synthesis in the nervous system.
- B. Agranoff, University of Michigan, Ann Arbor: Regional brain protein synthesis in rat brain after hypoglossal axotomy.
- L. B. Cohen, Yale University, New Haven, Connecticut: Optimal methods for measuring spike activity.

J. Haselgrove, University of Pennsylvania, Philadelphia: Spectroscopic analysis of the metabolic intermediates of living and freeze-trapped brains.

- J. Greenberg, University of Pennsylvania, Philadelphia: Flow-metabolism couple in the brain.
- R.R. Miselis, University of Pennsylvania, Philadelphia: Application of [14C] iodoantipyrine cerebral blood flow method to a behavioral problem The vasomotor hypothesis for drinking to angiotensin II.

#### Session 4

- D. Ingvar, University Hospital, Lund, Sweden: Normal and abnormal distribution of activity in the human cerebral cortex.
- P. Roland, Bispebjerg Hospital, Copenhagen, Denmark: Macrophysiological dissection of the human brain.
- M. Reivich, University of Pennsylvania, Philadelphia: FDG technique—Physiologic and clinical studies.
- M. Phelps, University of California, Los Angeles, School of Medicine: The measurement of local cerebral glucose metabolism in man with positron computed tomography—Factors which effect the accuracy of local estimates and applications in visual and auditory stimulations.
- W. Cobbs, University of Pennsylvania, Philadelphia: Abnormalities in cerebral glucose metabolism in patients with visual field defects.
- R. Bajcsy, University of Pennsylvania, Philadelphia: Perception and recognition of 3-D shapes—A computer science point of view.
- J.A. Feldman, University of Rochester, New York: Global activity questions suggested by connectionist theory.
- C.J. Vierck, Jr., University of Florida College of Medicine, Gainesville: The spinal somatosensory pathways as model systems for neural coding by convergent interactions.

#### Session 5

- J.H. Kaas, Vanderbilt University, Nashville, Tennessee: Microelectrode mapping methods for subdividing the scinatosensory system.
- E.L. Schwartz, New York University Medical Center, New York: Computational anatomy in striate and extrastriate primate visual cortex—Spatial mapping as a structural basis for perceptual coding.
- M. Gazzaniga, New York Hospital-Cornell Medical Center, New York: Cognitive testing of the separate hemispheres—Split brain approaches to metabolic studies.

## Gene Amplification and Aberrant Chromosomal Structures October 4-7

During the past 5 years there has developed a body of literature and a group of investigators concerned with chromosomal abnormalities in cultured animal cells and in human tumors. These abnormalities include the presence of extrachromosomal elements called double minute chromosomes as well as expanded regions of chromosomes called homogeneously staining regions. Other investigators studying mechanisms of resistance to various agents that kill cells, including cancer chemotherapeutic agents, have found that one common mechanism of resistance involves selective amplification of specific genes. The amplified genes can be present in homogeneously staining regions of chromosomes, or can occur on double minute chromosomes. Thus, these two different areas of investigation—chromosomal abnormalities and drug resistance resulting from gene amplification—appear to be converging.

In October 1981, approximately 50 investigators, including workers in such diverse fields as bacterial genetics, DNA repair-replication, drug resistance, chromosome structure, and developmental biology met at Banbury Center to share current results and concepts.



#### Session 1 Examples of Gene Amplification

Chairperson: G. R. Stark, Stanford University Medical Center, California

- P. C. Brown, Stanford University, California: Gene amplification and methotrexate resistance in cultured animal cells.
- C. Bostock, University of Edinburgh, Scotland: Amplification of *dhfr* genes in mouse cells.
- J.R. Bertino, Yale University School of Medicine, New Haven, Connecticut: Gene amplification in a human leukemia line K-562.
- M.C. Weiss, Centre National de la Recherche Scientifique, Gif-sur-Yvette, France: *dhfr* amplification in rat hepatoma variants.
- J.L. Biedler and P.W. Melera, Sloan-Kettering Institute for Cancer Research, Rye, New York: Antifolate and vincristine resistance in animal cells.
- M. Tien Kuo, University of Texas System Cancer Center, Houston: Vincristine-resistant Chinese hamster ovary cells.
- C.T. Caskey, Baylor College of Medicine, Houston, Texas: *hprt* variants and reversion resulting from gene amplification.
- K.E. Mayo, University of Washingotn, Seattle: Regulation of amplified and transfected mouse metallothionein genes.
- I. Andrulis, The Hospital for Sick Children, Toronto, Ontario, Canada: Amplification of asparagine synthetase genes in CHO cells.

#### Session 2 Gene Amplification

Chairperson: J.L. Biedler, Sloan-Kettering Institute for Cancer Research, Rye, New York

- G. Levan, University of Gothenburg, Sweden: Double minute chromosomes, C-minus chromosomes in mouse cell lines.
- J.M. Trent, University of Arizona Health Sciences Center, Tucson: Metothrexate treatment and chromosomal aberrations in human tumors.
- J.D. Minna, National Naval Medical Center, Bethesda, Maryland: Chromosomal aberrations in human oat cell tumor cell lines.
- S.A. Endow, Duke University Medical Center, Durham, North Carolina: Replication of ribosomal genes in *Drosophila*.
- A.C. Spradling, Carnegie Institution of Washington, Baltimore, Maryland: Gene amplification during development in *Drosophila*.
- R.J. Schwartz, Baylor College of Medicine, Houston, Texas: Actin gene amplification in muscle development.
- V. Walbot, Stanford University, California: Nuclear gene amplification in maize and B chromosomes.
- R.E. Kellems, Baylor College of Medicine, Houston, Texas: Control of dihydrofolate reductase DNA replication and mRNA production.

#### Session 3 Molecular Structures of Amplified DNA Sequences Chairperson: C. Bostock, University of Edinburgh, Scotland

R.T. Schimke, Stanford University, California: *dhfr* gene structure and structure of amplified DNA sequences in various mouse cell lines.



- J. Hamlin, University of Virginia, Charlottesville: Amplified DNA sequences in MTX-resistant CHO cells. L.A. Chasin, Columbia University, New York, New York: Dihydrofolate reductase gene structure in amplified and *dhfr*-deficient CHO cells.
- G.R. Stark, Stanford University Medical Center, California: On the structure of amplified DNA sequences in PALA-resistant cells.
- G.M. Wahl, Salk Institute for Biological Studies, San Diego, California: Analysis of CAD gene amplification using molecular cloning, gene transfer, and cytogenetics.
- F. Gilbert, University of Pennsylvania School of Medicine, Philadelphia: Chromosomal aberrations in human neuroblastomas and retinoblastomas.
- P.E. Barker, Yale University School of Medicine, New Haven, Connecticut: Structure of aberrant chromosome structures in human tumor cell lines.
- H. Hubbell, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania: Molecular structure of DMs from a human colon carcinoid cell line.
- D.L. George, Johns Hopkins University School of Medicine, Baltimore, Maryland: Amplified DNA sequences in mouse tumor cells—Association with DMs and HSRs.

#### Session 4 Mechanisms of Gene Amplification

Chairperson: R.T. Schimke, Stanford University, California

- S. Lavi, Weizmann Institute of Science, Rehovot, Israel: Carcinogen-mediated amplification of DNA sequences in CHO cells.
- T.D. Tlsty, Stanford University, California: Enhanced generation of MTX resistance in cultured animal cells.
- A. Varshavsky, Massachusetts Institute of Technology, Cambridge: Phorbol esters and gene amplification.
- M. Botchan, University of California, Berkeley: Chromosome excision and/or amplification promoted by viral origins of replication.
- P.C. Hanawalt, Stanford University, California: DNA repair pathways in mammalian cells.
- W.A. Haseltine, Sidney Farber Cancer Institute, Boston, Massachusetts: Studies on DNA repair in bacteria.
- R.H. Rownd, Northwestern University Medical School, Chicago, Illinois: Use and lack of use of insertion sequences in amplification events in bacteria–Possible mechanisms of amplification in bacteria.

#### Session 5 Chromosomal Alterations

Chairperson: S.A. Latt, The Children's Hospital Medical Center, Boston, Massachusetts

- S.A. Latt, The Children's Hospital Medical Center, Boston, Massachusetts: Use of flow sorting to study amplified DNA sequences.
- R. Kaufman, Massachusetts Institute of Technology, Cambridge: Transfection and amplification of *dhfr* genes in animal cells.
- J. Roberts, Columbia University College of Physicians and Surgeons, New York, New York: Amplification and correction of transformed genes.

J.D. Rowley, University of Chicago, Illinois: Nonrandom chromosome changes in human leukemia.

- J.L. German III, New York Blood Center, New York: Human chromosomes and the generation of somatic cell diversity.
- J. Yunis, University of Minnesota, Minneapolis: High-resolution chromosome banding in the study of human neoplasia and birth defects.
- G. Klein, Karolinska Institute, Stockholm, Sweden: Gene dosage, gene expression, and tumorigenesis.

## Patenting of Life Forms, October 18-21

The Supreme Court's 1980 decision that artificial strains of microorganisms themselves could be patented, as well as processes for making or using these strains, symbolized for many people the growing commercialization of techniques of molecular biology which hitherto had been regarded as tools for investigating the foundations of genetics. The decision brought two cultures, patent law and fundamental biology, into sudden contact. Each knew little of the other. Both biologists and lawyers began asking to what extent patenting of inventions, so central to the pharmaceutical industry but with a much more subtle impact on the electronics industry, would govern the commercialization of the new recombinant DNA techniques. To remove some of the uncertainty, leading patent lawyers and scientists heard reviews by scientists of some of the immense diversity inherent in manipulations of microorganisms and by lawyers of the application of patent law to such organisms. The conference concluded with a review of recent changes in American and European patent laws and practices and the possibility of more change soon.

#### Session 1 Scientific Issues

- J. Hicks, Cold Spring Harbor Laboratory, New York: The life cycle of the common microbial hosts, with emphasis on yeast—the most complex.
- M. Scharff, Albert Einstein College of Medicine, Bronx, New York: Monoclonal antibodies. What defines a permanent cell line, differentiating what is novel or unique; what parameters distinguish one hybridoma from another?
- C.M. Croce, Wistar Institute of Anatomy and Biology, Philadelphia, Pennsylvania: Monoclonal antibody systems with potential for diagnosis of pancreatic and other forms of cancer.
- H. Heyneker, Genentech, Inc., South San Francisco, California: Vector systems and expressions in E. coli.
- A. Ullrich, Genentech, Inc., South San Francisco, California: Gene transfer—Moving a human gene to a mouse genome.
- S. Brenner, Cambridge University Medical School, England: Recombinants that are the same but different.

#### Session 2 Open Forum on Scientific Issues

Chairperson: N.D. Zinder, Rockefeller University, New York, New York

#### Discussants:

N.H. Carey, Celltech, Slough, Berkshire, England

P.A. Sharp, Massachusetts Institute of Technology, Cambridge

J. Davies, Biogen, SA, Geneva, Switzerland

J. Sambrook, Cold Spring Harbor Laboratory, New York

#### Session 3 Legal Issues

- D.W. Plant, Fish & Neave, New York, New York: Primer on law on patents and other intellectual property.
- B.I. Rowland, Townsend and Townsend, Palo Alto, California: Should the fruits of genetic engineering be patentable?



- V. Vossius, Vossius, Vossius, Tauchner, Heunemann, Rauh, Munich, Germany: Discussion of items I and II as they relate to European and German patent law.
- T.D. Kiley, Genentech, Inc., South San Francisco, California: Assuming patentability, what property rights should accrue to workers in this field?
- J.W. Schlicher, Genentech, Inc., South San Francisco, California: The extent to which antitrust and patent misuse law limits the manner in which patents are acquired, enforced, and licensed.
- N.J. Reimers,<sup>1</sup> R.G. Ditzel,<sup>2</sup> and W.P. O'Neill,<sup>3</sup> <sup>1</sup>Stanford University, California; <sup>2</sup>University of California, Berkeley; <sup>3</sup>DNAX Research Institute, Palo Alto, California: Problems in enforcing patents and in commercializing patented subject matter in the genetic engineering field.
- A.H. MacPherson, Skjerven, Morrill, Jensen, MacPherson, & Drucker, Santa Clara, California: Surviving in an industry that largely eschews patents-electronics.

#### Session 4 Open Forum on Legal Issues

Chairperson: Hon. G. Rich, United States Court of Customs and Patent Appeals, Washington, DC

#### Discussants:

G.M. Gould, Hoffmann-La Roche, Inc., Nutley, New Jersey

C. H. Herr, E.I. duPont deNemours & Company, Wilmington, Delaware

A.E. Tanenholtz, US Department of Commerce, Patent & Trademark Office, Washington, DC

#### Session 5 Revision in Patent Law and the Patent Court System Affecting the Patenting of Life Forms

#### Discussants:

N.E. Noonan, House Committee on Science and Technology, Washington, DC E.L. Bernard, Bernard, Rothwell & Brown, Washington, DC G.M. Karny, Office of Technology Assessment, US Congress, Washington, DC

## **Environmental Effects on Maturation**, November 1-4

To what extent are such environmental factors as nutrition and chemicals, artificial or natural, having such effects on children as stunting their physical growth or mental development, predisposing them to such long-term effects as cancer, or increasing the chance that these children, when they become adults, will have children of their own with birth defects? Experts on human, primate, and small animal development, including biochemists, pediatricians, psychologists, and pharmacologists, considered what is presently known about environmental risks for children, including risks to the developing brain, liver, and reproductive organs. The issues were considered in order to help plan research for better understanding of the risks faced by farm workers' children in an environment where pesticides are used heavily. Among many issues, participants considered the paradox presented by young animals actually showing increased resistance to some chemicals, even though, as rapidly growing organisms, the animals may have been expected to show increased vulnerability.

#### Session 1 Routes of Exposure: Skin and Lung

Chairperson: V. Hunt, Pennsylvania State University, University Park

- H.I. Maibach, University of California School of Medicine, San Francisco: Percutaneous absorption-Neonate compared to the adult.
- L. Frank, University of Miami School of Medicine, Florida: Maturational aspects of exidant-induced lung injury.
- R.C. Spear, University of California, Berkeley: Farmworker exposure to pesticide residues-Reflections on differential risk.

#### Session 2 Routes of Exposure: Gastrointestinal Tract

Chairperson: D. Barltrop, Westminster Children's Hospital, London, England

D. Barltrop, Westminster Children's Hospital, London, England: Lead/nutrition.

- C.M. Schiller, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina: Effects of toxins on gastrointestinal function-Developing systems.
- S.J. Henning, University of Houston, Texas: Development of feeding behavior and digestive function.
- E.P. Savage, Colorado State University, Fort Collins: Pesticides in human breast milk.

#### Session 3 Metabolism, Liver and Gastrointestinal

Chairperson: G.L. Lucier, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina

- H.P. Hoensch, University of Tubingen, Federal Republic of Germany: Absorption and metabolism of xenobiotics in the intestine.
- E.S. Vesell, Pennsylvania State University, Hershey: Dynamically interacting factors that affect the response of developing individuals to toxicants.
- S.D. Murphy, University of Texas Health Science Center, Houston: Toxicity and metabolism of organophosphorus insecticides in developing rats.
- G.L. Lucier, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina: Imprinting of hepatic metabolism by neonatal hormone.

#### Session 4 Kidney and Immune Systems

Chairperson: L.I. Kleinman, University of Cincinnati College of Medicine, Ohio

- L.I. Kleinman, University of Cincinnati College of Medicine, Ohio: The effect of lead on the maturing kidney.
- R.J. Kavlock, US Environmental Protection Agency, Research Triangle Park, North Carolina: The ontogeny of the hydropenia response in neonatal rats and its application in developmental tox-icology studies.
- J.N. Udall, Massachusetts General Hospital, Boston: Macromolecular transport across the developing intestine.
- M.I. Luster, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina: Altered immune functions in rodents perinatally treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin, phorbol-12-myristate-13-acetate and benzo(a)pyrene.
- T. Kalland, University of Bergen, Norway: Long-term effects on the immune system of an early life exposure to diethylstilbestrol.

#### Session 5 Central Nervous System

Chairperson: R.J. Bull, US Environmental Protection Agency, Cincinnati, Ohio

K. Suzuki, Albert Einstein College of Medicine, Bronx, New York: Development of myelin.

- R.B. Kearsley, New England Medical Center Hospital, Boston, Massachusetts: Cognitive assessment of developing infants.
- L.W. Reiter, US Environmental Protection Agency, Research Triangle Park, North Carolina: Organo-tin exposure in developing rodents.
- R.E. Bowman, University of Wisconsin Primate Laboratory, Madison: Some behavioral sequelae of toxicant exposure during development.
- R.C. Vannucci, Cornell University Medical College, New York, New York: Vulnerability of the immature brain to hypoxia-ischemia.

#### Session 6 Maturation of the Reproductive System, Including Neuroendocrine Aspects Chairperson: J.H. Clark, Baylor College of Medicine, Houston, Texas

J.H. Clark, Baylor College of Medicine, Houston, Texas: Sex steroids and maturation in the female.

- B.S. McEwen, Rockefeller University, New York, New York: Estrogens-Influences on brain development and neuroendocrine function.
- C.W. Bardin, The Population Council, New York, New York: The differentiation of the male reproductive tract.
- R.W. Goy, Wisconsin Regional Primate Research Center, Madison: The developmental actions or effects of androgens in Rhesus monkeys.
- D. Kupfer, Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts: Xenobiotics.
- D.R. Mattison, National Institute of Child Health and Human Development, NIH, Bethesda, Maryland: Prepubertal ovarian toxicity.
- P. Walker, Le Centre Hospitalier de l'Université Laval, Quebec, Canada: Long-term susceptibility resulting from brief perinatal manipulation of thyroid function.

#### Session 7 Epidemiological Perspectives

Chairperson: H.W. Berendes, National Institute of Child Health and Human Development, NIH, Bethesda, Maryland

- J.E. Norman, Jr., National Research Council, Washington, DC: Breast cancer in women irradiated in early life.
- R. Illsley, Institute of Medical Sociology, Aberdeen, Scotland: Impact of early-life factors on pregnancy outcomes.
- D. Snowdon, Loma Linda University School of Health, California: Age at baptism into the Seventh-Day Adventist Church and risk of death due to ischemic heart disease—A preliminary report.
- G.G. Nahas, College of Physicians & Surgeons of Columbia University, New York, New York: The Ledermann model applied to the frequency of marihuana use among U.S. high school seniors.

#### Session 8 Lessons from Pharmacokinetics and Human Responses

Chairperson: C.M. Berlin, Jr., Pennsylvania State University, Hershey

- L.K. Garrettson, Virginia Commonwealth University, Richmond: Age-related development of theophylline-Pharmacokinetic responses of children.
- B.R. Sonawane, University of Pennsylvania, Philadelphia: Developmental aspects of acetaminophen hepatotoxicity-Influence of age and acute starvation.
- J.S. Partin, State University of New York, Stony Brook: Reye's syndrome and its association with salicylates.
- A.H. Neims, University of Florida College of Medicine, Gainesville: Some drug host aspects of drug therapy in pediatrics.
- J.M. Tanner, University of London, England: Conference summary.

### Construction and Use of Mammalian Viral Vectors, December 3-6

At this conference 49 DNA and RNA tumor virologists presented and discussed the most recent advances in the use of tumor viruses as cloning vectors. The progress in this field can be judged by comparing this conference with the 1980 Banbury meeting on Construction and Use of Mammalian Viral Vectors. One year ago, the only viral vectors constructed and used were SV40 and adenovirus; papilloma and RNA tumor viruses were merely discussed as potential vectors. In contrast, during the 1981 meeting, work with a great variety of vectors, including both DNA tumor viruses (SV40, polyoma, papilloma, adenoviruses, herpesvirus) and RNA tumor viruses (MoMLV, MoMSV, HaMSV, ASV, SNV, MMTV) was presented.

#### Session 1 SV40

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

- G.C. Fareed, University of California, Los Angeles: Expression of influenza virus hemagglutinin using SV40 vectors.
- M.J. Gething, Imperial Cancer Research Fund Laboratories, London, England: Cell-surface expression and secretion of influenza hemagglutinin from simian cells infected with SV40-HA vectors.
- P. Gruss, NCI, National Institutes of Health, Bethesda, Maryland: The expression of viral and cellular p21 ras genes using SV40 as a vector.
- D.H. Hamer, NCI, National Institutes of Health, Bethesda, Maryland: Regulation of a metallothionein gene cloned in animal virus vectors.
- M. Horowitz, Massachusetts Institute of Technology, Cambridge: SV40 as a vector for cloning eukaryotic sequences and controlling elements.
- R. Treisman, Harvard University, Cambridge, Massachusetts: Expression of human  $\beta$ -globin genes in Cos-7 and HeLa cells.
- A. Levinson, Genentech, Inc., South San Francisco, California: Expression of hepatitis B surface antigen using SV40-based vectors.

#### Session 2 RNA Tumor Viruses

Chairperson: G. Vande Woude, NCI, National Institutes of Health, Bethesda, Maryland

- E.M. Scolnick, NCI, National Institutes of Health, Bethesda, Maryland: Properties of transmissible retroviruses containing the thymidine kinase gene of HSV.
- S. Watanabe, University of Wisconsin, Madison: Encapsidation sequence required for retrovirus vectors.
- C. Tabin, Massachusetts Institute of Technology, Cambridge: The utilization of a retrovirus as a eukaryotic vector for transmitting cloned DNA sequences.
- J. Sorge, Cold Spring Harbor Laboratory, New York: Retrovirus vector independent of selectable markers.
- R. Mulligan, Massachusetts Institute of Technology, Cambridge: Construction of transmissible retrovirus cloning vehicles carrying dominant-acting genetic markers.

#### Session 3 Papilloma, Polyoma, Simian Virus

Chairperson: J. Sambrook, Cold Spring Harbor Laboratory, New York

- P.M. Howley, NCI, National Institutes of Health, Bethesda, Maryland: Expression of selective traits in mouse cells transformed by a BPV69T-SV2gpt hybrid DNA.
- R. Breathnach, Faculté de Medicine de Strasbourg, France: Bovine papilloma virus I-pBR322 and polyoma-pBR322 recombinants as eukaryotic vectors.
- D. DiMaio, Harvard University, Cambridge, Massachusetts: Intact bovine papilloma virus-human DNA recombinant plasmids that propagate as episomes in mouse and bacterial cells.
- M. Botchan, University of California, Berkeley: Enhanced transformation mediated by bovine papilloma virus.
- M. Fried, Imperial Cancer Research Fund Laboratories, London, England: Use of a polyoma virus vector.
- R. Contreras, Laboratorium voor Moleculaire Biologie, Gent, Belgium: Expression of human fibroblast interferon  $\beta_1$  gene by transfection of monkey cells with an SV40 vector.
- P.J. Southern, Scripps Clinic and Research Foundation, La Jolla, California: Mammalian cell transformation with SV40 hybrid plasmid vectors.

#### Session 4 RNA Tumor Viruses

Chairperson: E.M. Scolnick, NCI, National Institutes of Health, Bethesda, Maryland

- S. Broome, Harvard University, Cambridge, Massachusetts: A Rous sarcoma virus gag gene product modulates on RNA levels in transfected cells.
- E. Gilboa, Princeton University, New Jersey: Transduction and expression of nonselectable genes using retrovirus-derived vectors.
- G. Vande Woude, NCI, National Institutes of Health, Bethesda, Maryland: Use of retroviral sequences in cotransfection, activation, and rescue of *onc* genes.
- I.M. Verma, Salk Institute, San Diego, California: Expression and regulation of rat growth hormone gene in mouse cells.
- G.L. Hager, NCI, National Institutes of Health, Bethesda, Maryland: Analysis of glucocorticoid regulation by linkage of the mouse mammary tumor virus promoter to a viral oncogene.
- M. Kriegler, University of California, Berkeley: A retroviral LTR contains a new type of eukaryotic regulatory element.

#### Session 5 Adenovirus, Herpesvirus

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

- C.S. Thummel, University of California, Berkeley: Precise positioning of SV40 DNA in adenovirus expression vectors by a combination of in vitro and in vivo recombination.
- Y. Gluzman, Cold Spring Harbor Laboratory, New York: Helper-independent adenovirus vector.
- K.L. Berkner, Massachusetts Institute of Technology, Cambridge: Adaptation of adenovirus as a cloning vehicle.
- N. Frenkel, University of Chicago, Illinois: A novel eukaryotic-virus vector-The herpes simplex virus amplicon.
- N.D. Stow, University of Glasgow, Scotland: Propagation of foreign DNA sequences using a novel herpes simplex virus vector.
- B. Howard, National Institutes of Health, Bethesda, Maryland: Vectors which may be propagated by integration into the *E. coli* chromosome.



